BSHG

The Newsletter of the
British Society for Human Genetics

Issue 45
June 2011

BSHG News

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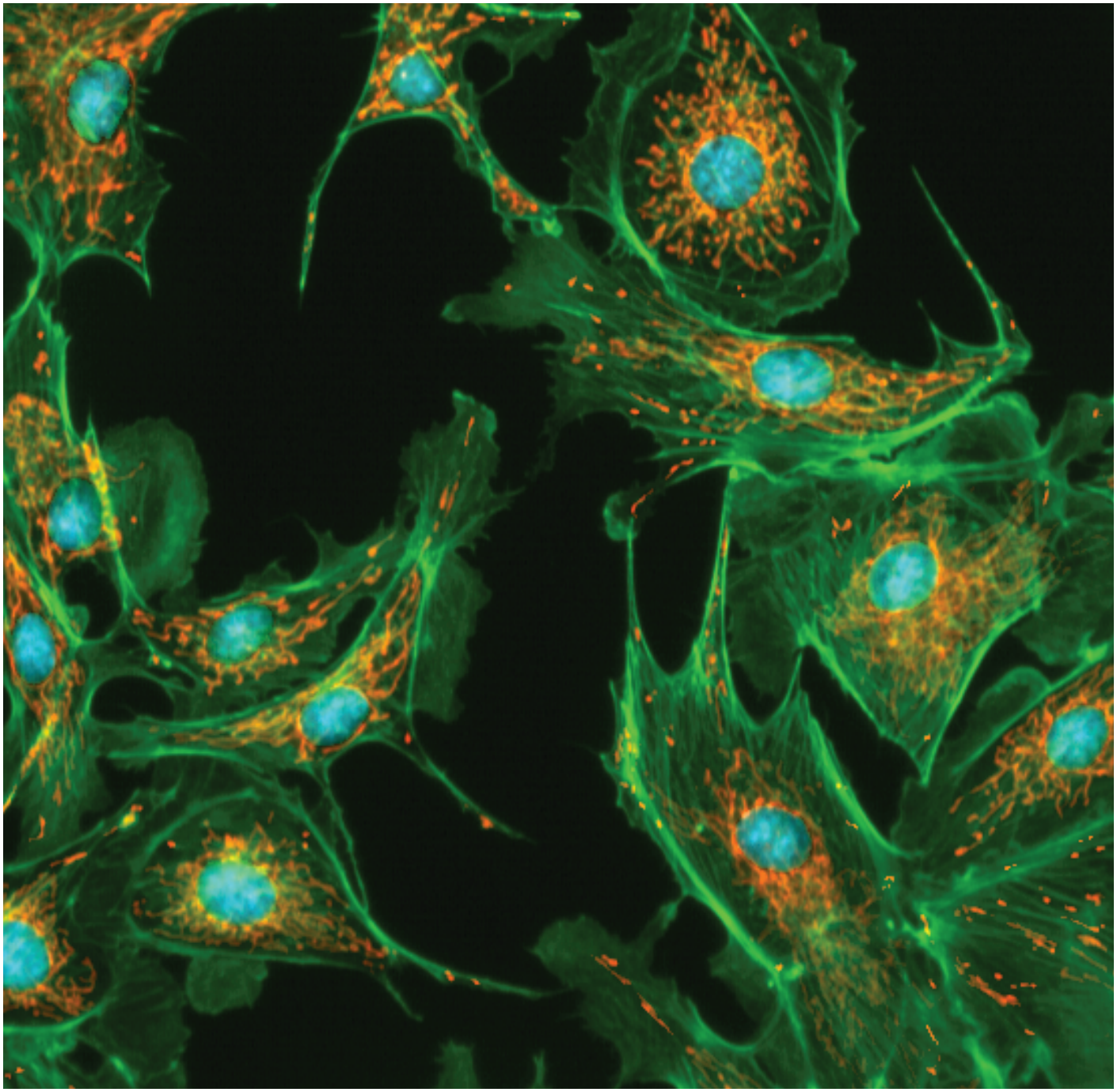

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From the newsletter editor

In this issue of BSHG News, we continue the series of excellent invited lead articles with Ewan Pearson's overview of the impact that genetics can have on the clinical management of diabetes, in which he brings his experience in genetics to bear on his work as a clinical endocrinologist.

Chris Patch makes her final contribution to the newsletter as Chair of the BSHG before she hands over to John Burn in September. Chris has taken the opportunity to reflect on the opportunities and challenges for our specialty presented by the genomic era.

Two eminent members of the BSHG have received prestigious awards in 2011: John Crolla reports that Professor Pat Jacobs was awarded the March of Dimes prize in developmental biology, and Professor Dian Donnai has been awarded the ESHG Education prize. Kate Glover reports the retirement of another prominent figure in the UK genetics community, Val Davison.

The BSHG relies on you to help identify copy for the newsletter. If you have a good idea for an article, please get in touch with me. My contact details are at the end of the main section.

Helen Middleton-Price

From the Chair

Chris Patch, Guy's

The Battelle report has announced that the $3.8 billion investment in the Human Genome Project (HGP) has generated $796 billion in economic impact (www.battelle.org/spotlight/5-11-11_genome.aspx, also reported on PHG Foundation website http://www.phgfoundation.org/news/8538/). This includes hundreds of thousands of jobs created in academic and commercial sequencing and research, and does not yet take into account the full long-term impact on health, innovation and knowledge generation. Although the report is focused on the USA and does not include the rapidly developing genomic industries in other HGP partners, including the UK, it is likely that there will be similar economic impact here.

Alongside this evidence for the economic benefits of the HGP, I remain concerned about the potential disbenefits caused by the possible inappropriate application of developments from this exciting science (eg: Direct to Consumer tests), as well as how we ensure the rapid implementation of sound testing strategies in healthcare. There is also an interesting tension developing between the idea of the genome as 'information' – within the changing context of information sharing, information exchange and privacy (eg: Facebook, Twitter etc) – and a more traditional medical/healthcare view. It is tempting in this time of change, economic uncertainty and NHS restructuring to retreat into a position based on inertia.

Listening to presentations at the ESHG conference in Amsterdam, and looking forward to the exciting programme for the BSHG conference, it does feel as if this period of uncertainty, combined with the incredibly fast moving developments in technology (and other developments, including the recognition of clinical genetics as a medical speciality in Europe) is providing a catalyst that will drive progress forward.

The science and technology is on the verge of delivering rapid and specific diagnoses for patients, as well as targeted screening, therapy and treatment, and a greater understanding of both normal and abnormal function. Other developments are, perhaps, equally as important as they offer enhanced opportunities to use the science for the benefit of individuals, families and whole populations. The recognition by the European Parliament of clinical genetics as a medical speciality allows for recognition of laboratory scientists, genetic nurses and counsellors (www.eshg.org/111.0.html). The BSHG has already supported the various professional groups in their aims for recognised training and statutory registration, and it is necessary that these initiatives continue to maintain momentum; the BSHG will have an important role engaging with the proposed Board of Medical Genetics of the ESHG.

Remaining in Europe, the European strategy on rare diseases – 80% of which are disorders that are predominantly genetic – has the potential to impact positively on the care of the patients and families whom we see every day in the clinic, and who participate in our research. I and other members of the Society worked with Rare Disease UK in preparing the strategy for the UK. (www.raredisease.org.uk/). This is also an important initiative; the BSHG and members of the UK genetics community have a long history of working in partnership with our patients, clients and their families for mutual benefit.

The clinical implications of genetics in diabetes

Ewan R Pearson, University of Dundee

As I come to the end of my time as Chair of the BSHG in September, I am encouraged by our progress towards sustainability, working in partnership with our constituent bodies and wider groups; the UK genetic medicine community is in a strong position to move forward. Undoubtedly there are economic benefits to be realised from the new technologies and science which will continue well into the future. These have to be complemented by appropriate professional and service developments, pushing for improvements in healthcare but with consideration of the wider consequences of genomic medicine. The BSHG is in a strong position to have a central role in this revolution, and it has been my privilege to work with you over the last two years to maintain and strengthen the Society so that it can continue to play its full part.

Diabetes is a highly heterogeneous condition where the diagnosis, made solely on the basis of hyperglycaemia, conceals multiple aetiologies. Classically we think of diabetes as being of two types: Type 1 diabetes, caused by autoimmune destruction of the beta-cell leading to absolute insulin deficiency; and Type 2 diabetes, which is usually diagnosed after deciding someone does not have Type 1 diabetes. As we understand more about the aetiology of diabetes it is apparent that this dichotomy is simplistic and there are many aetiological subtypes of diabetes now described.

Genetics of diabetes

Type 1 and type 2 diabetes are classical polygenic traits. The recent flurry of genome wide association studies in all disease areas has been particularly fruitful in Type 1 and Type 2 diabetes, resulting in considerable insight into the genetic aetiology and molecular biology of these two conditions. Whilst we would hope that ultimately this would yield new therapeutic options in diabetes, at present the results of these genetic studies have no direct impact on clinical practice.

Many monogenic subtypes of diabetes are described (see Hattersley, Bruining et al 2009). There are two types where recent developments have impacted directly on clinical care: Maturity Onset Diabetes of the Young (MODY) and Neonatal diabetes. MODY was named on clinical grounds in the 1970s as a form of diabetes that presents at a young age (usually before the age of 25), but like type 2 diabetes, does not initially require insulin treatment. MODY is believed to account for 1-2% of diabetes. The genetic aetiology of MODY began to be unravelled in the mid 1990s and OMIM now lists 11 subtypes. Of these, many are very rare. The most common are caused by mutations in Glucokinase, Hepatocyte Nuclear Factor (HNF) 1A, HNF4A and HNF1B. The clinical characteristics of these are well described in (Hattersley, Bruining et al 2009).

Diabetes that develops before the age of 6 months, variably termed neonatal diabetes or infancy onset diabetes, is rarely autoimmune in origin. Other than the transient form of neonatal diabetes due to altered methylation at the 6q24 locus, and rare syndromic forms of permanent neonatal diabetes, the genetic aetiology of neonatal diabetes was not well understood. However, in 2004-6, activating mutations in two genes, KCNJ11 and ABCC8, that encode the beta-cell KATP channel were described to cause neonatal diabetes (Gloyn, Pearson et al 2004) (Babenko, Polak et al 2006; Proks, Arnold et al 2006) and explain about half of all neonatal diabetes. Subsequently many novel genetic aetiologies of neonatal diabetes have been identified (Rubio-Cabezas, Klupa et al) but it is this group with KATP defects where dramatic clinical impact has been seen.

Sulphonylurea sensitivity and insulin cessation in patients with MODY due to an HNF1A mutation

A patient with an HNF1A mutation may present young, with marked hyperglycaemia and be assumed to have type 1 diabetes, and thus be treated with insulin, or may present more gradually at a later age and be assumed to have type 2 diabetes. Whilst making a diagnosis of HNF1A MODY was helpful in knowing how someone's diabetes might progress, and in providing information to family members on diabetes risk, it was only in 2003 that the key clinical importance of making such a genetic diagnosis became clear. In a randomised trial of sulphonylureas and metformin in patients with diabetes due to

"So the challenge remains to ensure patients … have equal likelihood of being diagnosed with MODY"

HNF1A mutations and Type 2 diabetes, the fall in fasting plasma glucose to gliclazide was 3.9-fold greater in patients with HNF1A mutations than their response to metformin (p=0.002); as expected, no difference in response to gliclazide or metformin was apparent in those with type 2 diabetes (Pearson, Starkey et al 2003). This study highlighted, for the first time, the importance of genetic aetiology in determining response to treatment in diabetes and has led to change in clinical management of patients with HNF1A mutations. Sulphonylureas are now recommended as the first line anti-diabetic therapy for these patients. Excitingly patients who have been assumed to have type 1 diabetes and treated with insulin, who are subsequently found to have a HNF1A mutation have been able to transfer off insulin onto sulfonylurea therapy (Shepherd, Pearson et al 2003).

Insulin independence in neonatal diabetes

A further example of how identifying monogenic diabetes can impact dramatically on diabetes treatment can be seen in the recent discoveries in neonatal diabetes. The activating mutations in KCNJ11 and ABCC8 genes result in the pancreatic KATP channel becoming insensitive to the increase in intracellular ATP:ADP that results from glucose metabolism. Thus the pancreatic beta-cell does not secrete insulin in response to hyperglycemia. Sulphonylureas bind to the KATP channel and close this channel, thus promoting insulin secretion. The discovery of mutations in this channel has subsequently led to successful transfer of patients with neonatal diabetes who had lifelong insulin treatment to oral sulfonylurea therapy with near normalization of blood glucose (Sagen, Raeder et al 2004; Pearson, Flechtner et al 2006). To find a patient, who may well be in mid-adulthood, who has been insulin dependent from soon after birth, and transfer them to a sulphonylurea tablet with resultant 'cure' of their diabetes is a unique experience in clinical medicine.

The challenge: dissemination and awareness

With such dramatic examples of how genetics can impact beneficially on the clinical management of diabetes, one would think that finding monogenic diabetes was an important priority in the diabetes clinic. Yet a fascinating report from Exeter highlights major disparity in the prevalence of monogenic diabetes around the UK (Shields, Hicks et al). There are clear areas of interest (eg the South West of England) where the number of cases of MODY in the population is high. Yet there are areas where there appears to be no MODY whatsoever! So the challenge remains to ensure patients across the whole of the UK have equal likelihood of being diagnosed with MODY. Potential solutions to this include the more widespread use of Genetic Diabetes Nurses (www.diabetesgenes.org) and the use of simple biomarkers (such as hsCRP, or Urinary C-peptide) to help identify patients with possible monogenic diabetes cost effectively.

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Professor Pat Jacobs awarded the March of Dimes prize in developmental biology, 2011

John A Crolla, Salisbury

Professor Patricia Jacobs

Patricia Jacobs OBE, FRS, needs very little introduction to the clinical and scientific community in the United Kingdom but over the past 12 months, she has been awarded two highly prestigious international awards which set her apart as one of the outstanding contributors to the discipline of human cytogenetics over the past 50 years.

In 2010, Pat was given the rare honour of being elected as a foreign associate of the National Academy of Sciences of the United States of America. The National Academy of Sciences was founded by President Abraham Lincoln in 1863 and election to the Academy is considered one of the highest honours that can be accorded a scientist. Pat therefore joins a very select group of non US citizens who have been thus honoured and is one of very few husband and wife members as her husband Professor Newton Morton is also an Academy member.

On the 2 May 2011 in Denver Colorado, Professor Pat Jacobs was jointly awarded, with David Page, the highly prestigious March of Dimes Prize in Developmental Biology. The prize recognises researchers whose work has contributed to our understanding of the science that underlies birth defects. One of the nominators for the award commented "I consider Patricia Jacobs the mother of human cytogenetics and David Page the father of the human Y chromosome". When reading this citation Pat commented "thank God I am not considered the grandmother of human cytogenetics"! Previous recipients of the March of Dimes award include several Nobel Laureates and from the UK winners have included Mary Lyon, Sir Martin Evans, Sir Richard Gardner, Sydney Brenner and Dame Ann McLaren.

At the award dinner in Denver, Pat gave an acceptance speech outlining the highlights of her 50 years in population cytogenetics (so far). She started in human cytogenetics two years after the discovery of the correct human chromosome number of 46, and her first appointment was to a scientific position with Michael Court Brown, who was then the director of the newly created Medical Research Council's group for Research into the General Effects of Radiation. Fortunately, at the beginning of her appointment, there were very few radiation samples for analysis and Pat was offered bone marrow from a man with a form of male infertility which had been first described in 1942 by Harry Klinefelter. The analysis of the bone marrow chromosomes led to the discovery, in collaboration with the Edinburgh based endocrinologist John Strong, of the first sex-chromosome abnormality (47,XXY) in our species. In turn, this observation stimulated the discovery of a number of key human cytogenetic discoveries which provided an essential link between chromosomes and abnormal human development and also led to the rapid implementation of the new medical discipline of Clinical Genetics.

The March of Dimes Prize also recognises Pat's many other outstanding contributions to human cytogenetics including (a) population cytogenetics detailing the rate of chromosome abnormalities in human newborns, (b) the contribution of chromosomal abnormalities to human morbidity and mortality, especially her pioneering work on the cytogenetics of spontaneous abortions and the origins of numerical chromosome abnormalities, (c) her work on the cytogenetics of Fragile X Syndrome, (d) and more recently her work on the origin of structural chromosome abnormalities. Throughout her career (so far), Pat has always embraced new technologies especially those which have provided quantum advances in our understanding of the underlying pathogenicity of chromosome abnormalities. Pat is still actively involved in chromosome research and in her acceptance speech at the March of Dimes she provided an outline of her ongoing interest in the frequency and possible pathogenic consequences of cryptic chromosomal mosaicism in humans.

Pat Jacobs therefore joins an elite group of highly distinguished scientists who since 1996 have been honoured with the March of Dimes Prize in Developmental Biology. Typically, Pat has already decided to spend the cash prize on furthering her research on mosaicism. I am sure that all member of the British Society of Human Genetics will like to join Pat's colleagues in Salisbury and her many scientific collaborators and friends throughout the world, in congratulating her on this outstanding and thoroughly deserved achievement.

Professor Dian Donnai awarded the ESHG Education prize

Professor Dian Donnai received her award from professor Jörg Schmidtke, President-Elect of the European Society of Human Genetics at the ESHG's annual conference in Amsterdam in June 2011

Congratulations to Dian Donnai, who was awarded the 2011 ESHG Education Award, one of only two annual awards made by the European Society of Human Genetics. The citation reads:

"The ESHG wishes to recognise Professor Dian Donnai's longstanding significant contribution to the clinical genetic sciences, education of students and clinical geneticists worldwide, the creation of the Manchester Dysmorphology Conferences which have contributed significantly to strengthening the collaboration between dysmorphologists in Europe and beyond, her wonderful dysmorphology workshops at the ESHG meetings and her excellent clinical genetic books."

From jeans to genes: an e-VAL-uation of genetic testing past, present and future

Kate Glover, West Midlands Regional Genetics Laboratory

On a cold, wet December morning, 120 delegates gathered together in a beautiful canal side location in Birmingham, to bid a fond farewell to one of the most influential genetics professionals of our era.

The first morning session was a trip down memory lane. Jonathan Waters took us on "a long strange trip" over the last 35 years and described the journey from G banding through FISH. We then followed the journey of how Prenatal Diagnosis and Cancer Genetics had evolved and were reminded of how Val had been instrumental in instigating the use of automation in diagnostic genetics in Birmingham.

The rest of the morning was taken up with talks on the history behind the development of the Genetics Professions and the early days of Training and Education and how Val was involved in the set up of the quality assurance scheme, NEQAS. Professor Sir John Burn then treated us to us to some more patient based discussions around the fascinating potential applications of Genetic Therapeutics in muscular dystrophy disorders and the use of aspirin to prevent cancers.

The first session of the afternoon focused on the emergence of new technologies and a reminder of how fast moving the world of Genetic technologies is. Nigel Carter of the Sanger Institute described how sequencing is set to revolutionise diagnostic genetic services. He described the exciting DDD project (Deciphering Developmental Disorders) that is being carried in collaboration with 23 genetic counselling centres around the UK. The potential information this study will provide is vast and has the eventual aim of allowing arrays to be designed with higher resolution, more targeted data.

John Crolla then described how he perceives the future of Prenatal Diagnosis with the main focus for the next six years being the introduction of free fetal DNA testing as the gold standard for aneuploidy screening. Ann Curtis followed with a talk about the need for "old dogs to learn new tricks", so that Genetic services are able to move forward with the new technologies.

The final session of the day focussed on the changes that Val had been involved in more recently with perhaps the most notable being her pivotal role in the development and implementation of MSC. Professor Sue Hill charted how Val's involvement would be a lasting legacy in the development of a more broadly qualified workforce in Clinical Science. Beverley Searle addressed the group with a very moving talk from a patient's perspective and made reference to all the personal sacrifices Val has made in order to raise funds and awareness for the charity Unique.

Val is not retiring entirely. She will still be involved in the UKGTN and has recently been appointed to the role of Lead Scientist for the West Midlands region.

It is however with a certain amount of sadness that those of us who have had the privilege to work with Val over the years are saying goodbye. It is perhaps fitting to conclude this summary of Val's symposium with some words that Gordon Lowther used during his surmising of his thoughts on words containing the word Val; VALete "Be well/stay strong – the commonest form of goodbye in Latin".

Delivering the benefits of genetics in mainstream medicine

Philippa Brice and Hilary Burton, PHG Foundation

Patients with inherited disorders are cared for throughout clinical medicine. An important element of this care may be provided by clinical genetics services, with their specialist expertise in diagnosis of syndromic disorders, understanding of inheritance patterns, and focus that is inclusive of family members. With increasing capabilities for molecular diagnosis of these disorders, the role of genetics services in using and interpreting genetic tests effectively has been paramount.

Over recent years, many genetic services have developed 'joint clinics' with other specialties to provide care for patients with inherited disorders in that specialty – for example joint cardiac, renal or neurology clinics. However, it can be anticipated that demand for genetic elements of clinical management will continue to rise, driven by availability of new scientific and clinical knowledge and new technologies and also by the increasing number of patients identified via improved diagnosis, cascade testing and population screening. The introduction of whole-genome sequencing technologies is likely to accelerate this situation.

The current picture

Current UK policy, as set out in the 2003 White Paper Our inheritance, our future: realising the potential of genetics in the NHS, is based on an expectation of diffusion of genetics expertise from clinical genetics into new areas of medicine. To a certain extent this has taken place, but research from the PHG Foundation over recent years has identified serious limitations with this approach. Strategic health needs assessments for inherited forms of ophthalmic and cardiovascular disease have revealed many issues likely to be shared by other services working to integrate expanding genetics elements. Most important is the need for diagnosis and ongoing management of the clinical phenotype, which must be undertaken by those with specialist knowledge of inherited disease within a given specialty. Secondly, is the recognition that, although geneticists and other specialists working together can provide excellent joint care, it is already impossible to provide equitable access to such services across the UK, a situation that will be exacerbated by increasing demand.

A new approach

Policy analysis by the PHG Foundation, including consultation with a wide range of stakeholders, suggests that an alternative paradigm is needed for the effective application of genetics for inherited disorders in mainstream medicine. This challenges the concept that genetics services themselves will necessarily become more 'mainstream', since they will continue to be highly specialised.

Rather, we propose that other clinical specialties should take new ownership of genetics in terms of assuming greater clinical responsibility for individual patients with inherited disease; and integrating new genomic expertise and technologies into their own professional competencies and clinical pathways. Substantial leadership and support will be required from clinical genetics services to manage this change and to provide continuing expertise where required, for example in recognition of syndromes, management of families or with tests that are difficult to interpret.

