

3. Genetics Working Party

Membership

Professor Christopher Ludlam	Chairman
Professor John Pasi	Secretary
Dr Paula Bolton-Maggs	
Dr Peter Collins	
Dr Tony Cumming	
Dr Gerry Dolan	
Dr Alan Fryer	Joint Committee for Medical Genetics
Dr Peter Green	
Professor Frank Hill	
Dr Marian Hill	Chairman Laboratory Network
Dr David Perry	
Ms Christine Harrington	UK RCN Haemophilia Nurses Association
Dr Heather Skirton	Association of Genetic Nurses and Counsellors

Remit

The Genetics Working Party was re-established by UKHCDO in 2004 with the following remit to:-

- Support and receive reports from the Haemophilia Laboratory Genetic Network
- Promote the establishment of Haemophilia Genetic Counsellors
- Implement systems for establishing family files and genetic registers at Haemophilia Centres
- Make representation to seek funding support for developments
- Promote appropriate developments in genetic services
- Establish secure arrangements for samples at Guy's Hospital
- Monitor and consider effects of any proposed gene therapy trials for haemophilia in the UK

The main activities of the Working Party during the year are summarised below:

UKHCDO Report "Clinical Genetic Service for Haemophilia"

During the year the Working Party has developed a computer database for storing information on members of haemophilia families to enable a genetic register to be established and for family files to be compiled. The database is an enhancement to the UKHCDO HCIS. The pilot version is currently being trialled in several Haemophilia Centres.

UKHCDO needs to consider local arrangements for genetic databases. It is probably not appropriate for all Haemophilia Centres to have a computerised system. One option would be "regional" databases to which appropriate Haemophilia Centre staff could have access.

Haemophilia Laboratory Genetic Laboratory Network

The Network has continued to flourish. An external clinical audit of the Laboratory Genetic Service against UKHCDO standards has been completed and the report is being developed. A report of the Network's activities is appended (**Appendix 1**)

Gene Therapy for Haemophilia B

The Working Party had a presentation by Dr Nathwami and Professor Tuddenham of a proposed project on gene therapy for haemophilia B. Over several meetings the Working Party had a creative dialogue with the Principal Investigators and the Protocol and Information Sheet have been amended in the light of suggestions. The Working Party Chairman was invited to a specially convened meeting of the Gene Therapy Advisory Committee at which the proposal was discussed. The Protocol has now been approved by GTAC. Recently Professor Pasi has become one of the Principal Investigators. Recruitment to the study will commence later this year, or early next year.

Consent and Confidentiality in Genetic Practice

This Report compiled by the Joint Committee on Medical Genetics on behalf of the British Society for Clinical Genetics, Royal College of Pathologists and Royal College of Physicians has now been published (available at rpath.org). Guidance is offered on a wide range of issues related to confidentiality with respect to genetic investigations. The guidance given in the UKHCDO Report on Clinical Genetic Service for Haemophilia is consistent with the recommendations of the Consent and Confidentiality Report. Dr Tony Cumming compiled a synopsis of the Report and this is attached (**Appendix 2**).

Appendix 1

UKHCDO Haemophilia Genetic Laboratory Network 2006 Update

The UKHCDO Haemophilia Genetic Laboratory Network currently meets two times / year.

Previous meetings were held on:-

13th October 2005 / Dublin

3rd April 2006 / Edinburgh

Haemophilia Genetic Laboratory Network Directory

The directory is now posted on UKHCDO website, in addition to links to Best Practice Guidelines for genetic testing in haemophilia A and B, published in 2005

Audit of haemophilia network labs

A national audit of network laboratories was carried out during 2005, which proved to be a very valuable exercise. Laboratories were audited by teams consisting of Consultant Haematologists and Clinical Scientists. Information on laboratory profile, facilities, service provision, quality and links with clinical and laboratory services was obtained. An overview report of this audit is currently being prepared by representatives of UKHCDO Genetic Working Party and the Laboratory Network and a further audit of network laboratories has been proposed for 2007.

