European School of Genetic Medicine

Basic and Advanced Course in Genetic Counselling

Bertinoro, Italy, April 30 – May 6

Bertinoro University Residential Centre
Via Frangipane, 6 – Bertinoro

Course Directors:
F. Forzano (Galliera Hospital, Italy) H. Skirton (Plymouth University, UK)

Basic and Advanced Course in Genetic Counselling

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BASIC AND ADVANCED COURSE IN GENETIC COUNSELLING

Bertinoro University Residential Centre (Italy), April 30 - May 6, 2014

Arrival day: Tuesday April 29th

Wednesday, April 30th – BASIC

14.00 – 14.30	Introduction to the course **F. Forzano**
14.30 – 15.30	Setting the scene – aims, process and outcomes of genetic counselling **C. Patch**
15.30 – 16.30	Inheritance models and risk assessment **M. Soller**
16.30 – 17.00	**Coffee Break**
17.00 – 18.00	Prenatal diagnosis: scenarios and issues **M. Soller**
18.00 – 18.30	Discussion

Thursday, May 1st – BASIC

Morning Session

9.00 – 10.00	Molecular analysis: old and new diagnostic tools **M. Iascone**
10.00- 11.00	Cytogenetics: current status and future perspectives **J. Baptista**
11.00 – 11.30	Coffee Break
11.30 – 12.30	Genetics of intellectual disability **F. Forzano**
12.30 – 13.30	**Lunch Break**

Afternoon Session:

14.00 – 15.30	Concurrent Workshops A-B
15.30 - 16.00	**Coffee Break**
16.00 – 17.30	Concurrent Workshops B-A

Workshop A: case discussion, clinical
Workshop B: case discussion, lab

Friday, May 2nd – BASIC

Morning Session

9.00 - 10.00	Basic concepts on dysmorphology **F. Forzano**
10.00 – 11.00	Cancer genetics: scenarios and issues **D. Turchetti**
11.00 – 11.30	**Coffee Break**
11.30 – 12.30	Practical ethics - consent, confidentiality and disclosure **C. Patch**
12.30 – 13.30	**Lunch Break**

Afternoon Session:

14.00 – 15.30	Concurrent Workshops C-D
15.30 - 16.00	**Coffee Break**
16.00 – 17.30	Concurrent Workshops D-C

Workshop C: role play, prenatal
Workshop D: role play, cancer

Saturday, May 3rd – CROSSOVER

Morning Session

9.00 – 10.00	Predictive and not: understanding the mixed message from our DNA sequence **C. Janssens**
10.00 – 11.00	Counselling for predictive testing **A. Tibben**
11.00 – 11.30	Coffee Break
11.30 - 12.30	Psychological issues in antenatal screening and testing **H. Skirton**
12:30 - 13.30	**Lunch Break**

Afternoon Session:

13.30 –14.00	Why do we need counselling skills? **E. Razzaboni**
14.00 –16.00	Revision of basic Rogerian counselling skills **H. Skirton**

Sunday, May 4th – ADVANCED

Morning Session:

9.00 – 11.00	Using Transactional Analysis in genetic counselling practice – theory and practice using scenarios **H. Skirton**
11.00 – 11.30	**Coffee Break**
11.30 – 12.30	Genetic screening and testing in children **A. Tibben**
12.30 – 13.30	**Lunch break**

Afternoon Session:

13.30 –15.00 Discussion of difficult cases brought by students
All faculty

15.30 – 16.00 **Coffee Break**

16.00 –17.00 What are my professional qualities and pitfalls?
A. Tibben

Monday, May 5th – ADVANCED

Morning Session:

9.00 – 11.00 Grief and loss issues – theory and personal awareness
H. Skirton

11.00 – 11.30 **Coffee Break**

11.30 – 13.30 Counselling skills practice using scenarios
All faculty

13.30 – 14.30 **Lunch break**

Afternoon Session:

14.30 –15.30 The Counsellor end: self-awareness tools, occupational stress and burnout syndrome
E. Razzaboni

15.30 – 16.00 **Coffee Break**

16.00 –17.00 Using supervision effectively
A. Tibben & E. Razzaboni

Tuesday, May 6th – ADVANCED

Morning Session:

9.00 – 10.00 Discussing difficult issues with clients
H. Skirton

10.00 – 11.00 Skills practice
H. Skirton

11.00 – 11.30 **Coffee Break**

11.30 – 12.30 Family dymanics
A. Tibben

12.30 – 13.30 Evaluation and feedback

13.30 Lunch and home

An application has been made to the EACCME for CME accreditation of this event.
*The application for European accreditation has been granted **35 European CME credits** (ECMEC) by the European Accreditation Council for Continuing Medical Education (EACCME).*

ABSTRACTS OF LECTURES

Wednesday, April 30

Setting the scene – aims, process and outcomes of genetic counselling

C. Patch
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In the past twenty years the demand for clinical genetic services and genetic counselling has increased enormously alongside the major advances in genetic science. Although accurate genetic counselling relies on a firm medical diagnosis, accepted definitions of genetic counselling also emphasise the educative and counselling components.

There may seem to be little in common between the science of genetics and counselling. Individual genetic counselling clients will often have questions and concerns about a genetic illness that could be important for themselves or their families. They may not only require information that is technically correct, but also some assistance to understand the information provided and to appreciate its relevance to their own lives, values and emotional reactions.

Genetic counselling can act as a bridge between the science of genetics and the understanding and feelings of its clients. Genetic counselling is a communication process that deals with the occurrence, or risk of occurrence, of a (possibly) genetic disorder in the family. The process involves an attempt by appropriately trained person(s) to help the individual or the family to

(1) understand the medical facts of the disorder;

(2) appreciate how heredity contributes to the disorder and the risk of recurrence in specified relatives;

(3) understand the options for dealing with the risk of recurrence;

(4) use this genetic information in a personally meaningful way that promotes health, minimizes psychological distress and increases personal control;

(5) choose the course of action which seems appropriate to them in the view of their risk and their family goals, and act in accordance with that decision,

(6) make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder' (Eurogentest 2009).

Genetic counselling should always be based on a diagnosis that is as accurate as possible. This increasingly involves interpretation of complex genetic analyses. The activities that take place within a counselling session include:

Taking a family medical history which is necessary to provide reliable information

Giving and interpreting genetic information with skill, presenting it in a non-judgmental way.

Supporting the patient or client particularly when they are making difficult decisions or at times of stress related to their genetic issues.

In the UK, most genetic counselling in provided in Regional Genetic Services by multi-disciplinary teams including medically trained specialist clinical geneticists and genetic counsellor colleagues. These colleagues are supported by laboratory scientists. Genetic diagnoses are usually made by clinicians - clinical geneticists or other medically qualified doctors - but clients can often be helped by discussions with non-medical genetic counsellors. In this session we will introduce the framework of genetic counselling and put it into context with the aims of this course.

Eurogentest (2009) Recommendations for genetic counselling related to genetic testing.

http://www.eurogentest.org/professionals/documents/info/public/unit3/final_recommendations_genetic_counselling.xhtml (accessed 14th April 2014).

