Abstracts

Cancer Genetics Group Spring Meeting
22 & 23 May, 2006
Birmingham, U.K.

Introduction

The Cancer Genetics Group (CGG) is a British multidisciplinary organisation. The purpose of the CGG is to improve the quality of care of patients and their families with any condition resulting in hereditary tumours. Eligible members are those with an interest in hereditary predisposition to cancer including clinicians, counsellors and scientists. Membership is affiliated through the British Society of Human Genetics. At least one scientific meeting of the CGG is held every year. Normally there is a two-day spring meeting at a host city in the UK and a single day winter meeting in London. More information on the CGG can be found on the CGG web site www.srl.cam.ac.uk/cggwebsite/cgg.htm

[1]

Cellular Response to Irradiation in Carriers of BRCA1 and BRCA2 Mutations


It is not known whether individuals who are heterozygous for germline BRCA1 and BRCA2 mutations have an altered cellular response to irradiation. We have investigated 53 BRCA1 and BRCA2 mutation carriers who have never had a malignancy and age-matched unaffected controls.

We found that peripheral blood lymphocytes from BRCA1 and BRCA2 mutation carriers have normal cell cycle kinetics and apoptotic response to irradiation compared with age-matched unaffected controls. However, we detected an increased number of chromosome breaks post irradiation using the G2 assay (P=0.002) and the S phase enrichment assay (P=0.011) in BRCA1 mutation carriers compared with age-matched controls. BRCA2 mutation carriers also had an increased number of chromosome breaks per cell compared to their matched controls using the S phase enrichment assay (P=0.045).

In an attempt to identify a cause for this altered cellular response to irradiation, the gene expression profiles of peripheral blood lymphocytes from five BRCA1, five BRCA2 and five age-matched controls pre and post irradiation were measured using human U133 Plus 2.0 arrays. BRCA1 expression in BRCA1 mutation carriers compared with the age-matched controls was reduced by 43% compared with controls (p=0.038) post 2Gy and by 41% post mock treatment (p=0.032). There was a non-significant reduction in BRCA2 protein expression post irradiation in BRCA2 mutation carriers of 34% compared with controls (p=0.24). We detected a number of consistently altered genes in response to irradiation in mutation carriers with BRCA1 or BRCA2 haploinsufficiency and discuss the functional implications of these.

[2]

Flow Chart for Cancer Genetics Studies at St George’s Hospital


Clinical trials are legion and often overlap or have competing interests. We at St George’s Hospital have devised a flow chart for Cancer Genetics to ensure that patients have the greatest opportunity to be involved in appropriate research studies. This has helped clarify entry and exclusion criteria for various studies and improved overall recruitment.

The flowcharts (Figures 1-4) include the following studies: EMBRACE, IMPACT, POSH, PROSE, UKFOCSS, POETS (Mirena coil study), CARBOPLATIN BRCA TRIAL, IBISII, FABCC, BRCA3, SIB PAIR, EUROPAC, FH01 and CORGI. This can be easily tailored for other centres with a different selection of studies. Copies can be collected from Dr Julian Barwell.
Breast cancer (BRCA mutation carrier) trials

**FEMALE**

BRCA mutation carrier

Unclassified variant

Female negative predictive test

Guy’s LOH Summer 2006

Affected with breast cancer (at any age)

Unaffected with breast cancer

Unaffected with breast cancer

Affected with breast cancer

Prophylactic breast/ovarian surgery (PM/PO)

UKFOCSS PROSE-controls

EMBRACE

**POSH**

Age <50 and treated Since January 2001

Age >50

Relapsed

Yes PM/PO

No PM/PO

CARBOPLATIN

Impact

5 years

Prostate cancer 5 year study

Unaffected

Not between 40-69

40-69

BRCA mutation carrier

MALE

**CAPP2 + 2 CAPP3 (2008)**

POET (Mirena coil study)

