

IMPACT OF PATERNAL AGE, EJACULATORY ABSTINENCE LENGTH AND SEMEN QUALITY ON THE OUTCOMES OF INTRACYTOPLASMIC SPERM INJECTION (ICSI) IN AN EGG-SHARING DONATION PROGRAM

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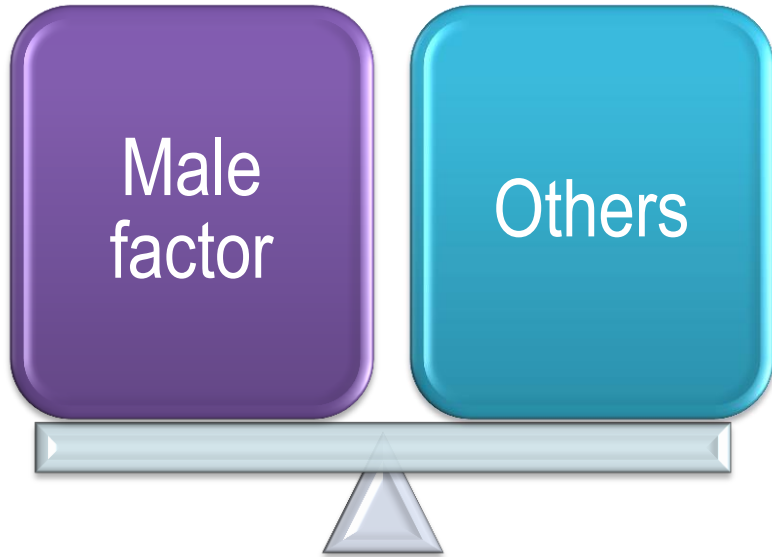
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INTRODUCTION

