What is genetic counselling?

Dr Anna Middleton
Principal Social Scientist
Genetic Counsellor
Cambridge, United Kingdom

Vice-Chair Association Genetic Nurses and Counsellors
Genetic counselling

- In the UK it is done in Regional Clinical Genetics services and Genomic Medicine Centres
- Specialist centres with outreach clinics
- Team of staff
**The team**

**See patients**
- Clinical Geneticists (doctors)
- Genetic Counsellors (nurse or MSc Genetic Counselling)
- [Research nurses, clinical nurse specialists, psychologists, social workers]

**Don’t see patients**
- Lab staff (arrays/sequencing/other)
- Research teams
Train to be a Genetic Counsellor

- MSc Genetic/genomic counselling or nursing route (i.e. not via a laboratory training)
- Registration (ensures competency and standards across profession)
- Recognised profession internationally

ASGC
Australasian Society of Genetic Counsellors

National Society of Genetic Counselors

GC-SA
Genetic Counsellors South Africa

GCRB
Genetic Counsellor Registration Board
Genetic counsellors see whole families

- Starts with the ‘proband’
- Information is shared in the family
- Relatives may then be seen
- Separate hospital notes
Reasons for genetic counselling

My mum had ovarian cancer at a young age, am I at risk?

I’ve had an abnormality picked up on pregnancy scan, the obstetrician thinks the baby has something genetic, please do testing

I’ve got a family history of Duchenne Muscular Dystrophy, am I at risk of having an affected child?
Aims of Genetic Counselling

Information

Support, empathy
• Provide information about a genetic condition
• Explain how the condition is inherited and the chance of it occurring
• Provide testing to clarify risk
• Understand the options available for management
Aims of Genetic Counselling

- Make decisions appropriate to personal and family situation
- Make the best possible adjustment to the disorder or risk
- Place factual genetic information into the family context
- Integrate lay knowledge with factual information
Genetic Counselling Consultation

- Find out the patient’s reason for referral
- Draw pedigree
- Assess genetic risk
- Explain inheritance patterns
When drawing the pedigree...

- Listen, pick up cues especially when taking family history
- Can be intrusive process
- Visual impact of pedigree
- Surprises, e.g. TOP, adoption, non-paternity
- Grief and loss
• Use pedigree to work out pattern of inheritance

• Work out risks of inheriting family condition (e.g. 50/50 chance of passing on or 1 in 4 chance of passing on)

• If passed on, work out risks of disease (‘penetrance’ and ‘expression’)

Working out who is at risk....
Mutations in genes don’t always equal disease

- Deletion in Duchenne Muscular Dystrophy = disease
- Deletion in breast and ovarian cancer gene = increased risk of disease
- Deletion in CCR5 gene = resistance to HIV
- Deletions can just be polymorphisms
Genetic Testing

- Discussion about practical and psychological implications of test result
- Diagnostic testing (adult, child, foetus, embryo)
- Predictive/presymptomatic testing
- Carrier testing
Genetic Screening

- Different to ‘genetic testing’
- Testing across a population group
- Testing of ‘healthy’ person to try to predict disease
- E.g newborn screening
- Prior probability of disease low
- Opportunistic screening with sequencing
• Considers the ‘patient’ and the extended family
• Often only seen once
• Focus is around the condition, not broader, e.g. not relationship counselling
• Advice not given but plenty of information
• May be referred on for therapeutic counselling
Given overview of genetic counselling

Role play a genetic counselling session

Explore how genomic technology has impacted on practice

End with some case studies
The work of a genetic counsellor in the UK

Christine Patch  PhD RN Registered Genetic Counsellor
Consultant Genetic Counsellor
Guys & St Thomas’ NHS Foundation Trust London
Reader
Florence Nightingale Faculty of Nursing and Midwifery KCL London
Guy’s 1988

- 2 clinical GCs (both nurses)
- 1 research nurse (DMD/BMD)
- 1 Consultant, 1 Clinical SpR, 2 Research SpRs
- Majority of GC work: prenatal RMA
- Few single gene tests possible (no CF, no HD)
- Co-counselling with geneticists
- Teaching of health professionals
- Bereavement work (much post-TOP)
3 Consultant genetic counsellors (all RN and registered GC)
3 senior GC (all reg GC 1 RN)
7 Genetic counsellors (6 reg GC 1 RN)
1 cardiac genetics nurse (employed by cardiology)
2 Cancer risk assessment nurse
2 Research nurses-recruitment to and managing of multicentre studies
12 Consultant, 2 Clinical SpR