Inheritance models and risk assessment

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Division Clinical Genetics
Lund University Hospital,
Sweden

Mendelian inheritance (or **Mendelian genetics** or **Mendelism**) is a theory of how hereditary characteristics are passed from a parent to their offspring. The theoretical framework was initially derived from the work of Gregor Johann Mendel, an Austrian monk, published in 1865 and 1866. He conducted hybridization experiments in garden peas and from these experiments he deducted the Mendel´s Principles of Heredity. Mendel summarized his findings in two laws: the **Law of Segregation** and the **Law of Independent Assortment.**

His work was "re-discovered" by three European scientists, Hugo de Vries, Carl Correns, and Erich von Tschermak.

Background information

A normal diploid human cell has 46 chromosomes, half are maternally derived and half are paternally. During production of new gametes (gametogenesis) —the normal complement of 46 chromosomes is divided to 23 (meiosis) to ensure that the resulting haploid gamete can join with another gamete to produce a diploid organism. An error in the number of chromosomes is termed aneuploidy. In independent assortment, the chromosomes are randomly sorted and the gametes end up with a random mix instead of a pre-defined "set" from either parent, gametes are therefore considered to be assorted independently. The number of possibilities - combinations maternal/paternal chromosomes in the gametes is large.

A **Mendelian trait** is caused by a change (mutation) in a single gene. For a disease to occur a mutation has to be present either in both alleles (recessive trait) or only in one of the alleles (dominant trait). Examples of recessive diseases are; cystic fibrosis, thalassemias and different metabolic diseases, and of dominant diseases; achondroplasia, neurofibromatosis and retinoblastoma. A disease controlled by a single gene contrasts with a multi-factorial disease, which is caused by genes in several loci (and the environment) as well as those diseases inherited in a non-Mendelian fashion. Diseases can also be either autosomal (disease-gene is on one of the chromosomes 1-22), or X-linked (disease-gene is on the X-chromosome).

Inheritance Models

Autosomal dominant

Only one allele is mutated. The disease-gene is located on an autosome (chromosomes 1-22). A person with a dominant disease has a 50 % risk to pass the disease to their offspring. Men and women are equally affected. Many times there is a history of the disease in the family, but the affected person can also be the first one (new mutation). Many diseases have a variable expressivity and reduced penetrance.

Autosomal recessive

Both alleles are mutated. Both parents are healthy carriers and have a 25 % to have another child with the same disease. Men and women are equally affected. Most often there is no family history, unless the parents are related (consanguity).

X-linked dominant

The disease-gene is located on the X-chromosome. A person with a dominant disease has a 50 % risk to pass the disease to their offspring. Many times the disease is lethal for male fetuses. Skewed X-chromosome inactivation plays a role in the severity of the disease in females that are affected.

X-linked recessive

The disese-gene is located on the X-chromosome. Males are more often affected compared to females. Women are most often healthy carriers, with a 50 % risk to transmit the disease-gene. Skewed X-chromosome inactivation plays a role in the severity of the disease in females that are affected. Affected males can't transmit the disease to their sons, but all their daughters will be carriers.

Nontraditional inheritance

- Imprinting diseases (Angelman, PraderVilli): Some genes become imprinted in either maternal or paternal meiosis (or later in the course of formation of the germ cells). The phenomenon is also called epigenetic modification. It leads to inactivation of the gene (by methylation). It can disappear or happen again in next meiosis. It is not exactly known when imprinting occurs, but most probably it occurs in an early phase of the germ cell formation. However, it might also happen after fertilisation.
- Uniparental disomy (UPD); a chromosome has only one parental origin
- Dynamic unstable mutations (Huntington, Dystrophia myotonica, Fragile-X)): a trinucleotide repeat becomes pathogenic when the number of repeats exceeds a certain limit. In previous generations there may have been mildly affected individuals, but as the number of repeats increases more severe phenotypes appear (anticipation: the symptoms become more severe or start earlier in later generations).
- Mitochondrial inheritance: about 1% of the DNA in the cell is mitochondrial
- (Homoplasmy = all mitochondria in a human is identical /Heteroplasmy = some mitochondria is normal, some mutated). A female may be symptomless if she has a heteroplasmic mitochondrial mutation but her children might be severely affected children
- Multifactorial inheritance: environmental factors and genes interact. There are additive or interactive effects of different gene loci. Diseases do not follow Mendelian inheritance patterns - still they can be enriched in families or in populations (Example many "common disorders" and congenital malformations).

Ethical and practical issues in counseling and riskestimations

- Always draw a pedigree.

- Thorough family history – consider if the disease can have many "faces", i.e Fragile.X, syndromes with malformations
- New mutations
- Variable expression/penetrance of the diseases
- Nontraditional inheritance – consider how this affects pedigree, counselling, etc
- Presymptomatic testing? Pros/Cons?
- Carrier-frequency in a population?/ Carrier- testing?
- Riskestimation, for example to calculate a risk for the partner to be a carrier
- Hardy-Weinbergs law. How to do this?
- Prenatal testing? Is it possible, is it wanted?
- Information of the disease and follow-up for carriers; in for example presymptomatic testing.

Prenatal diagnosis: scenarios and issues

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Division Clinical Genetics
Lund University Hospital,
Sweden

Prenatal diagnosis or prenatal screening is testing for diseases or conditions in a fetus or embryo before it is born. The aim is to detect birth defects, for example chromosomal abnormalities such as Down syndrome, hereditary diseases and neural tube defects.

Techniques

Diagnostic prenatal testing can be invasive or non-invasive. Invasive methods are for example amniocentesis, which can be done from about 15 weeks gestation, and chorionic villus sampling, which can be done approximately between 10 and 12 weeks gestation.

Non-invasive techniques include ultrasonography, nuchal translucency and maternal serum screens. If an elevated risk of chromosomal or genetic abnormality is indicated by a non-invasive screening test, the more invasive techniques are offered.

Because of the miscarriage risks associated with amniocentesis and CVS procedures, many women prefer to first undergo screening so they can find out if the fetus' risk of birth defects is high enough to justify the risks of invasive testing. Around weeks 10-11, nuchal thickness scan (NT) may be offered which can be combined with blood tests for serum markers like PAPP-A and beta-hCG, that correlate with chromosomal abnormalities, in what is called the First Trimester Combined Test.

Methods for non-invasive genetic tests for Down Syndrome, trisomy 18, and trisomy 13 using fetal DNA in the mother´s blood are on their way, as well as methods for testing for some of the Mendelian disorders.

Which Women/couples should be offered prenatal diagnosis

- Women over the age of 35
- Women with high risk estimation in screening
- Women who have had previous babies with a birth defect, especially heart or genetic problems
- Women who have a family history of a genetic disease or ethnic backgrounds prone to genetic disorders, or whose partners have these
- Women who are pregnant with multiples (twins or more)
- Women who have previously had several miscarriages

Genetic analysis - techniques

Genetic analysis of the cells from amniocentesis or CVS can include chromosomal analysis, genomic array, PCR, FISH or molecular genetic analysis of a known mutation in the family. PGD is a genetic testing method used combined with in-vitro fertilization for preimplantation genetic testing.