Infertility: 15% of the couples



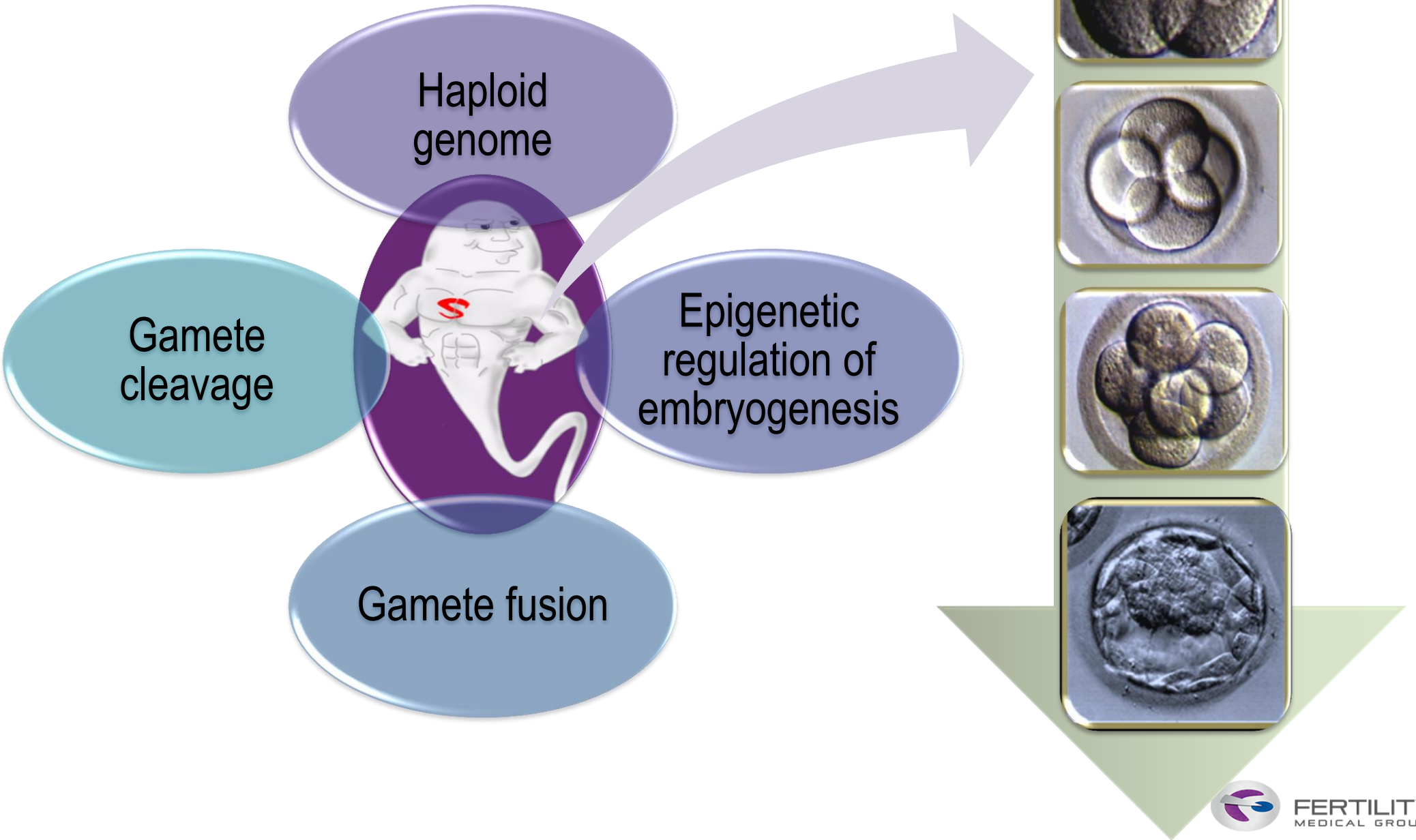
Male partner factors



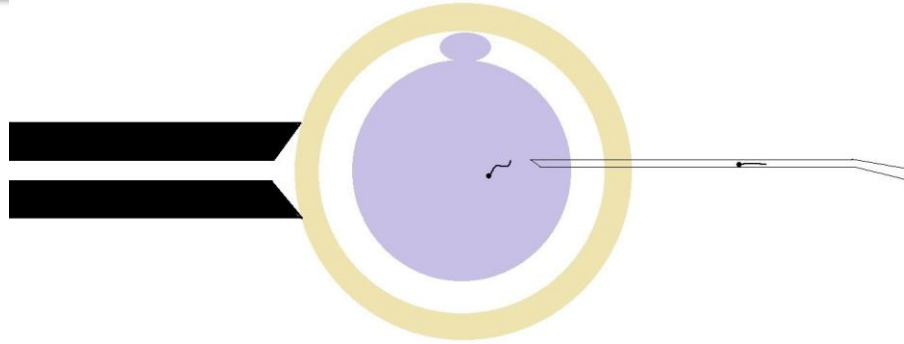
IVF

Most of the existing literature focuses on female infertility or on the fertility of both partners

INTRODUCTION

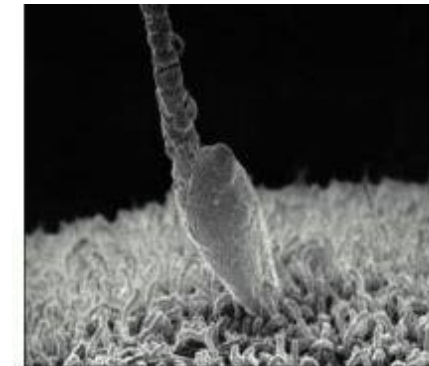


INTRODUCTION



concerns about
the contribution of
the male factor to
IVF outcomes

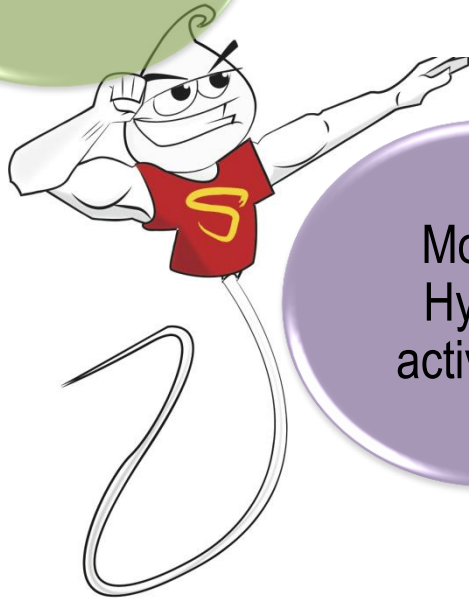
ICSI improve outcomes over conventional IVF for
male factor infertility



Molecular Biology of the Cell, 4th ed.

