

APPENDIX 5
Working groups results

September 20th 2006

Focus Group 1: Prevention

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Specific topic to be discussed: FETAL ALCOHOL SYNDROME (FAS)

• **Background information**

Fetal alcohol syndrome (FAS) is an important public health problem and thought to be a leading preventable cause of intellectual impairment worldwide. FAS is a diagnosis given to children who have been exposed to maternal alcohol consumption during pregnancy. The number and severity of symptoms may range from mild to serious. The degree to which a fetus is affected depends on the duration and amount of maternal alcohol intake, greater amounts and a longer duration causing more severe symptoms. However, only smaller proportion of pregnancies exposed to alcohol will result in FAS. This is presumably due to the genetic differences in ethanol metabolism of the mother and the fetus (1).

The first diagnostic criteria for FAS were established in 1973. Individuals with FAS have 3 basic characteristics: dysmorphic facial features, growth deficiency and central nervous system dysfunction. Prenatal alcohol exposure has been also associated with different cardiac, skeletal, renal, ocular and auditory abnormalities (2). There have been several updating of guidelines for referral and diagnosis of FAS, the more recent ones being more accurate and based on up-to-date scientific evidence and current clinical experience (3, 4, 5). Terms used to describe the spectrum of effects that result from prenatal exposure to alcohol, include fetal alcohol effect, alcohol-related birth defects (ARD), and alcohol-related neurodevelopmental disorder (ARD). For all these manifestations recently a common term has been introduced - fetal alcohol spectrum disorder (FASD), defined as the range of effects that can occur in an individual whose mother drank alcohol during pregnancy. These effects may include physical, mental, behavioural and/or learning disabilities with possible lifelong implications. For present FASD is not intended for use as a clinical diagnosis (5). In USA in 2002 CDC organized a scientific working group that issued guidelines for referral and diagnosis of FAS while the work on FASD is in progress (Appendix 1) (5). It seems that these guidelines are now widely accepted in USA. On the other hand, in Europe there is still no definite consensus on the diagnostic criteria for FAS. Some of the diagnostic guidelines or checklist systems

use different cut-offs and some of them are not sufficiently specific to ensure diagnostic accuracy leading to the inconsistencies in the FAS diagnosis.

- **Prevalence**

The prevalence of FAS in Europe is not yet accurately documented due to lack of research, underreporting of alcohol consumption, differences in access and attendance for antenatal and paediatric services, lack of knowledge and standard diagnostic criteria. Nearly all prospective epidemiological studies on FAS have been conducted in USA. These studies report FAS prevalence rates from 0.2 to 2.0 cases per 1,000 births. Using this prevalence rates we can estimate that among the approximately 5 million infants born each year in Europe, around 5000 will be born with FAS. The high prevalence rate for FAS in the USA (1-2 per 1,000 live births) and the relatively low rate reported in some studies from Europe (0.08 per 1,000) does not correspond to observed alcohol consumption (6). On the contrary, there is evidence that the alcohol consumption in Europe is increasing (7). A recent study from Italian province of Lazio found a prevalence of 3.7 to 7.4 per 1,000 children. The rate of FASD was 20.3 to 40.5 per 1,000 and estimated at 35 per 1,000 overall or between 2.3 and 4.1% of all children (8). This highly exceeds previously published estimates of both FAS and FASD. Thus, despite the progress made in the epidemiology of FAS, the magnitude of the problem in Europe is still not fully appreciated.

- **Pregnancies at risk**

Available data show that low socioeconomic status is strongly associated with women's alcohol use before and during pregnancy. Some populations (e.g. Native Americans or Indigenous Australians) are particularly vulnerable and at the higher risk for alcohol related fetal spectrum of disorders. Women at high risk for alcohol use when pregnant tend to be younger, less educated, single, and unemployed. Other variables associated with high-risk status for maternal alcohol use were past sexual abuse, current or past physical abuse, smoking, using other drugs, living with substance users. Other contributing factors for high-risk classification include feeling sad, believing that drinking any amount of alcohol while pregnant was acceptable, and being able to hold four or more drinks.

- **Alcohol consumption before pregnancy as a risk factor for FAS and FAS-related disorders**

US studies show that 15% of women of childbearing age could be classified as moderate or heavy drinkers. Binge drinking reported about 13% of women (five or more drinks at one occasion). Among pregnant women in America 13% continue to use alcohol, approximately 3% report binge drinking or frequent drinking (i.e., seven or more drinks per week) (9). Alcohol consumption before pregnancy can be considered the main significant risk factor for alcohol consumption during pregnancy. Therefore this group of women must be regarded as “high risk”.

- **Prevention**

Prevention of FAS and related disorders is of paramount public health importance. Estimates of lifetime cost varied from \$596,000 in 1980 to \$1.4 million in 1988 and we can assume that there is a significant increase in the costs from that period (10). Our goals in the prevention of FAS are to define the problem of alcohol consumption in European region, to raise the awareness of the population and health professionals and to develop programs that are effective and targeted to specific populations for reducing the risk of an alcohol-exposed pregnancy.

- **Recommendations by the focus group**

After a thorough discussion and the analysis of recent studies concerning prevention of FAS (11-19), the focus group has recommended the following specific actions, targeting primary, secondary and tertiary prevention of FAS and fetal alcohol spectrum disorders.

The first step is to study the prevalence of FAS in population-based surveys in Europe, and to determine the existing knowledge and state of the art on health education and promotion in the field of alcohol consumption. In this way we can follow up and evaluate the outcome of future preventive strategies and policy development.

At primary level, two types of activities are needed – health promotion and specific actions. Health promotion should be especially aimed at the following target groups: children, medical professionals (in particular primary health care providers), young women, low socio-economic groups and media. A broad variety of health information methods can be applied – leaflets, articles in journals, TV and radio spots, warning labels on alcoholic beverages etc.

Women of childbearing age should be advised to limit their alcohol consumption to no more than one unit a day when they are planning pregnancy and to sustain completely from drinking while pregnant. This can be done by primary health care clinicians (family physicians, obstetricians) while discussing the family planning and other aspects of reproductive health. The integration of information about FAS prevention together with other available and ongoing prenatal programs (for example folic acid) can be easily done with comparatively good cost-benefit ratio and low burden for the national healthcare systems. Above recommendations could be planned, organized and monitored by a working group (WG) on FAS at EU level.

Apart from the general information about the harmful effects of alcohol consumption during pregnancy, primary prevention should incorporate specific screening strategies to identify and intervene with women at risk for alcohol-exposed pregnancy.

Specific actions must also include establishment of a unified FAS case definition that will put the basis for the setting up of a surveillance system at both national and international levels. For this purpose a group of experts should evaluate different checklists and agree upon common diagnostic criteria for FAS and FASD

providing a balance between too conservative and too broad diagnostic criteria. Studies utilising different diagnostic criteria in a single population will help to define the optimal diagnostic system.

Secondary prevention can be effective if done simultaneously at prenatal and postnatal levels. Pregnant women should be asked about their alcohol consumption during routine antenatal clinic visit. The detection of the women at risk for FAS can be improved by using one of the standard screening tools (e.g. AUDIT, TWEAK, and T-ACE). Even a brief interruption of drinking habits for women at risk can significantly reduce the incidence of FAS. We should continue to evaluate the usefulness of biomarkers from maternal blood or meconium in the detection of alcohol exposure. A detailed fetus ultrasound screening can detect facial dysmorphism, growth retardation and/or associated anomalies, thus assuring timely diagnosis and adequate follow up of both the mother and child. Apart from this, counselling must be a significant activity within the secondary level prevention of FAS. The early diagnosis in the neonatal period can be improved by applying age-appropriate evaluation system. Further screening for FAS should be performed in infancy/school period when additional neurological, cognitive and behavioural characteristics may become apparent.

At tertiary level, guidelines for referral and global healthcare management of children with FAS must be elaborated, that will guarantee optimal quality of life and adequate health, social and educational services. Such guidelines can be prepared at EU level by a working group on FAS.

**Appendix 1. Diagnostic criteria for FAS developed by the scientific working group of
CDC, (July 2004, last revision May 2005)**

1. Facial dysmorphism

Based on racial norms, individual exhibits all three characteristic facial features:

- Smooth philtrum
- Thin vermilion border
- Small palpebral fissures

2. Growth retardation

Confirmed prenatal or postnatal height or weight, or both, at or below the 10th percentile, documented at any one point in time (adjusted for age, sex, gestational age, and race or ethnicity).

3. Central nervous system abnormalities

I. Structural

1. Head circumference \leq 10th percentile for age and sex.
2. Clinically significant brain abnormalities observable through imaging.