Female

Male

No previous malignancy

HNPCC MUTATION CARRIERS

Unclassified variant

Prostate cancer 5 year study

Unaffected

Not between 40-69

40-69

BRCA mutation carrier

Male negative predictive test

Adapted for St George’s Hospital Clinical Genetics

Last updated:
July 2006
Julian Barwell Ed 5635
Albert Njindu Anand Saggar
### Study where mutation identified

<table>
<thead>
<tr>
<th>Study</th>
<th>Contact</th>
</tr>
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</table>
| **PROSE** Prevention and Observation of Surgical Endpoints An estimation of breast and ovarian cancer risk reduction after the use of risk-reduction surgery and to evaluate psychosocial endpoints in women who carry BRCA1 and BRCA2 mutations. | Elizabeth Bancroft  
0207 808 2136  
elizabeth.bancroft@rnh.nhs.uk  
The Royal Marsden Hospital |
| **POSH** Prospective Outcomes in Sporadic Vs Hereditary breast cancer. A prospective, case-controlled, observational study of treatment choices and outcomes in young women with breast cancer | NCRN Trevor Batt 0208 661 3049  
South West London Cancer Research Network  
Sue Gerty 02380795171 Southampton  
Closure Date: June 2006 (Jan 2006 for new centres) |
| **CARBOPLATIN/DOCETAXEL** A chemotherapy trial in relapsed breast cancer patients. | Dr Andrew Tutt  
andrew.tutt@gstt.nhs.uk  
020 7188 4237 Guy’s Hospital, London |
| **EMBRACE** Epidemiological Study of Familial Breast Cancer in BRCA1 and BRCA2 mutation carriers | Dr Susan Peock 01223 740616  
Strangeways Research laboratories, Cambridge  
Closing date: 30 September 2009 |
| **IMPACT** Identification of Men with a genetic predisposition to Prostate Cancer | Elizabeth Bancroft  
0207 808 2136 |
| **POET** Prevention Of Endometrial Tumours study The use of a progesterone releasing intra-uterine device (Mirena coil) in women with HNPCC at high risk of developing endometrial tumours. | Professor Shirley Hodgson  
020 8725 5279  
shodgson@sgul.ac.uk  
St George’s Hospital, London |
| **CAPP- Colorectal Adenomas/carcinoma Prevention Programme for proven HNPCC mutation carriers CAPP2 + F/U of UK CAPP2 patients (recruitment now completed) CAPP3-Starts 2008** | Gail Barker 0791 233 1414  
www.capp2.com  
Institute of Human Genetics, Central Parkway  
Newcastle Upon Tyne |
| **UKFOCSS** UK Familial Ovarian Cancer Screening Study Evaluation of ovarian screening in primary relatives of affected member of high risk families. | Professor Ian Jacobs  
0845 155 5000 ext 9165  
ian.jacobs@uelh.nhs.uk  
University College Hospital, London |

### Lay and Professional Understanding of Cancer Genetics Activities in the UK

Cooke S., Crawford G., Lucassen A., Parker M., Hallowell N.

In the UK, DNA testing for hereditary cancers and high-risk cancer surveillance takes place either as part of research protocols (and thus requires ethical approval) or is offered as an NHS clinical service. The route chosen may depend on arbitrary factors. There is a need to determine the impact that current research governance arrangements have on research and clinical practice in cancer genetics. This multidisciplinary project investigates healthcare professionals’, patients’ and regulators’ understanding of cancer genetics activities within the UK. It looks at how these groups conceive of the research-clinical practice distinction, and aims to identify any perceived ambiguities and practical and/or ethical problems that are generated for the different actors. Semi-structured interviews (n=100) are currently being carried out with 3 groups: healthcare professionals who are involved in cancer genetics research and/or provide a clinical cancer genetics service/refer patients to such a service; patients involved in cancer genetics research (DNA and/or clinical studies) and regulators who play a role in the regulation of clinical research or clinical practice.
Cancer genetics trials: Untested or no familial mutation identified in affected individuals

