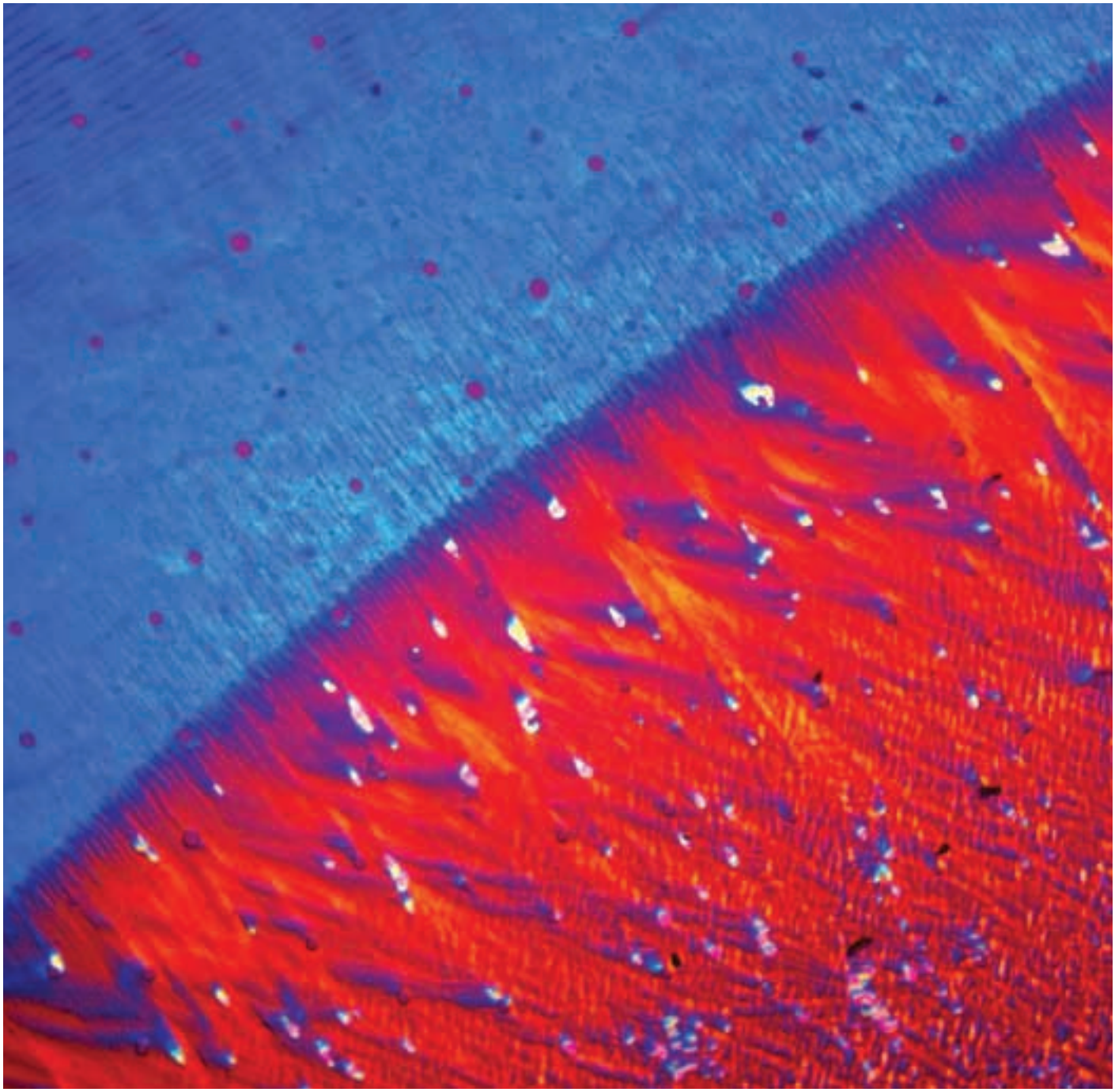
BSHG

The Newsletter of the
British Society for Human Genetics

Issue 37
November 2007

BSHG News



From the Newsletter Editor

Welcome to the November 2007 edition of *BSHG News*. In the BSHG section of this issue we have several excellent articles, including Paul Brennan's on the potential for a cardiac genetic referral deluge; Lyn Chitty on free-fetal DNA testing; John Burn's parallel universe; Marion McAllister on outcome measures for clinical genetics services; and Rob Elles and Gert Matthijs on the Myriad Genetics' appeal against a BRCA1 patent rejection by the European Patent Office.

We are launching a new element of the newsletter in this issue; *HIGHLIGHTS* is an opportunity for members to update the rest of us about recent publications by writing a brief, jargon-free summary for *BSHG News.* This has the advantage of directing fellow geneticists to find out about recent work, and may even improve your citation rate! In this edition, Sian Ellard and colleagues' paper on mutations in permanent neonatal diabetes – published in the American Journal of Human Genetics – initiates what I hope will become a regular feature.

Finally, the Competition to find a *BSHG News* cover image is still open, but not for long! If you would like to see your image on next year's newsletter, make sure you send it to me by the end of November.

Helen Middleton-Price

A Message from the Incoming BSHG Chairman

Rob Elles

I am very pleased and a bit daunted to be taking office as Chairman of the British Society for Human Genetics; the Society is growing in size, scope and stature, exemplified by the British Human Genetics Conference, which has gone from strength to strength, thanks most recently to out-going Chairman Richard Trembath and Eamon Maher and the Scientific Programme Committee.

The Council Away Day in May allowed us to step back and set goals (see New directions presented to the Society in York in this issue of *BSHG News*), and I hope I will be able to help achieve at least some of them during my period in office.

Wrestling with the day-in day-out struggles of the clinic and laboratory, it is hard to see beyond the next consultation or report deadline, but I am sure that Genetic Medicine has a great future. The trick will be to maintain a focus on the high-value work that is our bread and butter whilst making appropriate links as genetics expands into mainstream medicine, and new technologies and research findings create new possibilities for diagnosis and treatment.

One of the great rewards of working in Medical Genetics is the collaboration within the UK network. Financial pressures, business-orientated Foundation Trusts and powerful technologies may challenge this way of working. This means we must re-state the benefits of joint working and ensure the network is strengthened; one of our strongest arguments may be the potential of linking service and research to clinical trials, and we should look hard at these possibilities.

Internationally UK Genetics is well respected and in the last ten years UK geneticists have played leading roles in European health-related research and more recently in the European Society of Human Genetics. There is value in building on this experience and asking what we can offer to the developing economies. I am interested in working with a new BSHG International Group to develop links on both a development and commercial model.

I look forward to working with Council, with Ruth Cole and her team in Birmingham, and with the Society's members; I would welcome hearing from you at any time: rob.elles@cmmc.nhs.uk

In Memoriam: Dr Marina Seabright

Dr Marina Seabright, who discovered the method for trypsin G-banding that opened up a new era in medical genetics in 1971, died in late July 2007, not far from the laboratory in which she made her breakthrough. Her Lancet paper (Seabright, 1971) became a citation classic with more than 1294 citations, according to Google Scholar, and was followed by 17 years in which Marina was instrumental in building up the Wessex Regional Cytogenetics Unit as the major laboratory for cytogenetics in central southern England.

Marina's parents were Italian, living in Calabria. She studied medicine at Palermo, Sicily, where she met and married a young English naval lieutenant, Harold Seabright, whose family came from Hampshire. Her husband brought Marina back to England and she applied to Bristol University to continue her medical studies. Due to the large number of ex-service people applying she was unsuccessful and so, in 1947, came to work in the pathology service at Salisbury General Infirmary. She rapidly mastered the laboratory techniques and became an Associate and then a Fellow of the Institute of Medical Laboratory Technology with her thesis on the differential centrifugation of white blood cells. She was for some years the Senior Technician in Haematology but, in 1965, she set up the Cytology laboratory and, in the late 1960s, developed an interest in Cytogenetics, her practical skills allowing the production of good chromosome preparations.

Marina's great contribution to Cytogenetics was her technique of trypsin banding. Like a number of other seminal discoveries in Cytogenetics, there were elements of both chance and persistence in her story which has not received quite the same detailed attention from recent historians as that given to some of her contemporaries (e.g. Harper, 2006). One day in 1967, she was examining a Leishman stained chromosome preparation and was surprised to find that the chromosomes had “strange stripes” across the chromatids. Despite trying to retrace every step of the staining protocol, including the use of a few drops of the coffee that she had been drinking at the time, she was unable to reproduce the banding pattern and senior colleagues unanimously dismissed the striped chromosomes as artifacts. However, four years later, Lore Zech and Torbjorn Caspersson elegantly revealed the fluorescent bands that could be used to identify each chromosome using quinacrine mustard (Caspersson et al, 1971). While appreciating that this was a great step forward, Marina felt that the resolution needed improving and wondered if artificially uncoiling the chromatids before staining them would enhance the differentiation between the bands. As she remembered trypsin being used to ‘relax’ the coils of Vicia Faba chromosomes in the past, Marina tried trypsin on human material; a few sets of chromosomes showed both the banding pattern of her 1967 original and were comparable to the new fluorescent bands. In retrospect, Marina believed she must have produced the original by using a pipette contaminated with trypsin that had been previously used for harvesting a culture of fibroblasts but, this time, she had no doubt about the significance of her finding. It took only a few days to replicate, refine and standardize the method. The great value of her method lay in its simplicity, speed, low cost and the ability to characterise each individual pair of chromosomes with confidence under the light microscope. Trypsin banding rapidly transformed medical genetics and is still the most common method of chromosome banding used worldwide today.

Marina went on to study the effects of radiation on chromosomes and was awarded a PhD by the University of Southampton for this work. Not long after this, she was appointed Consultant Scientist and Director of the Regional Cytogenetics Unit in Salisbury. Under Marina, and as a direct consequence of her enthusiasm, the Unit thrived and budded off a series of huts and cabins at the rear of the Infirmary. When diagnostic molecular techniques arrived, Marina embraced them, setting the pattern for integration between cytogenetics and molecular genetics which we now recognize as essential. She became a Member of the Royal College of Pathologists and did a great deal for the profession as the first Secretary of Association of Clinical Cytogenetics and

Assistant Editor of the Journal of Medical Genetics. She ran a happy and productive Unit and colleagues record that it was always a pleasure to go to her room and talk about any problem, related or unrelated to cytogenetics.

Towards the end of her career Marina became a familiar figure at international meetings, which suited her gregarious personality, her interest in people and her forthright, incisive manner of expressing her opinions. Few who met her will forget the physically tiny but seemingly larger than life figure with the gruff voice and strong Italian accent. As her retirement approached in 1987, there was general concern that any replacement would seem dull and ordinary in comparison, but Marina was successful in recruiting Professor Patricia Jacobs who was able to build on the foundations that Marina had laid and use the excellent records of the laboratory as the basis for research on a wide range of cytogenetic topics.

Marina Seabright retired from her appointment as Director on 31 December 1987. On the same day, her appointment as an Officer of the Order of the British Empire, for her contribution to cytogenetics, was announced in the New Year Honours list.

John Barber, Annette Cockwell, Tony Herbert, Nick Dennis, John Harvey and Alan McDermott

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Acknowledgements

We are indebted to Marina herself for the Citation Classic article she wrote in 1981 which is held at the University of Pennsylvania Garfield Library and can be accessed via http://garfield.library.upenn.edu/classics1981/A1981LH21000001.pdf .

We are also grateful to the late Dr Robert Pinkerton for the profile of Dr Marina Seabright written on her retirement for the Bulletin of the Salisbury Medical Society.

Professor John Hilton Edwards FRS

Just as *BSHG News* was going to press, we heard the sad news that Professor John Edwards died in October. A full obituary will appear in the next edition. Our thoughts are with his family at this sad time.

Interested in benefiting from a Jeans for Genes grant award?

Jeans for Genes is a UK registered charity whose mission is to raise funds to support individuals and families affected by genetic disorders and to advance medical research into the causes, cure, prevention or relief of such disorders. This year Jeans for Genes is accepting applications from UK charities for grants ranging from £500-£25,000. Successful applicants will be those requesting funds for projects that extend the reach of Jeans for Genes into the genetic disorder community.

Jeans for Genes Day is one of the most popular one-day national charity appeals in the UK. On Jeans for Genes Day, Friday, 3 October 2008, children and adults nationwide will be asked to wear their jeans to work or school and to make a donation. Over £24 million has been raised by Jeans for Genes since the Charity was founded in 1996.

If your charity is interested in finding out more about benefiting from a Jeans for Genes grant, please visit http://www.jeansforgenes.com/grantapplication

The closing date for applications is Friday, 4 January 2008.

Gathering storm? Feel the breeze…cardiac genetics in the UK: an update

Paul Brennan, Northern Genetics Service

Over the last 10 years the subspecialty of cancer genetics has grown and defined itself. Cancer family history now accounts for a significant proportion of all referrals to regional genetics services. This explosion in activity has been driven in no small part by the growing awareness of familial cancer across a variety of medical specialities, creating clinical demand for cancer risk assessment and genetic testing; and the prominence given to familial cancer by the development of disease-specific management guidelines (particularly the NICE familial breast cancer guidelines). Service development has, in addition, been spurred by recommendations in the 2003 genetics white paper and facilitated by the creation of cancer networks, which have provided many centres with formal access to cancer clinicians, service improvement teams and a setting in which service development and change management are a cultural norm.

This explosion is going to happen to cardiac genetics over the next decade. So, what are the similarities to cancer genetics? Firstly, inherited cardiac diseases are not rare. Common single gene cardiac diseases probably affect around 1 in 250 people in the UK[1], although individual incidences (new diagnosis rates) remain largely unknown. Of the 100,000 annual sudden cardiac deaths in the UK – deaths which can confidently be attributed to heart disease – up to 10,000 of them are genetic (typically, cardiomyopathy and premature coronary artery disease secondary to an inherited dyslipidaemia); in addition, around 50% of cases of the 500 or so annual unexplained deaths in young adults are thought to be caused by inherited disease (typically inherited arrhythmia). Like cancer, in addition to clearly defined single gene disorders, some common cardiac diseases have a significant 'polygenic' component to their aetiology.

Secondly, support group lobbying and national level policy development in the form of 'Chapter 8'[2] are raising awareness of both sudden unexplained / cardiac death and inherited heart disease within the Department of Health, cardiac networks and cardiologists, and referral rates are starting to climb. Cardiac networks are not as well developed as cancer networks, but their functions, remit and philosophies are the same.

Chapter 8 has led to the creation of the National Sudden Cardiac Death and Inherited Cardiac Conditions Delivery Group (co-chaired by Alison Cox of Cardiac Risk in the Young {CRY} and Mike Yates from the Department of Health), and the National Coroners and Pathologists Special Interest Group (co-chaired by Mike Yates and Dr Perry Elliott of The Heart Hospital). These committees are largely focussed on services that respond to sudden death at present. A blueprint for inherited heart disease centres has been produced by Professor Bill McKenna and sent to all cardiac networks for consideration. Particular care has been taken to ensure that the role of genetics services is clearly delineated. Marfan syndrome is excluded from this document, although from a genetics service's point of view this is an important patient group and is another potential cause of sudden, potentially preventable, death. Although the blueprint recommends the creation of a relatively small number of specialist joint services – some covering a number of adjacent cardiac networks – this is merely a discussion point at present.

Are we ready for an explosion in referrals? The survey I undertook in late 2005 demonstrated one key observation: a striking variation in cardiac genetics service provision on many levels. Referral rates to genetics services varied from <10/yr to 600/yr (hypertrophic cardiomyopathy, the upper figure being a cardiologist-run cardiac genetics service with no close link with the local clinical genetics service); the type of services offered ranged from frequent, large multidisciplinary clinics to dedicated genetics clinics for inherited heart disease, whereas 37% saw inherited heart disease in general clinics; and there was little consistency in the uptake and use of diagnostic genetic testing. Few centres were geared-up to respond to a significant increase in referrals in 2005.

Two years later, this work needs to be repeated and expanded. Referrals are now different in rate and complexity. Some centres are beginning to think about demand management measures to reduce inappropriate referrals. Since 2005, hypertrophic cardiomyopathy and long QT syndrome diagnostic genetic testing has been transferred from the Oxford Genetics Knowledge Park to UK-GTN and a number of other laboratories have developed tests for these diseases. Many centres are unable to obtain funding for these tests, despite published evidence demonstrating their utility, and we need to understand the scale of the problem. Wales, Scotland and Northern Ireland need to be considered in their own rights. An updated survey will be undertaken during late 2007 and 2008 by the Foundation for Genomics and Population Health, under the leadership of Dr Hilary Burton (whose report on metabolic services[3] will give you a flavour of what the scope of the survey is likely to be). Critically, this study will also address the epidemiology of inherited heart disease so we can begin to understand the likely demand on services. Your centre will be asked to contribute information to this survey and I would urge you to do so.

The 2006 BSHG York meeting also saw the birth (although gradual emergence is

probably more apt) of the UK Cardiovascular Genetics Interest Group (see http://groups.google.co.uk/group/UK-CGIG). At present this has a rudimentary website and discussion group but I hope it will develop, link with cardiologists and become a lively society that plays a key role in the way services – and research – develop.

Over the next few years we will see the emergence of clinical cardiac genetics as a subspecialty in its own right, just as we have seen with cancer genetics. Clinical services will need to grow in capacity and complexity, in collaboration with cardiologists and exploiting cardiac networks. We will need national guidelines (I know, you're still waiting for that Marfan guideline: it'll be worth the wait, honest) and difficult discussions with healthcare commissioners around issues like genetic testing. But it's been done before with cancer, with some success, and we have to embrace the challenge.

If you felt the breeze and want to know more, it's not too late to register for the 'Challenges of clinical cardiovascular genetics' symposium in Cardiff, 22-23 November (see http://www.wgp.cf.ac.uk/listEvents.htm).

[1] Hypertrophic cardiomyopathy is estimated to affect 1/500 people, of which at least 50% is the result of a single gene fault; dilated cardiomyopathy affects 1/100 – 1/200 people, of which 20-40% have evidence of familial disease; familial hypercholesterolaemia is thought to affect 1/500 people.
[2] The affectionate term given to the latest chapter of the coronary heart disease National Service Framework (Department of Health. National Service Framework chapter for arrhythmias and sudden cardiac death. 4 March 2005. Available at: http://www.dh.gov.uk/en/Policyandguidance/HealthandsocialcaretopicsCoronaryheartdisease/DH_4117048)
[3] Available at http://www.climb.org.uk/Research/metabolic_pathways.pdf

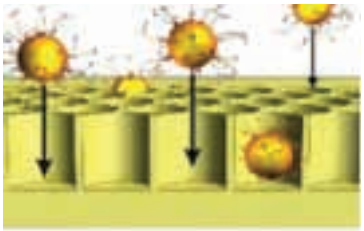
Life in a parallel universe: exploring the value of massively parallel sequencing by synthesis in clinical diagnostics

John Burn, Newcastle

A new approach to DNA sequencing called 'massively parallel sequencing by synthesis' has been developed which has great promise for diagnostics. In essence, small fragments of DNA, bound to beads sit in each of over a million tiny wells in a glass plate. As the bases are washed across the plate, a light flash is released for each letter that binds to the single strands in each well. A camera records these flashes then the computer deduces the sequence of each overlapping fragment and assembles the complete sequence. In theory, we should be able to set up individual runs, which sequence several genes in each of several patients. The preparation is complex but the individual machine runs take only around 12 hours. There are a host of technical challenges to overcome but the promise is that we will be able to sequence cheaper and faster than before. As a proof of principle, Roche Diagnostics are working with a team at the Institute of Human Genetics in Newcastle, led by Ann Curtis, to see if we can provide a complete sequence of BRCA1 and BRCA2 for several probands simultaneously. The glass plate can be segmented into 16 sections so the first idea will be to see if we can achieve both gene sequences in 16 probands simultaneously. This would offer a substantial cost improvement on present methods. A second set of experiments will explore the possibility of pooled sample analysis which might further improve productivity.

Members who came to the BSHG Sunday evening session heard Elizabeth Bryan's moving and insightful lecture based on her new book Singing the Life, which gave a doctor's personal perspective of BRCA1 in the family. The following Thursday she gave a similar lecture at the Centre for Life in Newcastle. To attract public interest, I gave interviews to our local media and linked her talk to our acquisition of the Roche genome sequencer FLX with funds from our regional development agency One North East. The following day the nationals picked up the story and produced the usual spectrum of variations on a theme. If patients ask about this, the answer is that the new approach shows great promise but is still under development and will not be ready for diagnostic use for several months.

Hopefully, 2008 will see us able to reduce the turnaround time and cost for sequencing these genes and others like them. Solution to one problem may raise new challenges, as easier diagnosis might lead to increased numbers of families needing counselling. If the early promise of the new drug class known as PARP inhibitors is maintained, this might become easier as these drugs selectively kill malignant cells deficient in BRCA1 or BRCA2. The first call on the new tool will be to identify eligible cancer sufferers to recruit into the clinical trials now commencing.



Elizabeth's book, Singing the Life, is now available from Amazon.

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Myriad Genetics' appeal against a BRCA1 patent rejection by the European Patent Office (EPO)

Rob Elles, Manchester
Gert Matthijs, Leuven

Myriad has tried hard to appeal against the EPO rejection of key elements of its BRCA1 patent claims and regain its original claims on the entire BRCA1 gene, sequence and protein, and all possible applications; it has, however, failed.

In the last week of September in Münich, the EPO Appeal Board heard arguments put by lawyers for the patent holder on their second patent claim on the BRCA1 gene (formally the patent is co-owned and thus defended by the University of Utah Research Foundation and the NIH, but in reality, Myriad Genetics is defending its case). This was an appeal against the earlier limitation of the patent claim. The patent claim rests on a short 300 bp probe and a few other gene sequences required to detect the BRCA1 gene.

The arguments were countered by Mr William Bird and his co-workers, who defend the case on behalf of a large group of European genetics societies and institutions, including the British Society for Human Genetics, and by Mr Jacques Warcoin, who represents the Institut Curie and two other French institutes, very much in concert with the attorneys representing the Dutch Ministry of Health, the Swiss Social Democrat Party and Greenpeace.

Gert Matthijs, a diagnostic scientist from Leuven, who has played a leading role in coordinating the opposition, reported that Myriad's attorney tried many arguments to convince the Appeal Board to grant a broad patent, and to neglect the errors in the sequence that were present in the original claim. This would have run counter to previous case law at the EPO and these arguments were effectively countered by the opposition attorneys and rejected.

Gert mentioned that at times during the sessions, the situation became theatrical and even "Dante-esque" with tensions rising high. Also, the Appeal Board was composed of five, rather than the normal three members, and the hearing took a full four days, illustrating that the BRCA1 case is, indeed, one of the most complex disputes in patent history.

To clarify the situation: this appeal concerned the second of three BRCA1 patents:

- Patent 1, granted in 2001, originally claimed the diagnostic test for predisposition to familial breast and ovarian cancer. It was revoked following hearings in May 2004. Myriad Genetics has filed an appeal against this decision. A hearing is awaited.

- Patent 2, which was rejected in the appeal described above, originally claimed the gene and protein sequence of BRCA1, and all possible applications, but was limited to a claim on a probe and a few other gene sequences to detect the BRCA1 gene after the first instance hearing in January 2005. This has now been confirmed.

- Patent 3, as originally granted, claimed a series of individual mutations. It was reduced to a single claim on a probe to detect the frequent Ashkenazi mutation 185delAG, in January 2005. The Myriad appeal has yet to be heard.