II. Neurological

Neurological problems not due to a postnatal insult or fever, or other soft neurological signs outside normal limits

III. Functional

Performance substantially below that expected for an individual's age, schooling or circumstances as evidenced by:

1. Global cognitive or intellectual deficits representing multiple domains of deficit (or significant developmental delay in younger children) with performance below the 3rd percentile (2 standard deviations below the mean for standardized testing)

or

2. Functional deficits below the 16th percentile (1 standard deviation below the mean for standardized testing in at least three of the following domains:

- a) cognitive or developmental deficits or discrepancies
- b) executive functioning deficits
- c) motor functioning delays
- d) problems with attention or hyperactivity
- e) social skills
- f) other, such as sensory problems, pragmatic language problems, memory deficits, etc.

4. Maternal alcohol exposure

- I. Confirmed prenatal alcohol exposure
- II. Unknown prenatal alcohol exposure

CRITERIA FOR FAS DIAGNOSIS

Requires all three of the following findings:

1. Documentation of all three facial abnormalities
2. Documentation of growth deficits
3. Documentation of CNS abnormality

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Focus group 2: Epidemiological data collection

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Topics covered:

1. The importance of epidemiological data collection of Rare Diseases (RD)

Data collection is useful in terms of: Epidemiology and Public health

Epidemiology

- to estimate the prevalence, incidence and mortality of RD
- to know the spatial and temporal distribution of RD
- to study the natural history of RD
- to conduct analytic and clinical trials of potential risk factor

Public health

- to provide indicators of access and quality of health care
- to plan health interventions
- to estimate costs of RD
- to eventually changes in the policy

2. **Mortality data** are not adequate to provide information on the indices of prevalence and incidence. The reliability of mortality data depends on accuracy of the vital registration systems of each countries.

3. How to identify cases

Experts have to establish standard case definition applicable for the purpose of data collection. Case definition for the purpose of clinical trial might be different from that of epidemiology.

To better identify cases, there is a need for:

- Continuous training for professionals
- Providing guidelines
- Create a network of check points
- Active case finding as much as possible

- Providing incentives to data providers
 - Potential use of database on delivery of specific therapies
4. Severity of RD: need for standardization (especially for genetic diseases)
 5. Inadequacy of ICD 9 and ICD 10 (We need for an ad-hoc classification with case definition)

Effective coding is critical to data collection because subsequent use of data depends *on storage and retrieval of causes using codes*. Problems with coding have a major impact on rare diseases. Only a few inappropriate coded cases can greatly influence rate.

The system of icd-9 (ICD9-CM) and icd10 are still not sufficiently precise for many RD.

6. **Numerator&Denominators**

There is a need to conciliate the following two conditions

- Estimates of epidemiological relevance can be achieved through the collection of significant numbers of cases from a relatively large population. (Robertson NP 1998).
- Case ascertainment of the best quality is possible when we focus on a limited population and do good follow up and monitoring with active case finding (Zivadinov R, 1998).
- Therefore, it is important to balance the two aspect of data collection: **quantity and quality**
- Personnel required for the establishment of a reliable register of one or more RD in a population of 10 million is likely to be in the order of 5-10 full time persons, including at least 2 scientists

Focus Group 3: Epidemiological Indicators

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Mortality Data for Rare Diseases

In discussing the use of mortality data for rare diseases, a number of issues were addressed by the Discussion Group. These issues are summarized below.

From single to multiple causes of death

Cause-specific mortality is one of the most reliable epidemiological indicators and can contribute to developing etiologic hypotheses, to tracing temporal changes in disease patterns, to describing the health status of different population groups, and to estimating disease prevalence (1, 2, 3). However, cause of death is generally expressed in terms of a single cause. Although this was probably adequate for describing mortality when public-health concerns mainly involved acute and infectious diseases, it has become less appropriate since industrialized nations have undergone the so-called “epidemiologic transition”, that is, the extensive diffusion of chronic diseases and the simultaneous decrease in acute diseases, especially infectious diseases. Consequently, the proportion of deaths due to chronic diseases has increased, yet these deaths often involve a number of coexisting conditions, which may not be linked by a direct etiologic chain, complicating the identification of a single underlying cause.

To more accurately describe mortality when deaths are due to concurrent causes and to better understand the associations among these causes, multiple cause-of-death records can be of use (1,2). These records contain not only the underlying cause (i.e., the disease/injury starting the chain of events leading directly to death) but also non-underlying causes (i.e., those resulting in the underlying cause, or contributing to death yet not part of the chain of events leading directly to death or immediately causing death). In some countries (e.g., Australia, South Africa, and the United States), multiple cause-of-death data have been routinely produced for a number of years. In Italy, though these data are not routinely collected or codified, the National Institute of Statistics (ISTAT) collects data on all causes of death exactly as written out in full by the medical examiner on the death certificate, beginning with 1995 mortality data.

Multiple cause-of-death data for rare diseases

Multiple-cause-of-death records are particularly useful in studying rare diseases. For example, some rare diseases are seldom the underlying cause of death (e.g., NF1, one of the rare diseases studied in **NEPHIRD**); thus data on non-underlying causes are particularly important. Moreover, for rare diseases that have been the focus of very few mortality studies (again, such as NF1), routinely collected mortality data can provide additional information, such as the mean and median age at death and the most common conditions associated with death (4).

The codification of rare diseases and data linkage among various sources

Mortality data are generally codified according to the International Classification of Diseases (ICD), though the specific version of ICD may vary by country. However, in ICD 9 and ICD 10, not all rare diseases have their own specific code. For instance, in ICD 9, a single code is used to classify both types of neurofibromatosis, two diseases that differ for a number of aspects, including lethality, although in ICD 11, specific codes for hundreds of rare diseases are expected to be added. For this reason, it would be useful to link mortality data with data on deaths from other sources, such as hospital discharge records and disease registries. Linkage would also be useful for acquiring a more complete description of the impact of the disease being studied.

Limitations in the use of mortality data

The validity and reliability of data are important concerns even when considering only a single cause of death; when considering multiple causes, there are obviously more data, which could mean more potential problems. The quality of mortality data depends of course on the accuracy of the death certificate, which in addition to causes of death includes other medical information, such as the sequence of conditions that resulted in death and other contributing medical factors. Demographic data are also recorded, such as age, gender, place of residence, marital status, and occupation.

Moreover, mortality data, which must be collected for all deaths and are generally verified by statistics institutes, are made available with a certain delay (usually a few years). However, this limit is only relative, given that trends in mortality are evaluated over long periods of time, except for severe or fatal diseases that emerge relatively suddenly (e.g., the onset of the AIDS epidemic in the mid-1980s). Another limitation concerns data linkage, which must be performed taking into account laws and regulations for safeguarding privacy.

Finally, for describing those rare diseases that are not lethal, other data sources - besides mortality information - must be taken into account.

Final recommendation

The final recommendation of the Discussion Group is to contribute to the understanding of rare diseases by using mortality data, which are routinely collected in all countries and are exhaustive and of fairly good

quality. Particular attention should be paid to multiple cause-of-death data, which can allow researchers to maximize the use of the diagnostic information on the death certificate and provide ways of looking at mortality data that go well beyond the typical examination of the underlying cause of death. Linkage of mortality data with data from other registries should also be considered, to combine the high quality of data from specific pathology registries with the completeness of mortality data.

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September 21st 2006

Focus Group 1: Diagnostic test

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Diagnostic test

Genetic testing is the analysis of a specific gene, its products or function, or other DNA and chromosome analysis, to detect or exclude an alteration likely to be associated with a genetic disorder (Harper P, J Med Genet 34: 749-752, 1997).

Diagnostic testing are fundamental to make a diagnosis (e.g. telomere analysis), to confirm a clinical hypothesis (e.g. Miller-Dieker syndrome and del17p13.3), to subclassify a disease (e.g. genetic deafness), to assess the disease severity (e.g. cystic fibrosis), to establish genotype correlations and plan the clinical follow-up (e.g. PTPN11 mutations in Noonan and Leopard syndromes), to prenatally diagnose chromosomal and single gene disorders.

Genetic testing services in the EU have substantially increased their activity in the past few years. Several External Quality Control (EQC) schemes have been funded either by international groups or by national governments or by private subscription.

Some important topics have been discussed within the focus group “Diagnosis and treatment: diagnostic test”, whose discussion leader were Dr. A. Utkus (Department of Human and Medical Genetics of Vilnius University, Vilnius, Lithuania) and Dr. F. Torricelli (Piastra dei Servizi Azienda Ospedalieri Careggi, Firenze – Italy).

1. Clinicians versus geneticists’ role in diagnostic tests

Since heterogeneity of some mutation (e.g. CFTR gene in cystic fibrosis, BRCA1 and 2 genes, etc) a whole and huge knowledge of pathology is essential in order to perform correct and complete

analyses. Therefore, clinicians and geneticists have to be considered at the same level and should share their knowledge and information. A full understanding of the pathophysiological and genetic aspects of a pathology are good prerequisite for molecular diagnosis testing of rare diseases.