- 40-70
  Post menopausal
  No HRT
  
  Atypical hyperplasia
  Or LCIS/DCIS
  FH BREAST CANCER

  IBISII
  FABCC
  BRCA3
  SIB PAIR STUDY

- FH01: Mammography trial evaluation of mammographic surveillance in women 40-50 with a family history
  
  1 FDR BC<40
  Bilateral FDR BC<50
  BC+ OC (1<60) (F/SDR)
  2 BC<60 (F/SDR)
  3 BC<60 (F/SDR)
  1 male BC FDR/2 SDR male BC
  2 SDR BC<50 or 1<50 + OC(pat)

  Age 40-44
  No breast cancer/DCIS
  No prophylactic mastectomy
  Not pregnant
  No negative predictive BRCA result

- UKFOCSS if >3S for FDR
  Modify with paternal transmission
  
  1 other breast cancer<50 in FDR
  Or 1 other ovarian cancer in FDR

  2 other breast cancers< 60 in FDR

  3 other CRC(<50) All FDR

- Cori
  1 other CRC
  Age unspecified

  1 colorectal adenoma<45 or dysplastic/>1 cm/villous polyps

- Ovarian cancer
  At any age

  3 individuals with adenomatous polyps at any age

- Bowel tumour
  CRC=colorectal carcinoma

1 colorectal adenoma<45 or dysplastic/>1 cm/villous polyps

PANCREATIC CANCER at any age

- Controls from unaffected family members

1 other adenocarcinoma of pancreas at any age or
1 other breast/ovarian/melanoma/gastric cancer
Suggestive of cancer susceptibility syndrome
Degree of relationship unspecified

1 diagnosed <60
Sib pair 1<65
3 any age

PROSTATE CANCER
Penetrance Estimates for BRCA1 and BRCA2 Based on Genetic Testing in the Service Setting

Evans D.G., Shenton A., Woodward E., Laloo F., Maher E.R.

1Academic Unit of Medical Genetics and Regional Genetics Service, St Mary’s Hospital Manchester M13 0JH, UK, 2Division Section of Medical and Molecular Genetics, University of Birmingham School of Medicine, and West Midlands Regional Genetics Service, Birmingham, UK.

Abstracts

Penetrance Estimates for BRCA1 and BRCA2 Based on Genetic Testing in the Service Setting

Evans D.G.1, Shenton A.1, Woodward E.2, Lalloo F.1, Maher E.R.2

1Academic Unit of Medical Genetics and Regional Genetics Service, St Mary’s Hospital Manchester M13 0JH, UK; 2Division Section of Medical and Molecular Genetics, University of Birmingham School of Medicine, and West Midlands Regional Genetics Service, Birmingham, UK.

Background: The identification of a BRCA1 or BRCA2 mutation in a familial breast cancer kindred allows genetic testing of at-risk relatives. However, considerable controversy exists regarding the cancer risks in women who test positive for the family mutation.

Methods: We reviewed 385 unrelated families (223 with BRCA1 and 162 with BRCA2 mutations) ascertained through two regional cancer genetics services. We estimated the penetrance for both breast and ovarian cancer for female mutation carriers (904 proven mutation carriers – 1442 females in total.

BBaacckkggrroouunndd::The identification of a BRCA1 or BRCA2 mutation in a familial breast cancer kindred allows genetic testing of at-risk relatives. However, considerable controversy exists regarding the cancer risks in women who test positive for the family mutation.

MMeetthhooddss::We reviewed 385 unrelated families (223 with BRCA1 and 162 with BRCA2 mutations) ascertained through two regional cancer genetics services. We estimated the penetrance for both breast and ovarian cancer for female mutation carriers (904 proven mutation carriers – 1442 females in total.

Conclusions:: Our data suggest that women with a positive family mutation may have a higher than previously reported risk of breast cancer. The penetrance for ovarian cancer was lower than previously reported. The results of this study will help to inform genetic counseling in the future.