- Myriad also has a patent on BRCA2. It has been limited in June 2005 to claim the detection of the 6174delT mutation in BRCA2 in the Ashkenazi-Jewish population. .

The recent appeal decision is important in a number of ways:

- the EPO had decided to deal with patent 2 first as the most fundamental of the three BRCA1 patents. This decision will affect the outcome of the two outstanding appeals. European scientists are particularly anxious that the EPO confirms the revocation of patent 1 which would strongly interfere with BRCA diagnostic services.

- the Appeal Board has confirmed the limitation on the scope of patent 2. This decision reaffirms case law that the correct DNA or amino acid sequence is an essential technical feature in patent claims. The decision will impact on the patenting of genes in general.

- this decision is definitive and further appeal is not possible. Myriad will not be able to obtain a claim on the (only) other frequent Ashkenazi in BRCA1mutation, 5382insC.

- As granted now, patent 2 is limited in scope and does not interfere with diagnostics in Europe.

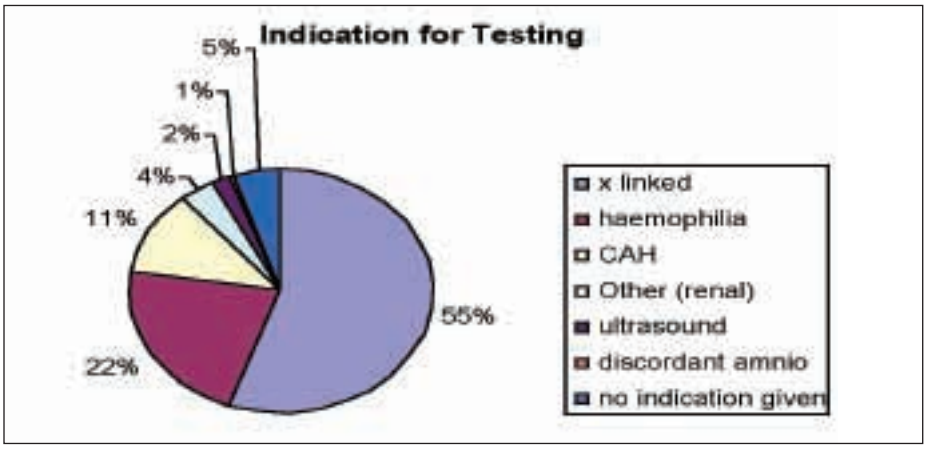
Further information: EPO website: http://www.epo.org/about-us/press/releases/archive/2007/20070927.html

Prospective Register of Outcomes Of Free-fetal DNA testing (PROOF) – results of the first year's audit.

Lyn Chitty[1,2], Bhaneeta Mistry[3], Julie Hogg[2], Cathy Meaney [3], Louise Thomasson [2], Gail Norbury[3], Geoff Daniels[4], Kirstin Finning[4] and Peter Martin[4].
[1]Clinical and Molecular Genetics, Institute of Child Health, [2]Fetal Medicine Unit, University College Hospital, [3]North East Thames Regional Genetics Laboratory, Great Ormond Street Hospital, London and [4]International Blood Reference Laboratory, Bristol

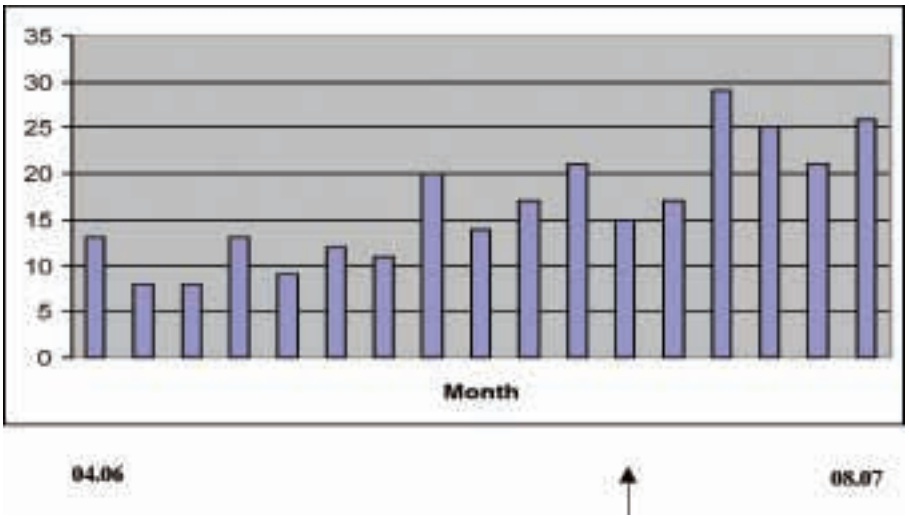
At the BSHG meeting in York in 2006, following a presentation of one unit's experience1, there was a request to provide more information with regard to the performance of free fetal DNA (ffDNA) for fetal sexing. At that time the authors undertook to conduct a national audit of all tests done in England in clinical practice. Approval for this was given following submission to the UCLH REC. An audit was performed of all requests for fetal sexing using ffDNA made to the two laboratories offering the test between 1 April 2006 and 31 March 2007. The test is offered by the International Blood Reference Laboratory in Bristol, who have been performing the test since 2003, and the North East Thames Regional Genetics Laboratory, Great Ormond Street Hospital, in London, which had recently developed fetal sexing using ffDNA and began offering it as a clinical service at the beginning of April 2006.

In the year commencing April 2006, 160 women were tested with 202 ffDNA tests performed. 28 tests were repeated as no result could be issued on the first test, and 14 repeats were required for marker testing. Different methodologies were used in the two laboratories, both based on real time PCR. The International Blood Reference Laboratory based their analysis on the DYS14 gene and the North East Thames Regional Genetics Laboratory used SRY. Indications for testing are shown in the histogram below. Of note, 22% of requests were because the mother was a carrier of haemophilia, although clinicians requesting the test reported that invasive testing for fetal sexing would not usually be requested for this indication.



The majority of tests were performed at seven weeks gestation or greater. 56.0% of results were reported within 3 days of testing and 91.3% within 7 days. When considering the time from receipt of sample in the laboratory to issue of report this was 72.0% and 98.7% respectively. No result was issued in eleven cases (6.8%). Fetal sex, as indicated at invasive testing, ultrasound or at birth, was ascertained in 139 (86.3%). Concordant results, in those with outcomes, were obtained in 96.2% of all cases. There were only six tests performed before seven weeks gestation and two of these gave discordant results. When analysing accuracy for tests done at seven weeks or more the accuracy was 97.6%. When considering tests done for X-linked conditions (excluding haemophilia), invasive tests were performed on only 55% of cases.

Analysis of the numbers of tests performed since 1 April 2006 showed a steady increase in requests with a third laboratory offering the test from March 2007.



"When analysing accuracy for tests done at seven weeks or more it was 97.6%."

In view of the experiences with testing over the last year, practices have changed in the two laboratories, the data from which are reported here in an attempt to reduce the incidence of discordant results. The IBGRL will only report as male a sample where seven of eight replicates have a CT value < 37, and female where a maximum of two replicates have a CT value >39. This has resulted in an increase in requests for a second sample to 20% and no report being issued in 8% of all samples, or 5.9% of those where repeat testing is performed. The GOSH laboratory found that the use of bi-allelic fetal markers used to confirm amplification of ffDNA was time consuming and only informative in 40%. This has been abandoned pending development of a universal fetal marker and the policy in this laboratory currently is to analyse two independent samples before issuing a result assessed on basis of standard deviation and Ct value between 6 replicates of duplicate extracts. Testing before seven weeks is not recommended. Early impressions are that these new measures should reduce the incidence of discordant results, but the audit will be continued for a further year to investigate trends.

Conclusions

- Fetal sexing using ffDNA is 97.6% accurate when performed > seven weeks.
- It reduces invasive testing in cases referred because of an X-linked condition by around 45%
- Criteria for reporting sex must be very stringent
- It is not possible to determine sex using ffDNA in around 4-6% of cases
- Further investigation of the aetiology of false positive males is needed.
- Development of sex-independent fetal markers is needed.
- Early ultrasound (in an FMU) can be offered to confirm sex from 12 weeks'.
- There appears to be a trend towards offering sexing using ffDNA rather than USS is some conditions, eg haemophilia where invasive testing would not usually be offered. This may have significant service and economic implications.

Acknowledgements.

The European Commission for the Special Non-invasive Advances in Fetal and Neonatal Evaluation (SAFE) Network of Excellence (LSHB-CT-2004-503243) funded the personnel collating the outcome data. We would like to thank all those who helped by returned outcome forms.

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1. Chitty LS, Stojilkovic-Mikic, Hogg J, Martin PG, Meaney C, Norbury G. Effectiveness of non-invasive prenatal diagnosis using free fetal DNA in the maternal circulation. J Med Genet 2006;43:suppl1:S30

HIGHLIGHTS – BSHG members' recent publications

Permanent neonatal diabetes caused by dominant, recessive or compound heterozygous SUR1 mutations with opposite functional effects

Ellard et al AJHG 81, 375-382

Recessively inherited loss-of-function mutations in the KCNJ11 and ABCC8 genes encoding the pore-forming Kir6.2 and regulatory SUR1 subunits of the pancreatic beta cell KATP channel are the most common cause of congenital hyperinsulinism. The opposite phenotype of neonatal diabetes is most frequently caused by heterozygous activating mutations in the KCNJ11 gene. In the present study we sequenced the ABCC8 gene in a cohort of 59 patients with permanent diabetes diagnosed before 6 months of age who did not have a KCNJ11 mutation. Mutations were identified in 16/59 patients and included eight patients with heterozygous de novo mutations. A recessive mode of inheritance was observed in eight patients with homozygous, mosaic or compound heterozygous mutations. Unexpectedly two of these patients were compound heterozygotes for an activating missense mutation and a frameshift mutation. These frameshift mutations result in premature termination codons and are predicted to be loss-of-function mutations typically associated with recessive hyperinsulinism. We propose that these loss-of-function mutations lead to a decrease in functional protein and that the majority of pancreatic KATP channels will be homomeric for the missense mutation. To our knowledge, this is the first disease phenotype reported to be a result of compound heterozygosity for both gain-of-function and loss-of-function mutations.

Towards outcome measures for clinical genetics services

Marion McAllister M[1,2,3], Katherine Payne[1,3], Rhona Macleod[2,3], Stuart Nicholls[1], Dian Donnai[1,2,3], Linda Davies[1,4]

[1]Nowgen, A Centre for Genetics in Healthcare
[2]Central Manchester and Manchester Children's University Hospitals NHS Trust
[3]Academic Unit of Medical Genetics and [4]Health Economics Research at Manchester, The University of Manchester

There is no accepted 'gold' standard model of providing a clinical genetics service but each approach to service delivery shares a common goal of aiming to improve patient benefits. Using existing measures of outcome it is not clear if clinical genetics services effectively meet this goal. Payment By Results (PBR) requires the NHS to quantify all activities, and so there is a need to identify or develop effective outcome measures. The aim of the Valuation and Evaluation of Genetics Services research theme at Nowgen was to commence work towards a core set of outcome measures for clinical genetics services. The first phase of this programme is now complete and this article reports on the findings of this first phase.

The research programme used a triangulation of three methods: a systematic review, a Delphi survey, and qualitative research using focus groups and interviews. The systematic review[1] aimed to identify existing validated outcome measures used in evaluations of clinical genetics services and the key domains described in these measures. Five databases were searched using structured electronic search strategies based on text terms relevant to (1) clinical genetics services (2) outcome measures and (3) validation methods. The systematic review identified 61 papers, which used 67 validated outcome measures. The identified outcome measures can be broadly classified into: non-genetics specific (37 measures) suitable for the evaluation of any healthcare service, and genetics specific (30 measures). The findings from the systematic review were used to design the Delphi survey[2], which aimed to explore genetics professionals' and patients' views about which outcome measures are most appropriate to value clinical genetics services. A two-round Delphi survey was completed by a panel comprising 115 genetics healthcare professionals and 72 patients and support group members. The survey contained 19 measures identified from the systematic review. Respondents assessed the usefulness of each outcome as a measure of patient benefit on a rating-scale (1=strongly disagree to 7=strongly agree). Figure 1 shows the percentage of the panel who rated the outcome domains as 'useful' (scored 5, 6 or 7) as a measure of patient benefit. Outcome domains that achieved consensus (at least 75% of panel rated 'useful') by the panel were: decision-making; knowledge of the genetic condition; perceived personal control; risk perception; satisfaction; meeting expectations; ability to cope; diagnosis accuracy and quality of life.

A follow-up survey will be posted on the Nowgen website in January 2008 exploring the views of the general public about appropriate outcome measures for clinical genetics services.

The aim with the qualitative research[3,4,5] was to develop a model describing the patient benefits of using clinical genetics services. Seven focus groups[3] (n= 33) and 19 one-to-one interviews[3,4,5] were conducted with patients of clinical genetics services, their representatives from patient support groups, and health professionals involved in provision of clinical genetics services. The total sample size was 55. Data was analysed using grounded theory methodology. The outcome of the qualitative research was a model of 'empowerment' describing the patient benefits of using clinical genetics services, and is shown in Figure 2. 'Empowerment', as constructed in this study, summarises what participants said they and the patients they represent are looking for when they attend a clinical genetics service. Empowerment enables a fulfilling family life, and emerged in this study as being a belief system that allows a person to feel in, or take control of their lives and have responsibility or autonomy over decisions and choices. Empowerment is made up of four contributing dimensions: (1) 'knowledge and understanding' about the family condition, (2) 'decision-making', or feeling able to make important life decisions in an informed way, (3) 'instrumentality', or feeling able to make effective use of the health and social care systems for the benefit of the whole family, and (4) 'future-orientation' or feeling able to look to the future having hope for a fulfilling family life, for oneself, one's family, and/or one's future descendents. The qualitative research also identified a series of process attributes, and a series of interventions that can facilitate empowerment, and these are also shown in Figure 2.

The qualitative research findings and the model of empowerment supports the following outcome domains as highly valued:

- Perceived personal control (PPC)
- Ability to make decisions
- Knowledge of the genetic condition
- Accuracy of diagnosis

When compared with outcome domains identified by the systematic review, empowerment is conceptually most similar to the concept of perceived personal control (PPC), and a measure of PPC has been developed for use in evaluations of clinical genetics services. The PPC measure has been validated for use in an Israeli population, but has not yet been validated for use with a UK population. However, empowerment includes some benefits not captured by PPC related to

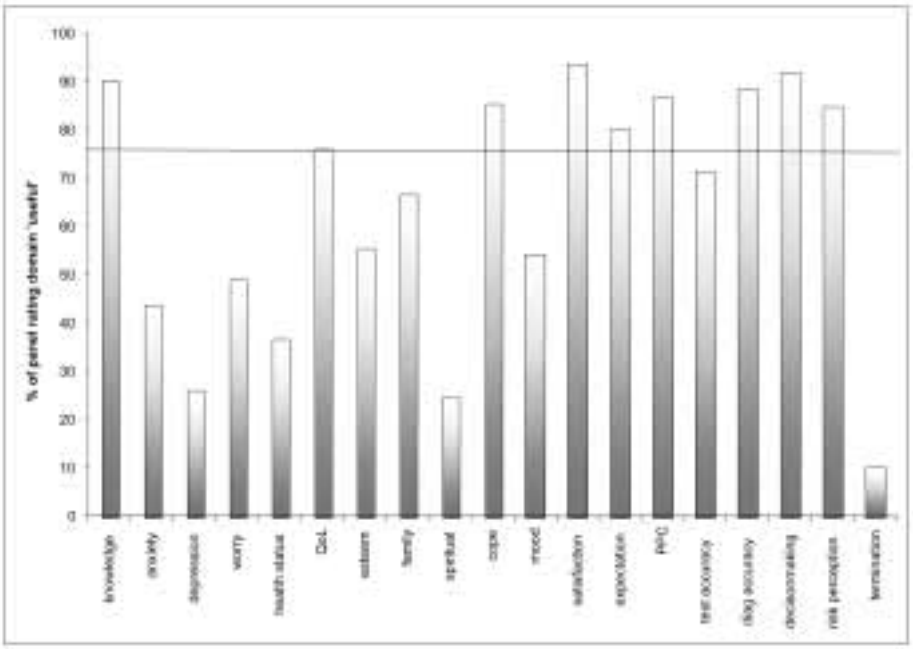
"There is no accepted 'gold' standard model of providing a clinical genetics service"

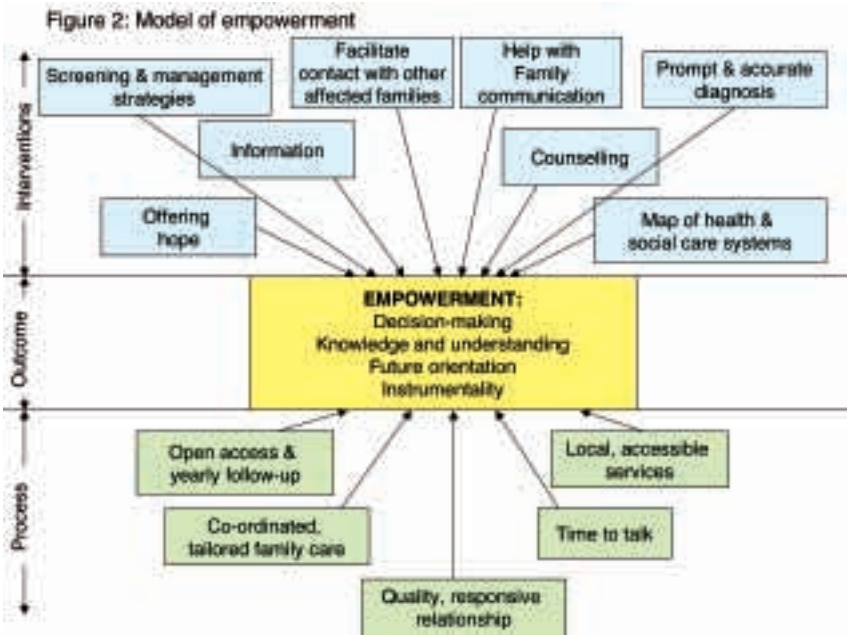
empowerment of other at risk relatives, and future generations.

This study has successfully triangulated three different research methods to provide evidence to begin developing a core set of outcome measures for clinical genetics services. The findings from the systematic review enabled a Delphi survey to identify those outcome domains, included in currently validated outcome measures, that are most highly valued by patients of clinical genetics services, and by genetics healthcare professionals. The qualitative research supports the findings from the Delphi survey, but also identifies some areas where current validated outcome measures do not fully capture the benefits that patients can get from using clinical genetics services. These areas include future orientation and empowerment of future generations. It is clear that the benefits of using clinical genetics services may not be realised for up to a generation or more, but that those benefits can still be appreciated by patients on behalf of their descendents. This aspect of patient benefit is not captured by any existing validated outcome measures used in clinical genetics services. The qualitative research has also identified interventions that a clinical genetics service can offer, as well as aspects of the service process that can maximise patient benefits. These findings will be useful in designing new models of service delivery.

A follow-up study is funded by a Medical Research Council post-doctoral training fellowship to enable Dr Marion McAllister to develop a validated measure of 'Empowerment' for use as an outcome measure for clinical genetics services. This is likely to involve further development and validation of the PPC measure, and Marion is collaborating with Professor Shoshana

Figure 1: Outcome domains rated as 'useful' by the Delphi panel





"Empowerment… allows a person to feel in…control of their lives"

NGRL Updates

NGRL (Manchester)

Rob Elles, Manchester

Shiloh at the University of Tel Aviv in Israel who developed the PPC. Dr Katherine Payne has been awarded an RCUK Senior Academic Fellowship focussing on the economics of genetics-related healthcare, which includes the development and application of economic methods to evaluate both genetics-related services and technologies and explore factors affecting their uptake in the National Health Service.

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5. McAllister M, Payne K, Nicholls S, Macleod R, Donnai D, Davies L. Patient empowerment in clinical genetics services. J Health Psychol (in press)

A workshop to discuss the achievements and plans of the NGRLs was held at BSHG York. To stimulate discussion we looked at the factors that will be important for the genetic diagnostic network over the next five years.

The NHS landscape

After the seven fat years around the Genetics White Paper investment will seven lean years follow? Financial pressures and the competitive environment formed by Foundation Trusts acting as stand-alone businesses are already causing tensions with the idea of networked service provision. The next five years may see less shared service provision through the UKGTN, more repatriation of tests and more duplication of effort. Or can we re-invent the network as automation takes hold and unit costs fall, continue to expand the volume and range of laboratory services we offer through UKGTN to new users and strengthen the specialist expertise built around the research interests in Regional Genetics Centres?

The Pathology Networks advocated in the Carter Report are now a reality. They form larger and more coherent service providers and give genetic laboratories new opportunities to exploit their modernised capability and their skills and expertise to offer molecular pathology services to Laboratory Medicine.

NHS Research and Development is being re-organised. The new emphasis on translational research may stimulate an increased rate of translation of genetic research findings into service. In recognising this trend the UK Genetics Services could work to develop itself into one of the recognised research networks.

Fewer newer technologies

To make a bold statement: in five years the present distinctions between cytogenetics and molecular genetics will cease to exist; we already see a convergence around common technical platforms such as array CGH and highly parallel sequencing. If we make the right organisational and purchasing decisions, these technologies will be effectively implemented. This is a huge challenge to the current organisation of our services and training of our staff. They will transform what we can offer, not just in throughput and turn-round time, but in qualitative terms giving us the capability to scan whole genomes at a fine level of detail, tackle locus heterogeneity and look at whole families of genes associated with phenotypes and whole pathways within the cell.

If we are to exploit these new capabilities and add value as scientific interpreters of genotypes then clinical scientists and technologists must learn, help develop, and integrate informatic tools. In five years time scientists will not be genotyping or karyotyping; they will be addressing web based information systems from their desk-tops to integrate large volumes of data into meaningful risks for patients. Genetic scientists must become bio-informaticians.

The pace of research will not slacken and will open potential new directions. In the single-gene conditions, new tests for genetic modifiers of phenotype will become relevant. Genetic diagnostics should look more intensively at somatic changes, working in partnership with the Pathology Networks. Clinical trials and treatments are likely to be come available for previously intractable inherited disease. In evaluating genetic tests this will change the balance of cost and benefit. Information as a hard-to-measure benefit will be replaced by a readily evaluated therapeutic gain.

Much will change over the next five years and as a network we need to be prepared and recognise the new opportunities for genetics services.

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NGRL MANCHESTER

NGRL (Wessex)

Nick Cross, Salisbury

Our forthcoming work program will focus predominantly on three key areas: (i) new mutation detection techniques including next generation sequencing, (ii) non-invasive prenatal diagnosis and (iii) array comparative genomic hybridisation (CGH). Below we give an update into our ongoing array CGH work plus a summary of a study of methylation-sensitive high resolution melt curve analysis that has recently been published.

Oligo array-cgh

The NGRL (Wessex) customised 4 x 44K oligo array design has now been ordered and printed for several other laboratories, a number from Western Europe and two in the U.K. There have also been a number of expressions of interest from other U.K. laboratories and from groups in other parts of the world. For further details of the array design parameters, please see (http://www.ngrl.org.uk/Wessex/array.htm and http://www.ngrl.org.uk/Wessex/microdel_collection.htm).