2. **Metabolic screening versus genetic testing**

Cystic fibrosis screening in USA was lead by Dr Utkus as example of successful transition to detect some of the most frequent mutations present at national level in US, where a precise number of mutations (25 mutations) was introduced in the minimum CF carrier screening panel (Richards CS and Grody WW, *Expert. Rev. Mol. Diagn.*, 4(1), 2004).

In Italy a law of 1993 (no. 548, of 23 December, 1993) established the development of programmes for the prevention and care of patients affected by cystic fibrosis. The programmes were to include primary prevention measures and the establishment of CF centres in each Italian region or group of smaller regions. CF neonatal screening programmes have been operating in some regions for many years, in some for a more limited period. Neonatal screening is based on an immunoreactive trypsinogen test, followed by genetic analysis (Castellani C, Bonizzato A, Cabrini G, *et al.* Newborn screening strategy for cystic fibrosis: a field study in an area with high allelic heterogeneity. *Acta Paediatr.* 86: 497-502, 1997; Castellani C, Picci L, Scarpa M, *et al.* Cystic fibrosis carriers have higher neonatal immunoreactive trypsinogen values than non-carriers. *AJMG* 135A: 142-144, 2005). Nevertheless, also on the basis of the personal experience showed by the component of the discussion group, genetic testing activities have to be performed only when a therapeutic approach is available for the pathology; furthermore, population metabolic screening are too expensive.

3. **Genetic test selection and diffusion of information at EU level**

The number of analyses performed during recent years has been increased in all EU Countries; in Italy, for example, the number of cytogenetic test performed increased from 150.000 to 250.000 from 1997 to 2004 and, during the same period, the number of molecular analyses performed for molecular analyses increased from 50.000 to 200.000 and three-quarter of analyses referred to only 10 genes (Dalla piccola, 2004).

Therefore, medical community, professional organization and health strategies should be adopted in order to promote diffusion of correct information about genetic test.

4. **Diffusion of genetic “passport”**

The diffusion of a genetic passport has to be considered as a tool to have complete and detailed information on a person is important to study the correlation between particular alleles and the capability of metabolizing various compounds. These problems are the subject of pharmacogenetics,

an individual field of current genetic research. The genes that determine the response to carcinogens and endotoxins code for proteins involved in metabolism (deactivation and detoxification) of xenobiotics. Such genes are known as environmental, or metabolism, genes and are characterized by a considerable population polymorphism. Examples of genetic passport are present in Russia (Development of a Biochip for Analyzing Polymorphism of the Biotransformation Genes. AS Glotov *Molecular Biology*, Vol. 39, No. 3, 2005, pp. 357–365).

Nevertheless, discussion group recognized that the use of genetic passport should be limited at legal reasons.

5. Recommendations should be adopted in order to assure safe and effective genetic testing of rare diseases in EU and to implement National experience with international ones
6. Laboratory accreditation

Laboratory tests must be validated before their application as diagnostic tools and their quality maintained throughout use, usually by operating under a Quality Management System, including, whenever possible, formal accreditation. Programs should be in place to assist the development from new research findings to diagnostic tests.

Furthermore, specific protocols should be shared by laboratories and standardized methods should be available and used by all genetic testing laboratories.

7. **Networking activities**

A network for all pathologies should be organized in order to send patients to specific reference centres. This networking activity should assure a reduction of error rate in the performance of analyses and a reduction of laboratories which perform the same analyses thus contributing to the creation of specific centres for detection of pathologies.

Focus Group 2: Counseling and Risk Communication

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We focused on cancer genetic counselling and risk communication

Genetic Counseling can be define as the **communication process** which deals with the human problems associated with the occurrence, or risk of occurrence, of a genetic disorder in a family (Ad Hoc committee on Genetic Counseling (1975). Report to the American Society of Human Genetics. American Journal of Human Genetics, 27, 240-242).

It is important to point out that the communication process has to be NON-Directive. The patients' autonomy in decision-making is an important issue in genetic counseling and has to be promoted by non-directive communication. Non-directiveness is a strategy to assist individuals to achieve a personal decision, discussing all relevant opinions in a relationship based on reciprocal trust and respect.

.This communication process involves an attempt by one or more appropriately trained persons to help the individual or family:

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

In genetic counseling we have to deal with risk continuously. But, what is the meaning of risk? Risk is a concept based on probability. It is the chance that an event, i.e. a disease, will occur within a given time period.

Dramatic advances in our understanding of the genetic basis for cancer have led to the development of new methodologies and tools for genetic cancer risk assessment. Cancer risk assessment is developing into a distinct discipline in which established empiric risk models are recast along with rapidly evolving genetic technologies for estimation of individual cancer risk. Identification of persons at increased risk for cancer allows application of potentially life-saving surveillance or preventive measures.

The basic premise is that cancer is a complex disorder, both biologically and socially.

Hallmarks of familial cancer include occurrence of cancer at an unusually younger age, (or in the less usually affected gender), vertical transmission of cancer within a family multifocal or bilateral disease in paired organs, multiple primary cancers in an individual, and clustering of unusual or rare cancers.

Comprehensive cancer risk assessment requires consideration of both personal risk factors (reproductive/hormonal history, exposures such as tobacco, and treatments such as radiotherapy) and thorough family history.

The most straightforward risk calculation is mendelian risk in the setting of a known familial mutation (50% for first-degree relatives, 25% for second-degree relatives, and so forth).

A more sophisticated approach takes into account age-specific penetrance estimates in a Bayesian modification of risk. In short, if a woman is unaffected at the age of 80 years, then the probability that she or any of her offspring is a carrier of a highly penetrant gene mutation is diminished. Bayesian calculations also can be used to gauge the significance of a negative result in an unaffected individual if the family diagnosis is certain (but the mutation is unknown) and the sensitivity of the genetic test well established.

Genetic testing for inherited susceptibility mutations is the most recent addition to the tools used for risk assessment and has the potential to provide more accurate risk estimation than any empiric risk-assessment tools.

Once we have calculated the risk we have to communicate it, and risk can be a difficult concept to explain, especially in the clinical setting. Usually, patients request certainties. But unfortunately, it is impossible to predict exactly what will or will not happen to an individual. People seeking for genetic counseling can be in a condition of great distress, vulnerability, anxiety, and they could be facing very stressful life events related to high-impact existential themes...health, disease, death or reproductive choices. They are not always capable or feel themselves capable to understand all these problems nevertheless they have to do important and urgent choices for their lives. In the field of Medicine and in particular in Medical Genetics rarely we can provide certainties. In a context of different grades of uncertainty what we can do is provide the information we have in an accurate, useful, understandable way not forgetting sensitivity and empathy toward who is trying to make his personal sense to this loss of control on his life and cope with.

It can be challenging for a health care provider to convey information in a way that is both personally **relevant** and **motivating** to individual patients.

The form in which risk is communicated may influence both decision-making processes and motivation to change behaviors such as undergoing testing or other medical procedures, engaging in behaviors that will protect or harm health, and adhering to recommended treatment or lifestyle advice.

Because of that, it is important that providers and patients understand **what risk is** and **how it can be altered**.

Difficulties in communicating diagnostic information are inherent in doctor-patient interactions. A very **specialized knowledge** has to be **interpreted** and **understood** by patients. The difficulties in such a task are further exacerbated when the **diagnosis** is a **risk** for a severe disease as cancer is. Diagnosis of a cancer (or just the risk of developing it) produces important psychological and relational reactions in people involved, individuals, couples, families. Intensity and quality of these reactions may vary considerably but if we just stop to think it would be the same for all of us like human beings.

When healthy “potential patients” are told of their risks for future disease, this can be a sensitive situation, prone to many **dilemmas** with **ethical** consequences.

In scientific contexts, risks are calculated on the basis of a variety of systematically established factors; while the risk judgments of individuals are assumed to be influenced to a greater extent by **personal experiences**, **moral values** and **social norms**.

The determination of risk status of an individual for development of a future disease is a complex process, involving **negotiation** between **different modes of explanation**. The health care professional in clinical practice has a mediating function between objective and relatively unambiguous scientific knowledge on statistically based risk (measurable uncertainty) and the individual’s experiences of ambiguous risk (unmeasured uncertainty). It is important to recognize that **tolerance** of risk varies greatly from person to person, and **patients’ risk perceptions** are often very different from their actual risks, leading to over – or underestimations of risk.

The amount of effort that patients are willing to make to **alter disease** risk may depend on their perceptions of **personal risk** and their **perceived ability** to make effective change.

There are many different ways to discuss risk.

We can use:

- Qualitative expressions,
- Quantitative expressions,
- Absolute risk,
- Relative risk, or
- Risk over different time periods.

But again, it is important to remember that it can be very challenging to communicate information in a way that is both **accurate** and **useful**.

In order to help counselors in the communication process, several authors have tried to establish guidelines for this communication process. For example, Schwartz and colleagues published some principles for cancer risk communicators that can be used in other types of risk communication.

