



Basic and Advanced Course in Genetic Counselling

Bertinoro, Italy, April 20 -24, 2018

Bertinoro University Residential Centre Via Frangipane, 6 – Bertinoro, Italy

Course Directors:

F. Forzano (Clinical Genetics Department Guy's & St Thomas' NHS Foundation Trust London UK), Giovanni Romeo (European School of Genetic Medicine and Univ.Bologna, Italy) A. Tibben (Dept of Clinical Genetics, LUMC, Leiden, the Netherlands)





Basic and Advanced Course in Genetic Counselling

Bertinoro, Italy, April 20-24

CONTENTS

3
7
32
33

Friday, April 20th – BASIC

9.00 - 9.10	Introduction to the course F. Forzano, A. Tibben
9.10 - 9.30	The 30 years of the European School of Genetic Medicine ESGM G. Romeo
9.30 - 10.15	Icebreaking
10.15 - 11.00	Cytogenetics and Molecular Genetics: past, present and future J. Baptista
11.00-11.30	Coffee Break
11.30-12.20	Genetics of intellectual disability F. Forzano
12.20-13.20	The Genetic Laboratory: instructional book M. Iascone
13.20-14.30	Lunch break

Afternoon Session:

14.30-15.30	Basic concepts on dysmorphology F. Forzano
15.30-16.15	Genetic services: aims, process, outcomes. Setting the agenda C. Patch & Z. Bruwer
16.15 – 16.45	Coffee break
16.45 - 18.15	Workshops session:
	A: CASE DISCUSSION, CLINICAL

A: CASE DISCUSSION, CLINICAL B: CASE DISCUSSION, LABORATORY C: HOW TO DRAW A PEDIGREE

Saturday, April 21st – BASIC

9.00 - 10.30	Workshops session:
	A: CASE DISCUSSION, CLINICAL B: CASE DISCUSSION, LABORATORY C: HOW TO DRAW A PEDIGREE
10.30 - 11.00	Coffee Break
11.00 - 12.00	Cancer genetics: scenarios and issues D. Turchetti
12.00 - 13.00	Prenatal diagnosis: scenarios and issues F. Forzano
13.00 - 14.30	Lunch Break
Afternoon Session:	
14.30 - 15.30	Practical ethics: consent, confidentially and disclosure C. Patch
15.30-16.00	Coffee Break
16.00 - 18.00	Workshops session:
	D: ROLE PLAY, PRENATAL E: ROLE PLAY, CANCER
Sunday, April 22 nd	– BASIC & CROSSOVER
9.00 - 11.00	Workshops session:
	E: ROLE PLAY, CANCER D: ROLE PLAY, PRENATAL
11.00 - 11.30	Coffee Break
11.30 – 12.30	Introduction to the course and Revision of basic Patient-Centered counselling skills A. Tibben
12.30 - 13.15	Skills practice (I) A. Tibben

13.15-14.30 Lunch Break

14.30 - 15.45	Skills practice (II)
	All Faculty

15.45-21.00 Social event tbd

Monday, April 23rd – ADVANCED

9.00 - 9.45	Counselling for predictive testing A. Tibben
9.45 - 10.45	Discussion of difficult cases brought by students All faculty
10.45-11.15	Coffee break
11:15 -12.30	Skills Practice (III) All faculty
12.30 - 14.00	Lunch break
Afternoon Session:	
14.00 - 14.45	Breaking the news: theory A. Tibben
15.45-15.45	Skills practice (IV) Breaking the news A. Tibben
15.45 - 16.15	Coffee break
16.30 - 17.30	Family dynamics: theory and awareness E. Razzaboni

Tuesday, April 24th – ADVANCED

9.00 - 9.30	Genetic testing in children (recommendations, legal frameworks and specific counselling issues C. Patch
9.30 – 10.15	Cross cultural issues Z. Bruwer
10.15-10.40	Grief and loss experiental exercises A. Tibben
10.40-11.00	Coffee break
11:00 -12.15	Grief and loss experiential exercises All faculty
12.15 – 12.30	Evaluation, closing remarks, farewell F. Forzano, G. Romeo, A. Tibben
12.30-14.00	Lunch and departure

ABSTRACTS OF LECTURES

Friday, April 20

The 30 years of the European School of Genetic Medicine G. Romeo

European Schoool of Human Genetic Medicine and Alma Mater Studiorum Università di Bologna, Italy

This year is the 30th anniversary of the foundation of the European School of Genetic Medicine (ESGM) which was started in 1988 in Sestri Levante (Italy).

In order to get a feeling of the origin and past history of the European School of Genetic Medicine you can read the article below which highlights the role of Victor A. Mckusick, one of its main founders. He passed away 10 years ago, on July 22, 2008.

The accompanying picture shows Victor together with his wife Anne when he received the Japan Prize from the Emperor of Japan a few months before his death. Anne, a faculty at Johns Hopkins Hospital and a distinguished rheumatologist, was attending all the courses together with Victor between 1988 and 2007. She passed away on September 17, 2017.

We miss them both.



www.nature.com/ejhg

PERSPECTIVE

The early years of the ESHG leading to the reform of 1988 and the spirit of the Sestri Levante school

Giovanni Romeo^{*,1}, Eberhard Passarge² and Albert de la Chapelle³

European Journal of Human Genetics (2017) 25, S6-S12; doi:10.1038/ejhg.2017.142

At the Third International Congress of Human Genetics in Chicago in September 1966 a group of human geneticists from Europe met and agreed that there should be a European Society of Human Genetics (ESHG). This was formally established in 1967, as reviewed elsewhere in this issue by Peter S Harper. As two of us (EP and AdlC) attended the discussion in 1966 and all three were involved subsequently in the early development of the ESHG we would like to add a few comments. Following its first annual meeting in 1967 in Copenhagen, the ESHG held meetings each year in various European cities arranged by different colleagues as local hosts, but not yet organised as a scientific society comparable to the American Society of Human Genetics.