Strategic policy recommendations

- Production of commissioning guidance and clinical pathways for all areas with substantial elements of inherited disease
- Efforts to address inequities in access to high quality services for inherited diseases
- Review of genetic test provision, in the context of national pathology modernisation and anticipated increases in demand
- Creation of a sub-specialised clinical workforce to provide expert care for inherited diseases (in addition to ongoing general heath professional education in genetics)
- Development and evaluation of models to ensure effective provision of specialised genetics support for other clinical services
- Evaluation and audit of inherited disease services

The future for specialised genetics services

It is important to emphasise that the proposed development of mainstream specialties to meet changing needs by embedding genetics as sub-specialisations in no way removes the need for clinical genetics services. Indeed, regional genetics services would have a crucial leadership role both in helping other specialties to incorporate genetics and for ongoing operational support. A strategic and co-ordinated response supported by all the stakeholders is vital to ensure that we deliver both the immediate and future benefits of advances in genetics for patients in a fair and equitable manner.

The full report Genetics and mainstream medicine is available for free download from www.phgfoundation.org

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The joint Indo-UK clinical genetic and genetic medicine teaching initiative

Dhavendra Kumar, Cardiff

Dr Bronwyn Kerr delivering the John Edwards Memorial Lecture in Bangalore, India (31 January 2010)

The awareness of clinical genetics in the healthcare is fast increasing in most developing countries such as India, Brazil, China and South Africa. However, there is apparent shortage of trained clinicians and health professionals providing this service. Demand for this service is rapidly expanding that is largely met by the private sector contributing to gross inequality in its provision. In addition, the provision of laboratory genetic services is also confined to certain laboratories that are in most cases research laboratories and only interested in selective conditions. There is tremendous opportunity for clinical and laboratory geneticists to offer their expertise and assist clinicians and professionals in these countries. During the last few years few UK-based genetic professionals have informally provided input in supporting only very few centres in India and elsewhere.

Welcome of Professor Frances Flinter at the opening ceremony in Chennai

Recently a series of joint Indo-UK genetic education symposia were organised by Dhavendra Kumar from Institute of Medical Genetics, Cardiff. The first symposium in this series (30-31 January 2010) was organised by Dr Meena Bhatt (Consultant in Clinical Genetics) at the Centre for Human Genetics, Institute of Applied Biology and Bioinformatics, Bangalore, India. It was focussed on Clinical Cardiovascular Genetics. The UK faculty was led by Dhavendra Kumar and included Bronwyn Kerr (Manchester), Rob Hastings (Bristol & Oxford) and Perry Elliott (Heart Hospital, London). Several eminent cardiologists and genetic professionals also participated in the symposium. Several topics were covered during the two day symposium. Feedback was generally very positive with several requests to repeat the event. Dr Bronwyn Kerr also delivered the Second John Edwards Memorial Lecture set up by Professor Sharat Chandra, a friend of the Late Professor John Edwards (Oxford) and formerly Professor of Genetics, Institute of Science, Bangalore.

Convenors of the Chennai symposium: Prof. Ramasamy Pitchappan (Director, Research and Education, Chettinad Health University) with Prof. Dhavendra Kumar (Consultant Clinical Geneticist, Institute of Medical Genetics, University Hospital of Wales, Cardiff.

Dr Rob Elles performing the Indian ritual at the opening ceremony of the Apollo Hospital symposium in New Delhi (26 March 2011)

This year two symposia were organised in India led by Dhavendra Kumar (Cardiff); the UK team included Robert Elles (Manchester), Frances Flinter (Guy's Hospital, London) and Leema Robert (Guy's Hospital, London). The first was held in Chennai, the capital city of the southern state Tamil Nadu ('Current trends in Clinical Genetics and Genomic Medicine, 21-24 March 2011). It was followed by the second symposium in New Delhi (Current practice of Genetic and Genomic Medicine, 26-27 March 2011) hosted by the Apollo Hospital, the largest health care provider in the private sector. Several clinical geneticists and genetic scientists from India (including one from Colombo, Sri Lanka, Dr Vajira Dessanayake) were invited on the faculty.

The programme at both symposia reflected the current trends in the clinical and laboratory genetic practice highlighting the key elements of the UK-style NHS clinical and laboratory genetics organisation and delivery of genetic services. The Chennai symposium attracted a mixed audience comprising of medical students, junior medical practitioners, specialist medical

"...there is ample scope and opportunity for ... UK NHS clinical and laboratory geneticists to engage in genetic teaching programmes in India and other developing countries"

Dr Rob Elles with Pro-Vicechancellors of the Chettiand Health University, Chennai, India

practitioners, laboratory scientists and research students. This was organised and hosted by the Chettinad Health University, a privately funded medical and health institution and tertiary hospital. The symposium was well organised by local hosts and organisers. The 3-day programme included dedicated talks from the UK team as well as team of experts from within India. Dr Rob Elles provided an overview on genetics and genomics in new emerging economies of the developing world. Professor Ishwar Verma, Head of the Genetic Medicine at the Sir Ganga Ram Hospital, New Delhi, introduced the status of medical genetics in India. A number of specialist topics were covered including prenatal diagnosis and pre-implantation genetic diagnosis (Francis Flinter), molecular genetics of heart failure (Dhavendra Kumar) and genetic management of congenital heart disease (Leema Robert). Some areas of genomic medicine were also covered including nanotechnology/nanogenomics, pharmacogenomics/ pharmacogenetics and personalised medicine. The symposium concluded with a dedicated session on genetic and genomic technologies facilitated by Dr Rob Elles. A number of presentations were made by laboratory scientists covering a range of genetic and genomic technologies. The general feedback from both the participants and the speakers was consistently positive and very encouraging with a clear indication of holding similar symposium in the future.

The next symposium was planned at the Apollo Hospital in New Delhi. This was jointly organised by the Departments of Medical Genetics at all the All India Institute of Medical Sciences and Department of Metabolic and Fetal Medicine at the Maulana Azad Medical College, both in New Delhi. The Apollo Hospital is one of the leading providers for healthcare in the private sector. This hospital group offered to host this symposium and was very well attended. Rob Elles managed to travel to New Delhi along with Dhavendra Kumar. The programme was largely focussed on clinical genetics and there was generally a very relaxed atmosphere. Several presentations were made on a variety of clinical genetic topics followed by active discussion. It was obvious that the expertise and interest in clinical genetics was enormous with consistently high standard of their knowledge. Feedback has been generally very positive and encouraging with a clear demand to hold similar symposium in the near future. Rob Elles attracted lot of attention with his offer to help diagnostic genetic laboratories to gain access to the network of European genetic testing laboratories and improve standards in line with UK/Europe/OECD guidelines.

The experience from these symposia has been encouraging and rewarding. This illustrates that there is ample scope and opportunity for a number of UK NHS clinical and laboratory geneticists to engage in genetic teaching programme in India and other developing countries. So far these were managed without any dedicated funding. The UK team gratefully acknowledges the local NHS trusts and organisations for allowing time and expenses. It is possible that this joint initiative could be partly supported by the government agencies such as Dept of Biotechnology, India who might be interested to support similar seminars or symposia in India. It is important that we more and more clinical and laboratory geneticists come forward and contribute in similar future initiatives. Any one who might be interested to join, please register your interest to Dhavendra Kumar. (Dhavendra.kumar@wales.nhs.uk; kumard1@cardiff.ac.uk).

Prof. Ishwar Verma, Leading Medical Geneticist of India, Head of Genetic Medicine, Sir Ganga Ram Hospital, New Delhi; Formerly Professor/ Head Genetics Unit, All India Institute of Medical Sciences, New Delhi, India

Bringing non-invasive prenatal determination of fetal sex using cell free fetal DNA into mainstream clinical practice

Melissa Hill and Lyn Chitty on behalf of the RAPID team

Clinical and Molecular Genetics, Institute of Child Health and Great Ormond Street Hospital for Children NHS Trust

The five year RAPID programme aims to improve the quality of NHS prenatal diagnostic services by evaluating early non-invasive prenatal diagnosis (NIPD) based on cell free fetal (cff) DNA in maternal plasma. A key achievement since our launch in July 2009 has been our collaborative work with the NHS service laboratories to inform the introduction of NIPD for fetal sex determination into routine clinical practice.

NIPD for fetal sex determination is highly accurate

The PROOF (Prospective Register of Outcomes of Free-fetal DNA Testing) audit is complete and has been published1. The audit assessed all cases referred for fetal sex determination using NIPD between 1.4.2006 and 31.3.2009 from two NHS laboratories; the International Blood Group Reference Laboratory (IBGRL) and the North East Thames Regional Molecular Genetics Laboratory (NETRMGL).

During the three years of the audit, testing was requested in 672 pregnancies. Indications included 123 referrals for DMD, 140 for haemophilia and 76 for CAH. In view of the experiences with testing over the first year, reporting criteria were changed to increase stringency and stipulate testing after 7 weeks gestation. In the subsequent 511 pregnancies the concordance rate increased to 401/403 (99.5% CI 98.2%-99.9%). No result was issued in 4% of pregnancies. The clinical utility of NIPD was clearly demonstrated as only 32.9% (174/528) underwent subsequent invasive testing.

NIPD for fetal sex determination is no more expensive than invasive testing

To investigate the incremental cost of NIPD for fetal sexing compared with traditional invasive testing two representative genetic conditions were chosen; DMD and CAH2. Care pathways were ascertained and used to identify the main NHS cost drivers of fetal sex determination. These included costs of NIPD, CVS (sampling and molecular testing), scans, and pregnancy outcomes. Data describing the proportion of known carriers at each point in the care pathways were derived from the PROOF audit.

NIPD was found on average to cost £255 per women tested, including sampling, laboratory testing and feeding back the results. Differences in mean costs per pregnancy for NIPD versus invasive testing were small for both DMD (mean difference –£87, 95% CI -£303 to £131) and CAH (mean difference –£193, 95% C.I. -£301 to -£84). The costs of NIPD were offset by the smaller proportion of women who required CVS, such that NIPD overall was not associated with higher costs compared with invasive testing.

Bringing NIPD for fetal sexing into routine clinical practice

To allow NIPD to enter mainstream clinical care approval by the UKGTN and recognition by commissioners is crucial. Gene dossiers for fetal sex determination for CAH and X-linked disorders (excluding haemophilia) have been approved by the UKGTN for three laboratories (NETRMGL, Birmingham and NGRL (Manchester)). RAPID worked with the service laboratories to facilitate the application which was supported by our evaluations of accuracy and costs. Care pathways and best practice guidelines have been developed to accompany the gene dossiers and these are available from the RAPID website.

At present NIPD for fetal sex determination has not been approved for haemophilia. This is because clinical utility is not clear. Invasive testing and termination are rare and information regarding fetal sex is used solely to guide delivery management which could be done later in pregnancy using ultrasound. RAPID is currently investigating costs and evaluating the attitudes of patients and clinicians regarding fetal sex determination for haemophilia.

With increasing numbers of referrals and several laboratories now offering NIPD for fetal sexing a quality assessment scheme is required. In collaboration with UK NEQAS and NGRL (Manchester) a pilot quality assessment scheme has been run with four laboratories that each tested three anonymised samples. An expanded pilot scheme will be undertaken in 2011.

Guidance for commissioners and public health teams is in the final stages of development. In addition, RAPID is working in collaboration with Genetic Alliance UK to survey the opinions of families accessing this test. Draft patient information has been developed and will be piloted in the coming months. The National Genetics Education and Development Centre are developing educational competencies and learning packages to support the health professionals who offer these tests.

What is next for NIPD?

NIPD for skeletal dysplasias (achondroplasia3 and thanatophoric dysplasia) is being offered in collaboration with NETRMGL on a research basis.

"Fetal sex determination using cffDNA is highly accurate when performed in NHS service laboratories using stringent reporting criteria"

Formal standards for testing are being developed. If you are interested in offering these tests to any patient please contact rapid@ich.ucl.ac.uk for information sheets for both health professionals and patients.

Summary

- Fetal sex determination using cffDNA is highly accurate when performed in NHS service laboratories using stringent reporting criteria.
- Parents should be advised of the small risk of discordant results and of the possibility that repeat testing may be required to resolve inconclusive results.
- NIPD has changed clinical practice, reducing the need for invasive genetic testing.
- The overall costs of NIPD were offset by the smaller proportion of women who required an invasive test and, as a result, NIPD is no more expensive than traditional invasive testing.
- NIPD can provide clinical benefits for many women by avoiding the risks of invasive testing, without additional costs to the NHS.

Further information about RAPID

Email: rapid@ich.ucl.ac.uk
Web: www.rapid.nhs.uk.

Acknowledgements

We thank the IGBRL, the NETRMGL and the many clinicians who assisted with the audit. We are also grateful to the patients and health professionals who have generously given their time to attend focus groups and/or interviews to allow us to explore stakeholder opinions.

Personnel were funded by the SAFE EU FP6 Network of Excellence, the RAPID NIHR Programme Grant and the Central and East London CLRN. The research funded is independent and the views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

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3. Chitty LS, Griffin DR, Meaney C, Barrett A, Khalil A, Pajkrt E, Cole TJ. New aids for the non-invasive prenatal diagnosis of achondroplasia: dysmorphic features, charts of fetal size and molecular confirmation using cell-free fetal DNA in maternal plasma. Ultrasound Obstet Gynecol. 2011 37:283-9.

Book Review

New Clinical Genetics 2nd Edition, Andrew Read and Dian Donnai, Scion

Mary Porteous, Edinburgh

Back in 1982 I was a 5th year medical student in Manchester on a paediatric rotation. Our assignment was to identify an interesting patient and write a case report. Unable to identify a truly fascinating case on the ward at Wythenshawe Hospital, which was full of children with constipation or RSV, I decided to contact the genetics department to see if I could be introduced to a child with Down syndrome and a heart defect (genetics and cardiology being my main interests at the time). I phoned the St Mary switchboard and spoke to a woman I mistakenly took to be Dr Dian Donnai and arranged to attend the clinic with my matriculation card. I duly turned up at the suggested time to the Genetics Department to find I was unexpected (I never found out who the woman on the phone was). I was passed to the head of the Molecular lab, Andrew Read who sat me down with a cup of coffee and inspired me with his enthusiasm and clear explanations of how genetic science was being translated into meaningful clinical results . We were then joined by Dian Donnai, who gave me an insight into genetic counselling and the importance of communication based on careful pre-clinic preparation. It was one of the highlights of my student education and probably the moment when I became convinced in my future career choice. I was therefore delighted to be asked to review the second edition of 'New Clinical Genetics' written by two of my early heroes.

This book is primarily aimed at medical students. Its integrated case based approach lends itself to a sustained period of reading rather than quick fact collecting. This is not a weakness as there are plenty more traditionally structured Clinical Genetic reference books available. Readers are invited to choose either to follow the 26 case studies through from referral to diagnosis and management or to concentrate on the science presented in the Background, Summary and Extension sections. Each chapter concludes with self-assessment questions pitched at a level which would stretch the average undergraduate (and occasionally your reviewer) quite significantly. Indeed Clinical Genetics trainees preparing for the Specialty Certificate Exam who complete the questions without difficulty have little to fear from the scientific component of the exam.

The case studies are realistic and stimulating rather than contrived. Those of us involved in Clinical Genetics teaching are all aware of the power of a case study to engage an audience. It can be challenging taking a non-exploitative but informative clinical photograph but the photographs used to illustrate the different cases in this book hit the right note. The standard of illustrations in general is very high with use of full colour where appropriate. I suspect that the book will catch the eye of anyone browsing the genetics section for an accessible introduction to Clinical Genetics. To quote one such browser who posted a review of the book on the Amazon website "Wonderfully written, it brings genetics to life."

At times I was slightly frustrated that page numbers were not given along with directions in the text to "see figure 2 or disease box 9" particularly when they were located in different chapters to the text. However when I remarked on this to a colleague she did not have the same problem and pointed out that the editor has used colour coding to distinguish case (green) from disease box (blue) and scientific extension (orange). Knowing this as well as the chapter in which the figure was to be found made searching easier. This will have been an extremely difficult book to edit because of the complexity of the case-based structure and generally I think the authors have been extremely well served by their editor, Jonathan Ray.

It is impossible for any book to keep up with the pace of change in Genetics and this book is no different. The "major challenge" of searching for mutations in the dystrophin gene referred to in the Duchenne case is reduced to near routine in the diagnostic laboratory. However, the authors have an eye to the future with discussion of the increasing role of microarrays and the arrival of massively parallel sequencing. In the absence of a personal tutorial over coffee from the authors, this book is the next best thing. I would certainly be happy to recommend it to medical students and postgraduate trainees.

Review

Teachers' TV programmes: Genetics and Medicine

Sandy Raeburn, Nottingham

In June 2010, Teachers TV issued a series of five videos on 'Genetics and Medicine' (1), covering important elements of genetics aimed at school students between the age of 14 and 16 (2).

In the six decades since the first satisfactory description of the human DNA structure (and correction of the human chromosome count to 23 pairs) progress in genetic understanding has burgeoned inexorably (3). Often, the drivers for the forward leaps of knowledge were improvements in the laboratory technologies.

Yet, in parallel with the new laboratory findings (indeed often preceding them!) there was steady but less dramatic progress in medical genetics (4). My view, then and now, was that scientists and the media lauded progress in laboratory research, whilst ignoring the equal or greater importance of clinical studies, of the wider family and of the community. Laboratory and clinical research in genetics are interdependent and complementary; they cannot be taught in isolation.

School genetic teaching, therefore, started with DNA and molecules; only later were the patient and family given (usually) sparse mention. For example, the earlier TeachersTV programme on 'Genetic Engineering' was launched in June 2007 and (with an otherwise excellent instructional approach) for the most part covered DNA technology, cloning (Dolly the sheep) leaving around three minutes for the medical implications of the Human Genome Project and less than two minutes on ethical issues.

This genetics and medicine series starts with real people with important disorders. In the first video a woman with a devastating family history of cardiac deaths introduced her own story, leading to the need for an implantable defibrillator for her and her teenage son. The condition, long QT syndrome, is due to potassium channel defects which affect heart muscle depolarisation. The laboratory steps to find out which of at least four genes was involved were covered next (there are now more than 10 genes implicated!). Then we turned to the clinical story of a family with severe eczema - vividly illustrated. The steps in research (5) to find the causes and risk factors were then summarised.

The second programme focussed on breast cancer, using the same format - clear clinical description and family details, preventive options including bilateral mastectomy (in a male as well) followed by the scientific explanations and challenges. As in the first programme, I was impressed with the teaching qualities of articulate, affected teenagers. The choices they faced and their clear summaries of the nature of their problems had as much educational value as the professional explanations. The family affected here by a rare cause of early onset breast cancer (not BRCA1 or 2) were also delightful in other ways, not least their positive drive and optimism when faced with impossible dilemmas and much sadness.

The three programmes on genomics and health consisted of round table discussions with a (science-orientated) professor of genetics, a bioethicist, and two senior clinical professors - both involved with active patient care as well as clinical genetic research. The chairman was a senior lecturer in science education. If anyone stepped away from real facts, the clinical experts brought them down to earth. Vice versa, clinical anecdotes were only used to illustrate the elements of personal choice.

School students might find this format, of debate between experts, less exciting than the personal stories of the first two programmes, but teachers could use the material provided to establish core class discussions, for example about personal privacy versus wrongful use of genetic testing.

Let me say that this series is excellent, well-balanced and up to date; it should inspire young people to study genetics more fully, either as a general interest or as a future career. I wish I were 50 years younger!

TeachersTV, their production team from Glasshead production company, the Nowgen Centre for genetics in healthcare (a partnership of the Central Manchester University Hospitals NHS Foundation Trust and The University of Manchester) and the Wellcome Trust who provided sponsorship should all be congratulated.

Sources & References

1) Teachers TV. These programmes are now available at http://www.youtube.com/nowgen

2) Three of these programmes lasted about 14 minutes each (Genes and Disease, Breast Cancer in the Family and a general discussion of Genetics, Society and Health); the two others are much shorter at around four minutes (Genomics, Personality and Health and Genomics, Decision-making and Risk).

3) Such advances include the cytogenetic changes in specific chromosomal disorders, cell culture techniques which modelled diseases of biochemical pathways, elucidation of those pathways, recombinant DNA technology, the first gene sequencing, molecular genetic diagnosis, etc.

4) For example, more precise family tree interpretations, systematic descriptions of specific syndromes with careful measurement of key signs and sub-classification of generic disease groups (like breast cancer or epilepsy), as well as better clinical management leading to longer survival and long-term follow-up studies which then clarified the natural history.

5) Case control studies, filaggrin gene identification, genome wide association studies (GWAS), etc.

National Genetics Reference Laboratories updates

NGRL
National Genetics Reference Laboratory | Manchester

Manchester

Andrew Devereau, Manchester

SNPCheck

Work is underway to develop an enhanced version of SNPCheck that will enable laboratories to personalise SNPCheck by creating their own profile and storing their primer pairs for faster re-analysis. We will be trialling the new version of SNPCheck over the next couple of months and the final release will be available later this year for subscription. For further information contact glen.dobson@cmft.nhs.uk.

DMuDB

EMQN members are now able to register for a subscription to the Diagnostic Mutation Database, through the EMQN website. We intend to launch DMuDB internationally by August 2011. Work is ongoing to adapt the database for this purpose, and we are continuing our consultation of current database users to ensure that any concerns and suggestions are considered as we move forward with this project.

We have recently been pursuing ways to make submission of data to DMuDB a quicker and easier process. To this end, we have been investigating the addition of DMuDB export functions to STARLIMS and Alamut. The Alamut integration has progressed to the stage where a first version of DMuDB export is now available in Alamut 2.0. Documentation of the new export functions can be found online at http://www.interactive-biosoftware.com/alamut/doc/2.0/reporting.htm. The required "template" file for DMuDB export is available at http://www.interactive-biosoftware.com/alamut/doc/2.0/templates/DMuDB_Alamut_Spreadsheet.xml. Bulk export can be performed by clicking the "Export for DMuDB" item in the "Mutations" menu. If you already have variant data in Alamut, have version 2.0 installed and have an NHS.net account (in order to send us the generated export data) we are interested in doing some initial trials of bulk export of data from Alamut to DMuDB. Please contact glen.dobson@cmft.nhs.uk if you would be interested in trialling this with us.

We are also working alongside our local STARLIMS implementation in Manchester to develop an export function to DMuDB. It is hoped that this will enable the function to be rolled out to other implementations in the future. We will update you when further progress with this has been made.

As always, we are interested in collecting variant data that laboratories would like to submit to the database – this can be sent to us via secure electronic routes, e.g. from an nhs.net account to cmm-tr.ngrlman@nhs.net, or by arranging for us to visit your laboratory to collect it in person. Please get in touch if you would like to submit your data: support@dmudb.net

Bioinformatics training

Our 2-day bioinformatics course for cytogeneticists and molecular geneticists, delivered in partnership with Nowgen, has been substantially revised. The new course was delivered for the first time in May and we are now taking bookings for a second run-through in September. We are also developing a distance learning-based assessment to be completed by attendees in their own time after they have attended the 2-day course. Our next bioinformatics course for clinicians is planned for October.