**EUROPA**

The **EUROPA** registry of hereditary pancreatic diseases: Gene identification, risk factors and screening protocol consensus

EUROPA Study Co-ordinator 0151 706 4168 Royal Liverpool University Hospital

**CORG**

C**O**lo**R**ectal Tumour Gene Identification Study.

The collection of families with multiple cases of colorectal neoplasia to identify novel predisposition genes through linkage and association using familial cases.

Professor Ian Tomlinson
ian.tomlinson@cancer.org.uk
020 7242 0200 Ext 2884
CRUK Lincoln Inn Fields

**SIB PAIR STUDY**

Breast cancer susceptibility gene identification in female sib-pairs where no cases or ovarian cancer are present in family.

Caroline Langman
caroline.langman@genetics.kcl.ac.uk
020 7188 1364 Guy’s Hospital, London

**UKFOCSS**

UK Familial Ovarian Cancer Screening Study.

Evaluation of ovarian screening in primary relatives of affected member of high risk families.

Professor Ian Jacobs
0845 155 5000 ext 9165
ian.jacobs@udh.nhs.uk
University College Hospital, London

**UKGPC**

UK Genetic Prostate Cancer Study (Open to 2012).

To identify susceptibility genes and study gene-environment interactions.

Michelle Guy
michelle.guy@ic.ac.uk
020 8661 3507 Institute of Cancer Research
assumed to carry the mutation) and also assessed the effect of mutation position and birth cohort.

**Results:** Breast cancer penetrance to 70 and 80 years was 75% (95% CI 72.5-77.5%) and 85% (95% CI 82.4-87.6%) respectively for BRCA1 and 80% (95% CI 77.6-82.4%) and 90% (95% CI 87.4-92.6%) for BRCA2. Ovarian cancer risk to 70 and 80 years was 60% (95% CI 65-71%) and 65% (95% CI 75-84%) for BRCA1 and 30% (95% CI 25.5-34.5%) and 37% (95% CI 31.5-42.5%) for BRCA2. These risks were only marginally reduced by excluding the index case from each family. We found evidence of a strong cohort effect with women born after 1960 having a cumulative risk of 40% for breast cancer by 40 years of age compared to <10% in women born before 1930.

**Conclusion:** In high-risk families, women who test positive for the familial BRCA1/BRCA2 mutation are likely to have cumulative breast cancer risks in keeping with the original estimates obtained from such families. This is particularly true for women born after 1960.

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**Abstracts**

**Fig. 1.** Breast cancer cumulative incidence by gene (BRCA1 or BRCA2)

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**[5]**

**Study Comparing Two Types of Screening Provision for People with von Hippel-Lindau Disease**

Fraser L., Watts S., Cargill A., Sutton S., Hodgson S.

1Department of Medical & Molecular Genetics, Guy’s Hospital, London, UK; 2Department of Clinical Genetics, Guy’s Hospital, London, UK; 3Cancer Research UK, Medical Statistics Group, Oxford, UK; 4Department of Public Health and Primary Care, University of Cambridge, UK

**Purpose:** Patients diagnosed with von Hippel-Lindau (VHL) disease require life-long surveillance for clinical manifestations of this multi-system disease. This descriptive study reports on two types of screening provision for VHL patients in the UK: single appointment One Stop clinics and multiple appointment Ad Hoc clinics.

**Methods:** One hundred and seventeen VHL patients from eight regional genetics centres were approached to take part. Seventy-two (61.5%) returned a completed study questionnaire. Fifty-four (75%) were screened at One Stop clinics. Comprehensiveness of surveillance, attendance rates, patient ratings of quality of care and levels of psychological morbidity were compared between the two types of service.

**Results:** One Stop clinics provided a more comprehensive screening service evidenced by double the number of site-specific examinations reported at Ad Hoc clinics. More patients at One Stop clinics attended regularly. There was no difference in patient ratings of quality of care between the two types of service. While levels of disease severity were similar between the two groups, a greater proportion of those screened at One Stop clinics were classified as anxious or depressed.