At the 1988 ESHG meeting in Cardiff a process to reform the Society was started as described by Brunner and Harper in this issue of the Journal (EJHG, 2017). In April of the same year 108 young geneticists from 16 European countries travelled to Sestri Levante, Italy, to attend the first week-long course in Medical Genetics, taught by the late Victor A McKusick (1921–2008) and by many of the European medical geneticists of the time (see Figures 1 and 2).

The model for this course was the 'Short Course in Medical and Mammalian Genetics' held in Bar Harbor, Maine, organised each year by Victor A McKusick and attended in 1968 by some young European participants, including the three of us. The support of the Istituto Gaslini (Genoa) and of the Federation of European Societies of Biochemistry (FEBS) made it possible to start the European equivalent of the Bar Harbor course 20 years later; this was quite labour-intensive as shown by its tight scientific schedule (Figure 3), consisting of morning lectures and afternoon practical workshops (but also characterized by long lunch breaks of about 2 h dedicated to the delicacies of Genoese cuisine...).

During subsequent years this model developed further into many more specialised courses (Cancer Genetics, Genetic Counselling, Molecular Cytogenetics, Eye Genetics, etc.) that became to be known as the European School of Genetic Medicine (ESGM). The 30th edition of the main ESGM course took place at the beginning of May 2017 in Bertinoro, Italy, with the new name 'Clinical Genomics and NGS'. It was attended by 89 students from all over the world (37 countries, Figure 4). Most of the ESGM courses have been supported consistently by ESHG fellowships. In what is more relevant for the history of ESHG, some of the highly motivated faculty of the 1988 course became the leaders of the reformed ESHG in later years, after the new statutes



FIRST COURSE IN MEDICAL GENETICS COUNTRIES OF PROVENIENCE

¹University of Bologna, Department of Medical and Surgical Sciences, Bologna, Italy; ²Universität Duisburg-Essen, Institut für Humangenetik, Hufelandstr, Duitsland; ³Human Cancer Genetics Program, The Ohio State University, Columbus, Ohio, USA E-mail: romeo@eurogene.org



Figure 2

proposed by a committee consisting of Christos Bartsocas, Charles Buys, Marco Fraccaro, Peter Harper, Jan Mohr, Anne de Paepe and Eberhard Passarge) were approved and implemented in 1991 at the Leuven meeting where one of us (GR) took office as the first democratically elected ESHG President and went on to found the EJHG the following year. We have placed so much emphasis on the ESGM courses because we believe that the reform and expansion of the Society became possible in part through these courses, which enabled so many people to become acquainted with each other, breaking down national, regional and linguistic barriers.

Initially Jan Mohr, the founding secretary-general, contacted one of us (EP) in 1987 and suggested that he should take over as secretary-general in due time. Such a change appeared to be a good opportunity to make the ESHG more democratic and inclusive by electing a board (president, president-elect, secretary-general) and a programme committee. Sup-ported by Peter Harper at the 1988 Cardiff meeting, the newly elected board took office in 1989 at the meeting in Groningen organised by Charles Buys (once again described by Peter Harper). All this happened at a time when Europe was going through great political changes—namely the fall of the Berlin Wall in November 1989, which led to the unification of East and West Germany in 1990, and the signing of major European treaties, such as Maastricht in 1993. It was a time of great enthusiasm and popular approval for the idea of building the European Union (EU) and implementing reforms, which for the first time in our history were being accomplished through peace and diplomacy.

In this climate of changes our small community of scientists was transformed into a democratic society of medical and clinical geneticists. We sometimes ask ourselves: was this achievement worth the time and effort invested in it? Among other indicators which can be used to answer this question, there is a simple observation based on the breakdown of students attending the main ESGM course in 1988 versus 2017 (Figures 1 and 4 respectively). This comparison docu-ments the success of ESHG in supporting programmes of advanced training in medical and clinical genetics that today are no longer limited to Europe but attract young geneticists from all over the world. This is a tangible result which shows that the reformed ESHG is having a tremendous impact on the practice and research in medical genetics far beyond Europe. The spirit that animated the European School of Genetic Medicine since its early days in Sestri Levante probably imprinted many young geneticists like Brunhilde Wirth (a student in the course of 1988; Figure 2) and Han Brunner (a young faculty member since the early '90s) who later became the driving force of the main ESGM course.

In conclusion, the reform of ESHG was useful, as evidenced by the universal acceptance and recognition of the Society's role in medicine and genetics. The success of the ESHG today is also shown by its excellent annual meetings under the guidance of its programme committee, and by its Journal that serves to unite geneticists from all over Europe and to let the rest of the world know what is happening in Europe. The three authors of this review were actively involved in the transformation of the ESHG from a somewhat loosely organized association to a well-organised scientific society in the late 1980s and early 1990s. AdlC and GR served as presidents during that period, EP as secretary-general, all elected by the membership assembly at annual meetings. During his Presidency GR founded the Journal, which he directed until 1995.

