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PERSPECTIVE

Dysmorphology and the ESHG

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The great advantage of the ESHG is that it is a broad church. Although for many years we fell into several distinct tribes, such as clinicians, cytogeneticists, molecular geneticists, counsellors, population geneticists, it is now apparent that for advances to occur, we all need to be part of 'the same family' working together and respecting each other's expertise. Although in some countries clinicians who specialise in dysmorphology see it as a subspecialty of paediatrics, most European countries regard dysmorphology as a specialty within genetic medicine, albeit often with a foot in the paediatric camp.

I came to genetics from paediatrics in 1977 when genetics was not a recognised medical specialty in the UK. I was stimulated to do so having been fascinated by patients with various syndromes I had seen on the wards. The prevailing view was that nothing could be done to prevent the problems in these children but I was struck by how little was known about the causes and how little information and support were available to these families. I responded to an advertisement 'married woman required part-time for two clinical assistant sessions in genetics' and realised that this was the specialty for me! In time, I was appointed to one of the first three training posts in genetics in the UK. I memorised the first edition of Smith's *Recognizable Patterns of Human Malformations* and tried to find others within the Clinical Genetics Society who shared my interests, such as Robin Winter and Michael Baraitser from Great Ormond Street Hospital in London. They started a half-day meeting for case presentations in 1980 http://www.histmodbiomed.org/sites/default/files/44869.pdf (pages 63–68).

Gradually an informal network built up with colleagues from UK, and we made contacts with colleagues with similar interests in France, the Netherlands, Scandinavia, Italy, Switzerland and Germany. As we all travelled, this network widened to include Eastern European countries and I remember a terrific session with great cases in Warsaw in the mid-1980s. Many of us attended the David W Smith Workshops on Malformations and Morphogenesis in the United States (founded in 1980) and formal conference series were also founded in Europe, such as the EuroDysmo meeting organised by Jean-Pierre Fryns and Claude Stoll in the Bischenberg Conference Centre near Strasbourg, although their first meeting was in Zaragossa, Spain (in collaboration with the French Club Européen de Conseil). I started the biennial Manchester Dysmorphology Conference series in 1984, later organised together with Jill Clayton-Smith and now also with Sofia Douzgou and Siddharth Banka. The informal network of dysmorphologists in Europe has been enormously productive for the delineation of rare dysmorphic disorders. I remember excellent presentations at ESHG and ASHG Conferences from multiple collaborating European authors on 'A clinical and molecular study of (…) syndrome', where the phenotypes and natural history of many disorders were established by the study of large cohorts and presenting either linkage data, recurrent microdeletions or chromosomal clues to gene location, and which later formed the basis for gene discovery.

ORIGINS OF THE DYSMORPHOLOGY WORKSHOPS AT THE ESHG CONFERENCES

Members of our informal network met up at European Society of Human Genetics conferences and stood in corners staring up at a light source with 35 mm slides or going through photographic prints. Others used to gather round and then bring cases for discussion the next day. I seem to remember we had a table in the poster halls at the Paris meeting in 1994 and London in 1996 but we did not want to follow the ASHG model of Curbstone Consults, where an individual participant met with a single 'expert'.

Our first formal workshop was in Genoa in 1997. Robin Winter and I ran a small session with about 50 attendees and an 'expert panel' that was asked to sit on the front row. It was quite a challenge with old fashioned projection, slides needing to be put in a carousel and the running order of those wanting to present cases on a flip chart. As soon as technology allowed, the London Dysmorphology Database was included in the session, necessitating double projection, which provided another challenge for the conference centre. Gradually the number of attendees increased, as well as the number of cases presented and there have been two workshops at each conference for the last ten years with attendance reaching 450 per session at the recent 50th Anniversary Conference in Copenhagen. Current facilitators are Jill Clayton-Smith, Sofia Douzgou and me.

Reflecting on the value of these dysmorphology sessions I think that (a) delegates from any country get to present cases in a supportive environment and often the best prepared and most interesting cases come from doctors in the most economically deprived countries; (b) senior colleagues from the major European centres actively participate and often offer to undertake investigations on cases from less developed centres—it is like a 'dating agency' since many discoveries and publications have resulted from these connections; (c) it has a real educational aspect since doctors new to dysmorphology get to see how more experienced colleagues formulate a differential diagnosis and use new diagnostic technologies.

DYSMORPHOLOGY AT THE EUROPEAN SCHOOL OF MEDICAL GENETICS

Since the European School of Genetic Medicine was founded by Giovanni Romeo in 1988, dysmorphology has been an integral part of the flagship annual course in Medical Genetics (now the Clinical Genomics and NGS course) in Bertinoro di Romagna. This has great logic since the topics covered demonstrate the breadth of clinical genomics from features in an individual patient to the latest applications of technologies and understanding of genetic mechanisms.