**Conclusion:** The study findings suggest that an optimum screening service for VHL patients is one based on One Stop clinics offering comprehensive surveillance and psychological support.

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**[6]**

**Gene-Related Cancer Spectrum in Families with Lynch Syndrome**

Geary J., Sasiemi P., Hodgson S.

1Department of Medical Genetics, St George’s University of London, Cranmer Terrace, London, SW17 0RE, UK; 2Cancer Research UK Department of Epidemiology, Mathematics & Statistics, Cancer Research UK Clinical Centre at Barts and The London, Wolfson Institute of Preventive Medicine, Charterhouse Square, London EC1N 6BA, UK

We obtained cancer details and age at diagnosis in mutation carriers and their 1st and 2nd degree relatives in a cohort of 132 families with Lynch Syndrome and known MMR mutations. The relative incidence of
cancers in Lynch Syndrome families was compared to that in the general population (RR), Table 1. Colorectal cancer was the most common site (64% and 55% in individuals from families with MLH1 or MSH2 mutations respectively). Mean age at diagnosis in MSH6 families was 57.7y compared to 42.7y in both MLH1 and MSH2 mutation families. Endometrial cancer was more common in MSH2 mutation carriers, RR 53 (25 for MLH1), and even more common in MSH6 families, median age at diagnosis 49y. Gastric cancer accounted for 5% of cancers in both MLH1 and MSH2 mutation families (RR 12), 53% diagnosed before 50y, 28% before 40y age, with clustering within MSH2 mutation families. Seven cases of small intestinal cancer occurred in MSH2 and MLH1 mutation families (RR 25). Six of seven families with renal cancer had multiple cases; the majority were in MSH2 mutation families, and familial clustering was significant. 19 of 27 ovarian cancers seen were in MSH2 mutation carriers, 70% diagnosed before 50y, where age known. There were 9 cases of sebaceous skin cancer, 3 in two MLH1 and 6 in four MSH2 mutation families. 14 of 22 cases of pancreatic cancers seen were known to be diagnosed below 60y, youngest at 29y. We found only a slightly increased RR (1.7) of breast cancer, and no familial clustering.

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Number of Cancers</th>
<th>Familial Relative Risk</th>
<th>Odds Ratio</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>MLH1</td>
<td>MSH2</td>
<td>MSH6</td>
</tr>
<tr>
<td>colorectal</td>
<td>301</td>
<td>262</td>
<td>14</td>
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<td>colorectal &lt;40 years</td>
<td>71</td>
<td>58</td>
<td>1</td>
</tr>
<tr>
<td>non-colorectal &lt;40</td>
<td>22</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>endometrial</td>
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<td>58</td>
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<td>gastric</td>
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<td>16</td>
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<td>30</td>
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<td>4</td>
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<tr>
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<td>2</td>
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<tr>
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<td>480</td>
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</table>
performed the list is unranked and anyone in a list of qualifying relationships can consent. It is not clear whether this also applies to the handling of a tissue block in order to extract DNA. The current common and statute law around access to records and samples will be discussed highlighting inconsistencies and suggesting consistent pragmatic approaches.

[8]

Identification of Men with a Genetic Predisposition to Prostate Cancer: Targeted Screening in BRCA1 and BRCA2 Mutation Carriers and Controls: the Impact Study

Mitra A.V.1, Bancroft E.K.2, Eeles R.A.1-2 on behalf of the Impact Steering Committee

1Institute of Cancer Research, London; 2Royal Marsden Hospital NHS Foundation Trust, London

**Key words:** prostate cancer, genetics, screening

This international collaboration aims to conduct the largest screening study of men with a known genetic predisposition to prostate cancer. Prostate cancer may be an indolent disease and screening the general population is controversial, with no established reduction in mortality. Mutations in BRCA genes may increase the relative risk of prostate cancer by up to 23-fold. We aim to establish whether male BRCA1 and 2 mutation carriers indeed have a higher prostate cancer incidence, are at risk of aggressive prostate cancer and if a targeted screening programme is feasible in this population. We will also undertake proteomic profiling of urine and serum in these men.