In genetic testing there are several issues that need consideration before the sample is taken:

Few examples: Is it possible to diagnose the requested disease at this moment? Is the mutation known? Is the right laboratory notified? Is the right method for analysis planned? What time limits are there to have results “in time” Has the family been properly informed about the testing? How will the couple be informed after testing?

Ethical and practical issues

The option to continue or abort a pregnancy is the primary issue after most prenatal testing. Still many difficult decisions often follow prenatal testing or screening. A genetic counselor has to ensure that information about testing options and results is given in a non-directive and supportive way and that the parents are well informed if they have to consider abortion vs. continuing a pregnancy. A lot of “background” factors can influence decisions and consideration for example cultural background, religion, and former family experiences.

Thursday, May 1

Molecular analysis: old and new diagnostic tools

M. Iascone
Medical Genetics Laboratory,
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Italy

Technological advances in molecular genetics had signed the pace of progress in our ability to diagnose genetic diseases. Molecular genetic tests usually study single genes or short lengths of DNA to identify variations or mutations that lead to a genetic disorder. Now this approach is changing due to the recent introduction of new sequencing technology in clinical practice. The lesson will focus on old and new techniques used to diagnose diseases caused by different pathogenetic mechanisms, in particular:

- diseases caused by dynamic mutations (triplets expansion in the promoter region of the FMR1 gene, Fragile X syndrome)
- diseases caused by imprinting defects (methylation-specific PCR for evaluation of methylation status of a DNA region and use of STR markers to detect deletions or uniparental disomy, Prader-Willi /Angelman syndrome).
- diseases caused by total or partial deletions/duplications of single genes (MLPA, multiplex ligation-dependent probe amplification, Alagille Syndrome).
- diseases caused by known point mutations (single bases substitutions or indels) detectable by targeted methods (real-time PCR for detection of single known mutation or reverse dot blot and similar for arrays of known mutations, Cystic Fibrosis).
- diseases without hotspots mutations detectable only by DNA sequencing.

At the basis of almost all molecular analyses, there is the **polymerase chain reaction** (**PCR**). This is a technology used to amplify a single or a few copies of a piece of DNA across several orders of magnitude, generating thousands to millions of copies of a particular DNA sequence. Developed in 1983 by Kary Mullis, PCR is now a common and often indispensable technique used in research and diagnostic labs for a variety of applications. The method relies on thermal cycling, consisting of cycles of repeated heating and cooling of the reaction for DNA melting and enzymatic replication of the DNA. Primers (short DNA fragments) containing sequences complementary to the target region along with a thermostable DNA polymerase are key components to enable selective and

repeated amplification. As PCR progresses, the DNA generated is itself used as a template for replication, setting in motion a chain reaction in which the DNA template is exponentially amplified. PCR can be extensively modified and is at basis of the majority of tests used in a molecular genetics lab. PCR and capillary electrophoresis allows the detection of triplets' expansion or by amplification of chromosome specific markers the detection of parental origin of chromosomes to detect uniparental disomy. One o the modifications of PCR, is represented by **Methylation-specific PCR** (**MSP**), used to detect methylation of CpG islands in genomic DNA. DNA is first treated with sodium bisulfite, which converts unmethylated cytosine bases to uracil, which is recognized by PCR primers as thymine. Two PCRs are then carried out on the modified DNA, using primer sets identical except at any CpG islands within the primer sequences. At these points, one primer set recognizes DNA with cytosines to amplify methylated DNA, and one set recognizes DNA with uracil or thymine to amplify unmethylated DNA. MSP is, for example, used in Prader-Willi/Angelman syndrome genetic testing.

MLPA (**Multiplex Ligation-dependent Probe Amplification**) is a multiplex PCR method detecting abnormal copy numbers of genomic DNA segments (usually exons). Although for most hereditary conditions, (partial) gene deletions or duplications account for less than 10 % of all disease-causing mutations, for many other disorders this is 10 to 30% or even higher still. The inclusion of MLPA in clinical settings can therefore significantly increase the detection rate of many genetic disorders. Although MLPA is not suitable for genome-wide research screening, it is a good alternative to array-based techniques for many routine applications. Typical for MLPA is that it is not target sequences that are amplified, but MLPA probes that hybridise to the target sequence. The MLPA reaction can be divided in five major steps: 1) DNA denaturation and hybridisation of MLPA probes; 2) ligation reaction; 3) PCR reaction; 4) separation of amplification products by electrophoresis; and 5) data analysis.

During the lesson, particular emphasis will be given to old and new **sequencing techniques** that are revolutionizing the approach to genetic testing. Sequencing technologies have evolved rapidly over the past 5 years. **Semi-automated Sanger sequencing** has been used in clinical testing for many years. It is based on chain-termination method developed by Frederick Sanger in 1977. The Sanger method was soon automated and was the method used in the first generation of DNA sequencers and is still considered the gold standard of clinical sequencing. However, its limitations include low throughput and high cost, making multigene panel laborious and expensive. Recent technological advancements have radically changed the landscape of medical sequencing. **Next-generation sequencing (NGS)** technologies utilize clonally amplified templates, which are then sequenced in a massively parallel fashion. This increases the throughput by several orders of magnitude decreasing the cost of sequencing. NGS technologies are now being widely used in clinical setting. Three main

levels of analysis, with increasing degrees of complexity, can now be performed via NGS: disease-targeted gene panels, whole-exome sequencing (WES), and whole-genome sequencing. All have advantages over Sanger sequencing in their ability to sequence massive amounts of DNA, yet each has challenges for clinical testing.

For example, the results of NGS genetic tests are not always straightforward, which often makes them challenging to interpret and explain. During the lesson an overview of current limits of clinical application of NGS will be addressed.

Cytogenetics: current status and future perspectives

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Medical Genetics Unit
Bologna University Hospital S.Orsola-Malpighi
Italy

The early days

The study of chromosomes and their structure is the subject of cytogenetics. The year 1956 marked the beginning of modern human cytogenetics when Tjio and Levan defined the number of chromosomes in man as 2n=46 and Ford and Hamerton confirmed this finding. In 1959, the first chromosome abnormalities were described: Jacobs and Strong reported an additional chromosome X in a case of Klinefelter syndrome, Lejeune *et al.* showed the presence of an extra chromosome 21 in Down syndrome and Ford *et al.* demonstrated a 45,X karyotype in a case of Turner syndrome. These first discoveries were rapidly followed by other cytogenetic reports that established the medical applications of cytogenetics.

Because of the limitations of the early methods used in clinical cytogenetics, numerical abnormalities, in which the chromosome complement is different from 2n=46 were the first type of chromosome abnormality described. However, the existence of a number of large structural rearrangements, including Robertsonian translocations, was also documented at this time, but it was the introduction of chromosome banding techniques that initially allowed much more detailed characterisation of structural chromosome rearrangements.