Istituto S Internatio Pediatric	cientifico nal School ^S Spillofihē	G.Gaslini of SestfilLevante scho	FEBS (Fe Biochem	deration of European cal Societies)
	EUR	OPEAN GOROMEODET	ALEDICAL GENETICS 7, April 6-12 1988 AM	5
<u>WEDNESDAY</u> 8.30-12.30	5 V.A.McKu introduc A.M. Fri G.Romeo A.Cao phenotyp S.Ottole beta-tha gene exp J.Ott (No	sick (Baltimor tion to principl (Genoa): DNA pol (Cagliari): BN a-genotype relat adhi (Milano): lassemias and i ression.	e): History of Me es of human geneti Introduction to m ymorphisms and dis eta-thalassemias: ionship and detect Molecular mechan nherited abnormali uction to analysis	dical Genetics: an cs wolecular genetics ease molecular basis, ion isms of defects in ties of gamma-globin of genetic linkage
18-18.30: 18.30-20: 5	 Workshop computer in Man, of these Questions T.Caskey Devroped 	1: pedigree an ized programs (L Possum, London programs will co from students (Houston): Lo	nalysis and risk c inkage, OnLine Me Dysmorphology Data ontinue throughout esch-Nyhan diseas	alculation. Use of ndelian Inheritance base): demonstration the course. e: molecular basis,
<u>THURSDAY</u> 7 8.30-12.30 4 15-17.30: 18-18.30: 18.30-20: 4	M.Fergusc mutations <u>6 C.Junien</u> and acqui <u>4 M.Rocchi</u> mapping >Workshop Questions <u>6 A. de la</u> Clinical, determina	<u>cccola</u> (Rome): Me <u>n-Smith</u> (Cambring (Paris): Molecu red chromosomal (Genoa): Cyto 2: Clinical cyto from students <u>Chapelle</u> (Helsin cytogenetic tion	athods of cytogene idge): From chrom lar characterizati rearrangements ogenetic methods ogenetics hki) and <u>M.Ferguso</u> and molecular	tic analysis osomal to molecular on of constitutional for physical gene <u>n-Smith</u> (Cambridge): aspects of sex
FRIDAY 8 8.30-12.30: 41 15-17.30: 18-18.30: 18.30-20: 1	Session A.Piazza M.Baur (B M.Sarfara mendelian G.Romeo (Workshop Questions R.Norio (on population g (Turin): Princ onn): Linkage Di Zi (Cardiff): disorders Genca): Consangu 3: problem solvi from students Helsinki): The F	enetics coordinate iples of populatic sequilibrium Risk calculation inity and disease ng session on popu innish disease her	ed by <u>R.Ceppellini</u> on genetics for recurrence of in Italy ulation genetics
<u>SATURDAY</u> 9 S.30-12.30: 45 20 21 22 Afternoon:	Session of <u>M.Baur</u> reconstru <u>V.A.McKus</u> J.Mohr (C <u>M.Sarfara</u> <u>H.H.Roper</u> strategie Trip to condition	n linkage coordi (Bonn): Comp ction <u>ick</u> (Baltimore): openhagen): Some zi (Cardiff): Ex <u>s</u> (Nijmegen): M s Portofino (by s)	nated by <u>J.Ott</u> (N outerized prograu The human genome e highlights of lin clusion mapping Mapping of X-linked boat or bus dep	ew York) n for haplotype (status of the map) nkage studies in man d genes and research pending on weather
SUNDAY 10 8.30-12.30: 24 25 26 15-17.30: 18-18.30: 18.30-20: 2: 21	A.M.Frisc M.Bobrow H.H.Roper G.Romeo (Barcelor Workshop Questions G.Andria Smith (C sulphatas	<u>hauf</u> (London): T (London): Ducher <u>5</u> (Nijmegen): My (Genoa), <u>J.Mc</u> a): Review on cy 4: Molecular ger from students (Catanzaro), <u>A</u> ambridge): Mole e deficiency in	The methods of revo ine muscular dystro otonic dystrophy <u>hr</u> (Copenhagen) stic fibrosis reso letics (I) <u>Ballabio</u> (Naples icular and clinica man	arse genetics ophy and <u>X.Estivill</u> earch), and <u>M.Ferguson-</u> 1 aspects of steroid
MONDAY 11 8.30-12.30 3 3 3 15-17.30 18-18.30 18.30-20 3	9 <u>K.Berg</u> risk fact <u>G.Uterman</u> populatic multifact <u>G.Bianchi</u> models 2 <u>R.B.Barbe</u> rats 3 <u>A.Sidoli</u> hypertens Workshop Questions <u>T.Caskey</u>	(Oslo): Genetic ors n (Innsbruck n variance of orial hyperlipid (Milan): Essent r (Milan): Sel (Milan): Disli ion: molecular as 5: Molecular gen from students (Houston): Gene	s of coronary hear quantitative lipo lemia ial hypertension ection and breedin poproteinemias, a malysis of multifi etics (II) Therapy	rt disease and its cributing to the protein traits and in man and in animal ng of hypertensive atherosclerosis and actorial diseases
TUESDAY 12 8.30-12.30: 31 31 31 31 31 31 31 31	Session o <u>M.Cordone</u> <u>P.Durand</u> J.C.Kapla analysis <u>M.Pembrey</u> DNA analy Panel dis	n prenatal diagn (Genoa): Ob-Gyn (Genoa): Biochem <u>n</u> (Paris): Str (London): Pract sis and the asso cussion on genet	osis coordinated H togenetics tical Genetics ategies of prenata tical aspects of pr ciated counselling tic counselling and	by <u>J.C.Kaplan</u> al diagnosis by DNA renatal diagnosis by g prenatal diagnosis
15-17.30: 44 18-18.30: 18.30-20: 44	R.Norio diagnosti Workshop Questions G.Bernard	(Helsinki): c aid in clinica 6: Review of pro from students i (Paris): The o	Use of a manua [:] 1 genetics blems <u>r</u> ganization of the	data bank as a human genome

Figure 3

 $\frac{\text{WEDNESDAY}}{\text{Optional guided excursion to the Cinque Terre (by boat or train + walking)}}{10}$



Figure 4



Giovanni Romeo

Professor of Medical Genetics at University of Bologna Medical School (2001-2012). Degree in Medicine (1965); Internship & Residency in Paediatrics, University of Bologna Medical School (1965-1967); Research Fellow, Genetics Division, Department. of Pediatrics, Johns Hopkins Medical School, Baltimore, Md. (1968-1971).