These principles included:

1. To make clear the main message,
2. To provide context
3. To acknowledge uncertainty, and
4. To remember health

First at all, we have to delineate the main message clearly.

We have to define the outcome under consideration. *Diagnosis, heredity, specific morbidity, or death from disease.* The risk can be presented in numbers or in words. If it is presented in numbers, we can use percentage or proportions. But also, the risk can be framed in negative or in positive terms.

Breast Cancer Risk framed in negative terms

Lifetime incidence of breast cancer in develop countries		
	Probability of developing breast cancer between ages 20 - 80	Proportion
No affected relatives	7.8 %	1:13
One affected first degree relative	13.3 %	1:8
Two affected first degree relatives	21.1 %	1:5

Lifetime mortality of breast cancer in develop countries		
	Probability of dying for breast cancer between ages 20 - 80	Proportion
No affected relatives	2.3 %	1:42
One affected first degree relative	4.2 %	1:24
Two affected first degree relatives	7.6 %	1:13

Breast Cancer Risk framed in positive terms:

Lifetime changes of NOT having breast cancer in develop countries		
	Probability of developing breast cancer between ages 20 - 80	Proportion
No affected relatives	92.2 %	12:13
One affected first degree relative	86.7 %	7:8
Two affected first degree relatives	78.9 %	4:5

Lifetime chances of NOT die because of breast cancer in develop countries		
	Probability of dying for breast cancer between ages 20 - 80	Proportion
No affected relatives	97.7 %	41:42
One affected first degree relative	95.8 %	23:24
Two affected first degree relatives	92.4 %	12:13

Also, we have to provide the time frame. It is not the same the risk for the next year, (*e.g., in the next 5 year* or life-time).

The best way of risk communication depends on the individual client and the aim of genetic counseling and the right way of framing risks must be tailored to the individual client and the specific counseling situation.

The data have to be presented clearly, we have to clearly specify to whom the data apply (*e.g., gender, age, risk factors*), and we have to present benefit and harm symmetrically

We have to provide context. We have to present both chance of diagnosis and death or morbidity to reflect disease lethality. We can also specify important competing risks for death, compare the risk with familiar events or compare the risk factor or intervention under consideration against other known factors to be clear that all factors do not change risk by the same amount.

We should acknowledge uncertainty and remember that **Risk is only a measure of probability and not an absolute answer.**

One of the main objectives of medical care is to improve the health of the population and scary messages do not make people feel healthier and may generate unrealistic expectations about disease risk and treatment benefit.

The fundamental purpose of risk communication is to provide individuals with the facts they need to make personal informed decisions. Increasing the public sense of vulnerability to inspire a healthy behavior undermines well-being and may result in net harm.

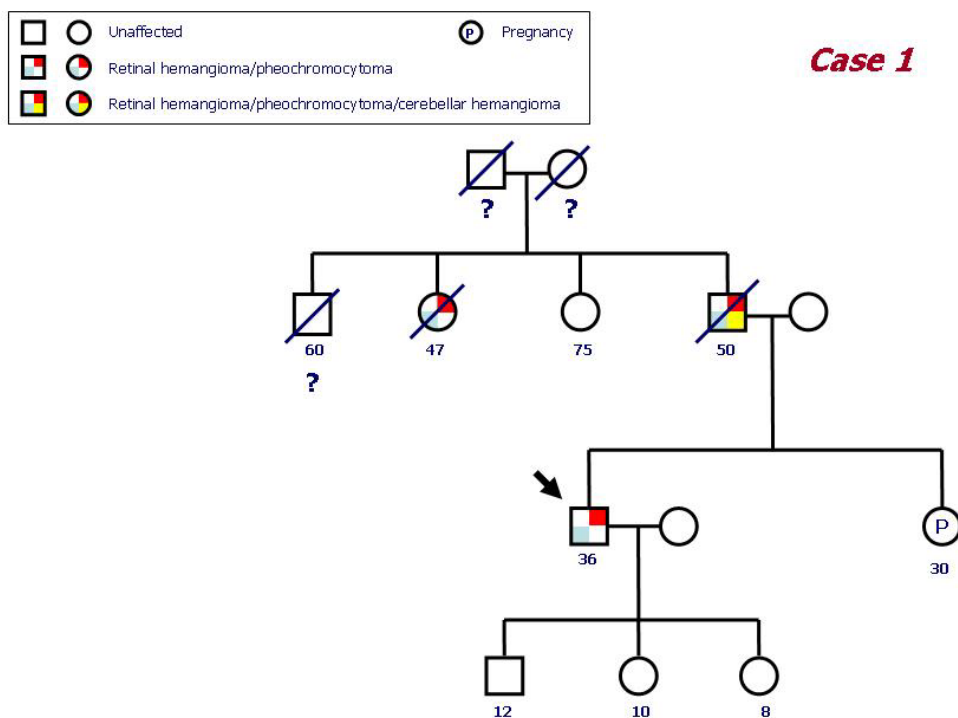
Communicators should be sensitive about the potential side effects of their messages.

Several clinical cases were used to point out some of the problems dealing with Counseling and risk communication:

Case # 1

A 36-year-old man presented with a 6-month history of palpitations and headaches and high blood pressure refractory to calcium channel blockers and beta blockers. Urine studies showed elevated catecholamines and a CT revealed bilateral 6-cm adrenal masses suspicious of pheochromocytoma. His past medical history was significant for retinal hemangioma in the right eye. His family history was significant for a father and aunt who died of adrenal tumors. His father was also diagnosed of both retinal and cerebellar hemangiomas. His aunt also had retinal hemangiomas.

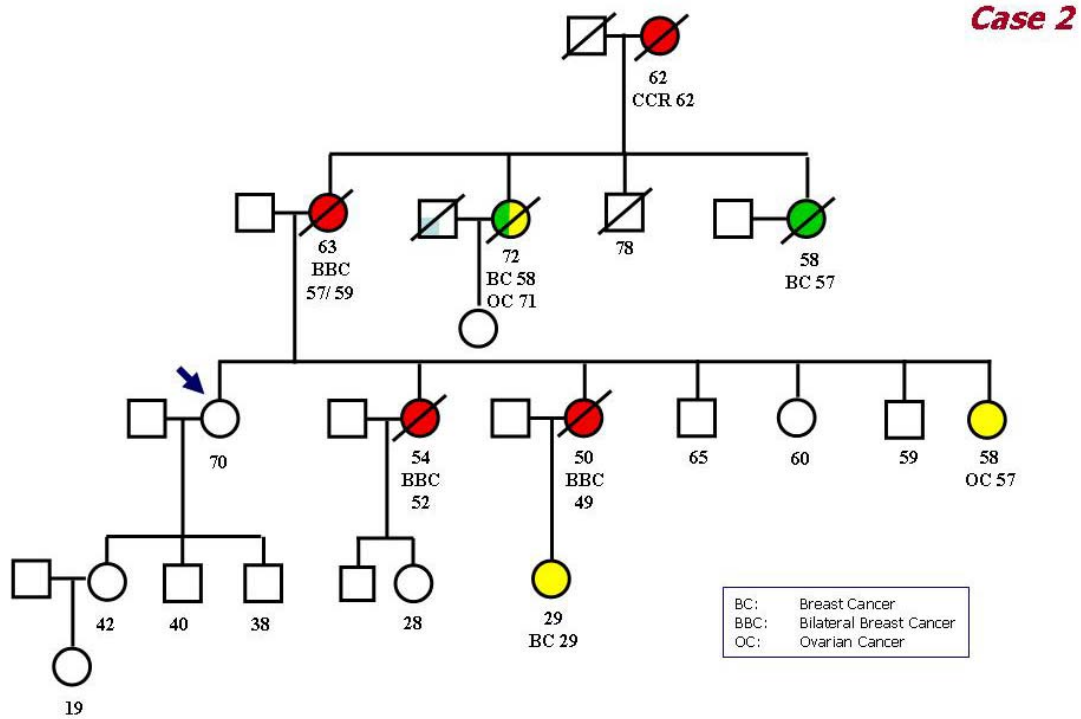
At the end of the visit the patient demands genetic counseling.



Case # 2

A 70 year-old woman and her 42 year-old daughter sought consultation regarding cancer risk. They reported that the niece of the mother, recently affected by ovarian cancer, tested “positive” for *BRCA1*, but did not want to discuss any of the details of the testing or the specific results. The woman and her daughter who sought consultation could not afford to pay out of pocket for *BRCA1*, which was not covered by their insurance.