In Salisbury we have now run over 50 customised arrays (200 individual samples) and are detecting pathogenic imbalances ranging from ~175 Kb up to several megabases. In the coming months, we will be looking at the next iteration of the customised design to take into account the new printing formats which Agilent plan to have available by May/June 2008. From a diagnostic perspective the revised formats will include 8 x 60K and 4 x 180K, the latter being automatable using the Tecan hybridization station. With the 8x60K format, the promise of high throughput/density oligo array cgh will become a reality. With our experience to date with Agilent's e-ARRAY facility and the availability of oligos for the pseudoautosomal region, we will have to maintain a balance between sensitivity and the overall utility of future array designs. From recent studies of pathogenic X chromosome imbalances detected by array-cgh (e.g. Froyen et al 2007. Hum Mutation 28:1034-1042), it is clear that future designs should incorporate comprehensive X and autosomal coverage. We would welcome any feedback on our current design and ideas for the forthcoming upgrade. For further information please contact John.Crolla@salisbury.nhs.uk.

Methylation-sensitive high resolution melt curve analysis

Angelman syndrome (AS) and Prader-Willi syndrome (PWS) are two distinct neurodevelopmental disorders which are caused primarily by deficiency of specific parental contributions at an imprinted domain within the chromosomal region 15q11.2-13. Lack of paternal contribution results in PWS either by paternal deletion (~70%) or maternal uniparental disomy (UPD) (~30%). Most cases of AS result from the lack of a maternal contribution from this same region, by maternal deletion (~70%) or paternal UPD (~5%). Analysis of allelic methylation differences at the SNRPN locus discriminates the maternally and paternally inherited chromosome 15 and can be used as a diagnostic test for AS and PWS. We have used methylation-sensitive high resolution melt curve analysis (MS-HRM) with the DNA binding dye EvaGreen to analyse methylation differences at the SNRPN locus in anonymised DNA samples from PWS (n=39), AS (n=31) and normal control samples (n=95). Results from the MS-HRM assay were compared to those obtained using a methylation-specific PCR protocol that is used commonly in diagnostic practice. Using the MS-HRM assay, 97.6 % of samples were unambiguously assigned to the three diagnostic categories (AS, PWS, Normal) using automated calling with an 80% confidence percentage threshold and the failure rate was 0.6%. One sample showed a discordant result for the MS-HRM assay when compared to MS-PCR data. We conclude that MS-HRM is a simple, rapid and robust method for screening methylation differences at the SNRPN locus and could be used as a diagnostic screen for PWS and AS.

White HE, Hall VJ and Cross NCP. Methylation-Sensitive High-Resolution Melting-Curve Analysis of the SNRPN Gene as a Diagnostic Screen for Prader-Willi and Angelman Syndromes. Clin Chem. 2007 Sep 21; [Epub ahead of print]

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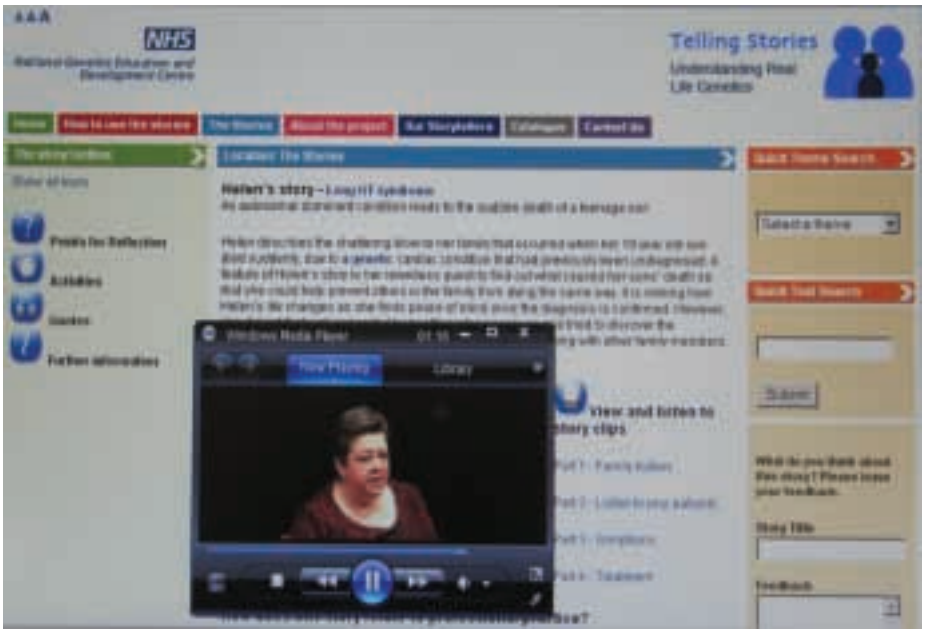
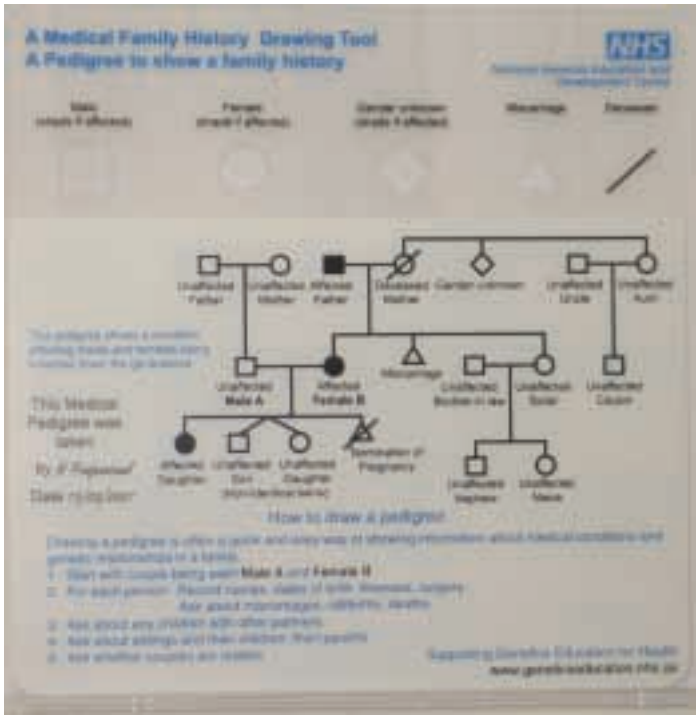
NHS National Genetics Education and Development Centre Update

Silvana Ioannou, Birmingham





The NHS National Genetics Education and Development Centre staff were pleased to meet many of you at our stand at the BSHG annual conference in York in September.

Since our last report we have been developing genetics education resources to support those learning genetics, teaching genetics, developing genetics services, and applying genetics in practice. Our website (www.geneticeducation.nhs.uk) provides information on resources, courses and learning support materials for each of the different healthcare groups.

Events

We would like this opportunity to invite the Regional Genetics Centres from around the country to our two open days, An Update for Regional Genetics Centres, on the 20 and 29 November, at the NHS National Genetics Education and Development Centre in Birmingham to find out about the range of our work in genetics education, including: genetics learning outcomes for medical students, foundation trainees, non-genetics SpRs and GPs; patients views on receiving genetic information; explore the Centre's online resources and discuss genetics education with Centre staff.

Competences for genetics in clinical practice for non-genetics healthcare professionals

The Centre undertook a joint project with Skills for Health and a cross section of health professionals from the UK to identify what genetics activities were appropriate to health professionals outside specialist genetics services. The activities were translated into competences with specific performance criteria, knowledge and understanding. The competences have been approved as National Occupational Standards.

Genetics Education Resources

1. Following discussions with speciality education bodies, the Centre has been collaborating with Regional Genetics staff to develop guidance to maximise the teaching and learning opportunities of non-genetics medical trainees in the outpatient genetics clinic. The finalised guidance will be sent out to all the regional genetics centres.

2. Telling Stories, Understanding Real Life Genetics is a teaching and learning tool available online at geneticseducation.nhs.uk/tellingstories. This genetics education resource contains patient stories and the experiences of families and health professionals that illustrate the impact of genetics on clinical practice. Each powerful story is accompanied by a story tool box of further activities and points of reflection which makes the most of teaching and learning experiences.

3. The Centre has developed a Medical Family History Drawing Tool for all health professionals learning or teaching taking a pedigree to illustrate a family history. This template includes a step by step guide to taking a family history. If you would like a Medical Family History Drawing Tool please email silvana.ioannou@geneticseducation.nhs.uk

Genetics Education Courses

The NHS National Genetics Education and Development Centre will be hosting a series of interactive Teaching Genetics courses, the first of which is aimed at the educators and trainers of Specialist Registrars (SpRs). This course will be held on Thursday, 31 January, Wednesday, 27 February and Tuesday, 8 April 2008. The course provides grounding in teaching genetics to health professionals including identifying how to engage people when teaching, how to communicate genetics concepts. For more information about the Teaching Genetics course, or to register, please visit our website, www.geneticseducation.nhs.uk.

Publications

The Centre will be publishing a series of reports, the first of which presents the views and experiences of patients and their families about how they received genetic information, in which they give their preferences and recommendations for receiving information. The Centre is preparing to send out this report to all the regional genetics centres. The other reports planned for the next few months include

- Workforce competences in genetics for non-genetics health workers – implementation into practice.
- Learning outcomes in genetics for medical students and non-genetics Specialist Registrars.
- Guidelines for teaching and learning in the genetics outpatient clinic.
- Attitudes of practicing pharmacists towards pharmacogenetics and the skills required to deliver a pharmacogenetics service.
- A review of genetics content in the biology A-level and International Baccalaureate examinations.
- A toolkit for supporting genetics service developments.

Did you know about OrphaNews Europe?

OrphaNews Europe is a bi-monthly, free, electronic newsletter which has been established for over two years. With a focus on rare diseases, which encompasses most genetic diseases, it is highly relevant for members of the BSHG. With it, you can stay up to date with:

- Research and public health policy news at a national, European and international level.
- New syndromes and genes published in PubMed.
- Funding opportunities for research.
- New orphan drug designations and authorisations.
- Events and publications.
- News from patient organisations.

Go on, subscribe today at:

- www.orpha.net/actor//cgi-bin/OAhome.php?Ltr=EuropaNews

FamilyTalk

FamilyTalk is a research project exploring family communication between children and young people and their parents about genetic conditions and genetic risk information. The project aims to examine the process involved and language used depending on the family members, the developmental stage of the children, the genetic condition and its potential outcomes.

We hope to be able to find out more about the different strategies used by families to discuss genetic conditions, and how effective these are by exploring children's and young people's understanding. The findings will inform the development of ideas and tools and provide a source of advice to help other parents talk to their children depending on their child's stage of development. This will also help health professionals in the support and advice they provide to families.

FamilyTalk is funded by the Department of Health and carried out by a team of researchers at Birmingham University. The project has been informed by the Genetic Interest Group (GIG) and a team of lay adviser families, including children, young people and their parents, and has been approved by the Liverpool Paediatric Ethics Committee.

Recognising that there are many sensitive issues involved, we have agreed with the research ethics committee to recruit families who have appropriate support networks via support groups. We are willing to attend meetings to discuss the project further, and answer any questions. Families are carefully assessed to ensure parents have discussed the genetic condition with their children previously, well in advance of their participation and recruitment to this study.

We are interviewing parents or guardians and children and young people in families affected by cystic fibrosis, Duchenne muscular dystrophy, familial adenomatous polyposis, neurofibromatosis, sickle cell disease or thalassaemia. We use a variety of participatory techniques to engage children and young people. We would also like to interview the parents in families affected by Huntington disease to explore the issues they face in deciding when and how to discuss this late onset genetic condition with their children.

All family members' interviews are treated confidentially and they take place at a time and place that suits them.

If you are involved with a support group and may be willing to introduce the project to its members please contact us for further information. You can also find further information on our website: http://www.healthsci.bham.ac.uk/FamilyTalk/

If you are interested in learning more about this research please contact

Gill Plumridge, Tel 0121 415 8740 or email: g.plumridge@bham.ac.uk or

Alison Metcalfe, Tel 0121 4142666 or email: a.m.metcalfe@bham.ac.uk or

Jane Coad Email: j.coad@bham.ac.uk

Genethics Club

Got a difficult ethicolegal issue? Don't forget Genethics Club! (www.genethicsclub.org.uk) Genethics Club is a national forum for professionals working in clinical or laboratory genetics. The format is like dysmorphology club: clinical case discussions, or issues/dilemmas (real or hypothetical, clinical or policy) around a central plenary talk. Each day usually runs from 10.30-4.30. Two of the meetings each year are held in London and one outside London. If you would like to host a genethics club, please let us know.

Provisional dates for 2008:

30 January 2008, Regent's Park College, London (Plenary: Research or clinical care? Examining the boundary in field of Cancer genetics)

July 2008, date tbc Edinburgh tbc

13 October 2008, London (venue tbc)

There is usually a small charge for attendance (~£10 depending on venue). CPD approval – 5 points per day.

Contact Mike Parker (michael.parker@ethox.ox.ac.uk), Tara Clancy (Tara.clancy@cmmc.nhs.uk) or Anneke Lucassen (A.M.Lucassen@soton.ac.uk) for further information.

BSHG AGM Minutes

New directions presented to the Society in York

The BSHG Council Away Day held on 15 and 16 May in Southampton aimed to look at the next seven to ten years, identify key strategic areas and help the Society develop an action plan.

The context for new proposals was discussed at the workshop; most of the Society's members and activities are related to the NHS and features in the current landscape are the reform of the research and development system with the creation of the National Institute for Health Research and Office for Strategic Co-ordination of Health Research. There is a new emphasis following the Cooksey report of the need to strengthen translational research and clear patient benefits as the outcome of research. At present Genetics is not recognised as one of the research networks and geneticists must work hard to become a de facto research network.

The recent period when specialised genetic services have benefited from central funding was closing and a tougher financial climate may follow and genetic services must adapt to this new environment.

Outgoing President Richard Trembath presented a summary of the workshop and three new directions for the Society at the AGM in York:

1. Re-emphasising the aims of the Society and strengthening its structure

- A new Chief Executive Officer post was proposed to help the BSHG achieve its strategic goals, promote the public profile of the Society, and strengthen its financial base. A robust proposal for sustainable funding will be a pre-requisite to appointment of this new post.
- The Society will improve interactions with other medical societies and disciplines (for example the social sciences) and strengthen its relationship with patient groups and industry.
- The BSHG will take actions to ensure that the value of belonging to the Society membership is clearer, retain existing members, and recruit beyond its current base (NHS employed professional staff).
- The Society will consider the benefits and issues involved in the adoption of one or more Patrons.

2. New directions for Human Genetics in healthcare:

- Genetic interventions are changing from a focus on information to the patient towards improved prevention of and management and therapy for genetic conditions. There is an important role for the Society to encourage and facilitate education and training for example in the management and analysis of clinical trials.
- The Society should help strengthen the infrastructure of the genetic network to meet the changing needs of service and research; promoting the updating, standardisation and communication of clinical and laboratory information systems.
- The BSHG recognises the increased relevance of genetic interventions to common conditions and will encourage geneticists to work with colleagues in other disciplines for example in setting standards in clinical care pathways.

3. Actions to influence policy development:

- The BSHG will help ensure that Genetics is recognised as an NHS research theme; supporting the candidature of members of the community to the College of the NIHR.
- The Society will encourage the retention of an identifiable Genetics Policy function within the Department of Health.
- The BSHG will strengthen its effectiveness in responding to issues of public interest.

Changes in Genetics are happening already, the flavour of the conference this year was distinctly therapeutic and not just diagnostic, the training of both scientists and clinicians will need to evolve to reflect this evolving and shifting emphasis. The Society aims to ensure that its membership continues to thrive and expand in this changing climate.

Notice Board

Welcome to New Members

48 new members were elected to the British Society for Human Genetics in September:

Dr Ismail Alrashdi (Clinical Genetics)
Mrs Neena Arora (Cytogenetics)
Miss Elspeth Badger (Cytogenetics)
Mr Leigh Batten (Molecular Genetics)
Dr Jessica Buxton (Human Genetics)
Miss Rebecca Collier (Genetic Counsellors)
Miss Anne-Marie Coupe (Molecular Genetics)
Mrs Lyndsey Croft (Cytogenetics)
Miss Pooja Dasani (Genetic Counsellors)
Miss Barbara de Oliveira (Cytogenetics)
Mrs Ahinora Dimitrova (Cytogenetics)
Mr Navaratnam Elanko (Molecular Genetics)
Mr Drew Ellershaw (Cytogenetics)
Miss Kim Gratton (Cytogenetics)
Miss Elinor Groves (Cytogenetics)
Mrs Alison Hall (Human Genetics)
Mr Abraham Hayibor (Cytogenetics)
Dr Ketil Heimdal (Clinical Genetics)
Miss Tatiana Jakubcova (Molecular Genetics)
Prof Janusz Jankowski (Molecular Genetics)
Dr Nayana Lahiri (Clinical Genetics)
Mrs Elaine Levinson (Genetic Counsellors)
Mrs Maria Masood (Genetic Counsellors)
Miss Katherine May (Genetic Counsellors)
Miss Jenna Mcluskey (Molecular Genetics)
Dr Jayne Minton (Molecular Genetics)
Mr Hood Mugalaasi (Molecular Genetics)
Mrs Tina Nanji (Cytogenetics)
Miss Akua Nkreumah (Cytogenetics)
Dr Suzanne O'Shea (Molecular Genetics)
Mrs Emily Packham (Molecular Genetics)
Dr Siddramappa Patil (Clinical Genetics)
Miss Claire Pearce (Cytogenetics)
Miss Jennifer Platt (Cytogenetics)
Miss Hannah Pulker (Molecular Genetics)
Miss Stacey Sandell (Molecular Genetics)
Miss Fabiana Ramos Vasques (Cytogenetics)
Miss Sandra Ramos (Molecular Genetics)
Mr Richard Sayers (Genetic Counsellors)
Mrs Beverley Setterfield (Cytogenetics)
Dr Una-Marie Sheerin (Clinical Genetics)
Miss Helen Shields (Cytogenetics)
Miss Alison Skinner (Molecular Genetics)
Dr Ingrid Slade (Clinical Genetics & Cancer Genetics)
Mr Paul Stevens (Cytogenetics)
Dr Nicola Taverner (Genetic Counsellors & Cancer Genetics)
Mrs Annette Wakeling (Cytogenetics)
Miss Lorna Williams (Cytogenetics)

BSHG News Editors


Deadline for contributions for next issue is Friday 11 January 2008

BSHG Editor: Dr Helen Middleton-Price
BSHG Executive Officer: Mrs Ruth Cole

Nowgen - A Centre for Genetics in Healthcare, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU

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Email: helen.middleton-price@cmmc.nhs.uk

Travel Awards

How to apply for Travel Awards

Applications should be sent to Mrs Ruth Cole, the Society's Administrator in Birmingham. Priority will be given to young investigators presenting results at major meetings. Applications should state the benefit to the applicant of receiving a travel award and clearly explain the part which the applicant played in the work. Another award cannot be granted to a successful applicant for three years. A small review committee has been formed to review applications for these awards. There are four DEADLINES a year for applications:

1 January **1 April**
1 July **1 October**

PLEASE NOTE: To qualify for a travel award applicants must have been a member of the Society for at least one year. It is highly unlikely that retrospective awards will be given.

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

Conference Reports

National Coalition for Health Professional Education in Genetics (NCHPEG) Annual Meeting, USA, January 2007

Clara Gaff

My first impression of Washington DC was one full of 'operators' as all of the (mostly Washington-based political/biotech/medical) passengers on the airport shuttle moved rapidly from polite chit-chat to an incisive assessment of each other's position, interests and utility. In a more relaxed way, the NCHPEG meeting was similar: a diverse range of health professionals, researchers and educators learning more about others' 'take' on genetics. With a theme of pharmacogenomics, it was hardly a surprise that many pharmacists were present, but there was also good representation of other allied health professionals such as dieticians and social workers as well as the usual genetics specialists. The 'can do' attitude and sense of optimism about the advent of pharmacogenomics into clinical care was refreshing. I was surprised that there is already a clinical, consultative pharmocogenomics service at Cincinnati Children's Hospital, providing a 2 day turn-around service and enabling physicians to tailor doses of some psychiatric medications to genotype. Francis Collins gave an overview of advances in personalised medicine. A special mention is needed for Peter Farndon, who conveyed the aims and eccentricities of the NHS (something I have struggled to come to grips with over the last 3 years) so coherently in a short 30 minutes. So – thank you for giving me this opportunity.

European Human Genetics Conference Report, Nice 16-19 June 2007

Marie Leema Robert

The beautiful city of Nice provided a wonderful setting for this year's meeting. With direct flights from Bristol and Exeter, travel to Nice was so simple. In the age of heightened security in our airports, my poster tube bore the brunt of bazooka jokes. Nice is well worth visiting. The sunshine, seafood and blue beaches should be enough temptation. The hotels are neat, spacious and affordable with plenty of good restaurants.

In spite of some initial hitches with equipment failure, the meeting ran smoothly with plenty of excellent sessions. The facilities were great and organisation including time keeping was excellent. The sessions on ciliopathies, new metabolic diseases and preimplantation genetic diagnosis were fascinating. The genes for several syndromes like Donnai-Barrow, Meckel Gruber, Joubert and Crisponi syndrome have been cloned and 5 more novel X-linked MR genes have been identified.

With 1413 posters to view, there was plenty of stimulating information to keep everyone occupied. It was fascinating to see delegates carrying their cameras everywhere. I later found out that as people viewed posters they also took digital photographs to study in detail later and for reference. Now why did I not think of that?

I would like to thank the BSHG for the travel award which enabled me to attend this conference.

Competition

Do you have a beautiful or unusual image relating to human genetics that you think would be suitable for the front cover of *BSHG News*?

If you do, the image is of high quality (at least 300dpi on A5), you hold copyright and would like to see it on the front cover of our newsletter, please send the image to *BSHG News* Editor, Helen Middleton-Price (helen.middleton-price@cmmc.nhs.uk).

The person whose image is chosen for in 2008 will receive a bottle of champagne and the satisfaction of knowing that their image is preserved for eternity by *BSHG News*. The competition will close on 30 November 2007.

Winners will be chosen by the *BSHG News* Editor, whose decision will be final.