Best practice guidelines

We are currently working with the CMGS to update the best practice guidelines for the Interpretation and Reporting of Unclassified Variants (UVs) in Clinical Molecular Genetics which were developed in 2007. A workshop took place in March and a revised draft of the guidelines is now being developed. As with the existing guidelines, the revised version is being developed in collaboration with the Dutch laboratories.

Tools analysis

As part of our 2011-12 work programme we intend to expand our tool analysis project. This will advance the analysis already performed on in silico missense and splice site prediction tools, and tie these tools in to our curation and quality management of the data within DMuDB. Our long-term aim is to provide a regularly updated indication of the performance of individual tools. If you have any questions about this programme, please contact kathryn.robertson@cmft.nhs.uk.

NATIONAL GENETICS REFERENCE LABORATORY
WESSEX

Wessex

Nick Cross, Salisbury (ncpc@soton.ac.uk)

Future of the NGRLs

Contrary to expectations, both NGRLs have received notification that they will continue to receive funding from the DH until March 2012, the end of our current contract period. Funding for 2011/2 however has been significantly reduced and it has been made clear that there will be no central money available from the DH after March 2012. Efforts are ongoing to search for alternative funding sources to keep key elements of our programme going beyond this time.

"The CMGS/NGRL pilot study to evaluate diagnostic use of next generation sequencing (NGS) is ongoing"

Next Generation Sequencing

The CMGS/NGRL pilot study to evaluate diagnostic use of next generation sequencing (NGS) is ongoing. One hundred and forty samples of known genotype have been collected from eight participating regional genetics laboratories and their mutational status confirmed in Salisbury. These have been sent out to a number of technology vendors and service providers to perform targeting and sequencing experiments. The study aims examine the effectiveness of different targeting/sequencing pipelines for analysis of multiple genes using seven colorectal cancer genes as a model system. The study currently comprises eight different targeting/sequencing pipelines including targeting by Agilent, Illumina, Fluidigm, and Raindance and sequencing on the Applied Biosystems (SOLiD), Illumina (GAII) and Roche 454 (GS-FLX) platforms. We are currently in the data acquisition phase and expect to have a full data set by the end of June 2011. Initial data for RainDance targeted material that has been sequenced across the three different platforms, is currently being analysed. As well as evaluating technical aspects of the workflows the data is also being used to evaluate a number of different analysis approaches including both commercial packages and open source software. We are interested in the potential to examine additional sequencing methodologies (for example Ion Torrent) using the targeted material already generated. If anyone is interested in collaborating in this study for example providing alternative sequencing for one of the targeted panels or using data for comparative analysis of software, or would simply like more information please contact chris.mattocks@salisbury.nhs.uk.

Array CGH

The NGRL array CGH team continues to collaborate with the International Standardised Cytogenomic Array (ISCA) consortium initiative and have submitted fully anonymised retrospective data to help determine the populaton frequncies and pathogenicity of recurring microdeletion and duplication syndromes. An update of the NGRLs scientific collaboration with ISCA was given by John Crolla at the ACC/CMGS joint meeting in Durham on 6th April 2011.

Dr Shuwen Huang and Annette Cockwell have recently completed an evaluation of the use of a combined ELUCIGENE® QST*R-PL and array CGH using an 8 x 15K array design when applied to tissues derived from spontaneous abortions, neonatal deaths and fetuses with multiple congenital abnormalities. This study (to be submitted for peer review in the next month) clearly demonstrated that a combination of QF-PCR and array CGH for most solid tissue referrals is the preferred route for diagnostics in this patient cohort. The full Power Point of the presentation at the ACC/CMGS meeting can be found on the NGRL website.

The NGRL together with Prof Steve Robson (Newcastle) and Prof Lyn Chitty (UCL), have recently been awarded funding from the Efficacy and Mechanism Evaluation Programme (MRC/NIHR joint funding) for a technical evaluation of the use of array CGH in prenatal diagnosis. The study is called the Evaluation of Array Comparative genomic Hybridisation in prenatal diagnosis of fetal anomalies (EACH) and will involve recruitment of patients from eleven fetal Medicine Units. The QF-PCR, conventional karyotyping and and array CGH will be carried out in seven Regional Genetics laboratories. The recruitment criteria for the EACH study are fetuses with a normal qfPCR result and; (1) one or more structural anomalies identified at the 11-14 or 18-21 week ultrasound screening scan or (2) an isolated nuchal translucency (NT) above 3 mm at the 11-14 wk ultrasound screening scan undergoing conventional karyotyping by amniocentesis or CVS for clinical indications. The EACH study is due to start in the autumn. For further information please contact John Crolla (john.crolla@salisbury.nhs.uk).

Non invasive prenatal diagnosis

(i) Fetal sexing and fetal independent markers: A retrospective optimisation of RASSF1A and SRY real time PCR has been completed and a prospective evaluation is ongoing with 90 samples analysed to date. As part of this RASSF1A/SRY study we are collaborating with a company specialising in droplet digital PCR (QuantaLife) to explore methods for accurately determining the cell free fetal DNA load in maternal plasma samples (abstracts submitted to ACMG and ESHG, manuscript in preparation). We recently participated in a RAPID organised workshop to compare the quality of cell free fetal DNA (cffDNA) obtained using three different DNA extraction kits and the results of using two genotyping assays (to detect SRY and DYS14) for non-invasive prenatal genotyping for fetal sex.

(ii) NIPD of aneuploidy: We are assessing the use of NGS-based approaches to NIPD of aneuploidy and have prepared eight libraries, using several different assay designs, which will be sequenced in May/June 2011. The optimal assay design will be evaluated further using a large cohort cf fetal DNA samples to determine whether the methodology is suitable for detection aneuploidy.

If you would like any more information please contact Helen White: hew@soton.ac.uk

We welcome feedback from the genetics community on our current work programmes and suggestions for future work either directly to myself or to the individual project leads. For details on all our activities at NGRL (Wessex) as well as individual contact details please see our website www.ngrl.org.uk/wessex.

Announcements

Invitation to British geneticists with links to the Indian subcontinent

British genetics professionals (clinical geneticists, genetic counsellors/nurses, laboratory scientists, research and academic) originating from and/or having links with any part of the Indian subcontinent (India, Pakistan, Bangladesh, SriLanka, Nepal, Bhutan, Myanmar/Burma) are invited to join this new group. The main objective of the group is to raise awareness and promote healthcare applications of genetics and genomics in any country of the subcontinent. Members will engage in educational and research activities on a voluntary basis in their own time and with their own resources. In addition members would take on other tasks such as advising, mentoring and helping fellow genetics professionals during visits to the UK. All BSHG members sharing similar objectives are also welcome to join the group.

Please contact Dhavendra Kumar (02920 744 4037 or kumard1@cf.ac.uk) OR Ajoy Sarkar (0115 962 7728 or ajoysarkar@yahoo.co.uk).

Reference materials survey

The National Institute for Biological Standards and Control (NIBSC) has made various genetic reference materials over the past few years (see June 2010 Newsletter) and would like to receive some feedback, both on the utility of the current materials and on laboratories' priorities for the list of future reference materials. If you would like to have some input, then please follow this link to our questionnaire:

http://www.nibsc.ac.uk/science/diagnostics/human_genetic_diagnostics.aspx

Contact: Paul Metcalfe
paul.metcalfe@nibsc.hpa.org.uk 01707 641250

New comprehensive molecular genetic test for Glycogen Storage Disease

A new molecular diagnostic screen of all 18 genes known to cause Glycogen Storage Disease is now available in the DNA Laboratory at GSTS Pathology, Guy's Hospital, London.

All 284 exons of the 18 genes are captured simultaneously with a bespoke Agilent Sure Select in-solution hybridisation array, then subjected to massively parallel sequencing using Illumina's next generation sequencing by synthesis technology. All target regions (coding exons and splice sites) will be covered by over 30x read depth. Any regions having less than 30 reads will be subjected to standard PCR amplification and fluorescent capillary Sanger sequencing, and detected variants will also be confirmed by standard capillary sequencing.

The methodology has been verified to detect known point mutations and indels up to 38bp, and whole exon CNVs.

For further details please contact either Dr Steve Abbs in the laboratory: stephen.abbs@gsts.com tel: 020 7188 2582; or Dr Charu Deshpande in Clinical Genetics Charu.Deshpande@gstt.nhs.uk tel: 020 7188 1363.

Noticeboard

Genetic Testing of Children: Report of a working party of the British Society for Human Genetics 2010

is available on the BSHG website:
http://bshg.org.uk/GTOC_2010_BSHG.pdf

Call for participants: young peoples' experience of NF1

Jenny Barke, PhD Student, Centre for Appearance Research, University of the West of England, Coldharbour Lane, Bristol, BS16 1QY.

Neurofibromatosis Type 1 (NF1) has been found to have a significant impact on quality of life and psychological adjustment for some individuals (1). However it is impossible to predict what kinds of challenges a person with NF1 may face. Psychological problems can stem from an altered appearance caused by neurofibromas and from the unpredictability of the condition (2).

Adolescence is generally recognised as a time during which appearance becomes more significant for young people; it is during this time that neurofibromas often first appear and become particularly noticeable. Not knowing how the condition will progress makes adolescence a time of uncertainty for those with NF1.

Despite the potential impact of NF1 on quality of life and psychosocial adjustment during adolescence there is limited research that examines the lived experience of young people with NF1. Therefore this research aims to explore the psychosocial impact of NF1 on adolescents' lived experience by examining both resilience and challenges being faced, in order to identify any support needs and the factors that might help positive adjustment. The overall aim of this research is to inform the future provision of care for young people with NF1.

Research plan

The first stage of this research is a series of exploratory interviews with 1) health professionals; 2) young people aged 14-24 with NF1 and 3) parents of young people with NF1. These interviews will be used to develop surveys to further investigate areas identified in the exploratory interviews.

Interviews with young people and parents are currently taking place. If you know of any families or individuals who are suitable for this research and may be interested in taking part in a research interview, please contact Jenny Barke for further information.

Interviews with health professionals are complete, and the survey for health professionals who work with people with NF1 can be found at http://tiny-url.org/NF1. It takes less than ten minutes to complete and entries can be entered into a draw to win a £50 M&S voucher (Survey closes 30 June 2011).

For further information on any aspect of this research please contact Jenny Barke.

References:

1. Graf A, Landolt MA, Mori AC, Boltshauser E, Quality of life and psychological adjustment in children and adolescents with neurofibromatosis type 1. Journal of Pediatrics 2006;149:348-353.

2. Ferner RE, Huson SM, Thomas N, Moss C, Willshaw H, Evans DG, Upadhyaya M,Towers R, Gleeson M, Steiger C, Kirby A. Guidelines for the diagnosis and management of individuals with neurofibromatosis 1. Journal of Medical Genetics (JMG), 2007, 44(2), pp. 81.

jenny.barke@uwe.ac.uk 0117 328 1891

British Human Genetics Conference 5-7 September 2011 University of Warwick, UK

Scientific Programme

Carter Lecture: **"Making eyes: genes and networks"** given by Professor Veronica van Heyningen

BSHG Lecture: **"Evolution of the Cancer Genome"** given by Professor Mike Stratton

Symposia:

Fanconi Anaemia - Prof Christopher Mathew, Dr Marc Tischkowitz, Dr Ruth Newbury-Ecob, Dr Stefan Meyer, Prof Nazneen Rahman

Reflections on the Psychosocial and ethical aspects of emerging technologies - Prof Mike Parker, Dr Christine Patch, Dr Marijke Wevers, Dr Celine Lewis

Genetics and Genomics in the Developing World - Dr Dhavendra Kumar, Dr Thomas Williams, Dr Manj Sandhu

Approaches to Complex Disease - Dr Eleftheria Zeggini, Prof David Van Heel, Prof Jane Worthington

Animal Models of Genetic Disorders - Dr Tamar R Grossman, Dr Ferenc Mueller, Dr Lyle Zimmerman

Clinical Management of Genetic Disorders - Dr Susan Huson, Dr Glenda J Sobey, Prof Phil Beales

Cancer pathogenesis and genomic architecture - Dr Peter Campbell, Dr Lyndal Kearney, Prof Thorsten Zenz

NeuroGenetics - Dr Lisenka Vissers, Prof Sanjay Sisodiya, Prof David Skuse

Treatment Strategies for Genetic Disorders - Dr Simon Jones, Prof Irwin McLean, Dr James Bainbridge

Workshops:

Novel Insights into the Genetics of Acute Lymphoblastic Leukaemia and Myeloproliferative Neoplasms - Prof Nick Cross, Prof Christine Harrison, Dr Amy Sherborne, Dr Lisa Russell

Variable phenotypes in genetic conditions - Implications for genetic counselling - Prof Jeremy Turk, Prof Robert Stockley, Dr David Honeybourne, Dr Nils Krone

Somatic Mutation detection in the context of targeted therapies – Prof Tim Maughan, Dr Clive Mulatero

Neurodevelopmental Disorders - Dr Hayley Archer, Prof Jill Clayton-Smith, Dr Jeanne Amiel

Education:

Clinical Trials

Next Generation Sequencing

Debate: **"This house believes that Synthetic Biology should be used to design new forms of life"** Prof Alison Metcalfe, Dr Chris French, Prof Paul Martin, Dr Ainsley Newson

Plenary and concurrent sessions from submitted papers

Further Information from:

The Conference Office, British Society for Human Genetics, Clinical Genetics Unit, Birmingham Women's Hospital, Edgbaston, Birmingham B15 2TG.
Tel: +44 (0)121 627 2634 Fax: +44 (0)121 623 6971 Email: bshg@bshg.org.uk
Website: www.bshg.org.uk
Registered Charity No. 1058821

British Society for Human Genetics Annual General Meeting

Monday 5 September 2011 at 17:30 at the British Human Genetics Conference to be held at the University of Warwick

Agenda

1. Chairman's Report

2. General Secretary's Report

3. Treasurer's Report

4. Conference Organiser's Report

5. Any other business

If there are any matters which members wish to raise would they please send them to the General Secretary, Dr Chirag Patel, Clinical Genetics Unit, Birmingham Women's Hospital, Edgbaston, Birmingham. B15 2TG by Monday 8 August 2011 email: chirag.patel@bwhct.nhs.uk

Welcome to New Members

24 new members were elected to the British Society for Human Genetics in January 2011

Mr Alaa Ali Alhazmi	CGG
Dr Kate Baker	CGS
Miss Harvinder Bangar	BSHG
Miss Hayley Elizabeth Bennett	Lab Trainees
Dr Claire Bonshek	CGS
Mrs Veronica Buchanan	ACC
Ms Alice Callard	AGNC/CGG
Dr Rachel Ann Clark	Lab Trainees
Miss Melissa Connolly	Lab Trainees
Miss Annet Damhuis	CMGS
Miss Modupe Esubiyi	CMGS
Mr Adam Colin Gunning	CMGS/CGG
Mrs Nichola Hart-Holden	CMGS
Miss Lucinda Hordley	CMGS
Mrs Lowri Hughes	Lab Trainees
Dr Chloe Mak	CMGS/CGG/SGPPH
Ms Joanne E Morgan	CMGS
Mr Brendan Mullaney	CMGS
Miss Roopal Patel	CMGS
Dr Nicola Ragge	CGS
Mr Wesley James Simpson	CMGS
Dr Alice Stellman	CGS
Mrs Leanne Sian Willoughby	ACC
Miss Izabela Wojcik	Lab Trainees

Travel awards

How to apply for Travel Awards

The Travel Award is for current members who have been a member of the Society for at least one year, for travel to overseas conferences, meetings, etc. There are no travel awards available to attend UK based conferences.

It is highly unlikely that retrospective awards will be given.

Applications should be sent to Mrs Dina Kotecha, the Society's administrator in Birmingham, with the applicant's date of birth stated. There is no set form but please give as much information as possible, and if you have submitted or had an abstract accepted please enclose a copy indicating whether it is a spoken or poster presentation. It will be treated in strict confidence.

Priority will be given to young investigators presenting results at major meetings.

Applications should state the benefit of the award to the applicant, and should clearly explain the part the applicant played in the work. A further award will not be made to a successful applicant within three years.

A small review committee has been formed to review applications for these awards. There are four deadlines per year for applications:

1 January	1 April
1 July	1 October

The successful applicant will be expected to write a brief report for the BSHG newsletter and may be asked to present the work at one of the Society's meetings.

Conference reports

American College of Medical Genetics Annual Meeting, 16-20 March 2011, Vancouver, BC, Canada

Sara Levene, Guy's

The meeting was held in Vancouver at its Harbourside convention centre, overlooking the water and mountains beyond. The breathtaking views and lovely city made it a great conference location.

The meeting included much discussion of genomics and whole genome analysis and their use in clinical practice. As a clinician from the UK, I felt at times that I had landed on another planet amongst colleagues who seemed not to bat an eyelid at the suggestion of using whole genome sequencing in newborn screening! There were a number of highlights of the conference for me, and this included a lecture on translational genomics and health outcomes as a new research discipline. There was also a very interesting symposium on chromosomal mosaicism, which highlighted a shocking finding from research on rejected PGD embryos, that most human cleavage stage embryos contain chromosomally unbalanced blastomeres.

I was very lucky to able attend this meeting, and was grateful to the BSHG for a travel grant in order to present my abstract entitled 'Jewish Genetic Disease Screening in the UK, Rational or Rationing?' My own presentation was part of a wider symposium on global perspectives on screening for Jewish Genetic Diseases, and included speakers from the USA and Canada.

Forthcoming conferences

International meeting Genetics, epigenetics and evolution of sex chromosomes (French Genetics Society (SFG)/ Jacques Monod Institute, University Paris-Diderot): 9-10 June 2011

Venue: Paris, France
Website: http://www.sfgenetique.org

Fundamentals of next generation sequencing: 14 June 2011

Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: Public Sector £125.00 Early Bird (up to 30 April), Private Sector £175.00 (up to 30 April), Public Sector £200.00 (After 1 May), Private Sector £250.00 (After 1 May).
Contact: Angela Davies Tel: 0161 2763200, email: angela.davies2@cmft.nhs.uk or
Contact: Kate Mulryan Tel: 0161 2763205, email: kate.mulryan@cmft.nhs.uk

Next generation sequencing bioinformatics: 15 June 2011

Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: Public Sector £175.00 Early Bird (up to 30 April), Private Sector £225.00 (up to 30 April), Public Sector £225.00 (After 1 May), Private Sector £275.00 (After 1 May).
Contact: Angela Davies Tel: 0161 2763200, email: angela.davies2@cmft.nhs.uk or
Contact: Kate Mulryan Tel: 0161 2763205, email: kate.mulryan@cmft.nhs.uk

Next generation sequencing bioinformatics: 16 June 2011

Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: Public Sector £175.00 Early Bird (up to 30 April), Private Sector £225.00 (up to 30 April), Public Sector £225.00 (After 1 May), Private Sector £275.00 (After 1 May).
Contact: Angela Davies Tel: 0161 2763200, email: angela.davies2@cmft.nhs.uk or
Contact: Kate Mulryan Tel: 0161 2763205, email: kate.mulryan@cmft.nhs.uk

Familial breast cancer: family history & risk assessment: 22-24 June 2011

Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: £650.00
Contact: Kate Mulryan
Tel: 0161 2763205,
email: kate.mulryan@cmft.nhs.uk

7th ISABS Conference in forensic, anthropological and medical genetics and Mayo Clinic lectures in translational medicine: 20-24 June 2011

Venue: Bol, Island of Brač, Croatia
Contact: ISABS (info@isabs.hr)
Website: www.isabs.hr

(BSHG) British Human Genetics Conference: 5-7 September 2011

Venue: University of Warwick
Contact: Dina Kotecha
(bshg@bshg.org.uk)
Website: www.bshg.org.uk

(HGV2011) 12th International Meeting on Human Genome Variation and Complex Genome Analysis: 8-10 September 2011

Venue: Claremont Hotel Club and Spa, Berkeley, CA, USA
Website:
http://www.hgvmeeting.org/hgv2011

VII World Conference on Bioethics (SIBI): 19-22 September 2011

Venue: Gijón, Spain
Contact: International Society of Bioethics
Website: www.sibi.org

Bioinformatics for cytogeneticists and molecular geneticists: 20-22 September 2011
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: £275.00 Early Bird (up to 31 May), £325.00 (After 1 June).
Contact: Tom Hancocks Tel: 0161 9017190, email: tom.hancocks@cmft.nhs.uk

Intensive course - Publish or perish. Intensive course on research and publishing in the field of bioethics: 3-6 October 2011
Venue: Leuven, Belgium
Contact: Pascal Borry PhD and Chantal De Keersmaecker (chantal.dekeersmaecker@med.kuleuven.be)
Website: www.masterbioethics.org under Intensive Courses

12th International Congress of Human Genetics / ASHG American Society for Human Genetics annual meeting (ICHG/ASHG): 11-15 October 2011
Venue: Montreal, Canada
Contact: paulinem@ashg.org
Website: http://www.ichg2011.org/

Bioinformatics for clinical geneticists: October (date to be confirmed)
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Contact: Tom Hancocks Tel: 0161 9017190, email: tom.hancocks@cmft.nhs.uk

An Introduction to q-PCR: 3-4 November 2011
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Contact: Kate Mulryan Tel: 0161 2763205, email: kate.mulryan@cmft.nhs.uk

Fundamentals of next generation sequencing: 8 November 2011
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Contact: Angela Davies Tel: 0161 2763200, email: angela.davies2@cmft.nhs.uk or Kate Mulryan Tel: 0161 2763205, email: kate.mulryan@cmft.nhs.uk

Next generation sequencing bioinformatics: 9 November 2011
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Contact: Angela Davies Tel: 0161 2763200, email: angela.davies2@cmft.nhs.uk or Kate Mulryan Tel: 0161 2763205, email: kate.mulryan@cmft.nhs.uk

The Third Cardiff Symposium on Clinical Cardiovascular Genetics: 24-25 November 2011
Venue: Cardiff
Contact: Angela Burgess Email: burgessam@cf.ac.uk Tel: 029 2068 7267

Personalised medicine: 8 December 2011
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Contact: Kate Mulryan Tel: 0161 2763205, email: kate.mulryan@cmft.nhs.uk

Biomarkers in research and clinical practice: 9 December 2011
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Contact: Angela Davies Tel: 0161 2763200, email: angela.davies2@cmft.nhs.uk

An Introduction to miRNA and siRNA: 26-27 January 2012
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Contact: Kate Mulryan Tel: 0161 2763205, email: kate.mulryan@cmft.nhs.uk

British Human Genetics Conference: 17-19 September 2012
Venue: University of Warwick
Contact: Dina Kotecha (bshg@bshg.org.uk)
website: www.bshg.org.uk

BSHG News Editor

Deadline for contributions for next issue is 30 November 2011

BSHG Editor: Dr Helen Middleton-Price
Nowgen - A Centre for Genetics in Healthcare, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU

Tel: 0161 276 3210
Fax: 0161 276 4058
Email: helen.middleton-price@cmft.nhs.uk

Editorial

Welcome to the ACC section of the BSHG News. It feels a bit like in this issue we are sponsored by the CMGS but I will get to that later. Are you missing the hard copy? Why not print out a lab copy (double sided so as not to waste paper). Peruse it in the tearoom, or the banding room – if CPA will allow. I have now returned from maternity leave and it is Stuart's second edition. We should be completely on the ball but we are still only human (honest).