Fluorescence in situ hybridisation (FISH)

Although conventional cytogenetics is an essential technique in the identification and characterisation of chromosome rearrangements, this methodology has a resolution limited by the capacity of the human eye of ~3 to 5Mb. More recently, the advent of FISH has permitted the study of chromosomes at resolutions significantly higher than afforded by conventional cytogenetic analysis. The technique is based on the hybridisation of a labelled DNA or RNA probe to patient genomic DNA. Radioactive isotopic labels were used initially, but were later replaced with

fluorochromes, rendering the technique safer and easier to use. Furthermore, the availability of fluorochromes of different colours enables the testing of more than one probe simultaneously. This technical advance allied to the increasing accessibility of probes generated by the Human Genome Project promoted significantly the use of FISH.

Array Comparative Genomic Hybridisation (Array CGH)

Recently, the application of DNA probes to microarrays has emerged as a powerful technology in genetics studies. Array CGH enables the detection of copy number changes by competitively hybridising differentially labelled test and reference DNA to arrays of spotted and mapped clones. Thus, the technique allows the rapid screening of the whole genome at a resolution determined by the density of the markers spotted onto the array.

Next Generation sequencing (NGS)

NGS enables a fast and cost effective way to determine the whole DNA sequence of an individual, hence allowing for the identification of the whole catalogue of DNA variants in a given genome. Alternatively, a NGS assay might be designed in order to target not the whole genome, but specific genomic regions, for example the exons and in that case the assay is named exome sequencing. Irrespective of the chosen design for a NGS experiment, the final outcome is that data on all variants present in a DNA sequence is obtained and quite often the amount of data generated is overwhelming.

Future perspectives

The field of Human Genetics has greatly benifited from technological advances. At this point in time, it seems obvious that the main challenge faced by human geneticists rests with the interpretation of the data obtained, specially by array CGH and NGS assays. Although a set of criteria has been put in place to aid in this interpretation in many cases a definitive answer just cannot be given to patients. Hopefully, we will be in a position to tackle these shortcomings when a large enough number of individuals' genomes has been analysed. Thus far, the study of normal individuals has demonstrated that human genome variation is considerable and further studies are necessary to help to gauge its full contribution for human diversity and susceptibility to disease.

Genetics of intellectual disability

F. Forzano
Medical Genetics Unit, Galliera Hospital,Genova
Italy

Intellectual Disability (ID) is a common condition which affects 1-3% of people worldwide, and is currently defined as "an impairment of general mental abilities that impact adaptive functioning in conceptual, social and practical domains" with onset in the developmental period.

A genetic cause can be found roughly in a half of the cases, being much more likely as the IQ progressively decrease.

Among the genetic causes it is possible to make a gross distinction between multiple genes defects and single genes defects.

The first group include genomic imbalance (deletion or duplication) which involves various contiguous genes and which can be identified through standard karyotyping (resolution 3-5 Mb) or molecular karyotyping (FISH and array-CGH, resolution 25Kb-1Mb). The contribution of each of the genes located within the critical region to the phenotype can be different, and sometimes it is possible to identify one major gene responsible for the core phenotype. Almost 10-15% of the patients affected by genetic related ID carry an overt or subtle chromosomal abnormality.

The second group includes a few hundreds of genes spread throughout all chromosomes. More than 200 genes are located on the X chromosome. Among these, FMR1 is responsible for the most frequent inherited form of MR, Fragile-X syndrome, which affects 1 in 6000 people. On the contrary, all the other genes individually account for a very small proportion of ID disorders.

The functions of the genes involved in ID can be very diverse and include the structure, the function or the metabolic environment of neurones.

To search the causes of ID is important for many reasons: to define a prognosis, to start a proper care plan, to provide a specific recurrence risk and to get a proper support to the family.

Guidelines on the evaluation of mental retardation have been established through Consensus Conferences, one of the foremost has been from the American College of Medical Genetics in 1997.

As the research advances, new genes are identified and new techniques available, thus improving both knowledge and tools that can drive clinicians in the diagnostic process. It's now emerging that ID can be the end result of a number of different abnormal pathways, no-one of them overriding the others, which underlie the huge complexity of our intellectual processing. So unraveling the causes of ID phenotypes will ultimately be important to understand how the brain develops and works and eventually to find out possible specific treatments.

Friday, May 2

Basic concepts on dysmorphology

F. Forzano
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Italy

The term “Dysmorphology” has been coined by Dr. David W. Smith in the 1960's to generally define the study of human congenital malformations, particularly those affecting the “morphology” (anatomy) of the individual.

A few years later, Dr. Jon Aase, a former Dr Smith’s student, elaborated much more this concept and stated that "As a scientific discipline, Dysmorphology combines concepts, knowledge, and techniques from the fields of embryology, clinical genetics and pediatrics. As a medical subspecialty, dysmorphology deals with people who have congenital abnormalities and with their families."

The clinical examination of the morphology of referred patients has proved essential for the delineation of hundreds of syndromes and has been a key tool for the discovery of many “disease genes”. A structural defect is in fact an inborn error in morphogenesis, and the study of these anomalies ultimately lead to an extended knowledge on genetic mechanisms which regulate normal embryonal development too.

The dysmorphological assessment relies on a careful analysis of congenital anomalies. While major malformations are obvious at birth and usually lead to a prompt referral for a medical evaluation, minor malformations have no clinical consequences and can easily be neglected. However, the recognition of these minor malformations might be the essential clue for the detection of a genetic condition, which can allow to establish the more appropriate intervention for the child and the whole family.

Since the evaluation of minor malformation is largely subjective, new computer-based 3D techniques have recently being developed to analyse facial features in an objective, operator-independent way and to assist clinical training in pattern recognition.

Databases like OMIM, London Medical Databases, Possum are useful tools commonly used by dysmorphologists to achieve a diagnosis in difficult cases.

With the introduction of new cytogenetic and molecular testing, the traditional path from phenotype to genotype in dysmorphology has now become a two-way road.

In fact large scale testing of patients with developmental problems has brought to the identification of several 'new' microdeletion/duplication syndromes through so called 'reverse dysmorphology', that is, using a genotype to phenotype approach.

The combination of all these new tools and techniques makes Dysmorphology nowadays a very exciting and dynamic branch of Clinical Genetics. The parallel improvement in both phenotyping and genotyping and their continuous reciprocal interaction will ultimately lead to a profound knowledge on pathogenesis of a number of diseases and also on physiological development and functioning.

Cancer genetics: scenarios and issues

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Policlinico S. Orsola-Malpighi,
Bologna, Italy

Cancer is always a genetic disease, as it is the result of multiple genetic defects in cells. In the majority of cases, the accumulation of genetic changes in a tissue is random, and in this case the tumour is termed sporadic. In a fraction of cases, however, all the cells of the body carry an inborn genetic defect, which increases the chance that certain tissues would become cancerous. This type of cancer susceptibility can be passed down to the offspring, and cancer occurring in such predisposed individuals is therefore regarded as "hereditary".

Observation of large populations of individuals revealed that as much as 5-10% of cancer cases show marked familial clustering suggesting hereditary cancer predisposition. This is a small fraction of the total cancer burden, if compared to those attributed to dietary risk factors (35%) and to smoking (30%). Nevertheless, if one estimates that 5-10% of the most common cancers, like breast, colorectal and prostate cancer, are associated with a genetic predisposition, it becomes clear that the absolute number of hereditary cancer cases is significant. Moreover, the identification of cancer genetic syndromes allows for the identification of individuals at increased risk, who can benefit from specific prevention strategies.

