Organisation of the PGD Centre

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Overview

- Setting up a PGD Centre
- Organisation of the PGD Centre
- Preparation for clinical PGD
- Misdiagnosis
- Accreditation
- External quality assessment
- ESHRE PGD Consortium
- Future of PGD/PGS
- What makes a good PGD Centre?

Setting up a PGD centre

- Two ways

- IVF centre and PGD centre in the same institute – preferred
- Transport PGD

Organisation of the PGD Centre

- Highly successful IVF unit
- Patients need genetic and specific PGD counselling
- Biopsy performed by trained embryologist
- Diagnosis performed by molecular biologist/cytogeneticist
- Accredited lab
- Patient information leaflets and consents
- Excellent communication between IVF centre and diagnosis lab
- Join the PGD Consortium

Successful IVF Unit

- No point doing PGD in an IVF unit with poor results
- Need experience in biopsy
- Selecting embryos on genetic and chromosomal status
- Morphology rarely taken into consideration

Pretreatment workup

- FISH
  - Sexing need to check for polymorphisms
  - Translocation protocols developed by cytogeneticist
  - For PGS – polymorphic sites
- PCR
  - Confirmation of mutation on proband and relatives
  - Suitable informative markers to detect contamination
  - Experienced molecular biologist
- Arrays
  - Depends on if for molecular or cytogenetic
  - Validation of WGA and array
  - Experienced clinical scientist

Workup of diagnosis

- Validation of method
- Full authorised report
- Protocol logged into lab system
- Prior to cycle – internal quality assessment of all reagents and equipment

Clinical cycle

- Full consultation, information leaflets, relevant consents
- Need good number oocytes/embryos
- Patients must not have unprotected sex
- All cumulus cells removed (maternal contamination)
- ICSI for all molecular diagnosis (paternal contamination)
- Medium to support blastocyst growth
- Clear identification of biopsied cell and embryo number
- Ensure correct embryo transferred
- Appropriate witnesses throughout diagnosis
- Full authorised report logged in PGD and IVF centre

Misdiagnosis

- Analysis of untransferred embryos
- Prenatal diagnosis
- Follow up of pregnant patients
- Follow up of babies born
- Wilton et al, 2009

Possible causes of misdiagnosis

- Allele dropout
- Contamination - sperm/cumulus/DNA/cells
- Mosaicism
- Transferring wrong embryo
- Unprotected sex

Key points for biopsy/diagnosis lab

- Counselling
- Appropriately trained staff
- Aware of misdiagnosis possibilities
- Quality control
- Records
- ISO/accreditation

Accreditation

- ISO 15189
- Every country has national body
- How can the consortium help?
- QM workshop
- Paper on accreditation of a PGD laboratory, Harper et al, 2010
- Establish an accreditation advisory panel
  - Discussion with national accreditation bodies
  - Offer centres help with accreditation process

ISO 15189

- **Management requirements**
- Organization and quality management
- Quality management system
- Document control
- Review of contracts
- Examination by referral laboratories
- External services and supplies
- Advisory services
- Resolution of complaints
- Identification of control of non conformities
- Corrective action/Preventative action
- Continual improvement
- Quality and technical records
- Internal audits
- Management review

ISO 15189

- **Technical requirements**
- Personnel
- Accommodation and environmental conditions
- Laboratory equipment
- Pre-examination procedures
- Examination procedures
- Assuring quality of examination procedures
- Post-examination procedures
- Reporting results

EQA FISH

CEQA Cytogenetic European Quality Assessment

- web: www.ceqa-cyto.eu
- Cytogenetics European Quality Assessment scheme (CEQA)
- Ros Hastings, Joyce Harper, Edith Coonen, Paul Scriven
  - 2008 – pilot in three stages: PGD and PGS on line analysis and submission of retrospective case.
  - 2009 – 27th June, participants meeting
  - 2009 – EQA. Robertsonian and reciprocal translocation cases in two stages