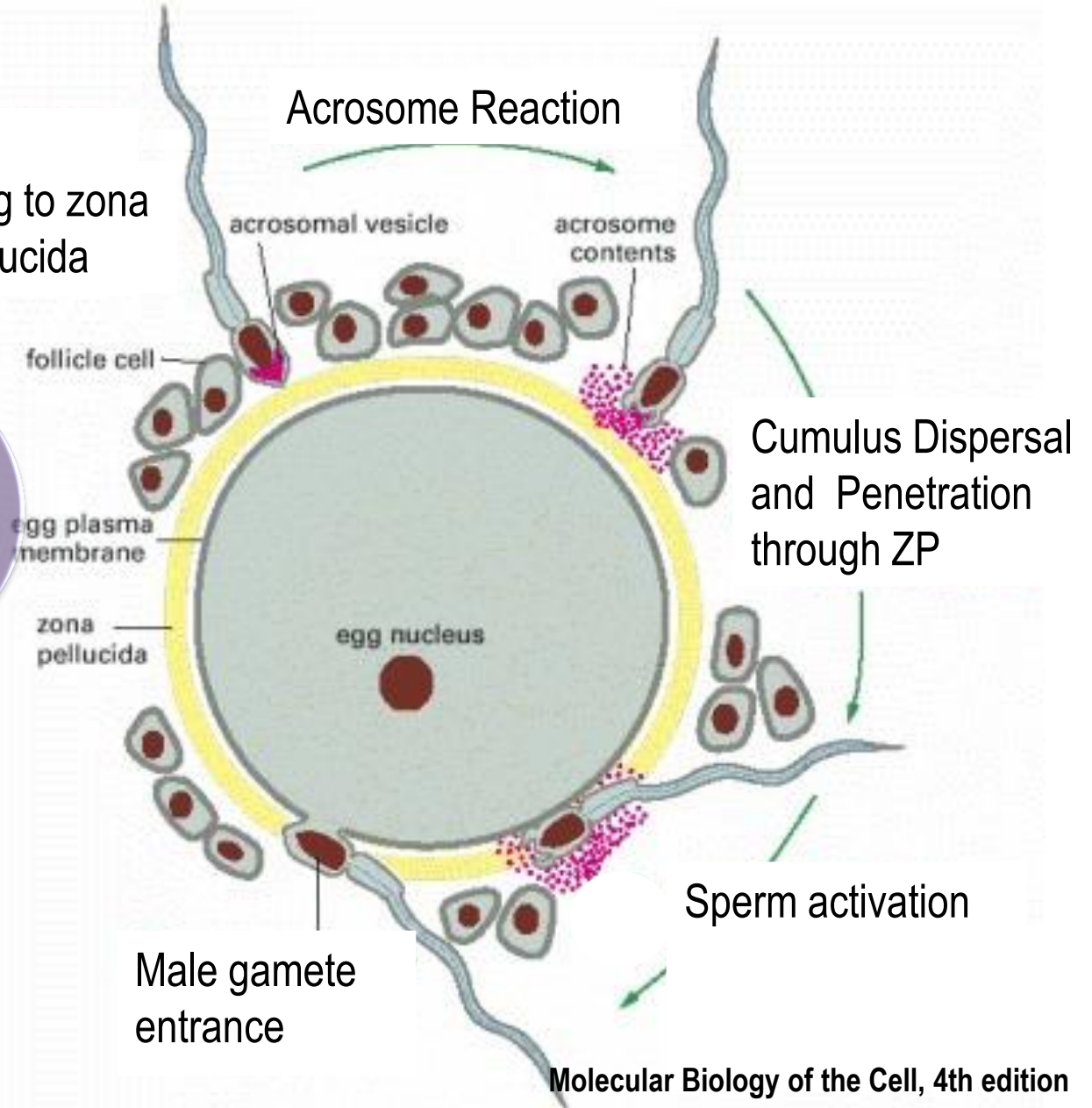
INTRODUCTION

Capacitation

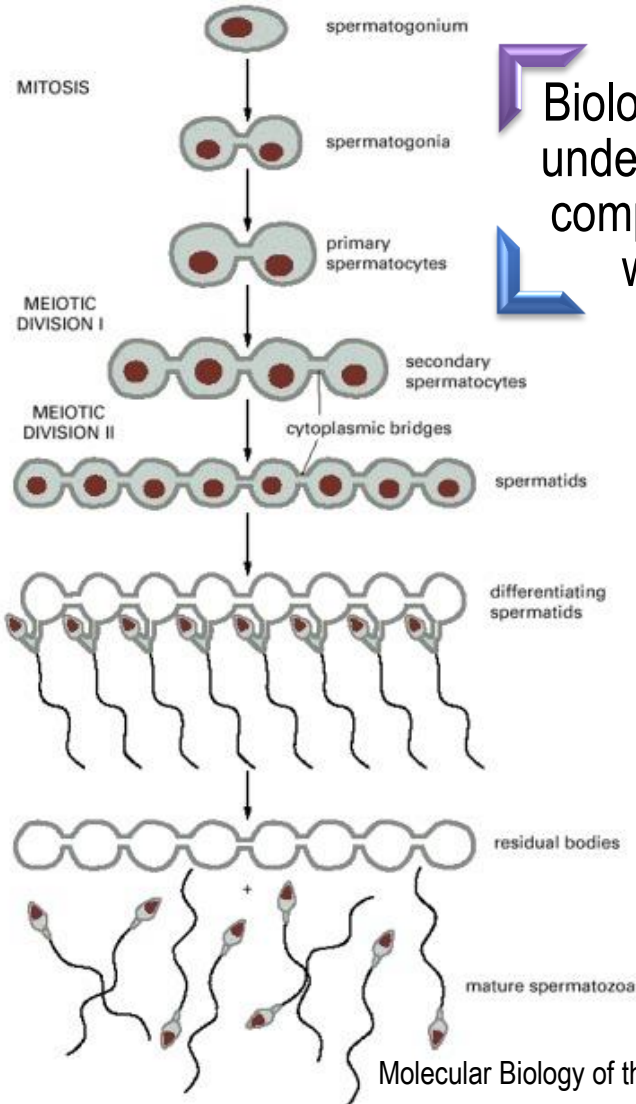


Motility
Hyper-
activation

Binding to zona
pelucida



INTRODUCTION



Biological clock underestimated compared with women

Recently, the potential role of paternal age has been investigated with conflicting results



Human Reproduction
Advanced Access Publication

Chapuis

Sp blas
Aurélien Ch
Emmanuel

Journal of Assisted Reproduction and Genetics
<https://doi.org/10.1007/s10815-018-1256-8>

ASSISTED REPRODUCTION TECHNOLOGIES

Abnormal sperm concentration and motility as well as advanced paternal age compromise early embryonic development but not pregnancy outcomes: a retrospective study of 1266 ICSI cycles

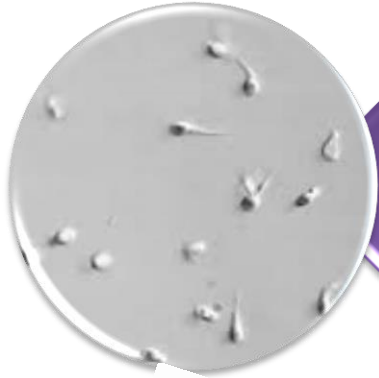
Alessandro Bartolacci¹ · Luca Pagliardini² · Sofia Malieva² · Andrea Salonia^{3,4} · Enrico Papaleo¹ · Paola Viganò²

Received: 26 April 2018 / Accepted: 29 June 2018
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...many Mullet^{1,2,3} · ...
...mir Hamamah^{1,2,3} · ... Sophie Bringer-Deutsch⁴

Men produce sperm through the entire life

INTRODUCTION



The same is true for impact of abnormal sperm parameters on embryo implantation

ANDROLOGIA 30, 91-95 (1998)

The outcome of clinical pregnancies after intracytoplasmic sperm injection is not

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R. Mercan, S. E. Lanzendorf, J. Mayer, Jr., A. Nassar, The Howard and Georgeanna Jones Institute for Women's Health, De Virginia Medical School, Norfolk, USA

Z.P. Nagy, J. Liu, H. Joris, G. Ver

Human Reproduction, Volume 10, Issue 5, -
<https://doi.org/10.1093/oxfordjournals.humrep>

Chapuis et al. Basic and Clinical Andrology
DOI 10.1186/s12610-016-0045-4

RESEARCH ARTICLE

Sperm

ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Journal Article

Effect of the male factor on the clinical outcome of intracytoplasmic sperm injection combined with preimplantation aneuploidy testing: observational longitudinal cohort study of 1,219 consecutive cycles

Basic and Clinical Andrology

Access

CrossMark

Deutsch



MED.