Medical geneticist with a wide international research experience documented by his leadership role during the past 30 years in different Institutions: Genova (Istituto G Gaslini), Lyon (International agency for Research on Cancer) and Bologna Medical School. Major research interests: Hirschsprung disease, RET protooncogene, consanguinity studies and genetic epidemiology, mtDNA mutations in cancer. He has published more than 380 papers in peer-reviewed international journals.

In collaboration with the late Prof. Victor McKusick in 1988 he founded the European School of Genetic Medicine, now located in Bertinoro, Italy, attended so far by more than 7000 students and devoted to the advanced training in genetics and genomics of young geneticists and health professionals from Europe and elsewhere in the world.

In 1992 he became the first democratically elected President of the European Society of Human Genetics (ESHG) and founded the European Journal of Human Genetics which he directed up to 1995.

Among other prizes, he was awarded the ESHG Educational Award in 2005 and the Arno Motulsky-Barton Child Award for Excellence in Human Genetics Education in 2011 by the American Society of Human Genetics. During the past 15 years he developed several research and educational projects in Oman.

S10



Eberhard Passarge, MD (1935), is a US-trained German human geneticist at the Medical Faculty Essen of the University of Duisburg-Essen, Germany. He became a founding member of the ESHG after attending the discussion of forming a European Society of Human Genetics at the Third International Congress of Human Genetics 1966 in Chicago. He served as secretary-general of the ESHG 1989-1991. He was host of the annual meeting of the ESHG in Essen in 1984 on 'Cancer and Genetics'.

He graduated as MD at the University of Freiburg (1960), had postgraduate training in Hamburg and Worchester (MA), specialized in Paediatrics and Genetics in Children's Hospital Cincinnati, Ohio and Cornell Medical Center New York. He was Head of the Division of Cytogenetics and Clinical Genetics at the Department of Human Genetics, University of Hamburg, Germany, 1968-1976, and moved to Essen in 1976. From 2010-2014 he was Intermediary Chairman, Department of Human Genetics, University of Leipzig, Germany.

His main interests are the scientific investigation of hereditary and congenital diseases and the application of this knowledge in genetic diagnosis and counseling. He is author or co-author of about 250 articles in international, peer-reviewed journals. His experience in academic teaching is reflected in his single author book Color Atlas of Genetics, its 5th edition in press, to be published by Thieme Medical Publishers Stuttgart-New York, in 2018.

EP was President of the German Society of Human Genetics 1990-1996, of which he became an honorary member in 2011. He is music coordinator at the University of Duisburg-Essen where he organizes the annual festive university concert. He was elected to be an honorary member of the university senate in 2016. He was awarded prizes from scientific institutions in Germany, Romania, Czech Republic, and India.

(Institute of Human Genetics, Emeritus Director, University Hospital Essen, Hufelandstr. 52, 45122 Essen, Germany)



Albert de la Chapelle is a Distinguished University Professor and Cancer Scholar at The Ohio State University. He received his MD in 1957 and PhD in Human Genetics in 1962 at the University of Helsinki. He received board certification in Internal Medicine but soon left clinical medicine for genetics. He became Finland's first Professor of Medical Genetics in 1974 and remained at that position until 1997 when he moved to The Ohio State University to start a program in Human Cancer Genetics. In the European Society of Human Genetics he served as a Board member 1966-1995, Chairman of the Aims and Statutes Committee 1990-1991, and President 1993-1994. His major honors include: Memberships in the Academy of Finland, the Royal Swedish Academy of Sciences and the US National Academy of Sciences. Dr de la Chapelle started as a cytogeneticist specializing in mechanisms of sex determination. He then turned to molecular genetics, pioneering the mapping and cloning of those Mendelian disorders that are enriched in the Finnish founder population, clarifying the molecular basis of over a dozen of these disorders. He is best known for his role in determining the molecular basis of hereditary cancer, notably the role of the mismatch repair genes in Lynch syndrome. He detected the phenomenon of microsatellite instability in hereditary cancer. He has pioneered the translation of these molecular events into clinical work and cancer prevention. Presently his laboratory is heavily committed to the study of the genetics of thyroid cancer.

Cytogenetics: current status and future perspectives

Júlia Baptista

Department of Molecular Genetics, Royal Devon and Exeter NHS Foundation Trusts and University of Exeter Medical School, Exeter, UK

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 subset of genes or in the entire 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. The availability of datasets from normal populations such as ExAC and gnomAD and of clinically affected patients such as ClinVar, are key to help us interpret the variants identified.

Future perspectives

The field of Human Genetics has greatly benefited 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, especially by array CGH and NGS assays. This is more so as the NHS sets itself to move to the mainstreaming

of genomics. 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

Clinical Genetics Department Guy's & St Thomas' NHS Foundation Trust London UK

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.

The Genetic Laboratory: instructional book

M. Iascone

Medical Genetics Laboratory, AO Papa Giovanni XXIII, Bergamo, Italy

Technological advances in genetics had signed the pace of progress in our ability to diagnose genetic diseases. Molecular genetic tests usually studied single genes or short lengths of DNA to identify variations or mutations leading to a genetic disorder. Now this approach is changed due to the recent introduction of new sequencing technology in clinical practice. The lesson will focus on the impact of these new technologies on the work, organization and skills of genetic labs.

Basic concepts on dysmorphology

F. Forzano

Clinical Genetics Department Guy's & St Thomas' NHS Foundation Trust London UK

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

Aims Processes and Outcomes of Genetic Counselling

C. Patch

Genomics England London UK, and Faculty of Nursing, Midwifery & Palliative Care, King's College London, UK

Z. Bruwer

Genetic and Developmental Medicine Clinic, Sultan Qaboos University Hospital, Oman

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 includes medical information, accepted definitions of genetic counselling also emphasise the educative and counselling components. Advances in the science related to genomic medicine also raises questions about what is genetic counselling and how our existing models fit with the knowledge genereted through the scientific developments. 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).