GC work : 48% of appointments, predictive testing, multidisciplinary clinics, prenatal clinics, PGD.
60% of workload high risk cancer family history
Teaching of health professionals

No routine prenatal screening counselling, no post TOP beeavement, little co-counselling
Episode of care in a health setting

- Referral to Genetics team
- Patient seen by appropriate person(s) in team, according to diagnosis and issues
- May require collection of information prior to appointment
- Summary letters
- Follow up as required
What types of patients are seen by genetic counsellors

• Any who do not need a medical diagnosis
  – Predictive/presymptomatic testing-where gene mutation known
  – Cancer risk assessment and testing
  – Reproductive choice-prenatal/PGD
  – Explain genetic test results
New roles

• Multidisciplinary/specialist clinics e.g. rare diseases, eye genetics etc
  – Genetic counselling
  – Management

• Clinical Nurse Specialists
  – Eg Cardiac genetic nurses
Role of genetic services

- Diagnosis
- Risk assessment
- Options
- Decision-making
- Adjustment to status

What is patient’s agenda

knowledge of condition’s natural history
is testing available? for pregnancy? to check baby?
risks – to self and relatives (e.g. their grown up children)
management
support for family’s situation

Clinicians agenda

enable patient to make informed decision
no recommendations/decision making for patient
Give accurate information
appropriate information
layman’s language

support patient in their choices (non-judgemental)
alert other health carers to patients decision,
risks and management issues
What actually happens:

- Introduce self
- Summarise referral letter
- Check patients view of the situation and what they hope to gain from the session. *were they sent?*
- Explain what you, the counsellor, can offer
- Agree on a plan
What actually happens:

- **Listen**, pick up cues especially when taking family history
- **Confidentiality** – (as far as possible, discuss family communication and the need of proband to share information)
- Translate complex genetic information into lay language
- Pace the information delivery appropriately
- Common themes:
  - burden of the genetic condition/risk of it happening again
  - Guilt/blame
- Consider previous loss (loss through death, loss of self esteem, loss of control, previous abandonment and abuse) - can be reactivated through process
- Meet the **patients’ needs** as well as following own agenda
What actually happens:

• Summarise and repeat key points such as risk figures and inheritance
• Allow silences, tears, talk about deceased family members
• Provide contact number
• Write to summarise details
‘Non directive counselling’

• Term derived from Carl Rogers in his writing about client centered therapy
• Aims to enable person/couple make a decision that is right for them. Particularly in pregnancy or in predictive testing for known gene mutations
• This assumes there is a choice and no pressure from public health policies
Supervision

• Technical term for counselling engagement with others
• Group or individual supervision is recommended
• Helps to be aware of own issues so that you recognise why a consultation was challenging
Talking about our project SWAN UK: "Joining SWAN UK has made a massive difference to my life. I have some great friends and always know where to turn to if I need some help."

SWAN UK member 2012

Helping those with genetic conditions

Genetic Alliance UK is the national charity of over 150 patient organisations supporting all those affected by genetic conditions.

Our aim is to improve the lives of people affected by genetic conditions by ensuring that high quality services and information are available to all who need them.

Our Mission

Our mission has three main elements:

* Supporting:
We seek to raise awareness of genetic conditions and improve the quality of services and information available to patients and families.
• What about your services?
Genetic counselling is a communication process that deals with the occurrence, or risk of occurrence, of a (possibly) genetic disorder in the family. The process involves an attempt by appropriately trained person(s) to help the individual or the family to

(1) understand the medical facts of the disorder;

(2) appreciate how heredity contributes to the disorder and the risk of recurrence in specified relatives;

(3) understand the options for dealing with the risk of recurrence;

(4) use this genetic information in a personally meaningful way that promotes health, minimizes psychological distress and increases personal control;

(5) choose the course of action which seems appropriate to them in the view of their risk and their family goals, and act in accordance with that decision;

(6) make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder.

http://www.eurogentest.org/professionals/info/public/unit3/final_recommendations_genetic_counselling.xhtml
Role play

- Anna is seen in clinic to discuss family history of breast cancer
Genomics in the clinic

(Genomic counselling?)

