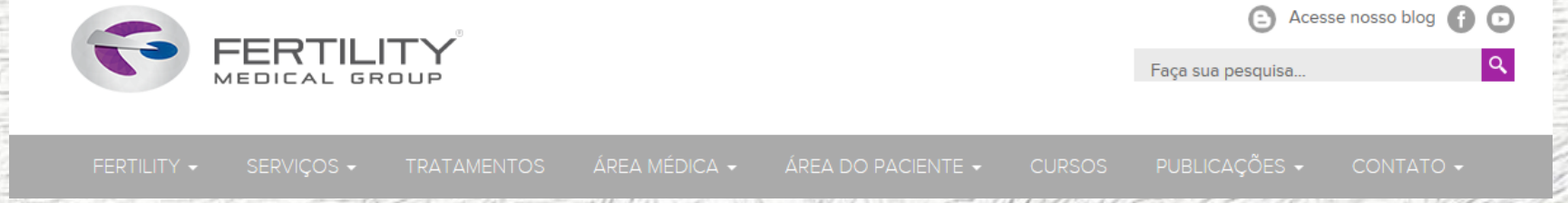
II Workshop Internacional de Genética Reprodutiva

Diagnóstico Genético Pré-implantacional: aplicação e resultados na Clínica de Reprodução Assistida

Edson Borges Jr.

CHROMOSOME

II Workshop Internacional de Genética Reprodutiva



http://fertility.com.br/producao-cientifica-2016/

CHROMOSOME

II Workshop Internacional de Genética Reprodutiva

Agenda

1- PGS/PGD: conceitos
2- Survey IVF-Worldwide
3- Técnicas e Resultados
4- Eficácia e Limitações
5- Segurança
6- Análise crítica e considerações

CHROMOSOME

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CHROMOSOME

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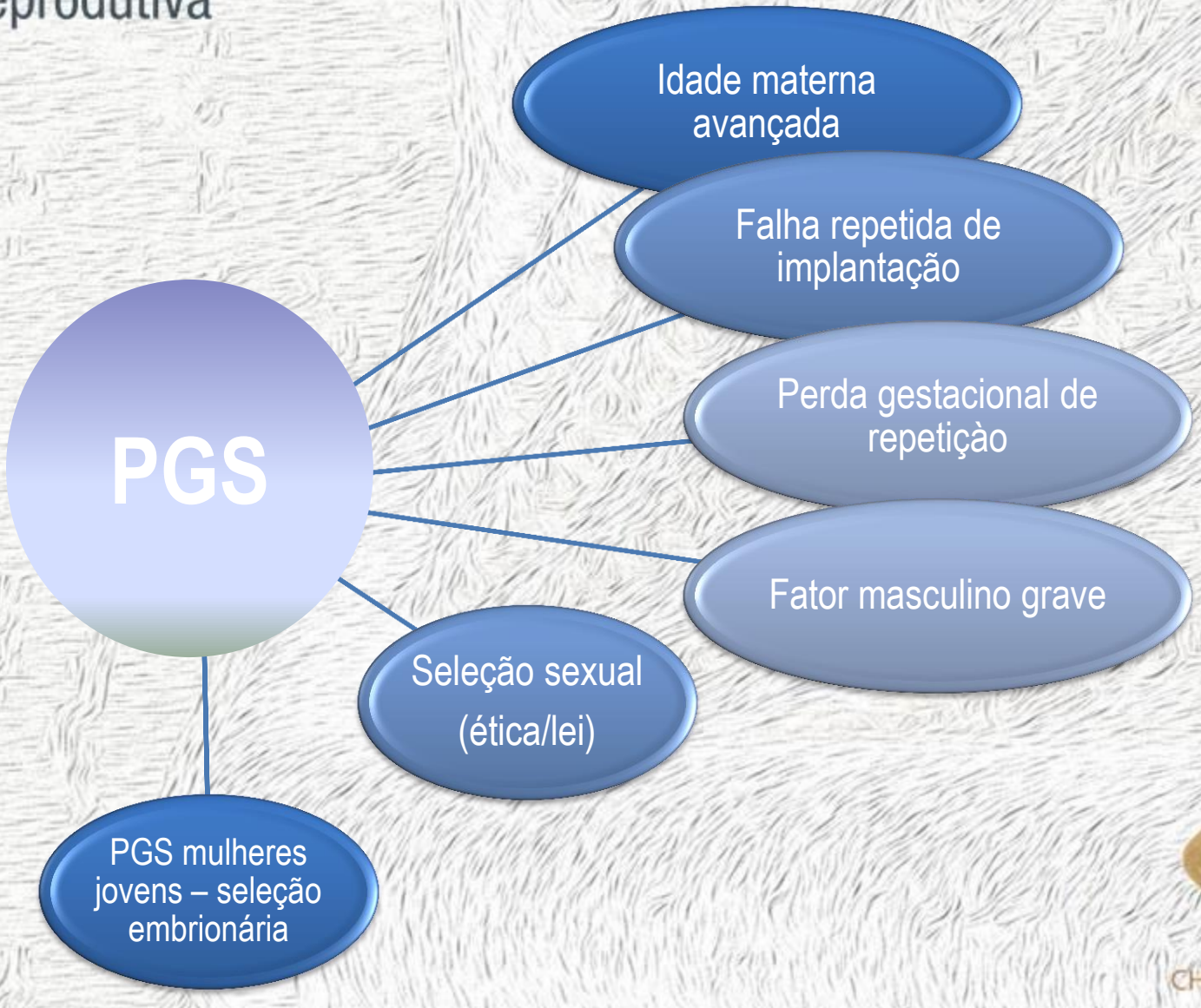
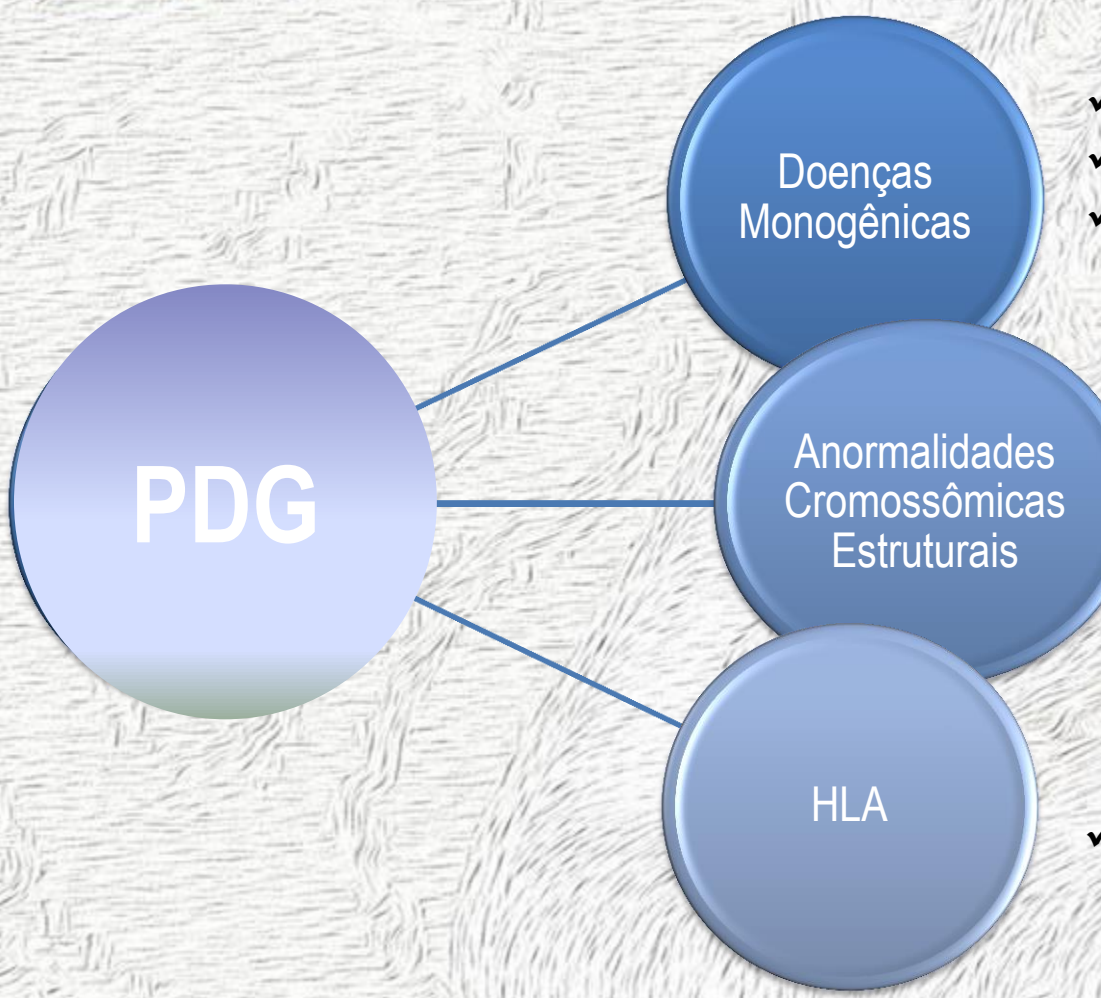
Diagnóstico Genético Pré-Implantacional



CHROMOSOME

II Workshop Internacional de Genética Reprodutiva

Diagnóstico Genético Pré-Implantacional



- ✓ Autossômica Recessiva
- ✓ Autossômica Dominante
- ✓ Doenças dos Cromossomos Sexuais

- ✓ Translocações
- ✓ Deleções
- ✓ Inversões
- ✓ Duplicações

- ✓ Antígeno de Histocompatibilidade

CHROMOSOME

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CHROMOSOME

II Workshop Internacional de Genética Reprodutiva

RESEARCH & EDUCATION

IVF WORLDWIDE

Preimplantation genetic screening (PGS) : what is my opinion

The purpose of the current survey is to evaluate the extent and patterns of use of PGS worldwide, and to gain an insight on the views and opinions of the ART community on the use of PGS

This survey includes the responses of 386 IVF Units from around the globe responsible for 342,000 cycles.

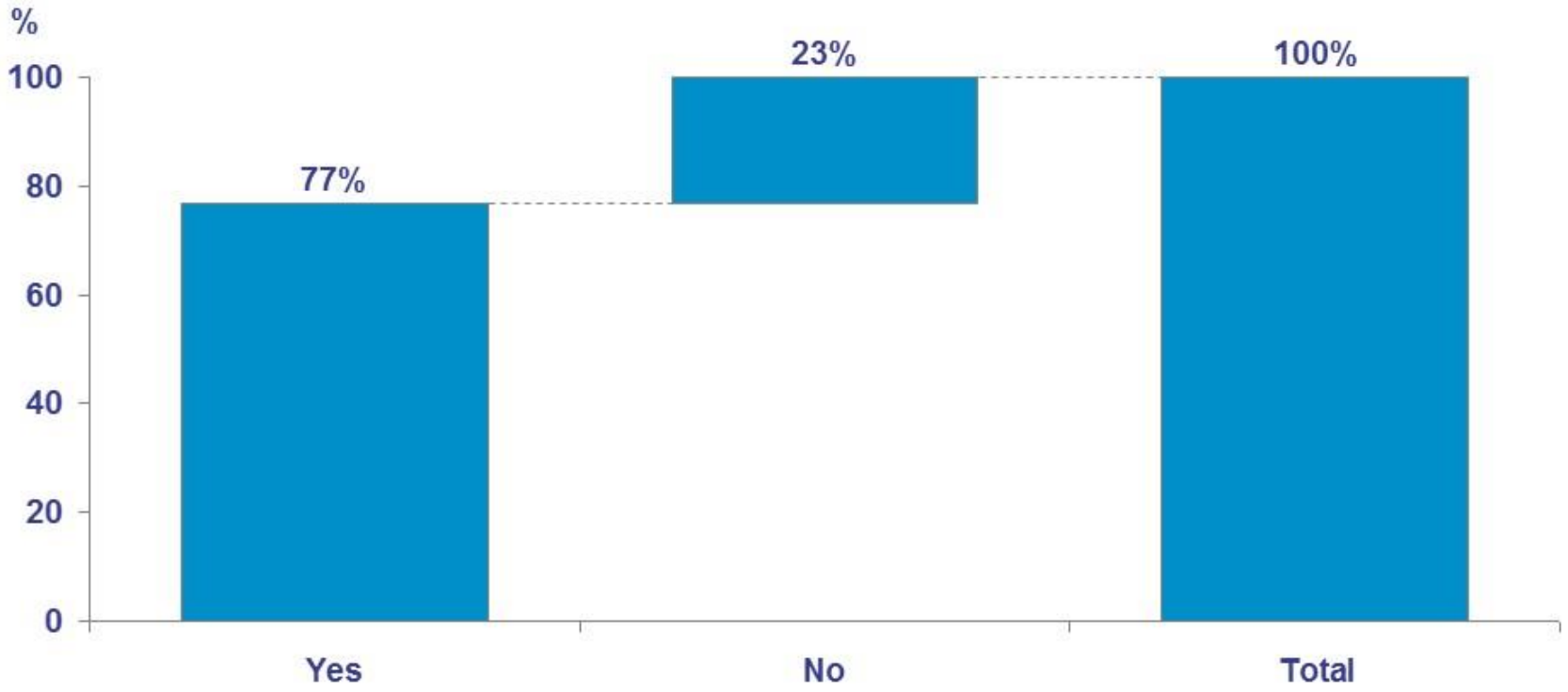
The results clearly emphasizes the role of preimplantation genetic screening (PGS) in current practice and supports the Position Statement on PGS issued by prominent leaders in the field during the 1st COGEN Meeting in Paris 2015