**Methods**

850 tested BRCA1/2 mutation carriers and 850 tested non-carriers will be recruited over 5 years in 39 centres. Annual serum PSA will be taken. If PSA is less than 3, the test will be repeated the following year. If the PSA is greater than 3, prostate biopsy will be offered. In the event of a cancer diagnosis, treatment will be according to local centre guidelines. Serum, plasma and urine samples will be taken to investigate proteomic profiles of these fluids in an attempt to identify more specific markers for prostate cancer.

100 men will be recruited by the end of 2006. Baseline PSAs, prevalence of undiagnosed prostate cancer, and the age of onset in male BRCA1 and 2 mutation carriers will be compared with the control group. Analysis of proteomic profiles will be established between BRCA1 and BRCA2 carriers, controls negative for these mutations and carriers and non-carriers with a diagnosis of prostate cancer.

**Results** (see graphs)

Recruitment started in November 2005; 24 men have been enrolled, 10 BRCA2 carriers, 8 BRCA1 carriers and 6 controls. One BRCA1 carrier has a PSA of 3.8 and is currently awaiting a biopsy. All other men have a PSA less than 3. The one man with a PSA greater than 3 also has a free total PSA of 11%. In total, 3 BRCA1 carriers have a free total PSA less than 15%; all other men have levels above this value.
Disseminating BRCA2 Test Results Identified in the Research Context to Relatives of Deceased Prostate Cancer Patients: a Qualitative Study of Relatives’ Experiences

Ormondroyd E.1, Moynihan C.1, Ardem-Jones A.2, Eeles R.1, Davolls S.1, Watson M.1

1Institute of Cancer Research, Sutton, UK; 2Royal Marsden Hospital, Sutton, UK

This study was established as an adjunct to an earlier, national study at the Royal Marsden Hospital and UK Institute of Cancer Research, which detected pathogenic BRCA2 mutations in a number of men diagnosed with prostate cancer before the age of 55 (Edwards et al., 2003). The men had died before the results of that study were available, and the Clinical Genetics team at the ICR/RMH attempted to contact the next-of-kin, offering an information/counselling session.

The current study is a psychosocial evaluation of the impact of being contacted about the existence of a genetic fault in a deceased relative. A snowball sampling strategy has been used to recruit relatives with whom the next-of-kin has shared this information. We are exploring:

• relatives’ reactions to learning about the genetic test results in their deceased relative,
• prior and current perceptions of risk, and risk management decisions,
• communication with other relatives,
• information and support needs,
• whether relatives perceive that they have experienced benefit or harm as a result.

Participants, some of who have and some have not elected to have genetic counselling, include partners, adult children and siblings of the deceased men. Semi-structured, in-depth interviews with twelve relatives are currently being analysed using a grounded theory approach. Findings will be discussed, including the importance of the role of the communicator, who may not be the closest relative. Effective communication and subsequent handling of the information, whether or not this includes engagement, is dependent on a positive relationship.

Grief in Cancer Genetics

Phil C.

East Anglian Medical Genetics Service, Department of Clinical Genetics, Box 134, Addenbrooke’s Hospital, Hills Road, Cambridge, CB2 2QO

A 63-year-old gentleman was seen for HNPCC predictive testing following the identification of an MSH2 mutation within the family. Mr A was at 50% risk of inheriting the familial MSH2 mutation. Mr A had suffered multiple close bereavements due to cancer in the family and he had also lost his wife to breast cancer at the age of 46 years. Mr A arrived at the appointment keen to have a predictive test to ‘prove he did not have the gene’. Mr A was from a large cancer family who were all now being seen for predictive testing. The family’s anxiety had been heightened by the sudden loss of a 46-year-old family member to pancreatic cancer. This case highlights the importance of seeing each family member as an individual in their own right and also that their experience of the cancers in the family will be unique to each of them. There may be further experiences of cancer outside of the blood family that the individual has experienced. The case also shows that cancer within families can heighten individuals’ awareness of their own mortality, but with genetic cancer conditions this also links into feelings of guilt with the realisation of their children’s mortality.