INTRODUCTION

EA

The same lack of consensus is noted when it concerns the ejaculatory abstinence length

Recomendations for EA

1 2 3 4 5 6 7



ESHRE
NAFA



WHO



Effect of EA on seminal parameters and sperm quality



Effect of EA on embryo development and implantation

The scientific evidences behind these recommendations are limited

OBJECTIVE

To evaluate the effect of paternal age, ejaculatory abstinence length and semen quality on ICSI outcomes in recipients' cycles in an egg-sharing donation program

MATERIALS AND METHODS

- STUDY DESIGN

Historical cohort study

268 oocyte donor cycles
(19-35 y-old)

Between January/2015 and May/2017

Egg-sharing donation program

427 oocyte recipient cycles
(26-59 y-old)

Paternal Factors

General Mixed Models

Post-hoc power for the sample size: **95.7%**.

MATERIALS AND METHODS

Predictive variables

Paternal age

Ejaculatory abstinence length

Sperm count

Progressive sperm motility

Total motile sperm count

Response variables

Fertilization rate

High-quality embryos rate on D3

Normal embryo development rate on D3

Blastocyst development rate




High-quality blastocysts rate

Implantation rate

Pregnancy rate

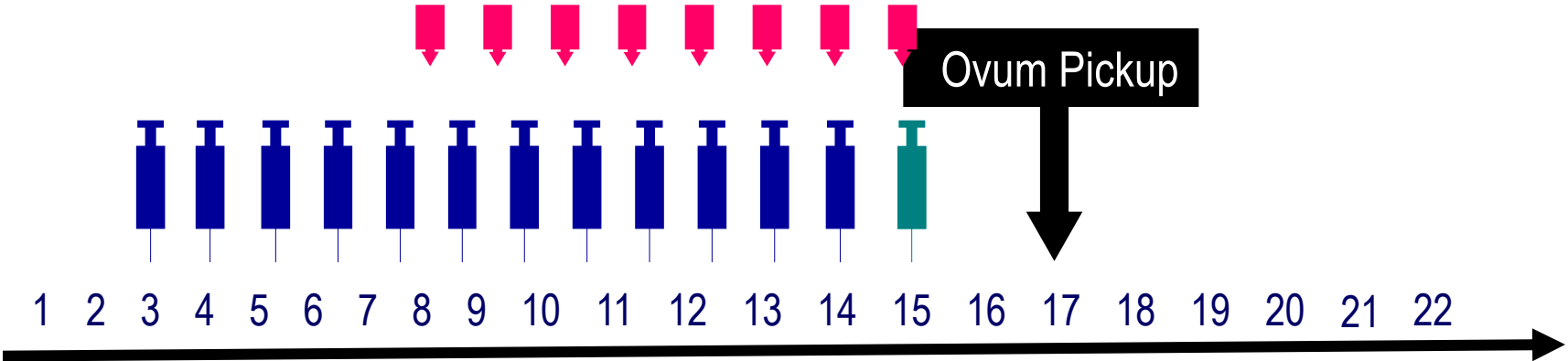
MATERIALS AND METHODS


Controlled Ovarian Stimulation

-  GnRH Antagonist
-  Recombinant FSH
-  Recombinant hCG



E2




Menses

MATERIALS AND METHODS



Incubation, denudation and nuclear maturation evaluation



ICSI performed after denudation for donors or 3 hours after warming for recipients