Genes involved in hereditary cancer predisposition belong to three main classes:

1. **Oncogenes** are genes that are normally involved in cell growth and proliferation and cause cancer when they are over-expressed, amplified, or mutated (gain of function).
2. **Tumour suppressor genes**, on the other hand, normally regulated cell growth, and only result in malignant progression when their negative control is impaired (loss of function).

3. Similarly to tumour suppressor genes, also **DNA repair genes** cause cancer predisposition through a loss of function, which allows for multiple genetic defects to accumulate in the cell genome, leading to the malignant phenotype.

Unlike oncogenes, a monoallelic mutation of which is sufficient to cause cancer, tumor suppressor and DNA repair genes generally require that both the alleles are mutated for cancer to develop.

There are very few instances of oncogenes involved in hereditary cancer syndromes: RET mutations cause Multiple Endocrine Neoplasia 2, while mutations in MET are responsible for Familial Papillary Renal Carcinoma Syndrome. Conversely, mutations in tumor-suppressor genes account for the majority of cancer syndromes, such as the Breast Ovarian Cancer Syndrome, caused by mutations in BRCA1 and BRCA2 genes, and Hereditary Melanoma, caused by mutations in the CDKN2A gene. Talking of repair genes, a dysfunction of the mismatch repair caused by mutations in one of the responsible genes results in Hereditary Non-Poliposis Colorectal Cancer (HNPCC, also known as Lynch Syndrome).

Recognizing the hereditary cases among all cancer patients is sometimes easy, when the family history is highly suggestive, but can be difficult in many cases. The usefulness of specific familial and/or clinical features in the identification of inherited cases will be discussed in the lecture. In addition, for some cancer types, such as breast and colorectal cancer, probabilistic models are available to predict the probability of mutations in specific genes and to assess individual cancer risk.

Genetic testing may find the causative mutation in a number of families, which helps identify asymptomatic carriers in the family; nevertheless genetic heterogeneity (rare or undiscovered genes) and the existence of possible alternative mechanisms of gene alteration (undiscovered type of mutations) hamper the ability of genetic testing to detect the underlying defect. Limitations of testing must be taken into account when counseling people from cancer-prone families and planning prevention and surveillance. In the near future, next-generation sequencing technologies are expected to lead to an enormously increase in the detection rate of genetic tests. At the same time, however, we will face increasing troubles with interpretation and communication of genetic test results, as variants of unknown significance will become more common, a number of "incidental findings" will be detected and penetrance of rare genes will be uncertain.

Whenever the efficacy of available risk-reduction strategies is not definitely demonstrated, a non-directive approach should be adopted in counselling patients at increased risk for cancer. The purpose of counselling may include helping the individual explore feelings about his or her personal risk status and make a healthy adjustment to that risk status. Either alone or in consultation with a mental health provider, professionals offering cancer genetic counselling attempt to assess whether the individual's expectations of counselling are realistic and whether there are factors suggesting

unusual risk of adverse psychological outcomes after disclosure of risk and/or genetic status. To limit the chances of adverse consequences of risk assessment and communication, in addition to a continued follow-up by the counsellor, the availability of psychological support, preferably provided by mental health professionals with experience in cancer genetics, is recommended.

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Practical ethics - consent, confidentiality and disclosure

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Principles regarding consent for procedures and protecting the confidentiality of medical information are enshrined in codes governing ethical practice. They are also subject to statutory oversight which may vary according to the area of administration. It can be argued that medical genetics is no different from other medical specialties. However the practice of clinical genetics may give rise to situations where issues of consent and confidentiality do require special consideration. In relation to consent for procedures the key aspects are that i) the person understands the nature and risks of the procedure to which they are consenting and ii) that the person gives consent without coercion.

In this session we will consider cases where there may be special issues relating to consent and confidentiality. The text below is adapted from 'Applied genetics in health care'. In genetic healthcare settings, consent most often relates to:

1.Taking a family history

Consent can generally be assumed if the proband provides the information requested, providing that the process and reason for taking the pedigree have been explained. However, when using the pedigree to counsel other family members, the confidentiality of the original proband must be respected. For this reason, it may be appropriate to take a new pedigree when seeing a different branch of the family.

2. Obtaining specific medical history from the proband and/or other relatives

It is frequently necessary to request medical notes on the proband in order to advise him or her properly, consent must be sought to view or request medical records. The purpose of viewing records of other family members must be explained to them and written consent obtained.

3. Obtaining blood or tissue samples

Permission to take a sample must be explicitly given by the client. This is sometimes written consent, but if the procedure has been explained the co-operation of the client in giving the sample is usually deemed to be evidence of consent. For example, if a client lifts his sleeve and presents his arm after being asked to consent to a blood sample, this would be evidence that the client has given consent.

4. Performing genetic tests

The exact nature of the tests and the implications of the result must be explained to the client . It is good practice to give the client written information as well as a verbal explanation, and written evidence of consent must be recorded. Risks associated with genetic testing might include the discovery of false paternity, this should be mentioned if a possibility. Other aspects of consent for genetic tests include whether consent is given for the sample to be stored and the possible outcomes of the test. Separate consent should be obtained for use of the sample in research and to share the results with relatives in the process of their own testing.

5. Issues arising from Genome Sequencing

The advent of whole genome approaches to genetic analysis in the research setting and in the clinic has led to number of different analyses of how to approach the issue of 'health related' actionable incidental findings. This discussion is still ongoing with different approaches being suggested. The

spectrum ranges from a bio-informatically targeted approach to analysis based on the clinical question which minmises the possibility of uncovering the information unrelated to the genetics test, to an opportunistic screening approach deliberately targeting genetic variants that have actionable health consequences. Whatever approaches are used there are challenges for consent and confidentiality.

Confidentiality

Confidentiality of personal information is a basic tenet of healthcare and is considered so important to the rights of the client that it is enshrined by law in many countries. However, there may be provision under some statutes for the healthcare professional to disclose the client's confidential medical information, if not disclosing would result in serious but avoidable harm to others. This is the case in UK law. A good example covered in law would be where a person had a serious infectious disease that was putting others in the community at risk.

In a genetic healthcare setting, the situation may be complex, as the information about the genetic structure of one individual may (and often does) have implications for other family members. Where this occurs, the proband is usually encouraged to share the information with relatives who may be affected, especially if screening or treatment is available that would reduce the health risk. It is usual to offer support in the form of written information that can be given to relatives and contact details so that they can seek more information and guidance from the genetics team if they wish.

When an individual refuses to share information with relatives, there is always an underlying reason that might not be obvious to the practitioner. The situation is rarely urgent, and effort spent in gaining the proband's confidence and allowing time for psychological adjustment to their status can often be helpful in enabling the proband to share the information. However, this is not always the case and then the decision about whether to break confidentiality may arise.