We have another good selection of articles this issue so many thanks to all who contributed.

Our lead article covers the proposed merger of the ACC and CMGS. This is the first of many articles which will be informative to the CMGS readership as well as cytogeneticists. It comes at an important time for these two converging disciplines as members should have been balloted by the time our next issue is released in January 2012. Check it out for the joint web page address to keep you up to date.

On a similar theme we have an interesting article from Jonathan Waters about the evolution of Royal College of Pathologists (RCPath) examinations. This outlines the situation with the cytogenetics and molecular genetics sub-disciplines amongst other changes. In addition, see the RCPath website www.rcpath.org for sample short answer questions from the clinical genetics exam to get an idea of the new format even though they are a bit more clinical.

NHS Scientist Training Programme (STP) trainee Amy Llewellyn gives us a conference report for what was a very successful joint spring meeting. The abstract booklet, presentations and posters are all available at the spring meeting website www.springmeeting.cytogenetics.org.uk/

Thanks go to Duncan Baker from the Sheffield cytogenetics laboratory who brings us their Cytovision experience and the UKCCG for two articles covering their background and current news.

There are two articles of specific interest to the genetic technologist readership. The first is advanced warning of the annual genetic technologist (GT) meeting, calling for presentation ideas and perhaps more importantly for discussion topics. The second is some positive preliminary news from the GT survey.

Finally, young, fit and enthusiastic STP trainees are running for a charity close to our hearts and Stu brings in the news matrix.

Enjoy this bumper edition and keep the articles coming! Don't forget to use the resources available to you including the ACC discussion forum which remains open and will be a great tool for UK labs if we are not afraid to use it www.geneticstraining.org.uk/forum/

Hazel

More about the proposal to merge ACC and CMGS

Angela Douglas and David Baty

An article in the last BSHG news (issue 44) outlined the increased collaboration between the ACC and CMGS and the benefits of a single professional body. This article aims to elaborate further on where we go from here.

If the memberships approve through ballots of the 'special resolution' to dissolve the current societies, ACC and CMGS will be dissolved and replaced with a new professional body and we will merge the memberships.

In order to proceed we need the following: Consent from two-thirds (66.7%) of CMGS members attending an annual or extraordinary meeting. The ballot is to take place at an extraordinary meeting at the BSHG conference in September and proxy voting will apply to this meeting.

Consent from three-fourths (75%) of ACC members, testified by their signatures, to an instrument of dissolution in the form prescribed by the Treasury Regulations. A postal ballot will take place between May and September and proxy voting will apply to this postal ballot.

If the memberships agree to the dissolution of the current bodies:

- A new 'shadow' organisation will be set up
- The executive committee of the new organisation will be initially formed from existing executive members of ACC and CMGS

Association for Clinical Cytogenetics

CMGS Clinical Molecular Genetics Society

Examinations in genetics – update

Jonathan Waters PhD FRCPath waterj@gosh.nhs.uk
Chair RCPath SAC for Genetics and Clinical Embryology

- This interim committee will run alongside the existing ACC and CMGS executive committees and be tasked with the details of winding down the ACC and CMGS and establishing the new professional body.

The aim is to launch the new body at the Joint Spring meeting in 2012 (Birmingham). The new body will be a charitable organisation and possible names will be sought from the current memberships. The executive will choose a name from the members proposed names.

The new executive team will comprise 12 members serving a three year term of office: Five Office Bearers (Execs); Chair, Deputy Chair, Treasurer, Secretary, Deputy (Membership) Secretary and seven Ordinary Members; 5 of which will hold responsibility as Chairs for the following subgroups:

1. Genetics Education and Training (exists)
2. Professional Best Practice and Audit
3. Scientific
4. Communication
5. Bioinformatics and Information (exists)

The future Chairs shall be elected from one of the residing committee members by the committee members, the rest of the committee members to be elected from the membership by membership.

Engagement with the membership is imperative. A joint web page has now been set up providing a forum to post information about the process for comments, suggestions and questions http://www.geneticlabs.org.uk/

Currently there are a number of drivers for change for examinations in genetics for Fellowship of the Royal College of Pathologists (FRCPath). The Specialty Advisory Committee (SAC) for Genetics and Clinical Embryology at the Royal College of Pathologists (RCPath) is responsible for advising the college on the content, scope and format of examinations in genetics. This article aims to summarise the current situation from the SAC perspective. The drivers for change are:

a) Modernising Scientific Careers (MSC) and in particular the requirements of the Genetics Healthcare Scientist Training Programme (STP)

This programme aims to provide comprehensive training across both cytogenetics and molecular genetics and to provide an understanding and awareness of how genetics fits into patient care pathways.

b) The 'convergence' of the sub-disciplines of cytogenetics and molecular genetics

The convergence of the two sub-disciplines is well recognised with increasing overlap in technologies and increasingly sophisticated use of information technology.

To meet the requirements of both a) and b) a single FRCPath Part 1 examination will be offered in genetics from spring 2015. This will replace the existing separate Part 1 examinations in cytogenetics and molecular genetics. There will be sufficient flexibility to cater for those trained via MSC Higher Specialist Training (HST) as well as for those whose training has been acquired within the existing sub-disciplines. The Part 2 viva component of the examination will also (and in fact already does) reflect this convergence.

In addition, there is increasing use of shared questions between cytogenetics and molecular genetics as we move toward a single examination. There will be a move away from essay questions to short answer questions in the written paper and a greater use of computer-based scenarios in the practical examination is being explored with the College.

c) FRCPath in the 'molecular pathology of acquired disease'

The college has identified a need for a clinical scientist cohort within pathology who are trained and qualified to FRCPath level in the application and interpretation of technologies (genomics, metabolomics and proteomics) in acquired disease. Development of this is a separate piece of work with input from significant stakeholders at the College outside genetics – notably in histopathology. This examination could be appropriate for scientists in genetics laboratories who specialise, or wish to specialise, in the genetics of acquired disorders. It must be emphasised that this examination is some way off and may not ultimately be

Examinations in genetics – update cont

sufficiently flexible to accommodate multiple entry routes.

d) Diploma-level examination in 'laboratory genetics for clinicians'

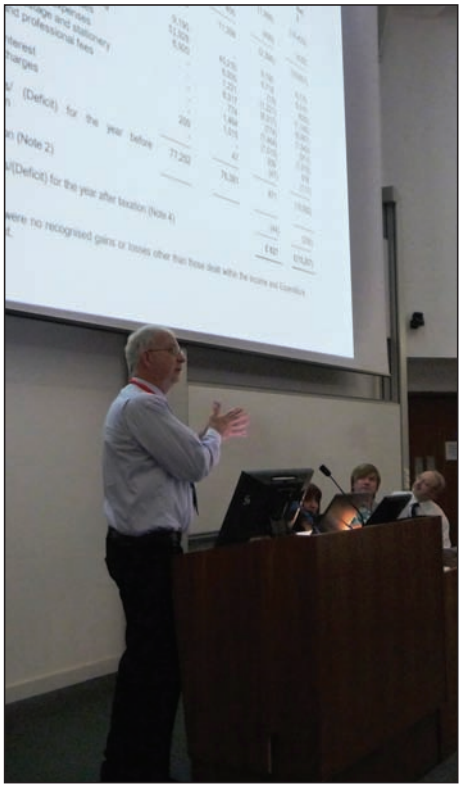
This examination is being developed to meet demand from clinical geneticists at the point of exit from their Royal College of Physicians (RCP) training who require an examination in genetics. The exam will be overseen jointly by RCP/RCPath and hosted by the RCPath.

I would like to acknowledge the help of Dr Fiona MacDonald who, as Chair of the Panel of Examiners in Genetics at the RCPath and a member of the SAC, has been particularly involved in these developments.

ACC/CMGS spring conference Durham 2011

Amy Llewellyn, STP Trainee, Nottingham

Like many people, Durham is a place I've often admired from afar. The striking Norman cathedral and nearby castle sit majestically on top of a hilly peninsula surrounded by the River Wear, captivating passing rail users. So I was delighted that the Northern Genetics Service chose Durham as the venue for this year's ACC/CMGS Spring Conference, giving me the opportunity to finally explore this historic University City. The occasion also provided a fitting finale to the career of legendary cytogeneticist, laboratory head and local resident Dr John Wolstenholme, who opened the proceedings with a brief history of the area.



We heard about St Cuthbert and the Prince Bishops, but rather more predictably, array CGH (aCGH) was the focus of many ACC talks with several speakers presenting their investigations into its application in prenatal and solid tissue analysis, with promising results. We were updated on the now well-established use of aCGH as a front-line test for patients with developmental delay in the Newcastle, Liverpool and Wessex labs, with the obvious benefit of increased diagnostic yield. The message from several speakers seemed to be that as (oligo) arrays are increasingly replacing karyotypes, the need to work closely with clinical geneticists to discuss results and share data is greater than ever.

As an STP trainee, I was interested to hear guest speaker Claudia Haferlach talk about the need to incorporate both cytogenetic and molecular techniques for the efficient risk classification and therapeutic stratification of haematological malignancies. Her talk and several others also mentioned the potential use of whole genome next generation sequencing (NGS) for the detection of genomic imbalances and balanced rearrangements, as well as detecting mutations at a molecular level. NGS seems to be highly applicable to diseases with a broad spectrum of mutations and may be particularly useful for tumour diagnosis as Adrienne Flanagan and later Graham Taylor both explained.

Antigoni Tzika seemed to be ahead of the game, with her assessment of the Illumina

GAII NGS platform for copy number analysis, which showed that it performs at least as well as aCGH. However, amongst all the talk of emerging technologies, Melody Tabiner's award winning presentation about her investigations into a complex 7;13;11 rearrangement reminded us that conventional karyotyping still has an important role in today's cytogenetics lab.

NGS featured heavily in the CMGS line-up. Over several talks we learnt about different methods for targeted enrichment, different NGS platforms and heard comparisons of analysis software. It was interesting to hear about the NGS services now available in Leeds and Oxford for BRCA, HNPCC and hypertrophic cardiomyopathy, and progress in the development of an NGS service for patients with X-linked learning disabilities in Cambridge.

I find it really fascinating and heartening to hear about advances in the treatment of diseases we diagnose, so I particularly enjoyed the talk by guest speaker Kate Bushby on the latest treatment prospects for muscular dystrophy. Likewise, Doug Turnbull gave an interesting talk on mitochondrial disease and techniques to prevent its transmission while Jenna McLuskey spoke passionately about PGD successes in Scotland.

Other highlights included the talk by trainee prizewinner, Nicola Ibberson, who spoke about the use of hybrid mini-gene assays to confirm the pathogenicity of predicted splice site variants. I was impressed with the automated, barcoded and largely paperless STARLIMS workflows presented by Sian Ellard from the Exeter lab.

The two conference dinners took place in the Great Hall of Durham Castle, a superbly Hogwarts-esque venue. Afterwards the ceilidh dancing got everyone on their feet and some people on the floor. This year's conference may have been the last of its kind, as the ACC and CMGS will soon be joining forces to form a single unified society, provided they get the votes from their membership. Could next year's meeting in Birmingham finally see the 'cytos' and 'molecules' officially integrated, sharing conversation and ideas over the conference dinner table? Clearly collaborations already exist: cytogenetics and molecular genetics trainees from St. George's (Mala Vast and Mariana Grobler) presented their joint project to compare FISH and MLPA for 1p19q deletion testing in oligodendroglial tumours. A nice example of multidisciplinary team working, combining the skills of histopathology and neuropathology with both genetics disciplines.

The mood of the conference was strongly in favour of the merger. It makes sense to me as a hybrid trainee; I routinely suffer from an identity crisis. It seems clear that both disciplines face similar challenges for the future: how can we quickly and confidently interpret the variation we are picking up as our use of high-resolution arrays and NGS rapidly increases? How will we cope with the onslaught of data and will those of us without informatics training be able to keep up?

Many thanks to everyone at the Northern Genetics Service for putting together such a rich and varied programme and thanks to my labs in Nottingham for enabling me to attend the whole week.

Sheffield diagnostic genetic services experience with the Genetix Cytovision GSL-120 scanning system

Duncan Baker

Never a lab to shy away from change, Sheffield brought in the GSL-120 Image Analysis system in September 2010. There were high hopes for tackling our sizable postnatal backlogs and consequently relieving work pressures in other areas. We firstly assembled a small team to understand the machine in detail and supervise its introduction, as it was felt that the wisest approach was to limit the number of people modifying the system. This started with one week of initial training with Genetix, and then we were left to play with it and get some validation tests done before a second visit. We had already been using the Cytovision manual capture technology so were familiar with some aspects of the system. We found the new aspects user friendly and not too brain straining to understand and use.

The machine itself has been hidden away in the darkest corner of the FISH dark room, and now any FISH analysis done using a microscope is performed with the accompaniment of the rattling and whirring of the scanner which runs for most of the day and all night.

The G-band postnatal analysis had the largest backlog and we targeted this area for validation first. We tested it on the most subtle abnormals and low level mosaics available to us. Postnatal blood analysis went live in November with metaphase FISH analysis close behind. Our cell selector (classifier) appears to be working well and with a pre-analysis karyotyping step added to our procedures the time taken to analyse has reduced significantly. The backlog is steadily decreasing and analysts are now spending more time helping to relieve work pressures in other areas, to spread the benefit of the image analysis system. We haven't made the step to a paperless analysis system but the system does enable us to do so and we are moving in that direction.

The one downside I can think of is that the appearance of 10 large monitors for cytovision analysis has reduced our own personal desk space. If you are tidy this is ok, if you are like me then it causes chaos!

One early concern was how well would staff take to the new method of analysing, would they be reluctant to give up the microscope? Fortunately, once people had received some training and were in front of the computer screen with nicely captured chromosomes they were soon converted and the analytical grumbles are now related to the occasional inconvenience of being reduced to finding cells down a microscope.

As with any computer system there are the occasional niggles, however with the help of Genetix staff and cytogeneticists from other labs with Cytovision experience to call on these have been kept to a minimum.

Interphase FISH has just gone live with some good quality images. Validation of bone marrows, amniotic fluids and solid tissues is nearly complete and planned to go live within a month. Meanwhile, my microscope is gathering dust.

For Sale: 30 well maintained microscopes!

In the spotlight – Leukaemia Research Cytogenetics Group

Dr Lucy Chilton, Leukaemia Research Cytogenetics Group, Northern Institute for Cancer Research

The UK Cancer Cytogenetic Group (UKCCG) was established in 1988 with the remit of improving leukaemia cytogenetics within the UK by bringing together the cancer cytogeneticists from all over the country to discuss developments and problems. A number of research projects were carried out, which led to joint publications from the group. In 1992, with funding from Leukaemia and Lymphoma Research (LLR), formerly Leukaemia Research Fund, Professor Lorna Secker-Walker formed the Leukaemia Research Cytogenetics Group. She also developed a bespoke database for the collection of cytogenetic information from patients registered on UK acute leukaemia treatment trials, backdated to 1990. Professor Christine Harrison became head of the group in 1997. From the original location at Royal Free Hospital, London, in 2001, the group moved to the Cancer Sciences Division, University of Southampton. In 2008 it moved again to its current location in the Northern Institute for Cancer Research, Newcastle University. Originally, from the collection of karyograms, the group reinterpreted karyotypes from these patients and stored the information in the database. Currently this database holds cytogenetic, genetic and clinical information on around 27,000 patients. Over the years, the research of the group has expanded to include state-of-the-art technologies, fluorescence in situ hybridisation (FISH), multiplex ligation-dependent probe amplification (MLPA), array-based comparative genomic hybridisation (aCGH) and recently, next generation sequencing.

Leukaemia Research Cytogenetics Group Update

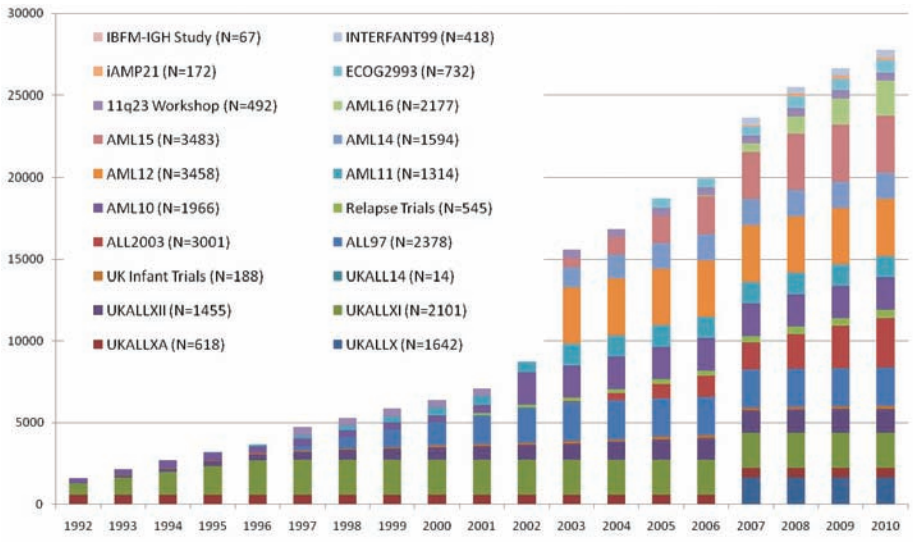
Dr Lucy Chilton, Leukaemia Research Cytogenetics Group, Northern Institute for Cancer Research

The group has an international reputation in leukaemia cytogenetics and has published widely in the field. The wealth of genetic information available within the database has allowed them to provide accurate incidences and prognostic information on established chromosomal abnormalities, as well as facilitating the discovery of novel genetic changes. One example was the identification of a new abnormality: intrachromosomal amplification of chromosome 21 (iAMP21). Children with this aberration were shown to have a poor outcome. Modified therapy for these patients has improved their prognosis in current trials. Professors Christine Harrison and Anthony Moorman have recently been awarded a new 5 year specialist programme grant from Leukaemia and Lymphoma Research to expand their research into the new treatment trials.

Thank you!

With the help of the UKCCG laboratories and the Clinical Trials Units the database has continued to grow. We currently have samples for 95% of patients enrolled on active trials. The completeness of the database has allowed us to continue our research and provide a resource to UKCCG members. We would like to take this opportunity to thank you all for your support.

Annual accrual of cases to the LRCG database



Cytokine receptor-like factor 2 (CRLF2) in ALL

We are continuing to investigate the role of CRLF2 deregulation in B-cell precursor (BCP)-ALL. We have recently published the outcome data for patients with CRLF2 deregulation in relation to other chromosomal abnormalities in childhood BCP-ALL (Ensor HM, Schwab CJ, Russell LJ et al. Blood 2010). We are currently looking at associated deletions involving B-cell differentiation genes and cell cycle control genes and the clonal heterogeneity of these deletions within leukaemic samples. We are also, as part of a successful fellowship application, developing functional assays to assess the biological functions of CRLF2 deregulation using human CD34 positive umbilical cord blood cells in in vitro and in vivo assays.

Leukaemia Research Cytogenetics Group Update cont

Screening for copy number changes in ALL

Following the publication of our pilot study using the P335 IKZF1 MLPA kit (Schwab et al, Genes Chromosomes Cancer, 49(12):1104-13), we have now screened more than 1000 paediatric BCP-ALL and 300 Philadelphia negative adult ALL samples for copy number abnormalities in genes previously reported to be of interest in BCP-ALL. Manuscripts are now in preparation reporting the incidence, association with cytogenetic subgroups and prognostic significance of these findings. In particular, we are investigating the role of IKZF1, which has been associated with a poor outcome in a number of studies.

In vivo oncogenomic screening strategies

This is a five year European Research Council funded project which commenced in May 2010. Our primary objective is to develop high throughput functional screens to identify important driver oncogenes and tumour suppressors where other techniques have implicated a large number of candidates. In our initial experiments we have established models of leukaemia from cells carrying deletions of 6q and iAMP21, abnormalities that are thought to harbour respectively novel tumour suppressor genes and oncogenes. To date, we have demonstrated that these transplanted cells can express GFP and luciferase from integrated lentivirus constructs, which will allow us to monitor their progression in vivo.

Further characterisation of iAMP21

Our search for the initiating mechanism in iAMP21 continues with whole exome and paired end sequencing of a single patient.

ALL Trials

Infants under 1 year of age can now be registered on the INTERFANT 06 Study. There has been a good response to date, with 27 patients entered so far.

The amended adult MRD-ALL Study is recruiting well.

UKALL14 has recently opened and includes risk stratification based on cytogenetics.

UKCCG meeting 2011

John Swansbury, The Royal Marsden Hospital & The Institute of Cancer Research

The 33rd meeting of the United Kingdom Cancer Cytogenetics Group was held in Newcastle on 15 and 16 March 2011. The two-day format was as successful as it had been when first used in 2010, with no shortage of excellent material and presentations. There is no other UK meeting to match it for interest and relevance, and this is reflected in its popularity and attendance. The profession must record its thanks to Leukaemia & Lymphoma Research (LLR, formerly the Leukaemia Research Fund) which provides substantial financial support, such that there is no charge to attend, and that one delegate from each lab has their expenses met. Other welcome financial support came from Genetix, NECCR and OGT, again being evidence of the importance of this gathering.

The European guest lecture was given by Dr Alex Kohlmann, Munich: 'Next-generation sequencing in myeloid malignancies: Perspectives from daily routine diagnostic operations.' Other guest lectures were given by Dr Jacqueline Boultwood (LRF Molecular Haematology Unit, Oxford), Dr Duncan Baird (Medical Genetics, Haematology and Pathology, Cardiff), Professor David Grimwade (King's College, London) Dr Roberta La Starza (University of Perugia, Italy) and Professor Steve O'Brien (Royal Victoria Infirmary, Newcastle upon Tyne). A different insight was provided by Dr Simon Bailey (RVA, Newcastle upon Tyne) describing the very limited resources available to treat children's cancer in Malawi: a telling statistic was that

UKCCG meeting 2011 cont

he has devised a treatment for Burkitt lymphoma that costs around £100 and will save around 40% of cases, compared to a cost of more than £75,000 in the UK, which saves many more.

The other presentations came from within the profession, and were no less interesting. Many of these came from the home of the UKCCG, the LLR Cytogenetics Centre in Newcastle, headed by Professor Christine Harrison. The LLR supports the UKCCG meetings in recognition of the data and material that UK labs provide to Christine's unit and her team uses this to undertake a truly impressive range of research leading to a wide range of publications. Some of this work has a direct impact on trials and treatment, which is a great side-benefit from the diagnostic studies that are routinely done in our labs. Equally welcome are the various case studies and presentations from labs around the UK.