Forthcoming conferences

The Muscular Dystrophies: 19 November 2007
Venue: New Lecture Theatre, Royal Society of Medicine, 1 Wimpole Street, London, W1G 0AE
Email: genetics@rsm.ac.uk Book on-line at: www.rsm.ac.uk/genetics

Family History, Genetics and Insurance: 22 November 2007
Venue: Central Hall Westminster, William Sangster Room, Storeys Gate, Westminster, London SW1H 9NH
Email: mb-gaic@dh.gsi.gov.uk

A two day intensive course in Biobanking: 26 – 27 November, 2007
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: £375.00
Contact: Dr Mark Leech Tel: 0161 276 3200, email: mark.leech@cmmc.nhs.uk

Molecular Genetics for Cytogeneticists: 6 – 7 December, 2007
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: £180.00
Contact: Dr Mark Leech Tel: 0161 276 3200, email: mark.leech@cmmc.nhs.uk

A two day intensive course in Real Time PCR: 12 – 13 February, 2008
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: Please enquire
Contact: Dr Mark Leech Tel: 0161 276 3200, email: mark.leech@cmmc.nhs.uk

Bioinformatics for Cytogeneticists and Molecular Geneticists: 6 – 7 March, 2008
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: £195
Contact: Dr Mark Leech Tel: 0161 276 3200, email: mark.leech@cmmc.nhs.uk

Clinical Genetics Society Spring Conference: 12-13 March 2008
Venue: St George's Hall, Liverpool
Contact: Clinical Genetics Society, Clinical Genetics Unit, Birmingham Women's Hospital, Edgbaston, Birmingham. B15 2TG
Tel: 0121 627 2634
Fax: 0121 623 6971
email: cgs2008@bshg.org.uk

Association of Clinical Cytogeneticists Spring Conference: 31 March – 1 April 2008
Venue: Merseyside Maritime Museum, Liverpool
Contact: Peter Howard and Angela Douglas, Regional Genetics Laboratory, Liverpool Women's Hospital, Crown Street, Liverpool. L8 7SS Tel: 0151 702 4229/4232 email: peter.howard@lwh.nhs.uk and angela.douglas@lwh.nhs.uk

Clinical Molecular Genetics Society: 2-4 April 2008
Venue: Carnatic House, University of Liverpool
Contact: Roger Mountford and Julie Sibbring, Regional Molecular Genetics Laboratory, Liverpool Women's Hospital, Crown Street, Liverpool. L8 7SS Tel: 0151 702 4219/4225 email: roger.mountford@lwh.nhs.uk and julie.sibbring@lwh.nhs.uk

Molecular Genetics for Genetic Counsellors: 23 – 24 April, 2008
Venue: Nowgen, The Nowgen Centre, 29 Grafton Street, Manchester M13 9WU
Cost: £180.00
Contact: Dr Mark Leech Tel: 0161 276 3200, email: mark.leech@cmmc.nhs.uk

Association of Genetic Nurses and Counsellors: 15 May 2008
Venue: St Albans Conference Centre, London
Contact: Jennifer Wiggins, North Thames Regional Genetics Service, Great Ormond Street Hospital for Children NHS Trust, Great Ormond Street, London. WC1N 3JH

Cancer Genetics Group: 20-21 May 2008
Venue: Cardiff
Contact: Ian Frayling, Institute of Medical Genetics, University Hospital of Wales, Cardiff. Tel: 029 2074 4203 email: ian.frayling@cardiffandvale.wales.nhs.uk

European Human Genetics Conference, Barcelona, Spain: 31 May - 3 June 2008
Venue: CCIB Conference Centre, Barcelona, Spain
Website: www.eshg.org/eshg2008/

SIDS 10th International Conference 2008, Portsmouth, UK, 23-26 June 2008
Venue: Portsmouth, UK
Website: www.sids2008.org.uk

XX International Congress of Genetics: Understanding living systems: 12-17 July 2008
Venue: Berlin, Germany
Contact: email: info@geneticsberlin2008.com website: www.geneticsberlin2008.com

XXII International Congress of the European Society for Philosophy of Medicine and Healthcare: European Bioethics in a global context: 20-23 August 2008
Venue: Tartu, Estonia
Contact: Bert Gordijn, Secretary of the ESPMH, Nijmegen, The Netherlands
email: b.gordijn@efg.umcn.nl

British Human Genetics Conference: 15-17 September 2008
Venue: University of York
Contact: British Society for Human Genetics, Clinical Genetics Unit, Birmingham Women's Hospital, Edgbaston, Birmingham. B15 2TG
Tel: 0121 627 2634 Fax: 0121 623 6971
email: york2008@bshg.org.uk website: www.bshg.org.uk

Editorial
June 2007

The ACC section of this BSHG newsletter is dedicated to the memory of Marina Seabright and the enormous contribution that she made both professionally and personally to the cytogenetics profession. The respect and high esteem in which she is held by her colleagues, is reflected in the article which features in the main section of the newsletter. Deepest sympathy is extended to her family and friends on behalf of the entire cytogenetics community.

In this issue we have a report back from the 6th European Cytogenetic Conference which was held in Istanbul in July, as well as feedback on the recent MRCPath written examination. The inaugural ACC Research Project Grant Award has been made and details of the projects and lucky recipients can be found in this issue. Mandeep Bahra also gives us his 'take' on the cytogenetic profession. We also have a bit of a 'fun' article – You know you've worked too long in a lab when…; how many of those are familiar to you?

A big thanks to all the contributors to this issue. It is wonderful to be spoilt for choice for articles instead of being restricted to only a few and wondering just how we are going to fill our pages. Keep those articles rolling in!

Finally, I would like to take this opportunity to thank Chris Wragg for his help and support over the past three years and to welcome Simon McCullough to the editorial team.

"One day your life will flash before your eyes. Make sure it's worth watching." Anon

ACC Research Project Grant Awards for 2007

Jonathan Waters, GOS, London

The Project Grant review committee, on behalf of ACC Council, was delighted to be able to make two awards in this financial year.

The two successful projects were from Dom McMullan and Dr Louise Brueton (Birmingham) for a project entitled: 'Screening of X-linked Mental Retardation Patients using Exon Resolution arrays' and from Dr Kalliroi Stergianou and colleagues (Nottingham and Warwick) for a project entitled, 'Evaluation of technologies for detection and quantification of foetal DNA in plasma in a clinical setting'.

There was a small but high quality field of submissions. Both successful projects which were multi-disciplinary in approach, showed evidence of clear, well-defined outcomes of potential clinical value within a reasonable time frame. We look forward to feedback from both groups on their progress in due course.

Subject to ratification by ACC Council, further award(s) may be made in 2008 and submissions will be invited in the same way as this year.

New Name

Following acceptance by the membership at the September 2006 AGM, the Association of Clinical Cytogeneticists is now the Association for Clinical Cytogenetics.

A Turkish Delight – The 6th European Cytogenetics Conference (ECA 2007), 7-10 July, 2007, Istanbul Convention and Exhibition Centre, Turkey.

Steve Hellens, Newcastle

Friday, 6 July: Middle of summer and yet a 3am start means I am leaving home in the dark with a long day of travelling ahead of me. The flight from Newcastle to Istanbul via Paris was uneventful. However, we arrive in Istanbul at 5pm to find that our posters are still somewhere in Paris (try not to allow the check-in staff to place your valuable work into the hold). Another one and a half hours sorting this out at lost property, means that we have to take a taxi through the city's main rush-hour to our hotel. We finally arrive at 7.30pm local time at the Savoy Hotel in the very centre of the city. My room has a spectacular view across the Bosphorus, but no time for that now, must unpack, have a very quick shower to cool down (one of many) and get out to see the city. Hotel reception rings the airport for us – our posters should arrive tomorrow morning.

Saturday: No posters yet. Registration for the conference is scheduled for anytime before 2pm, so we can fit in a visit to St. Antoine's Church & the Galata Tower prior to the conference. The Galata Tower gives magnificent views of the city and the Bosphorus, has served the city as a fortress, fire headquarters, prison, etc. and is now a quality restaurant. Registration is very quick & efficient; we are delighted to be informed that our posters have been allocated slots in poster session 2 and therefore are not required until Monday. The first session is dedicated to the ECA Working Groups and the influence of array technology on genetic diagnosis is indicated immediately in these early presentations and discussions. Our first view of the main auditorium makes me think 'Thank goodness I'm not doing a talk' - but it is very impressive. An official welcome and introductory lecture by Professor Albert Schinzel is followed by a very entertaining Opening Ceremony, with music by Tulughan Ugurlu (a local singer/songwriter/composer) telling the history of Istanbul and dancing by the Mevlevi dervishes. After a short bus trip to Istanbul University, we are treated to a superb Welcome Reception with delicious food & wine in a beautiful outdoor setting next to a large spotlighted mosque.

Sunday: The day starts early (posters have still not arrived) with an excellent presentation by Wendy Bickmore on the spatial organisation of the human genome within the nucleus. Griet van Buggenhout presents an interesting view of older patients with clear diagnoses where their clinical features are difficult to recognise. Steven van Vooren describes his complex bioinformatics project of mining the literature and prioritising genes in the DECIPHER website. The afternoon is comprised of two separate concurrent sessions – the first Chromosome Instability or Gamete Chromosomes and then New Microdeletion Syndromes or QA in Cytogenetics. All four sessions look very inviting and I find it extremely difficult to choose – not unlike Sunday evening where we struggle to eat all that is on offer at a Turkish banquet in a traditional Islamic restaurant. Back at the hotel – there are still no posters – reception rings the airport again and we are assured that they are on their way.

Monday: An earlier start today, we have to display our posters at 8am (yes, they arrive just in time). The day starts with a brilliant session on Cancer Cytogenetics culminating in a very-assured presentation on Neuroblastoma MLPA analysis by our colleague Andrea Elliott. We are so busy congratulating her, that I miss the start of the plant cytogenetics session. It is very important that I attend the micro-array presentations in the afternoon and it is much easier picking my way through the second group of concurrent sessions. However, I still regret not being able to hear the presentations on PGD & PND. On Monday evening we have a great time – Andrea is more relaxed and we enjoy a delicious meal at the Cicek Pasaji (Flower Passage).

Tuesday: Today starts with another fascinating session on Genome Architecture, including a very interesting presentation on evolutionary neo-centromeres by Mariano Rocchi. The final

session is another array-CGH session with talks describing how aCGH enables us to further characterise different chromosome abnormalities. The conference is concluded in great style with Richard Redon explaining normal CNV in the genome.

Wednesday: We have time for a little more sight-seeing before having to check-out of our hotel at lunchtime. We manage to visit the Hagia Sophia (a Byzantine church, which became a mosque at the beginning of the Ottoman era), the Sultanahmet Camii (Blue Mosque), the Topkapi Palace (home of the Ottoman Sultans) and the Misir Carcisi (Spice Bazaar).

On the flight home, I mull over the last few days. Overall the visit to Turkey is a great success. It is my first trip abroad to an international cytogenetics conference, the conference has been most informative, whilst I have really enjoyed the experience of Istanbul & its culture. I very much appreciate this opportunity and I would like to thank the ACC for their Travel Award. I need to write the review for the BHSG Newsletter – I think I'll call it 'A Turkish Delight'.

Please note: All three travel award recipients submitted articles, however due to space restraints we are only able to publish one. Ed

Membership of The Royal College of Pathologists 2007

Teresa Davies, Chair, Genetics Examination Panel

Membership of the Royal College of Pathologists (MRCPath) is a mark of professional standing and esteem achieved through 1 of 3 possible routes: examination, publications or at the invitation of Council. The latter 2 routes are for academic and distinguished pathologists and are inappropriate for trainees.

Potential candidates should always visit the RCPath web site for the most up to date information, including guidelines and regulations and must ensure they read them and follow them carefully.

In genetics, a small number of candidates achieve MRCPath through publications each year but the most common route is by examination.

The MRCPath examination consists of an assessment of the candidate's knowledge of the specialty and their ability to apply that knowledge in the practice of their specialty.

2007 saw the separation of the Part 1 written and practical examinations into 2 sessions, Spring and Autumn. This was done to give more time for marking and moderation and to relieve the pressure on the examiners, candidates and the examination department.

It is encouraging to see the number of candidates sitting the part 1 examination. This year there were 7 candidates for the part 1 written in cytogenetics with 7 passes and 12 candidates in molecular genetics with 9 passes.

General feedback is presented elsewhere in the BSHG newsletter.

The practical examinations are to be held in October.

There continues to be a disappointingly small number of candidates sitting the part 2 examinations, which is held once per year in Spring. There were 3 candidates in cytogenetics with 2 passes and none in molecular genetics.

However it is encouraging that a number of proposals for part 2 written work have been submitted for approval this year and several pieces of written work have been presented for assessment with the view of sitting part 2 oral in 2008.

A lot of work is being undertaken by the College examination department and the examination panels to improve the examination process and standards in all disciplines. This has included holding training sessions for all examiners.

All of the work, setting and marking the exams, assessing written work and conducting orals is carried out by the small genetics exam panel, which has 11 examiners in molecular genetics and 9 in cytogenetics.

A special thanks to them for all of their hard work.

Teresa.Davies@nbt.nhs.uk

MRCPath Part 1 in Clinical Cytogenetics, Spring 2007 - Feedback prepared by Examiners for The Royal College of Pathologists

Katie Waters and Lorraine Gaunt

Seven candidates sat the written papers in March. It has become a tradition to provide general feedback on performance in each of the questions. This year all the candidates passed. We hope the feedback will encourage others to sit the examination next year. The practical examination will be held 11-12 October 2007 and we wish all candidates sitting the exam success.

Paper 1

1. Explain the principles underlying the following techniques, illustrate with examples of application in a clinical cytogenetics service

   a. C-banding
   b. Multiplex ligation dependent probe amplification
   c. Sister chromatid exchanges
   d. Unique sequence fluorescence in situ hybridisation probes

   This question required that the candidates were knowledgeable of both traditional cytogenetic and current molecular techniques. Generally the question was well answered, however, the weaker areas were C-banding and SCEs. Some candidates included a diagram to illustrate the principle of a technique. This was particularly appropriate for MLPA (range 12-14, 6/7 candidates).

2. What is X-inactivation, how is it mediated, and for what purpose? How, using cytogenetic and molecular genetics methods, can X-inactivation status be assessed in a female? How can skewed X-inactivation lead to disease?

   Many will have noticed that this question appears more often than would be expected by chance alone on the Cytogenetics MRCPath exam paper. This is because traditionally it is poorly answered. At first sight it appears long, multifaceted and demanding; on the other hand the examiners have provided a nascent plan. The quality was better this year, and as with a number of the questions, showed significant evidence of rehearsal from study groups. That aside, its not an easy question and the poorer candidates were either too superficial in their response, or inaccurate in their detail, specifically with respect to the first part of the question. Interestingly there was little knowledge of the molecular techniques used for X-inactivation. With the overlap between our two disciplines increasing and the fact of a joint question on each paper, future candidates are encouraged to fact find more widely. (range12-14: 6/7 candidates)

3. Explain the relationship between particular types of DNA repeat sequences and recurrent structural chromosome abnormalities. Illustrate with examples of constitutional abnormalities.

   Generally this was a well answered question with a common structure adopted by many candidates and reflecting the many recent publications from a variety of sources. Candidates did well in covering this increasingly vast subject and in documenting the range of repeat sequences and examples of their apparent role in formation of chromosome abnormalities. Some individuals described specific chromosome rearrangements in detail, others took a broader approach. Both approaches were acceptable. All candidates passed the question with a score range of 13-14. (6/7 candidates

4. Describe the clinical features and genetic causes associated with the following karyotypic findings. What are the main differential diagnoses:

   a. 46,XX karotype in a phenotypic male
   b. 46,XY karyotype in a phenotypic female

   Sex reversal is a subject area that candidates would have been expected to have reviewed and revised. This was a straight forward question and most candidates who attempted it covered the expected diagnoses for both parts and achieved a pass (range 12-14, candidates 5/7).

5. Describe the disease and cytogenetic/molecular defects in the following

   a. Burkitt's lymphoma
   b. Infant leukaemia
   c. Multiple myeloma

   This was the least popular question on paper 1 with only four candidates attempting it with varying success. It is important that if candidates select a question like this that they have knowledge in all the areas that the question specifies as this will be needed to pass. Half the candidates covered Burkitt's lymphoma and multiple myeloma adequately. Infant leukaemia was poorly covered with some candidates opting to write about childhood leukaemia instead. (range 10-14, 4/7 candidates)

Paper 2

1. A recent report evaluating the use of array comparative genomic hybridisation (aCGH) in the investigation for idiopathic learning disabilities suggests it should be considered

as a first line investigation.

Describe the issues, (biological, scientific, and technical) which would need to be taken into consideration prior to aCGH as a first line investigation being introduced for these patients into a diagnostic genetics laboratory.

In terms of question spotting (anticipation) this is surely the most obvious question for the 2007 paper and yet the most poorly answered even though again the examiners had provided a potential structure for the candidate, and the information is easily available (for example http://www.ngrl.org.uk/Wessex/microarray_wshop06.html, and many other sources.) The issue generally was insufficient detail and explanation and the examiners were not convinced that all candidates understood the issues behind their key words (range 12-14 - 5/7 candidates)

2. Describe the screening options available to achieve a detection rate for Down Syndrome greater than 75% with a false positive rate of 3%. How would the choice of these options by obstetricians affect prenatal diagnoses referrals to a cytogenetics laboratory?

A timely question for Spring 2007 with a real potential for the shape of our services to change, potentially quite dramatically. The examiners wished to be reassured of the candidates' knowledge of the screening programme and the range of possible effects on the prenatal diagnostic service, not all of which are immediately obvious. The question attracted a range of answers that varied not so much in the detail, but in the depth of knowledge and apparent understanding and perhaps the question allowed the examiners to separate the 'rote learners' from the 'thinkers' (range 11-14) (6/7 candidates).

3. Discuss the diagnostic and prognostic value of identifying acquired cytogenetic abnormalities in acute leukaemias.

This question was generally well answered with candidates, in particular, demonstrating an up to date knowledge of recurrent abnormalities in AML and ALL. This question produced some very good answers (range 12-14, 6/7 candidates).

4. Write fully interpreted reports for the following findings:

a. A mosaic supernumerary bisatellited marker chromosome in a PHA stimulated culture of a blood sample from a child with developmental delay, which is shown by fluorescence in situ studies to be derived from chromosome 22
b. Mosaicism for chromosome 14 in a cultured chorionic villus sample referred with a positive first trimester Down screening result
c. 10% of metaphases from a blood sample from an infant with unexplained neurological problems show rearrangements involving 7, 14 and X
d. A 46,XY karyotype in a cultured postnatal fetal skin tissue sample which was referred for confirmation following a rapid prenatal test result (for copy number of chromosomes 13, 18 and 21) on uncultured chorionic villi which indicated trisomy 18.

Supplement your answer with any additional aspects you may have taken into consideration but which you have not included in your report.

This question was specifically written in response to the poor report writing demonstrated in the 2006 practical paper. The examiners wanted to establish knowledge, which we asked for in the second part of the question, as well as interpretation and application of that knowledge. The responses were disappointing; underpinning knowledge was demonstrated, but the translation of that into a report suitable for the referring clinician was much less strong and candidates are advised to take note of this as they prepare for the Autumn practical examination. One candidate failed to provide any reports, although demonstrating a good understanding of the issues which would need to be considered when a report was to be compiled. That individual was given a 'fail' score for the question. Don't lose sight of the question amidst the detail (range 10-14).

5. Your service commissioners are undertaking a review of cytogenetic services and have invited you to write a report detailing what changes/developments in services and workforce can be expected in 5 years time. What developments and improvements would you put into your report and why?

Most candidates focused on the changes/developments aspect of the question and identified the main drivers as automation, array technology and service 'modernisation'. It was disappointing that some candidates did not consider the future training requirements of the workforce or skill mix in their answers (range 12-14,

You know you've worked too long in a lab when...

1. You wonder what absolute alcohol tastes like with orange juice

2. You can tell what cheap and expensive white coats look like

3. You can't watch CSI without cursing at least one scientific inaccuracy

4. You use acronyms for everything and never stop to elaborate

5. Liquid nitrogen is only about a 1/3 as dangerous as you thought

6. You always seem to use the microscope after the person with the impossible close together eyes

7. Accident reports are badges of honour

8. You've wondered why you can't drink distilled water in the lab - it should be clean?

9. You give the lab equipment motivational pep talks

10. When a non-scientist asks you what you do for a living you roll your eyes and talk science at them until they've loss the will to live (mainly for fun)

11. You have to check the web to find out what the weather is outside

12. You realise that almost anything can be classed as background reading

13. People wearing shorts under a lab coat disturb you slightly as they look as though they might be naked underneath

14. Safety equipment is optional unless it makes you look cool

15. Warning labels invoke curiosity rather than caution

16. The Christmas night out reveals scientists can't dance, although a formula for the movement of hands and feet combined with beats per min is found scrawled on a napkin by a waiter the next day

17. You know which part of the lab you can chill out in undisturbed on Friday afternoon

18. You decide the courses and conferences you want to go on by the quality of the food served

19. You are strangely proud of the collection of junk you've stolen from vendors at trade shows

20. You've used dry ice to cool beer down

21. No matter what the timings in the experiment protocol there is always time for lunch in the middle

22. As has been pointed out to me on several occasions - You can no longer spell normal words but have no trouble with spelling things like immunohistochemistry or Waldenstroms macroglobulinaemia

23. Burning eyes, nose and throat indicate that you haven't actually turned on the fumehood/downdraft bench

24. Your slightly too fond of the smell of (pick one or many) Xylene//Ethanol//Alcoholic handwash/Acetic acid

25. You've left the lab wearing a piece of PPE (personal protective equipment) because you forgot you had it on

26. You have made some kind of puppet out of a nitrile glove and kept it as a pet.

27. You still get amusement out of "freezing" things in liquid nitrogen

28. Blinking fast has saved your eyesight on more than one occasion.

29. You've removed your gloves to find a small hole which has left you with either - wrinkly old person hands, a brightly coloured finger (histologists especially) or a burning sensation and dermatitis at some point.

30. You've bent down to pick something up off the floor only to scatter the contents of your top pocket under the largest machine in the lab

Junior Liaison Committee (JLC) – In the Spotlight

Mandeep Bahra

Throughout my few but eventful years (so far) in cytogenetics, working in five different labs, I have had the good fortune to meet and work with a very diverse group of people. This has broadened my horizons somewhat and I think I'm better for it. Just in monetary terms, this job has funded many a travelling experience, from the pyramids in Cairo to Earnest Hemingway's home in Cuba! The afore-mentioned diverse group of people have presented many opportunities which would probably not come my way if I worked in another profession. Some have helped me conquer my fear of roller-coasters, while others have simply helped boost my self confidence. This new-found confidence has led to a day out gliding, a flying lesson and, last month, my colleagues and I seized the opportunity to unleash our inner 'Tarzan' and "Go Ape"! (see pic).

My point is simply this: Whatever our hobbies, interests, likes or dislikes, as junior members, we all face the same problems, obstacles and challenges professionally. That's why the JLC exists. If you have any queries about training, CPD, registration, etc., feel free to contact us. It's been said before but I'll say it again, if we can't help we can usually direct you towards someone who can. So take an interest in your profession, it can work wonders for you!

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ACC News Editors

Deadline for contributions for next issue is Friday 11 January 2008

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Attention all Genetics Technical Staff

GACTAC **CMGS** CTGAACTGACTACGTACTGAACTG
CTACGT ACTGAACTGACTACGTACTGAACT
TACTGAACTGACTACGT **CLINICAL MOLECULAR** ACTGAA
ACGTACTGAACTGACTA **GENETICS SOCIETY** ACTGAACTG

Association for Clinical Cytogenetics

This is your chance to do something positive and show just how valuable you actually are within your lab.

The Associated Genetic Technologists Committee (AGTC) consists of ten technical staff from the CMGS and the ACC, five from each discipline. We aim to promote technical staff, to give them a positive career structure and formal recognition as Genetic Technologists within either Molecular Genetics or Cytogenetics. To this end, the AGTC are founder members of the Voluntary Registration Council (VRC) which has been set-up to mirror the Health Professions Council (HPC). This will make the eventual transfer from the VRC to the HPC as simple as possible, with hopefully everyone who is on the voluntary register being automatically transferred to the HPC without jumping through any more hoops and an extraordinary fee for grandparenting.

From the six disciplines currently members of the VRC, 42 people have registered and of these, 22 are Genetic Technologists – nine Molecular Geneticists and 13 Cytogeneticists. So, although we aren't off to a racing start, we are beating the other five disciplines put together.

Let's have a big surge and get even more people on the VRC – remember, you must have been a full time MTO2 or above for at least three years (or equivalent part time) plus have either a recognised degree or a further three years experience within a NHS lab. With approximately 400 technical staff from both disciplines throughout the country, it is hoped that many will apply soon. New Guidance notes have been recently written; however, at this time, the AGTC has decided against producing a 'template' report as it is strongly felt that this is very specific to each person and every application is assessed according to individual competences. Please see the VRC website, www.vrcouncil.org and follow the ACC /CMGS link for details.