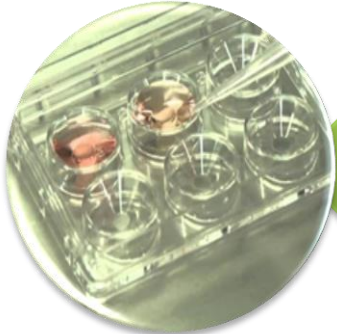


Embryo culture until day 5



One or two blastocysts transferred

MATERIALS AND METHODS



Vitrification and the warming: Cryotop method



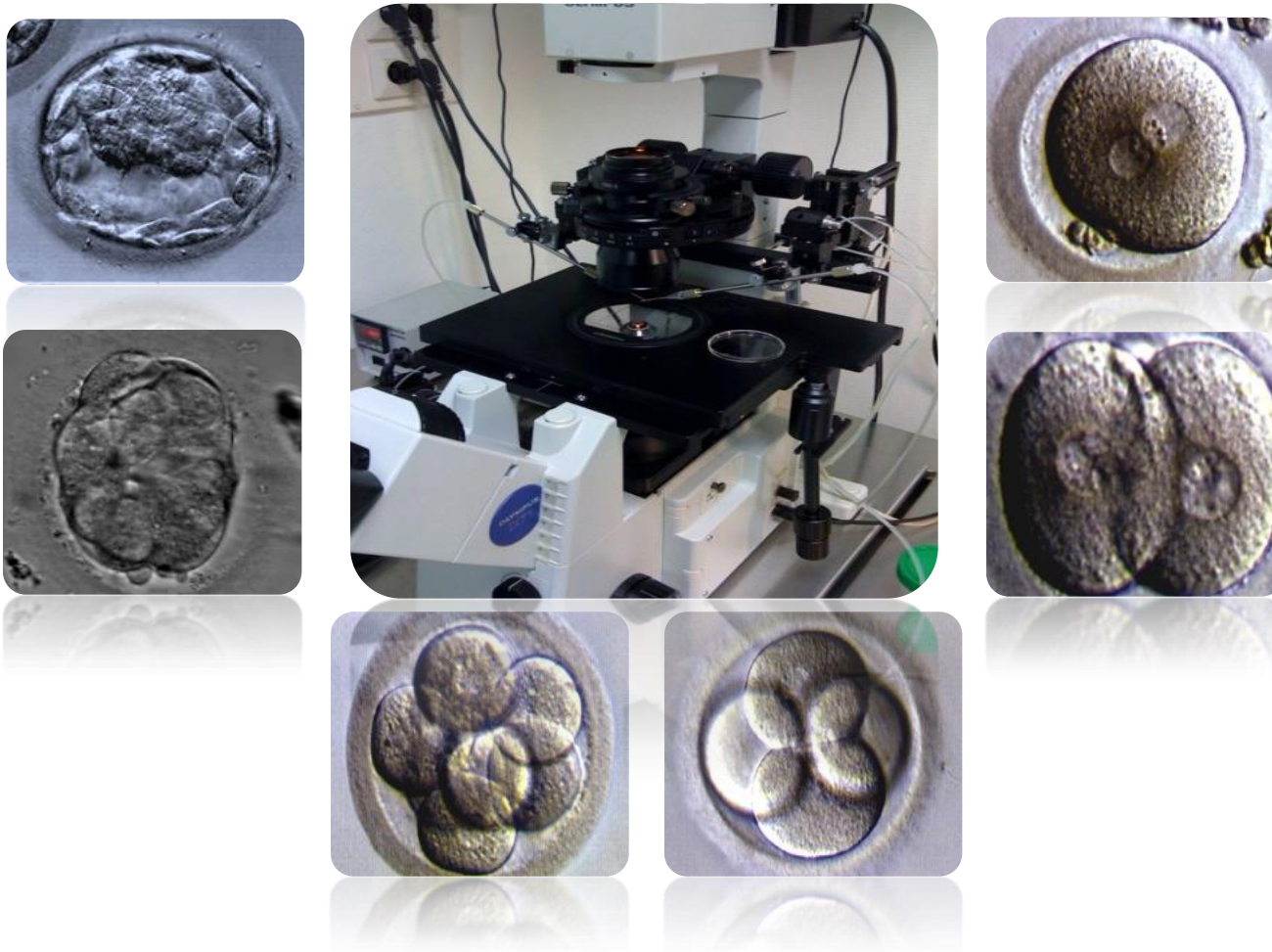
Semen samples were evaluated according to the threshold values established by the WHO in 2010



Sperm preparation: 2-layered density gradient centrifugation technique

MATERIALS AND METHODS

- EMBRYO MORPHOLOGY



RESULTS

Association between paternal age and ICSI outcomes

Variables	Paternal Age			
	B	SE	CI	p
Fertilization rate	-0.276	0.085	-0.442 – -0.110	0.001
High-quality embryos rate on D3	-0.040	0.017	-0.072 – -0.006	0.021
Normal embryo development rate on D3	-2.750	0.8625	-4.441 – -1.059	0.001
Blastocyst development rate	-0.070	0.035	-0.139 - -0.002	0.043
High-quality blastocysts rate	-44.058	20.248	-84.065 - -4.051	0.031
Implantation rate	-0.060	0.007	-0.075 - -0.045	< 0.001
Pregnancy chance	Exp(B): 0.664		0.457 – 0.967	0.033

RESULTS

Association between ejaculatory abstinence length and ICSI outcomes

Variables	Ejaculatory Abstinence Length			
	B	SE	CI	p
Fertilization rate	-0.083	0.847	-0.442 - -0.110	0.765
High-quality embryos rate on D3	-0.003	0.015	-0.006 – -0.001	0.028
Normal embryo development rate on D3	-0.300	0.014	-0.058 – -0.020	0.036
Blastocyst development rate	-0.589	0.243	-1.067 - -0.111	0.016
High-quality blastocysts rate	13.812	88.143	-160.341 – 187.966	0.876
Implantation rate	-0.012	0.003	-0.203 - -0.353	< 0.001
Pregnancy chance	Exp(B): 0.051	1.803	0.001-1.870	0.103

RESULTS

Association between sperm count and ICSI outcomes

Variables	Sperm Count			
	B	SE	CI	p
Fertilization rate	0.075	0.020	0.035 – 0.115	< 0.001
High-quality embryos rate on D3	2.296	7.074	-11.587 – 16.179	0.746
Normal embryo development rate on D3	-0.884	0.568	-1.999 - 0.232	0.120
Blastocyst development rate	2.155	0.884	0.420 – 3.891	0.015
High-quality blastocysts rate	-36.970	27.177	-90.666 - 16.727	0.176
Implantation rate	0.025	0.003	0.020 – 0.031	< 0.001
Pregnancy chance	Exp(B): 0.920	0.167	0.658 - 1.284	0.617