CHROMOSOME

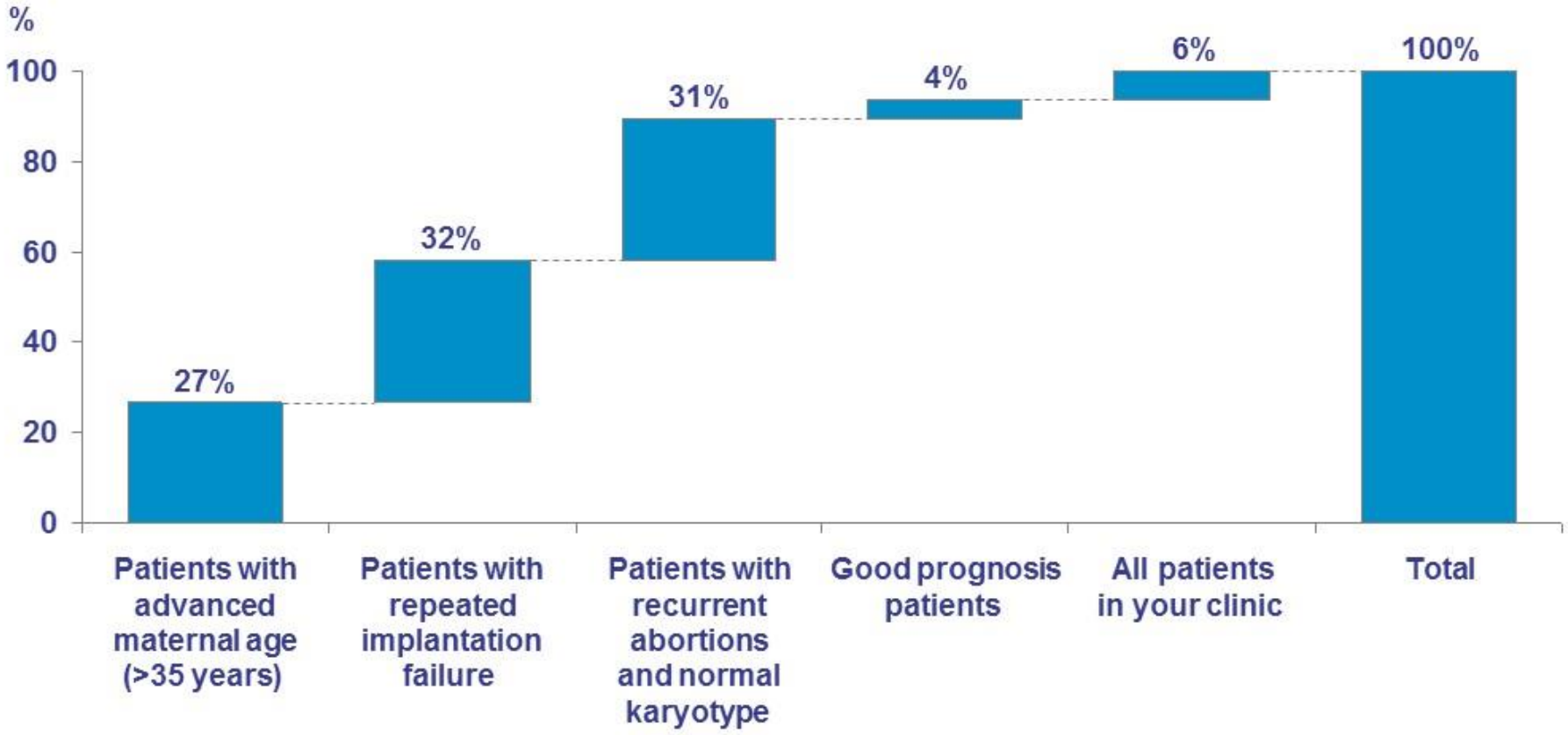
Number of cycles in units

Continent	IVF Cycels	IVF units
USA & Canada	65,800	97
South America	18,500	34
Australia & New Zeland	22,300	21
Asia	83,900	78
Europe	137,900	137
Africa	14,200	19
TOTAL	**342,600**	**386**

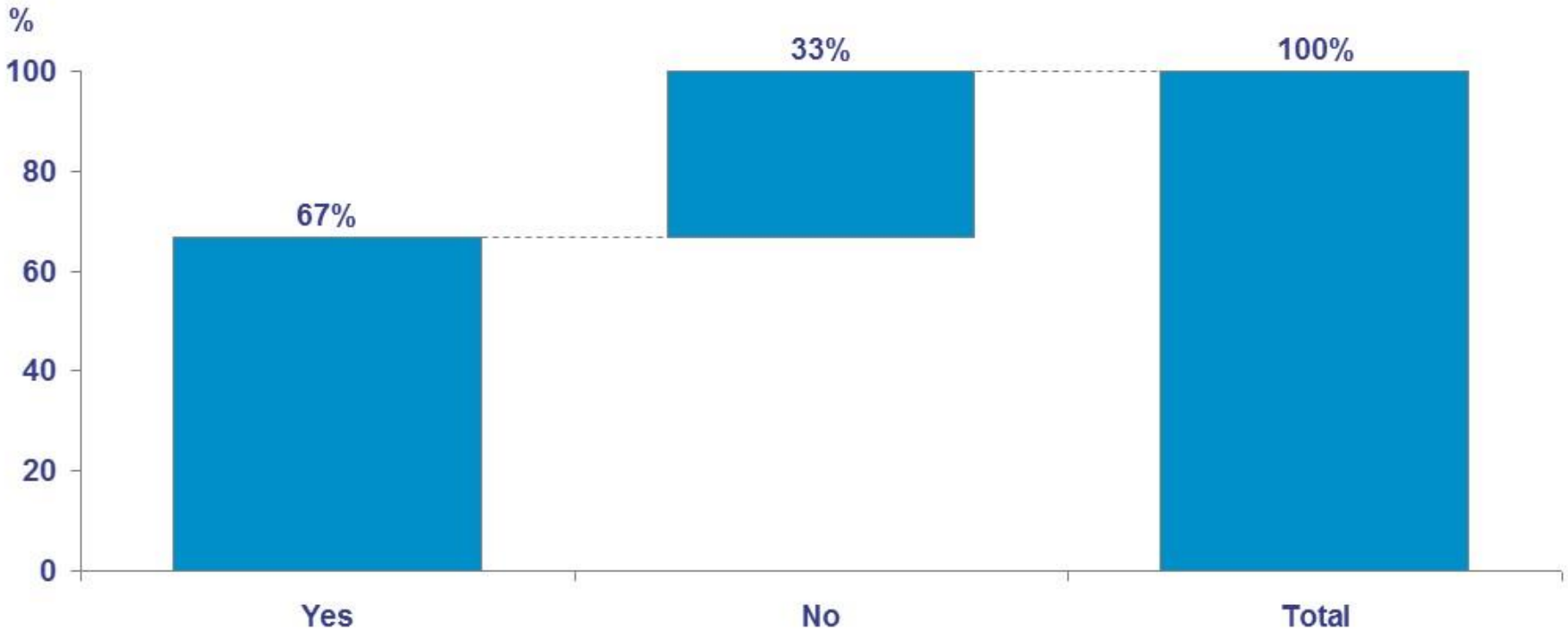
Is PGS used in your clinic?



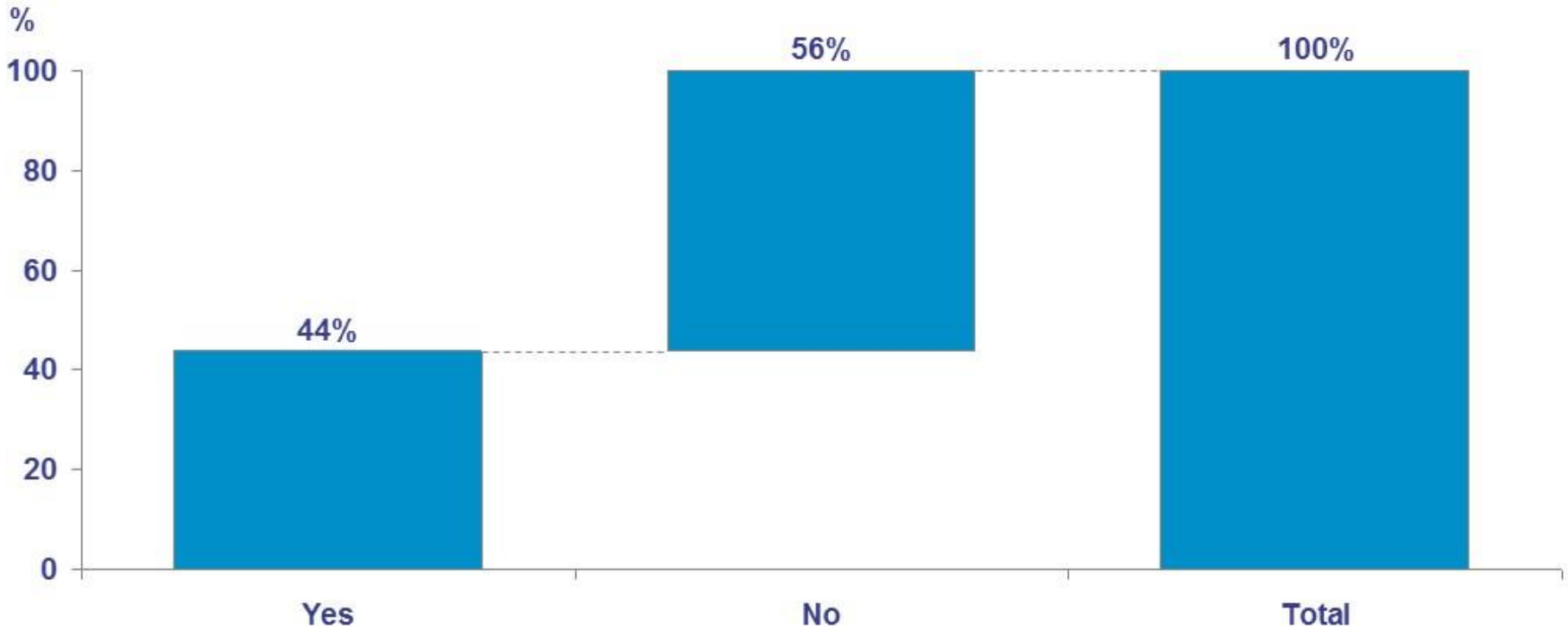
1) Which patients are being offered to include PGS in their treatment cycle?



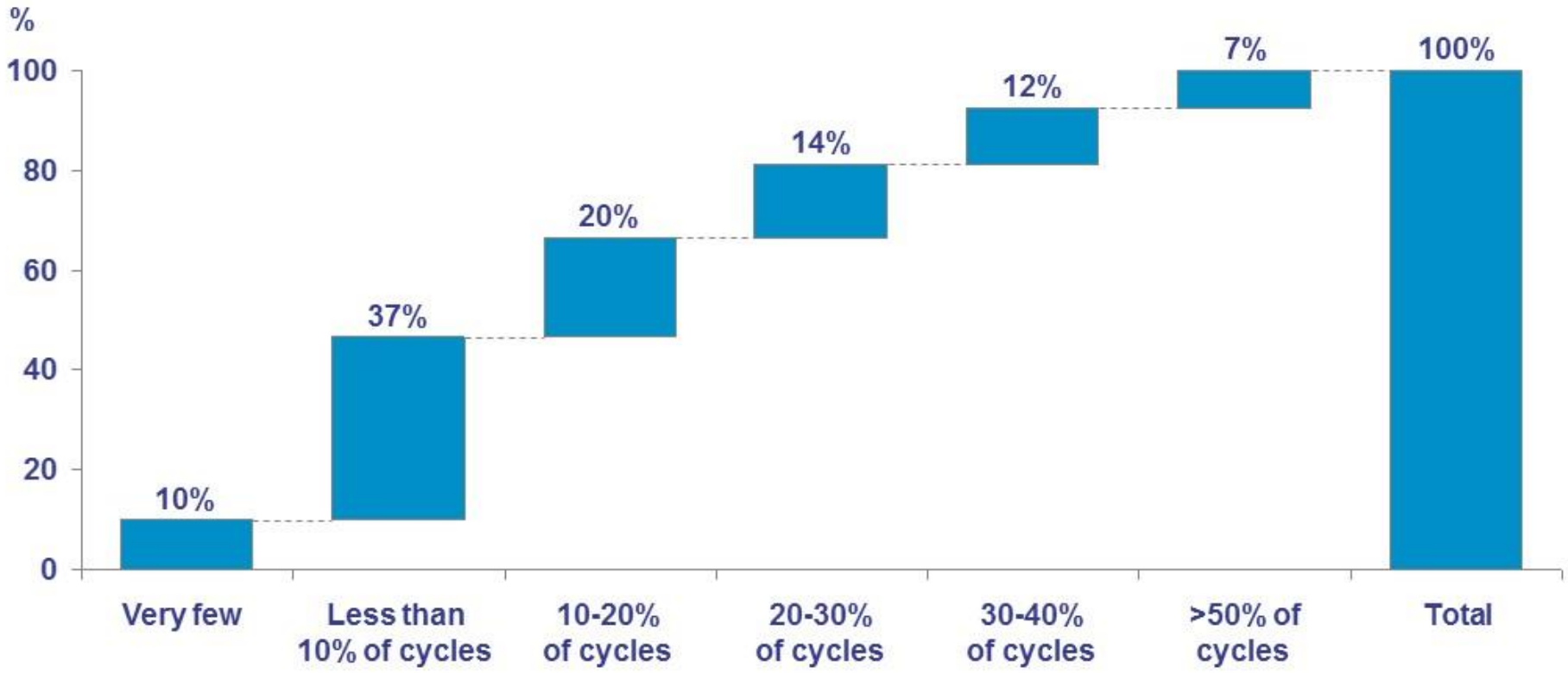
2b) All patients are included irrespective of ovarian reserve