The AGTC is painstakingly sorting through many details; it is a wonderful opportunity to be recognised as professionals, and we want to get it right. There are new CPD guidelines being drafted which will go on the website, as well as huge steps being taken for future education and training; a new technical competence training manual is being developed, building on a 1st degree. This involves a large amount of communication at many levels, as well as addressing funding needs, in order that Genetic Technologists will be able to attain statutory regulation, something the Clinical Scientists already enjoy.

The ACC have generously provided a one off Training for Trainers course specifically for senior technical staff. This was free to ACC members, and with 18 places available, this led to quite a number of technical staff joining the professional body. All the GTs who attended this course thoroughly enjoyed it and are very grateful to the ACC. We are hoping the CMGS can offer something similar if there are any spare places. If you feel you would benefit from attending this course, ask your Head of Laboratory if it is possible.

With both the Cytogenetics and Molecular Genetics meetings overlapping by one day at the next Spring Conference in Liverpool, the AGTC have approached the organisers to hold a study session, which, if successful could become part of future BSHG meetings. This follows on from the very successful and well attended technical study day on 28 June 2006 in Birmingham. We are hoping that as many people as possible attend these meetings.

But we need you to stand up, join the professional bodies and show that being a Genetic Technologist is your career, not just a stepping stone to being a Clinical Scientist. Without you joining the CMGS or ACC and applying to be on the voluntary register, then the AGTC will not have enough leverage to influence matters that will in turn affect our careers. We want to be recognised as competent professionals in our own right and with the professional bodies backing us, we can develop positive training programmes and a career pathway for all technologists.

Editorial

Ann Kershaw and Sarah Smalley

Hello and welcome to the AGNC section of BSHG news. It has been a struggle to convince you all to send us your contributions, but thank you to those who have. Before whetting your taste buds with details of what to expect in this edition we would first of all like to apologise to Alison Lashwood whose update on PGD from Guy's Hospital printed in the last edition was in fact sent as an e-mail and not as an article intended for publication. So apologies to Alison and to our readers if this did not appear to be as scholarly as her usual handiwork.

As for what to expect this time round, we have a piece on losing your BSHG virginity by our newest Trainee Genetic Counsellor, feedback from the AGNC Annual General Meeting and an overview of the International Society for Nurses in Genetics (ISONG) Conference in Bristol. We also have an article from Dr Chris Patch on the work she has been doing with the HGC, an update from the Genetic Counsellor Registration Board, and not forgetting our regular feature, Guess the Genetic Counsellor.

We hope that you enjoy reading this issue and that some of you might be inspired to send your contributions for the next one. If not, we may have to start nominating authors and of course we would be happy to receive nominations for any of your friends or colleagues!

With best wishes

Ann Kershaw and Sarah Smalley

Through the eyes of a BSHG virgin

Mabella Farrer, Cambridge

I arrived in a pool car with my colleagues feeling like a small child being taken by their family to a large family occasion where you know you will see very few familiar faces. Daunted by the prospect of having to make conversation with people who you don't know, and your knowledge of the subject being severely limited, this new trainee genetic counsellor had arrived for her first BSHG conference.

For those experienced geneticists and scientists, you will have to excuse me as, as a trainee genetic counsellor, I went to the counselling presentations rather than the ones that I knew would be over my head. When, on pondering the meaning of a title, I came up with nothing (as yet, but hopefully in many years time I would understand it), the solution was to pick another lecture!

There were times however when two presentations appealed, but they ran concurrently: a clash. So should I run from hall to hall, hoping that the concurrent sessions are keeping to time, or choose one hall and stay put for that session? My decision was to sit still and not risk walking in late to a presentation that had already started, finding myself unsure of whether it is the one I wanted to hear, or the tail end of the previous talk.

The sessions this year must have been exceptional as even though it felt like the heating was on strike, and fingers and toes were turning blue, attention was still focussed on the presentations. For those who attended the spoken presentation 'Children's Understanding of Testing for a Genetic Illness', I am sure that we will all remember the pictorial images depicting concepts such as 'what is family tree?' where one child had actually drawn a pedigree, although rather neater than some

I've seen in various clinical notes! It is worth highlighting that none of us have an excuse now for drawing pedigrees with scrappy circles and squares as pedigree drawing tools were being given away, even if they did not have the same take home appeal as the torches, pens and animals that were also available.

The end of day one brought the wine tasting quiz, an event that was most welcomed (it appeared by all). I am however unsure as to the ratio of those actually knowing which wine was what: thinking they knew: and pure guesswork. I was definitely in the last category but it certainly assisted the networking, and got everyone chatting.

The ethics sessions spanned the two ends of the spectrum with regard to testing and termination of pregnancy. Views ranged from anti-abortion for any reason to testing to such an extent that you could choose to have a child who would be artistic or musical, or with an IQ above a chosen figure. These talks were further discussed over coffee with gusto! Sandwiched between two extreme ends of the spectrum was a reminder to us all from Antenatal Results and Choices (ARC) that each person, couple and family are individual, and the decisions they face when learning that their pregnancy is not going as they expected are personal to them. This presentation also reminded us of the services out there which can provide such expert support to these families.

Day two spoken presentations focussed on cardiac disease, risk communication and management. The afternoon led me to the young researcher's forum, where we heard about publishing research and how the peer review system works. There was also time to view the posters and see some of the work that is going on round the country.

Networking (some would say gossiping) was a must – catching up with old friends and colleagues as well as being introduced to more eminent people by those you were with was a big part of this conference. For me it was a start to putting names to faces, and faces to article authors whose work I have read and critiqued as part of the MSc.

Tuesday evening arrived and it appeared that we must be a scary bunch of people as on arrival at the racecourse for the conference dinner, we were informed that the horse racing providers had done an NHS clinic special, they Did Not Attend. As compensation however, extra champagne was ordered (for those who do not work in clinics, sadly champagne is not routinely ordered for us when patients don't attend), and the dinner went ahead without a hitch and with much laughter and many a joke.

Meeting so many when knowing so few was a daunting prospect, but the conference was a friendly place, the presentations were interesting and informative, and the networking was inspiring. I am sure that for all of us our genetics family/circle grows with each meeting as we get to know more people, make new friends and learn from each other. I am looking forward to many future conferences and meetings.

mabella.farrer@addenbrookes.nhs.uk

The desserts certainly went down with a smile

Report from the AGNC Annual General Meeting (AGM) on behalf of the AGNC Committee

Jennifer Wiggins, GOSH, and Janet Birch, Liverpool

In the June newsletter and at Spring Meeting in March we asked members for their views on moving the AGM from the BSHG Conference to a regular slot at the Annual Spring Meeting. The question arose because attendance at the AGM has fallen. The AGNC Constitution states that 'The quorum for the AGM shall be twenty five percent of ordinary members and five committee members including at least two officers' (1995, amended 2004).

After consideration of the responses received from members and as we have not had the required membership numbers at the last two AGM's at York the Committee has made a decision to move the AGM to Spring Meeting from 2008. We hope that this will ensure that we have a quorum should any future issue require a vote. The decision was announced to those members present at the 2007 AGM.

The Committee plans to keep the location of the AGM under review and will continue to evaluate numbers in attendance. The AGNC business/update slot that was previously held at Spring Meeting will now take place at the BSHG Conference.

Goodbye!

Fiona Robson has now completed her full term of 6 Years on the Committee during which time she has performed a sterling job as Treasurer. We are very pleased to say that Fiona will still be an active member of the CSSWG and the Committee would like to thank her for all of her hard work on behalf of the AGNC membership.

Mark Longmuir has now taken over office as Treasurer and we look forward to him keeping a canny eye on our finances.

There will be no changes to membership of the Genetic Counsellor Registration Board (GCRB) this year. Kathy Barnes, Chair and Anna Middleton, Vice-Chair have agreed to remain on the Board for their second term. Re-election is not needed if the individual is an Officer of the Board. The AGNC committee would like to thank the Registration Board for all their hard work over the past year.

Welcome

We are pleased to announce that Greta Westwood has been elected to the Committee following the recent vote. We look forward to working with Greta and would like to thank all of the nominees for their enthusiasm and support for the AGNC.

Newsflash.....

You should have received a free copy of AMICUS magazine with the BSHG mailing. The edition includes an article written by Sarah Coulson about life as a Genetic Counsellor and AMICUS have kindly donated these copies to the AGNC membership.

AGNC Spring Meeting 2008

The AGNC Spring meeting will be held on Thursday, 15 May, 2008 at St. Albans Conference Centre, London EC1N 7RD. We will be accepting abstracts for spoken and poster presentations this year and are also looking specifically for clinical case studies. The electronic abstract submission page will appear on the AGNC website on 1 December, 2007 and close 15 February 2008. Registration for the Meeting will start in March and the last day for registration is 2 May 2008. The maximum number of delegates is 110-120, so it is important to book early. If you have any questions about the Meeting please contact Jennifer Wiggins at wiggij@gosh.nhs.uk.

The International Society for Nurses in Genetics (ISONG) Conference in Bristol

Vicki Wiles, Cambridge

When a conference session starts at 8.15am on a Sunday morning you can be sure it's something to do with Americans. The International Society for Nurses in Genetics (ISONG) decided to hold its 20th Conference and first International meeting in Bristol but this wasn't an American meeting held in the UK, but rather a fascinating gathering of delegates from 23 countries. I went, along with Gilly Bromilow (Exeter, AGNC Vice Chair), who chaired a session, to represent the AGNC.

The conference had been largely and ably organized by Dr Heather Skirton (University of Plymouth), ex-President of ISONG, who has done much to reach out to developing genetic counselling training centres worldwide in order to offer shared support and ideas. ISONG members have evidently greatly valued her energy and committment.

John Burn started the conference in style with a classic Burnesque key address titled 'the trouble with nurses and counsellors…'; Dr Chris Patch (Guy's Hospital) spoke about the work of the Human Genetics Commission, which is an organization to be proud of internationally. We heard too, about family history taking in Iceland (Vigdis Stefansdottir), Israel (Sivia Barnoy), Ireland (Mary Quinn Griffin), Japan (Kumiko Tsujino) and amongst families of Pakistani origin in the UK from Shagufta Khan (West Midlands) in, what was for me, one of the best sessions, comprising as it did humour, intriguing cultural detail and moving insights.

Previous Trainee Genetic Counsellor Anna Clee (St George's Hospital) presented her work on the role of spiritual belief in predictive testing very well. Caroline Benjamin (Liverpool), Sally Watts (Guy's Hospital), and Marion McAllister (Manchester), and Maggie Kirk (University of Glamorgan) also presented their wide ranging work.

The ISONG Conference Bristol

Gilly Bromilow, Exeter

Concurrent sessions made for hard choices about what to go to and I missed the metabolic session which included a presentation on the potential role of pharmacological chaperones for the treatment of lysosomal storage disorders such as Fabry disease and Gaucher disease. However I did hear Jeanne Gottlieb's (Miami) brave exploration of the role of the American nurse from 1900-1950 which described how the eugenics movement had a major impact on professional nursing. Her analysis of the move to patient autonomy and the importance of its maintenance was impressive. Marcia Van Riper (North Carolina) spoke movingly about how a genetic condition in the family can affect families in surprising ways, using six cases as examples. Meanwhile Fiona Ulph's presentation (University of Nottingham) on how 7-11 year olds view genetic concepts certainly got everyone talking, as 89% of children in their sample thought a blood test was a serious medical procedure requiring an anaesthetic.

I came away with a strong sense that UK Clinical Genetics is playing a key role in leading the way in good practice expansion in Europe. International meetings such as this are important to share ideas and to help us understand that many of the issues, we as GCs deal with on a day to day basis, cross cultural and national boundaries.

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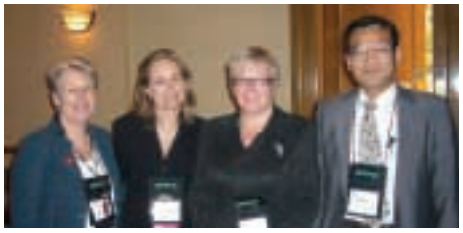
ISONG Conference Committee



Chairing a session is almost as nerve racking as presenting, but not quite! However I was pleased to be asked to represent the AGNC at an international meeting, together with Vicki Wiles and found it an exhilarating, but exhausting four days. Starting at 8.15am each day was definitely a challenge, especially as Vicki and I were staying a distance away from the venue. The speakers came from a wide variety of countries (23 in all we were told) and I was full of admiration for everyone presenting, especially those who presented in a foreign language.

I will not repeat Vicki's précis of the sessions, but will just add that I was struck by how much the AGNC both as an organisation and as individual members can reach out to other genetic counselling organisations across the world. By the exchange of ideas and experience and becoming involved in exciting new ventures we can all extend and improve our knowledge and thereby improve the service to our patients.

The AGNC reciprocity working party has been doing sterling work in looking at other registration arrangements, and meetings like this can only improve the opportunities available. So thank you to Heather and to ISONG for the wonderful networking opportunity, and congratulations on a successful and illuminating conference.

Gillian.Bromilow@rdeft.nhs.uk

Direct to Consumer Genetic Tests

Christine Patch, Guy's Hospital

The UK Human Genetics Commission is the Government's advisory body on current and potential developments in human genetics and the likely impact on human health and healthcare as well as the social, ethical, legal and economic implications. I have been a member since 2003 and have been chair of the genetics services subgroup. I thought it might be interesting to present a short report from my perspective, not on behalf of the HGC, on one piece of work we have recently undertaken. We have been considering again the question of genetic tests supplied directly to the public.

There is interest in the framework for the quality assurance and regulation of genetic tests and testing services with bodies such as Eurogentest, OECD, The Council of Europe and others actively considering the various issues.

Whilst regulation of NHS-based genetic tests has been enhanced by creation of the UK Genetic Testing Network, there is currently a regulatory gap concerning commercial genetic testing providers.

HGC considered this in detail through a public consultation exercise which culminated in the Genes Direct report published in 2003. This report did not favour an outright ban on all direct to consumer (DTC) genetic tests but did recommend that some genetic tests might be best provided via medical referral. A mechanism for pre-market review of tests and a code of practice for DTC testing services were amongst the report's key recommendations.

"There is currently a regulatory gap concerning commercial genetic testing providers"

To put this in context a brief summary of relevant events is presented below.

1996 – Establishment of Advisory Committee on Genetic Testing (ACGT)

1997 – Publication of ACGT's code of practice on genetic testing services supplied direct to public

1999 – ACGT's work subsumed within the newly established Human Genetics Commission (HGC)

2001/2 – HGC review the Sciona service against ACGT code of practice. As a result the HGC restated its advisory role rather than a regulatory role.

2002 – HGC begins public consultation on future of regulation

2003 – Publication of Genes Direct, the HGC's report on the future of regulation

2003 – EU IVD Directive regulating diagnostic tests comes into force in UK, enforced by the MHRA

2003 – United Kingdom Genetic Testing Network established to promote equity of access to genetic services, ensure they are of high quality, evaluate the effectiveness of new genetic tests for the NHS and to influence the NHS commissioning mechanisms.

2003 – DH white paper on genetics supported the UKGTN as having a major role in supporting integrated genetic testing services

2007 – HGC Follow up to Genes Direct workshop

Adapted from Stuart Hogarth, David Melzer, Ron Zimmern. The regulation of commercial genetic testing services in the UK: A briefing for the Human Genetics Commission. www.hgc.gov.uk/Client/document.asp?DocId=97&CAtegoryId=8

In January 2007, the HGC held a follow up workshop to consider the recommendations of the Genes Direct report and make further recommendations. The recommendations which aim to enhance the current regulatory mechanisms, focused on three areas: pre-market review of tests, quality assurance and advice and advertising. The report will be published shortly and will be available on the HGC website together with other relevant documents and details of other areas the HGC is involved in.

Christine.Patch@gstt.nhs.uk

Advance Notice

The Association of Genetic Nurses and Counsellors Spring Meeting

Thursday May 15, 2008
St. Albans Conference Centre,
Leigh Place, Baldwins Gardens, London,
EC1N 7RD

First call for abstracts: November 2007

Guess the Genetic Counsellor

This time you have two chances to guess who is behind the disguise.

Answers in the next edition.

Last edition, the Counsellor behind the mask was Sarah Smalley, Genetic Counsellor, Cambridge and AGNC newsletter editor.

Update from the Genetic Counsellor Registration Board (GCRB)

Patricia Finnemore, Principal Genetic Counsellor, Southampton

Congratulations to the following who registered in July 2007
Glen Brice
Tara Clancy
Catherine Falconer
Selina Goodman
Catherine Higgins
Mark Longmuir
Lorna McLeish
Charlotte Riddick
Catherine Willis

Last chance for the grandfather clause
For those without degrees who completed at least 2 years whole time equivalent work as genetic counsellors before 1 March 2002, (Applicant Guidelines, p6) March 2008 is the last chance to submit intention to register.

New registration will be annual, in September, from 2008.

Renewal of registration
Renewal of registration is required every 5 years and will take place annually in March. The renewal fee is £100.

The GCRB will notify those due to renew 6 months in advance. Renewal requires1500 hours (or 40 weeks) of work in a role directly related to genetic counselling in the 5 years prior to the renewal, plus 30 hours per year continual professional development during those 5 years and 2 references, one from a senior colleague and one from a manager. For details see www.agnc.org.uk/registration/renewal

Assessors
Thank you to all who have assessed portfolios. More assessors are always required. Genetic counsellors with five years experience are eligible to train as assessors, at the Board's expense, with two yearly refresher courses.

Forfeit of £200 registration fee
Please be aware that, unless there are extenuating circumstances, which have been recorded on the form on the website, the fee will be forfeited if

1. The portfolio is not submitted on time (Applicant Guidelines p14 para 1)

2. Minor amendments are not submitted within 4 weeks of receipt of the Post Interview Report (Applicant Guidelines p5, para 3)

3. Significant amendments are not submitted at one of the next two consecutive submission dates (Applicant Guidelines p5, para 5)

4. Significant amendments are unsatisfactory, requiring a new portfolio (Applicant Guidelines p5, para 6)

The Guidelines
Modifications and clarifications are constantly required. The GCRB will update the Guidelines annually and publish a new edition in January each year. So each new cohort submitting intention to register in March should use the edition for the current year.

AGNC News Editors

Deadline for contributions for next issue is Friday 11 January 2008

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Editorial
Recurring Themes…

Sue Huson, Manchester

My focus for this issue is on recurring themes. Those of you who have worked with me will know I am a 'last minute' person. This is my first recurring theme; although I am slightly better than I was, there is still a way to go! First, an apology to my co-editors in Manchester: I left it too late to involve you! Next, a big thank you to everyone for the fantastic response to my last minute call for articles. I hope by the time you have read the newsletter, you will agree there is lots to interest everyone. Particularly exciting are the forthcoming meetings: our first joint CGS with our Dutch colleagues and the Fundamentals of Genetics course which Helen Firth has organised. The latter has been talked about for years (possibly even when I was training!), so we are grateful to Helen for finally making it happen.

My next recurring theme is on our ability to let others volunteer while we sit back and let them get on with it. I asked you for feedback on content of the newsletter and received very little, so have taken an editorial decision on what it should be.

The main recurring theme I wanted to talk about are the ones that I am sure we all spend countless hours discussing in our own departments. I am now working in my fourth genetics centre (having trained in Cardiff and at the Kennedy Galton Centre and being a Consultant in Oxford before Manchester). In all of them we had a weekly meeting which has taken various formats but all included an 'admin slot' and case discussion. Common to all departments have been frequent discussion about

- Missing case notes and how to deal with them

- Typing and (for some of us) dictation backlogs

- Collecting data for Trusts and GENCAG

- Agreeing department policy on common clinical situations

- Maintaining a high calibre journal club

- And, having just made a coffee, this reminds me: just who is responsible for the pile of washing up in the sink (particularly on clinical meeting day)?

With regard to data collection my personal view is, the sooner we as a profession can agree a standard data set that we can easily record, the better. Many other specialties have already achieved it. So I was pleased to see in Alan's column that the Lead Clinicians are meeting soon to discuss data collection.

With regard to the other topics, I thought the newsletter might be able to help. So I have introduced a 'Sharing Practice' column and Oxford has kindly let me publish their BSHG poster on the use of voice recognition software. I look forward to receiving contributions from any person/department who thinks they have a particularly good solution to something.

The other thing I am introducing is a Clinical Conundrum column. This is so we can share areas of development where we are uncertain what departmental policy should be. The subject that stimulated this was a discussion at our own clinical meeting about how we were counselling couples with Robertsonian translocations about UPD 14/15. Everyone had a slightly different data source etc. Perhaps some things are so common that CGS should have agreed counselling guidelines?

In summary, therefore the themes I would like to follow in the newsletter are:

- National feedback from Council (thanks Alan, you are doing a great job!) and our representatives on the various national bodies

- Reports back from subspecialty group meetings – our first two appear in this issue

- Sharing practice

- Clinical Conundrums

- Clinical updates- from the experts on different conditions

- Research updates/call for patients etc

- Etcetera…to include anything else.

So at last, a whole editorial, and no mention of my favourite genetic disease…but haven't got through the whole newsletter without mentioning skiing…please see 'Skiing and CPD' in Etcetera.

From the CGS President

Alan Fryer, Liverpool

Greetings CGS members!
This is my opportunity to update you on CGS activities since the last newsletter. Council met in June and a number of items were debated. I was able to feedback from the BSHG Away Day and those of you who attended the BSHG AGM at York will know that a number of important proposals came out of that – particularly the suggestions that BSHG should consider having a chief executive officer and a patron to help promote the development of the Society, consider a closer relationship with the Journal of Medical Genetics (possibly even a franchise whereby we co-own the journal with BMJ Journals) and also the possibility of offering the option of joining ESHG in with BSHG membership (hopefully at a discounted price).

It was also clear that we within CGS need to work closely with BSHG. Someone remarked that BSHG should be greater in influence than the sum of its component parts and I am sure this is true. Two items particularly struck me – firstly the research agenda. Richard Trembath reminded everyone of the change in NHS research funding and the Society needs a clear strategy if we are to tap into the system. This also came up at the Joint Committee where it was mentioned that labs were now finding it increasingly difficult to obtain funding for small projects. Within CGS the possibility of setting up a clinical genetic research network has been on the agenda for sometime but what sort of network? Currently, research links are informal but do we want to develop a network that has an oversight body that reviews requests etc. How would we fund the infrastructure to support this and would it help us attract research monies? Karen Temple is giving some thought to this and I am sure it will be a debating topic at the Council Away Day in January.

One problem that Rob Elles identified is that we all have different computer systems within our clinical services that largely do not speak to each other – this is something that we need to look into. I went to a meeting arranged by the Human Genetics Commission in August along with representatives from "Connecting for Health" (CfH) and we will be pursuing the possibility of CfH helping us. As Rob reminded us, we are likely to see increasing numbers of clinical trials of novel therapies in inherited disorders and we want to be in the position to recruit patients into such studies. I thought we had some exciting talks at York (particularly Hal Dietz's talk on Losartin) that reminded us of the changing scene and the likely need for clinical geneticists to be involved (and trained) in areas such as these which have been largely outside our practice in the past.

The second area that struck me was that of International links. At BSHG Council, Rob Elles described his efforts to engage developing genetic services in India – the proposal was that they may want to buy in UK expertise and training with UK specialists visiting and helping in the establishment and development of services. Whilst the emphasis was on laboratory expertise, clinical expertise was also included. In CGS we have been pursuing an alternative strategy of inviting overseas fellows to visit the CGS meeting and spend a week in one or two UK centres to develop a "twinning" approach. We are in the final stages of developing an application form for this – I suspect we may not have this in place for Spring CGS in 2008 but hopefully by 2009, it will be up-and-running. As a result of all these discussions it was clear and accepted by BSHG that we should have an "International Interest Group" within BSHG with all of the affiliated societies represented. I have already had a lot of interest from colleagues within CGS. It is also clear that many of you already have overseas links with developing services and perhaps one of the first things the "International Interest Group" will do is to identify all of this activity.