There is a slight discrepancy between the name (UKCCG) and the product, in that the great majority of the content is haematological and rather little comes from other cancers. To some extent this is inevitable, given that the majority of routine diagnostic cytogenetics in the UK is still based in haemato-oncology. However, expansion into other cancer types is accelerating, and no doubt the UKCCG and its meetings will continue to grow in popularity, variety and significance.

Talks from the 2011 meeting are available here: http://research.ncl.ac.uk/lrcg/

UKCCG 2011: Anthony Moorman (LLR) and Roberta La Starza (Italy) talk shop

Annual meeting for Genetic Technologists/ Practitioners: October 2011

Association for Clinical Cytogenetics

CMGS CLINICAL MOLECULAR GENETICS SOCIETY

The Annual Meeting for Genetic Technologists/Practitioners will be hosted in Newcastle this year in October with an actual date still to be arranged. It is open to all genetic technologists/practitioners working in cytogenetics and molecular genetics departments.

Proposed format: A morning of troubleshooting based forums with feedback and follow up via the discussion board http://geneticstraining.org.uk/forum/ and an afternoon of presentations.

Aim: To increase communication between labs up and down the country in order to share information on good practice more effectively. This will allow for better development of the services we offer.

Discussion forums: We propose a series of small focus groups to discuss ideas, problems and techniques that may benefit routine lab work. We would like to address problems that labs are actually experiencing. Please email suggested topics you would like to see included in the focus groups, for ideas of examples please see the flyer in the Spring Conference packs.

Presentations: Please think about any talks you might like to present as October is fast approaching.

The success of this event relies upon input from colleagues now. Please support and encourage any ideas for discussion or presentation amongst your staff.

Venue: Newcastle upon Tyne

Contact: Simon Cammack, Northern Genetics Service, Institute of Human Genetics, Central Parkway, Newcastle upon Tyne, NE1 3BZ Tel: 0191 241 8803

Email: Simon.Cammack@nuth.nhs.uk

Brief news from the Associated Genetic Technologists Committee (AGTC) survey 2011

Anne Reilly (AGTC Chair)

A survey of Genetic Technologist (GT) staff was undertaken over February and March 2011. This was very successful and we would like to thank all those who took part. We had over 200 responses and we are currently evaluating the data. This will help us to ascertain more accurate figures on a number of issues: how many GTs are members of the ACC or CMGS; how many GTs are registered with the Voluntary Registration Council; what GTs would like their professional bodies to do for them and what more can be done to encourage GTs to join a professional body and become registered.

In summary, the number of Genetic Technologists joining a professional body is continuing to grow with approximately 45% of GTs now members of either the ACC or the CMGS.

The number of Genetic Technologist joining the voluntary register also continues to rise; there are currently 149 Genetic Technologists on the voluntary register (figures last updated October 2010).

The information gathered from this survey should help support our application to HPC or other registration/accreditation body.

Unique running opportunity

Celia Brown (London)

The frequent trips to Nottingham to attend lectures have been a great way for us MSC Healthcare Scientist trainees to get to know each other. In addition to the odd post-lecture drink or trip to Pizza Express, a group of us began to go running together. It all started quite by accident as we passed each other jogging along the canal or stretching in the Premier Inn car park and the idea was formed to start a running group for when we were in Nottingham. Soon we had amassed 5 or 6 regulars and it was after a few enthusiastic outings that we got the adrenaline-fuelled idea of entering a running event together. Pretty soon this idea had spiralled into entering the Great North Run half marathon no less, to raise money for the charity Unique.

Unique running opportunity cont

Many of us have volunteered for Unique and experienced first hand the vital work they do supporting, informing and bringing together individuals and families affected by rare chromosomal disorders. The study days that they run prove a rare opportunity for individuals and their families to meet and gain information and support from healthcare professionals and each other. We all felt fundraising together could help us raise as much money as possible for this great charity. It's going to take a lot of blood, sweat and tears to make it through 13.1 miles so please give us lots of incentive and sponsor us. You can visit our fundraising page at www.virginmoneygiving.com/team/STPrunningteam. Also look out for us on the day we'll be in Unique yellow!!

Thanks for your support from the STP running team:

Celia Brown (London)
Philip Dean (Bristol)
James Eden (Birmingham)
Amy Llewellyn (Nottingham)
Maha Younes (Sheffield)

News matrix

ArrayCGH embryo screening success
Italian scientists have reported a 70% clinical pregnancy rate using arrayCGH to screen embryos in patients with recurrent miscarriage arising from parental balanced rearrangements.

www.cambridgenetwork.co.uk/news/article/default.aspx?objid=81524

Review calls for the use of arrays in autistic spectrum disorder
A review of 507 children from Kirch Developmental Services Center in Rochester, US with autistic spectrum disorder has found abnormalities in 2.3% after karyotyping and in 0.04% following fragile X DNA analysis prompting the authors to call for the use of frontline arrays in this patient cohort…

www.ncbi.nlm.nih.gov/pubmed/21525079

…particularly given the 7% abnormality rate reported by the multi-centre Autism Consortium last year using arrayCGH.

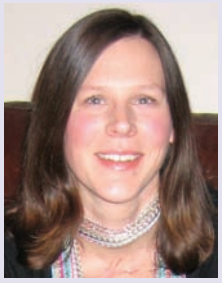
www.ncbi.nlm.nih.gov/pubmed/20231187

Combined 22q11.1-q11.21 deletion with 15q11.2-q13.3 duplication identified by array-CGH in a 6 year old boy
Greek scientists have reported a deletion associated with DiGeorge syndrome co-existing with a duplication of 15q11.2-q13.3 (associated with a syndrome in its own right), in a 6-year-old boy presenting with growth retardation, dysmorphic features and learning difficulties.

www.moleculartcytogenetics.org/content/4/1/6

Stem cell lines show high genetic variation
An international collaboration has shown that both embryonic and induced pluripotent stem cells show a greater degree of genomic variation than other cell types in culture, with cells rapidly acquiring profound gains and losses during differentiation and reprogramming, calling into question their stability and clinical safety in human trials.

http://www.bionews.org.uk/page_86148.asp



ACC News Editors

Deadline for contributions for next issue is 30 November 2011

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Editorial

Welcome to the AGNC section of BSHG News. In this edition Laura Boyes reports back on the AGNC census results. If you want to know what percent of the 168 responding genetic counsellors are Registered and how many of us are doing home visits then read on. It's also good to note that in recognition of increasingly constrained NHS funding, the AGNC are offering more study awards to enable GC's to attend meetings and conferences.

This issue's genetics centre in focus is Sheffield. I'm intrigued to see that they are based in two charming Victorian houses and were originally set up in 1963. For those of us in big NHS blocks this looks delightful. Thanks to Judy Tocher for revealing how they work and reminding us who is who.

See this issue also for updates from the Genetic Counsellor Registration Board (GCRB) on newly registered GC's and changes to the Registration process. This edition also includes summaries of the talks and social events at the very successful Spring Meeting in Belfast in April. Please note next year's meeting is planned for Tuesday, 17 April 2012 here in Cambridge. Why not make a weekend of it and do some college visiting and punting beforehand? You can even get to see the site where Watson and Crick (with the crucial help of Rosalind Franklin) worked out the structure of DNA in 1953 and have a drink in the pub they went to celebrate in.

Vicki Wiles, Cambridge

AGNC update

Laura Boyes, AGNC Committee

Since our last newsletter Aoife Bradley and the team in Belfast hosted a fantastic two day spring meeting. Thank you for your hard work arranging such a rich and diverse programme and for organising the glorious sunshine. There was an impressive array of presentations both from locals and from our talented membership. Look out for a more detailed conference report in this newsletter.

Spring Meeting 2012
We are delighted that the team at Cambridge have volunteered to host the one-day 2012 AGNC spring meeting. The planned date is Tuesday, April 17.

The British Human Genetics Conference
(Warwick 5-7 September) is fast approaching. With symposia including 'the ethical and psychosocial impact of emerging technologies' and 'the variable phenotypes of Mendelian conditions', we hope many genetic counsellors will be able to attend. This year we are offering an increased number of AGNC travel awards to facilitate attendance at conferences in these lean times. Each award is for £100, to be used towards travel or registration fees. If an excess of applications is received, priority will be given to applicants giving a spoken or poster presentation but historically there have been relatively few applications for these awards, so we'd encourage AGNC members to apply.

Representation on external committees
We would like to thank all those who have volunteered to represent the AGNC on various external bodies. Your enthusiasm and the commitment of your time are very much appreciated. Jessica Shearn from Southampton will be the additional representative on the Clinical Governance Committee and Glen Brice from St Georges,

AGNC update cont

London will be our representative on the United Kingdom Genetic Testing Network (UKGTN). The AGNC has been invited to have representation on the Human Genome Strategy Group. Chris Patch has agreed to represent the AGNC on the Service development working group and Georgie Hall will represent the profession on the Education, Engagement and Training working group. The AGNC would like to acknowledge and thank Naz Khan, Genetic Counsellor from Manchester for her contribution to these groups.

Census results

Thank you also to all who completed the AGNC census this year. Anita Bruce presented the results at the AGM in Belfast and a full report will be available on the AGNC website shortly. The 168 responses showed we are a diverse group with an approximately even number of genetic counsellors with an MSc and an experiential background in nursing, midwifery, health visiting or social work. Just over half of responders are GCRB registered and just less than a quarter are GCRB mentors/assessors. 28% (and 45% of those from an MSc background) are not union members. We would advise individuals to be members of a union for your own protection and support.

We revised some of the questions this year to help determine whether GC's roles are changing. Here are some highlights from the responses:

- Two-thirds of us have a mixed cancer and general clinical workload, with most having at least a 40% contribution from each.
- For GC's who undertake prenatal work, three-quarters estimate it to be up to 10% of their work.
- Many undertake additional activities such as research, education and management. This usually constitutes up to 10% of overall work but for some is significantly more.
- Pre-clinic contact varies but for the majority is less than 10% of their clinical work. One quarter undertake no pre-clinic work.
- For three-quarters, GC only appointments comprise more than 40% of their clinical work. For one-third it is >90%.
- Home visits appear to be rare for 95% of us and two-thirds undertake little co-counselling.

We also asked for your thoughts on use of the AGNC email group. You told us it was a useful forum for sharing ideas and practices and gaining support from each other. We'd like to encourage everyone to use it in this way, to feel safe in doing so and to be receptive to others' enquiries. We explored a suggestion for a discussion forum on the AGNC website but this is unlikely to be practical to use or manage. Hopefully you don't find it too onerous to ignore or delete emails less relevant to you.

It is inspiring and heartening to see the valuable work taking place throughout our profession, particularly when many are facing difficult times in the NHS, universities and allied organisations. Now, as ever, it seems particularly important to support development; personally, within your centre and in the genetics community as a whole, as we all work to promote and protect our genetics services for patients in the future.

Profile of Sheffield Clinical Genetic Service

Judy Tocher, Sheffield

The early years

It all started in 1959 when Dr Eric Blank came to Sheffield to take up the post of Reader in Medical Genetics. In 1963, in collaboration with the university, he established the Centre for Human Genetics. This was the first joint university-hospital venture of its kind in the country. Initially they performed chromosome analysis, and later provided a clinical service with genetic counselling, for the old North Trent region. The first genetic nurse employed was Margaret Johnson. The clinical service expanded in 1990 with the appointment of Dr Oliver Quarrell and two genetic nurses, Alyson Bradbury and Carol Giblin.

Population

The service now covers a population of 1.8 million and serves South Yorkshire, North-East Derbyshire, North Nottinghamshire and North Lincolnshire. Our department is part of Sheffield Children's NHS Foundation Trust, with offices located in two large stone built Victorian houses on the main Sheffield Children's Hospital site.

Staff

Currently there are four full time consultants:

- Dr Jackie Cook
- Dr Oliver Quarrell
- Dr Michael Parker
- Dr Diana Johnson

Dr Sobey, Consultant Dermatologist, is based in the department and runs the Elhers Danlos syndrome (EDS) service.

We have two SPRs:

- Dr Lisa Robertson
- Dr Meena Balasubramanian

There are seven genetic counsellors/genetic nurse specialists, working a mixture of full and part time hours, equating to 5.4 wte genetic counsellors.

- Alyson Bradbury (Current Clinical Lead)
- Jessica Bowen (Registered)
- Helen Fairtlough
- Helen Howie
- Sharon Pagdin
- Judy Tocher (Registered)
- Leanne Mercer (Registered in USA and Canada)

- Nicola Crawford: Clinical Genetics Manager
- Cathryn Dow: Cancer Co-ordinator
- Joanne Lemmon: EDS service Co-ordinator
- Louise Nevitt: Clinical Research Officer
- Kirsty O'Donovan: DENDRON Research Assistant
- Nadia Pepper: Research Assistant/ Monitor for Euro HD Registry

We are all supported by an excellent administrative team.

Consultants: Left to right – Oliver Quarrell, Jackie Cook (white top), Glenda Sobey (blue scarf), Diana Johnson (brown shirt)

Genetic counsellors: Left to right back row – Jessica Bowen, Helen Howie, Judy Tocher
Left to right front row – Alyson Bradbury, Helen Fairtlough

"As in all departments, the role of the genetic counsellor has evolved and changed over the years"

Map of clinic locations

Clinics

We hold clinics in Sheffield and regional district general hospitals, with the furthest located 75 miles away.

Specialist clinics

We are involved in an ever increasing number of multidisciplinary clinics. Specialist clinics currently attended by a consultant or genetic counsellor include:

- Eye clinic
- Renal clinic
- Cleft lip and palate clinic
- Paediatric polyposis clinic
- Skeletal dysplasia clinic
- NF2 clinic
- NF1 clinic
- MEN clinic
- Oncology gynaecology clinic

We hold a weekly joint prenatal clinic with the fetomaternal medicine unit and are a satellite clinic for Guy's hospital PGD service.

In addition the department hosts the northern branch of the Ehlers Danlos syndrome National Diagnostic Service, headed by Dr Glenda Sobey with one wte genetic counsellor post shared between Jessica Bowen and Judy Tocher. Children and adults with suspected complex EDS are referred with an aim of establishing the diagnosis more effectively and providing holistic care for this challenging group of conditions.

We have a monthly meeting with the South Yorkshire Regional Inherited Cardiac Conditions Service. Cases are discussed so that the most appropriate care is offered to streamline cardiac screening and genetic testing.

Closer links with the histopathologists have led to a monthly case discussion meeting. Consultants attend regular Paediatric Neurogenetic & Paediatric Neurodisability Multi Disciplinary Team meetings.

Laboratories

The Cytogentics and DNA laboratories are located nearby in the main hospital and have recently merged to become the Sheffield Diagnostic Genetic Service.

The Role of the Genetic Counsellors

As in all departments, the role of the genetic counsellor has evolved and changed over the years. We hold a weekly new referrals meeting to discuss cases and allocated them appropriately. Some cases are brought straight to a clinic appointment; others have a pre-clinic telephone call from one of the genetic counsellors. A small number of cases, with specific clinical need, receive a home visit and we are active in trying to maintain this. In addition we hold a separate weekly cancer genetics meeting to discuss the cancer referrals.

The genetic counsellors co-counsel in some Consultant led clinics and also run our own GC led clinics, with a mixed caseload of both cancer and general genetics. The genetic counsellors maintain a focus on the psychosocial aspects of genetic counselling, in both our pre-clinic work to prepare families before clinic and with follow up afterwards.

We have had two trainee genetic counsellors, both now in substantive posts. All the genetic counsellors were involved in mentoring or clinical supervision in some capacity. The whole department found this a valuable and worthwhile experience.

The genetic counsellors all actively participate in journal club, audit and contribute to the teaching activities of the department.

Genetic Counselling Registration Board (GCRB)

Aoife Bradley, Belfast

Congratulations to the following who registered in January 2011

Jessica Bowen
Claire Brooks
Hilda Crawford
Kim Dymant
Mabella Farrer
Theodora Gale
Ruth Glew
Hazel Hailey
Catherine Hartigan
Rupinder Jassi
Nasaim Khan
Peter Marks
Katherine May
Sara Pasalodos
Genevieve Say

The work of the GCRB continues apace, with the views of the profession and those undertaking registration and mentoring processes constantly being sought. The GCRB endeavours to grow and develop in line with feedback from the membership as well as continually auditing and evaluating the process to ensure registration is fair, robust and transparent. There are currently 151 Registered Genetic Counsellors.

Sign-Off Mentors

The role of mentors for candidates undergoing registration has changed. Mentors are now known as Sign-Off Mentors (SOM), and have an increased role in examination, observation and signing off work within the candidate's portfolios. Any Registered Genetic Counsellor (RGC) wishing to become a SOM must complete the Sign-Off Mentor training. SOM's should be RGC's with at least 5 years experience in a genetic counselling post and be easily accessible to the candidate (for example working in the same department, where possible). To act as a SOM they must also have completed the SOM training within two years prior to acting as SOM. Existing GCRB trained mentors will be able to perform the SOM role until 2013 to allow additional training to be completed. A list of SOM's is available on the GCRB website. A SOM training day in July 2011 is now fully subscribed but it is hoped to offer a further training day later in the year.

Counselling Courses

The GCRB would like to remind members of the AGNC of a change to the requirements for registration with regard to counselling courses for applicants applying under the Set B criteria. From 2012, at least 30 hours of counselling training must be obtained from an academically accredited course and the candidate must show evidence of having passed a formal assessment / examination as part of the course.

Reciprocity Guidelines

The GCRB would also like to let members know of changes to the Reciprocity guidelines for overseas applicants for registration. The guidelines and requirements are not greatly altered from the previous guidelines with the exception that SOM's will be required to observe five genetic counselling sessions / genetic outpatient appointments carried out by the applicant and will have to include their observations in their reference on the candidate. Updated guidelines and application forms for overseas applicants will shortly be available on the GCRB website. We will also be sending a representative to the Transnational Alliance for Genetic Counselling (TAGC) meeting in October this year to contribute to a better understanding of United Kingdom registration requirements internationally, and also to learn more about training and registration abroad.

Portfolio Assessments

The GCRB have changed the method used to evaluate portfolios to make the process more like the evaluation of academic courses which undergo external examination and evaluation. Candidates who submitted their portfolios on 1 April 2011 will be the first cohort undergoing the new registration process. Again, the changes instituted and the new assessment process will be fully evaluated and subject to change or alteration if necessary.

The GCRB members are listed below and further details are accessible on the GCRB website, www.gcrb.org.uk

Jan Moore (Chair); Barbara Stayner (Vice Chair); Lorna McLeish (Secretary); Lesley Snadden (Treasurer); Heather Skirton (Board Moderator); Gillian Scott (Company Secretary); Aoife Bradley, Diana Scotcher and Sally Watts (Members); Dr Melita Irving (Medical representative); Krystle Kontoh (Lay representative); Maureen Taylor (Board Administrator).

The AGNC Spring Conference 2011, Belfast

Aoife Bradley, Belfast

Well what can I say about the Spring Conference held on 7 and 8 April, 2011? After many months of planning and putting all together, the day finally dawned, and what dawns we had. Belfast definitely put her 'pretty skirts' on for our delegates from all over the UK and from as far away as Australia.

The format of the Conference was changed this year with regard to the plenary sessions, where the Organising Committee tried to choose a subject matter and give a number of presentations with sessions lasting 20 minutes each, instead of the hour usually given to plenary speakers. From the evaluation forms returned it would appear delegates found this format to be very suitable, feeling their attention spans were more than up to this. It also provided a showcase for many talented and interesting speakers whom the Organising Committee had found it very difficult to decide between.

Thursday commenced with papers presented by the membership. The Organising Committee had received so many excellent submissions that presenters had only 15 minutes to present their papers. Well done to all those who presented, and to the Chairs, who kept all sessions to time throughout the Conference - a feat in itself. From a personal point of view it is extremely difficult to pick a highlight as I enjoyed all of the presentations, but Lisa Jeffers certainly left me wanting to hear much more about her PhD findings. The two presentations by Anna Middleton and Gillian Crawford on incidental findings with regard to whole genome studies raised some interesting ethical points and issues. After lunch, in plenary session one, the highlight for me was Dr Melissa Hill's presentation on non-invasive prenatal diagnosis using cell free fetal DNA. Then, after a reviving cup of tea or coffee, plenary session two, with its emphasis on BRCA gene changes. The presentation by Dr Hinds was very insightful and interesting with regard to prophylactic surgery, Dr Quinn was enthusiastic and inspiring about her research work and Hazel Carson presented the patient perspective beautifully showing how her determination to help other BRCA carriers has culminated in the support group she has started in Northern Ireland.

Thursday night was the conference dinner. With one table of delegates trying to drink the central display on the table and another delegate trying to rope the hotel manager, Gary, into being the judge for a rather surreal competition (ye shall remain nameless here), as we would say here in Belfast 'the craic was 90'. Many delegates then decided to try some of the Belfast night-life. The Crown Bar, the oldest surviving bar in Belfast, was visited by many to sample some of the 'black stuff' as well as the atmosphere. Then, for those die-hards up to it, they were led to Fibber Magee's for a bit of traditional music and a hooley.

Friday, dawned bright and clear with yet more sunshine. Two whole days of good weather would you believe it! The plenary sessions on Friday morning, concentrating on cardiac genetics, lysosomal storage disorders and the Traveller Community were again too difficult to pick a highlight from. Special mention I feel must be made of the presentations by Dr McKee on the genes that built the pyramids and Dr Bradley on the Irish Giants – both amusing and educational. The presentations by the membership that afternoon were many and varied and again were of such a high standard I find it impossible to pick a favourite or highlight. Special mention should also be made of the posters submitted, all of which were of a very high standard, with the AGNC having a poster prize for the first time this year, which was won by Stephanie Oates, many congratulations.

Some delegates stayed on after the close to spend the weekend sampling other delights of Belfast and Northern Ireland. Many more said this was their first ever visit here but it certainly wouldn't be their last. All that remains for me to say is a big thank you to the AGNC Committee for their help and support with the Conference – but particularly – the hugest possible thanks to the genetic counselling team in Belfast who all worked hard to pull it together and make it such a success. Thank you ladies – and well done! I hope all those who attended enjoyed the Conference, the famous and infamous 'Norn Iron' hospitality and the craic.

AGNC Conference 2011- a trainee's perspective

Eshika Haque, Glasgow

On the 7 April 2011, a group of people known as genetic counsellors, descended upon a very sunny Belfast. This is because the Association of Genetic Nurses and Counsellors annual Spring Meeting was kindly hosted by our Belfast colleagues this year.

As a trainee genetic counsellor I feel that I learn the most from my colleagues. Therefore, though all the talks were thoroughly enjoyable, I felt that I benefitted the most from the papers and case studies that were presented by the membership. One also has to mention the fantastic talk given by Dr Fiona Stewart on the lysosomal storage disorders and the exciting work that Anna Middleton is currently undertaking with the Deciphering Developmental Disorders (DDD) project. The Glasgow Genetics Centre was also quite well represented with my colleagues Sarah Gibson, Mark Longmuir and Cathy Watt giving presentations on various cancer genetics related issues. It was interesting to hear about genetic counselling and the Irish travelling communities as I seldom get a chance to work with this particular ethnic group.