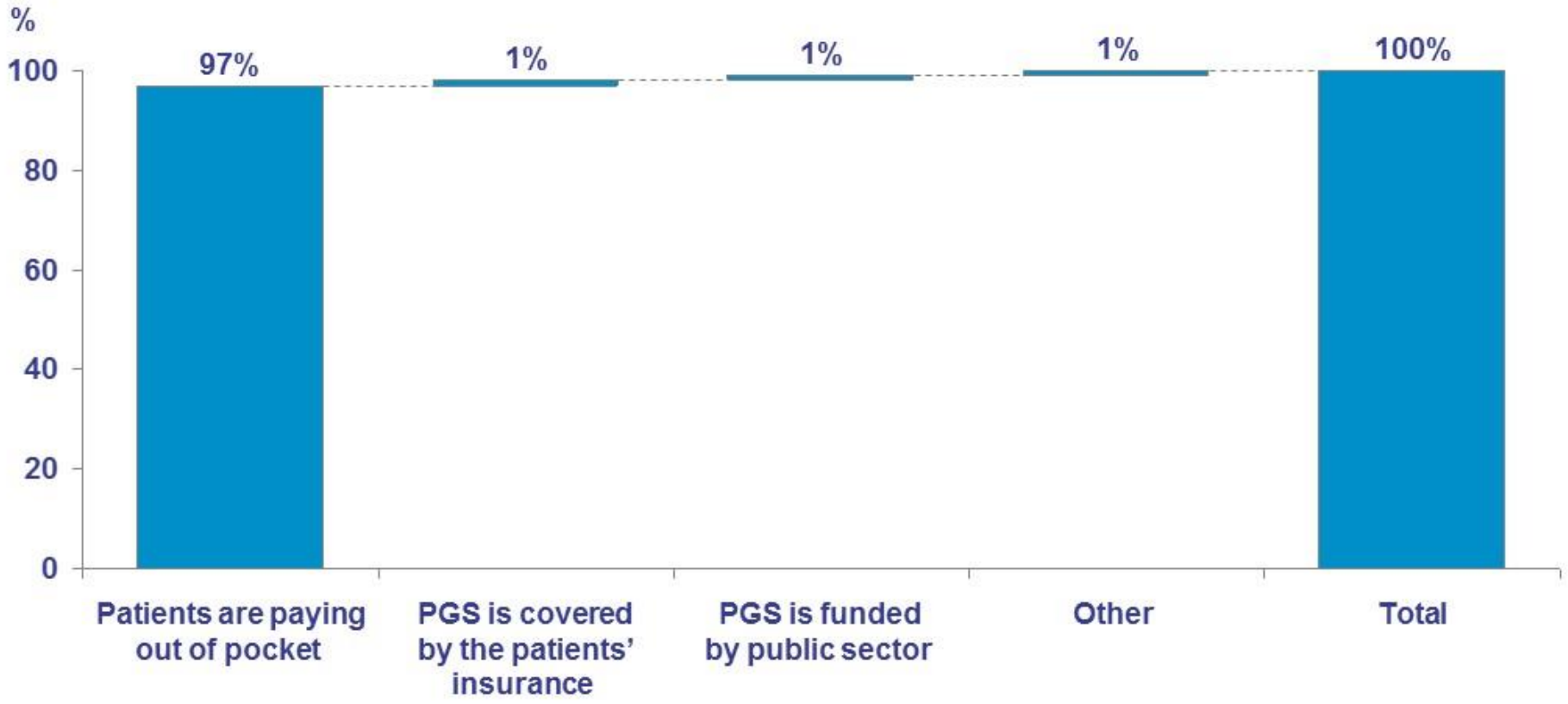
2c) A minimum of embryos/blastocysts are necessary for inclusion irrespective of ovarian reserve



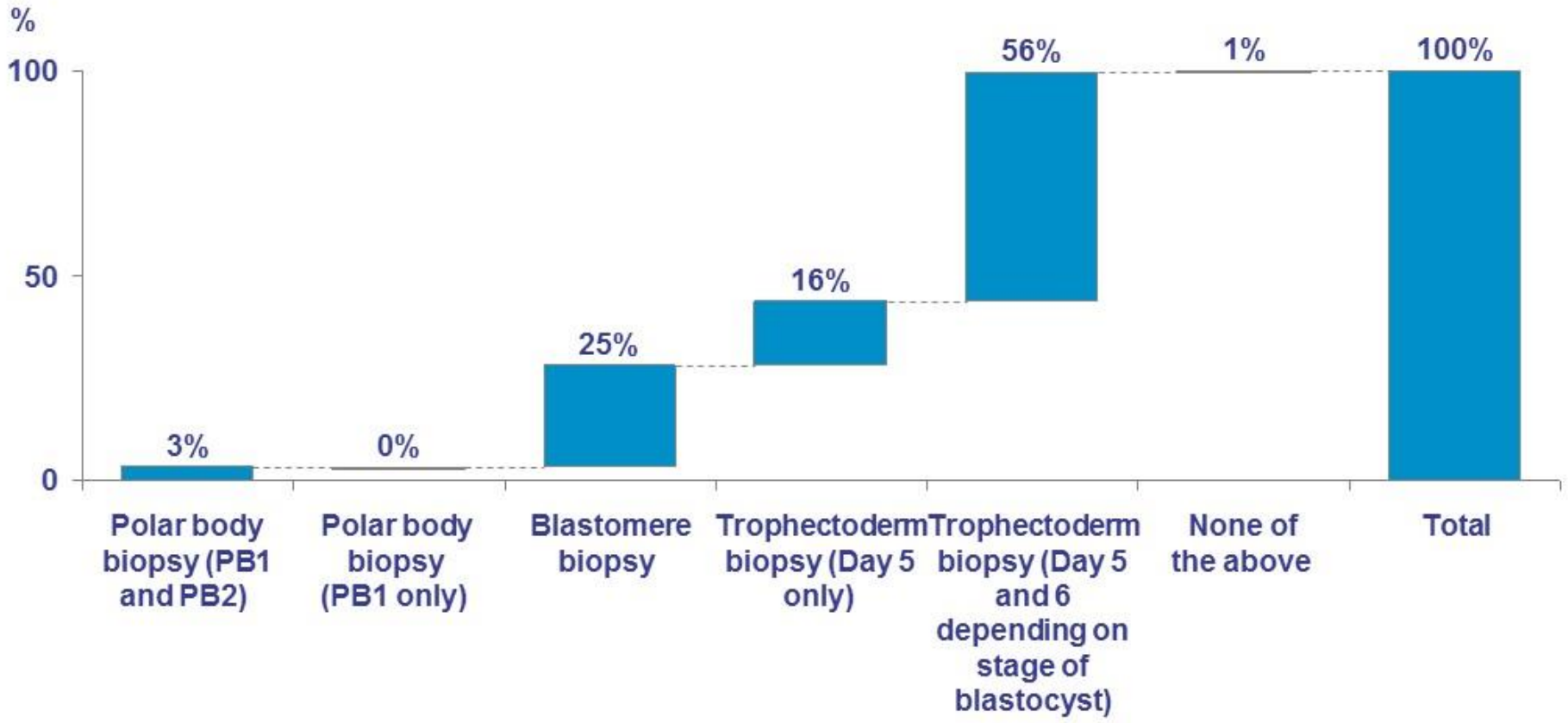
3) To what extent is PGS being used in your clinic?



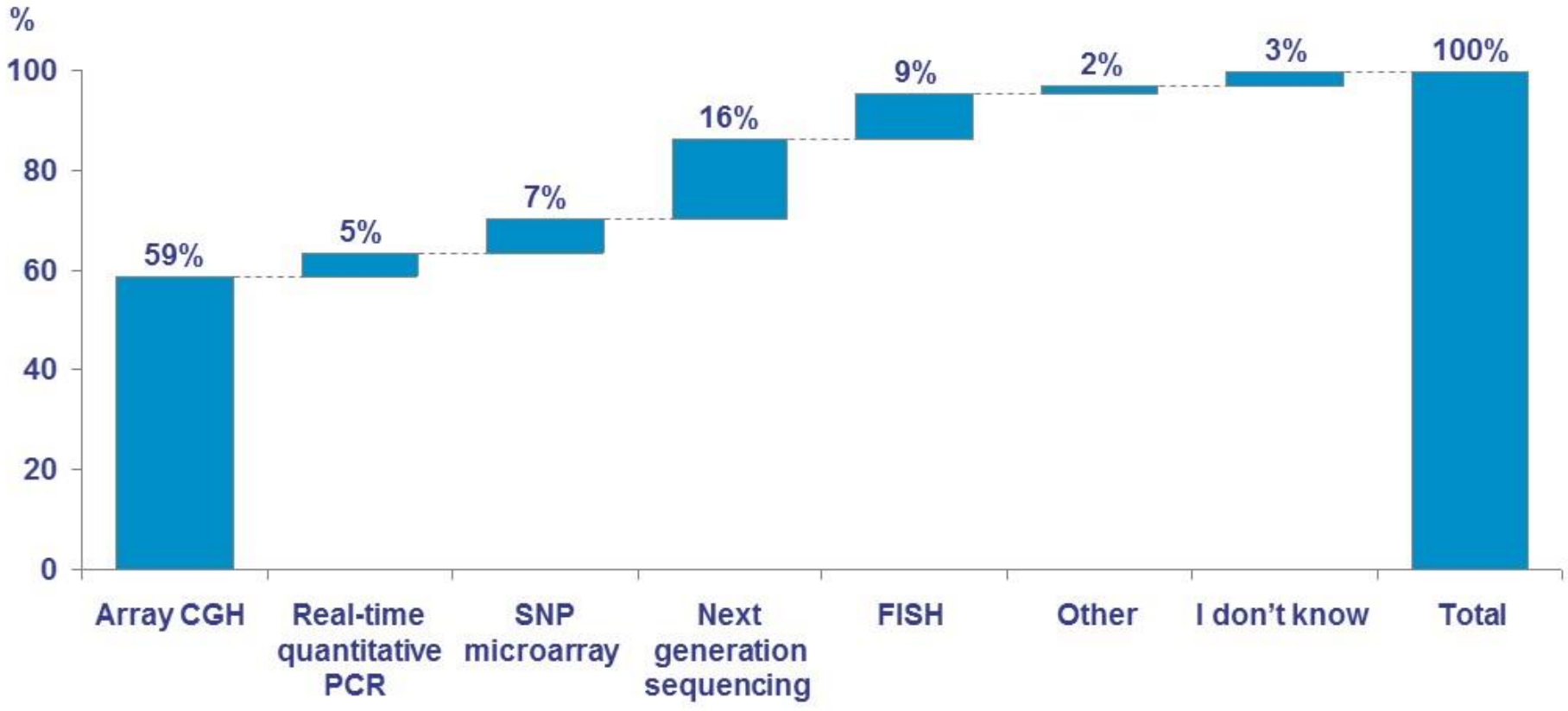
4) Who is responsible for the funding of the PGS part of the IVF cycle?



5) At what stage of development are the majority embryo biopsies being performed in your clinic?



7) Which method of genetic testing is predominantly used in your clinic for determination of embryo ploidy status?



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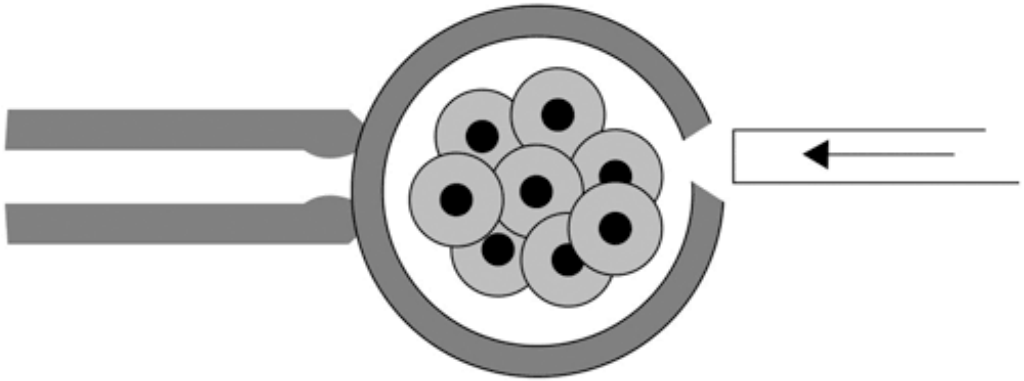
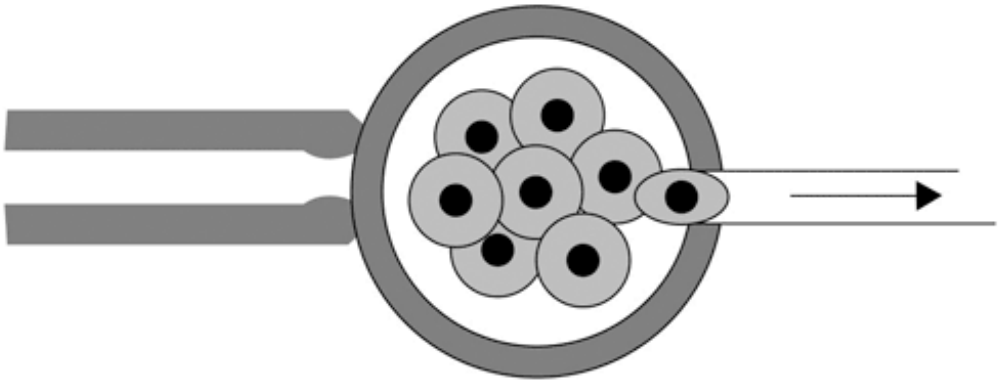
CHROMOSOME

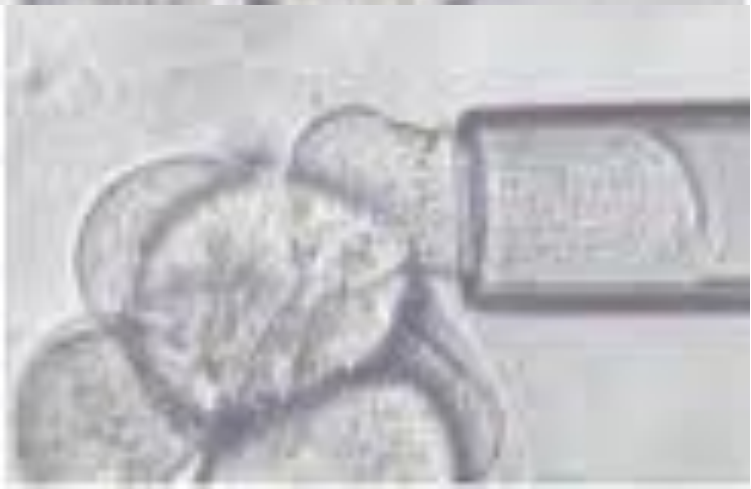
Embryo Biopsy



The 8-cell embryo is held by a holding pipette
and a hole is made in the zona pellucida



A blastomere is aspirated into a biopsy pipette,
and then can be genetically tested.