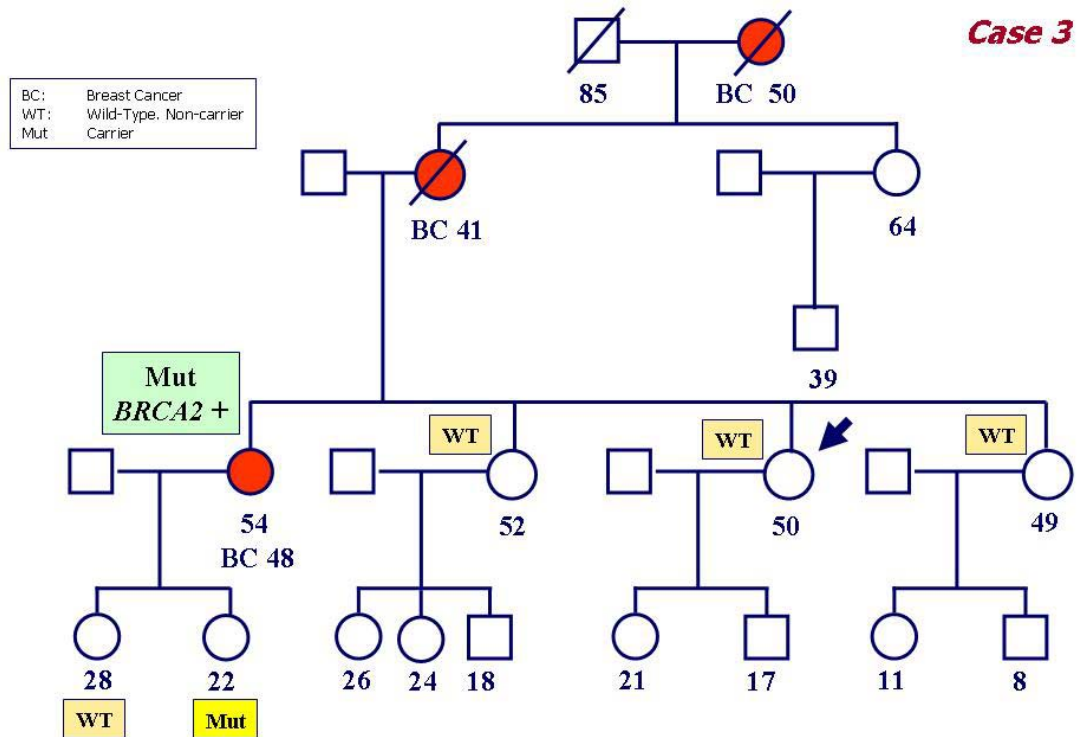
Can you help them to estimate their risk?



Case # 3

Mary, a 50 year-old woman, soughs consultation regarding her breast and ovarian cancer risk. She reported that her sister was diagnosed of breast cancer when she was 48. Her mother and grandmother were also diagnosed of breast cancer. Recently, her sister was tested “positive” for *BRCA2*, and after a very short counseling process Mary decided to be also tested for the same mutation. Two days ago Mary received her test result that was negative for her sister *BRCA2* mutation.

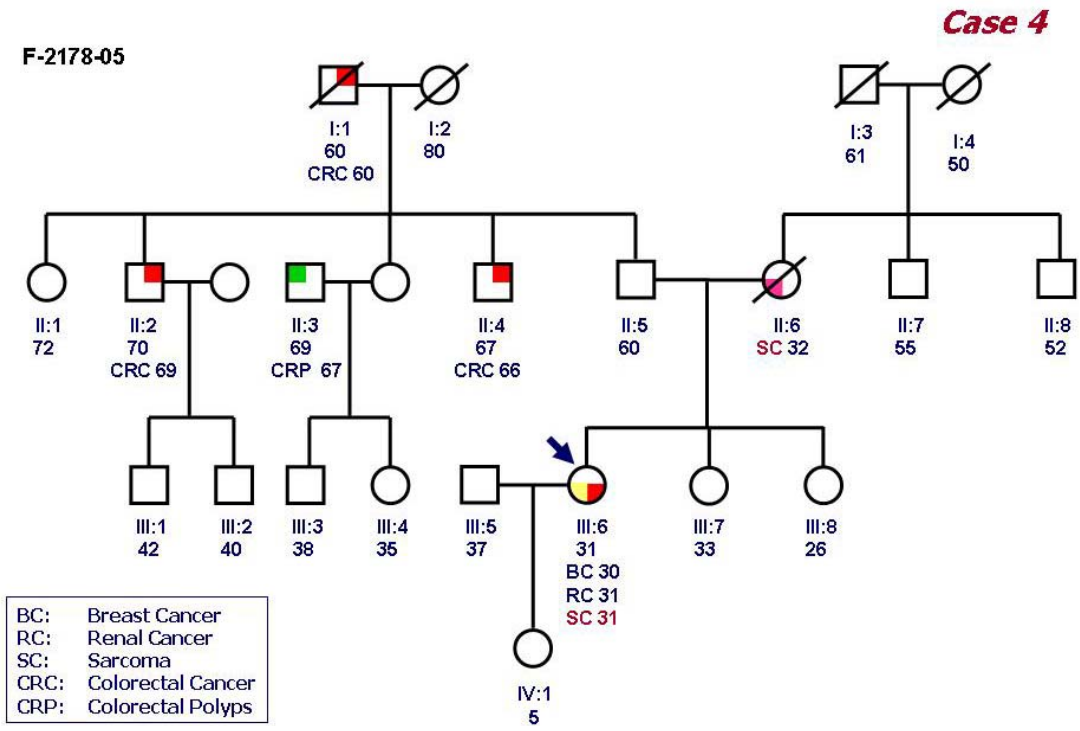
Can you help her to estimate her risk?



Case # 4

A 31 year-old woman sought genetic counseling and testing.

She had breast cancer at age 30, renal cancer at age 31, and recently she has been diagnosed of soft tissue sarcoma at age 31. Her mother died of a sarcoma at age 32. Her father is healthy at the age of 60. However, two uncles and her grandfather were diagnosed of colorectal cancer.



Case # 5

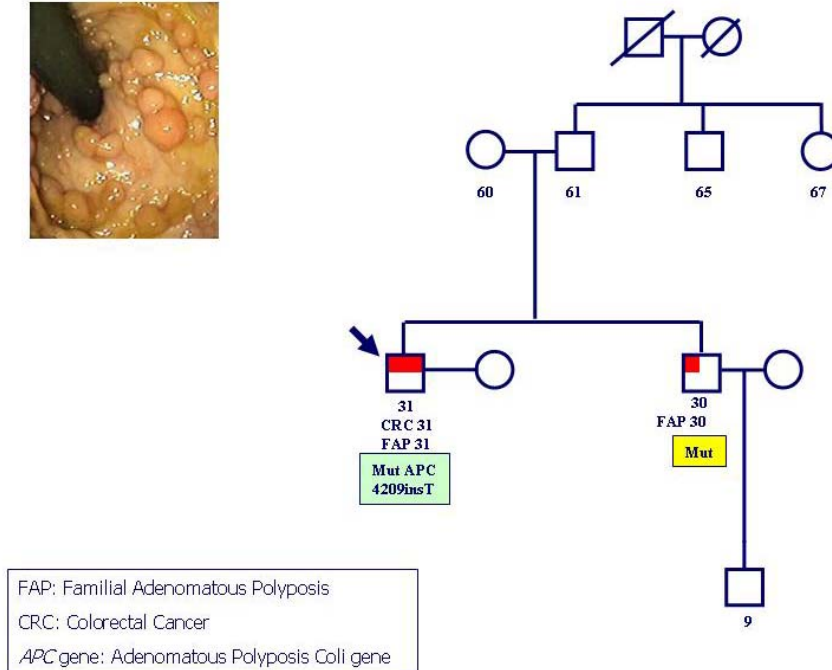
A 31 year-old man and his family sought genetic counseling.

He has recently been diagnosed of colorectal cancer in the context of a Familial Adenomatous Polyposis (more than 2.000 polyps in the entire colon). His brother has been diagnosed of having more than 1.000 polyps in the entire colon by a screening colonoscopy.

Can you help the entire family?



Case 5



From the real clinical cases discussed in the FOCUS GROUP emerged a common sense of how complex is the communication in the context of genetic counseling and, with more tips from the facilitator about the cases carried on, how the reality is always more complex than expected. Experiences like this, with health professionals working in the genetic field, from different countries and different backgrounds, could be very useful in sharing personal experiences and best practices.

As conclusions we would like to remark that:

1. Counseling is a Non-Directive communication process which deals with the human problems associated with the occurrence, or risk of occurrence, of a disorder.
2. Risk is the probability that an event will occur within a given time period.
3. Risk messages can be communicated in many different ways.
4. Risk information can be used to help individuals identify factors that influence health,
5. It can be very challenging to communicate information in a way that is both **accurate** and **useful**.
6. Its important to pay attention to psychological, ethical social, legal aspects involved in genetic counseling and risk communication

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Focus Group 3: Therapies and rehabilitation

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Therapies and rehabilitation

Many barriers undermine the access to treatment of patients with rare diseases. Among the others it is worth mentioning the availability of health care centre, the delay in diagnosis, the limited knowledge and experience of health care workers, the availability of a specific drug for the disease and, when available, the cost of the drugs. The aspects on health maintenance organization shall be privileged in the present discussion.