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 this session we will introduce the framework of genetic counselling and put it into context with the aims of this course starting with agenda setting for counsellor and client

Resources

Eurogentest Recommendations for genetic counselling related to genetic testing.

http://www.eurogentest.org/index.php?id=673 (accessed 1st April 2018).

Middleton A, Hall G, Patch C Genetic Counselors and Genomic Counselling in the United Kingdom Molecular Genetics & Genomic Medicine 2015 3(2) p 79–83

Veach PA, LeRoy BS, Bartels DM 2003. Structuring the genetic counseling session: Initiating, contracting, ending and referral. In Facilitating the genetic counseling process. A Practice Manual. New York, NY: Springer p 93-97

Saturday, April 21

Cancer genetics: scenarios and issues

D. Turchetti

Univ. of Bologna, 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.

References:

- Offit K.: Clinical Cancer Genetics. Risk Counselling and Management, Wiley-Liss 1998
- Genetic Cancer Risk Assessment and Counseling: Recommendations of the National Society of Genetic Counselors Journal of Genetic Counseling, Vol. 13, No. 2, April 2004
- http://www.nci.nih.gov/cancerinfo/pdq/genetics/overview
- http://www.nci.nih.gov/cancerinfo/pdq/genetics/risk-assessment-and-counseling
- Robson. M. and Offit. K.: Management of an inherited predisposition to breast cancer. N Engl J Med 2007; 357:154-62
- Hendriks YMC et al.: Diagnostic approach and management of Lynch Syndrome (Hereditary Nonpolyposis Colorectal Carcinoma): A Guide for Clinicians. CA Cancer J Clin 2006; 56: 213-225
- Stadler ZK et al: Cancer Genomics and Inherited Risk. J Clin Oncol 2014; 32: 687-698.

Prenatal diagnosis: scenarios and issues

F. Forzano

Clinical Genetics Department Guy's & St Thomas' NHS Foundation Trust London UK

All the couples face a 3% risk of having children with congenital anomalies. Prenatal screening refers to different kind of testing offered during pregnancy, which include a combination of US scans, metabolites dosage and fetal DNA analysis on maternal blood, aimed to investigate a portion of this risk, primarily related to the more frequent chromosome aneuploidies, as trisomy 21, and malformations, as neural tube defects.

Prenatal diagnosis refers to testing offered to selected couples who are at risk of specific disorders, or to pregnancies identified at high risk through prenatal screening.

The aim of prenatal screening and diagnosis is to identify fetal anomalies in order to drive the management of the pregnancy and to allow the parents to make autonomous reproductive choices.

Parental personal views and feelings, cultural and ethical issues, time constraint and uncertainties on prognosis make this setting particularly challenging.

The explosion of available techniques of genome analysis is now opening up new scenarios in which a thorough fetal genome could be prenatally investigated, thus enriching the debate on which the scope of prenatal testing should be as well as the ethical issues implicated.

Practical ethics - consent, confidentiality and disclosure

C. Patch

Genomics England London UK, and Faculty of Nursing, Midwifery & Palliative Care, King's College London, UK

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

Traditional models of consent may need to be reviewed given the uncertainties and open-endedness of genomic medicine. It may be impossible to gain valid consent if full understanding of the details surrounding what findings may be returned, storage and use of data is required. In addition it is not possible to give assurances about the unknwn uses of information in the future. Broad consent has been suggested as a model going forward in the development of a genomic medicine service in the UK based on learning from the 100,000 genome project. It is suggested that this involves '*entering a relationship with agreed ground rules about mutual responsibilities and rights*'.

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 minimises 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.

However a very strict interpretation of confidentiality could affect patients adversely depriving them of information taht may affect there own health care. In adition thesharing of limited patient inofrmation is necessary for variat intrepretation. These are current chalnegs to our previous understandings of confidentiality. As more information is stored centrally it may be that clinicians have access to familial information without any breach of confidence.

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 <u>https://www.acmg.net</u>

Davies S, C. Annual Report of the Chief Medical Officer 2016, Generation Genome. London: Department of Health, 2017

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/631043/CMO_annual_report_generation_genome.pdf (accessed 1st April 2018)

Joint Committee on Medical Genetics Consent and confidentiality in genetic practice: Guidance on genetictesting and sharing genetic information. A report of the Joint Committee on Medical Genetics 2nd edition2011(accessed1stApril2018)http://www.bsgm.org.uk/media/678746/consent and confidentiality 2011.pdf

Background document for revision of guidance: consent and confidentiality in clinical genetic practice. <u>http://www.bsgm.org.uk/media/1075617/background_document_to_consent_and_confidentiality_revision</u> <u>1_.pdf</u> (accessed 1st April 2018)

Kalia SS, Adelman K, Bale SJ et al. Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics. Genet Med 2017; 19: 249-255

Middleton A, Marks P, Bruce A et al. The role of genetic counsellors in genomic healthcare in the United Kingdom: a statement by the Association of Genetic Nurses and Counsellors. European Journal of Human Genetics 2017; 25: 659-661

Middleton A et al Position statement on opportunistic genomic screening from the Association of Genetic Nurses and Counsellors (UK and Ireland) (2014) Eur J Hum Genet. 2014 Jan 8. doi: 10.1038/ejhg.2013.301

Skirton H, Patch C and Williams J (2005) Applied Genetics in Health Care. Taylor Francis. Abingdon 2005

Sunday, April 22

Introduction to the course and Revision of basic Patient-Centered counselling skills

A. Tibben

Dept of Clinical Genetics, LUMC, Leiden, the Netherlands

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 f 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 had 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 an 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 helpful 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

On 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 'golden standard' for the personcentred counsellor is the ability to hold every person in unconditional regard. Whilst this itself a challenge, it helps to reduce value judgements of the client and therefore increases the likelihood that the client will free to make the decision that is best for them.