RESULTS

Association between progressive sperm motility and ICSI outcomes

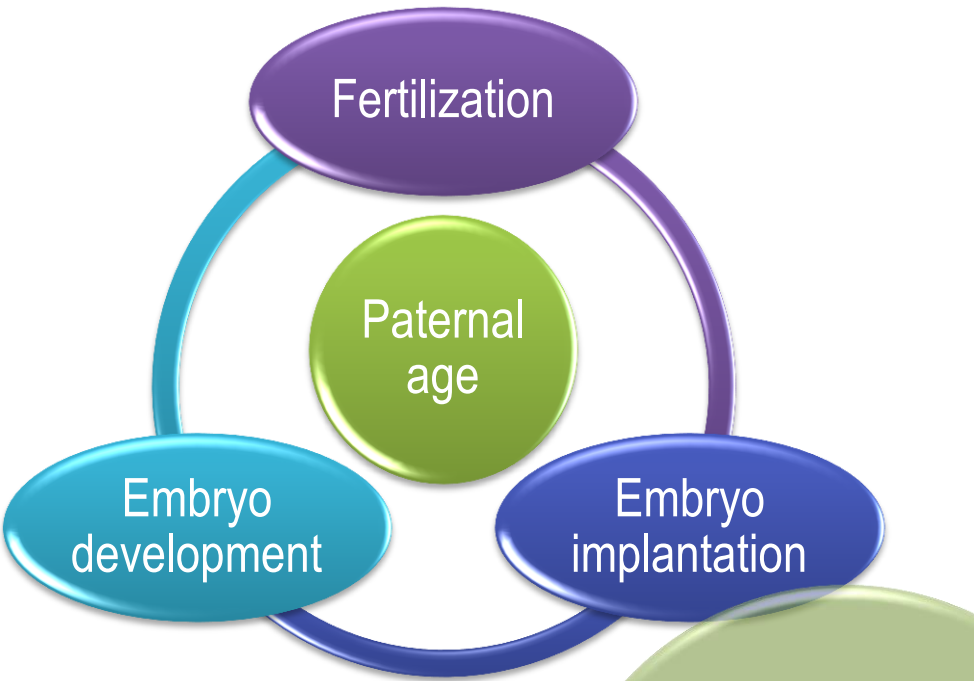
Variables	Sperm Motility			
	B	SE	CI	p
Fertilization rate	-0.003	0.0462	-0.093 – 0.088	0.951
High-quality embryos rate on D3	-1.573	20.270	-41.352 – 38.206	0.938
Normal embryo development rate on D3	0.017	0.077	0.002 – 0.032	0.024
Blastocyst development rate	0.412	0.586	-0.739 - 1.563	0.483
High-quality blastocysts rate	-5.955	5.453	-16.729 - 4.819	0.277
Implantation rate	0.183	0.010	0.163 – 0.204	< 0.001
Pregnancy chance	Exp(B): 1.037	0.031	0.974 - 1.104	0.253

RESULTS

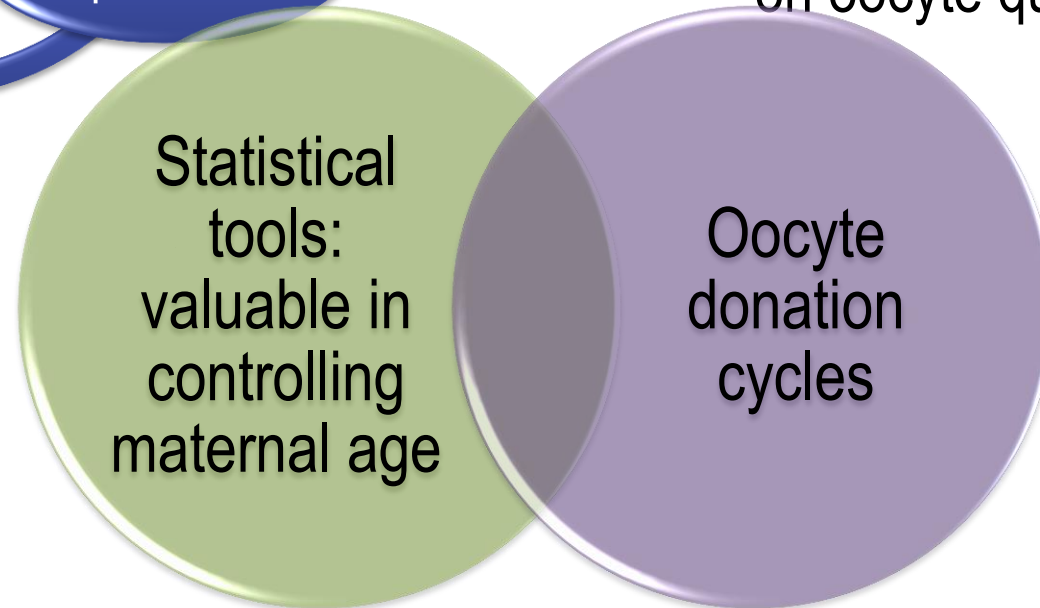
Association between total motile sperm count and ICSI outcomes

Variables	Total Motile Sperm Count			
	B	SE	CI	p
Fertilization rate	-0.007	0.030	-0.065 – 0.051	0.809
High-quality embryos rate on D3	2.841	2.297	-1.667 - 7.350	0.216
Normal embryo development rate on D3	-2.914	2.327	-7.480 - 1.652	0.211
Blastocyst development rate	1.057	0.508	0.060 – 2.054	0.038
High-quality blastocysts rate	9.779	6.442	-2.949 - 22.508	0.131
Implantation rate	0.008	0.003	0.002 – 0.014	0.009
Pregnancy chance	Exp(B): 0.957	0.062	0.845 - 1.083	0.475

DISCUSSION



Bias of the effect of maternal age on oocyte quality



DISCUSSION

Oocyte
donation
cycles

Egg
sharing
donation
population

VS

**Decreased IVF
outcomes:**

(Frattarelli et al.
2008; Luna et al.
2009)

**No effect of
paternal age on
IVF outcomes**

(Whitcomb et al.
2011; Begueria et al.
2014; Ghuman et al.
2016)