Our discussion receives great help from the EurordisCare survey, which collected a series of important information, with the aid of the rare disease associations and patients. Some of these questions are of great importance to understand which problems are to be solved first, and may be of great help for, in the management of rare diseases:

- a) **delay from early symptoms to confirmatory diagnosis.**
 - 25% of patients had to wait between 5 and 30 years;
 - 40% of patients first received an erroneous diagnosis
 - This led to erroneous medicinal treatment for 33% of patients, to surgery for 16% of patients, to 10% for psychological care
- b) **patient mobility:** 25% of patients had to travel to a different region to obtain the confirmatory diagnosis, 2% to a different country
- c) **communication of diagnosis**
 - was announced in unsatisfactory or unacceptable terms or conditions in 45.5% of cases
 - the genetic nature of the disease was not communicated to the patient or family in 25% of cases (given the genetic origin of 80% of rare diseases)
- d) **genetic counselling**
 - genetic counselling was performed only in 50% of cases

- discussion on the diagnosis and genetic risk was engaged in 40% of cases
- patients or their parents engaged in debate within their family to help diagnose or prevent other cases in 80% of cases
- within the latter conditions, discussion helped diagnose other family members in 30% of cases (10% affected; 20% healthy carriers).

From this information, a series of important questions arise; among these, chiefly two key questions;

- 1) How to identify persons with rare diseases as early as possible
- 2) How to ensure optimal treatment of patients with rare diseases

Rare diseases hit only a limited number of persons. Only few specialists, often scattered all over a country, are able to put forward correct diagnosis and therapies, however also these specialists may end up in visiting only few cases during their life. In order to respond to such a problem, the common idea promoted so far, was to identify big institution, with personnel and facilities (infrastructure and equipment) able to manage rare diseases. In this way patients with rare diseases will most likely access to one centre increasing the number of cases treated in there. This would better expose health care workers to rare disease cases, increasing their knowledge, experience and therefore ameliorating their ability to understand and manage the specific disease.

Several indications are given by different countries, under different public health administrative structures. We propose a discussion on some of these, even though we are aware that some solutions we propose require time, money and good will, but these are part of a practical scheme for social improvement, not utopia.

The Neurofibromatosis clinic established in Turku and described by Dr. Peltonen provides an example of such a referral hospital for patients with Neurofibromatosis 1 (NF), which is a model to expedite the access to adequate treatment

NF clinic includes one coordinator consulting specialist of different fields when necessary. The range of specialists available are listed below:

Neurofibromatosis clinic:

- Genetic counselling
- Orthopaedic
- Dermatology
- Ophthalmology
- Paediatric surgery
- Paediatric neurology
- Neuropathology

- Laboratory investigation
- Etc..

Institutions dedicated to a single rare disease has advantages and disadvantages. Some of these follow:

Advantages:

- one institution has great visibility. Everybody knows where it is and therefore it is easy to access
- one institution collects all clinical cases in the territory. The doctors and other personnel belonging to the institution are expert in all aspects of the disease
- one institution can manage the different clinical aspects of the disease, can undertake clinical research (because of the number of patients that is more likely to recruit)
- one institution can provide comprehensive care to patients including referral to patients associations and to other institution/organisations dealing with the social aspects of the disease
- one institution can better manage the follow up within the territory: for example establishing linkages with General Practitioners

Disadvantages:

- one single institution is physically far from the great majority of patients. Patients must travel long distance; sick children need the support of their parents who are forced to stay out of their house, far from their other children with a very high economic and emotional cost
- often patients looking for help in a country need a first tentative diagnosis in order to be properly referred to the specific specialised centre. This is a great weakness of the system considering that appropriate diagnosis is still a major problem in many countries as general practitioners and specialists are not able to recognise the disease and therefore to properly advice patients
- there are some 7000 rare diseases. Such a big number of specialized institutions can be built all over the EU? Even if they are built, to what extend will those be able to serve the need of patients widespread all over the EU?
- Can we think of prioritising some diseases? In case, which ones? Which criteria should be used?

Suggestions for a discussion

- 1) **Considering the present status.** Several highly specialized and well known institutions exist and perform important job in EU. Some of them (as the one here described by Drs. Juha and Sirku Peltonen during our Meeting in Roma) are dedicated to a “single syndrome”, as neurofibromatosis is. This condition is optimally studied from several clinical and experimental points of view,

including genetic counselling, and offer an excellent answer to the needs of patients. This solution has a very strong cultural and expertise basis, and is a rich resource for the community. Some other institutions can have a wide cultural background, e.g., leukodystrophies, i.e., a wide group of diseases which can be studied with analogous cultural instruments. Well, in both cases patients need not only these highly specialized institutions. They need other “intermediate” structures, as well. They need at first, a wide cultural basis for the diagnosis; they need also a clinical help near their home, to perform therapy and follow-up controls;

- 2) **Considering the present status: which centralised structures are presently working?** Some structures do exist in the field of rare diseases, and we need to know how many, and for what diseases, and where they are. We suggest that the first step can be to have a better knowledge of existing structures, and an inventory list of such specialised Institutes can be outlined. A list for rare diseases organisations is working within EURORDIS, and is referred to more than 260 rare disease organisations. Perhaps these organisations may help compiling such a list, and suggesting further connections within these Institutions.
- 3) **Another suggestion can be forwarded:** these organisations may propose adding, on the web, the names of those doctors, scattered all over the territory, who performed studies on one or another particular disease, and can facilitate the management of patient recruiting-diagnosis-treatment. For example: If I write the word “neurofibromatosis” on a research motor as google, the Turku Institute should appear. Clicking on it, further indications can enrich the cultural weight of the Institute: the name(s) of institutions/doctors who may be of help for neurofibromatosis, nearest to the city of patients; and the names and addresses of associations of patients, and so on. In any cases, patients need more than highly specialized institutions. They need also “intermediate” structures able to provide a diagnosis; to provide clinical help near their home, to perform therapy and follow-up controls on a day to day base.
- 4) **Is it possible to identify criteria to develop a list of priorities for the selection of rare diseases on which highly specialized institutions should be built?** May be we can, in certain circumstances. Apart from cases of well known and stabilized Institutions, which are part of the cultural heritage of a Nation, we can suggest to adopt at least three criteria to identify priority rare diseases:
 - 1) the existence of new effective treatment and/or diagnostic or screening procedures and/or drugs for a certain disease;
 - 2) the possibility of grouping several rare diseases, which may be studied together, because of their clinical expression (e.g., central nervous system, or cardiovascular system, and so on) and/or their aetiology (e.g., genetic-metabolic);
 - 3) the possibility of collecting large amounts of resources (funds, personnel, equipments) from private/public sources, and the contemporary availability of a critical mass of investigators expert on a specific disease or a group of diseases.

In order to promote the establishment of such centres, it could be important to consider the provision of incentives such as the release of certification or the allocation of financial support, as well. Different Countries in Europe put forward interesting proposals in the field of rare diseases/orphan drugs (e.g., Denmark, France, Germany, Hungary, Italy, Poland, Spain, Sweden, The Netherlands, United Kingdom). Several countries launched a national plan for rare diseases, and within the Plan, some of them designed a number of referral departments/centres located within universities/hospitals, whereas others chose providing funding to specialised centres of reference, or to patients' organizations, or to support clinical research into rare diseases.

5) **Which perspectives for the future?** Much work needs to be done:

A) Information for the great public

B) Information for the workers in health structures and for the medical schools

C) Information for the “continuing medical education”,

Can we suggest that a National Plan for rare diseases should be adopted in all EU countries? All these points shall receive help through the web correct diffusion

Other important issues to be addressed in the future in the context of care and treatment

Rehabilitation

In addition to the pharmacological treatment of the disease or of its signs and symptoms, it is essential to support the reintegration of the patients within the society. This would imply an appropriate physical rehabilitation, when necessary, and a continue or ad hoc psychological support to patients. Assistance and help should be given also to the family of the patients as they are directly involved in the management of the patients and often it is an heavy, constant physical and psychological burden difficult to coop with.

It is therefore important to consider the impact of the disease on the quality of life of the patient to understand how to ameliorate it with treatment, care and any other non clinical support that may be needed.

The integration of the patients within the society should receive more attention as it is the base to ensure a normal and meaningful life to person that too often are marginalised because of their disease. In this optic, it is important to work towards the establishment of an enabling environment which should include a better school system, a better workplace as well as a better social support for people affected with rare disease.

Education and information

The enabling environment previously envisioned cannot be achieved without the engagement of the general population. It is important to better sensitise the general population on such important issues as it will help to

increase the understanding of the problems, to avoid discrimination, to share important preventive information and to build a critical culture on rare diseases.