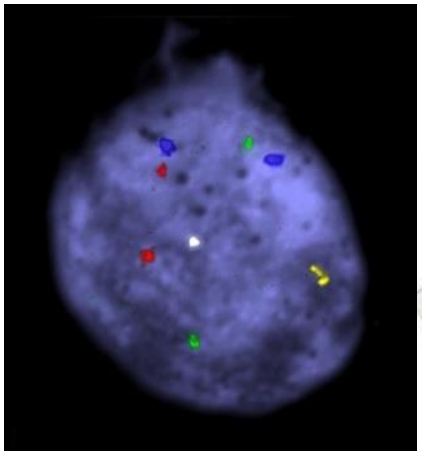


FERTILITY MEDICAL GROUP

Técnica

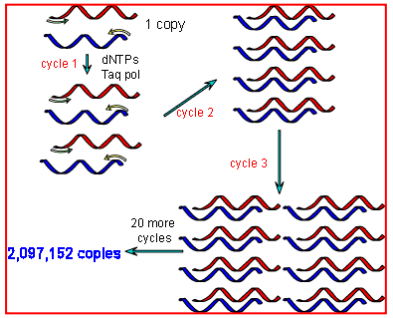
- X,Y,13,14,15,16,18,21,22

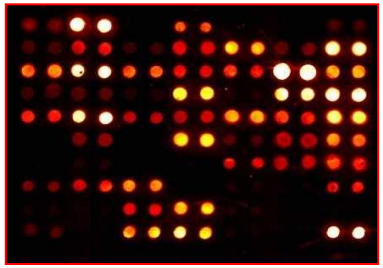
Blastômero com núcleo visível



PGS-FISH

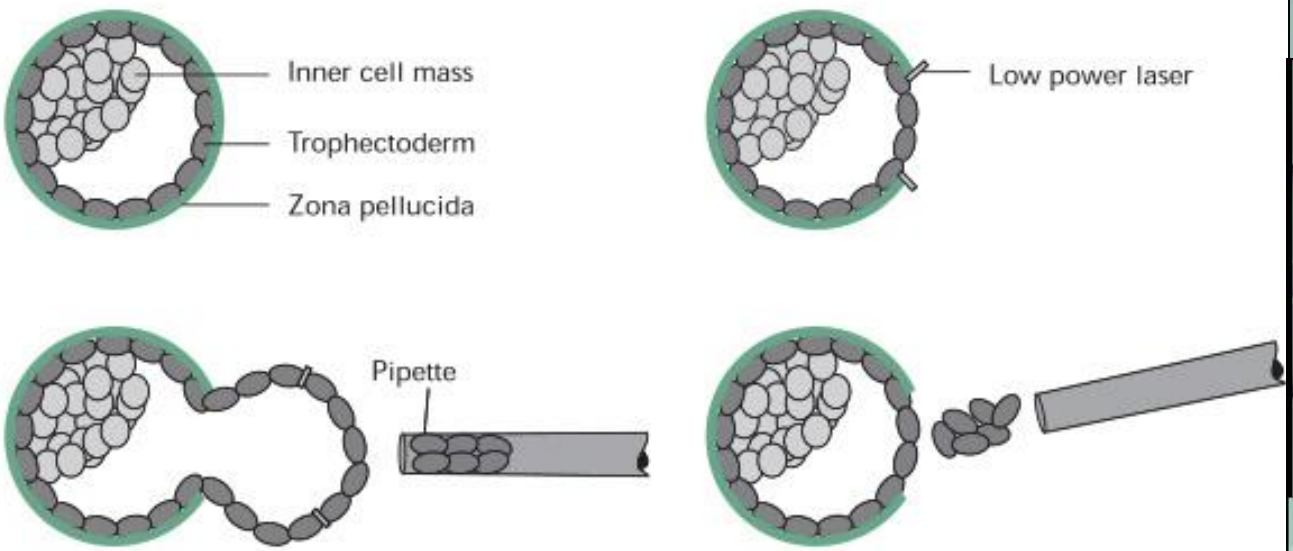
PGD-PCR



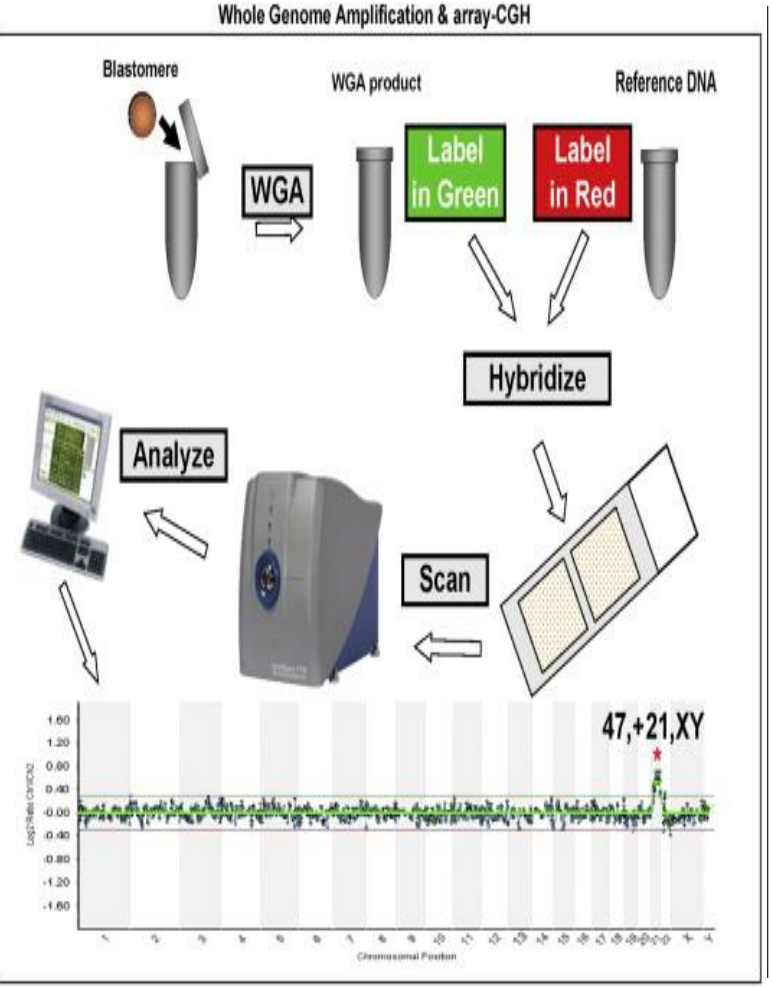


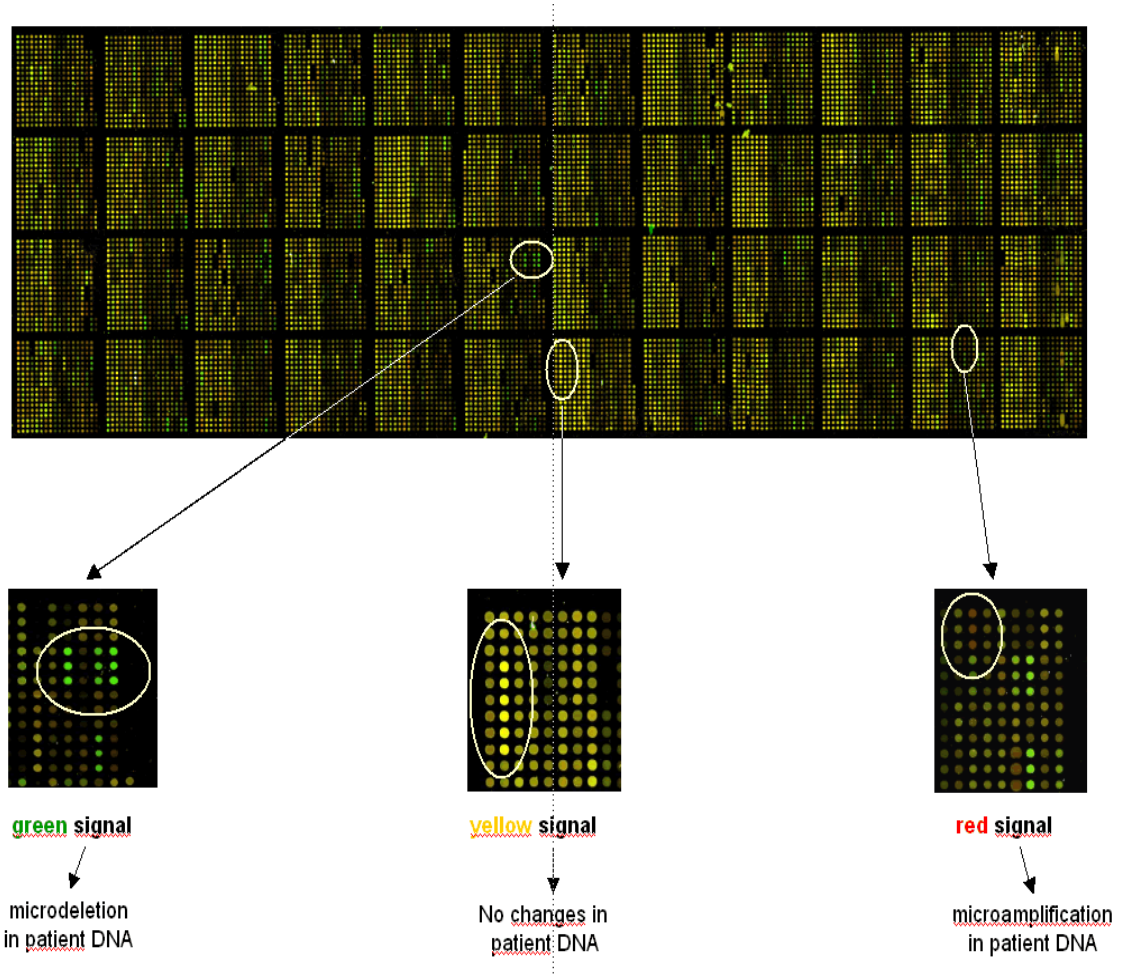
- **Doenças Autossômicas Dominantes**
  - Distrofia Miotônica
  - Doença de Huntington
- **Doenças Autossômicas Recessivas**
  - Fibrose Cística
  - b-talassemia
  - Atrofia Muscular Espinhal
- **Doenças Ligadas ao Cromossomo X**
  - Síndrome do X-frágil
  - Distrofia Muscular de Duchenne
  - Hemofilia