Women’s Experiences of a Favourable Test Result from Predictive BRCA1/BRCA2 Genetic Testing

Rose S.

London

This study explores the experiences of women who have undergone predictive BRCA genetic testing and received negative (favourable) results. Data were gathered using questionnaires and semi-structured interviews from nine women who had undergone testing during the period 2001-2003.

The study indicates that for many women, although their new cancer risk status is understood in terms of numerical value, the implications of this risk status are not fully realised. High cancer worry following testing indicated that a favourable result did not provide sufficient reassurance. Family experience was particularly influential in an individual’s risk perception.

Fear of breast cancer led to requests for inappropriately frequent breast surveillance but a lack of breast awareness amongst the women. Whilst genetic testing was motivated by a desire for control of the future, genetic testing was only one of many factors influencing the women’s attitudes to cancer.
The findings indicate a need for better education of women regarding breast awareness and the rationale behind surveillance practices, as well as further genetic counselling for women with high cancer worry irrespective of their test result. Further research is required to sample a greater number of women.

Summary of the ‘Interesting Cases’ Session

Lucassen A.

CGG secretary

The last few December CGG meetings have seen a dedicated slot for the discussion of interesting and/or difficult cases. This has proved highly popular with the membership and all of the 130 or so members present at the December 2005 meeting voted for its continuance and also inclusion at the summer CGG meetings. The 1.5-2 hour slot was designed to facilitate more informal discussion than possible in the scheduled talks and plenaries. We asked for any cases with ongoing management problems, clinical queries, ethical or legal dimensions or just learning points. This broad remit allows a variety of cases to be discussed, allowing members to benefit from the experience of a national group of experts and stimulating broader discussion than many find possible in busy local departmental meetings.

The cases range from unusual presentation of conditions or clusters of cancer, interpretation of laboratory results, to the age-old ethical dilemma of the management of families in which for example paternity has been misattributed. An example of the latter was presented at the meeting: A father, known to have a mutant high-risk cancer gene, had asked that both his two daughters be tested for the mutant gene, even though he knew one was not his biological daughter. He had asked for this deception so that she would not find out about her paternity through the lack of an offer of predictive testing. There was general consensus that entering into such deception was problematic and that further facilitation of family discussion might find other resolutions to the problem. Another presented case queried the duty to contact at-risk relatives who had not been informed of their high risk status by the tested relative: A father who had tested positive for a BRCA1 mutation had declined to tell his daughters, currently in their mid 30s, for fear of ‘upsetting’ them. The audience was very much divided in opinion about this matter and it was agreed that there is little in the way of professional guidance to help decide. The ‘great debate’ at this year’s British Society of Human Genetics (website) will debate this very issue, in the wake of several recent publications which demonstrated that relatives did not object to, and indeed in some situations expected, direct contact from the genetics service rather than an affected relative (Newsom et al., Suthers et al., 2005). One of the other issues discussed was the inadvertent testing of CHEK2 status in all people tested for BRCA2 (because of its inclusion as a positive control in the commercial ARMS kit). Many of the clinicians present were unaware of this, and the issue came to light when a GP referral specifically asked for CHEK2 status in the light of the Peto et al. Lancet paper (2005) which demonstrated a high risk of breast cancer (up to 60% lifetime risk) in first-degree relatives of individuals with bilateral breast cancer who were heterozygous for the del1100C allele. There was agreement that a much larger dataset was required before such lifetime risk figures could be used in genetic counselling, but also a concern about using this allele as a positive control if its risk is unclear.

The above gives a flavour of the session, in which several other interesting cases were discussed.