Young
fertile
oocyte
donors

DISCUSSION

This creates an interesting situation

Oocytes from the same cohort can be compared

The impact of paternal age on the functionality of oocytes derived from infertile-couples can be analysed

This is different from most other published studies in which data comes from oocyte donor populations

DISCUSSION



Embryo development and
implantation competence

ANDROLOGY



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ANDROLOGY

ORIGINAL ARTICLE

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Keywords:
Ejaculatory abstinence, ICSI, semen quality,
sperm DNA fragmentation

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Revisiting the impact of ejaculatory abstinence on semen quality and intracytoplasmic sperm injection outcomes

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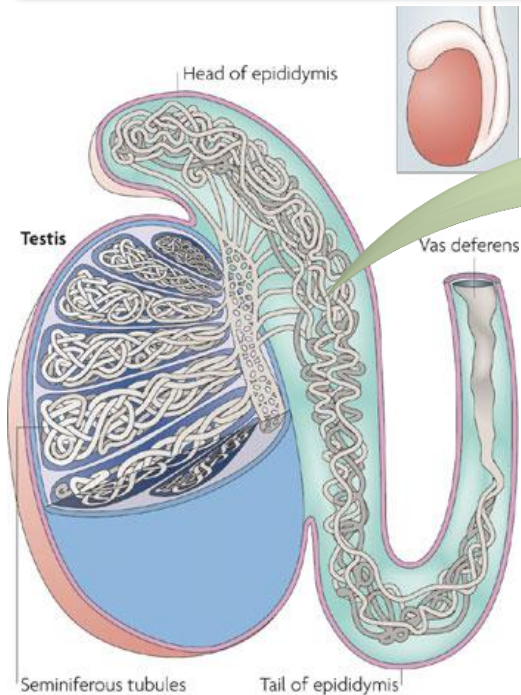