Alterações gênicas

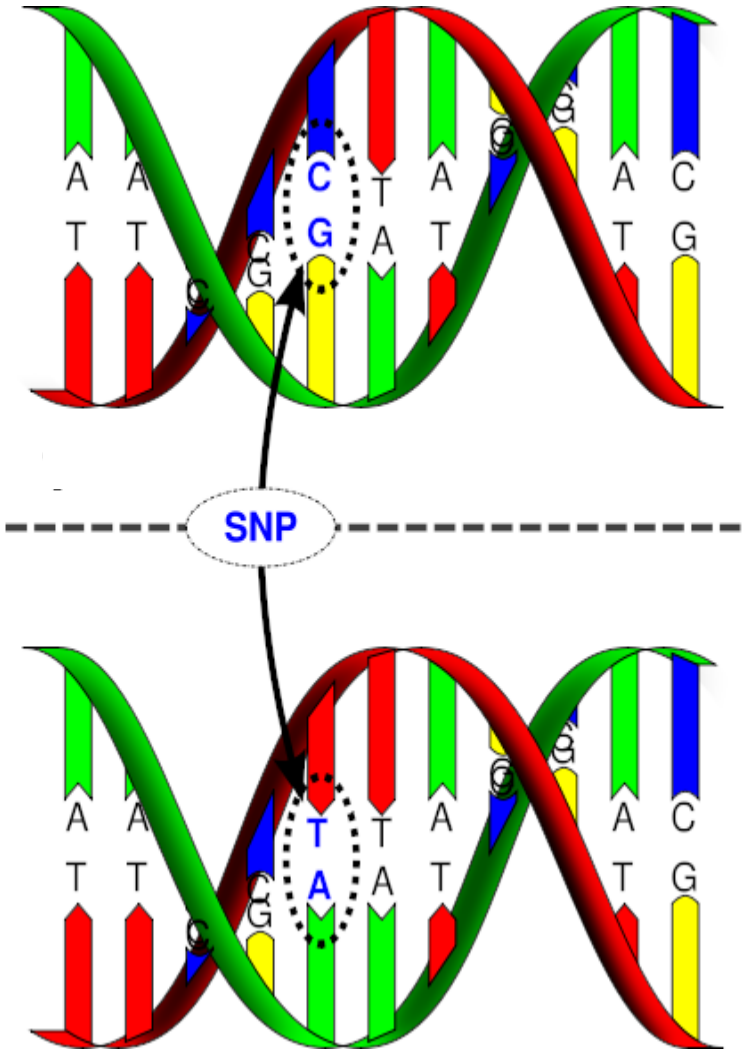

Inner cell mass
Trophectoderm
Zona pellucida
Low power laser
Pipette

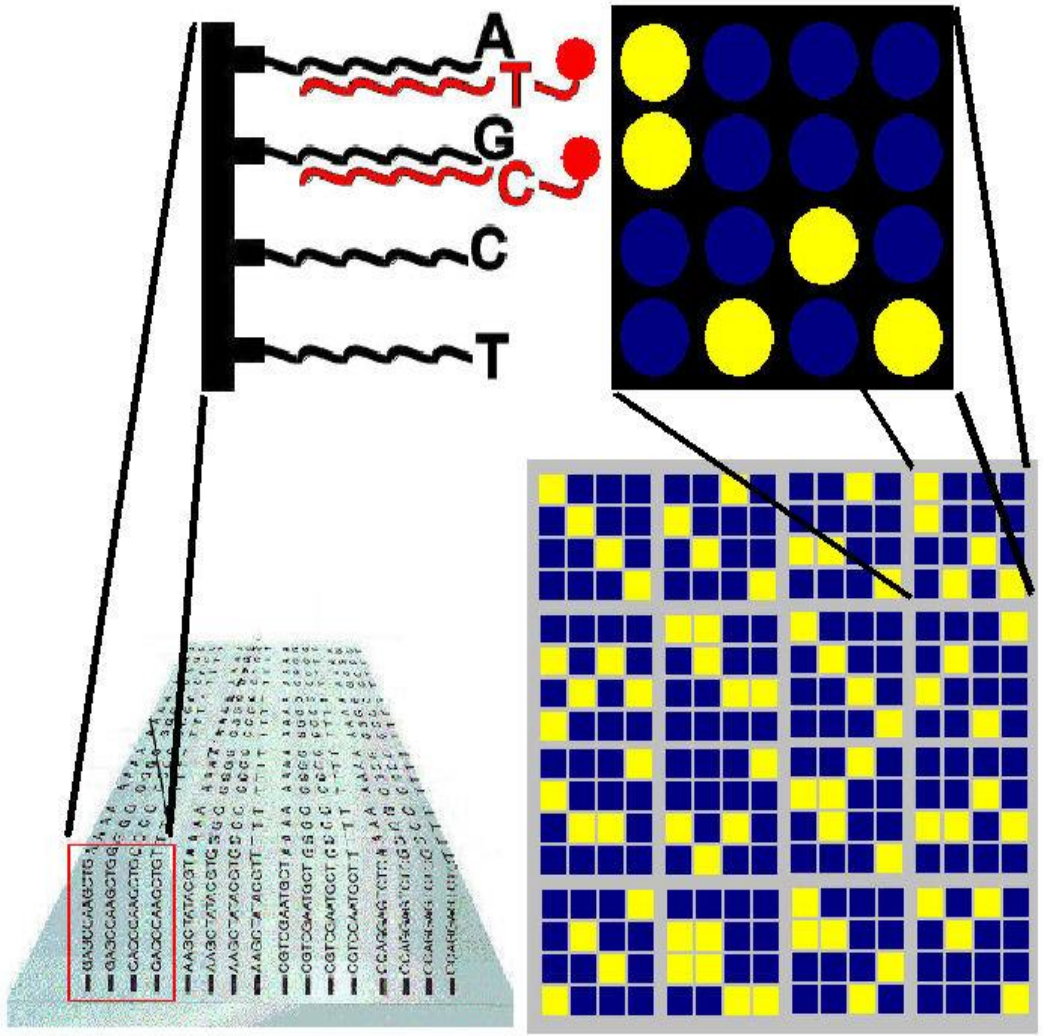
CGH - ARRAY


Whole Genome Amplification & array-CGH
Blastomere
WGA product
Reference DNA
WGA
Label in Green
Label in Red
Hybridize
Analyze
Scan
47,+21,XY

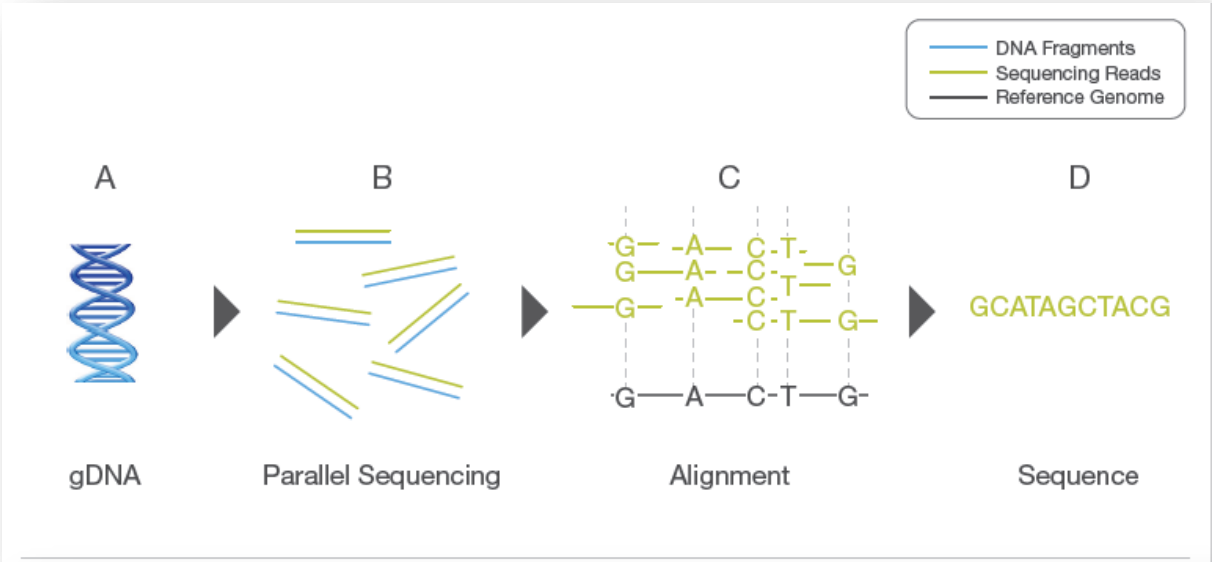

green signal
microdeletion in patient DNA
yellow signal
No changes in patient DNA
red signal
microamplification in patient DNA

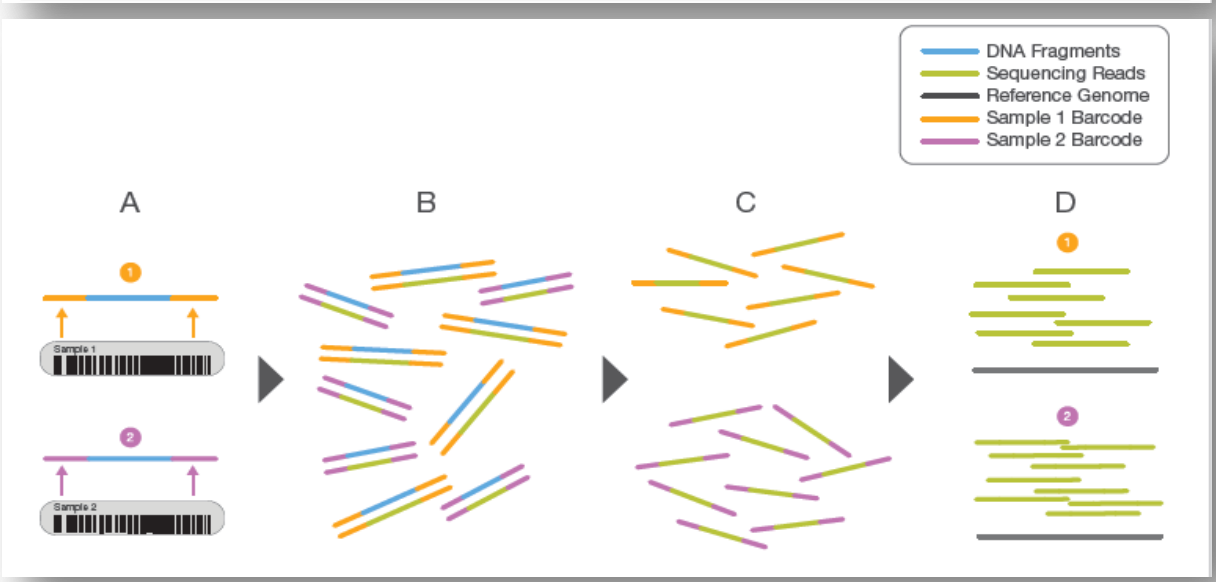
SNP - ARRAY





NGS – Next Generation Sequencing





FERTILITY MEDICAL GROUP

Dados FERTILITY 2012 – 2015

Ano	Procedimentos	PGS/PDG Ciclos	%
2012	1068	93	8,7
2013	1055	110	10,4
2014	1047	118	11,3
2015	1085	114	10,5
TOTAL	***4255***	***435***	***10,2***

FERTILITY 2012 - 2015: Resultados – técnica FISH

	N	%
Nº de casos	286	-
Nº de embriões obtidos	1959	-
Nº de embriões biopsiados	1455	74,3%
Nº de médio de embriões biopsiados/paciente	5,1	-
Falha técnica	25	1,7%
Normais	589	40,5%

Dados FERTILITY 2012 – 2015: PGS FISH (Day 3) *vs* ICSI

	PGS	ICSI	ICSI_D5 ≤35a	ICSI_D5 >35a
Ciclos	286	3481	779	685
Idade	39,2	36,4	31,9	38,9
Embriões transferidos	1,7	2,1	2,1	2,2
Taxa gestação / transferência	34,0%	38,3%	51,7%	37,8%
Taxa implantação	29,5%	28,3%	40,8%	27,0%
Taxa de abortamento	15,9%	14,0%	9,9%	14,5%
Gestação múltipla	23,1%	30,1%	36,8%	26,0%

Dados FERTILITY 2012 – 2015: PGS FISH (Day 3) *vs* ICSI

	PGS	ICSI_D5 >35a
Ciclos	286	685
Idade	39,2	38,9
Embriões transferidos	1,7	2,2
Taxa gestação / transferência	34,0%	37,8%
Taxa implantação	29,5%	27,0%
Taxa de abortamento	15,9%	14,5%
Gestação múltipla	23,1%	26,0%

p>0,05

FERTILITY MEDICAL GROUP

FERTILITY 2012 - 2015: Doenças avaliadas	Casos	%
Acidúria metilmalônica	2	3,8%
Amiotrofia espinhal	3	5,8%
Anemia falciforme	10	19,2%
Ataxia espinocerebelar	7	13,5%
Fibrose cística	2	3,8%
Gangliosidose	2	3,8%
Hemofilia	2	3,8%
HLA	3	5,8%
HLA associado à outras doenças	(15)	-
Imunodeficiência combinada grave (SCID)	4	7,7%
Rins policísticos	1	1,9%
Síndrome de Marfan	1	1,9%
Síndrome de Wolfran	1	1,9%
Talassemia	9	17,3%
X-frágil	5	9,6%
TOTAL	***52***	

FERTILITY 2012 - 2015: Resultados – técnica PCR

	N	%
Nº de casos	52	-
Nº de embriões obtidos	395	-
Nº de embriões biopsiados	283	71,6%
Nº de médio de embriões biopsiados/paciente	5,4	-
Falha técnica	21	7,4%
Normais	66	23,3%
Portadores	101	35,7%

FERTILITY 2012 - 2015: Resultados – técnica HLA

	N	%
Nº de casos	18	-
Nº de embriões biopsiados	122	-
Falha técnica	7	5,7%
Compatíveis	15	12,3%

Dados FERTILITY 2012 – 2015: PGD (Day 3) *vs* ICSI

	PGD	ICSI	ICSI_D5
Ciclos	52	3481	1464
Idade	35,0	36,4	35,2
Embriões transferidos	1,5	2,1	2,1
Taxa gestação / transferência	26,3%	38,3%	45,2%
Taxa implantação	28,1%	28,3%	34,2%
Taxa de abortamento	12,5%	14,0%	11,7%
Gestação múltipla	42,9%	30,1%	32,8%

P<0,05

FERTILITY 2015: Resultados – NGS

	N	%
Nº de casos	20	-
Nº de embriões obtidos	190	-
Nº de embriões biopsiados	73	-
Nº de médio de embriões biopsiados/paciente	3,6	-
Nº de embriões analisados	70	-
Nº de médio de embriões analisados/paciente	3,5	-
Falha técnica	0	0,0%
Normais	17	24,3%

Dados FERTILITY 2015: NGS (Day 5) *vs* ICSI

	NGS	ICSI	ICSI_D5 ≤35a	ICSI_D5 >35a
Ciclos	20	3481	779	685
Idade	38,4	36,4	31,9	38,9
Embriões transferidos	1,5	2,1	2,1	2,2
Taxa gestação / transferência	37,5%	38,3%	51,7%	37,8%
Taxa implantação	33,3%	28,3%	40,8%	27,0%
Taxa de abortamento	0,0%	14,0%	9,9%	14,5%
Taxa de gestação continuada	37,5%	30,1%	41,1%	28,6%

Dados FERTILITY 2015: NGS (Day 5) *vs* ICSI

	NGS	ICSI_D5 >35a
Ciclos	20	685
Idade	38,4	38,9
Embriões transferidos	1,5	2,2
Taxa gestação / transferência	37,5%	37,8%
Taxa implantação	33,3%	27,0%
Taxa de abortamento	0,0%	14,5%
Taxa de gestação continuada	37,5%	28,6%

P<0,05

FERTILITY MEDICAL GROUP

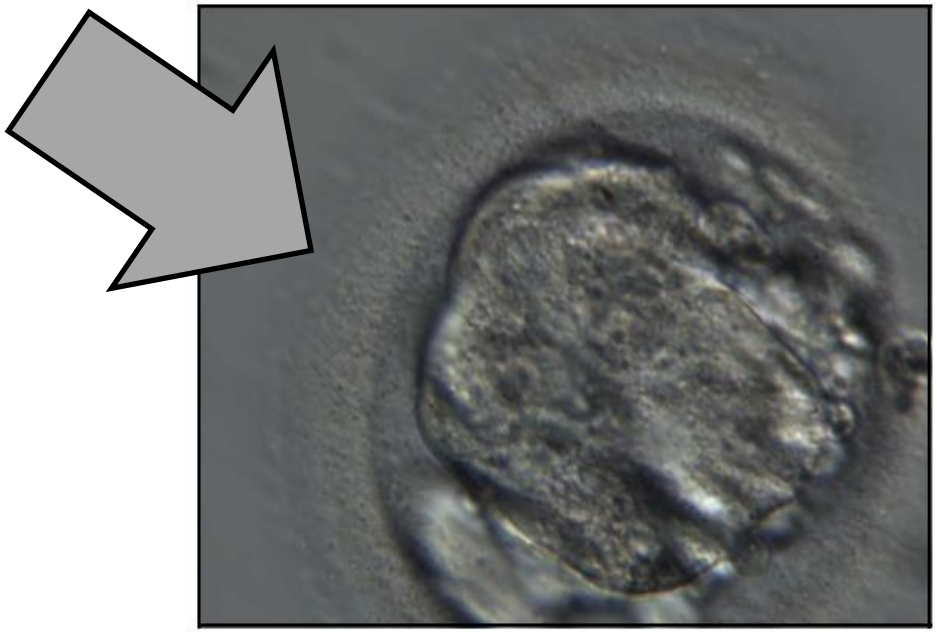
J Assist Reprod Genet (2012) 29:1305–1309
DOI 10.1007/s10815-012-9862-3

GENETICS

Preimplantation diagnosis for β-thalassemia combined with HLA matching: first "savior sibling" is born after embryo selection in Brazil

Rita C. S. Figueira · Amanda S. Setti · Sylvia S. Cortezzi · Ciro D. Martinhago · Daniela P. A. F. Braga · Assumpto Iaconelli Jr. · Edson Borges Jr.