External QA

The network has made valuable contributions to the development of the UK-NEQAS EQA Scheme for haemophilia genetic testing, which now has full scheme status. All network laboratories are registered, undertaking two exercises per year, which cover a range of different approaches to mutation detection in haemophilia. Scoring includes clerical accuracy and interpretation in addition to correct test result. NIBSC and UK-NEQAS are currently establishing EBV immortalised cell lines for use as standards and EQA material.

Mutations and Inhibitor Risk

The network has reviewed the mutation-associated risk of inhibitor development in response to replacement blood factor therapy. Guidelines for recommendations on genetic reports have been established and accepted by the UKHCDO Inhibitor working party.

Nomenclature

Implications of adopting HGVS recommendations on mutation nomenclature were raised at the ISTH Scientific Standardisation Committee Meeting by network representatives. This has particular relevance for nucleotide and amino acid numbering systems in many haemostatic proteins. An international working party has been set up to discuss this and will include a member of the UKHCDO genetic laboratory network. The HGVS recommendations for mutation description has been adopted through-out the laboratory network

Haemophilia Genetic Data Storage

Implications of the proposed incorporation of genetic results within a local version of the national HCIS database have been discussed.

Retention and Storage / Human Tissue Act

Implications for long-term storage of samples from haemophilia patients have been discussed. Variability noted between different Trusts.

Haemophilia Alliance

The Network is represented on the “Haemophilia Alliance.”

Publications

A poster (Provision of a Molecular Genetics Network for Haemophilia care in the United Kingdom) was presented at the World Federation for Haemophilia Meeting in Vancouver. This had positive feedback, and was thought to represent a good model for haemophilia genetic services.

Future network activities:

Network-wide studies

The network laboratories were invited to consider several areas of research that could be carried out on a network-wide basis, including evaluating the implications of recently described Xq28 polymorphism on testing for F8 intron 22 inversion, evaluating the incidence of mutations leading to 1-stage/2-stage assay discrepancy, and developing a network-wide approach to the investigation of ‘difficult diagnostic cases’.

Training / Education

The network is working towards organising a number of workshops with particular relevance to haemophilia genetic testing. This includes approaches to mutation detection, investigation of ‘difficult and unusual cases’, Quality management, internal audit and preparation for CPA.

Appendix 2

Selected key points from consent and confidentiality in genetic practice: guidance on genetic testing and sharing genetic information

Report of the Joint Committee on Medical Genetics (RCPATH, RCP, BSHG)
April 2006

Aim of report

To clarify issues of consent and confidentiality in clinical genetic practice (but much of the report is relevant to other specialities), particularly with regard to the Data Protection Act 1998 and the Human Tissue Act 2004. The report also takes into account the Human Tissue (Scotland) Bill.

Consent – General Aspects

- Consent is the process to ensure that a patient understands the nature and purpose of giving a sample or undergoing an intervention. It is recognised that consent cannot always be totally comprehensive.
- Except in exceptional circumstances consent should be obtained prior to a clinical or laboratory or laboratory test (with genetic implications) being undertaken, and consent should have been obtained before medical genetic information is disclosed
- DH guidelines place the **onus for gaining consent with the clinician requesting the genetic information or the sample**. Gaining consent may be delegated to a suitably trained and qualified individual.
- In current practice, **the laboratory is not required to confirm and document consent**.

Genetic Laboratory Request Form

Recommended statement for inclusion on request forms:

In submitting this sample, the clinician confirms that consent has been obtained:

- a) for testing and possible storage
- b) for the use of this sample and the information generated with it to be shared with members of the donor's family and their health professionals (if appropriate)

Consent for continuing and further investigations

Original consent remains valid if a further investigation remains within the scope of the original consent (e.g. use of a new method where previous investigations had not detected a mutation).

Regarding consent for future testing of a sample, it is recommended that spoken and written information should be given, and confirmed by the use of a consent form.