As a trainee genetic counsellor it is always nice to go to the AGNC conferences. Not only do you get to see other colleagues from different centres but you also get to meet people who are directly linked to your profession such as the cardiac nurse and Huntington's disease specialist, both of whom gave talks on their individual specialties in Belfast. It is nice to get a better understanding of how the different NHS specialties work together to give optimal service to our patients. I always feel very fortunate to go to these meetings and come away with a lot of valuable information that I hope will shape and better my practice as a genetic counsellor in the future. A big thank you to our Belfast colleagues for organising such a wonderful event.

New guide for families on breast cancer family history services

Ross Kester, Breakthrough Breast Cancer

Finding out about a family history of breast cancer and exploring management options can be a daunting process for some. To help, Breakthrough Breast Cancer has produced a single guide bringing together all the key information in one place. Their aim is for the guide to help women plan the management of their breast cancer risk in partnership with their family history or genetics team. This great guide combines national standards of services and care and what people can expect when accessing family history and genetics services in the UK with first-hand experiences of women who have used these services.

Order free copies for your service at breakthrough.org.uk/publications or 08080 100 200.

AGNC News Editor

Deadline for contributions for next issue is 30 November 2011

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Editorial

Well it's all change at the top of CGS, which allows me to say "wha gwan Mr President?", a phrase my two year old uses at every opportunity. A prize of a small amount of kudos goes to the person who recognises the origin of that quote. Indeed Mr President tells us what's going on later in this issue. I would like to add my voice to Peter's, and I am sure everyone else's in thanking Frances for the invaluable work she has given the society during her tenure.

Meanwhile, the National Commissioning Group (NCG) has clearly been using its money wisely, with news about more specialist clinics, for Bardet Biedl and Xeroderma Pigmentosum. Let us hope that the financial pressures on the NHS don't force this extremely valuable group to stop supporting more highly specialist, but valuable services. If there are other NCG-funded services, which have not yet publicised themselves in these pages, please feel free to submit an article for the next edition.

As a primarily web-based entity myself these days, I find the CGS website a very useful resource, expertly managed by Adam Shaw, and many of the documents arising from Council's efforts are on there, or soon will be. Make sure you check it out often, and let Adam know if there are things you think should be on there, or need to be reviewed.

Finally, congratulations to Daniela Pilz for a very successful conference, we all learnt a lot about DNA repair defects.

Natalie Canham (KGC)

Letter from the President

Peter Turnpenny

My first task is to say a big 'thank you' on behalf of the CGS to my predecessor, Frances Flinter, who discharged her presidential duties with characteristic efficiency and commitment. Always able to speak on our behalf with great succinctness and clarity, she also appears, quite effortlessly, to understand how the NHS works! It is a challenge to follow her example, and indeed a long line of distinguished presidents over the years. Thanks are also due to Sarah Smithson and Emma Hobson who stepped down from the Council after their 3 year term of office, replaced by Shane McKee and Carole Brewer in a strongly contested election.

The CGS Spring Conference was a real success and a tribute to Daniela Pilz and her team for the hard work and preparation. Two excellent symposia, some ground-breaking pieces of exciting research, and a presentation by this year's International Scholar from East Jerusalem, was topped off by a very high quality group of talks for the SpR prize – well done to Siddharth Banka (Manchester). Such a showing bodes well for the future of Clinical Genetics, though on a cautionary note only 8 of the 15 available training posts were filled at the national recruitment round.

Regional Genetic Centres are beginning to confront the reality of financial constraints within the NHS. This ranges from promised development money being withheld to very unpleasant cuts to existing budgets. Though the parliamentary process is currently 'paused' we should be under no illusion that there will be a return to the status quo. It is a little early to know the full implications of what lies ahead but a joint workshop of the CGS Council and Lead Clinicians Group is planned for early 2012. In the meantime, the updating of several CGS documents is intended to support those centres joining battle with their Trusts or Commissioners over the nature of a Consultant's work. I refer to 'Roles of a Clinical Geneticist' and 'Guide to Consultant Job Planning', both available on the Society's website. A very full description of our work and service, reworked from an earlier version, will in due course appear in the RCP's updated dossier, 'Consultant Physicians Working with Patients', and this also may prove useful.

There have been four areas of significant activity in recent months.

1. Considerable effort is under way to prepare the knowledge-based assessment (Specialty Certificate Examination) for Clinical Genetics under the leadership of Mary Porteous. This will take place under the aegis of the Royal College of Pathologists. Sample questions will soon be posted on the website.

"our unique skills and expert contributions are recognised by our colleagues in other specialties"

2. The scope of international work is expanding with the formation of a more formal 'interest group' and Council agreement that money is available for Travel Scholarships to any Clinical Geneticist resident in the UK. This includes mutually beneficial educational, training and/or research visits to centres in developing countries as well as recognised centres of excellence. More details and an application form can be found on the website.

3. A small group, led by Annie Proctor, will input to the RCP's important project on Transitional Care (from paediatric to adult medicine). As Clinical Genetics spans all medical specialties I believe we have a lot to offer here.

4. We have been asked to provide additional expertise to the clinical sciences section of the MRCP examination, something to which Alex Henderson has been contributing single-handedly recently. The call for help attracted enormous interest and Alex will be joined by Catherine Mercer and Jonathan Berg, and a small back-up group will also be involved more peripherally.

In March Dr Bassam Abu-Libdeh, this year's CGS International Scholar, spent a few days in Exeter followed by a couple of days in Salisbury at the Wessex Laboratories. My wife and I took him to Salisbury one Sunday afternoon and stopped off en route to visit Stonehenge (see picture). He was amazed that he had never heard of the place and, when he asked us the meaning of 'henge', we were amazed at our own ignorance (we now know it is derived from an older word for 'hanging stones').

It is good that our unique skills and expert contributions are recognised by our colleagues in other specialties but we need to be mindful of our profile among undergraduates and junior doctors. I was reminded of this over Easter. Our medical daughter, who is half-way through her StR training in an acute medical specialty, in close proximity to one of the biggest genetic centres in the country, told me quite bluntly that most of her friends know almost nothing about Clinical Genetics, if they have heard of us at all. We therefore cannot presume that our existence is well known, let alone understood, and we must take every opportunity to connect with students and postgraduates. We can at least be more positive than one of my other (non-medical) daughters, who describes her father's work to her friends in these terms: "He draws a family tree, takes a blood test, and then gives bad news!"

Launch of National Xeroderma Pigmentosum Service

Bob Sarkany and David McGibbon (Photodermatology Unit) and Shehla Mohammed (Clinical Genetics) Guys

We are delighted to let you know that our bid for a nationally-funded service for Xeroderma Pigmentosum (XP) was successful. The first National Commissioning Group (NCG) XP multidisciplinary clinic was held at St Thomas' Hospital in April 2010. The new service's model of care is distinctive in that the aim is for patients to continue to be managed by their local Consultants, with the new service providing outreach support and highly specialist services where needed.

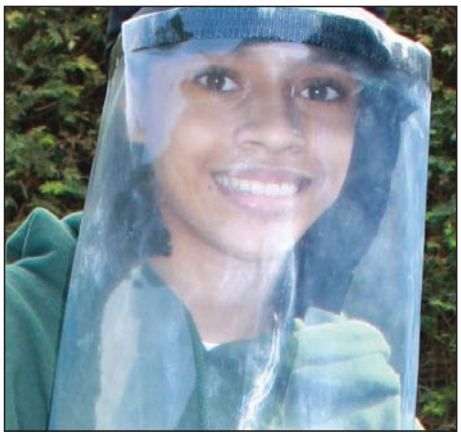
Why was a National Service needed?

Over the last five years we had held multidisciplinary XP clinics a few times a year. Experience from those underlined the need for specialised and coordinated care and the Department of Health agreed with us when we applied to the NCG for funding last year.

The average life expectancy in XP is 32 years, with death usually from metastatic melanoma or the progressive neurological degeneration that affects one in four patients. Some patients have dramatic sunburn reactions from early infancy, but half of all patients are not overtly photosensitive, and present insidiously with gradually increasing freckling in exposed skin as ultraviolet-induced DNA damage accumulates in exposed skin during childhood, paving the way for future skin cancers.

As XP patients cannot repair the DNA damage, meticulous photo-protection from early childhood, including UV-protective

"After 6 months of the Service, 35 of the 100 British patients had been assessed in the multidisciplinary clinic"



visors, window films and daylight avoidance, is the only way to avoid skin cancers and eye damage. This is particularly hard for the patients who do not sunburn and do not feel that the sun is doing them any harm. Not surprisingly, patients become isolated and can encounter problems at school, compounding the pressures faced by families. This can aggravated by visual damage, and the insidious neurological involvement damaging hearing and causing learning problems.

We felt that there was a need for a coordinated national service, with outreach nurses supporting specialists to look after their patients locally, and a one stop multidisciplinary clinic providing highly-specialist services. As well as dermatology and clinical genetics input, our clinic provides specialist XP ophthalmology and neurology support, and audiometry. The patient support group emphasised the lack of support for families, and our clinical psychologist works with the families to find ways to manage the complex nature of this condition. The extreme photoprotection required (for the eyes as well as the skin) is difficult, but is the only way to improve the long term outlook, so we provide specialist photoprotection advice. Our dermatological surgeons concentrate on removing skin cancers from faces already scarred by a lot of previous surgery.

Where are we now?

After 6 months of the Service, 35 of the 100 British patients had been assessed in the multidisciplinary clinic, and we have excised 13 skin cancers, diagnosed significant eye pathology in 11 patients and significant neurological disease in 10 patients. Consanguinity among the parents of children with the disease has turned out to be a major issue in many families. Patient feedback has been very supportive. They have particularly appreciated the amount of time available to explain things to them, and the psychological support. As well as upgrading photoprotection measures in almost everybody seen so far, we have discovered that, unless taking oral supplementation, all the patients are seriously vitamin D deficient.

Who made it happen?

None of this could have happened without the XP Support Group. Sandra Webb started this patient support group ten years ago after her son Alex (above) was diagnosed with XP. When you see pictures of a boy with XP with all the right clothing, gloves and visor, you know that's Alex. They are a fund of information and every February organise a get-together weekend for the families. Sandra has been involved in the NCG Service from its inception. She is on hand at every clinic and the Support Group organises and pays for trains and hotels so that patients can come to the multidisciplinary clinic from anywhere in the country.

The lab diagnostic service

We are very fortunate in having the involvement of Professor Alan Lehmann (FRS). He is the scientist who discovered much of what is known about DNA excision repair and about the pathogenesis of XP, and he has contributed his expertise at all our multidisciplinary clinics from the beginning. For decades Prof Lehmann has provided diagnostic testing in his research lab. He diagnoses XP by measuring DNA repair after UV exposure in fibroblasts cultured from the patient's skin biopsy. His diagnostic service finally has secure funding as part of the NCG service. The diagnostic service is now expanding to provide complementation grouping and mutation analysis as a result of the NCG funding.

The future

We are currently focussing on developing the outreach nursing, and expanding what the multidisciplinary clinic can provide. In the longer term we will trial new treatments as they come along, but for now photoprotection, excision of tumours, and holistic care of patients and their families are the mainstays of treatment.

If you want us to see your patient

If you have any patients with XP, or if a patient might have XP, do feel free to involve

Launch of National Xeroderma Pigmentosum Service cont

us in jointly caring for them. You can refer them to us in the Photodermatology Unit at St John's Institute of Dermatology or The Clinical Genetics Department at Guys. The service is centrally funded so there is no paperwork for Consultants referring from England or Scotland. Consultants in Wales need approval from the Welsh Health Board and the situation is probably similar for patients from Northern Ireland. Patients' travel, hotel arrangements and expenses are all looked after by the XP Patient Support Group.

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A national Bardet-Biedl Syndrome clinical service

Elizabeth Forsythe and Philip Beales, Institute of Child Health

The National Commissioning Group (NCG) has awarded joint funding for hospitals in London and Birmingham to provide a national Bardet-Biedl Syndrome (BBS) clinic, effective from April 2010. This service provides both multidisciplinary clinical assessment and laboratory diagnostics for patients with confirmed or suspected BBS. The successful bid was led by Professor Philip Beales in collaboration with the Laurence-Moon-Bardet-Biedl patient support group (LMBBS). The service operates on two hospital sites in each city - Guy's Hospital and Great Ormond Street Hospital in London, and Birmingham Children's Hospital and University Hospital Birmingham. Teams in both cities are supported by clinical nurse specialists and family liaison officers from the LMBBS. The molecular diagnostic service is based at Great Ormond Street Hospital, and genetic analysis is available for BBS1-BBS14.

What is the purpose of the national BBS clinic?

BBS is a rare pleiotropic disorder and patients require specialist multidisciplinary care resulting in frequent hospital attendances. Many patients are blind or severely visually impaired and making the journey for hospital visits can pose a considerable challenge. The national BBS clinical service offers a one-stop clinic where patients are reviewed by a clinical geneticist, nephrologist, ophthalmologist, endocrinologist, clinical psychologist, dietician and clinical nurse specialist. The clinic provides annual follow-up and aims to ensure appropriate management for all patients with BBS and reduce the number of hospital attendances.

Which patients are eligible?

The national BBS clinical service although funded to receive direct referrals from England and Scotland also welcomes referrals from Wales and Northern Ireland under local agreements. Primary clinical features include: rod-cone dystrophy, post-axial polydactyly, obesity, renal anomalies, learning difficulties and hypogenitalism or genital anomalies. Patients usually present with a combination of several features, but some may present with only one or two as the phenotype is highly heterogeneous and typically evolves over several decades.

Current service arrangements

Referrals are accepted from clinicians of all speciality backgrounds including general practice. Patients can also be referred via the LMBBS (www.lmbbs.org.uk). Clinical assessment occurs either in London or Birmingham depending on geographical location. Paediatric and adult clinics are held separately. In addition to review by clinicians the assessment includes comprehensive blood profiling and detailed ophthalmological assessment. Family liaison officers from the LMBBS attend all the clinics and provide pre-clinic support including help with travel and accommodation.

How to make a referral

By letter/phone/email:
Professor Philip Beales
Molecular Medicine Unit
Institute of Child Health
30 Guilford Street WC1N 1EH

Email: p.beales@ich.ucl.ac.uk
Phone: Tel: 020 7242 9789
or www.lmbbs.org.uk

Trainees' Column

Rob Hastings (Research Fellow, Oxford)
Robert.Hastings@cardiov.ox.ac.uk

One of the main areas of development in training is the impending introduction of the Knowledge Based Assessment 'exit' exam. This is due to commence next year and is intended to be taken in the penultimate year of training. It will be administrated by the Royal College of Pathology but the work of the SAC, particularly Professor Porteous, in creating an appropriate exam at the minimum possible cost is much appreciated. The likely cost should be below £500, significantly less than those in several other specialties. Having said this, further costs for trainees, who already self-fund several courses and conferences and are largely in unbanded and frequently less than full time jobs, is rarely truly welcomed.

The exam will be criterion-referenced, meaning that a 'pass mark' will be set prior to the exam, with the intention of this being a competence exam reflecting clinical practice. Unfortunately there are not the resources to run a pilot exam round or to 'bench mark' questions to ensure this is set at an appropriate standard. However, five questions will be released prior to the exam to give an idea of style and standard expected. All the questions will be based on the updated curriculum and will be a requirement for completion of training.

In terms of funding there are welcome developments by the CGS to start introducing travel awards, available to both consultants and trainees. These are not intended to cover courses or conferences within the UK. The aim is really envisaged to help fund time in an overseas institution, whether that is in a developing country or a world-renowned centre. This is meant to be for educational purposes, both learning and teaching, and forming links with overseas centres. However these awards will remain intentionally flexible to allow support for any activities deemed worthy of supporting. Further details will be circulated in due course.

The academic committee, headed by Professor Goodship, continues to aim to support trainees in research, whether they are specifically academic trainees or not. The standard of research performed by trainees was clearly evident in the registrar presentations at the CGS Spring Conference. One issue raised has been access to relatively small amounts of funding to perform small or pilot projects. Hospitals often have local charitable funds which are very accessible for this, but there are several charities that award funding in specific areas of research. Professor Goodship is collating these so if you are aware of any such funds please let her know (j.a.goodship@newcastle.ac.uk).

News from the Medical Genetics section of the Royal Society of Medicine

Melita Irving (Guys)

Prizes: The Hiscox Young Trainee of the Year 2010, second prize of £1,000 and RSM membership was awarded to medical genetics section member Dr Manju Kurian who had previously been awarded the Alan Emery Prize.

The Ellison-Cliffe Travelling fellowship is an award of £15,000 for fellows of the RSM wishing to travel abroad for more than six months in pursuit of further study, research or clinical training relevant to their specialist field. To find out more about this prestigious prize see the RSM website (www.rsm.ac.uk).

Membership: Membership of this historic institution offers the opportunity to benefit from the many educational events held regularly, as well as providing access to comprehensive library facilities and eligibility to apply for prizes and awards. High quality accommodation at competitive rates is also available to members. Join now online: www.rsm.ac.uk

Minutes of Clinical Genetics Society AGM held 10th March 2011 at SOAS

Secretary Elisabeth Rosser (GOSH)

The AGM began with the President, Frances Flinter, reviewing the work and achievements of the Society over the last year.

The Vice President, Peter Turnpenny discussed the proposed changes to the constitution. These proposed changes had been discussed and agreed in the Council meeting the previous night and had been circulated to all members. No comments were made. The changes to the constitution were proposed by Adam Shaw and seconded by Judith Goodship, they were accepted by the meeting.

The Secretary, Elisabeth Rosser, presented a brief report.

The Treasurer, Amanda Collins presented the accounts and explained the changes in the accounting year, in that accounts will now be presented January to December so that they are not a year out of date when presented to conference. Two sets of accounts were presented. The first set covered the period from April 2009 to March 2010. It was proposed that these be accepted by Daniela Pilz and seconded by Sahar Mansour. The accounts from April 2010 to December 2010 were also presented. It was proposed that these were accepted by Sue Price and seconded by Miranda Splitt. Both sets of accounts were accepted by the meeting.

Thanks were expressed to Daniela Pilz for the organisation of the conference and to Dina Kotecha and Eileen Connop for their organisation of the conference.

The role of President passed to Peter Turnpenny.

CGS News Editor

Deadline for contributions for next issue is 30 November 2011

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Editorial

As we go to press, the Editorial pate is being scratched in puzzlement at the absence of copy. Was it something this editor wrote in the last issue? Perhaps something frightfully non-PC sneaked past the Editor-in-Chief? Suffice to say: articles are a little thin on the ground in this issue. One is refreshed after a glorious fortnight in the South of France, where one's time was divided almost equally between having a good time and marking FRCPath scripts. Modesty forbids sending snaps of my working holiday: not for those of a delicate disposition!

Many thanks to Tracy Lester for writing up our feedback on this year's Part 1 examination. All I would add is that clarity of thought is most important: Non-Invasive Prenatal Diagnosis cannot possibly reduce the miscarriage rate to zero, (but it might reduce it to background level!).

I have also included a piece on the reliability of published information; we've all seen dodgy information on the internet, but we need to be cautious about apparently reputable sources as well.

Finally, I draw your attention to three articles that appear elsewhere in this issue: firstly, an advert for the Annual Meeting of Genetic Technologists/Practitioners; secondly, details of the proposal to merge the ACC and CMGS, from Angela Douglas and David Baty; and thirdly, Jonathan Waters writes about the future shape of the FRCPath exams, reflecting the growing overlap between the different genetic disciplines.

Items sadly excluded from this issue include the startling discovery that a mutation in FOXC-2 gave Elizabeth Taylor a second set of eyelashes, thereby contributing to her renowned beauty. Where do they get these gene names from?

It only remains for me to renew my plea for any of you who can hold a pen or operate a keyboard, to put a few words together about anything that is remotely to do with clinical molecular genetics. As ever, it will be gratefully received and faithfully applied.

Martin Schwarz

Feedback on the FRCPath Part 1 written examination 2011

Tracy Lester, Oxford and Martin Schwarz, Manchester

Fourteen candidates sat the written examination on March 22nd 2011. Congratulations to the seven who passed; we hope the remaining seven who were unsuccessful on this occasion won't be deterred from making another attempt. This feedback is designed to help the 2012 candidates with their preparation and to encourage others to sit the examination in future years. Problems with exam technique were a factor for many of this year's candidates, particularly in structuring essays in a logical way and in ensuring that the questions were addressed properly. It may be that exam preparation has concentrated too much on memorising information without including practice at argumentative writing. Future self-help courses should try to address this by stimulating discussion among students. Three of the questions this year were common to the cytogenetics and molecular genetics papers.

Paper 1

(1) Discuss, with examples, how genetic approaches in cancer have contributed to the advance of stratified medicine.

This question was common to the cytogenetics and molecular genetics papers. Examiners were looking for a definition of stratified medicine, and a description of the link between genetic tests and the medical treatment (including names of drugs and populations tested), using several examples from different types of cancer. All candidates were able to identify at least one example of a cancer drug treatment that is stratified by a particular genotype, with herceptin/breast cancer and gefitinib/small cell lung cancer being frequent choices. Better answers included several examples from a broad range of cancers as well as a good description of stratified medicine, and gave a good historical perspective showing how stratified drug treatment in cancer (and other areas) had developed and is continuing to develop. Those answered less well either contained irrelevant material, insufficient examples, or did not fully address the question.

(2) Explain how molecular pathology relates to phenotypic variability in three genes associated with phenotypic heterogeneity.

All candidates that attempted this question were able to correctly identify three genes where phenotype varies according to genotype. FMR1 was universally chosen, with other less popular choices including PMP22, DMD, APC and CFTR, amongst others. Good answers described the mechanistic link between the genotype and the phenotype for all three of their chosen examples, eg linking loss of FMR1 expression due to methylation of the expanded allele in the 5'UTR to the phenotype of fragile X syndrome, whereas premutations result in FXTAS due to a toxic gain of function of the mRNA. Candidates that performed less well described the mutations and the associated phenotypes, but did not explain the molecular pathology.

(3) Describe the underlying genetic cause(s) of TWO of the following conditions, and briefly outline techniques used in their investigation.

a) FSHD
b) AS/PWS
c) CF

This was the most popular question on paper 1, being attempted by all candidates. Only two candidates chose to write about FSHD, with the majority choosing CF and AS/PWS. Examiners were looking for a description of the disorder, with a comprehensive description of the underlying genetic causes. A brief description of the techniques and their application in the investigation of the disorders was also expected.

Performance was mixed on this relatively straightforward question. Answers to CF generally contained a description of the types of mutation class with examples of mutations falling into each category; however, some answers failed to mention that some mutations are population specific and so the tests used generally target specific mutations. For AS/PWS, imprinting was not always described well, with some candidates failing to describe the parental origin of the genetic causes found in the two disorders. Techniques were also not linked to the type of lesion that they detect, with a few candidates showing confusion in this area.