Christine Patch PhD RN
Consultant Genetic Counsellor
Reader
Florence Nightingale Faculty of Nursing and Midwifery London

Guy’s and St Thomas’
NHS Foundation Trust
Specialist roles
• Diagnosis
• Explanation of technical issues
• Interpretation of results
• Exomes
• Genomes
• Specialist counselling skills
• ??????

Mainstream roles
• Support
• Adaptation
• Decision-making
• Current drivers

  – Technological and scientific development
    • Sequencing technologies
    • Laboratory rationalisation
    • Changing business models
    • Managing expectations
    • Direct to consumer testing offers

  – Changes to health services
    • Training
    • Managing expectations
    • New ways of working
    • Strained financial resources
Reality of WGS

Role of genetic counsellors?

Challenges for genetic counsellors
When exploring a clinical diagnosis.....

- Large deletions
- Large duplications
- Cancer genes
- ID genes

Diagnosis

- Large deletion in a cancer gene
- Change in a known developmental disorder gene
- Uncertain pathogenicity
What is 100,000 genome project
http://www.genomicsengland.co.uk

Genomics England, with the consent of participants and the support of the public, is creating a lasting legacy for patients, the NHS and the UK economy through the sequencing of 100,000 genomes: the 100,000 Genomes Project.

Genomics England was set up by the Department of Health to deliver the 100,000 Genomes Project. Initially the focus will be on rare disease, cancer and infectious disease.

Read more...
• New technologies
  – How much (too much ?) information
  – Utility of information
• Organisation of services
  – What is role of genetic services?
  – Who should provide genetic/genomic health care
• Quality assurance
  – Technology
  – Services
  – Professional
Genetic technologies evolution

Karyotype >3-5Mb

aCGH > ~ 2kb

Fluorescent in situ hybridisation

Sequencing 1bp
• UK - Arrays recommended as first line test since 2010.
• Varying technologies
• Varying algorithms for determining pathogenicity
  – NB does not detect balanced rearrangements

– best practice guidelines
  www.cytogenetics.org.uk/prof_standards/ACC_array_bp_dec2011_2.00pdf
American College of Medical Genetics Genetics in Medicine 2011 13 676-679, 680-685
ISCA
CNV detection rate=25%
87% too small to be detected by G-banded chromosome analysis
33% of imbalances are definitely pathogenic
34 different established genomic disorders detected in 430 patients
Imbalance for 6 different susceptibility loci detected in 205 patients
Most common genomic disorder: 22q11.2 deletion syndrome (n=64)
Most common susceptibility locus imbalance: 16p11.2 (n=60)

Ahn et al.(2013) Array CGH as a first line diagnostic test in place of karyotyping for postnatal referrals – results for four years clinical application for over 8,700 patients
• Challenges
  – Interpretation

• 4 year old boy learning difficulties
• Parents mild learning difficulties
INHERITED CHROMOSOME IMBALANCE DETECTED

del(3)(p26.2;p26.2)(4,331,005-4,553,083)x1 del(6)(q22.31;q22.31)(123,581,324-124,208,360)x1

Follow-up report:

Array CGH analysis of DNA from ______ has been carried out using oligonucleotide arrays with ~44,000 probes across the genome. This test identified two regions of imbalance:

1) A short arm of chromosome 3. The imbalance comprises approximately 22.7kb of material from band p26.2 and lies between 4,331,005 bp and 4,553,083 bp from the chromosome 3 short arm telomere.

2) A long arm of chromosome 6. The imbalance comprises approximately 627kb of material from band q22.31 and lies between 123,581,324bp and 124,209,360 from the chromosome 6 short arm telomere.

The deletion, duplication and sample identity have been established using custom MLPA probes specific for bcl within the regions of imbalance.

No other imbalance was detected (excluding previously published polymorphisms).

Follow-up studies on DNA from ______ parents __________ using the same custom MLPA probes, have shown that Alan's mother carries both the chromosome 3 short arm deletion and the chromosome 6 long arm duplication. These imbalances are therefore likely to be polymorphisms of no clinical significance; however any unusual features shared by Alan and his mother may be associated with either of these imbalances.