This article presents the first Brazilian clinical experience demonstrating feasibility of combined PGD and HLA matching for β-thalassemia major, designed to preselect for transfer only those unaffected embryos that are HLA antigen compatible with a sibling needing cord blood transplantation.

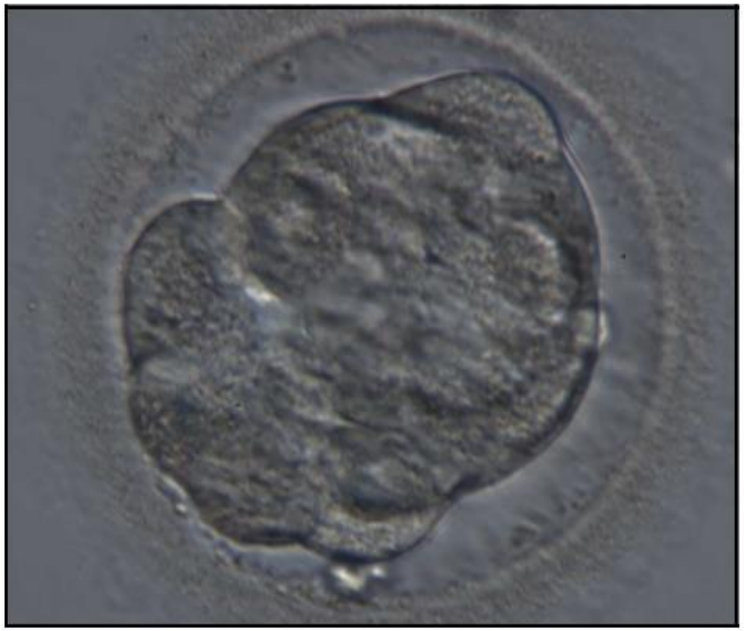


Timestamp

13/06/2011 07:53:52

Comment

Embrião 13 - Transferido
Dia +5 - Compactando
(Compacto na
transferência)
Resultado de PGD:
Normal, HLA compatível



Timestamp

13/06/2011 07:55:41

Comment

Embrião 15 - Transferido
Dia +5 - Compacto
Resultado de PGD:
Traço materno, HLA
compatível

ESTADÃO.COM.BR

Transplante inédito de cordão e medula cura menina com talassemia

A doadora, Maria Clara, de 1 ano, nasceu após ter sido selecionada geneticamente para não carregar o gene da talassemia e ser 100% compatível com a irmã, Maria Vitória, de 6

19 de abril de 2013 | 2h 05

ARTICLE IN PRESS

Reproductive BioMedicine Online (2016) ■■, ■■-■■

ELSEVIER

www.sciencedirect.com
www.rbmonline.com

Reproductive BioMedicine Online

ARTICLE

Assisted reproductive techniques in Latin America: the Latin American Registry, 2013

Fernando Zegers-Hochschild [a,b,c,*], Juan Enrique Schwarze [c,d], Javier A Crosby [a,c], Carolina Musri [a,c], Maria Teresa Urbina [c,e] on behalf of the Latin American Network of Assisted Reproduction (REDLARA)

PGS/PGD

- 86 centros – 12 países
- 1920 ciclos – 56% blastocisto
- ~ 4 embriões analisados / ~1 embrião normal
- 208 gestações clínicas, 174 partos, 199 cças nascidas

Human Reproduction, Vol.30, No.8 pp. 1763–1789, 2015
Advanced Access publication on June 12, 2015 doi:10.1093/humrep/dev122

human reproduction

ESHRE PAGES

ESHRE PGD Consortium data collection XIII: cycles from January to December 2010 with pregnancy follow-up to October 2011†

M. De Rycke[1,*], F. Belva[1], V. Goossens[2], C. Moutou[3], S.B. SenGupta[4], J. Traeger-Synodinos[5], and E. Coonen[6]

- Thirteen sets of data on 45,073cycles / 7,751 babies born
- 62 registered centers
- Inherited chromosomal abnormalities: 6,968 cycles
- Monogenic disorders: 9,267 cycles
- Sexing for X-linked diseases: 1,484 cycles / social: 753 cycles
- Aneuploidy screening: 26,737 cycles
- FISH: 78% (I-XII) – 68% (XIII) – array: 355 cycles (6%)
- Clin preg rate (% per OR / % per ET): 22/28

Human Reproduction, Vol.30, No.8 pp. 1763–1789, 2015
Advanced Access publication on June 12, 2015 doi:10.1093/humrep/dev122

human reproduction ESHRE PAGES

ESHRE PGD Consortium data collection XIII: cycles from January to December 2010 with pregnancy follow-up to October 2011†

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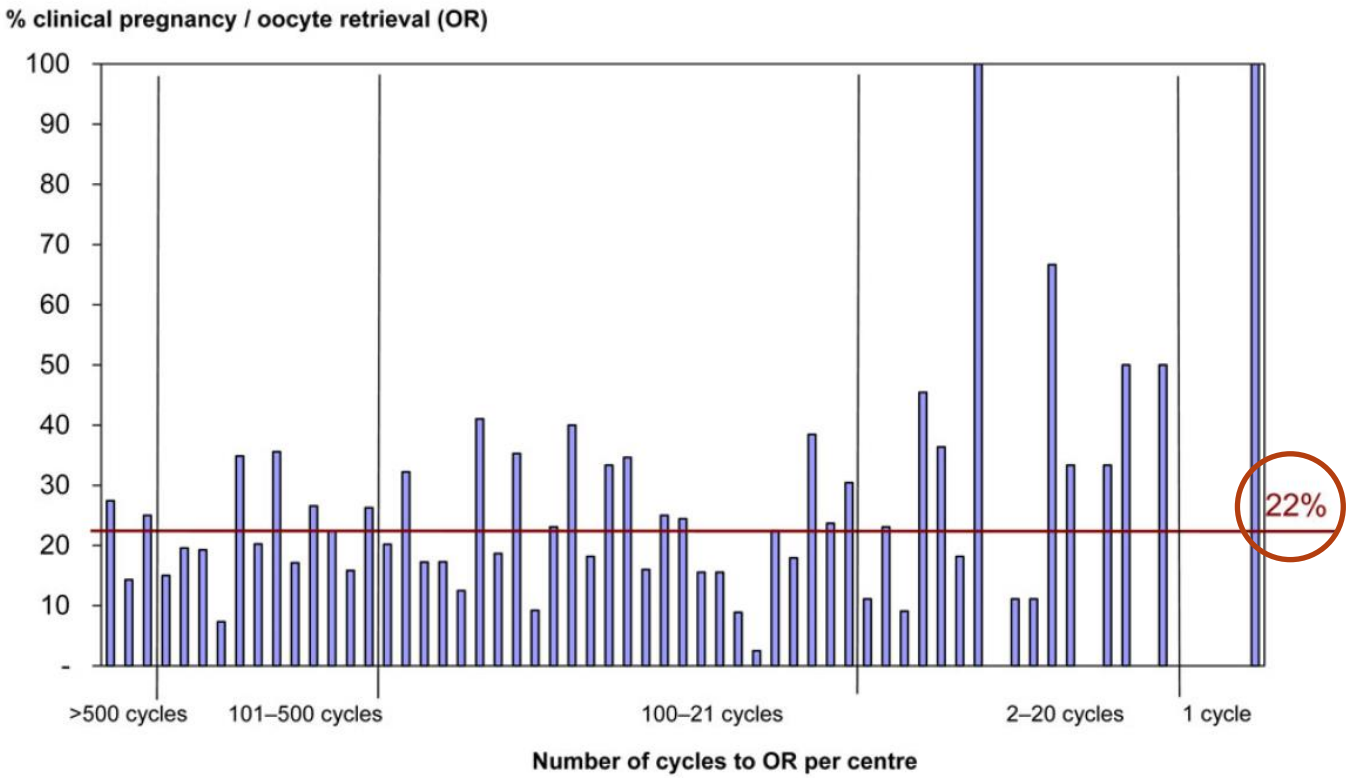

Figure 1 Clinical pregnancy rates per centre. OR: oocyte retrieval.

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CHROMOSOME

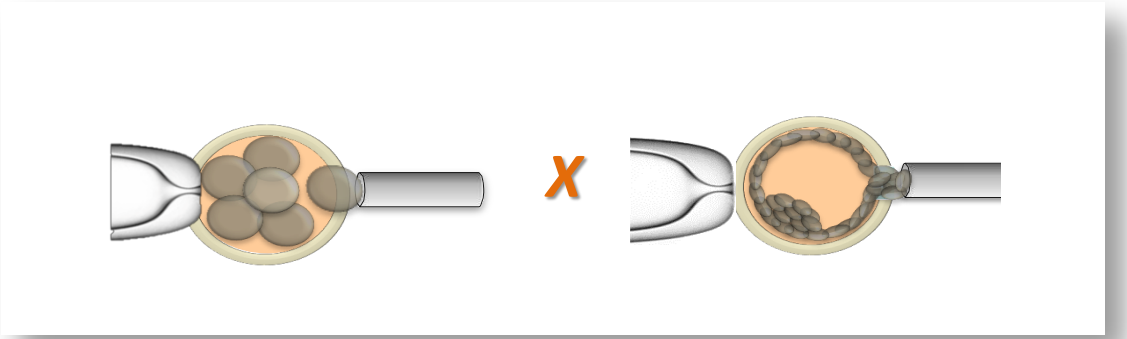
Cleavage-stage biopsy significantly impairs human embryonic implantation potential while blastocyst biopsy does not: a randomized and paired clinical trial

Richard T. Scott Jr., M.D.,[a,b] Kathleen M. Upham, B.S.,[a] Eric J. Forman, M.D.,[b] Tian Zhao, M.S.,[a] and Nathan R. Treff, Ph.D.[a,b,c]

[a] Reproductive Medicine Associates of New Jersey, Morristown; [b] Division of Reproductive Endocrinology, Department of Obstetrics, Gynecology, and Reproductive Sciences, Robert Wood Johnson Medical School, Rutgers University, New Brunswick; and [c] Department of Genetics, Rutgers–State University of New Jersey, Piscataway, New Jersey

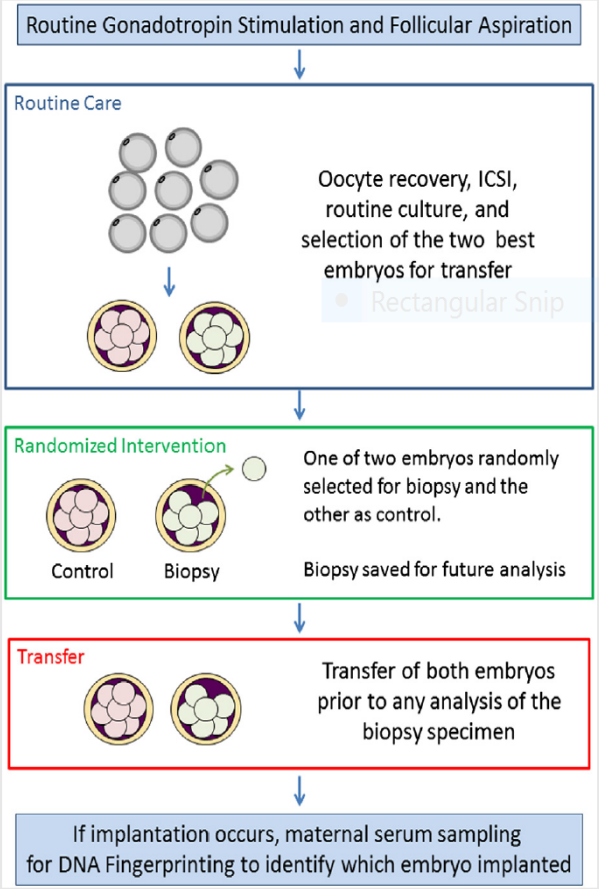
Fertility and Sterility® Vol. 100, No. 3, September 2013 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2013.04.039



FERTILITY MEDICAL GROUP

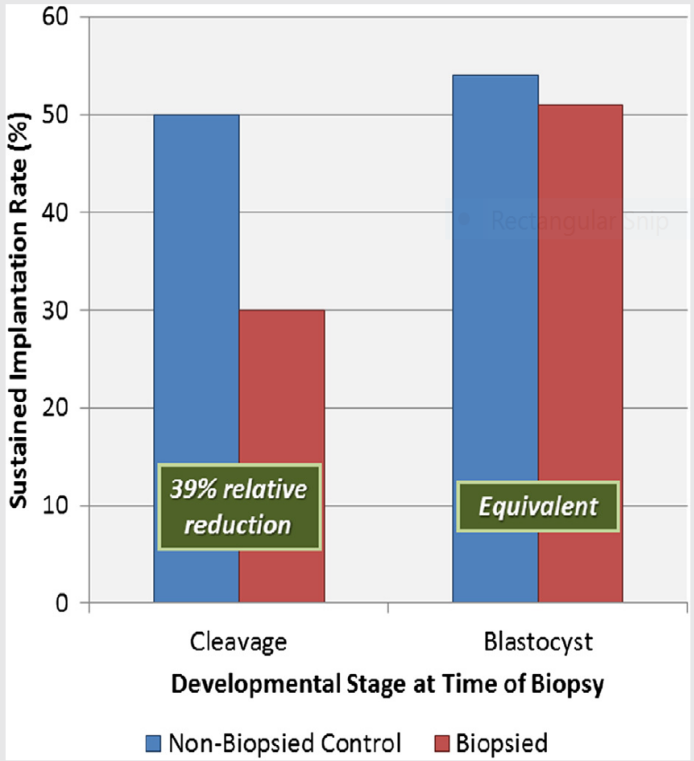
FIGURE 1



Study design to assess the impact of biopsy at the cleavage stage (day 3) on embryonic reproductive potential. The randomized paired experimental design allowed each patient to serve as her own control. An equivalent methodology was used to determine if trophectoderm biopsy at the blastocyst stage affected embryonic potential. ICSI = intracytoplasmic sperm injection.