(4) Describe the principle features of the mitochondrial genome. Give examples of mitochondrial disorders with differing patterns of inheritance and outline testing strategies to aid diagnosis.

This question was attempted by the majority of candidates. The principle features of the mitochondrial genome were generally described well, but several candidates performed less well on the second part of the question. In particular, knowledge of disorders with autosomal inheritance was poor, and a list of methods used to identify mutations was given, rather than testing strategies. Good answers included biochemical and histological assays in the testing strategy

as well as molecular methods, and explained how these could be used to target molecular testing.

(5) Briefly explain the meaning of FOUR out of five of the following terms, giving examples drawn from human molecular pathology:

a) Anticipation
b) Copy number variant
c) Exonic splice enhancer
d) Gene conversion
e) Kozak sequence

This question was also popular, with all twelve candidates choosing to write about terms a) to d). HD was a popular choice for explaining the phenomenon of anticipation, with good answers linking the increased expansion size to the increase in severity and reduction in age of onset, often by using a hypothetical pedigree. Examples illustrating the role of CNVs in molecular pathology included subtelomeric rearrangements and developmental delay, and contiguous gene deletion syndromes. Better essays also described the mechanisms by which CNVs can lead to disease. SMN2 was universally chosen as the example to illustrate an ESE, however a few answers failed to link this to its role in molecular pathology. SMN1/2 was also a popular choice for describing gene conversion, with better answers also giving other examples as well.

Paper 2

(1) You are invited to contribute to a Commissioning Review. How would you justify the service that a diagnostic genetics laboratory provides? What cost improvements and service improvements would you recommend? What developments of the service and associated staffing would you request over the next five years and why?

This question was common to the cytogenetics and molecular genetics papers, and proved to be one of the least popular questions. The quality and organisation of the answers was variable, illustrating a presumed lack of experience of some of the candidates. Service justification was generally poor, with few candidates giving good reasons why our service is important or why it should be funded. A number of candidates lost marks through not addressing the question, for example by concentrating too heavily on quality assurance, or by not discussing the effects of service developments on staffing. Cost improvements often focussed on local laboratory actions (such as cheaper consumables, more efficient tests), with fewer candidates offering suggestions at the strategic level, such as resource sharing between local labs or centralisation. 'Consolidation of services' was suggested by a few candidates, but without further explanation. Service improvements universally focussed on next generation sequencing, with only a few candidates mentioning aCGH, use of cffDNA for PND, or molecular diagnostics as other possible developments. Many candidates who gave enthusiastic support to next generation sequencing (for example, in BRCA1 and BRCA2 screening) did so without discussion of cost-effectiveness or efficiency. Only one candidate managed to secure a pass mark for this question, which was very disappointing.

(2) Summarise the types of adverse event that can happen in a diagnostic genetic laboratory, with particular emphasis on the analysis of prenatal samples. Outline the policies and procedures required to minimise such events. What should happen if an adverse event occurs?

This question was also common to the cytogenetics and molecular genetics papers, but few candidates did well in what should have been a relatively straightforward question. Those candidates who scored poorly tended to do so through a failure to address the question; principally by failing to discuss policies and procedures, by not focussing on events that can happen during prenatal diagnosis, or by not fully describing the procedure to follow if an adverse event occurs. As with the previous question, candidates that performed less well showed a lack of experience with laboratory management, describing standard practice in their own laboratory (such as tube transfer checks, filling in an adverse event form) without really explaining the reasoning behind these procedures. For example, recording reagent batch numbers is not carried out just to meet CPA requirements.

(3) In your opinion will non-invasive prenatal diagnosis be established as a reliable diagnostic procedure for the analysis of single gene disorders within the next five years? Explain your answer.

This question was attempted by the majority of candidates, but very few answered it well. Most answers were factually correct, showing revision of this subject, however few addressed the actual question which was asking for a justified opinion rather than a description of non-invasive PND. Nevertheless, it was encouraging to see answers in both the 'Yes' and 'No' camps, with supporting evidence for each. Identification of the specific problem of detecting maternally

inherited alleles in a background of significant maternal contamination was not addressed in several answers. Good answers used examples from the literature to show how this problem is currently being addressed and how developments in technology could also help to overcome this problem.

(4) Describe the following techniques, giving examples of their uses and limitations in the diagnostic genetic laboratory:

a) haplotype analysis
b) real-time PCR
c) reverse-transcriptase PCR
d) array CGH

In most cases the diagnostic uses of these techniques were covered reasonably well. Candidates tended to lose marks mainly for a failure to describe the technique adequately, or to address the limitations of the technique in question for diagnostic genetic testing. A minority of candidates also showed some confusion, particularly with regard to haplotype analysis.

(5) Describe mechanisms by which a female carrier of an X-linked condition could exhibit clinical symptoms. Illustrate using examples from diagnostically important disorders.

This was the most popular question on paper 2, being attempted by all candidates. All candidates identified skewed X-inactivation as a mechanism, but there was some misunderstanding about how this results in disease. A few candidates did not address the question and instead produced an essay that focussed on X-inactivation only, others failed to identify other mechanisms that could result in disease, or listed potential mechanisms without explaining how they can result in disease.

Table 1. Summary of answers

Question	1-1	1-2	1-3	1-4	1-5	2-1	2-2	2-3	2-4	2-5
No of answers	9	9	14	12	12	9	11	12	10	14
Average score	12	13	12	13	12	12	12	12	13	12
No of passes (13-15 marks)	4	4	5	5	3	1	4	2	2	4
No of fails (<13 marks)	5	5	9	7	9	8	7	10	8	10

A Tale of Two Risk Figures or: "Don't believe everything you read in scientific journals"

The assessors for the European External Quality Assessment scheme for Cystic Fibrosis are faced, as in any other QA scheme, with coming up with different testing scenarios each year. In fact, this is usually no more than asking the same question in a slightly different guise. One way of doing this is to change the country of origin of the fictitious patients, in order to make the risk calculations a little more interesting. In the 2010 scheme, we created a couple in which one (Caitlin Flanagan) had a sister who died from CF. Caitlin was from Belfast, Northern Ireland and on testing was found not carry a mutation. Her partner (as yet untested) had no family history of CF and was also from Northern Ireland. What could be simpler?

The two risk calculations are both quite straightforward, but require two pieces of information: the mutation detection rate for the Northern Irish population of any given kit, and the population carrier frequency. The former figure is determined by each laboratory, but the latter is widely available in the form of published population figures – or so we believe! For CF, the assessors recommend two key publications for mutation frequencies: one from Phil Farrell in Wisconsin (Bobadilla et al, 2002) and the other from the World Health Organisation – a report of a joint meeting of various interested parties, entitled "The Molecular Genetic Epidemiology of Cystic Fibrosis". Both are considered to be reputable sources of mutation rates and prevalence figures. Both quote a Cystic Fibrosis prevalence in Northern Ireland of 1 in 5,350; the WHO paper cites Bobadilla in its general list of references; Bobadilla cites Giovanni

Romeo (1989) specifically for the 1 in 5350 figure.

The reason this figure needed further investigation was that it simply did not fit in with the rest of the United Kingdom and the Republic of Ireland. For the UK, we generally use a figure of around 1 in 2,500 and the National Centre for Medical Genetics in Dublin quotes a figure (unattributed) for Ireland of 'approximately' 1 in 1461. Previously published figures for Northern Ireland go from 1 in 1600 (Carter, 1977), 1 in 1666 (Stevenson, 1959) to 1 in 1857 (Nevin, 1979) – the latter being perhaps the most reliable.

Further sleuthing unearths the root of the anomaly; Romeo's paper cites two widely differing figures for Northern Ireland: 1 in 1700 and 1 in 9000, both attributed to Art Beaudet's chapter on CF in the now-superseded 6th edition of Scriver's well-known "Metabolic basis of inherited disorders" (the same chapter now in the 8th edition is by Michael Welsh). The 1 in 1700 figure can easily be accounted for, but the 1 in 9000 remains a mystery. I think I might have a copy of the 6th edition somewhere……

So where did the 1 in 5350 figure come from? Simple! A schoolboy's attempt to average Romeo's two figures (1700 plus 9000, divided by 2 equals 5350!). [Notwithstanding the dubious wisdom of averaging two widely disparate figures, the average of those two prevalence figures would be approximately 1 in 2860!]. So, the next time you cite a paper for a particular piece of evidence, don't take it at face value!

CMGS News Editor

Deadline for contributions for next issue is 30 November 2011

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Editorial

I am writing this at the end of a successful spring meeting, expertly hosted by Alan Donaldson and colleagues in Bristol. It was a very interesting programme, highlighting many of the new challenges that face us in the field of cancer genetics, from incidental findings to stratified medicine. The next CGG meeting will be the one day winter meeting at Guy's on 2nd December. This will follow the usual format of research update, discussion of difficult cases and a key note speaker. The two day spring meeting in 2012 will be combined with the Dutch group. It will be held in Newcastle on 14th and 15th March.

In the Chair's message Anneke Lucassen has provided a comprehensive update on many of the current issues in cancer genetics. The lead article is a comment from the Research Department of Gynaecological Oncology at UCL on the newly published NICE guidelines for early detection and treatment of ovarian cancer which can be found at www.nice.org.uk/CG122. Still on the subject of NICE guidance, the Guideline Development Group for review of the Familial Breast Cancer guidelines is currently being formed. Andrew Cuthbert represented the CGG at the scoping meeting about this guidance. He has provided a comprehensive summary of the key issues discussed at that meeting in this edition of the newsletter. New innovations in clinical practice is the theme of the next section with Gill Crawford describing how the team at Southampton have introduced personal health records for their VHL patients, Julian Adlard introducing the new testing service that has been set up in Leeds for patients with phaeochromocytoma and paraganglioma and Jo Campbell describing the rapid BRCA testing service that has been established by GSTS at Guy's Hospital. In the last section Jonathan Hoffman provides insight into the experiences of a local research team running the IMPACT study and Caroline Huang explains about a study that she is setting up. Finally, there is a reminder about how to apply for a CGG bursary.

In order to make the newsletter relevant and interesting we need your input. The editors for the next edition will be Emma Woodward and Lisa Jeffers. Their contact details can be found at the end of this section. Please do get in touch if you have something to contribute or if you would like to discuss the possibility of submitting an article.

Best wishes, Chris Jacobs

Chair's message

Anneke Lucassen

Another newsletter deadline approaches with frightening speed. The Cancer Genetics Group continues to thrive and, as I write, we are very much looking forward to the Spring two-day meeting in Bristol. Alan Donaldson, Sally Yerbury and colleagues have done an excellent job of lining up what promises to be a very interesting programme. Since we haven't met as a group since the last newsletter, I thought I'd take this opportunity to update the readership on some cancer genetics related activities.

Most CGG members will know by now that NICE are updating their recommendations on the management of people with a family history of breast cancer. Andrew Cuthbert attended an initial scoping meeting on behalf of CGG. Gareth Evans is lead clinician for the guidelines and guideline development group members will be appointed over the next few months. We look forward to hearing the outcome of these discussions.

The Association of British Insurers (ABI) and government announced last week that the long-standing concordat and moratorium on genetic testing in the UK has been extended to 2017. The concordat and moratorium applies to the use of predictive (rather than diagnostic) genetic test results and means that people can insure themselves and their families, even if predictive genetic testing shows they have inherited a familial condition. The moratorium applies to life assurance and critical illness insurance. Where applications exceed £500,000 and £300,000 respectively, insurance companies are allowed to seek an exemption from this moratorium, but to-date Huntington's disease is the only condition for which such an exemption has been given. The moratorium was

"…the Human Genetics Commission published a report on the concept of genetic discrimination"

introduced in 2001 and has been renewed several times, now to 2017 with the next review due in 2014. The Human Genetics Commission (HGC) now oversees this process (since GAIC, the Genetics and Insurance Committee, was disbanded). Of course, since the" bonfire of the quangos" introduced by the current government, the HGC is now also under threat, certainly as an independent commission. The department of health plans to reconstitute it as an expert advisory committee, but at the time of writing its new role or terms of reference have yet to be fully defined. We may therefore need yet a further committee to take on oversight of the insurance moratorium.

Despite these uncertainties the HGC has had some recent output relevant to cancer genetics, which seems appropriate to mention here. This month the commission published a report on the concept of genetic discrimination and whether it can be accurately defined and distinguished from other forms of discrimination. A lively seminar and debate in January 2010 started these discussions and the report covers the relevant philosophical background, the UK legislative framework and international perspectives, especially in relation to the US 'GINA' legislation (the Genetic information non-discrimination act). A summary of the report is on the HGC website (www.hgc.gov.uk). Similarly a report on intellectual property and DNA diagnosis is likely to be of interest to all those who have followed the Myriad BRCA patenting story. Less relevant to cancer genetics specifically, more to genetics as a whole, but a beautiful example of sensationalist headlines, is the HGC report on preconception genetic testing. The Daily Telegraph headline ran 'Test children's genes before they have sex' on their front page, which resulted in a lot more press coverage.

With my 'ethics hat' on I will also briefly mention some relevant output from the Nuffield Council of Bioethics (NCOB). Many of you will know NCOB is an independent body that examines and reports on ethical issues in biology and medicine. It celebrates its 20 year anniversary this year and since it is funded by the Nuffield Foundation, the Wellcome Trust and the Medical Research Council its future is currently more secure than bodies such as the Human Genetics Commission. Approximately half of the reports issued by NCOB have genetics as a main focus or discussion point highlighting what we know from our practice - that there are plenty of ethical challenges. One of the latest reports: Medical profiling and online medicine - the ethics of 'personalised healthcare' in a consumer age considers 'over the counter genetic testing' from the perspective of a lay person without a significant family history and the potential pitfalls of buying a genetic test and the problems with interpreting results. The CGG readership will be very familiar with the potential pitfalls of direct to consumer tests and these are further illustrated in a 2010 report from the United States Government Accountability Office (see http://www.gao.gov/new.items/d10847t.pdf for a full copy of the report). The group sent samples from five different donors to five different companies and received very conflicting advice, for example on breast and prostate cancer risks ranging from below average to above average on the same sample. They then also sent off the same samples but with a fictitious family or personal history and showed how this too made a difference to the interpretation of the same genetic tests. For those of you who have patients attending your clinic with the results of such tests, this makes interesting reading.

For ethical issues in clinical practice, Genethics club (www.genethicsclub.org) continues to thrive with its three yearly meetings. Manchester Nowgen centre hosted the first meeting of 2011. The next meeting is in Cardiff on July 20th and then London on November 10th. If you'd like to attend, want to host a future meeting or have any issues you want to see debated, please get in touch.

Statement re NICE guideline April 2011 from the research department of gynaecological oncology, UCL

Ian Jacobs
Usha Menon
Ranjit Manchanda

NICE has recently published guidelines (April 2011) which include advice on the care of women with symptoms which may be due to ovarian cancer. There are no randomised trials in this area. The evidence on which the guidance is based is limited to retrospective studies documenting the pattern of symptoms women experience prior to diagnosis of ovarian cancer. It is hoped that by encouraging GPs and others to act on these symptoms the guideline will help reduce the time to diagnosis of ovarian cancer. NICE recommends performing a CA125 blood test followed by an ultrasound scan in women who have any of the following symptoms on a persistent or frequent basis (particularly more than 12 times per month): persistent abdominal distension or bloating; feeling full (early satiety) and/or loss of appetite; pelvic or abdominal pain; increased urinary urgency and/or frequency; newly diagnosed irritable bowel syndrome over the age of 50. This has not been formally tested in a clinical trial.

Several points need to be emphasised:

1. There is NO evidence one way or the other, that acting on these symptoms will alter time to diagnosis, stage, survival or deaths from ovarian cancer.

2. There is a possibility that this recommendation will cause anxiety for women with symptoms who do not have ovarian cancer. Only 1 in 500 women who have the symptoms listed above will actually have ovarian cancer, i.e. >99% women with these symptoms do not have ovarian cancer.

3. The recommendation will lead to diagnostic testing and in some cases to unnecessary surgical investigation with complications in women who do not have ovarian cancer. NICE estimates that only 1 in 157 women with an abnormal CA125 and 1 in 26 women with an abnormal CA125 and ultrasound scan will have ovarian cancer (i.e., 96 % to >99% women with abnormal tests will not have ovarian cancer).

4. NICE is not recommending screening for ovarian cancer amongst healthy symptom free women. The efficacy of screening for ovarian cancer is being investigated in the national ovarian cancer screening trials – UKCTOCS (in the general population) and UKFOCSS (in the high-risk population) which will report in 2014-15. Within these national screening trials women undergo a combination of CA125 blood tests and/or ultrasound scans on a regular basis with the aim of picking up ovarian cancer early, before the occurrence of symptoms.

We are pleased to see this focus on the problem of ovarian cancer and acknowledge that the NICE guideline development group had a difficult remit as they were asked to focus on aspects of diagnosis and initial management of ovarian cancer that are controversial or uncertain with a lack of high quality evidence. With regard to symptoms, they have “made a call that lack of evidence should not preclude the possibility of timely and appropriate referral of women with possible ovarian cancer”. Not everyone would agree that this is justified and there is a high likelihood that the recommendations will lead to anxiety and unnecessary diagnostic or surgical intervention for a large number of women, leading in some cases to serious complications. It is a concern that many of the women who have positive results will not have been adequately informed in advance about the lack of an evidence base and the potential consequences of these recommendations

The guidelines recommend research in women with ovarian cancer to explore the relationship between symptoms and stage/survival and a population based study that records both the duration and frequency of symptoms. We are disappointed that there is no emphasis on the need to address the key issue - the lack of prospective evidence from clinical trials, that a symptom based intervention has an impact on stage, survival, mortality or at a minimum, on time to diagnosis of ovarian cancer. Conducting a trial to document these end points should have been a priority and it is a serious concern that the recommendations are likely to make it impossible to conduct such research.

Familial breast cancer guideline review: Scope workshop 14 March 2011, Manchester: draft Scope summary

Andrew Cuthbert

(see Published Draft Scope 30.03.11 – 28.04.11 http://www.nice.org.uk/nicemedia/live/13269/53866/53866.pdf)

Remit

i) National Collaborating Centre for Cancer (NCC-C) commissioned by NICE to update CG41 (2006) as part of the guideline review cycle – in particular to:

a. Review the existing threshold for BRCA1/2 mutation screening
b. Develop guidelines for offering mutation screening unaffected women with a substantial risk of a BRCA1/2 mutation where there are no affected candidate to test
c. Review chemoprevention (Tamoxifen) for unaffected women with a heightened risk
d. Review provision of surveillance for women with an increased risk
e. Other suggested topics:
- Guidance for high risk women on taking HRT following pre-menopausal oophorectomy

ii) Develop a short clinical guideline for the management of women and men diagnosed with breast cancer who also have a (strong) family history, thus filling the gap they fall into between CG41 and the 2009 Early Breast Cancer Guidance (CG80). Suggested topics:

a. Risk threshold for offering BRCA mutation screening to women with a personal history of breast cancer
b. Scope for BRCA/P53 testing in <4weeks to inform treatment
- Does a delay affect outcomes (such as bilateral/contralateral surgery vs lumpectomy, use of radiotherapy in TP53 patients)?

c. Is mastectomy more effective than conservative surgery with radiotherapy in TP53 mutation carriers?
d. Thresholds for offering risk-reducing mastectomy
- Timing of discussion with patient

e. Who should be explaining the outcomes of testing?
f. Specific surveillance for affected family members with a history of breast/ovarian cancer.

Group discussion

About thirty stakeholders from diverse interest groups attended plus ten NICE/NCC-Cancer officials. After preliminary comments the meeting broke into three facilitated discussion groups. Each group gave feedback, albeit brief due to time limits. Comments are to be incorporated in to an amended scope for public consultation at the end of March.

CG41 Update:

i) Arguably the most difficult problem will be the provision of surveillance for moderate risk women currently under CG41. According to Julietta Patnik, plans for the National Breast Screening Programme (NBSP) to manage moderate risk women have stalled. Their proposed risk thresholds are nothing like those in the current guideline. Their modelling defines moderate risk as being ≥4x to ≤8x RR at age 40, (>6% risk from 40-50). Gareth Evans argued 90% of those currently meeting CG41 moderate risk criteria would not have been offered screening under NBSP proposed criteria.

ii) Probability threshold for BRCA testing (affected individuals) - currently there is no universally agreed and implemented tool for calculating mutation probabilities. A consensus is required on how a probability is to be calculated and what the threshold will be.

iii) The current 20% threshold is not consistently used, many centres already use 10% which is likely to be in the updated guideline.

iv) Introduction testing for unaffected women with a substantial carrier risk; again no agreed method for calculating and a level will need to be set (?20%).

New Short Clinical Guideline for women with breast cancer and a family history:

i) Offering BRCA mutation screening to women with breast/ovarian cancer: again, how should mutation probabilities should be calculated and at what thresholds need to be determined

ii) Section on the impact of delaying testing on outcomes alludes to PARP-i type therapies and is probably too early to scope – it was suggested that this is not included at this stage but perhaps to be included in the first update after licensing.

iii) Section on the effectiveness of Risk Reducing surgery
_ What should the threshold be for offering risk-reducing surgery - how should this be assessed? – no comments
_ When is it not appropriate to offer surgery? – no comments

iv) Who should discuss mutation screening, its outcomes and at what time?
_ A strong feeling this should be a Clinical Geneticist/Genetic Counsellor

Timetable

30/03-28/04: publication of Scope and consultation – see NICE website for comments proforma
31/03/11: Advert for applications to the GDG 10+ healthcare professionals, 3 patient/carer reps, a panel of experts (see NICE Website)
04/07: Agreement on Scope
18/07/11: First GDG meeting
09/10/12: First draft submitted
Final publication TBC

Guideline Development Group

Chair, Maggie Alexander (Breakthrough Breast Cancer), Lead Clinician, Gareth Evans
Period for applications to other positions has now closed (including a Clinical Geneticist and a Genetic Counsellor)

Personal health records

Gillian Crawford

The Wessex Clinical Genetics have recently introduced personal health records for our Von Hippel Lindau (VHL) patient cohort.

Because VHL patients have multiple appointments with multiple clinicians a soft handbag size friendly plastic wallet was designed as a patient held personal health record. It includes pages for general information (GP and Consultant details), appointment and scan dates with outcomes and future plans. It also includes screening guidelines for VHL and a pocket at the back to insert a copy of our VHL patient information booklet. The record is not designed to replace medical/genetic records but as a resource for patients so they can collate their health details in one place and to promote a sense of control in a condition which is often characterised by an apparently never ending series of appointments with a wide range of health professionals

An initial batch of 10 records has been given to VHL patients to evaluate. This includes newly diagnosed, established and adolescent patients. The records will then be adapted and amended based on their feedback. We have already included aspects of this personal record in our prophylactic mastectomy care pathway and are considering designing new page inserts which can be used for other multi system genetic disorders (e.g. Nf2). I would be pleased to hear from other centres on their experiences of implementing patient held health records. Please contact gc@soton.ac.uk

Phaeochromocytoma and paraganglioma – a new testing service in development in Leeds (Yorkshire Regional Genetics Service)

Julian Adlard
Ruth Charlton

Phaeochromocytomas and paragangliomas (phaeo/PGL) are tumours arising respectively from the adrenal medulla or from extra-adrenal neuroendocrine tissue. They may develop anywhere in the sympathetic or parasympathetic systems from the pelvic floor to the base of the skull. Those arising in the parasympathetic system (typically in the head and neck) are usually non-secretory, whereas those arising in the sympathetic system including phaeochromocytomas are more likely to produce excess catecholamines. Whilst the majority of these tumours are benign, a proportion are malignant. Even in benign cases, undiagnosed hypertensive crises can prove fatal, local pressure effects may cause problems, and there are other important associations if the tumours are part of a genetic syndrome.