Resources

American College of Medical Genetics and Genomics ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing
Update published April 1st 2014
https://www.acmg.net

Joint Committee on Medical Genetics Consent and confidentiality in genetic practice: Guidance on genetic testing and sharing genetic information. A report of the Joint Committee on Medical

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PhGFoundation Clinical whole genome analysis: delivering the right diagnosis http://www.phgfoundation.org/reports/15237/ (accessed 14th April 2014)

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United States Department of Health and Human Services. Office for Civil Rights- HIPPA. Medical Privacy – National standards to protect the privacy of personal health information (accessed 14th Aril 2014) http://www.hhs.gov/ocr/hipaa/finalreg.html

Saturday, May 3

Predictive and not: understanding the mixed messages from our DNA sequence

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When whole genome and whole exome sequencing are introduced into health care, and offered directly to consumers in commercial settings, the landscape of genetic testing will drastically change. The information that is obtained from sequencing is much more complex than the results of traditional genetic testing: where traditionally a test is undertaken to inform a single health outcome, genome sequencing can inform the diagnosis of, or susceptibility to, numerous diseases.

Genome sequencing is envisioned to ultimately replace conventional forms of genetic testing. The technology will become so inexpensive that it will be straightforward to sequence the entire genome and only interpret the loci of interest. This prospect has already led to an intense debate on what to do with the remaining unreported data. The return of incidental findings is one of many concerns accompanying the introduction of genome sequencing in health care. Others include issues around privacy, discrimination, insurability, and patient and consumer protection.

The opportunities for the return of incidental findings, discrimination and stigmatization depend on the predictive ability of a test. Therefore, the discussion of these concerns in the context of sequencing should start from a critical assessment of the predictive ability of DNA, which is paramount because the genome does not have an 'overall' predictive ability as such. Rather, genome sequencing should be seen as one assay that consists of numerous tests. The predictive ability depends on what is predicted, in whom and how (using which specific information from the DNA).

For a constructive debate on ethical and societal issues, health care professionals, policy makers, legislators and the public need to be aware of the possibilities and limitations of sequencing. A good understanding of what can (and cannot) be predicted from our DNA is necessary to ensure a responsible introduction of genome sequencing in health care and an effective regulation of commercial DNA testing. This paper provides a concise explanation on how DNA can be both predictive for some diseases and not predictive for others.

Based on the following manuscripts and papers:

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Kalf RR, Mihaescu R, Kundu S, de Knijff P, Green RC, Janssens AC. Variations in predicted risks in personal genome testing for common complex diseases. Genet Med 2013.

Janssens ACJW, van Duijn CM. An epidemiological perspective on the future of direct-to-consumer personal genome testing. Investig Genet 2010;**1**(1):10.

Janssens AC, van Duijn CM. Genome-based prediction of common diseases: advances and prospects. Human molecular genetics 2008;**17**(R2):R166-73.

Janssens ACJW, Aulchenko YS, Elefante S, Borsboom GJJM, Steyerberg EW, van Duijn CM. Predictive testing for complex diseases using multiple genes: Fact or fiction? Genet Med 2006;**8**(7):395-400.

Counselling for predictive testing

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Genetic counselling has been perhaps the most important way of assisting families with a hereditary disease in managing the consequences of the disease, and in helping individuals at-risk to find creative solutions for their problems. The increased awareness of the genetic aspects of a disease, and genetics in general, together with the more widespread availability of genetic centres have contributed to a more appropriate approach for those who ask for assistance in making important life decisions. Clinicians involved with families with a hereditary disease may prefer to refer their patients to a clinical genetics centre to address the genetic questions. The way such questions are dealt with can have a profound impact on the attitude of individuals at risk, their partners and children, and on further relatives. Before the availability of predictive or susceptibility testing, general counselling of the genetics of a hereditary disease was the most important issue that led individuals at risk to visit the genetic counsellor. Currently, people often apply for general genetic counselling when they have only recently first learned of a hereditary disease in their family, although many of them come with the intention to discuss predictive or prenatal testing. Most people seen for genetic counselling regarding a hereditary disease are the asymptomatic children of an affected patient, seeking reassurance for themselves and their (future) children. Sometimes people apply for predictive testing because they have the opinion that a test result might solve their psychological or family problems. Those professionals who have much experience with general

counselling and predictive testing know that alternative ways of coping with personal risks and, subsequently, life decisions might be preferable in some cases.

Genetic counselling involves a process of consultation by which information is imparted to individuals or families affected by or at risk for a genetic disorder. It includes information on the nature of the disorder; the size and extent of genetic risks; the options, including genetic testing, that may help clarify the risks; the available preventive and therapeutic measures, and the provision of psychological, social and practical support. In the context of genetic testing it may include responding to the concerns of individuals referred and their families, discussing the consequences of a test, and enabling them to choose the optimal decision for themselves, but not determining a particular course of action (American Society of Human Genetics 1975). The definition emphasises the two-way nature of the interaction between the test candidate and the counsellor. Moreover, counselling is considered as a process, taking place over a period of time. This process allows the assimilation of the potentially distressing information regarding diagnosis, prognosis, risk, emotional reactions, family dynamics etc. The counselling process allows attention for the autonomous decisions taken by the test candidate. The appropriateness of the decisions can be discussed and weighed extensively. This all requires 'appropriately trained persons' which implies special knowledge and skills distinct from those needed in other medical and counselling interactions (Platt-Walker 1998).

Individuals at risk for HD often come for genetic counselling to discuss aspects of the disorder they find difficult to deal with. Exploring with them their experiences, emotional responses, goals, cultural and religious beliefs, financial and social resources, family and interpersonal dynamics, and coping styles has become an integral part of the counselling process. Many individuals at risk with life long experience with a specific hereditary disease have no full awareness of how the disorder has influenced their psychological make up. An experienced counsellor must be able to recognise and bring forth these responses. He or she can identify normal and maladjusted responses, reassure candidates that their reactions are normal, prepare them for the near future, new issues and emotions that may come up, and help them to mobilise the resources needed to encourage coping and adjustment.

A central assumption of genetic counselling has been the non-directive approach. This assumption is often misunderstood in a way that non-directiveness does not mean that the counsellor should by no means express their personal views, opinions or feelings (Kessler, Kessler et al. 1984; Djurdjinovic 1998). An individual at-risk can expect that the counsellor is willing to provide some guidance when needed to enable him or her to proceed in his own process of consideration. Yet, it requires from the counsellor a level of introspection and awareness of his or her personal feelings and interests in order not to be coercive. The lack of treatment options and future perspectives may

facilitate the psychological defences of professional persons such as denial and displacement of responsibility. Families can be threatening to those professionals who have difficulties in working with conditions that cannot be cured. Although the defences protect professionals from the difficult and unsettling task of providing genetic counselling to healthy relatives at risk, they may prevent caregivers from establishing a relationship that is characterised by confidentiality, respect for autonomy and empathy (Martindale 1987). Permanent education and increase in awareness of the psychodynamics involved may lead to creative and constructive thinking about the current deficiencies in care and counselling services provided for families with a hereditary condition.