Basic counselling skills that we will discuss and practice are:

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

Monday, April 23

Counselling for predictive testing

A. Tibben

Dept of Clinical Genetics, LUMC, Leiden, the Netherlands

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 atrisk 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.

- American Society of Human Genetics, A. H. C. o. G. C. (1975). "Genetic counseling." <u>American Journal of</u> <u>Human Genetics</u> 27: 240-242.
- Baker, D. L., J. L. Schuette, et al., Eds. (1998). A guide to genetic counseling. New York, Wiley-Liss, Inc
- Djurdjinovic, L. (1998). Psychosocial counseling. <u>A guide to genetic counseling</u>. D. L. Baker, J. L. Schuette and W. R. Uhlmann. New York, Wiley-Liss: 127-170.
- Kessler, S., H. Kessler, et al. (1984). "Psychological aspects of genetic counseling. III. Management of guilt and shame." <u>Am J Med Genet</u> **17**(3): 673-97.
- Martindale, B. (1987). "Huntington's chorea: some psychodynamics seen in those at risk and in the responses of the helping professions." <u>Br J Psychiatry</u> **150**: 319-23.
- Platt-Walker, A. (1998). The practice of genetic counseling. <u>A guide to genetic counseling</u>. D. L. Baker, J. L. Schuette and W. R. Uhlmann. New York, Wiley-Liss: 1-26.

Breaking the news: theory

A Tibben

Dept of Clinical Genetics, LUMC, Leiden, the Netherlands

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.

Family dynamics: theory and awareness

E. Razzaboni

AO Modena, Italy

Genetic disease affects entire families, not just individual members. Although only some family members may receive genetic information directly from health service, genetic involves the whole family system. From a medical perspective we pay attention to the whole family

Family Dynamic is a broad term used to describe the patterns in which members of a family unit interact with each other. The concept of family dynamics is of interest for those working in genetic counseling services. The concept suggests that there is a set of behaviors indicative of healthy and unhealthy family dynamics. Family dynamics may have triggered the request for genetic counseling/testing. Insight into family dynamics may enhance understanding of the client's motives and resources. Family dynamics may have strong impact on coping with counseling and test outcomes. Insight into family dynamics may enable to provide tailored support and - if necessary – referral.

Usually we assume that the genetic information is true and that person understands the information and believes it to be true, but, this assumption fails to consider that the fact that families have their own social reality, which might be less influenced by objective medical fact than by internal family processes and relationship.

In families, shared understanding is affected by:

- 1. the degree of openness and frequency of communication (conversation orientation)
- 2. the extent to which authority shapes meaning (conformity orientation).

The resulting family communication patterns affect interactions with health-care practitioners, as well as, many family processes.

Insight to these patterns can lead to strategy to work more effectively with different family types.

Reference:

Clara L. Gaff and Carma L. Bylund (2010). "Family Communication about Genetics. Theory and Practice". Oxford University Press

Tuesday, April 24

Genetic testing in children (recommendations, legal frameworks and specific counselling issues)

C. Patch

Genomics England London UK, and Faculty of Nursing, Midwifery & Palliative Care, King's College London, London UK

The necessity of screening and testing children at risk brings along its own sensitivities. Parents naturally wish 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 overshadowed 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.

The general opinion among professionals is that testing for serious adult-onset disorders holds potential for harm. Testing may 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.

This opinion is reflected in professional guidelines and has led to much debate amongst the professional and patient/family community. However the situation regarding carrier testing or testing for diseases with onset during childhood is more nuanced and most genetic counselling services would aim to work with parents to reach a decision in the best interests of the child and family as regards genetic counselling.

A family life overshadowed by the risk of a hereditary disease will obviously influence the way parents perform their parental tasks. 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 family stories and 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. Genetic counsellors can aid the family in communication of the information in an age and developmentally appropriate way Such work might increase the cohesion in the family and lead to new, constructive, and creative ways to deal with the disease.

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 made against the personal and family history and future. The decision must be understood as part of the entire family and individual coping mechanisms regarding the risks and the disease.

BBC Radio 4 Inside the ethics committee Genetic testing in children http://www.bbc.co.uk/programmes/b038hhs7

BSHG Report on the genetic testing of Children http://www.bsgm.org.uk/media/678741/gtoc_booklet_final_new.pdf (accessed 12th April 2016)

Ross et al. ACMG Policy Statement Technical report: ethical and policy issues in genetic testing and screening of children. Genetics in Medicine(2013): 15,P 234–245.

Grief and loss experimental exercises

A. Tibben

Dept of Clinical Genetics, LUMC, Leiden, the Netherlands

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 a few.

Worden (2000) wrote of four tasks of mourning:

Task 1: to accept the reality of loss

Task 2: to work through the pain of grief

Task 3: to adjust to a new environment

Task 4: 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 backed 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.

Grief and loss experimental exercises

All faculty

Advances in technology increasingly facilitate parental choice with regard to prenatal diagnosis (PND); however, there are many ethical, legal, and social and psychological issues related to the clinical offer of prenatal screening and testing that require consideration. As with other medical procedures, enabling the parents to make an informed choice is integral to good clinical care; however, this can be challenging because of the understandable reluctance of parents to anticipate an abnormality in the fetus and the unpredictable nature of their reaction to the results. Beliefs and values relate to cultural norms, and women from dissimilar cultural backgrounds may show varied psychological responses and attitudes towards information and prenatal counselling. Considering the complexity of the matter, psychological issues will be examined to guarantee adequate counselling.