Scott. Cleavage-stage biopsy is harmful. Fertil Steril 2013.

FIGURE 3



Implantation rates following a randomized paired analysis of the effects of cleavage- and blastocyst-stage biopsies on embryo reproductive potential. Sustained implantation and delivery of the biopsied embryo were significantly reduced compared with its control sibling when biopsy was performed on day 3 at the cleavage stage (McNemar chi-square: $P<.03$). A similar paired analysis demonstrated that the developmental potential of embryos undergoing trophectoderm biopsy at the blastocyst stage was equivalent to the nonbiopsied control siblings.

Scott. Cleavage-stage biopsy is harmful. Fertil Steril 2013.

ORIGINAL ARTICLE
doi: 10.5653/cerm.2011.38.1.31
pISSN 2233-8233 · eISSN 2233-8241
Clin Exp Reprod Med 2011;38(1):31-36

CERM

Does blastomere biopsy in preimplantation genetic diagnosis affect early serum β-hCG levels?

Yeon Jean Cho[1], Jin Yeong Kim[1], In Ok Song[1], Hyung Song Lee[2], Chun Kyu Lim[2], Mi Kyoung Koong[1], Inn Soo Kang[1]

[1]Department of Obstetrics and Gynecology, [2]Laboratory of Reproductive Biology and Infertility, Cheil General Hospital & Women's Healthcare Center, Kwandong University College of Medicine, Seoul, Korea

2000 – 2006
Biópsia Dia 3
1290 ciclos positivos avaliados

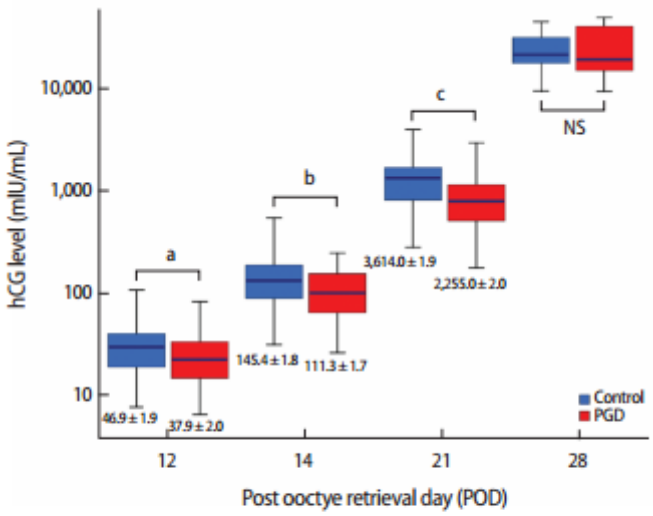


Figure 2. The highest and lowest quartile mean values of serum human chorionic gonadotrophin (hCG) on POD 12, 14, 21, and 28 in the preimplantation genetic diagnosis (PGD) and control groups. Values are presented as mean ± SD. NS, not significant.
[a]$p = 0.023$, [b]$p = 0.006$, [c]$p = 0.000$.

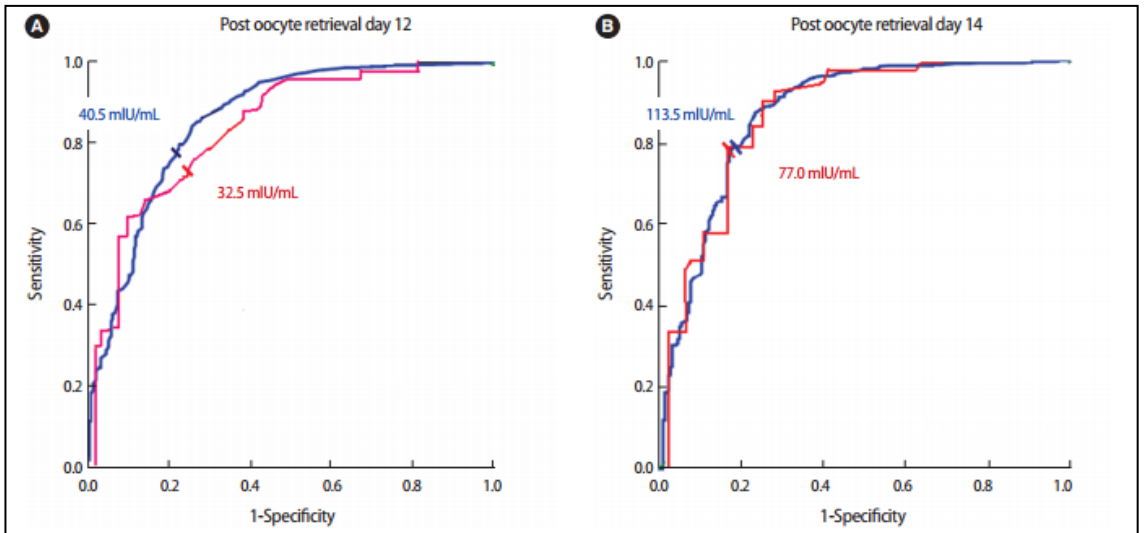


Figure 3. Nonparametric receiver-operating characteristic plots of calculated day 12 (A) and 14 (B) serum β-hCG levels to distinguish between viable pregnancies in both groups. Red line, preimplantation genetic diagnosis group; Blue line, control group.

FERTILITY MEDICAL GROUP

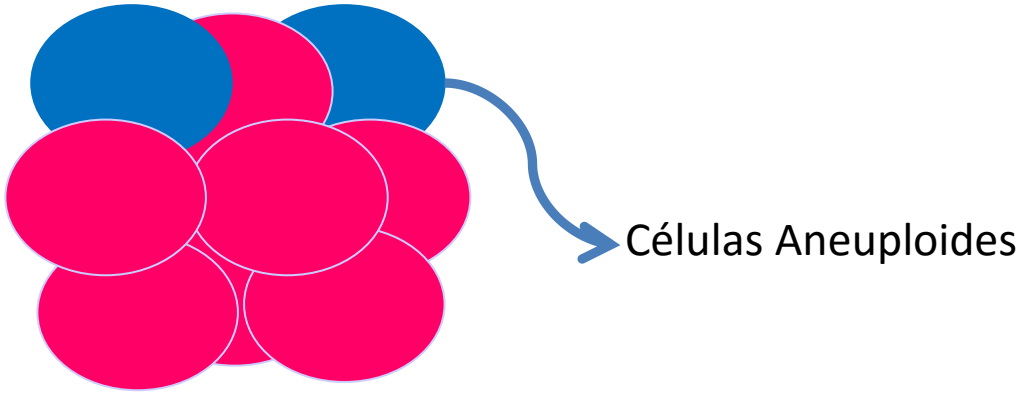
Biópsia em Estágio de Clivagem

LIMITAÇÕES

- Mosaicismo
- Autocorreção

EM DIA 3

Células biopsiadas podem não representar a totalidade das células do restante do embrião



- Embrião 8 cels : 91% mosaicos - 50% aneuploides
  - Abortos: 30% aneuploides
  - Natimortos: 20% aneuploides
  - Nascidos: 0.3% aneuploides

Autocorreção

Fertility and Sterility® Vol. 92, No. 3, September 2009

GENETICS

Preimplantation aneuploid embryos undergo self-correction in correlation with their developmental potential

Shiri Barbash-Hazan, B.Sc.,[a,*,#] *Tsvia Frumkin, M.Sc.,*[a,*] *Mira Malcov, Ph.D.,*[a] *Yuval Yaron, M.D.,*[b] *Tania Cohen, M.Sc.,*[a] *Foad Azem, M.D.,*[a] *Ami Amit, M.D.,*[a] *and Dalit Ben-Yosef, Ph.D.*[a]

[a] Racine IVF Unit and [b] Prenatal Diagnosis Unit, Genetic Institute, Lis Maternity Hospital, Tel-Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Existence of a possible self-correction mechanism of aneuploid embryos which occurs probably more significantly during development toward the blastocyst stage

Autocorreção

0015-0282/$36.00
doi:10.1016/j.fertnstert.2011.07.1087
Fertility and Sterility® Vol. 96, No. 4, October 2011

GENETICS

Self-correction in tripronucleated human embryos

Noelia Grau, Ph.D.,[a] *Laura Escrich, Ph.D.,*[a] *Julio Martín, Ph.D.,*[a] *Carmen Rubio, Ph.D.,*[a] *Antonio Pellicer, M.D.,*[a,b] *and María-José Escribá, Ph.D.*[a]

[a] Universitary Institute Instituto Valenciano de Infertilidad Valencia, and [b] Department of Paediatrics, Obstetrics and Gynaecology, University School of Medicine, Valencia University, Valencia, Spain

Half of ICSI-TPN embryos became self-corrected blastocysts

IDADE MATERNA AVANÇADA

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 5, 2007 VOL. 357 NO. 1

In Vitro Fertilization with Preimplantation Genetic Screening

Sebastiaan Mastenbroek, M.Sc., Moniek Twisk, M.D., Jannie van Echten-Arends, Ph.D., Birgit Sikkema-Raddatz, Ph.D., Johanna C. Korevaar, Ph.D., Harold R. Verhoeve, M.D., Niels E.A. Vogel, M.D, Eus G.J.M. Arts, Ph.D., Jan W.A. de Vries, Ph.D., Patrick M. Bossuyt, Ph.D., Charles H.C.M. Buys, Ph.D., Maas Jan Heineman, M.D., Ph.D., Sjoerd Repping, Ph.D., and Fulco van der Veen, M.D., Ph.D.

206 PGS cycles

202 Control cycles

Live birth rate: 24% with PGS and 35% in controls

IDADE MATERNA AVANÇADA

Human Reproduction, Vol.25, No.4 pp. 821–823, 2010
Advanced Access publication on February 2, 2010 doi:10.1093/humrep/dep476

human reproduction ESHRE PAGES

What next for preimplantation genetic screening (PGS)? A position statement from the ESHRE PGD Consortium steering committee†

Joyce Harper[1,12], Edith Coonen[2], Martine De Rycke[3], Francesco Fiorentino[4], Joep Geraedts[2], Veerle Goossens[5], Gary Harton[6], Celine Moutou[7], Tugce Pehlivan Budak[8], Pam Renwick[9], Sioban SenGupta[1], Joanne Traeger-Synodinos[10], and Katerina Vesela[11]

There is now ample evidence that PGS for advanced maternal age, using cleavage stage biopsy and FISH testing of a limited number of chromosomes is not a valid procedure and should be replaced by more appropriate approaches.

Human Reproduction, Vol.25, No.4 pp. 821–823, 2010
Advanced Access publication on February 2, 2010 doi:10.1093/humrep/dep476

human reproduction ESHRE PAGES

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Currently there is no evidence that routine PGS is beneficial for patients with AMA and conclusive data (RCTs) on repeated miscarriage, implantation failure and severe male factor are missing.

Human Reproduction Update, Vol.17, No.4 pp. 454–466, 2011
Advanced Access publication on April 29, 2011 doi:10.1093/humupd/dmr003

human reproduction update

Preimplantation genetic screening: a systematic review and meta-analysis of RCTs

S. Mastenbroek*, M. Twisk, F. van der Veen, and S. Repping

Center for Reproductive Medicine, Academic Medical Center, University of Amsterdam, Meibergdreef 9, 1105 AZ, Amsterdam, The Netherlands

*Correspondence address. Tel: +31-20-5663090; E-mail: s.mastenbroek@amc.uva.nl

Submitted on December 31, 2009; resubmitted on January 10, 2011; accepted on January 31, 2011

There is no evidence of a beneficial effect of PGS as currently applied on the live birth rate after IVF. On the contrary, for women of advanced maternal age, PGS significantly lowers the live birth rate.

Human Reproduction, Vol.30, No.2 pp. 473–483, 2015
Advanced Access publication on November 28, 2014 doi:10.1093/humrep/deu303

human reproduction

REVIEW *Reproductive genetics*

The clinical effectiveness of preimplantation genetic diagnosis for aneuploidy in all 24 chromosomes (PGD-A): systematic review

Evelyn Lee[1,*], Peter Illingworth[2], Leeanda Wilton[3], and Georgina Mary Chambers[1]

[1]National Perinatal Epidemiology and Statistics Unit, School of Women's and Children's Health, University of New South Wales (UNSW), Level 2, McNevin Dickson Building, Randwick Hospitals Campus, Sydney 2031, Australia [2]IVF Australia Pty Ltd, 176 Pacific Highway, Greenwich, Sydney 2065, Australia [3]Melbourne IVF, Victoria Parade, East Melbourne, VIC 3002, Australia

PARTICIPANTS/MATERIALS, SETTINGS, METHODS: Nineteen articles meeting the inclusion criteria, comprising three RCTs in young and good prognosis patients and 16 observation studies were identified. Five of the observational studies included a control group of patients where embryos were selected based on morphological criteria (matched cohort studies).