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Patients with rare dysmorphic disorders have been described as 'nature's exceptions' and it is certainly true that the study of abnormal development has informed knowledge of normal development. The spirit of the EGF courses is to bring together an expert faculty with young clinicians and scientists from Europe and beyond to understand each other's worlds, to share knowledge and encourage collaboration.

ESHG-SPONSORED AND PROMOTED DYSMORPHOLOGY COURSES AND NATIONAL MEETINGS

Regular European dysmorphology training courses attract young clinicians from all over Europe. They include the 'What I know best' series organised by Giovanni Neri and Raoul Hennekam in Rome and the annual ESHG-sponsored Manchester Dysmorphology Course. Most countries now hold national dysmorphology days where individual cases are presented and some teaching takes place. These include the *troisième jeudi* meetings in Paris, the Dysmorphology Club in London and the Dutch and German dysmorphology meetings. Han Brunner and I regularly contribute to the annual Karen Helene Ørstavik Dysmorphology meeting in Norway and The Danish Dysmorphology Meeting in Copenhagen which have both been running for around twenty years with ever increasing attendance and enthusiasm for the subject.

DYSMORPHOLOGY IS BECOMING 'SMART'

Although diagnosis in dysmorphology is often intuitive and based on experience and pattern recognition, no clinician can recognise all syndromes and 'new' disorders are continually being described. There has been a lack of consistency in the descriptive terms used in the literature, but now there is general acceptance that we need to adopt standard nomenclature for clinical features and many large-scale studies now use the Human Phenotype Ontology http://human-phenotype-ontology.github.io/. This is particularly important for the definition of newly recognised syndromes and for genotype-phenotype correlation. In some centres there is already an 'exome first' approach to diagnosis and this is likely to become more widespread, but assessment of the clinical phenotype remains essential to interpret the significance of variants.

Image recognition systems have been used in diagnosis and research for some years (eg, see Hammond P. *Arch Dis Child* 2007; 92: 1120–1126) but have usually required special equipment which limits application in the clinic. However a system using modern technologies with active clinical input, Face2Gene https://suite.face2gene.com/, can, for many common conditions, yield a diagnosis from a mobile phone image with the expectation that, as the system learns from clinical images, more rare disorders will be diagnosable.

EUROPEAN REFERENCE NETWORKS

A recent EU initiative for rare disorders is the formation of European Reference Networks (ERNs). It is hoped that these will share best practice for management including guideline development, facilitate further gene discovery and access to diagnosis and clinical trials and treatments across EU boundaries. ERN ITHACA (coordinator Jill Clayton-Smith) brings together experts in rare congenital malformations and rare intellectual disability disorders and will network with parents, and patients to develop best practice and initiate guideline development, where required. It will establish criteria for patient registry data, advance training for health professionals and facilitate research in dysmorphology. The network will work with existing networks in the field, while keeping patients at the centre of its activities. http://ec.europa.eu/health/sites/health/files/ern/docs/ernitha-ca_factsheet_en.pdf

SUMMARY

Dysmorphology, as with other disciplines within genomic medicine is evolving to harness new knowledge and technologies. However those in the field must never lose sight of the fact that each dysmorphic child belongs within a family and that they can bring joy, as well as concern as is abundantly clear when we are invited to attend patient support meetings. It is our duty to offer the best possible care for these families and it is a privilege to undertake research in the field.

Dian Donnai

Dian Donnai is Professor of Medical Genetics in the University of Manchester and Consultant Clinical Geneticist, Central Manchester University Hospitals NHS Foundation Trust. She trained in paediatrics and clinical genetics and has a major interest in the care and investigation of children with developmental disorders. She was the service head then academic head of the Manchester Centre for Genomic Medicine from 1997 to 2008 and is now Clinical Head of Saint Mary's Hospital where the Centre is based. Her research has focussed on elucidating the underlying causes of dysmorphic disorders; she founded the biennial International Manchester Dysmorphology Conference series in 1984, which has acted as a focus for many research collaborations and, with colleagues, runs the annual ESHG-sponsored European Dysmorphology Course. She was the founding country coordinator of Orphanet, UK and regularly contributes to the ESHG/European School of Genetic Medicine course in Bertinoro. She was awarded the Lifetime Achievement Award in Genetics by the March of Dimes in 2010, the ESHG Education Award in 2011 and the ASHG Arno Motulsky-Barton Childs Award for Excellence in Human Genetics Education in 2017. She has also been involved with genetic service development including a term as consultant advisor to the Chief Medical Officer of England (1998–2004). She was appointed Commander of the Order of the British Empire (CBE) in Her Majesty's New Year Honours in 2005 for services to medicine and was elected to the Academy of Medical Sciences in 2001. She was also president of the Clinical Genetics Society (1997–1999) and the European Society for Human Genetics (2009–2010) and, as a proud European, has served on both the ESHG Board and the Scientific Programme committee.