Cross cultural issues Z. Bruwer

Genetic and Development Medicine clinic. Sultan Qaboos University Hospital, Muscat, Oman.

Culture is a general term that can describe beliefs, values, custom, social interaction, life interactions and geography shared by a group of people. It reflects the ethnic, historic and linguistic categorization. In genetic counselling, psychosocial, beliefs and morals behind a decision making is usually addressed. It is essential that the counsellor has a cultural awareness to create a cross cultural competence in counselling.

Genetic counselling practice in a highly inbreeding society with consanguineous marriage preference should have an understanding about the cultural beliefs and motives towards consanguinity.

Sultanate of Oman is one of the Middle Eastern countries that has a high rate of consanguinity. The service of genetic counselling is fairly new and is provided with two governmental genetic centers available in the country. To adopt the service within context of culturally driven marriage preferences for cousins, premarital genetic counselling service is provided. It serves a role in enhancing the families' awareness towards prevention of recurrence of a familial genetic disorder. However, challenges exist due to the heterogeneity of the culture and limitations of resources. Creating self-awareness about ethnocultural of the counsellee empowers the counsellor to increase interactive competence for different cultures.

References

HAMAMY, H., 2012. Consanguineous marriages: Preconception consultation in primary health care settings. *Journal of Community Genetics*, 20111122, Jul, vol. 3, no. 3, pp. 185-192 ISSN 1868-6001; 1868-310X.

HAMAMY, H., ANTONARAKIS, S.E., CAVALLI-SFORZA, L.L., TEMTAMY, S., ROMEO, G., KATE, L.P., BENNETT, R.L., SHAW, A., MEGARBANE, A., VAN DUIJN, C., BATHIJA, H., FOKSTUEN, S., ENGEL, E., ZLOTOGORA, J., DERMITZAKIS, E., BOTTANI, A., DAHOUN, S., MORRIS, M.A., ARSENAULT, S., AGLAN, M.S., AJAZ, M., ALKALAMCHI, A., ALNAQEB, D., ALWASIYAH, M.K., ANWER, N., AWWAD, R., BONNEFIN, M., CORRY, P., GWANMESIA, L., KARBANI, G.A., MOSTAFAVI, M., PIPPUCCI, T., RANZA-BOSCARDIN, E., REVERSADE, B., SHARIF, S.M., TEEUW, M.E. and BITTLES, A.H., 2011. Consanguineous marriages, pearls and perils: Geneva International Consanguinity Workshop Report. *Genetics in Medicine : Official Journal of the American College of Medical Genetics*, Sep, vol. 13, no. 9, pp. 841-847 ISSN 1530-0366; 1098-3600.

MODELL, B. and DARR, A., 2002. Science and society: genetic counselling and customary consanguineous marriage. *Nature Reviews. Genetics*, Mar, vol. 3, no. 3, pp. 225-229 ISSN 1471-0056; 1471-0056.

TADMOURI, G.O., NAIR, P., OBEID, T., AL ALI, M.T., AL KHAJA, N. and HAMAMY, H.A., 2009. Consanguinity and reproductive health among Arabs. *Reproductive Health*, vol. 6, no. 1, pp. 17-17 ISSN 1742-4755; 1011-8617.

TEEUW, M.E., LOUKILI, G., BARTELS, E.A., TEN KATE, L.P., CORNEL, M.C. and HENNEMAN, L., 2014. Consanguineous marriage and reproductive risk: attitudes and understanding of ethnic groups practising consanguinity in Western society. *European Journal of Human Genetics: EJHG*, 20130807, Apr, vol. 22, no. 4, pp. 452-457 ISSN 1476-5438; 1018-4813.

TEN KATE, L.P., TEEUW, M.E., HENNEMAN, L. and CORNEL, M.C., 2014. Consanguinity and endogamy in the Netherlands: demographic and medical genetic aspects. *Human Heredity*, 20140729, vol. 77, no. 1-4, pp. 161-166 ISSN 1423-0062; 0001-5652.

WEIL, J., 2000. Psychosocial Genetic Counseling. Oxford University Press, USA.

FACULTY Who is Who

Family Name Name		Affiliation	E-MAIL
BAPTISTA JULIA		Department of Molecular Genetics, Royal Devon and Exeter NHS Foundation Trusts and University of Exeter Medical School, Exter, UK	juliacpb@gmail.com
BRUWER ZANDRE		Genetic and Developmental Medicine clinic/ Sultan Qaboos University Hospital, Muscat, Oman.	zandrebruwer@gmail.com
FORZANO FRANCESCA Loi		Clinical Genetics Department Guy's & St Thomas' NHS Foundation Trust London UK	<u>francesca.forzano@nhs.net</u>
IASCONE	MARIA	Medical Genetics Laboratory, AO Papa Giovanni XXIII, Bergamo, Italy	miascone@hpg23.it
PATCH CHRISTINE		Genomics England London UK, and Faculty of Nursing, Midwifery & Palliative Care, King's College London, UK	<u>Christine.patch@kcl.ac.uk</u>
RAZZABONI	ELISABETTA	AO Modena, Italy	<u>elisabetta.razzaboni@gmail.com</u>
ROMEO	GIOVANNI	European Schoool of Genetic Medicine & Alma Mater Studiorum Università di Bologna, Italy	egf.giovanni.romeo@gmail.com
TIBBEN	AAD	Dept of Clinical Genetics, LUMC, Leiden, the Netherlands	a.tibben@lumc.nl
TURCHETTI	DANIELA	Univ. of Bologna, Policlinico S. Orsola-Malpighi, Bologna, Italy	daniela.turchetti@unibo.it