Human Reproduction, Vol.30, No.2 pp. 473–483, 2015
Advanced Access publication on November 28, 2014 doi:10.1093/humrep/deu303

human reproduction

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Inclusion criteria

A cohort of patients using one of CGH, aCGH, SNP array or qPCR for PGD-A

Study with 20 and more patients

Papers written in English

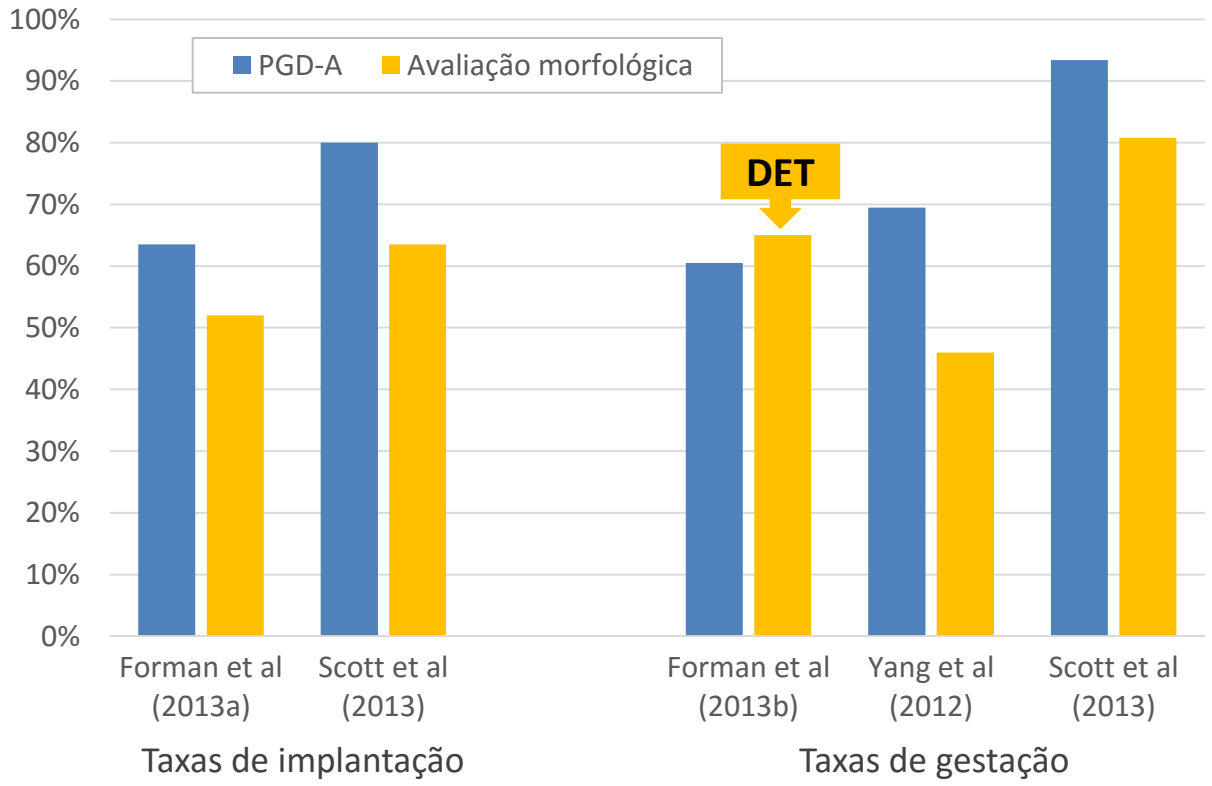
Experimental and observational studies

Inclusion of outcome measures that include either rates of clinical pregnancy, ongoing pregnancy, miscarriage or live births

Published in peer reviewed journal

Taxas de implantação e gestação com PGD-A:

ERCs com pacientes jovens

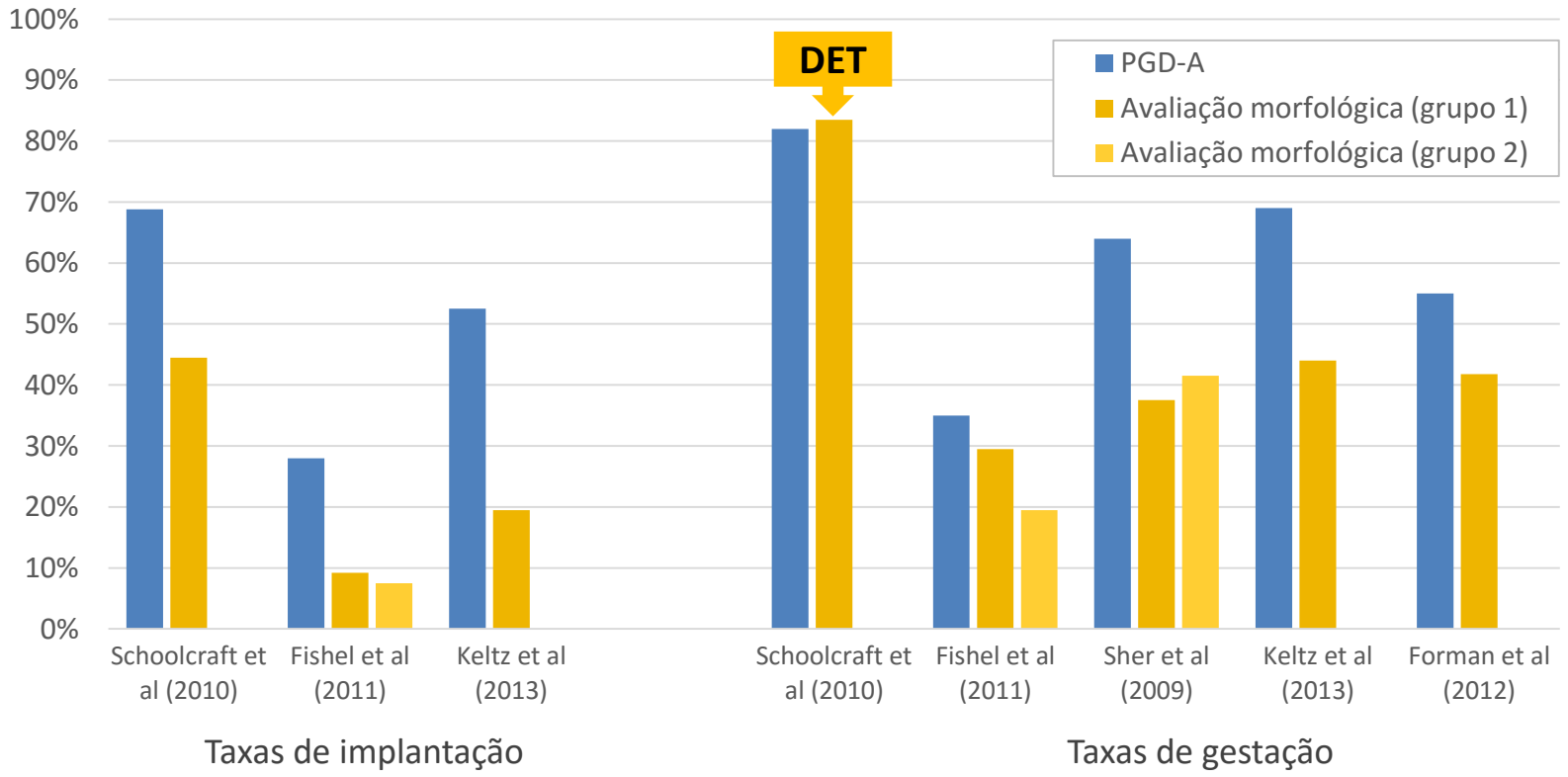


ERCs = estudos randomizados e controlados.

Lee E, *et al*. *Hum Reprod* 2015;30:473–83

Taxas de implantação e gestação com PGD-A:

Mulheres em idade materna avançada



ERCs = estudos randomizados e controlados.

Lee E, *et al*. *Hum Reprod* 2015;30:473–83

II Workshop Internacional de Genética Reprodutiva

Outcomes of in vitro fertilization with preimplantation genetic diagnosis: an analysis of the United States Assisted Reproductive Technology Surveillance Data, 2011–2012

Jeani Chang, M.P.H., Sheree L. Boulet, Dr.P.H., Gary Jeng, Ph.D., Lisa Flowers, M.P.A., and Dmitry M. Kissin, M.D., M.P.H.

Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

Fertility and Sterility® Vol. 105, No. 2, February 2016

- **PGD em 9,2% dos ciclos**
- **56% investigação de aneuploidias**
- **Mulheres ≤ 35 anos: taxas ~ gestação e nascimentos (numericamete menores)**
- ***Nos ciclos com transferência embrionária e investigação das ANEUPLOIDIAS:***

- **Mulheres ≥ 35 anos: menores taxas de aborto (aOR 0,55 – 0,62)**
- **Mulheres > 37 anos: maiores taxas de gravidez clínica, nascimento e de gestação múltipla (aOR: 1,18 – 1,43 – 1,98)**

II Workshop Internacional de Genética Reprodutiva

1- PGS/PGD: conceitos
2- Survey IVF-Worldwide
3- Técnicas e Resultados
4- Eficácia e Limitações
5- Segurança
6- Análise Crítica
7- Considerações

CHROMOSOME

Human Reproduction, Vol.25, No.1 pp. 6–8, 2010
doi:10.1093/humrep/dep428

human reproduction

EDITORIAL COMMENTARY

Children born after preimplantation genetic diagnosis show no increase in congenital anomalies

Joe Leigh Simpson[1]

College of Medicine, Florida International University, Miami, FL 33199, USA

[1]Corresponding address. Tel: +1-305-348-0570; Fax: +1-305-348-0651; Email: simpsonj@fiu.edu

In experienced hands, removal of one (or more) blastomeres does not result in an increase in birth defects.

The same should apply to polar body or blastocyst biopsy.

Whatever the controversy concerning efficacy of PGD/PGS in increasing pregnancy rates, patients may be informed that PGD/PGS is safe.

Human Reproduction, Vol.27, No.1 pp. 288–293, 2012
Advanced Access publication on November 2, 2011 doi:10.1093/humrep/der360

human reproduction

ORIGINAL ARTICLE *Reproductive genetics*

Neonatal follow-up of 995 consecutively born children after embryo biopsy for PGD

S. Desmyttere[1,*], M. De Rycke[1], C. Staessen[1], I. Liebaers[1], F. De Schrijver[1], W. Verpoest[2], P. Haentjens[3], and Maryse Bonduelle[1]

Embryo biopsy for PGD does not introduce extra risk to the overall medical condition of newborn children. Multiples born following embryo biopsy appear to be at lower risk for low birthweight compared with multiples born following ICSI.

Human Reproduction, Vol.28, No.6 pp. 1508–1518, 2013
Advanced Access publication on March 27, 2013 doi:10.1093/humrep/det073

human reproduction

ORIGINAL ARTICLE *Embryology*

The effect of preimplantation genetic screening on neurological, cognitive and behavioural development in 4-year-old children: follow-up of a RCT

P. Schendelaar[1], K.J. Middelburg[2], A.F. Bos[3], M.J. Heineman[2], J.H. Kok[4], S. La Bastide-Van Gemert[5], J. Seggers[1], E.R. Van den Heuvel[5], and M. Hadders-Algra[1,*]

PGS does not seem to affect neurological, cognitive and behavioral development of 4-year-old singletons; however, this data suggest that it may be associated with altered neurodevelopment in twins.

Human Reproduction, Vol.29, No.9 pp. 1968–1977, 2014
Advanced Access publication on July 3, 2014 doi:10.1093/humrep/deu165

human reproduction ORIGINAL ARTICLE *Psychology and counselling*

Cognitive and psychomotor development of 5- to 6-year-old singletons born after PGD: a prospective case–controlled matched study

C. Winter[1,2,*], F. Van Acker[3], M. Bonduelle[2], S. Desmyttere[2], F. De Schrijver[2], and J. Nekkebroeck[1,2]

[1]Department of Developmental and Lifespan Psychology, Vrije Universiteit Brussel (VUB), Pleinlaan 2, Brussels 1050, Belgium [2]Centre for Medical Genetics, UZ Brussel, Vrije Universiteit Brussel (VUB), Laarbeeklaan 101, 1090 Brussels, Belgium [3]Open Universiteit, Heerlen, The Netherlands

Human Reproduction, Vol.30, No.5 pp. 1122–1136, 2015
Advanced Access publication on March 6, 2015 doi:10.1093/humrep/dev036

human reproduction ORIGINAL ARTICLE *Psychology and counselling*

Psychosocial development of full term singletons, born after preimplantation genetic diagnosis (PGD) at preschool age and family functioning: a prospective case-controlled study and multi-informant approach

C. Winter[1,2,*], F. Van Acker[3], M. Bonduelle[2], S. Desmyttere[2], and J. Nekkebroeck[1,2]

[1]Department of Developmental and Lifespan Psychology, Vrije Universiteit Brussel (VUB), Pleinlaan 2, 1050 Brussels, Belgium
[2]Centre for Medical Genetics, Reproduction and Genetics, Reproduction - Genetics and Regenerative Medicine, Vrije Universiteit Brussel (VUB), UZ Brussel, Laarbeeklaan 101, 1090 Brussel, Belgium [3]Artesis, Plantijn Hogeschool, Lange Nieuwstraat 101, 2000 Antwerpen, Belgium

II Workshop Internacional de Genética Reprodutiva

Agenda

1- PGS/PGD: conceitos
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5- Segurança
6- Análise crítica e considerações

CHROMOSOME

II Workshop Internacional de Genética Reprodutiva

NGS – next generation sequencing

Vantagens

Melhor selecionamento permitindo *eSET*
Maior chance de gestação / transferência
Menor tempo para gestação
Menor chance de abortamento
Análise aneuploidias + SGD (*single gene defect*)

Limitações

Maior envolvimento laboratorial (hatching, observação contínua..)
Criopreservação (1/1 haste)
Novo ciclo de tratamento
Maior custo
Maior risco de não transferência

CHROMOSOME

II Workshop Internacional de Genética Reprodutiva

Diagnóstico Genético Pré-Implantacional

- *A biópsia embrionária é uma técnica DIAGNÓSTICA*; não muda o potencial genético do embrião
- Deve ser usado para SELECIONAMENTO EMBRIONÁRIO, com o objetivo de determinar quais embriões serão transferidos antes, baseado no seu potencial de implantação e diminuir o tempo para a gestação
- *Cada vez mais solicitada pelo casal, cujo principal objetivo é o diagnóstico das aneuplodias*

CHROMOSOME

II Workshop Internacional de Genética Reprodutiva

Diagnóstico Genético Pré-Implantacional

- *Indicado para mulheres com idade ≥ 37 anos*
- *Técnica a ser empregada: NGS*
- *FISH: deve ser abandonado para seleção embrionária. Para ANEUPLOIDIAS ???*
- *NGS: discordância de 3-5% entre células do trofectoderme e massa celular interna; diagnóstico do embrião e não do feto*

CHROMOSOME

Obrigado!

FERTILITY®
MEDICAL GROUP

edson@fertility.com.br