The continue training of health care workers is a “*conditio sine qua non*”. It is a essential to increase the skills and knowledge of the health care workers; different approaches can be suggested such as the inclusion of rare diseases within the curriculum of the medical school and the development of specific training sessions on rare diseases.

Because, always more often, clinicians, patients, mothers, friends and many others, look for information on the web, it would be important to ensure the development of website of controlled, good quality. The website could include e-forum that would form the basis to strengthen the collaboration among doctors, could be used to share information, experiences and may be to establish networks among patients, doctors and/or others in need.

In order to sensitive and provide appropriate information, it is important to develop information, education and communication materials to be distributed in hospitals, schools and any other relevant opportunities. Newsletter, brochure, pamphlet, poster are only few examples of written information materials. Also the engagement of the media could be further explore as often people rely on the information given by newspaper, magazine or the radio.

In this context the patients’ association can and should play a major role. There is need to strengthen the linkages between general practitioners, health centres, schools and patients’ associations. In addition patients’ association should be more involved when issues related to rare diseases are discussed as they have a unique insight that derived from their personal and direct experience.

Focus Group: Case Study: Haemophilia

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Introduction

There are about 38,000 haemophilia patients in European Union, the incidence of haemophilia being 1/10,000 inhabitants. Each year, about 750 babies are born with this disorder. Approximately 85% have haemophilia A (FVIII deficiency) and the remainder has haemophilia B (Factor IX deficiency). The severity of haemophilia is related to the amount of the clotting factor in the blood. About 70% of haemophilia patients have less than one percent of the normal amount and, thus, have severe haemophilia. The phenotype of the patients is based on assay of factor VIII or IX, by means of clotting (one-stage method is the most popular) or Chromogenic substrate methods. The genotyping is now easily achieved by means of screening tests, as CSGE or DHPLC, in order to select patients positive for Intron 22 inversion (about 40%) and, in the negative, to detect the exon carrying the mutation. The sequencing of the mutated exon allows the exact definition of the mutation. The knowledge of mutation, in the frame of affected family, is particular important to detect the facultative carriers before or during the pregnancy. This allows the prenatal diagnosis by means of villocentesis at 10-11 week of pregnancy. The voluntary interruption of pregnancy is particular frequent in under development countries (about 80%) and less frequent in the developed countries (about 30%) where good facilities are available for the treatment of the disease.

What' is the problem?

The most important challenges facing today the haemophilia patient, health care providers, and research community are safety of products used for treatment, management of the disease including inhibitor formation, irreversible joint damage, and life-threatening haemorrhage, and progress toward a cure. In the past 10 to 15 years, advances in screening of blood donors, laboratory testing of donated blood, and techniques to inactivate viruses in blood and blood products have remarkably increased the safety of blood products used to treat haemophilia. Although treatment-related infection with the AIDS virus or most of the hepatitis viruses is a thing of the past, these measures do not completely avoid viruses such as hepatitis A and Parvovirus B19. There is a great deal of concern about Creutzfeldt-Jakob disease (CJD), a rare transmissible nervous system disease that is inevitably fatal, being transmitted through transfusion. Recombinant factor VIII/IX, are manufactured by a process entirely free of human or animal proteins. Although the cost of these products exceeds that of the blood-derived product, it is clearly the treatment of choice for those, such as newborns, who have not yet been exposed to blood products or, if previously

exposed, not yet infected patients. All haemophiliacs of European countries have now available a treatment for bleeding which is totally free of any contaminating agents. On the contrary, the haemophiliacs of on development countries do not have these facilities, neither plasma-derived clotting factor concentrates: 80% of haemophiliacs world wide are lacking any form of therapy. While current treatment has greatly improved the outlook for most haemophiliacs, the development of antibodies (inhibitors) that block the activity of the clotting factors has complicated treatment for some patients. Approximately 15 percent of severe haemophilia A patients and 2.5 percent of haemophilia B patients develop such antibodies after exposure transfused factors. When inhibitors are present in large amounts, the patient may require very high and expensive quantities of transfused clotting factors to stem bleeding, and, in some instances, even that may not be effective. Immune Tolerance Induction (ITI) protocol have been developed with aggressive therapeutic approaches, which are terribly expensive (about €1.10⁶/year for a 20 kg child). The major cause of disability in haemophilia patients is chronic joint disease - "arthropathy" – caused by uncontrolled bleeding into the joints. Life-threatening haemorrhage is a constant risk. Traditional treatment of haemophilia has involved "on-demand" treatment, meaning that patients are treated with factor replacement only after bleeding symptoms are recognized. In several European countries the haemophiliacs are treated by periodic infusions (prophylaxis) regardless of bleeding status. This approach maintains the factor level high enough that bleeding, joint destruction, and life-threatening haemorrhage are almost entirely avoided. The cost of prophylaxis is huge more than €200,000/year/patient by the second decade of life. Even higher, is the cost of ITI, about €4,000,000/year/patient. The treatment decisions are not easy ones.

Conclusion:

The ultimate goal is to offer a cure for the disease. The challenge is to transfer normal genes into a patient so that they will produce the normal clotting protein. A small amount of active factor produced by the patient's own body will correct the disease. Although much remains to be studied before such treatment can be offered to patients, there have been a number of studies done in animals such as mice and dogs in which a factor VIII or IX gene has been inserted and has produced the proper blood product for periods that exceed one year. Major issues that remain to be resolved include the low level of production of the clotting factor, reduction of immune reactions that stop the production after a period, and development of ways to insert the gene directly into the body without manipulating cells outside the body

September 22th, 2006

Focus group 1: Social aspects

Discussion leader Andrew Knight (Australia)

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A. Questions and aspects raised by the group which can be considered to be universal:

How can a person with a rare disease find a better place in society?

What do we need to do to support the caregivers of a person with a rare disease?

How can we support professionals and patient advocacy groups?

At present social aspects are not recognized as important as they are - or as important as they should be regarded.

Theses:

Social aspects of rare disease have to be given greater importance

Social aspects are very individual and require individual solutions

Social problems of individuals need immediate solutions

Persons with rare disease should be integrated with other people in society

This will:

- decrease social impact of their disease
- increase awareness in the community

Obstacles:

Attitudes and ethical values in the society:

- People do not understand and appreciate diversity.
- History of separation of “different” people from mainstream society.

Suggestions:

- Provide training and education of the population and professionals in diversity.
- To increase health literacy of the population

B. Social problems and suggestions for the needs analysed according to different periods of life

1. Parenthood for a child with a rare disease

Problem

The illness pushes you out of “normality” – how do we minimise this for families with a child with a rare disease? Parents face a challenge to be able to live “normally” with their child and to help the child to develop social skills and other abilities required in life.

Suggestions

Group support for the family and siblings should be available to encourage the socializing process. The services needed should be arranged.

Services should be provided as much as possible at home, and the parents should be helped to learn to take care of the child at home.

Educational programs should be provided for people to learn to accept differences.

2. School

Problems

Families and children with rare diseases face different school systems and different problems depending on where they live.

The general school system is built upon expectations which may not match what a child with a disease can achieve. Children with disease do not fill the criteria necessary for integration into the current mainstream schooling system. Thus, disabled people are differentiated or disintegrated very early from the society.

Suggestion

Children with rare disease should be integrated into the general school system as they are part of general society.

To integrate the child, teacher should be trained in promoting and coping with diversity.

Improvement of health literacy in general population.

3. Adolescence

Problems

Transition from childhood to adult life requires learning of a range of social skills, coping etc. and may be delayed in a person with illness. Adolescence is a particularly difficult age in which to accept difference and contains a high pressure to be “normal”

Suggestion

Education towards accepting diversity.

Getting encouragement from patient organizations.

Meeting and sharing experience with other adolescents with the same disease.

4. Studying

Problems

Specific disabilities may prevent people from finishing studies or accessing tutoring systems.

Suggestions

Institutions such as universities must provide services to enable those suffering from rare diseases to receive appropriate education.

5. Adult life; work and employment

Problems

Unemployment, repeated short employment due to limited funding support of disabled people ; difficulty in finding permanent work, decreased performance in work, decreased ability to cope, poor transmission of information on the disease at work. Problems keeping or losing the job because the disease has caused changes in performance or requires frequent absences for medical or other interventions.

Suggestions

Some solutions already exist in some countries. The best solutions should be identified and spread.

Support systems by government: rights to have health care, own living accommodation, to get personal assistance etc. etc.

The company should be compensated if it employs a person with a disease. To receive this support, the patient has to have the illness officially recognized. In case of rare diseases, the requirement for recognition may even be refused because of the ignorance of the officials on rare diseases.