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Psychological issues in antenatal screening and testing

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Over the last half century, it has become increasingly possible to test a fetus for genetic or chromosomal conditions. Antenatal testing is a term applied when the fetus is at particular risk of a condition and the test is offered for that specific reason. The risk may be due to one of a range of reasons, for example a family history of a monogenic disorder, because the parents are carriers of an autosomal recessive condition or chromosomal translocation or because the mother is of advanced maternal age. Screening is offered to all women in the population, regardless of the prior risk. So for example, in some countries all women are offered antenatal screening for trisomy 21. The results do not provide a definite diagnosis, but give an indication of the level of risk in that

particular pregnancy. This allows the parents and professionals to make a decision about whether further tests are warranted.

There are many psychological factors that influence parental decisions about testing or screening. Their decisions will be affected by their attitudes to disability and abortion, as well as their reproductive history. Professionals have a duty to ensure that such tests are not seen as a 'routine' part of antenatal care. It is important that parents have both information about testing and screening and psychological support when making decisions. In this session we will discuss parent's views on screening and testing, and the roles of health professionals in this context.

Some relevant papers on this topic:

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Barr O, Skirton H. (2013) Informed decision making regarding antenatal screening for fetal abnormality in the United Kingdom: a qualitative study of parents and professionals. *Nursing and Health Sciences*, DOI: 10.1111/nhs.12034

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Stefansdottir V, Hardardottir H, Jonasson K, Skirton H, Jonsson JJ. (2010) Effects of Knowledge, Education, and Experience on Acceptance of First Trimester Screening for Chromosomal Anomalies. SOBS Acta Obstetricia et Gynecologica Scandinavica 89(7): 931-8.

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Why do we need counselling skills?

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Bad news may be defined as "any information which adversely and seriously affects an individual's view of his or her future". Bad news is always, however, in the "eye of the beholder," such that one cannot estimate the impact of the bad news until one has first determined the recipient's expectations or understanding. Different models of communication will be explored and learned to achieve communicational, emotional and relational skills. Furthermore, specific difficult issues in genetics will be analysed, such as: risk perception, autonomous decision, emotional impact and cultural differences

Revision of basic Rogerian Counselling skills

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In all healthcare settings, the use of counselling skills is helpful in enabling the client to discuss their health concerns and engage in shared decision-making about investigation and/or treatment. The core competencies for genetic health professionals include eliciting the client's concerns and exploring the psychosocial influences that have relevance to the genetic counselling for each family (AGNC, 2004). However, there will be sessions when the need to use counselling skills is more apparent, such as when the client is making difficult decisions or during periods of adjustment to changed circumstances. Active counselling may be undertaken by genetic counsellors who are appropriately trained to assist the client when the psychosocial issues are impeding adjustment to their genetic situation and therefore adversely affecting the client's quality of life.

Rogerian, or Person-centred, counselling

In every session of genetic counselling, it is important that clients are able to express their own concerns, questions and reactions, and to feel that the genetic practitioner has heard and addressed them appropriately. One model that is suitable for counselling in a genetic counselling context is the person- centred model based on the seminal work of Carl Rogers (1961). The central tenet of the

model is the belief that each person has the ability to solve his/her own problems and work through difficult situations using one's own resources. Support from another person enables the client to explore the situation in a safe emotional environment.

The aim of person-centred counselling is to facilitate the client to achieve self- actualisation through enhancing self-belief. The counsellor aims to hold the client in unconditional positive regard, and to demonstrate this. The empathic relationship is central to the counselling work.

Person-centred counselling is very appropriate in a genetic healthcare setting, as the practitioner does not profess to be 'an expert', who can solve the client's problems, but rather a supporter whose role is to reinforce the client's self-belief. Rogers described the 'core conditions' necessary for a helpful counselling relationship.

Core conditions

Genuineness

The counsellor is real to him or her self and to the client. To achieve this, the counsellor requires a considerable degree of self-awareness and a belief in the equality of the client.

Empathy

One description of empathy is being able to 'walk in the other person's shoes'. Whereas sympathy involves feeling sorry for the other person, empathy is more connected with trying to understand how the client feels, and communicating that understanding.

Warmth

Understanding the client is not facilitative unless that can be conveyed. The 'gold standard' for the person-centred counsellor is the ability to hold every person in unconditional positive regard. Whilst this itself a challenge, it helps to reduce value judgements of the client and therefore increases the likelihood that the client will feel free to make the decision that is best for them.

Basic counselling skills that we will discuss and practice are:

- Open questions
- Reflection of feelings
- Paraphrases of content
- Summaries of the dialogue
- Non-verbal communication
- Silence.

Sunday, May 4

Using Transactional Analysis in genetic counselling practice – theory and practice using scenarios

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Transactional analysis (TA) is a theoretical model of counselling that can help us to understand what is going on between us and the client. It was developed by Eric Berne and is one of the psychodynamic models of counselling.

Basic themes

All individuals have three ego states. These influence our thoughts and behavioural responses in a given situation. Individuals operate according to 'preconscious life scripts', that can however be changed. The counsellor's role is to facilitate the changing of scripts and to help the client reach the I'm OK – you're OK position.

- Parent

The instructor. The parental guide is internalised into the person, and becomes a psychological ego state. The parent state enables a person to operate in the social world, according to the rules of that world.

- Adult

In this state we are most likely to make judgements and exhibit behaviour that is appropriate to the situation. The Adult state is characterised by logical thinking, rather than the obedience to rules (parent) or acting on impulse (child). In the adult state, previous life experience is used, and information from the parent and child states are weighed up to find the relevant course of action.

- Child

The child ego state is characterised by the reactions and responses that were learnt as child. This means there is little modification of natural emotions.

Key concepts in TA

Transactions between individuals may be:

Complementary – where there is genuine understanding and communication e.g. adult to adult but can be parent to child or child to parent

Crossed – genuine communication does not occur, and there may be disruption to the relationship as a result of the crossed transaction e.g adult to parent or child to adult

Ulterior – the transaction seems to be outwardly straightforward but there is an hidden underlying motive

The OK / not OK position

In TA, each individual is viewed as worthy of respect, this is a similar to the basis of person-centred counselling. When a person has self-regard they are said to feel 'OK'. Feeling OK in later life is linked to the messages a person receives in infancy, childhood and adolescence.

Berne's theory also includes the approach a person has to others, hence the variety of possibilities:

I'm OK- you're OK

I'm not OK - you're OK

I'm OK - you're not OK

I'm not OK - you're not OK

These positions relate to life scripts. The individual conditioning a person receives early in life is called a 'life script'. In TA, the life script of the client is examined and the client may be challenged and supported in changing an inappropriate script.

The script consists of the series of messages conveyed to a child during formative years. The counsellor can support the client in challenging his or her life script.

During the session we will look at the theory and how we can apply TA in genetic counselling. . Some personal exercises will be used to help us understand the concepts.

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Genetic screening and testing in children

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There has been a long-standing consensus that the primary and strongest justification for genetic testing of children exists when the results will clarify the cause of current symptoms, when the onset of the condition may occur during childhood, or when the information will be used to embark on a course of care that must start during childhood to prevent or ameliorate later symptoms (American Academy of Pediatrics Committee on Bioethics, 1995). The necessity of screening and testing children at risk brings along its own sensitivities. The natural wish of parents is to ensure the safe and normal development of their offspring. However, in families at risk of genetic diseases, the future of a child can be shadowed by the chance that life may be shortened or adversely affected by the condition. Families who seek genetic counselling frequently wish to discuss the issue of telling their child about the condition in the family, and informing the child that they are at personal risk. This issue arises whether or not testing is available. The decision to tell may not be clear-cut, as the desire to inform the individual may be juxtaposed with reluctance to cause anxiety in the child (Skirton, 1998).