We understand that this family is attending the Genetics Clinic, Guy's Hospital.

Exam MLPA probes: 3,133bp; 776,155bp
Array findings probably unrelated to phenotypes in family
Challenges

- Variable Phenotype eg 16p 11.2 dup
‘Incidental findings’

Caroline Wright pertinent and non-pertinent findings
• Who should explain results
• Who should complete inheritance/validation/confirmation of pathogenicity studies
• New skills needed by genetic counsellor
• Close partnership working between genetic counsellor and medical consultant
Whole genome analysis

It is our view that using whole genome data in clinical diagnostic services within the NHS without first addressing these fundamental issues of diagnostic quality poses potentially unacceptable risks to patient safety, and quality of care. These risks include:

• Incorrect diagnosis (false positive or negative), leading to inappropriate patient care and decision making and threatening patient safety.

• Failure to provide a conclusive diagnosis for the patient and a continuation of their diagnostic odyssey.

• Inappropriate use of NHS resources.
• New Technologies
  – Impact on knowledge base of genetic counsellors/nurses

• Increasing impact of genomics to health
  – New ways of working, networking and multidisciplinary teams

• Strained financial resources
  – Constant evaluation of practice and services
  – Evidence of value
Genetic counselling is a communication process that deals with the occurrence, or risk of occurrence, of a (possibly) genetic disorder in the family. The process involves an attempt by appropriately trained person(s) to help the individual or the family to

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http://www.eurogentest.org/professionals/info/public/unit3/final_recommendations_genetic_counselling.xhtml
Attitudes towards returning data to participants in sequencing research

Dr Anna Middleton
Principal Social Scientist
Registered Genetic Counsellor
• Undiagnosed developmental disorder

• Current targeted testing – no answer

• Exome sequence as part of the Deciphering Developmental Disorders (DDD) project
‘INCIDENTAL FINDING’, OPPORTUNISTIC SCREEN
e.g. BRCA1

PERTINENT FINDING
Developmental Disorder gene

• Secondary variant
• Unsolicited finding
• Health related finding
• Ancilliary
  Etc etc
Objectives: to explore

Attitudes towards return of different types of genomic data

Attitudes towards the return of raw sequence data
Ethics and Genomics Survey

Sharing of Pertinent Findings

- Should Pertinent Findings from genome studies be made available to research participants?
  - Research participants should be able to receive pertinent findings if they want them
  - I don’t think pertinent findings from research projects should be available
  - I don’t know
Recruitment

10% Traditional Media

15% Direct Invitation

75% Social Media
Public = 4961

Genomic researchers = 607

Genetic health professionals = 533

Other health professionals = 843
75 countries involved
Q: What influences attitudes the most?

A: Our professional background rather than the country we are from.
Q: If Incidental Findings were categorized in the following ways (↓ below) what would you want to know?
Genetic Health Professionals (n = 533)
Public + Genomic Researchers + Other Health Profs (n = 6411)

- Life-threat, can be prevented
- Medications useful later
- Life-threat, cannot be prevented
- Not serious health importance
- Uncertain

%
Genetic Health Professionals (n = 533)

Public + Genomic Researchers + Other Health Profs (n = 6411)

P < 0.0001
Key messages

• People want data

• Treatability is important

• Genetic health professionals have more conservative views
  
Q: LETS ASSUME IT IS POSSIBLE TO RETURN IFS RELATING TO A CONDITION THAT IS SERIOUS AND PREVENTABLE.

DOES THE LEVEL OF RISK AFFECT WHETHER YOU THINK THE RESULT SHOULD BE RETURNED?
‘I’d be interested in knowing about a serious, actionable condition at these levels of risk...’
Even at ‘low risk’ some people still want data – (if it’s usable)

‘If its about me, I want to know’

‘I’ll decide how important this data is, not you’
Is there a profile to those who want data?
I want to know EVERYTHING!

Information Seeker

I just want some things.....

Information Discriminator
• Are you an....?

• Explored the profiles of each
• Adjusted for all potential confounding effects
• Only show data relating to significant odds ratios
Are more likely to be/want...

- Men
- Had previous genetic testing or genomic analysis
- Want their raw data
- Want low risk information
- From North America
- Not genetic health professionals
- Think genomic researchers should actively search for IFs

Information Seeker
Are more likely to be/want...