Although not known precisely, the incidence of diagnosed phaeo/PGL lesions is in the region of 1 in 100,000 per year, amounting to at least several hundred cases per year nationally. The underlying prevalence (including non-secretory benign lesions which are more likely to go undiagnosed) will be higher. A small proportion (~1 in 1000-2000) of patients with sustained hypertension will have a secretory tumour which may be undetected.

There are numerous phaeo/PGL predisposing genes which include VHL, RET, NF1, SDHB, SDHC, SDHD, SDHAF2, PRKAR1A, and TMEM127. Further susceptibility genes remain to be identified. The known genetic syndromes show autosomal dominant inheritance with the exception of SDHD which undergoes maternal imprinting, and therefore mutations are almost always phenotypically expressed after paternal rather than maternal inheritance.

Flags to hereditary rather than sporadic disease include recognised syndromic features, multifocal/bilateral/extra-adrenal disease, and presentation at younger ages (e.g. <45 years). Phaeochromocytomas presenting in childhood are usually genetic. It should be noted that genetic studies in patients with apparently sporadic disease have still identified a significant proportion with mutations. For example, in one registry study of 1149 cases (Erlic et al 2009) 14% were syndromic (VHL>MEN2>NF1) and 86% non-syndromic. Of the apparently sporadic cases, 19% had mutations identified in SDHB, VHL, RET or SDHD.

Approximately 1% of patients with NF1 will develop a phaeochromocytoma. Although, the penetrance of this manifestation of NF1 is relatively low, the high birth incidence of NF1 (~1 in 2500) means that a significant proportion of all phaeochromocytomas will be associated with clinical features of NF1, which should be assessed in the clinic.

Phaeo/PGLs develop in ~10-20% of patients with VHL disease (~1 in 40,000 incidence), with notable genotype-phenotype associations. The risk of phaeochromocytomas begins mainly from the mid-teens with median onset around 30. Paragangliomas have been occasionally reported.

About 50% of patients with MEN2A/2B (~1 in 30,000 incidence) will develop phaeo/PGL, and in 20% of cases this will be the first feature, presenting as young as 10 and on average around the mid-30s. MEN2 penetrance is variable between different RET codon mutations.

In reported series, the risk of phaeo/PGL due to the SDH genes appears to be over

70%, although could be over-estimated due to ascertainment bias. Most of the risk is over age 10, with median presentation around 30-35. There are phenotypic differences between the genes. For example, SDHD is more associated with head and neck paragangliomas, and SDHB is more associated with extra-adrenal sympathetic and malignant tumours.

Phaeochromocytomas may be seen in the Carney complex due to mutations in the PRKAR1A gene, although this condition is extremely rare with only in the region of 500 cases described worldwide.

TMEM127 mutations have been detected in ~30% of familial phaeo/PGL cases and in ~3% of apparently sporadic phaeo/PGLs with unknown genetic cause. Phenotypic features and penetrance are currently poorly defined.

In many cases of phaeo/PGL it will be important to identify if there is a genetic cause. This may allow more accurate assessment of additional risks to the affected patient, and to allow predictive testing and early screening/treatment (often from childhood) for at-risk relatives.

Yorkshire Regional Genetics Service has submitted a dossier to UKGTN for multiple testing for up to 8 of the recognised predisposition genes (excluding NF1). It is our intention to offer this service to external genetics centres (at a cost of ~£530) within the next few months. Testing includes analysis of entire coding region for point mutations and small insertion/deletion mutations in VHL, SDHB, SDHC, SDHD, SDHAF2, PRKAR1A, and TMEM127. Targeted analysis of RET exons 10, 11, 13, 14, 15, 16 will also be performed to detect mutations reported in association with MEN2/FMTC. Large deletions and duplications within VHL and SDHB/C/D genes will be detected by MLPA dosage analysis.

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Rapid BRCA testing service at Guy's (GSTS Pathology)

Joanne Campbell

In response to the increasing demand for a full screen of the BRCA1 and BRCA2 genes to be completed between an initial diagnosis of breast cancer and the date of surgical treatment, the DNA Laboratory within GSTS Pathology at Guy's Hospital, London has established a rapid BRCA mutation screen. This test will be available for individuals at risk of having a BRCA1 or BRCA2 mutation, who fulfil the clinical guidelines for mutation testing, for whom the presence or absence of a mutation might have implications for treatment options and who have received appropriate genetic counselling.

The Clinical Genetics department at Guy's Hospital have developed a pathway whereby in-region patients are sent an appointment for a rapid genetics assessment with a cancer genetics clinician within 5 working days of referral. If genetic testing is appropriate and desired by the individual following genetic counselling, a blood sample will be sent to the laboratory and the test will be completed within 15 working days.

Samples will be tested in the same way as for routine BRCA referrals, the entire coding regions of the BRCA1 and BRCA2 genes, including splice sites, will be screened for mutations by fluorescent Sanger DNA sequencing, and MLPA will be used to detect whole exon deletions and duplications, however samples will be prioritised and tested individually, rather than in a batch with other samples to facilitate the rapid turnaround time. The cost of this test is £950 to reflect the increased cost of testing samples individually, and the laboratory will be happy to receive referrals from other genetics centres.

Making an IMPACT - the experience of the IMPACT study at West Midlands Regional Genetics Unit

Jonathan Hoffman, Cancer Study Co-ordinator

Being a very small cog in the large machine that is a multi-national study would make it seem fairly insignificant to be reporting that to date: West Midlands Regional Genetics Unit has recruited 12 patients to such a study, IMPACT. Perhaps even in the grand scheme of things it is, but like the men who have so generously volunteered as recruits to this study, I feel I have gone on something of a journey. These are a few of my thoughts from along the way.

As many of you will relate to, as a clinical genetics centre, recruitment to studies can be in some ways something of a removed process. Paperwork goes back and forth between the Genetics Unit, the patients, and the study centres culminating in the recruitment of a patient. Quite often the closest contact you as a co-ordinating centre will have with a patient will be sight of the original copy of their hand written consent form. Of course this is by no means a criticism, just the nature of many cancer genetic studies. IMPACT however offers something different, a study where as a clinical centre one can offer a research opportunity that can directly benefit the patients. Not only that, but one that will be embarked upon alongside the patient, through five years of PSA testing, any interventions needed and all of the support along the way. The commitment that is asked of the men is not small and in turn, the involvement from the genetics department goes considerably beyond that of any other currently open study, and with that comes certain challenges.

Set-up wise IMPACT is a big undertaking with a host of logistical and organisational issues that must be negotiated before the thought of recruiting a patient is even considered. From this centre's point of view, seeing eligible men from the whole of the large geographical area of the West Midlands and surrounding counties is difficult. Each man needing a PSA test and possible referral to Urologist for a study protocol biopsy further convoluted any attempts for a smooth and streamlined study set up. For recruitment to the levels that we felt would justify the energies that would be going into the study, it was clearly going to take some careful planning. That is indeed where the majority of time and resources have been focussed to date.

With so much needing to come together, any kind of forward planning was made difficult. It was necessary for the proposed start date to be pushed back a number of times due to unforeseen delays to the process, however after many months and with practicalities finally overcome, came the 'Champagne moment' as the first batch of recruitment letters were posted.

So yes, fast forward several months and we now find ourselves with a total of 12 recruits to the study. The aspect that I have found the most encouraging is not just the level of uptake (so far approaching 40%), but that of these recruits, there has been equal uptake from both BRCA carriers and non-carriers. The BRCA negative men seem equally happy to commit to the uncertainties of the PSA screening program (through the control arm of the study) despite their own genetic status putting them at population risk for prostate cancer.

When asked why they had decided to take part in the study, the consensus of reaction from recruits focuses heavily on the level of cancer that there has been in family members, in particular in close female relatives. Regardless of the BRCA status of the individual, for all recruits there is a family BRCA diagnosis present, and it seems that it is this strong motivator that unites both of these groups of men. Through this sense of powerlessness and the desire to make some small difference, perhaps the IMPACT study gives these men the chance to take back a sense of control in some small way.

So is this all just a drop in the ocean, or do all these efforts represent something altogether more? Well the answer to this is not really important. What I can say though is that the whole process has provided a hugely positive and rewarding experience for myself and all of my colleagues involved in the study here in Birmingham. More importantly I firmly believe that this is also the case for the men who have been involved so far.

So here's to 12 real 'Champagne moments' and hopefully many more to come, not just here in the West Midlands, but across the many other centres working so hard on IMPACT around the UK and abroad.

Research into ethical and policy aspects of BRCA1/2 management

Caroline Huang

I am a research fellow at the University of Oxford Ethox centre, looking for participants in a research project that will explore the ethical and policy implications that arise in relation to the identification, care, and treatment of the BRCA1/BRCA2 gene mutations. The research project is being supervised by Professor Anneke Lucassen (University of Southampton) and Professor Michael Parker (University of Oxford).

By carrying out interviews with key stakeholders in British and American genetic screening practices and support systems, the project will draw upon a comparison of genetics practice in these two countries to examine aspects of clinical care such as the optimal level of information for patients to receive during counselling sessions, the amount and kind of surveillance services that are recommended to patients, and the quality of genetic education available to GPs. In addition to clinician-patient communication, the project will also look at how cancer genetics is impacted by other parties such as policymakers, genetic testing companies, medical researchers, advocacy groups, and insurers.

Preliminary conversations have been used to tailor the set of interview questions to reflect clinically relevant information and determine which identified areas of research are most interesting to stakeholders. Eventually, the results of the final qualitative interviews will be used to develop a set of quantitative measures for evaluating factors such as patient expectations for and satisfaction with the counselling and testing process. Ideally, this research project will lead to an improved set of guidelines for clinical-patient communication and foster an understanding of the political and legal implications of genetic services for BRCA1 and BRCA2 gene mutations.

If you are interested in taking part, please contact me and I can provide you with more details caroline.huang@merton.ox.ac.uk or (0)7917 392261 with any questions.

Cancer Genetics Group Travel Awards

The Cancer Genetics Group (CGG) would like to remind its members about the offer of Travel Awards. These are to encourage wider participation in its meetings and to support presentation of original cancer genetics research nationally and internationally. The CGG can make funding available on a discretionary basis as follows:

1) Up to three Travel Awards will be available annually to cover the registration, reasonable travel and accommodation costs for members to attend CGG meetings.

2) In addition members may apply for consideration of part-funding for relevant non-CGG meetings up to a maximum of £250 for European meetings and £500 for destinations outside Europe.

All awards are at the discretion of the CGG Steering Group. Priority will be given to CGG members in training who are presenting original cancer genetics research (oral presentation or poster) at a relevant Conference. Applications may also be considered from non-clinical members who do not have readily available sources of funding to attend CGG meetings.

You must be a CGG member and should apply in writing (or e-mail) to the Treasurer, Dr Julian Adlard at the address below. The application should include a brief CV, meeting details and value of attendance, a copy of any abstract and evidence of acceptance, total funding requested, other sources of funding sought, and a letter of support from the head of department. Successful applicants should acknowledge the CGG in their presentation and may be asked to write an article for the CGG section of the BSHG Newsletter as a condition of acceptance.

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Editorial

This is the third BSHG newsletter that the SGPPH has contributed to as an affiliated organisation. To date we have focused on the importance genetics becomes more mainstreamed in healthcare, both via the training of health professionals and by discussing the implications in primary care of genetic disorders. We have also looked at the implications of the advent of cheaply available whole genome testing, including genetic risk information in health messages and the implications for policy makers of genetic influences on some of the more complex disorders currently presenting a public health challenge in the UK.

The SGPPH focus for 2011 is to highlight issues around the clinical and public health implications of cutting edge genomic advances. This was the theme of our 2011 spring conference where the implications of a variety of different advances ranging from emerging cancer tests using gene expression arrays to the evolution of bacterial pathogens was discussed. In this current edition we have two papers looking at future directions in primary care and the implications of epigenetics for public health.

We are all aware of the financial constraints currently being placed on the NHS. A key cost pressure will be the implications of new technologies. Understanding the implications of the development of new knowledge and technologies will be essential if we are to make the case for effective and appropriate service development. The presidential address considers the need for strategic approaches to developing genetic services in Wales.

The SGPPH as a society is a special interest group specifically focused on the implications for policy and population health aspects of the growing knowledge about genetics. I would like to thank all contributors to the current edition and if any members (or non member) would like to contribute to future editions this would be welcome. These would need to be emailed to myself (tom.fowler@nhs.net). The format and style is outlined in BSHG News Issue 41, June 2009, pages 10 and 11.

Tom Fowler

The SGPPH President Report

Layla Jader, President of SGPPH

Since the Society for Genomics Policy and Population Health became a fully affiliated Special Interest Group of BSHG in April 2010 it has faced a number of challenges while growing into its new role. I am glad to say that we have overcome these challenges. We continue to hold a symposium at each BSHG Annual Conference and in addition will this year be holding the Open Debate on Synthetic Biology, which will hopefully be very interesting to many delegates. The difficulty SGPPH faced with the administrative support in organising our Annual Spring Conferences was at last resolved with a new partnership with the administrative office of the Wales Gene Park in Cardiff. This year we held our Spring Conference in April entitled 'Clinical and Public Health Implications of Cutting Edge Genomic Advances' with the new administrative support and it went well receiving excellent reviews from all the participants.

In my day job as a consultant in public health medicine I worked with the Chief Medical Officer for Wales and his Deputy in organising a one day genetic policy workshop in March 2010. This was held to re-examine and evaluate recommendations made in 2003 in a report - Genetics and Health in Wales: a Strategic Review, led by Professor sir Peter Harper. It was a very successful day and in writing a report collating all presentations and highlighting the main issues it was necessary to include my own public health commentaries and key points from a public health perspectives. One thing that struck me is that genetics is a rapidly evolving speciality that I think requires the establishment of an All Wales Advisory Group. This should deal with policy decisions on a continuous basis rather than at 7 yearly intervals. The other issue was the need to invest in

order to save money in the long run, not a concept easy to accept by those who hold the purse strings in the current environment. One example of this is that as genetic tests become cheaper and more easily available if a strategic approach is not taken in responding to these changes, then instead of reaping the benefits there is a real danger of an explosion of inappropriate testing that could collectively be very expensive.

What also struck me was how cardiologists who presented at the workshop were keen for the geneticists to do the genetic counselling rather than themselves. I found a similar notion with another group of professionals more recently in a different strategy group, haematologists caring for haemophiliacs stating very clearly that they don't do 'genetic counselling', they do 'genetic education', and that if 'genetic counselling' is needed they refer patients to genetic services. So genetic education including the basis of what constitutes a good genetic counselling has been and continues to be the biggest challenge in my view facing genetic services in UK.

My report also highlighted the great need to train and recruit bioinformaticians for Wales a new sub-specialty that has seen a rising demand. We live in a very interesting and challenging time as the world is changing around us.

Do epigenetic processes have implications for public health?

Graham Burdge, University of Southampton

It is becoming increasingly clear that gene polymorphisms alone are unable to explain completely differential risk of non-communicable diseases. Epidemiological studies have shown that the early life environment may induce phenotypic variations in the fetus which persist into adulthood. Furthermore, environmental constraint during early life, including unbalanced nutrition, poor nursing behaviour and exposure to environmental pollutants, increases risk of a range of non-communicable diseases such as obesity, type 2 diabetes mellitus, impaired cardiovascular function and osteoporosis. These phenotypic changes have been replicated animal modes of maternal under or over nutrition. Induction of altered phenotypes involves signals about the early life environment acting through processes which regulate developmental plasticity. The mechanism by which the quality of the early life environment is signalled to the fetus is not known. However, recent studies have demonstrated that epigenetic processes, specifically DNA methylation and covalent modifications to histones, are central to the mechanism by which the effects of the early life environment persistent into later life. Studies in animal models have shown that the effects of maternal nutrition on the epigenetic regulation of individual genes are highly specific, differ between sexes and that different nutrients induce different changes in epigenetic marks. Similarly, maternal behaviour during nursing or exposure to environmental pollutants also induce highly specific epigenetic changes in the offspring. There is now emerging data from studies in humans of the effects of famine and adverse physiological factors in early life which are consistent with the animal studies and support the view that epigenetic processes are important in differential risk of non-communicable diseases.

Epigenetic changes appear to retain plasticity beyond early life and unfavourable epigenotypes may be reversible, unlike genetic traits. Proof-of-principle experiments support this view, but suggest that such interventions need to be undertaken with caution. Furthermore, a recent study has shown that epigenetic marks in tissues collected at birth may have utility as biomarkers in predicting future disease risk.

Thus epigenetic factors are of potential value to publish health by providing a novel means of identifying and ameliorating disease risk. However, a number of technical and financial challenges need to be overcome before such translation into health benefit can be achieved.

Overview of genetics in primary care

Nadeem Qureshi, University of Nottingham

Information on inherited disease has been collated in primary care for several years, for example, through family history collection and screening programmes. However, primary care practitioners are not always aware of the genetics that they are exposed to. The genetic white paper offered an opportunity to improve the confidence and competency of these frontline practitioners but lack of sustained resources has limited mainstreaming of several innovative projects originally funded through this initiative.

Considering potentially appropriate interventions, the evidence base for primary care genetics services is disappointing. Recently a systematic review of the utility of the genetic family history in primary care was commissioned by the US National Institute of Health. This review identified the paucity of high quality research in the international literature, with the few studies identified focusing on familial cancer risk assessment. Although British studies have dominated previous research, with the disinvestment in genetic health service research over the past 5 years, this is unlikely to continue to be the case.

Hand in hand with building the evidence base, is implementing genetic educational strategies in primary care. PEGASUS, a National Screening Committee funded education project is a example of how this can be done. The original remit of the PEGASUS project was to support antenatal screening for sickle cell and thalassaemia. However the approach is generalisable to other genetic disorders and the experience from outreach work on familial cancer can add to our understanding.

Another powerful driver to improve genetic awareness among non-specialist are policy imperatives, in particular NICE guidelines. The two most obvious examples are the guidelines on Familial Cancer and Familial Hypercholesterolaemia. Other less obvious NICE guidelines can also enhance the profile of genetics. This is includes the Lipid Modification/Cardiovascular risk assessment guidelines.

The potential to incorporate genetics into British primary care remains untapped. Fundamentally we need to exploit transferable skills from routine practice, such as routine data collection and the ability of practitioners to communicate risk.

SGPPH News Editor

Deadline for contributions for next issue is 30 November 2011

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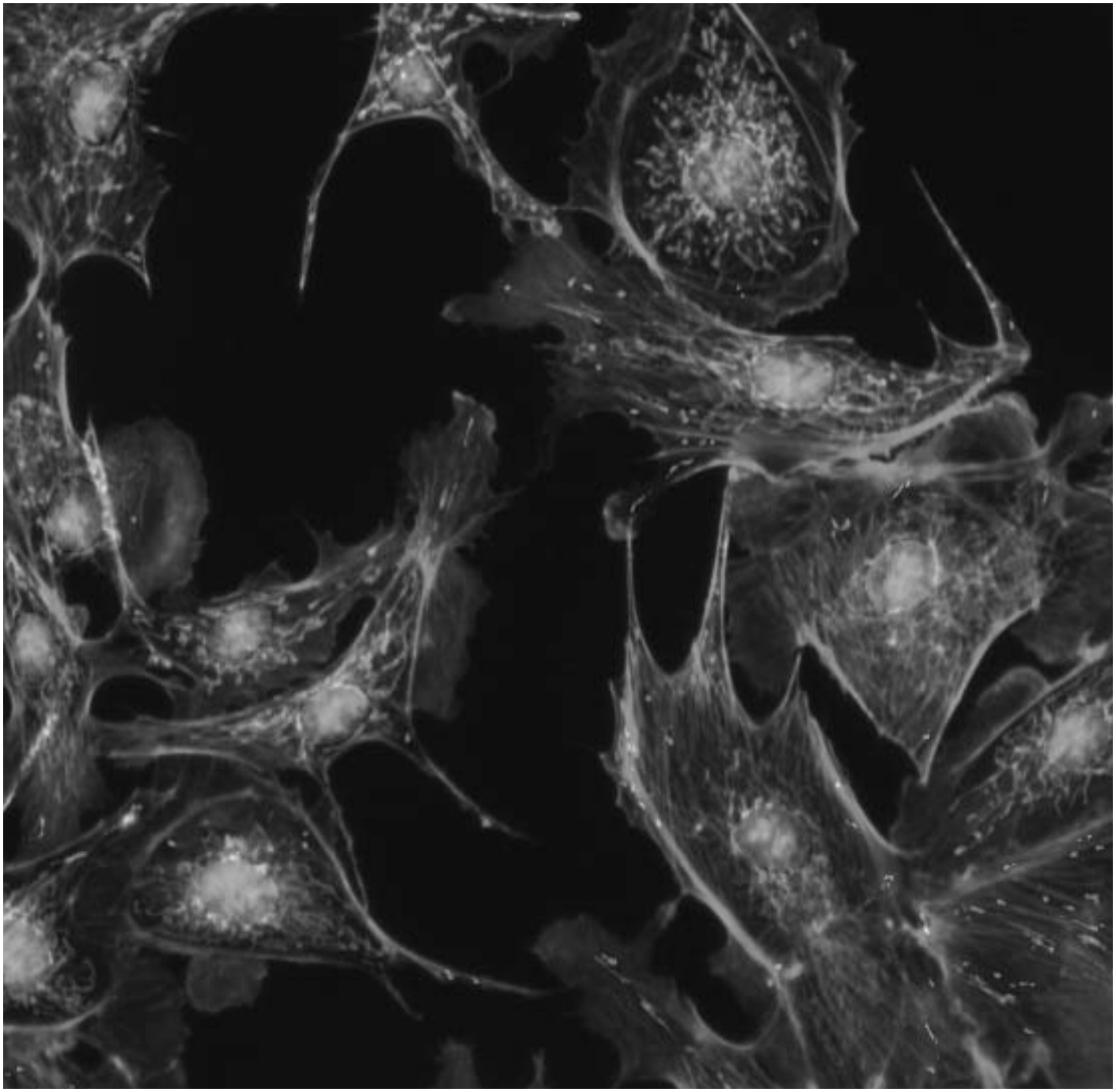

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