C. The role of professionals

Professionals can help alleviate social problems faced by people with rare diseases through:

- Spreading information on rare diseases among public health system.
- Increasing and improving the role of family doctors for people with rare disease.
- designing service provision so that as much as possible people can receive care at or close to home
- Research-oriented doctors could investigate whether general platforms of common diseases can be used for rare diseases.
- Help and support to and from the patient organisations.

Focus Group 3: Communication and Narrative Medicine

Discussion Leader: Daniela Zarri (Italy)

Rapporteur: Simonetta Pulciani (Italy)

Participants

Simone Baldovino (Italy)

Claudia Alberico (Italy)

Elisa Rozzi (Italy)

Stefanov Rumen (Bulgaria)

Janos Sandor (Hungary)

Clara Bonaldo (Italy)

Donatella Valerio Sessa (Italy)

Anna Luzzi (Italy)

Anna Colucci (Italy)

Ines Vallanzuolo (Italy)

Communication and Narrative Medicine

This short report summarizes the very long and productive discussion held during the focus group on “Communication and Narrative Medicine”.

The participants to this focus group were physicians, psychologists, patient association members and health operators, coming from Italy, Hungary, and Bulgaria.

This heterogeneous group pointed out different viewpoints on “Narrative Medicine” and its role and potentiality for a better therapeutic approach.

All participants agreed on the special power of narration, but not every body agreed on the tasks of Narrative Medicine, which prompted the discussion on topics such as Epidemiology and Empathy.

The Narrative Medicine could be used as reservoir of disease symptoms data to improve clinical knowledge acquired through epidemiological studies. The steering group analyzed the Narrative Medicine concept in order to find a link to compare symptoms data collected from questionnaires, with data extrapolated from the “illness stories”.

Many doubts were argued and expressed on the possibility to categorise and to analyze scientifically the data collected through the narration, which to date vastly differ from epidemiological approaches and protocols.

The Narrative Medicine has a long way to go before being widely accepted as tool to improve medical knowledge on diagnosis and therapy. Anyway, several participants have pointed out that it could be adopted as an effective and humane medical model.

The narration concept will devote more time to the therapeutic relational approach and may offer opportunities for empathic medical care.

Physicians, besides diagnosing and treating their diseases, should show more empathy towards those who suffer, and accompany their patients through their illnesses.

Empathy is a type of “emotional resonance”, which permits recognizing, perceiving and feeling the emotions of someone else.

Much consideration was expressed about the meaning of “emotional resonance” and its consequences in the medical-patient relationship.

The physiologists pointed out that “Empathy”, as defined by Carl Rogers, is:

“To perceive the internal frame of reference of another with accuracy and with the emotional components, but without ever losing the "as if" condition. Thus, it means to sense the hurt or the pleasure of another as he senses it and to perceive the causes thereof as he perceives them, but without ever losing the recognition that it is as if I were hurt or pleased and so forth”.

“Empathy” is not just a personal sensitivity to the “listening” approach of someone else. The attitude to communicate through “empathic” modalities can be acquired, and are desirable to enrich the narrative approach with other communication techniques, such as counselling.

Surprisingly, the focus group on “Communication and Narrative Medicine” concentrated just on the patients being the only narrators. Instead it would have been better to focus on discussions involving physicians, the patients’ families and other social groups that could use the narrative approach. All these participants through narration could better examine their relationships with each other and that of the patients.

From the “illness stories” physicians can be aware of the patients’ needs, communicate them to other health care professionals, and establish a communication ties with the public and the institutions to establish a more dedicated health care system.

No consensus was reached on task of Narrative Medicine and its potentialities and limits by those participating and time placed a restraint on the fruitful discussions continuing.

However, all participants agreed on the need of a more “humane” medical practice based on a constructive collaboration among physicians, health operators and those involved.

Focus Group 3: Quality of Life

Discussion Leaders: L. Padua (Italy). P. Caliandro (Italy)

Rapporteur: L.Ege (Denmark)

Participants:

Enzo Ricci (Italy)

Luisa Russo (Italy)

Marotta Lucia (Italy)

Franco Noli (Italy)

Mirando Siouti (Greece)

Annalisa Trama (Italy)

Quality of life

Dr Padua focused the discussion in which setting the quality of life can be used:

- To assess the efficacy of a medical procedure
- To assess the quality of a therapy To make an estimation of the needs of a population
- To improve the clinical decision
- To appreciate the differences in the health status of different patients.

After the introduction on QoL, the following topics were covered during the discussion group:

- To evaluate QoL in patients with deeply impaired clinical picture
 - Evaluating Health related QoL can be relevant both when the clinical picture is severe and when it is not severe. One of the major roles of QoL is to detect the evolution of the disease. QoL is used in clinical studies in order to integrate so-called ‘objective’ clinical data with ‘subjective’ scales. To reach a sufficient number of patients QoL is not good to measure individual persons, but useful to measure the implications of the disease in a sample.
 - To compare QoL of patients with different diseases and living in different countries The crucial point is to decide which available measurement should choose Generic instruments evaluate the HRQoL as a whole. Applicable to a wide range of different people with different type and severity of diseases, different cultures. Useful for comparisons and decision-making across different diseases and interventions. Specific instruments: have been developed on specific groups. They focus on the phenomenon of interest, can be more sensitive, more acceptable, do not allow comparisons QoL as a primary outcome measure in clinical trials HRQoL is the most important outcomes of clinical trials; useful to investigate variations in the way the diseases develops and can help the doctors to find out, what might be done. To evaluate the quality of life of parents. Different measures exist for adults and children. In small children, the parents’ reports of children’s the comparison between children’s and parents perspectives turns out to be of interest by itself. To utilise the results to improve social conditions

Focus Group 4: Case study: Prader Willi syndrome

Discussion Leader: A. Crinò (Italy), M. Dentamaro (Italy)

Rapporteur: G. Evans (UK)

Participants

G. Grugni (Italy)

P. Salerno (Italy)

V. Bonaldo (Italy)

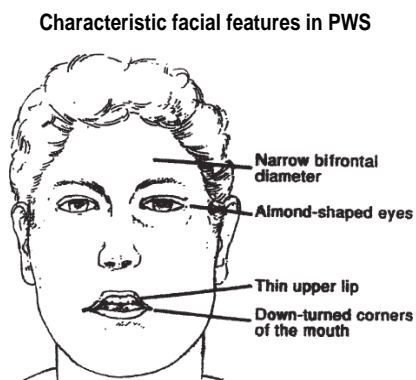
F. Noli (Italy)

C. Rigetti (Italy)

This focus group discussed about Prader Willi syndrome.

Prader-Willi syndrome (PWS) is the most common genetic cause of obesity. The syndrome is related to a paternally derived alteration on chromosome 15. It occurs in approximately 1:15,000-25,000 of births. PWS affects an estimated 350,000-400,000 people worldwide. The PWS Association (USA) is aware of around 3,500 cases in the United States, but the estimated pool of 17,000-22,000. The real prevalence of the syndrome is underestimated because of lack of knowledge about the disease.

In the first part of discussion, the dr. Crinò showed a power point presentation of the disease and a clinical case.



16-year-old boy

Reasons for admission in Hospital:

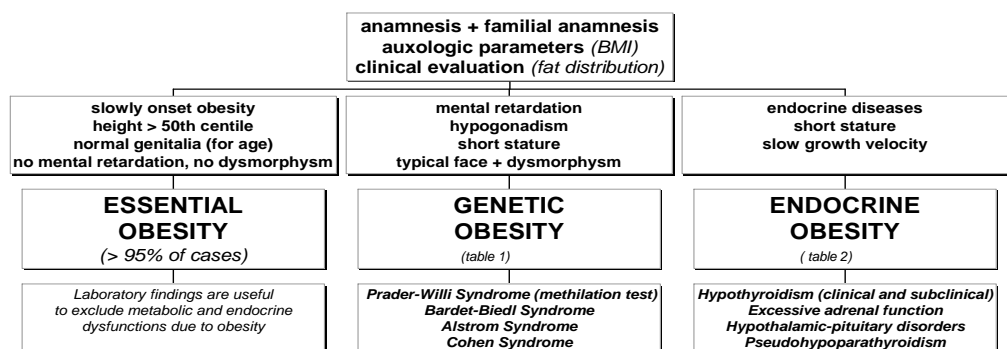
- Obesity*
- Hyperphagia*
- Hyperglycemia and mild glycosuria*
- Sleep disturbances*
- Dyspnoea*

The most important aspects of Prader Willi were underlined:

- the clinical aspects,
- the diagnosis,
- the treatment,
- the social aspect.

Very important is the role of a multidisciplinary approaches to this disease, for instance for the clinical aspects of hypotonia and of the obesity, which is deserve a differential diagnosis.

DIFFERENTIAL DIAGNOSIS OF PEDIATRIC OBESITY



During the Presentation of focus groups outcomes, dr. Evans summarized the conclusion of the discussion of the focus group with an exhaustive presentation.

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