- Women
- Not had previous genetic testing or genomic analysis
- From Europe
- Don't want their raw data
- Don't want low risk information
- Genetic health profs
- Think genomic researchers should NOT actively search for IFs
- Information Discriminator
‘Raw genomic data’ (sequence reads or called variants) on a hard drive

“Meaningless” (McGuire et al, 2008)

“Non-sensical” (Bredenoord et al, 2011)
“Yes, I’d want to be able to receive all of my raw genomic data”
Q: If you were given all of your raw genomic data from a research study, what would you do with this? (n = 6944)

- Seek interpretation: 62% (n = 4320)
- Nothing: 20% (n = 1358)
- Missing: 18% (n = 1266)
“I would seek out an interpretation”  
(n = 4320)
78% said ‘I wouldn’t do anything immediately with it, but would keep for future use’ (n = 926)

16% said ‘I wouldn’t know what to do with it’ (n = 194)

3% said ‘I would delete the data’ (n = 40)

3% ticked ‘other’ (n = 32)
There is an appetite for receiving raw genomic data

– For interpretation
– Just because it’s about me
Conclusions

- People want:
  - to be connected to the research process
  - the option to receive data

- There is a perceived value in the data
  - need to manage expectations
  - sign post to what they can do with it
Enormous thanks to:

- Mike Parker
- Caroline Wright
- Helen Firth
- Eugene Bragin
- Matt Hurles
- Kate Morley
- DDD ‘actors’ in films
- DDD team

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CASE 1: BENEFICENCE
USA Case

Anna aged 44
White American

Leonard aged 56, African American

Marie, aged 2

Severe developmental delay, dysmorphic features
• No significant family history in any relatives
• Marie is severely disabled. Parents very anxious and want to know everything about Marie’s possible prognosis
• WGS can be offered to find a diagnosis
• ACMG list for opportunistic screen is available
• List contains adult and child onset conditions
• Trio testing
‘INCIDENTAL FINDING’, OPPORTUNISTIC SCREEN

e.g. BRCA1

• Additional Looked For Findings

PERTINENT FINDING
Developmental Disorder gene
Broad Consent

- Different to specific consent for a particular condition
- Testing for conditions not heard of and have no emotional connection to
- List of conditions may change (as per 100kGP)
• Variant in P53 discovered in Leonard and Marie, “likely pathogenic” based on known research
  – (which has been done on data biased to affected people and without much ethnic diversity)
• Leonard is fit and well and has no family history of cancer (with many elderly relatives)
• How should we interpret this result?
The Ethical Dilemmas

• How to do good in the absence of strong data?
• What health screening should we offer Marie and Leonard? (Marie is severely disabled and annual MRI scanning is not feasible, would require a general anaesthetic)
• Extensive genomic data sharing is needed to confirm risks in specific ethnic groups
• How would you handle this situation?
• What do the family want?
• What have we offered them?
“It may help to explain the degree of uncertainty which surrounds the clinical utility of these [additional looked for findings] at the current time: the research effort to help us understand and interpret these findings will be ongoing throughout the project, and we will not know for certain what risks patients carry for some time.”
Jane

Robert

P

Profound deafness
Jane and Robert are both medically deaf, but also culturally Deaf

Sign language is first language (spoken and written English is second language)

Positive and proud to be Deaf

Generations of deafness (i.e. genetic/inherited)
• Jane and Robert have a preference for deaf children
• Concerned about having a hearing child
• Asked to chat through the chances of having a deaf or hearing child
• Would we offer pre-natal testing ‘just for information’ – risk of miscarriage from the amnio/CVS procedure
• Would couple ask for a termination of pregnancy, would we allow them?
The ethical dilemmas

- Balancing beneficence for the couple and family versus non-maleficence for a child that does not exist yet (although foetus exists)
- Parents right to have autonomy over pregnancy
- Hearing children might be disadvantaged in this family
- Health professionals balancing their focus between non-directiveness versus personal values
The outcome

- Jane and Robert had a deaf child
- They were relieved and delighted
- If the baby had been hearing, I would have referred them to the local social services for deaf people, to access speech therapy
Case studies HD
• Michael is 24 years old
• His mother who is a single parent is affected with HD.
• She has just gone into a residential home
• Michael is referred to talk about testing
• What issues may emerge
• What should we discuss
• Michael has a younger brother aged 14