PARTICIPANTS Who is Who

	FAMILY NAME	NAME	AFFILIATION	СІТҮ	NATION.	E-MAIL
1	AL BADER	SALHA	НМС	DOHA	QATAR	sbujassoum@hamad.ga
2	ALSULAIMAN	REEM	HAMAD MEDICAL CORPORATION	DOHA	QATAR	ralsulaiman@gm.slc.edu
3	BAHEER	SAJA	CHILDREN WELFARE TEACHING HOSPITAL	BAGHDAD	IRAQ	saja.baheer@yahoo.com
4	BERTONAZZI	BENEDETTA	SANT'ORSOLA MALPIGHI HOSPITAL	BOLOGNA	ITALY	benedetta.bertonazzi@aosp.bo.it
5	BUGREIN	НЕКМЕТ		DOHA	QATAR	h.bugrein@yahoo.com
6	CIANFLONE	ANNALIA	UNIV. OF GENOVA	GENOVA	ITALY	annalia.cianflone@gmail.com
7	CRUZ DELGADO	MIKAELA	KAROLINSKA UNIVERSITY HOSPITAL	STOCKHO LM	SWEDEN	irka.cruz-delgado@sll.se
8	EHN	ΕΜΜΑ	KAROLINSKA UNIVERSITY HOSPITAL	STOCKHO LM	SWEDEN	emmaehn87@gmail.com
9	ENGLUND	KATARINA	UNIV. HOSP. OF UMEA	UMEA	SWEDEN	katarina.englund@vll.se
10	FARHANGNIYA	MANSOUREH	IRANIAN BIOLOGICAL RESOURCE CENTER IBRC	TEHRAN	IRAN	mfarhangniya@yahoo.com
11	FRANČIĆ	KLARA	UNIV. OF RIJEKA	ZAGREB	CROATIA	klara.francic@gmail.com
12	IUHAS	OANA ALEXANDRA	THE REGIONAL CENTRE OF MEDICAL GENETICS ORADEA & CLINICAL MUNICIPAL HOSPITAL	BUCAREST	ROMANIA	bogdan.pantelimon@jinfotours.ro
13	KLINTENSTEDT	JENNY	REGION OSTERGOTLAND REDOVISNINGEN	LINKOPIN G	SWEDEN	jenny.klintenstedt@regionostergotland.se
14	KOMDEUR	FENNE	VUMC	AMSTERD AM	THE NETHERLANDS	f.komdeur@vumc.nl
15	KRAUS	SARAH	UNIV. OF CAPETOWN	CAPETOW N	UK - SOUTH AFRICA	<u>S.kraus@uct.ac.za</u>
16	LOUIZOU	EIRINI	BIOIATRIKI S.A	ATHENS	GREECE	louizoueirini1978@gmail.com

	FAMILY NAME	NAME	AFFILIATION	СІТҮ	NATION.	E-MAIL
17	OPREA	LUCIAN	MD COMMUNITY CARE CENTER	IMPERIAL	USA	lucian_oprea2006@yahoo.com
18	ORRE	ANNIKA	FOLKHALSAN VALFARD AB	VASA	FINLAND	annika.orre@folkhalsan.fi
19	PACHECO	NADJA PEKKOLA	KAROLINSKA UNIVERSITY HOSPITAL	STOCKHO LM	SWEDEN	nadja.pekkola-pacheco@sll.se
20	PARDO	MONICA	UNIV. OF BARCELONA	BARCELO NA	SPAIN	monica_pardo@hotmail.com
21	PAVLOVA	ZORNITSA	IMDL GENOME CENTER BULGARIA	SOFIA	BULGARIA	blackwingedone@abv.bg
22	PELLE	ALESSANDRA	UNIV. OF TOURIN, AOU SAN LUIGI GONZAGA	TURIN	ITALY	alessandraelisapelle@gmail.com
23	PERON	ANGELA	UNIV. OF MILAN	MILAN	ITALY	angela.peron@unimi.it
24	PINTARELLI	GIULIA	FONDAZIONE IRCCS	MILAN	ITALY	giulia.pintarelli@istitutotumori.mi.it
25	REEM	SALAH ELDIN	UNIV. OF KHARTOUM	KHARTOU M	SUDAN	Reem-salah-uok@outlook.com
26	ROWE	CHARLOTTE ALISA	UNIV. OF EXETER	EXETER	υк	charlottealisarowe@gmail.com
27	SANDESTIG	ANNA	REGION OSTERGOTLAND REDOVISNINGEN	LINKOPIN G	SWEDEN	anna.sandestig@regionostergotland.se
28	SCHWARZ	MARTIN	CHARLES UNIVERSITY	PRAGUE	CZECH REP.	nezzmar@gmail.com
29	STRODE	AIJA	RIGA STRADINS UNIVERSITY	RIGA	LATVIA	aija992@inbox.lv
30	TESI	BIANCA	KAROLINSKA UNIVERSITY HOSPITAL	ENSKEDE DALEN	SWEDEN	bianca.tesi@sll.se
31	TINCHEVA	SAVINA	IMDL GENOME CENTER BULGARIA	SOFIA	BULGARIA	savina.tincheva@gmail.com
32	TREVISAN	LUCIA	OSP. POLICLINICO SAN MARTINO	GENOVA	ITALY	lucy.a.trevisan@gmail.com
33	VIGGIANO	EMANUELA	AULSS 6	PADOVA	ITALY	emanuela.viggiano@aulss6.veneto.it
34	VINBERG	JOHANNA	KAROLINSKA UNIVERSITY HOSPITAL	STOCKHO LM	SWEDEN	johanna.winberg@ki.se
35	WILDERO - VAN WOUWE	LIESBETH	GHENT UNIVERSITY HOSPITAL	ZOTTEGE M	BELGIO	liesbeth.wildero-vanwouwe@uzgent.be