With regard to other matters, Council agreed that we should set certain expectations on those who represent CGS on various committees. We do get asked from time to time to nominate members to join certain committees/working parties and we try to be democratic and open and ask for expressions of interest via the CGS reps network. We agreed that in these circumstances, we should ask candidates to include a brief description of why they wish to put themselves forward and what they could offer in the role. They should also be made aware of their responsibilities for feeding back to CGS council (and the Newsletter please!- Ed) of their work on the committee/working party if appointed.

Much time at Council was spent discussing the GENCAG Quality markers annual survey. The results of this arrived very late this year – largely due to reduced numbers of staff and illness in the Department of Health NHS Genetics Unit – and this was very frustrating when we were asked to produce this year's returns before being able to digest last years. Nevertheless we had to recognise that these figures (time –consuming as they can be to assimilate) are what the commissioners of our services have asked for and as they are commissioning the service they are entitled to data on the quality of the services we provide and

Specialist Registrar slot

Lily Islam, Kennedy-Galton Centre

we have an obligation therefore to do our best to provide them. Of course some of the data collected in the survey are indicators of practice rather than "quality" and Michael Wright as our rep on GENCAG will be discussing the data collection at future GENCAG meetings.

The lead clinicians group have been trying to collect data on the costs of our service, having managed to persuade the powers that be that the indicative tariff that had been suggested was too low. What was clear is that considerable differences exist between centres in terms of cost per consultation and much depended on what was counted as a consultation and what was included in the costs. Centres varied in their practice regarding tests and differences of opinion and experience were expressed about whether tests should be "unbundled" from clinic appointments. There was however clear agreement that we needed some uniformity in what was being counted – for this reason the lead clinicians group are holding an away day in November to try and thrash this out.

Congratulations to Katrina Prescott for winning the SpR poster prize at York. I understand that the posters were of an extremely high standard, everyone who submitted their work should be congratulated. One drawback of being President is that I have discovered that one has to go to lots of meetings when at York and so I didn't get to spend as much time as usual viewing the posters at this year's conference. Of course later this year the nomination forms will come round to elect my successor and I hope you will give some thought to that. Trevor has also indicated his desire to relinquish the Treasurer's post and I hope there will be a good deal of interest in taking this on. Trevor has done a magnificent job and deserves the opportunity to hand on the baton.

Another person handing on a baton is Shane McKee our CGS webmaster. Shane has done a great job in developing the CGS website but he has been looking for a successor and we are delighted that Adam Shaw has agreed to take over. Thanks to Shane for all that he had done.

One last item, following the success of the joint UK-Dutch Cancer Genetics Meetings, I invited our colleagues from the Netherlands to consider occasional joint CGS meetings. They welcomed this and we are delighted that our first joint meeting will be in Liverpool in March (see *Etcetera* for details).

I am one of the two Specialist Registrar (SpR) representatives on CGS Council; we are in the process of electing Duncan Rourke's replacement. The registrars are grateful to Duncan for all his hard work on our behalf. Being London-based does tend to make one a little insular, so I was very pleased to meet many other SpRs from around the country at BSHG; tales of life at other centres can be illuminating! I'd like to extend a particular welcome to the new SpR (and StR – Specialty Registrar) members of CGS, with congratulations to those who successfully navigated the Modernising Medical Careers maze.

On a less positive note, it is unfortunate when meeting SpRs to hear a few common concerns being voiced repeatedly. I have been working with Duncan to highlight the concern of SpRs that there is a scarcity of consultant posts in clinical genetics. This perception has sadly been an influencing factor in the decision of a few SpRs to leave clinical genetics training in recent years. In spite of this, we are encouraged that our concerns are being taken seriously by our consultant colleagues, and we remain hopeful that the target number of consultant posts suggested by the Royal College of Physicians taskforce will be attained in future.

If registrars have other issues that they'd like discussed at CGS Council, please feel free to contact me on lislam@doctors.org.uk, or come and find me at Dysmorphology Club/CGS etc.

Subspecialty Group Reports

UK Cleft Genetics Group Meeting, Wolfson College, Cambridge, 6-7 September 2007

Jill Clayton-Smith, Manchester

The inaugural meeting of the UK Cleft Genetics Group was attended by a small but enthusiastic group of representatives from 8 of the 11 UK Cleft Networks. Most were clinical geneticists but the group also included a paediatrician and a genetic counsellor who have a special interest in clefting and we were joined over the two days by a paediatrician working with the Cleft NET.East network, a fetal medicine specialist and a plastic surgeon. Starting at 4pm on a Thursday afternoon we embarked on a full program of presentations and discussions about genetic causes of clefting, covering various aspects of diagnosis, management and research.

We began with a short dysmorphology session, to which all of us brought both known and unknown cases. This brought home to us the huge number of different syndromes which are associated with clefting, and provided an opportunity to discuss the types of patient we see and how we routinely investigate them. It's clear that there is a great deal of variation in practice in the different centres. Discussion of several patients with collagen disorders, for example, led to the realisation that an evidence-based diagnostic and management pathway for these conditions could be a useful outcome from these meetings. We shared useful practical information on centres offering diagnostic and research testing for clefting disorders and plan to comprise a specific database of this information.

The Lead Consultant Paediatrician for CleftNET.East came to talk about his role in the team and the results of a 4 year audit of medical problems in cleft patients, demonstrating that there are major benefits from involving paediatricians in the routine care particularly of the syndromic cleft group. We then went on to discuss the role of the genetic team in the cleft network, looking at which patients we need to see, how they should be identified, the process of taking family and medical histories and which investigations we do. We shared information about practice in our own centres including issues such as the routine use of myopia cameras and hip X-rays at the appropriate times to screen Pierre Robin patients for Stickler syndrome. More food for thought, and all of this was before dinner!

Meeting early on the Friday morning we discussed the results of a short survey looking at how cleft patients who needed to be seen by the genetic team were triaged. There was universal agreement that the Cleft Specialist Nurses play a key role in this. We heard about a study in the Northern Region using review of patient photographs by a Clinical Geneticist to decide which patients to see. Interestingly, all of the patients whose photographs were reviewed over 5 years and who were deemed to merit a genetic consultation had already been referred to the genetic department via other routes. We looked at how geneticists contributed to cleft teams in the different regions. This is very variable from one region to another, but we learned from each other as to what worked well. Funding for genetic input is also very variable and it's clear that some negotiation is needed in this area. Di George syndrome was inevitably mentioned at several points, particularly the issue of which patients to screen and when. Geneticists appear to be much more conservative than our surgical and paediatric colleagues in this respect. The results of a survey from Newcastle helped to confirm our opinion that patients with isolated clefts who have normal feeding and development don't have a high incidence of 22q11 deletions, but this was flagged up as an area where we would look further at the evidence base in order to make recommendations on best practice. We finished off the morning by discussing the available patient literature for cleft patients who are seen for a genetic opinion. There are several different leaflets available, but we agreed to decide on one which we were all happy with to use on a UK – wide basis.

After lunch we had a presentation on prenatal imaging of cleft lip and palate from a local Fetal Medicine Expert. Although 3D scans provide excellent images, particularly, as he pointed out when you look at the "reverse face" they still don't guarantee detection of palatal clefts and to be most reliable they should be done after 24 weeks of pregnancy. Nevertheless, a diagnostic 3D scan carried out by an expert is clearly a powerful way of imaging the fetal face. We went on to have a session on research into clefting disorders, looking at the ways in which we as members of the cleft team could facilitate this and getting an update on the various cleft projects which are currently being undertaken. We finished by formulating an action plan and all of us left with jobs to do, but convinced that this had been a fruitful meeting and with plans to hold another one in 2008. We hope that colleagues from other networks who weren't able to participate this time can make it then. A fuller version of the proceedings of this meeting should be available on the CGS website in due course. Many thanks go to Helen Firth for organising this meeting on our behalf.

Sharing practice: how to address those typing backlogs

Sue Huson, Manchester

Most centres seem to have experienced dictation backlogs at one time or other. These have often developed because funding has become available for extra clinical posts though national/regional/Trust initiatives but the funding didn't include admin support. I don't know a Consultant who doesn't feel that a significant part of their time is spent on admin jobs that could be done by their secretary were they not typing, so the developments in voice recognition software and outsourcing to digital transcription services seems attractive. In response to my comments on this in the last editorial Graeme Suthers e-mailed from Adelaide to say:

"We have tried a number of workarounds for dictation woes in SA. I use a lot of inserts - carefully worded paragraphs that I can slip in. This has been particularly useful as we developed the familial cancer service as it helped ensure accuracy and consistency as the counsellors began to do more letters. I have also tried dictation software. When it works, it is brilliant. But when it doesn't, it is very frustrating. I do not think the technology is ready for mainstream use yet. It needs a powerful PC, and even so, the performance declines erratically as the day proceeds. I know that radiologists and pathologists use it routinely, but I cannot get the reliable consistency that they seem to enjoy."

The Oxford team presented their work with voice recognition in a Poster at York; they kindly agreed that I could reproduce the contents in the Newsletter so we can all learn from their experience. All the clinicians do is dictate the letters on to the screen, check the content and then email it to the secretary. Oxford has the Shire system which creates the letter templates with a few clicks of the button and then all the secretary has to do is paste the text in. Some users create their own templates. Feedback from other users of voice recognition software and departments using digital transcription services are welcome for the next newsletter.

DEVELOPING A VOICE RECOGNITION SYSTEM FOR CLINICAL CORRESPONDENCE IN A REGIONAL CLINICAL GENETICS SERVICE

Dr Helen Stewart, Sarah Durell, Eileen Collier, Ghazala Fazil

Department of Clinical Genetics, Churchill Hospital, Oxford OX3 7LJ

Introduction

- It has been the norm for Clinical Genetic Services to prepare correspondence documenting clinical consultations with patients
- This practice has recently been recommended generally for all clinicians
- The Clinical Genetics Society Clinical Governance Sub-committee states that 90% of post clinic correspondence should be sent within two weeks following an appointment (1)
- GenCag collect data on the percentage of letters that are sent within two weeks following a diagnostic consultation. (GenCag quality markers)

Problem

- During 2006, the ORH Department of Clinical Genetics benefited from an expansion in clinical staff numbers which was not matched by a parallel increase in secretarial time
- The secretariat was depleted due to long term sickness and vacancies
- There was a gradual increase in numbers of patients seen
- Consequently there was a build-up of a backlog of typing such that letters were taking several months to be typed and sent out
- In 2005-2006 < 10% of letters were sent within 2 weeks of an appointment

Attempted solutions

- Appointment of temporary administrative staff
- Requests to dictate shorter letters
- Use of standard paragraphs

Voice recognition system solution

- Market research was undertaken to explore options for voice recognition systems
- Cost comparisons were made with digital transcription services that were favoured by ORH Trust
- Dragon Naturally Speaking voice recognition system was demonstrated to Department of Clinical Genetic staff
- Dragon Naturally Speaking was trialled by a few members of staff
- Feedback from administrative staff, genetic counsellors and medical staff was sought
- Work was undertaken with commissioners and Trust to allow procurement of Dragon Naturally Speaking
- Hands Free Computing was commissioned to supply hardware, install software and provide on-site training

Lexicon development

- The Department of Clinical Genetics provided approximately 500,000 words of anonymised text to Hands Free Computing to assist in their development of the Lexicon. It was agreed that the Trust would receive part of the proceeds from any future sales of the lexicon in acknowledgement of this contribution.

Introduction and roll-out of system

- Five clinicians and one secretary were trained in a 'pilot' and a training manual was devised
- Voice recognition training for all remaining

"This has taken a while to get going but now very impressed with the effect this has had on our workload"

clinical users was completed in 7 working days (22nd Jan – 2nd February 2007) with 2 people being trained per day.
• Additional training and ongoing support was carried out by Department of Clinical Genetics IT staff (GF)
• It would have been necessary to purchase additional training days had in-house expertise not been available
• It is necessary to dictate to a computer screen at all times. It has proven impossible to use the voice recognition system using a 'chip' to be transcribed by secretaries. This necessitates a change in working practice or use of a lap-top computer for work in peripheral clinics.
• Planned phased cessation of use of Dictaphones in April 2007 (general) and May 2007 (cancer)
• Clearance of backlog: July 2007 (general), pending (cancer)

What the staff thought…

• Secretarial – "This has taken a while to get going but now very impressed with the effect this has had on our workload"
• IT – "In-house IT support is required initially. The system runs smoothly after the user starts working on the system"
• GC – "Useful tool, quicker than audiotape dictation especially when macros and templates are set up." "Much easier to use than audio dictation during times of interruption, as you can easily see where you were up to in a letter."
• Medical staff – "Initial reluctance, perseverance, gradual acceptance, generally would not go back to audiotape use"
• Business manager – "System took longer to implement and was more complex for users than it appeared when demonstrated but pleased with overall impact on workload"

Costs and savings

• The voice recognition system cost in the region of £25,000 to introduce including the cost of on-site training and the purchase of digital recorders for all 22 users. In addition to the initial set up costs, there will be a recurring annual charge (c£5,500) for licence renewals and upgrades
• Digital transcription would have cost approximately £25,000 per annum based on 2006/7 activity levels (3657 patients seen). This assumes an average cost of £0.115 per line (costs quoted varied between £0.08 and £0.15 per line) and is based on each patient generating two letters with 30 lines of text in each. This does not include the cost of secretarial time spent 'matching' the anonymised letter with the patient and adding address details etc

Cost comparisons with digital transcription are similar in year one but thereafter save ~ £19,500 per year.

Pros and Cons

PROS	CONS
Reduced overall time for letters to be produced	Initial increased time to dictate letters
Reduced correction time	Need for change in work pattern or lap top to allow dictation in peripheral clinics
Reduced time for letters to be sent out	Perseverance required to learn system
Reduction of backlog of typing	Difficult if high levels of background noise e.g. shared office
Increased accuracy of enclosures	
Increased standardisation of letters	
Secretarial staff able to manage work load and expand range of work	
Reduced clinical risk	
Improved morale	

References

(1)"Clinical Standards for a Genetics Unit" The Clinical Genetics Society Clinical Governance Sub-committee 2005

Research News

Leber Hereditary Optic Neuropathy Treatment Trial

Patrick Chinnery, Patrick Yu Wai Man, Philip Griffiths, Newcastle

The Newcastle Mitochondrial Research Group has set up a double-blind, randomised, placebo-controlled trial of the efficacy of idebenone in the treatment of patients with Leber Hereditary Optic Neuropathy (LHON). This study is being sponsored by Santhera Pharmaceuticals (Switzerland) Ltd and has regulatory approval. We would like to invite clinicians in the UK to refer eligible patients and inform LHON families under their care of this trial.

We are recruiting LHON patients aged 14 to 65 who have experienced visual loss for less than 5 years. The objective of this trial is to determine whether oral administration of idebenone can improve visual outcome in LHON. The trial centre is based at the Royal Victoria Infirmary in Newcastle and patients will have to attend for a total of 6 visits over 8 months.

Trial website: http://lhon.ncl.ac.uk/

E-mail: LHON@ncl.ac.uk or P.F.Chinnery@ncl.ac.uk

Telephone: 0191-222-8334 or 0191-222-5101

Genetics of Oesophageal Atresia (GOA) Project

Vicki Martin, Charles Shaw-Smith, Cambridge

The recent cloning of the Charge, Feingold and AEG (anophthalmia-oesophageal-genital) syndrome genes, together with the availability of array-based cytogenetics, has greatly improved the chances of making a molecular diagnosis in patients with syndromic oesophageal atresia/tracheo-oesophageal fistula and clinical features within the CHARGE/VACTERL/del (22)(q11) phenocopy spectrum.

Following the award of a four year Wellcome Trust Fellowship to Charles Shaw-Smith in 2006, the GOA (Genetics of Oesophageal Atresia) project has now collected in excess of 60 samples from patients with syndromic oesophageal atresia/VACTERL association. There is currently a small team devoted to the project, led by Charles with research assistants Mekayla Storer, fresh from Brisbane Australia, and Vicki Martin, formerly a leading light of TOFS, the UK support group for families of children with oesophageal atresia and malformations in the VACTERL spectrum.

How do I enrol a patient?

Patients and families are enrolled through Clinical Genetic departments. If you have a patient with a phenotype that might be suitable, the simplest route is to contact Charles or Vicki by email and we will let you know if we are interested (usually we are). We will then send out a consent form, information sheet and short form for clinical details.

We don't have strict inclusion criteria but, broadly, the following patient groups are suitable:

- Oesophageal atresia with additional features – learning disability, developmental delay, dysmorphic features, significant growth problems
- CHARGE/VACTERL/22q11 phenotypic group without a molecular cytogenetic diagnosis

If you have patients with cytogenetic or array-based findings and phenotypes in the above group then, needless to say, we would be very interested to hear about them!

What analysis is being offered?

We are offering, on a research basis, the following:

- Mutation analysis of the CHD7 (CHARGE), N-MYC (Feingold), SALL1 (Townes-Brock), and SOX2 (AEG syndrome) genes. Others, including some of the Fanconi genes, are currently being added to the panel
- High-resolution array-CGH using the recently reported BAC tiling array

Advantages?

We are offering a 'one-stop shop' for syndromic oesophageal atresia. This is particularly useful in cases where the phenotype does not fall neatly within a particular syndrome. Testing is free of charge. If you are agonising over whether your patient should have CHD7 mutation analysis, then this study could be for you!

Disadvantages?

This is testing 'on a research basis'. Any potentially pathogenic variants identified have to be confirmed in a clinical laboratory. At the moment, we are happy to undertake this by arrangement with the Molecular Genetics Service at Addenbrooke's Hospital. As is usually the case with research projects, we are not able to undertake completion of testing within a particular timeframe.

Further information

Please contact Charles (css@sanger.ac.uk or charles.shaw-smith@addenbrookes.nhs.uk) or Vicki (vicki.martin@addenbrookes.nhs.uk) for further information.

Proteus Syndrome – Call for patients

Richard Scott, Nazneen Rahman, ICR, Sutton

As part of the ongoing Childhood Overgrowth study and in collaboration with Professors John Harper and Raoul Hennekam at Great Ormond Street, we are extending our research into asymmetric growth to include Proteus syndrome / severe and progressive asymmetric growth conditions. Building on findings from our recent work on asymmetric growth, we aim to identify the genes and molecular pathways underlying severe and progressive asymmetric growth conditions and to define the clinical phenotypes with which they are associated.

We would be very grateful to receive samples and clinical data from any case with severe and/or progressive asymmetric growth including patients with Proteus syndrome, Proteus-like phenotypes or isolated macrodactyly. We are keen to receive blood and/or abnormal tissue samples. Where available, we are also keen to receive normal tissue samples.

Patient information sheets, consent forms and a short questionnaire are available from Richard Scott (Tel. 0208 722 4455, email richard.scott@icr.ac.uk) or Nazneen Rahman (email nazneen.rahman@icr.ac.uk).

Lost In Translation: A New Agenda For Research

Katie Snape, Richard Trembath, Guy's

Taking advances in laboratory research and turning them into diagnostic and therapeutic tools for use within a clinical setting is not a new concept, so why is the newly-minted term "translational research" suddenly so popular? As a recently appointed Clinical Research Fellow (CRF) in Translational Research at Kings College London, I intend to find out…

The National Institute for Health Research (NIHR) has recently established five comprehensive Biomedical Research Centres, which, together with a number of more specialised centres, have the specific goal of developing patient-based clinical research. The centres are created by the formation of a partnership between a university and an NHS trust, and bring together senior NHS clinicians, academics, dentists, university staff, allied health professionals, NHS managers and patients under one roof – something many of them may have been trying to avoid for years. The process is designed to identify emerging translational opportunities arising from research work and to support and develop the partnerships required to ensure the delivery of real changes in clinical management. Their creation recognises many of the challenges involved in taking research from the bench to the bedside and service provision.

The GSTT/KCL Biomedical Research Centre1 made the early decision to appoint 11 Clinical and 10 Allied Health Professional Research Training Fellows to join the Faculty of Translational Research. These are drawn from the wide range of medical specialities represented within the BRC, and are based within a new Clinical Research Facility ideally situated on the 15th floor of Guys Tower with stunning views over the Thames to get those creative translational juices flowing.

As a CRF within the Department of Medical and Molecular Genetics, my specific project is outlined below. The project itself is typical of a traditional clinical genetics research project. However, working within a Faculty which places an emphasis on translational research supports training in clinical trial design and execution, through structured teaching and practical exposure. These skills are increasingly likely to be relevant to clinical geneticists as therapeutic interventions for genetic disorders moves from promise to reality.

A Clinical and Molecular Genetic Study of Adams-Oliver Syndrome and Related Disorders

The Adams-Oliver syndrome (AOS) was first described by Forrest Adams and CP Oliver in 19452. The disorder is characterised by the combination of scalp aplasia cutis congenita (ACC), with terminal limb abnormalities. The phenotype is highly variable, with extreme forms of the syndrome associated with mental retardation and neonatal death. Of interest, around a quarter of AOS patients have associated vascular abnormalities, including congenital heart disease, cutis marmorata telangiectatica congenita, arterio-venous malformations and pulmonary hypertension.

An emerging hypothesis proposes that the underlying gene is critical for normal blood vessel development, hence identification of the molecular basis of this disorder is likely contribute to an understanding of processes involved in vasculogenesis, and as such that we may be able to extrapolate findings into therapeutic targets for more common disorders related to abnormalities of vascular development, in true translational style.

Given the rarity of AOS we have

established a European Consortium, in conjunction with Dr Wym Wuyts in Antwerp, Belgium and Dr Martin Zenker in Erlangen, Germany, with the aim of identifying and characterising the gene(s) responsible for AOS.

The response from clinicians both nationally and internationally from calls for recruitment to this study has been extremely impressive, but needless to say we remain keen to identify any additional patients and kindreds with possible AOS phenotypes and are still actively recruiting for patients to become involved in this study.

- Minimal enrolment criteria are aplasia cutis/cutis marmorata in combination with terminal transverse limb defects.
- This study has multicentre ethics approval.

Please contact me for further information, details of ethics and patient information leaflets.

Dr Katie Snape, NIHR Clinical Research Fellow

Guy's and St Thomas' NHS Foundation Trust / King's College London NIHR Biomedical Research Centre

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1) http://www.guysandstthomas.nhs.uk/education/researchanddevelopment/biomedicalresearch

2) Adams FH, Oliver CP. Hereditary deformities in man due to arrested. development. J Hered 1945; 36: 2–7

Developing Medical Genetics Services and Research in Mumbai

Dr Zarine Patel, Mumbai

I read with interest the article entitled Setting up a Genetics Service in Banglore, India, by Meera Bhatt. We thought people would be interested in the work of our centre.

Genetics in Mumbai, India was initiated way back in 1977 when the Unit of Medical Genetics at the Institute of Research in Reproduction started genetic counselling. In 1986 the unit became the 20th permanent centre of the Indian Council of Medical Research (ICMR). Today it is the leading centre in the country in the field of medical genetics. Our mandate has been prevention of genetic disorders by genetic counselling, genetic screening, and prenatal diagnosis. We run an effective genetic counselling clinic, where 500 new cases are diagnosed and counselled every year. May I add that the first test tube baby was conceived at the same genetic unit in 1986 under the pioneering efforts of Dr J Peter. I took my formal training through WHO under Professor Malcolm Ferguson-Smith at the Duncan Guthrie Institute of Medical Genetics in Glasgow. Later with Professors Charles Rodeck, Stuart Campbell and Peter Harper. On my return the Genetics Centre was established and various projects were undertaken including a control programme of B-Thalassaemia by antenatal screening; the feasibility of introducing genetics services in family welfare programme and preconceptional folic acid in prevention of neural tube.