Use of samples as controls, QA, audit, education and training

DH guidance – **Tissue samples may be used as controls and for QA, audit, education and training without specific consent**, provided NHS bodies have an active policy of informing patients of such use. Under the Human Tissue Act consent is not required for the use of samples from living patients for these purposes.

Recording consent

GMC guidance indicates that patients may give informed consent either orally or in writing. A record in the notes signed by the clinician is adequate for most purposes.

Consent to clinical photography and video recording

The purpose and possible future use must be explained before consent is sought – patients must be aware that they can refuse without their care being compromised, or that they can require that material can be used only if it can be anonymised (a specimen consent form is provide at Appendix 3).

Use of medical records of family members

Living family members: current practice is to obtain written consent from family members to access their medical information.

Deceased family members: access to medical records is at the discretion of the person holding them, unless the deceased refused permission. Some hospitals exercise this discretion by requiring consent from the spouse.

The Human Tissue Act has introduced the concept of consent from “any qualifying relative” with regard to release of bodily material posthumously for genetic analysis – it is suggested in the report that ideally a similar concept should be applied to medical records.

Disclosure of information (for accurate genetic diagnosis / family studies)

If consent has been obtained - medical information can be disclosed - this should be documented

If the basis of consent for releasing information is unclear - a clinical judgement should be made by the health professional and documented, for example:

- 1. An individual wanting to undertake prenatal diagnosis may not wish anyone to know of the pregnancy until the test results are available. The necessity to seek consent from another family member for release of the information will lead to a breach of confidence for the pregnant woman. The public interest in keeping the consultant's pregnancy confidential may be more important than the public interest in requiring consent to the disclosure of a test result from a family member – this concept is recognised legally.*
- 2. It is not necessary to release the technical description of a family mutation to a person who has been tested and shown not to have inherited the mutation. If a family member is shown to have the mutation, this is now their personal medical information and may be divulged to them.*

If consent to release information has been refused – the rule of confidentiality is not absolute – it may be justified to break confidence where the aversion of harm by the disclosure substantially outweighs the patient's claim to confidentiality (see GMC guidance).

Clinical use of results from research laboratories

Acceptable as long as the patient appreciates that the results have been generated in a non-clinical service setting. Best practice is to confirm results in a NHS laboratory if possible.

Genetic investigations on stored samples / archived pathological material

Living patients – consent should be sought

Newborn screening programme – e.g. dried blood spots – specific consent for testing without the screening programme must be sought

Post-mortem examination material – covered by the Human Tissue Act.

- **N.B. Removal, storage and use of human tissue containing cells falls within the provisions of the Human Tissue Act – extracted DNA does not (but professional guidelines apply).**

Human Tissue Act, consent and DNA analysis

The Human Tissue Act defines tissue as material from a human body that includes human cells, with the exception of gametes, embryos outside the body, hair and nail from a living person. Cell lines and **extracted nucleic acid are excluded**, as is any other material created outside the human body. Anonymised material from living people used in a research ethics committee approved project is also excluded.

- **N.B. It is lawful for cellular material from a living person to be stored and used without any consent for clinical audit, QA and performance assessment (including evaluation of in vitro diagnostic devices), public health monitoring and health-related education and training.**

Cellular material and DNA stored before the Human Tissue Act was in force

Cellular material – existing (pre Human Tissue Act) holdings are excluded from consent requirements of the Act where they are used for scheduled purposes, or medical diagnostics, or any purpose if the material is anonymised. Scheduled purposes include use for other family members.

DNA – excluded from legal requirements of the Act regarding consent.

Criminal offence of non-consensual analysis of DNA

Applies to the holding of cellular material with the intention of DNA analysis without consent. Does not apply to holding and use of extracted DNA – professional guidelines apply,

- **N.B. DNA analysis of bodily material undertaken as part of the medical diagnosis or treatment of the person whose body manufactured the DNA is excluded from the criminal offence.**

Tony Cumming
September 2006