The advent of clinical exome- and genome-wide sequencing has provided faster, wider and far-reaching options for testing and screening (Green et al., 2013; van El et al., 2013) and the debate about predictive genetic testing of children has been cast in a new light by American and European recommendations (Clayton et al., 2014; Lucassen, Widdershoven, Metselaar, Fenwick, & Parker, 2014;)

The general opinion among professionals is that testing for adult-onset disorders holds more potential for harm than for benefit (Clarke & Flinter, 1996). Testing is only justified if onset is expected in childhood or adolescence, and if treatment options are available. Testing removes the individual's future right to make own decisions as an autonomous adult, it removes the confidentiality, expected for any adult undergoing the same test, and it may alter the upbringing and the pattern of relationships within the family ands with peers, with the inclusion of stigmatisation and discrimination. Hence, DNA tests for adult-onset diseases on asymptomatic children - at parental request - is generally not performed in most genetic centres.

A family life overshadowed by the risk of a hereditary disease will obviously influence the way parents perform their parental tasks (Fanos, 1997). An important task regarding their children is the establishment of a stable and safe environment for the family, which may become difficult if the

parents fear the disease. They also have a task in explaining facts and circumstances of the grandparent's disease and their personal risks, which requires openness and courage to discuss these issues with their children. Parents must be able to understand their children's' developmental capacities for coping with their risk and a disease and they must be able to express this understanding. They must assist in tolerating and expressing uncertainty and anxiety, and facilitate the change to new relationships and responsibilities.

Having considered the tasks of parents and children, the tasks of the counsellor can be made more explicit. The counsellor can increase the awareness of how a hereditary disease has specifically affected every member of the family. He or she can help to further discuss the traditions, the myths, and the coping strategies in the family regarding the disease. The counsellor can help to explore the underlying motives of the test request and consider this in the light of the developmental and parental tasks. The counsellor can give clarity about the developmental issues and tasks of each member, and facilitate openness and nonreactivity (that is being able to listen, hear the emotions and considerations of the other without counteracting immediately). Such work might increase the cohesion in the family and lead to new, constructive, and creative ways to deal with the disease.

It takes time, specific training and knowledge and much experience to be able to recognise and explore the specific themes in the family regarding their development. The themes and issues to be addressed include the individual beliefs, attitudes, and feelings about the disease and its impact in the family. Further, the impact on the current interactional framework of the family needs to be viewed. Subsequently, the way this framework is carried over into social contexts such as work, school, social life, and finally, what is the common theme that links to family legacies, loyalties, and traditions? Counsellors may benefit from the attainments of family system theory; education in the use of family dynamics could enrich their work (Carter & McGoldrick, 1998).

Test requests should be considered against the background of the specific age and role-related tasks that each member in a family with a hereditary disease has. The achievement of these tasks may have been extremely burdened by the occurrence of a specific disorder in the family. The test applicant's motives should be explored to enable him or her to make an informed decision. The decision should be hold against the personal and family history and future. The decision must be understood as part of or reflection of the entire family and individual coping mechanisms regarding the risks and the disease.

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What are my professional qualities and pitfalls?

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The relationship between client and professional in genetic counseling has historically been guided by the principle of non-directiveness, and more recently by shared decision-making. Moreover, good counseling practice implies that the counselor is aware of and addresses four psychological dimensions: 1. information transference, with the inclusion of digesting information, risk perception, cognitive adaptation, 2. mood, and emotional reactions to being at risk and the information provided, 3. the partner relationship and family dynamics through time and its impact on information and cognitive functioning, and 4. behavioral adaptation to being at risk, and after having received test results. Good counseling practice implies also that the counselor develops the ability to have attention for own emotions, moral values, personal unfinished business, and vulnerabilities. These countertransferential and attitudinal elements might restrict the development of a good relationship with the counselee but may also be a rich source for a fruitful working alliance. In this workshop we will explore how awareness of personal issues can enhance and enrich the professional relationship with counselees. For further reading see (Evans, 2006)
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Monday, May 5

Grief and loss issues – theory and personal awareness

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Loss is one of the most common experiences of families affected by genetic conditions and so is a key topic in genetic counselling. The loss can take many different forms besides death of family members. People may experience loss of confidence, relationships, work, social life or reproductive futures, to name only a few.

Worden (2000) wrote of four tasks of mourning:

Task I: To accept the reality of the loss

Task II: To work through the pain of grief

Task III: To adjust to a new environment

Task IV: To emotionally relocate the loss and move on with life. These tasks follow a cyclical pathway, rather than a longitudinal one and individuals may go back and forth between tasks.

In this session, we will look at grief, the ways in which grief manifests itself and the tasks of mourning. We will discuss how we can support individuals and families in the grieving process and how our own losses affect us as professionals.

The Counsellor end: self-awareness tools, occupational stress and burnout syndrome

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Self-awareness is an individual's tendency to pay attention and become aware to his or her own emotions, attitudes, and behaviour in response to specific situations. In the case of counsellors, self-awareness is their insight into how their emotional makeup influences patient care. Conceivably, such insight may improve counsellor' professional performance and counsellor – patient relationship. Specific approaches will be adopted to enhance counsellors self awareness and to avoid occupational stress and burn-out syndrome. In fact, poor self-awareness could lead to under or over estimate own coping strategy with occupational stress. During the class we will explore both

with frontal lesson and with exercise: empathy, burn-out symptom (how to recognise and how to prevent), self-awareness tools.

Tuesday, May 6

Discussing difficult issues with clients

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As professionals, we have all been involved in situations where we find it difficult to discuss a particular issue with a client. This may be because:

- we feel uncomfortable or embarrassed about the topic
- we are afraid we will not be able to manage the client's response to the conversation
- we have cues from the client that this is a difficult topic for them.

Whatever the reason, it is important that we take responsibility for broaching the topic, maintaining appropriate boundaries and making sure that the client is 'held' safely from an emotional perspective. In this session, we will discuss difficult issues, why we find them difficult and how we can improve our care of patients by learning to manage these situations better.
This will be an interactive session and before the session it will be helpful if you can spend some time thinking about a situation where you found the conversation with a client challenging.

Family dymanics

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The last decades, most attention has been given to individual psychological responses to genetic counseling and testing. Yet, an increasing awareness of the psychosocial challenges of genetics for patients, their partners and their core and extended families can be noticed. For disorders in which carrier, predictive, or confirmative testing is available, core time phases with salient developmental challenges of all family members involved need to be addressed, both pre- and post-testing, including a long-term adaptation phase. Professionals in clinical genetics have scarce training in family dynamics, but recognize the need for more knowledge and skills on these issues to improve clinical practice. I will introduce the Family Life Cycle model. This useful model clusters genetic

disorders based on key characteristics that define types of [1-3].We will discuss its utility for assessment and care in daily practice.

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