• He says he wants to be tested what do we do?
# Overview of guidelines/position papers (1991-2005)

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<th>Year</th>
<th>Source</th>
<th>Description</th>
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<td>1991</td>
<td>National Consultative Ethics Committee for Health and Life Sciences (France)</td>
<td>Opinion regarding the application of genetic testing to individual studies, family studies and population studies.</td>
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<td>1992</td>
<td>German Society of Human Genetics</td>
<td>Statement on post-natal predictive genetic diagnosis</td>
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<td>Swiss Academy of Medical Sciences</td>
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<td>Institute of Medicine</td>
<td>Assessing genetic risks. Implications for health and social policy</td>
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<td>1995</td>
<td>GIG</td>
<td>Response to the CGS report**</td>
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<td>American Medical Association</td>
<td>Testing children for genetic status</td>
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<td>1995</td>
<td>ASHG and ACMG (US)</td>
<td>Points to consider: ethical, legal and psychosocial implications of genetic testing in children and adolescents</td>
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<td>Opinion and recommendations on Genetics and medicine: from prediction to prevention’</td>
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<td>National Human Genome Research Institute</td>
<td>Promoting safe and effective genetic testing in the US</td>
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<td>BMA</td>
<td>Human Genetics: choice and responsibility</td>
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<td>Report on genetic testing for late-onset disorders</td>
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<td>Australian Medical Association</td>
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<td>Italian National Bioethics Committee</td>
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<td>Canadian College of Medical Geneticists</td>
<td>Position statement – genetic testing of children</td>
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<td>2000</td>
<td>ESHG</td>
<td>Provision of genetic services in Europe – current practices and issues.</td>
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<td>Danish Council of Ethics</td>
<td>Genetic investigation of healthy subjects – report on presymptomatic gene diagnosis</td>
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<td>American Academy of Pediatrics</td>
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<td>Japanese Society of Human Genetics</td>
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<td>Human Genetics Society of Australasia</td>
<td>DNA presymptomatic and predictive testing for genetic disorders</td>
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<td>Genetics-Medicine-Related Societies (Japan)</td>
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<td>2005</td>
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<td>Child testing policy</td>
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Testing in adolescence

- At request of doctor
- At request of parents
- At request of young person
Types of genetic testing in children

Presymptomatic testing- untreatable late onset disorders with no effective intervention (usually AD)

Adults requesting such testing are advised through counselling pre testing to prepare for results as can have major life impact. International guidelines followed.

Implications include;

Managing results, pos or neg
Limitations of prediction
Emotional impact
Social- family, friends
Practical- insurance, employment

Presumption no testing
Case study Reproductive choice

Sarah and John’s daughter was diagnosed with SMA1. Sadly she died at the age of six months. Sarah has now had two early miscarriages and in her words desperately wants another child.

What issues may emerge
Reproductive options for those at risk of having a child with a genetic condition

- Reproductive roulette
- Prenatal diagnosis & TOP
- Gamete donation
- Adoption
- Remain childless
- PGD
ACU, Guy’s Hospital
UCH, London
CARE, Nottingham
The Bridge Centre, London
Glasgow Royal Infirmary
IVF Hammersmith, London
Oxford Fertility Unit
ARGC, London
Edinburgh ACU
Blastocyst Biopsy Procedure

Blastocyst held in position

Trophectoderm cells extruded through small hole made in the outer coating of the embryo

Cells removed and sent for testing

FREEZE ALL EMBRYOS
Total babies born = 473

- Treatment cycle to embryo transfer = 71%
- Clinical pregnancy per egg collection = 32%
- Clinical pregnancy per transfer = 41%

- 343 singletons
- 121 twins (x 2)
- 15 triplets (5 x 3)

- Multiple pregnancy rate = 8%
- 50 ongoing pregnancies
Success and age

- <35yr CPR = 36%
- 35-37 CPR = 19%
- 38-39 CPR = 8%
- >39 CPR = 0%
• No treatment if BMI > 35

• No funding if BMI > 30

Risks:
- egg collection
- decreased success
- increased chance of miscarriage
- increased risks in pregnancy
• Is PGD the solution?