The Centre caters for the needs of families with blood disorders, some neurogenetic conditions, birth defects and all cases of primary amenorrhea. We carry out FISH studies in lymphocytes, in sperm, T-FISH in couples with recurrent spontaneous abortion and children with idiopathic mental retardation. We have a simple immunocytochemical test for screening for fragile-X syndrome and also an ELISA for HbA2 for B-Thalassaemia screening. Since this is a government organization all tests are carried out free of charge.

Newer initiatives have included preimplantation genetic screening for aneuploidies. This was set up after my training with Professor Joyce Harper at University College London .

We were pleased to read of more international links being developed through CGS/BSHG and if anyone would like to visit our centre please be in touch.

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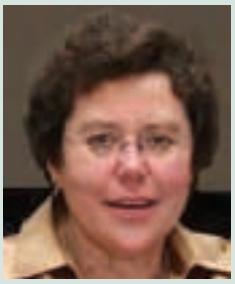
zmpatel@hotmail.com

CGS News Editor



Deadline for contributions for next issue is Friday 11 January 2008

Dr Susan Huson

Department of Clinical Genetics, St Mary's Hospital (SM2), Hathersage Road, Manchester M13 0JH

Email: Susan.huson@cmmc.nhs.uk

Tel: 0161 276 5152

Etcetera…

Inaugural Joint Meeting: UK / Dutch Clinical Genetics Societies, 12-13 March 2008

We welcome you to the beautiful St Georges Hall, LIVERPOOL UK for 2 exciting days of Clinical Genetics

Please note: March 11 Dysmorphology Club also in Liverpool at Alder Hey Hospital

FUNDAMENTALS OF CLINICAL GENETICS

A Course for Clinical Geneticists endorsed by the Clinical Genetics Society and the Specialist Advisory Committee of the Royal College of Physicians, London

Evening of Tuesday 8 Jan to
Friday 11 Jan 2008
At
The Wellcome Trust Conference Centre,
Hinxton Hall, Cambs, UK

This new 3-day course is open to Consultants and Specialist Registrars in Clinical Genetics. The programme for the first two days is designed to give all delegates an up-to-date overview of the fundamental aspects of genetics which underpin clinical practice. The third day of the course is designed especially for SpR's and focuses on dysmorphology and development and includes the course assessment.

We are very fortunate to have been granted permission to hold this course at the Wellcome Trust Genome Campus which has played a key role in some of the scientific developments to be discussed during the course. The course is sponsored by the Wellcome Trust and the Clinical Genetics Society. Full details, including the course programme and subsidised registration fees are available from p.garland@wtconference.org.uk. Numbers are strictly limited. Places will be allocated on a first come, first served basis with preference given to those still in training.

Course organiser: Dr Helen V Firth
Course tutors include:
Prof Andrew Wilkie
Prof Peter Hammond
Dr Jane Hurst
Prof Karen Temple
Dr Sarah Smithson

SKIING AND CPD?

Many other specialties, particularly surgical, combine educational events with skiing. Jane Hurst has come up with the excellent idea that we should launch a similar venture for clinical geneticists who trained pre-Calman. We mainly trained through apprenticeship and formal teaching was patchy…so regular and up to date CPD is much needed (well that's the official version!).The plan is that each member of the party would bring an update lecture on their favourite topic and we will learn before /after our day on the piste.

We would plan the first trip for spring 2009. A small prize will be awarded for the best group name which we hope will have a suitable acronym. For example, a group of female health professionals in the Swindon area have a LOST trip each year…the ladies only ski team.

So if you are interested please be in touch!

susan.huson@cmmc.nhs.uk
jane.hurst@orh.nhs.uk

NEW CONTACT DETAILS FOR THE LIVERPOOL SERVICE

Alan Fryer

- We have changed e-mail addresses and phone numbers.
- Our postal address is still at the Department of Clinical Genetics, Royal Liverpool Children's hospital (Alder Hey), Eaton Road, Liverpool, L12 2AP.
- Phone numbers are now:
  General enquiries: 0151-802-5000/5001/5002
  Secretaries: Dr Alan Fryer (0151-802-5004), Dr Ian Ellis (0151-802-5008), Dr Elizabeth Sweeney (0151-802-5005), Dr Lynn Greenhalgh (0151-802-5007), Dr Astrid Weber (0151-802-5006).
  Gail Mannion (genetic counsellor team leader): 0151-802-5032.
  Fax: 0151-802-5095/96.
- E-mails – have changed to name@lwh.nhs.uk instead of name@rlc.nhs.uk.

Editorial

Martin Schwarz

As we go to press, summer has had its last gasp with a couple of lukewarm days, and labs are making their preparations for the lab Christmas outing (tales and pictures for the January Issue please). Copy for this issue was sparse, but of high quality, so a big thank you to all contributors.

Thanks first to Debbie Bates for her seriously futuristic report from the San Diego meeting on novel sequencing technologies – but what exactly is "Ultra-deep sequencing"? Debbie tells us that Sanger sequencing chemistry might be a bit long in the tooth, and new and wonderful techniques are on the near horizon. The description of the bead-bound RNA polymerase method sounds incredible but feasible, if that's not oxymoronic.

It's nice to hear from Teresa Davies some encouragement to take the MRCPath, which remains the only 'public' exam that hasn't been 'dumbed-down' by successive Governments! It's useful, too, to have feedback on the answers provided by candidates; trainers will doubtless be busy as we speak, trying to rustle up some model answers.

I couldn't resist two somewhat esoteric pieces from the web. The first concerns the recreational use of genetics – yes, they've sequenced the genome of the Pinot noir grape (known in my neck of the woods as Spätburgunder, by the way). Perhaps they will now be able to answer the Ultimate Question as to whether Pinot noir really is a cross between Pinot meunier (Schwarzriesling) and Traminer – it's important! Your contributions on what Jilly Goolden would make of it all will be most welcome for the next issue.

The second piece requires no comment, but I can see a hint of a link with Debbie Bates's piece, in that they both mention 'Personal Genomics'. James Watson's Complete Genome on a DVD is just the seed...

On the home front, perusal of the Heads of Labs' email circuit is always fruitful, but can someone help me, please? I recently received an email in which the structure of UKGTN was described, detailing the make-up of the sundry (and numerous) associated committees, which seem to have reproduced in a rabbit-like fashion – or Topsy, if you prefer. I have not been able to find the email since then: I am now wondering if it was just one of those dreams that leave you with the uncomfortable feeling that the whole world's gone mad!

And a final plea to the agents employed by a certain large biotech corporation (yes, the one that holds all sorts of patents on DNA amplification techniques) – please stop going through my bins to try to find out how much Real Time PCR I'm doing. The answer is NONE!

The times, they are a-changing?

Debbie Bates
Sheffield Molecular Genetics Service

Next Generation Sequencing Technologies: Applications and case studies (San Diego, 21-22 March 2007).

Cambridge Healthtech Institute's inaugural Next Generation sequencing technology meeting was held earlier this year at the Mission Bay Hilton in sunny San Diego. It was a great two day programme covering novel sequencing technologies, platforms and future applications.

Sanger chemistry has dominated the last 30 years of DNA sequencing but with the 'Next Generation' field hotting up, I travelled across the Atlantic to see if sequencing in the NHS molecular genetics laboratory really could be poised for reform?

What do the new DNA sequencing platforms offer?

Sequencing-by-synthesis is a feature of some of the most promising new technologies appearing on the market. This includes approaches from 454 Life Sciences (Roche), Helicos and Illumina (Solexa).

454 Life Sciences were founded in 2000 by Jonathan Rothberg with the premise of achieving routine human whole genome sequencing in healthcare. Now acquired by Roche, 454 launched their FLX system earlier in 2007.

454's technology utilises an emulsion based PCR (emPCR) strategy in combination with pyrosequencing chemistry licensed from Biotage. High throughput is achieved by miniaturising a methodology with relatively short read lengths. This highly parallel approach is conducted in a PicoTitrePlate format and can generate 400,000 reads per run (4.5 hours).

Presenting at the meeting, Michael Egholm (VP of 454 Life Sciences, Molecular Biology) reported a 99.95% accuracy over a 250 base

Applied Biosystems SOLiD machine

"James Watson: the first human genome to be sequenced for less than a million dollars (or $1 million)"

read length; a very much improved performance over their initial instrument (GS20 model). 454's technology is amenable to ultra-deep sequencing of heterogeneous samples such as tumour biopsies. However, the nature of pyrosequencing leaves it prone to homopolymer problems.

Robert Strausberg (Venter Institute, CA) reported favourably on 454's characteristics. He presented data exploiting the sensitivity of ultra-deep sequencing to detect somatic mutations. Examination of glioblastoma samples detected mutations in the FGFR1 gene which could have easily been missed by the analysis of capillary electrophoresis (CE) chromatograms alone. Indeed, a digital output is emerging as one of the major attractions of many Next Generation platforms.

Egholm also revealed that 454 were sequencing James Watson's genome! Watson agreed only on the condition that he was not informed of any potentially deleterious variants. At the time of the meeting, 454 had generated approximately 3% of sequence derived from 'Project Jim' which did not map to the latest reference sequence; suggesting that perhaps the Human Genome Project (HGP) was only partially complete …or that it might be that extra bit of DNA which gives you an edge in life sciences research? [Just 'Sequencing', Jim, but not as we know it!]

'Project Jim' was completed in 2 months and is the first human genome to be sequenced for less than $1 million. At a ceremony held at the Baylor College School of Medicine, Richard Gibbs presented the 1962 Nobel Laureate with a DVD containing his genomic sequence. Much of this sequence information has been deposited in the public domain (www.ncbi.nlm.nih.gov/Traces/trace.cgi).

Applied Biosystems (AB) are not resting on their laurels. Michael Rhodes (Applications Manager, AB High-throughput Discovery) described how the company had evaluated a number of alternative sequencing technologies, from both academic and private sectors, before selecting and developing the SOLiD system (Sequencing by Oligonucleotide Ligation Detection). AB acquired Agencourt Personal Genomics (APG) and their novel adaptation of a sequencing-by-ligation method, originally developed by George Church's group at Harvard Medical School.

SOLiD technology also uses emPCR to clonally amplify DNA fragments. Products are randomly deposited onto an array for probing with fluorescent oligos. A 'strip and reset' two-base encoding method allows a double interrogation of each base to reduce errors. At the time of the meeting, SOLiD could achieve read lengths of up to 25 bases with a 98% raw accuracy, corrected to 99.99% using x20 coverage.

A single SOLiD run generates approximately 2G bases of sequence information (over 3 days). By employing a ligase based system, SOLiD avoids polymerase incorporation errors and the dephasing problems associated with sequencing-by-synthesis approaches.

Rhodes stressed the benefit of many Next Generation platforms permitting mate pair (paired-end) methodologies. It is possible to envisage how these approaches might be adapted to probe for rearrangements throughout the genome, producing a form of 'molecular karyotype'.

Sequence quality, error rates and read length all remain core concerns for the DNA sequencing community. However data storage capacity is emerging as a new issue for users. Handling and archiving data on this scale will be a fresh challenge for any diagnostic laboratory wishing to run a 'Next Gen' machine.

The $1,000 Genome: Fostering innovation thought competition.

The present cost of DNA sequencing needs to be significantly reduced in order to offer routine human genome sequencing and to make personalised medicine strategies a reality.

Jay Shendure (Harvard Medical School) presented some really neat solutions for capturing and sequencing only the expressed regions of the genome or 'exonome'. He proposed that one way of reducing the cost of human genome sequencing, to meet the $1,000 challenge, might be to limit analysis to coding regions alone. A strong believer that so-called 'junk' DNA is not inert, I was a little apprehensive about this approach. However, Sendure's targeting strategies would be ideally suited to the analysis of multiple loci which are known to be associated with a particular disease phenotype.

The X PRIZE Foundation was present at the meeting to promote the Archon prize for Genomics. The foundation is an educational non-profit prize institute whose previous initiatives have included the $10 million Ansari X PRIZE, which was awarded to Mojave Aerospace Ventures in 2004 for SpaceShipOne, a ground breaking private spaceflight vehicle.

The Archon X PRIZE for Genomics was launched in October 2006 as a vehicle to accelerate DNA sequencing technology developments and increase public awareness. It aims to challenge scientists and engineers around the world to deliver accurate, rapid and affordable genome sequencing. $10 million will be awarded to the first team to successfully sequence 100 human genomes in 10 days, at 99.99%

"'Next, Next Generation' sequencing technologies could include in vitro reading of a single DNA molecule by RNA polymerase"

accuracy and at a cost of <$10,000 per genome. The prize money has been provided by Stewart Blusson (President of Archon Minerals), a Canadian geologist who uncovered a trove of diamond mines in the Northwest Territories in the early 1990s.

Organisers plan to use the HGP sequence as a reference and to re-sequence random segments of the human genome to check on competitor concordance. Currently 454 and VisiGen are amongst those to have stepped up to the mark and enlisted.

It was reassuring so see that Archon have assembled a specialist committee to consider the social and ethical implications that will arise from advancing DNA sequencing technology and the prospect of personalised medicine.

'Next, Next Generation' sequencing technologies.

After getting to grips with the sequencing technologies currently breaking onto the market, the meeting turned to 'Next, Next Generation' methods. It was clear from this session that single molecule sequencing was a popular topic; providing the ultimate limit for miniaturisation. Without the need for amplification, one could theoretically select any DNA molecule from any cell and sequence it.

William Greenleaf (Applied Physics, Stanford) gave a fascinating and polished account of the potential for exploiting RNA polymerase's natural ability to 'read' the sequence of a single DNA molecule in vitro. In short, using optical traps as 3D springs and applying a force clamp to a bead-bound RNA polymerase molecule, real time measurements of the enzyme's movement along the DNA template could be observed. If the reaction is performed four times with each nucleotide delivered at a rate-limiting concentration, an alignment of the enzyme's characteristic rate-limited pauses permits deduction of the template DNA sequence.

RNA polymerase is highly possessive but with a reduced fidelity compared to most DNA polymerases, accuracy could be a concern. The technique is currently at a 'proof of principle stage'; achieving 95% accuracy over 30 bases. Greenleaf described his methodology as 'ultra-low thought-put'. Although it is difficult to imagine how one might parallelise the system, he proclaimed multiplexing the optical traps one of the next challenges.

Diagnostic laboratories and Next Generation sequencing.

Sanger/Capillary Electrophoresis (CE) sequencing was not completely shunned at the meeting. Stevan Jovanovich (Microchip Biotechnologies) presented the NanoBioPrepSEQ station. The system is designed to miniaturise and automate front-end Sanger sequencing preparation. Reactions are performed on a nano Litre scale in capillary channels and on chips, before analysis on standard CE instrumentation.

By using microfluidics and islands of automation, Jovanovich suggested Sanger/CE might be capable of meeting the $1,000 genome challenge and should not be disregarded quite yet. The reduced labour and downscaled reagent costs of this approach might appear more attractive to the average sized diagnostic laboratory than investment in a Next Generation platform at this stage.

Presently it is foreseeable to see a home for Next Generation hardware in large genome centres. Indeed, the metagenomics community are getting really excited about it all! The alternative sequencing field is fast moving; performance characteristics and the breadth of applications are constantly improving. However, it remains to be proven how these new technologies would fit into a typically sized diagnostic laboratory currently dominated by targeted re-sequencing.

The sheer sequencing capacity of a single Next Generation instrument run and changes to front-end preparation would require a revolution in workflow and the integration of many processes to insure efficiency.

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Attendance at this meeting was assisted by a travel award from the CMGS.

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454 Life Sciences: www.454.com
Microchip Biotechnologies: www.microchipbiotech.com

Membership of The Royal College of Pathologists 2007

Membership of the Royal College of Pathologists (MRCPath) is a mark of professional standing and esteem achieved through 1 of 3 possible routes: examination, publications or at the invitation of Council. The latter 2 routes are for academic and distinguished pathologists and are inappropriate for trainees.

Potential candidates should visit the RCPath web site for the most up to date information, including guidelines and regulations and must read and follow them carefully.

In genetics a small number of candidates achieve MRCPath through publications each year but the most common route is by examination.

The MRCPath examination consists of an assessment of the candidate's knowledge of the specialty and their ability to apply that knowledge in the practice of their specialty.

2007 saw the separation of the Part 1 written and practical examinations into 2 sessions: Spring and Autumn. This was done to give more time for marking and moderation and to relieve the pressure on the examiners, candidates and the examination department.

It is encouraging to see the number of candidates sitting the part 1 examination. This year there were 7 candidates for the part 1 written in cytogenetics with 7 passes and 12 candidates in molecular genetics with 9 passes.

General feedback is presented elsewhere in the BSHG newsletter.

The practical examinations are to be held in October.

There continues to be a disappointingly small number of candidates sitting the part 2 examinations, which is held once per year in Spring. There were 3 candidates in cytogenetics with 2 passes and none in molecular genetics.

It is, however, encouraging that a number of proposals for part 2 written work have been submitted for approval this year and several pieces of written work have been presented for assessment with the view of sitting part 2 oral in 2008.

A lot of work in being undertaken by the College examination department and the examination panels to improve the examination process and standards in all disciplines. This has included holding training sessions for all examiners.

All of the work, setting and marking the exams, assessing written work and conducting orals is carried out by the small genetics exam panel, which has 11 examiners in molecular genetics and 9 in cytogenetics.

A special thanks to them for all of their hard work.

Teresa Davies – Chair Genetics
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MRCPath Part 1 Examination

Part 1 Examination

Tuesday March 27th 2007

MOLECULAR GENETICS

First paper

Candidates must answer FOUR questions ONLY

Time allowed THREE HOURS

1. Explain the principles underlying following techniques, illustrate with examples of application in clinical molecular genetics

a. Di-deoxy DNA sequencing
b. western blotting
c. Multiplex ligase-dependent probe amplification (MLPA)
d. Immunocytochemistry/immunohis tochemistry

This question was answered by all candidates. The responses to this question were of mixed quality. Good answers provided succinct and accurate descriptions of the methods. Nobody mentioned dye primer sequencing, some people were unaware of the use of MLPA for methylation and point mutations.

2 What is X-inactivation, how is it mediated, and for what purpose? How using cytogenetic and molecular genetics methods can X-inactivation status be assessed in a female? How can skewed X inactivation lead to disease?.

This question was common to the cytogenetics and molecular genetics paper and was answered by all candidates. Generally this question was answered well. Good answers provided clear and accurate descriptions for each subsection of the question. Some missed the point that a polymorphic marker is needed to show the inactivation eg. the CAG repeat near the methylated sites in AR.

3 Describe how different types of repeat sequences in the genome (other than trinucleotide repeats and other microsatellites) can contribute to disease. Give examples. Describe possible mechanisms.

This question was answered in a satisfactory way by most of the nine candidates who attempted it. Unequal crossing over between repeats leading to duplications and deletions with the PMP22 gene used as the main example.

4 Define, with examples, the following:
• Random genetic drift;
• Founder effect
• X-linked dominant disease

How you would test if a common mutation was due to a Founder effect rather than recurrent mutation at a hot spot.

This question was answered well by most of the five candidates who tried it.

5 Describe how abnormalities in protein folding can cause diseases with gain-of-function, loss-of-function or dominant-negative mutational mechanisms. Give examples of diseases to illustrate the relevant principles.

This question was answered by ten candidates and caused many problems. Many applicants could not explain clearly what gain-of-function, loss-of-function or dominant-negative mutational mechanisms were. The applicants had a poor grasp of how mutations alter protein folding. HD, CF and OI were used as the main examples.

Part 1 Examination

Tuesday March 27th 2007

MOLECULAR GENETICS

Second paper

Candidates must answer FOUR questions ONLY

Time allowed THREE HOURS

1. The 2006 Nobel Prize in Physiology or Medicine was awarded to Andrew Fire and Craig Mello. It honours a discovery that has transformed biological research and may, in the future, prove useful in treating human disease. The discovery is called RNA interference, or RNAi.

Describe the basic principles of how siRNA (small interfering RNA) and miRNA (microRNA) regulate gene expression. Describe the possible physiological roles of this process, how this discovery has provided critical biological reagents for functional genomics (give examples) and describe how it may be useful for therapy of certain diseases (give examples and decribe possible risks of the methodology).

This question was answered by ten candidates and had answers that ranged from poor to excellent. The good answers showed a clear grasp of the concepts. The poor answers suggested that these applicants had not been exposed much to this approach. It is important that MRCPath applicants keep abreast of key developments across genetics.

2. A recent report evaluating the use of array comparative genomic hybridisation (aCGH) in the investigation for idiopathic learning disabilities suggests it should be considered as a first line investigation.

Describe the issues, (biological, scientific, and technical) which would need to be taken into consideration prior to a CGH as a first line investigation being introduced for these patients into a diagnostic genetics laboratory.

This question was common to the cytogenetics and molecular genetics paper and was answered by all candidates, Most answered this question well. The poorer

answers were compromised by a lack of detail on methodology and also a lack of appreciation of the bigger picture required for a screening service (i.e. issues outside the laboratory itself).

3. Define:

- Lod score; and the principles of genetic linkage analysis (Parametric linkage);
- Transmission disequilibrium test;
- Population stratification

Give examples of methods that can be used to limit risk of false positive results due to population stratification in genetic association studies.

This was an unpopular question only answered by three candidates and the marks were not good. We were surprised as population genetics is easy to prepare for and the question was straightforward.

4. What types of mutations give rise to the absence of a protein product of the expected correct size on a denaturing SDS gel? Describe why the protein is absent or has abnormal gel mobility and describe the experimental methods that you would use to define the relevant mechanisms.

This was answered by eleven candidates. Marks were spread over a wide range for this question. It is important that genetics trainees think beyond DNA as a diagnostic tool.

5. Huntington's disease: What is anticipation and what is the molecular basis for this phenomenon in HD? What is a prenatal exclusion test? - Describe the principles used with a hypothetical example? What is the evidence supporting the argument that HD is caused by a mutation that confers a toxic gain-of-function on the mutant gene product?

This was answered by all candidates. The marks on this question were fairly poor. Again, applicants did not often know what gain-of-function meant.

SUMMARY

Question									
1-1	1-2	1-3	1-4	1-5	2-1	2-2	2-3	2-4	2-5
No of answers									
12	12	9	5	10	10	12	3	11	12
Average score									
12	13	13	13	12	13	13	13	12	12
No of passes									
6	8	5	5	3	8	7	3	5	7
No of fails									
6	4	4	0	7	2	5	0	6	5

From The Web 1

Plying With Plonk: Pinot Noir Genome Sheds Light on Flavour, Health Effects of Red Wines

NEW YORK (GenomeWeb News) — A consortium of French and Italian researchers has sequenced the genome of a wine grape variety and found that it carries additional copies of genes linked to flavour, aroma, as well as the compound found in red wine believed to confer good health.

The draft sequence by the Public Consortium for Grapevine Genome Characterization hints at how vintners cultivated their crops for these desired phenotypes as far back as the Stone Age.

Its findings may also enable scientists to use the genome of Vitis vinifera, a Pinot Noir variety, to identify genes responsible for desired tastes and disease resistance.

For instance, the team found that compared to other flowering plants, grapevines have twice as many genes linked to essential oil production and other compounds responsible for a wine's aroma. They also have more of the genes that produce resveratrol, the compound in red wine associated with certain health benefits.