EQA Molecular

UK NEQAS

- Pilot
- Labs sent 'parental' &'affected relative' DNA samples from cell lines
  - Test DNA, report data and state if can offer PGD to couple
- Labs sent single cells representing 5 embryos
  - test cells and report results in regular format
  - interpret results into 'transfer' / 'no transfer'
- 2009/2010
  - Repeat pilot to determine performance criteria for full EQA scheme

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ESHRE PGD Consortium

- To survey the availability of PGD
- To collect prospectively and retrospectively data on the accuracy, reliability and effectiveness of PGD
- To initiate follow-up studies of pregnancies and children born
- To produce guidelines and recommended PGD protocols
- To formulate a consensus on the use of PGD
- To educate in the science of genetics and reproduction
- www.eshre,com

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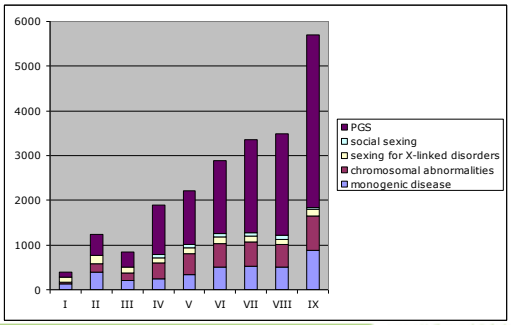
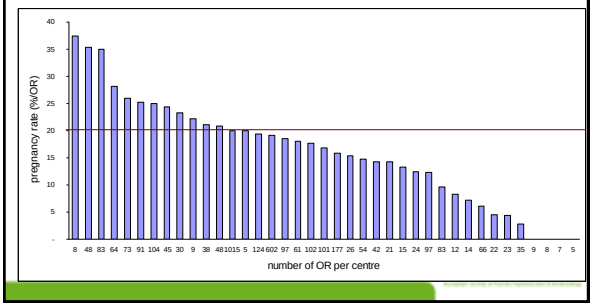
Evolution of PGD



Pregnancy rates by centre, data VIII



Consortium working groups

Aneuploidy screening: Chair Sjoerd Repping
- CLOSED – ESHRE PGS task force

Misdiagnosis: Chair Joanne Traeger-Synodinos
- Paper on causes of misdiagnosis – Wilton et al, 2009
- Study on follow up of untransferred embryos

Diagnostic laboratory accreditation: Chair Katerina Vesela
- Workshops 2008/2010
- Guide towards accreditation – Harper et al, 2010
- Accreditation advisory panel

Database: Chair Celine Moutou
- Setting up a new database
- Questionnaire on freezing

Guidelines: Chair Gary Harton
- Four guidelines prepared

Molecular methods: Chair Francesco Fiorentino
- Database of methods

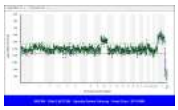
Consortium guidelines

- Organization of a PGD centre
- PCR-based PGD with Transport PGD
- FISH-based PGD with Transport PGD
- Biopsy for PGD in conjunction with the Embryology SIG

Future of PGD

- All stages of biopsy
- Arrays
- Increased number of diseases
- More controversial use of PGD



PGD


Single cells are removed from the embryo


Single cell


PCR


FISH

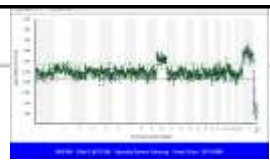

METAPHASE CGH

WGA


PCR


ARRAY CGH

PGS



- RCTs show it does not work using
  - FISH
  - Cleavage biopsy
- Look at PB or blastocyst
- Arrays
- Validate arrays – ESHRE PGS task force
- Harper et al, What's next for PGS? Hum Reproduction 2008, 2010
- Geraedts et al, 2009

Limitations of PGD

- Patients have to go through IVF
- Cost
- All embryos may be affected
- Making diagnosis from 1-2 cells
- Have been misdiagnosis
- Success rate lower than IVF

What makes a good PGD centre?

COMMUNICATION

Excellent IVF Platform

Excellent Diagnostics Laboratory

Integration of Services

Rigorous Quality Control/Quality Assurance

Commitment to Follow-up

Comprehensive Ethical Review

TRANSPORT PGD