SDF

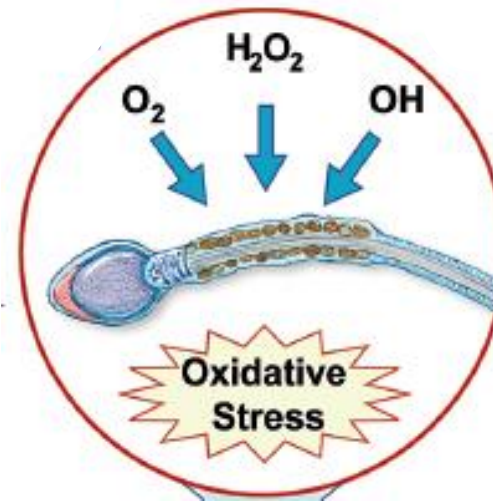


fertilization, blastocyst formation,
implantation, and pregnancy

DISCUSSION



Nature Reviews | Genetics

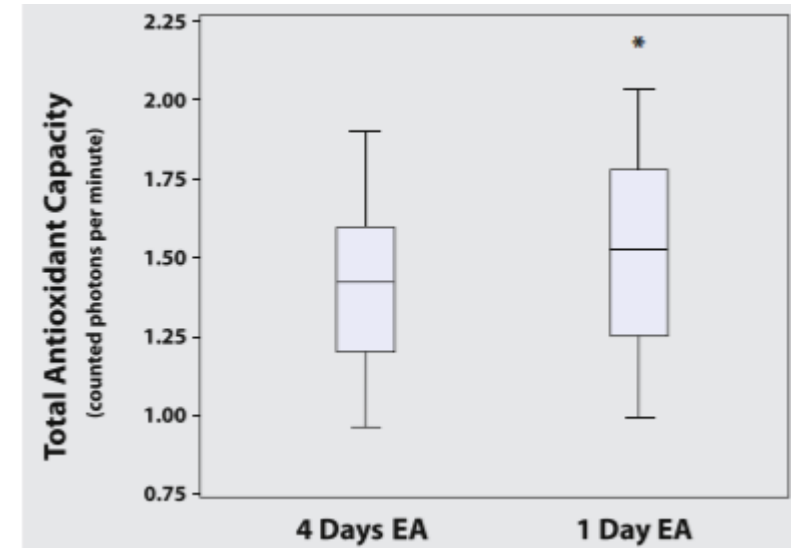


Kourouma et al., 2015

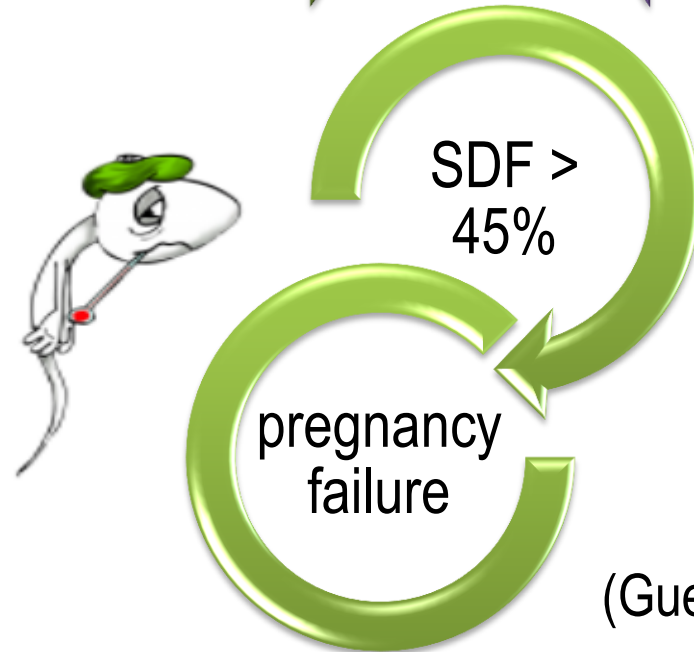
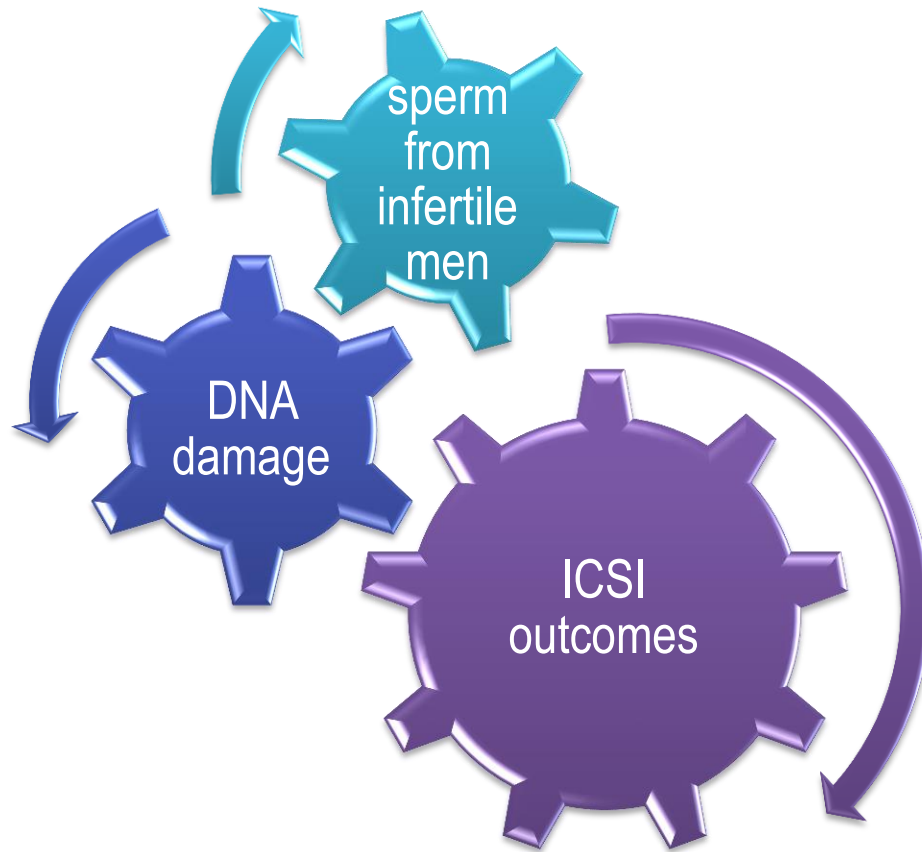
Influence of ejaculatory abstinence on seminal total antioxidant capacity and sperm membrane lipid peroxidation

Paul B. Marshburn, M.D.,^{a,b} Allie Giddings, M.D.,^b Stephanie Causby, M.S.,^{a,b} Michelle L. Matthews, M.D.,^{a,b} Rebecca S. Usadi, M.D.,^{a,b} Nury Steuerwald, Ph.D.,^c and Bradley S. Hurst, M.D.^{a,b}

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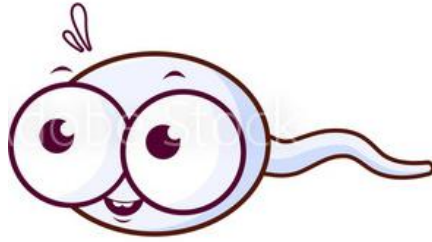
DISCUSSION



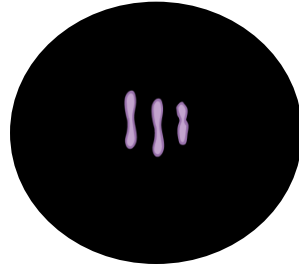
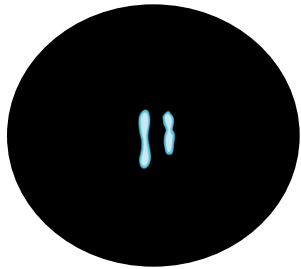
(Guerin et al. 2005)

Antonouli et al. 2019; Al Omrani et al. 2018;
Evgeni et al. 2015

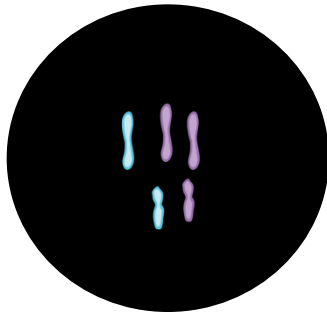
DISCUSSION



severe male factor



aneuploid embryos



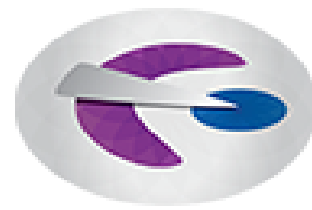
decreased implantation in
man with poor semen
quality

CONCLUSION

Increasing paternal age and EA, and poor semen parameters negatively impact ICSI outcomes, from fertilization to pregnancy

Therefore further tracking of the impact of paternal characteristics on ICSI outcomes should be encouraged

Despite paternal age is uncontrollable, and there are not so many things that can be done concerning semen quality, shortening of EA interval could be used as a strategy to optimize ICSI outcomes.



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DISCUSSION

Few studies focused on the influence of male factors on IVF outcomes

Paternal age

Seminal parameters

Ejaculatory abstinence length

ICSI outcomes

Conflicting results

Confound variables

Fertilization

Embryo development

Implantation