The draft sequence is the fourth produced for flowering plants, the second for a woody species, and the first for a fruit crop, the scientists wrote in their article, which appears as a Letter in Nature (27 September 2007).

Researchers led by Olivier Jaillon and Patrick Wincker of France's National Institute for Scientific Research at the Universite d'Evry "provided unexpected evidence for genome duplication" in a species that had previously been considered as true diploids on the basis of their genetics.

Writing that they selected grapevine "because of its important place in the cultural heritage of humanity," the scientists sequenced the PN40024 genotype of V. vinifera using a whole-genome shotgun strategy, with all data generated by paired-end sequencing of cloned inserts using Sanger technology on ABI3730xl sequencers.

The team produced a total of 6.2 million end-reads, representing an 8.4-fold coverage of the genome. Within the assembly, performed with Arachne, 316 supercontigs represent putative allelic haplotypes that constitute 11.6 million bases, they wrote in Nature. When considering only one of the haplotypes in each heterozygous region, the assembly consists of 19,577 contigs and 3,514 supercontigs totalling 487 Mb. This value is close to the 475 Mb reported for the grapevine genome size during January's PAG conference.

In their paper, the team notes that a "striking feature" of the grapevine proteome is the existence of "large families related to wine characteristics, which have a higher gene copy number than in the other sequenced plants."

For instance, the team has identified 43 genes encoding stilbene synthases, which help synthesize resveratrol, the grapevine phytoalexin linked to the health benefits associated with moderate red wine consumption.

Additionally, the researchers identified 89 functional genes encoding terpene synthases, which drive the synthesis of terpenoids, secondary metabolites believed to be "major components of resins, essential oils, and aromas of the plant.

The team writes that public access to the sequence will help identify genes underlying the agricultural characteristics of this species, including domestication traits. "A selective amplification of genes belonging to the metabolic pathways of terpenes and tannins has occurred in the grapevine genome, in contrast with other plant genomes, the researchers note.

"This suggests that it may become possible to trace the diversity of wine flavours down to the genome level," they write.

The genome could also enable vintners to devise grape strains less susceptible to the "large diversity of pathogens" that threaten them. Jean Weissenbach, one of the study's authors and director of Genoscope, the French national sequencing centre, said the sequence could help devise breeding programs to increase pest resistance.

From The Web 2

Google Buys Minority Stake in 'Personal Genomics' Startup

NEW YORK (GenomeWeb News) — Google has become a minority owner of early-stage personal genomics company 23andMe after investing $3.9 million as part of a round of private-equity financing.

23andMe co-founder Anne Wojcicki, who is married to Google president of technology and co-founder Sergey Brin, said in a statement announcing the funding yesterday that her company aims to "connect people with their genetic information" by allowing them to learn about their ancestry and inherited traits.

The Mountain View, California based company hopes eventually to allow many individuals to "work together to advance the overall understanding of the human genome."

23andMe's other co-founder, Linda Avey, has in the past worked for Affymetrix and Perlegen, according to the company's website. The site lists Avey's primary interest as "the acceleration of personalized medicine, using genetic profiles to target the right drug to the right person at the correct dose."

"Our goal is to connect you to the 23 paired volumes of your own genetic blueprint (plus your mitochondrial DNA), bringing you personal insight into ancestry, genealogy, and inherited traits," the website said. "By connecting you to others, we can also help put your genome into the larger context of human commonality and diversity.

"Toward this goal, we are building on recent advances in DNA analysis technologies to enable broad, secure, and private access to trustworthy and accurate individual genetic information," the company added. "Combined with educational and scientific resources with which to interpret and understand it, your genome will soon become personal in a whole new way."

[Hands up all those who were doing the 'fingers-down-the-throat' sign! –Ed]

CMGS News Editor

Deadline for contributions for next issue is Friday 11 January 2008

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Editorial

Chris Jacobs

Very many thanks to everyone who has sent me articles, paragraphs and letters for the newsletter. Please do keep them coming in for the next newsletter which is really not that far away. My email address is Chris.Jacobs@gstt.nhs.uk

This edition mainly focuses on breast cancer with a leading article from Gareth Evans, Chair of the CGG about breast screening for high risk women. Caitlin Ferguson, Senior Campaign Policy Officer at Breakthrough Breast Cancer has written about the new Breakthrough campaign to raise awareness about screening women with a family history of breast cancer. This may be helpful for some women, however, those who are not able to access screening according to NICE guidelines may also wish to contact their own Primary Care Trusts or their MP.

Staying with breast cancer and BRCA carriers in particular, the spotlight section has focussed on Guy's this time (now there's a surprise) but its come from a surgeon's perspective which I hope gives an interesting and original angle. Hisham Hamed, Consultant Breast Surgeon at Guy's and St Thomas' Trust kindly agreed (after only minor arm twisting) to write an article about managing breast cancer risk in BRCA carriers from the surgeon's perspective. Hisham is a member of the Guy's BRCA Carrier clinic team. Working together with other specialists has been a great learning experience for all those of us involved in the clinic and the lunchtime multidisciplinary meeting attended by geneticists, genetic counsellors, breast surgeons, gynaecologists, psychologists and oncologists often results in challenging and stimulating discussions.

It is exciting to see the launch of the new CGG website and we hope this will provide the membership with another way of communicating with each other. Like the newsletter, in order to be successful and useful, the website needs your input. Incidentally, this newsletter will go onto the web site after it has been published in the BSHG newsletter so you should find the May newsletter there soon and this newsletter should follow shortly.

Carole Brewer has provided us with a report on the very successful Spring meeting held in Manchester in May. With December fast approaching, it is a good time to remind everyone that the next CGG meeting will take place at Guy's Hospital on 7th December (not Saturday 8th as originally advertised by me). The December meeting should provide a helpful update on ongoing research studies as well as informing us about new studies. Hopefully, the meeting will be well attended. Please remember to let Gabriella Pichert, Anneke Lucassen or me know in advance if you have any cases to discuss.

With best wishes

Chris

Surveillance in Familial Breast Cancer

Gareth Evans

It is likely that annual mammography screening will identify over 60% of cancers in young women [1], but interval cancers do occur. The young breast is denser and more difficult to interpret. However, as relative risk to the general population at age 35 may be 40 fold, the high risk group needs to be treated as a special case. Although the first evidence for a significant survival advantage has emerged for the general population under 50 years [2,3]. the frequency of disease is probably too low to justify screening on economic grounds. However, our own work in Manchester has shown that impalpable small lesions are detected in the 35-49 year age group and that similar detection rates to the NHSBSP are attainable by targeted screening [4]. There are also the first signs of a mortality benefit, although this may not be the case for BRCA1 carriers who appear to have a worse prognosis [5,6]. Mammography may eventually be replaced by other more sensitive techniques such as MRI in BRCA1/2 mutation carriers [7], but the costs and scarcity of scanners may make MRI unviable outside a very high risk group. Currently MRI screening is recommended in the UK for BRCA1/2 and TP53 mutation carriers aged 30-49 as well as for individuals without mutations who are at very high risk (www.nice.org.uk). The very small dose of radiation involved with mammography has only a small theoretical risk of inducing a breast cancer [8]. Even cumulatively, this is unlikely to cause more than an extra breast cancer in 1 in every 10,000 women. This is not really comparable to a 40% lifetime risk. However, known carriers of TP53 mutations should probably not be screened with mammography. ATM gene mutation carriers are the currently the subject of a commissioned review. BRCA2 interacts with a protein involved in DNA repair and as such carriers may be more susceptible to radiation induced damage and we may also have to reassess risks in this group. Women screened for breast cancer may undergo fine

needle aspiration or open biopsy for screen detected lumps, which are entirely benign. This will be associated with at least a small degree of psychological and physical morbidity, but in experienced hands the risks of unnecessary biopsy are small [9].

There is concern that despite original publication of the NICE guidance in June 2004 [10] and update in 2006 for MRI guidance, implementation has been patchy across the England (Scotland is covered by SIGN guidance). In particular there are very few areas where MRI is being funded and even moderate risk mammography screening aged 40 to 49 remains a problem in many areas. This has been raised with Professor Mike Richards and Dr Julietta Patnick, Director of the National Screening Programme. We are hopeful that the situation will be resolved soon.

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SPOTLIGHT ON....GUY'S

Multidisciplinary Clinic for BRCA Carriers: The Surgeon's Perspective

Hisham Hamed

Risk Reducing Mastectomy (RRM), commonly known as prophylactic mastectomy, has been established as one of the most effective strategies in reducing the risk of breast cancer in women who are at significantly increased life time risk of breast cancer associated with BRCA mutations.

Women who are carriers of BRCA mutations are understandably very worried but equally highly motivated and eager to learn about how they can minimise their risks and address what is probably one of the most crucial decisions in their lives. Studies have shown that risk reducing surgery succeeds in alleviating women's anxiety. However, postoperative satisfaction and good quality of life is dependent on the amount of information women receive and the opportunity they have to take part in the decision-making.

Women who embark on RRM almost invariably expect to have immediate reconstruction and therefore the consultation should address available options in full details. The surgeon therefore should ensure that information is clearly understood. It is often extremely helpful to provide photographs, written information and other material such as the implants intended to be used. It is equally crucial that these women are given sufficient time to digest all the given information and are encouraged to return for further consultation if necessary.

Generally, the consultation should cover aspects of the mastectomy techniques. The option of nipple preservation (subcutaneous mastectomy) versus skin sparing mastectomy with sacrificing the

NEWS UPDATE

Feedback from the Cancer Genetics Group Spring Meeting – UK Cancer Genetics Group and Dutch Cancer Society, 22 – 24 May 2007, Manchester Conference Centre

Carole Brewer

nipple is often raised by women. Although there is no sufficient evidence of additional risk of developing breast cancer with subcutaneous mastectomy, there is no conclusive evidence of its safety.

There are several reconstruction options available to these women, ranging from insertion of silicone implant underneath the chest wall muscle to using autologous tissue either from the abdominal wall, TRAM (Transverse Rectus Abdominis Myocutaneous) or DIEP (Deep Inferior Epigastric Perforator) flaps or the area of gluteus maximus, S-Gap (Superior Gluteal Artery Perforator), .

Several factors are fundamental to the selection of reconstruction technique, not least, the patient's choice. Also consideration should be given to breast size that is often expressed in brassiere size, width of chest wall, abdominal panniculus, presence of abdominal scars and size of the buttocks and tissue laxity. The patient's general health and the likely post operative recovery are also important issues to address. It is particularly important to note any history of smoking, obesity, diabetes, use of steroids or anticoagulants as well as previous radiotherapy to breast or chest wall. Operative complications and expected cosmetic outcome should be emphasised in order to avoid unrealistic expectations and major disappointments.

This was the second joint venture between the UK and Dutch Cancer Groups following on the success of the meeting in Amsterdam in 2004.

John Burn gave the first talk, "Cancer Genetics: Where are we now? Where are we going?' This covered exactly 'what it says on the tin', with some interesting speculation and an entertaining illustration of the complexities of testing in polygenic disorders. All this and more was presented in John's usual inimitable style. As a bonus to all those who rose before dawn to be there for the start of the meeting, we were treated to photos of the wee'est member of the Burn Family – much to the admiration of all (only John could get away with this of course).

But seriously…after such an inspiring start which included ideas on how inherited cancer might be manipulated if only we understood it better, it was good to hear about the current management of the cancers seen daily in our clinics. It can only be an advantage to know what actually happens to our patients in a therapeutic setting. All three talks, on colorectal, breast and ovarian were well-judged in relation to the audience.

Before we go any further it has to be said that it was a very full programme,- altogether excellent, but very full. To me the next second session of the day was a paradigm of the rest of the meeting. This was an impossible-not-to-find-something-of-interest-whether-you–are-a-clinician-counsellor-researcher-or-psychologist, a real Licorice Allsorts sort of session, with something for everyone. How could this be? Well, first of all a bit of psychology; Nina Hallowell from Edinburgh talked about the perceptions amongst healthcare professionals of clinical practice versus research in cancer genetics. The distinction is clear cut for some, but less so for others. It also appears to be ever-changing - quite a challenge for governance! Then for something completely different…Louis Vitone, on behalf of the Europac team revealed that exocrine failure is an important risk factor for pancreatic cancer in hereditary pancreatitis (HP); in 150 families with HP cancer risk was not influenced by factors such as PRSS1 mutation, but diabetes increased the risk three-fold - important for risk stratification and targeting surveillance. Next up was Graeme Suthers and the genetic management of retinoblastoma (a tall order in only 10 minutes!). This was an eloquent update on what is a rather complex problem. Mosaicism is the key (either in the patient, or the parent); if you remember that it's easy! So remember to test both tumour and lymphocyte DNA. Finally in this session, Ros Eeles updated us on the IMPACT study of targeted prostate cancer in male BRCA carriers. Numbers are still small (57 at time of meeting), but expected to rise as new centres join up. So far, one prostate cancer has been diagnosed at only 48 years - an extreme but typical example of the young onset in BRCA carriers, who also appear to have a much poorer outlook - all the more reason to optimise a screening protocol.

There was good representation from the home team. In particular I enjoyed hearing Ian Frayling tackling the tricky issue of 'MSI, IHC or both?' and Jill Birch on Li Fraumeni syndrome. It was fascinating to get the perspective from both sides of the North Sea/English Channel as well as contributions from Europe, USA, Canada and Australia. It is always a pleasure to hear Hans Vasen

speak about cancer risk and surveillance in Lynch syndrome. Steven Narod presented the mature results of the Toronto MRI study in high risk women. There was a thought-provoking symposium on breast cancer treatment and prevention chaired by Jan Klijn, with Steven Narod and Tony Howell speaking. It is clear that the endocrine manipulation in breast cancer is not at all straight forward. It would be nice to expand on this, but there simple isn't space on this page! This particular session was finished off by an engaging talk by Michelle Harvey on the impact of lifestyle factors, especially diet, on breast cancer risk, including some fascinating data about weight gain. This is clearly an area we need to understand better. The idea that 'you can't do anything about your genes, but you can do something about you diet etc,' comes to mind.

Writing this now some time later (okay, quite some time later…) other highlights included a powerful session on Li Frameni syndrome, which, apart from anything else, reminded us what a truly devastating disorder it is. Mosaicism came up several times - not just in retinoblastoma, but also FAP where it is probably under-recognised in very good talk given by Frederik Hes from Leiden.

Overall, the programme was very well rounded and covered the common cancers from all perspectives, not just genetic but also providing insight into current treatment options and psychosocial aspects. I should mention that the meeting was organised back to back with the 10th International Meeting on psychosocial aspects of genetic testing and talks on psychosocial issues were also interspersed with the main programme over the first two days.

I have to confess that my attention towards the end of the meeting faded, having been struck down by a feverish cough which happily turned out not to be Legionella as I first feared, but sadly did mean that I had to miss the conference dinner at the Whitworth Art Gallery. So for those who have only stuck with this account in the hope of some snippets of juicy gossip, I will have to disappoint you. One can only guess at the fun and frolics that took place that night – hinted at perhaps by the odd rumour and number of empty seats in the auditorium the next morning. But perhaps some of those absentees had pseudo-Legionella too…

Breakthrough Breast Cancer Campaign for Family History Screening Services

Caitlin Ferguson

In the UK, around 5% of breast cancers are diagnosed in women who have a strong family history of the disease due to inherited faults in genes (such as BRCA1 and BRCA2) that lead to a high risk of developing breast cancer. Women who have inherited mutations in their BRCA genes have up to an 85% risk of developing breast cancer in their lifetime. A further 10-15% of breast cancer cases occur in women with a moderate family history of breast cancer. This means that around 8,000 cases of breast cancer a year will be diagnosed in women with a family history of the disease.

In 2004 the National Institute for Health and Clinical Excellence (NICE) published its Familial Breast Cancer clinical guidelines which recommended that women at a high risk of developing breast cancer due to their family history should be offered annual mammographic screening before the age of 50. A 2006 update to these guidelines additionally recommended the use of Magnetic Resonance Imaging (MRI) to screen some groups of high risk women. The age at which eligible women begin breast screening and the type of screening they are entitled to is dependent on their risk of developing breast cancer as indicated by their family history or an identified mutation in a breast cancer gene.

However, anecdotal evidence indicates that in many areas eligible women with a family history of breast cancer are not being offered breast screening according to the NICE guidelines. Barriers for eligible women wanting to access mammographic and MRI screening are likely to be occurring at a local level and may be due to a lack of MRI equipment and trained staff as well as competing claims for limited resources.

The Launch of the Cancer Genetics Group Website at www.ukcgg.org

Ian Ellis

At last the new CGG website has gone live. The web address is www.ukcgg.org. We are very grateful for the help of Rajesh Summan for helping to construct the website and to the CGG Website Steering Group - Carole Brewer, Hisham Ahmed, Ian Frayling, Paul Pharaoh.

The CGG website is laid out in a similar format to of the other BSHG constituent societies to help navigation. There is not much on the website as yet despite invitations to CGG members to submit material. Now that it is live, please do submit material. There is already a review of OncoVue the genetic test being offered by Opaldia. Probably the main use of our website will be for advising members of forthcoming meetings, submitting abstracts and for registration for CGG meetings.

There is also the facility for notifying members and visitors to the website of upcoming events, jobs, articles and news. There is also a research page that contains details of the POET (Prevention of Endometrial Tumours) study and you can also arrange for submission of your study to the website to keep collaborators and recruiters informed.

The website is there, please look at it and use it and do submit material. We need to discuss how we would like the website to evolve and particularly if we have someone who is IT and web page knowledgeable to act in the role of a web master or coordinator with Rajesh for submitting material and updating the website. In the meantime please send any materials to go on the website to me. Remember again, your website is at www.ukcgg.org.

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BRCA Carriers' Contact Group

Audrey Ardern-Jones and Liz Bancroft

A new 'Contact' group has recently been initiated by nurses from the Royal Marsden Cancer Genetics Unit. This group is for women in their twenties and thirties who are BRCA carriers and who are unaffected. Support Groups have been up and running for the past three years. The support groups are for BRCA carriers, both affected and unaffected. We had noticed that the younger unaffected age group were not attending the support groups and therefore decided to arrange the Contact group. We changed the name as well to make it different. The first session went very well with positive feedback; many of the young women were very happy to meet others as some felt very isolated. This group will take place every six months whilst the Support Group continuing every three months.

Breakthrough Breast Cancer, the UK's leading charity committed to fighting breast cancer through research, campaigning and education, is working together with its Genetics Reference Group (GRG) to ensure that these important breast screening guidelines are fully implemented. The GRG is a group of over 100 women with a family history of breast cancer and is part of the Breakthrough Campaigns & Advocacy Network (Breakthrough CAN), a community of individuals and organisations who campaign for improvements in breast cancer services, treatments and research.

Breakthrough is encouraging the Government to incorporate family history breast screening services into the national NHS Breast Screening Programme in order to ensure that resources are available for the service and to improve provision of screening for eligible women. On a local level, we hope to work with health care professionals and GRG members across the country to determine the availability of family history breast screening services in their locality, identify areas of best practice and campaign for improvements in regions where services are absent.

How can you help?
If you would like to help Breakthrough improve the provision of screening for women with a family history of breast cancer, please contact Dr Caitlin Ferguson, Senior Genetics Policy Officer, on 020 7025 2469 or caitlinf@breakthrough.org.uk. We would be particularly interested in any information you might have on the availability of family history breast screening services in your area.

If your work involves women with a family history of breast cancer, please encourage your patients to get involved with this campaign by joining Breakthrough's GRG at www.breakthrough.org.uk/genetics.

Research update

The Rocc (research or clinical care) study

Anneke Lucassen

Many of you have helped enormously with this study by giving us your views on the distinction between clinical practice and research in the field of cancer genetics. All the interviews have now been completed and the results are being evaluated. We will be disseminating our findings at the first Genethics Club meeting of 2008: 30th January 2008, to be held at Regents Park College, which is open to all BSHG membership. Please contact PIs of the study: Nina Halowell, Mike Parker or Anneke Lucassen for further details.

Call for families with more than one first-degree relative affected by myelodysplasia or acute myeloid leukaemia

Carolyn Owen

Familial occurrence of myelodysplasia (MDS) or acute myeloid leukaemia (AML) is rare but has provided a useful resource for investigation of predisposing mutations in these diseases. Germline mutations have been reported in RUNX1 or in CEBPA in several familial MDS/AML pedigrees; but the cause remains obscure in many other families. Unfortunately, most familial AML pedigrees are small and living-affected family members are limited. Genomewide linkage searches aimed at identifying disease-causing loci are difficult to perform with such small sample numbers.

Successful studies in other familial cancers have depended on collaborative efforts of many centres in order to obtain sufficient familial cases for examination. We are currently contacting authors of case reports of familial MDS and /or AML and would be interested in establishing collaborations with any groups that can provide samples of patients with familial MDS/AML. If you know of any families with more than one first-degree relative affected by MDS or AML that might be interested in participating in studies of the molecular cause of Familial MDS/AML, we would be most interested in discussing this with you. Any questions or correspondence can be directed to Carolyn Owen, Clinical Research Fellow Cancer Research UK Medical Oncology Unit, Barts and the London School of Medicine & Dentistry email: carolyn.owen@cancer.org.uk

The PARP Trial

Andrew Tutt

The PARP clinical trial evaluates a new treatment option for patients with advanced BRCA1 or BRCA2 associated breast cancer that has failed standard treatment. The study evaluates a new poly (ADP-ribose) polymerase (PARP) inhibitor. This inhibitor utilizes a special weakness of tumour cells that lack BRCA1/2 activity.

In this trial, which is designed to assess the efficacy and safety of KU-0059436, an oral PARP inhibitor is given twice daily. The study is a phase II study sponsored by KuDos Pharmaceuticals. It is a single arm, open label study where all participants will receive active drug. About 18 study centres across Europe, the US and Australia are currently participating.

Referred patients who are subsequently enrolled into this study will receive comprehensive informed consent counselling, individualized attention and excellent medical care, with the utmost privacy and security of their information. They may continue to receive routine standard and customary care from their local centre throughout the study and local colleagues will be kept informed of the patient's progress during the trial. Participants will be withdrawn from the study at any time, if it is in their best interests.

To discuss referral into the trial or for additional information, please contact Dr Andrew Tutt (Consultant Clinical Oncologist, Guy's Hospital) at 0207 188 4237, Andrew.tutt@gstt.nhs.uk

Key inclusion criteria

- Female, aged 18 years or older.

- Histologically or cytologically confirmed breast cancer that is locally advanced (not amenable to curative surgery and/or radiation) or has metastasised (Stage IIIB/IIIC or IV).

- BRCA1/2 associated cancer.

- One or more measurable lesions, not irradiated within 12 weeks of the first administration of IMP.

- ECOG performance status of 0 – 2/Karnofsky 100-50.

- Estimated life expectancy of at least 16 weeks.

- Failed at least one prior chemotherapy and/or endocrine therapy for advanced disease. No curative standard therapy exists.

- Adequate bone marrow, hepatic and renal function

Key exclusion criteria

- Less than 28 days from active therapy or high dose radiotherapy.

- Patients with brain metastases.

- Persistent grade 2 or greater toxicities (excluding alopecia) from any cause.

- Patients who are unable to swallow orally administered medication.

- Patients who are immunocompromised, e.g. patients known to be serologically positive for human immunodeficiency virus (HIV).

The list of in- and exclusion criteria is not complete. It will be the responsibility of the investigator to decide about the eligibility of study subject.

CGG News Editor

Deadline for contributions for next issue is Friday 11 January 2008

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