

*Simpósio
Comemorativo
dos 20 anos de
Reprodução Assistida
da **GENESIS***



20 **GENESIS**
anos
Assistindo a origem da vida

O Homem Infértil Presente e Futuro

Edson Borges Jr.



 Acesse nosso blog  

Faça sua pesquisa... 

FERTILITY ▾

SERVIÇOS ▾

TRATAMENTOS

ÁREA MÉDICA ▾

ÁREA DO PACIENTE ▾

CURSOS

PUBLICAÇÕES ▾

CONTATO ▾

<http://fertility.com.br/producao-cientifica-2015/>

Quando iniciar a avaliação?

⇒ Casais com vida sexual normal, após 1 ano de tentativas, sem anticoncepção e sem gestação

⇒ Antes de 1 ano

- Caso ♂ tenha um fator de risco conhecido para infertilidade (criptorquidia, patologia endócrina, varicocele, etc..)
- Caso ♀ tenha um fator de risco conhecido para infertilidade (idade > 35 anos, SOP, etc..)
- Caso ♂ / ♀ questionem seu potencial fértil

Etiologia da infertilidade

- fator masculino: 35%
- fator ovulatório: 15%
- fator tubo peritoneal } 35%
- fator uterino }
- fator cervical } 5%
- fator imunológico }
- ISCA: 10 %
- combinados: 35%
- fator psicossomático ?

ETIOLOGIA DA INFERTILIDADE MASCULINA

VARICOCELE	42,2
IDIOPÁTICA	22,7
OBSTRUÇÃO	14,7
♀ / ♂ normais	7,9
CRIPTORQUIDIA	3,4
IMUNOLÓGICA	2,6
EJACULATÓRIO	1,3
FALÊNCIA TESTICULAR	1,3

ETIOLOGIA DA INFERTILIDADE MASCULINA

- **fator masculino: 35%**
- Infertilidade idiopática: 25% dos homens
- Doença multifatorial com fenótipo heterogêneo

① *Envolver o marido na investigação e tratamento!!*

Propedêutica Laboratorial Masculina

- Espermograma com morfologia estrita (OMS 2010)
- Processamento Seminal Prognóstico
- Fragmentação do DNA do espermatozóide
- Quando alteração seminal importante
(conc < 2,0 milhões/ml): avaliação genética (cariótipo, microdeleção Y)
- Quando agenesia de deferentes: pesquisa de CFTR

World Health Organization reference values for human semen characteristics^{*,†}

Trevor G. Cooper^{1,10}, Elizabeth Noonan², Sigrid von Eckardstein³, Jacques Auger⁴, H.W. Gordon Baker⁵, Hermann M. Behre⁶, Trine B. Haugen⁷, Thinus Kruger⁸, Christina Wang⁹, Michael T. Mbizvo^{3,†}, and Kirsten M. Vogelsohn^{3,†}

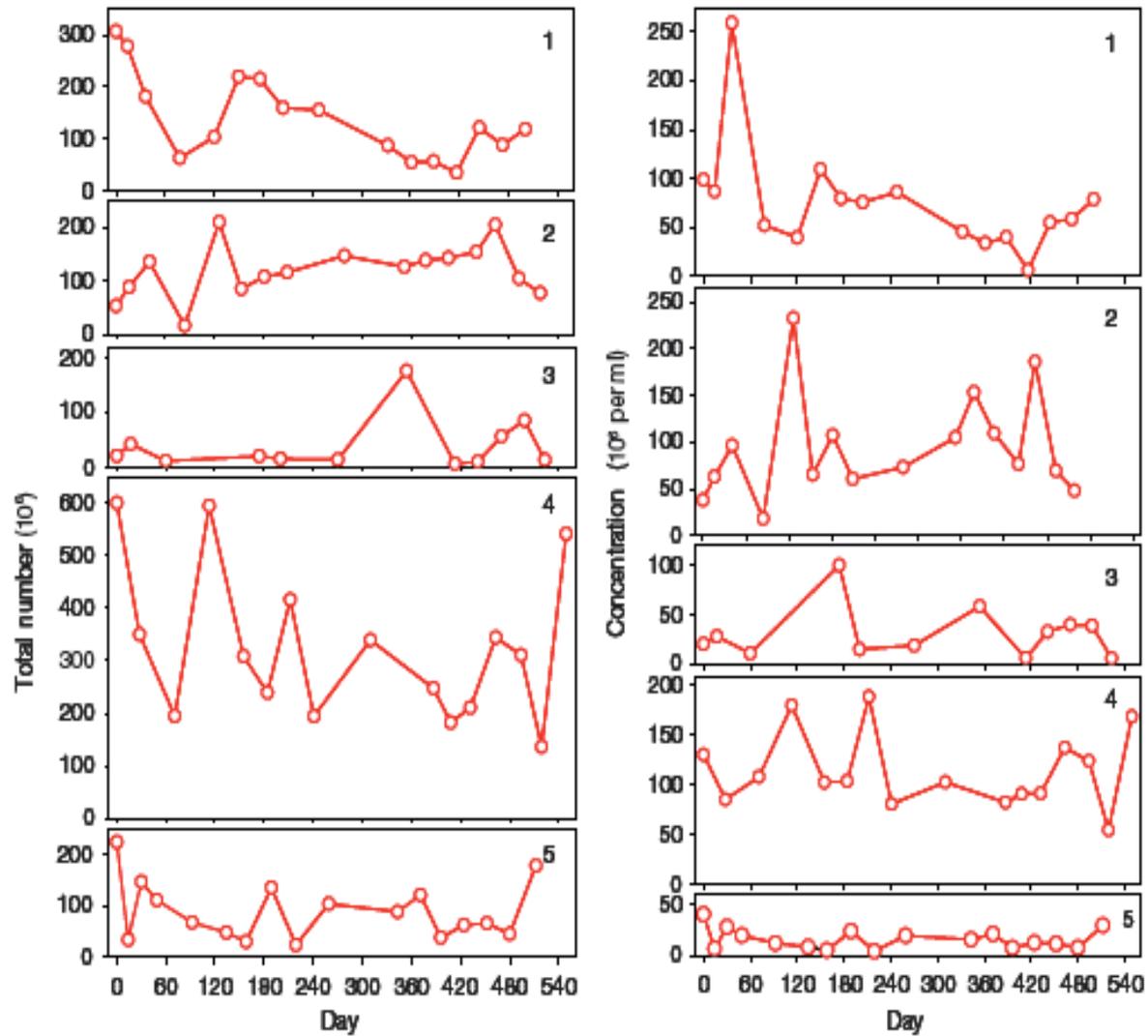
- 4.500 amostras seminais
- 14 países
- 4 continentes

WHO laboratory manual for the Examination and processing of human semen

FIFTH EDITION

- Volume: $\geq 1,5$ ml
- PH: $\geq 7,2$
- Cor: branco opaco ou branco acinzentado
- Liquefação: < 30 minutos
- Concentração: $\geq 15 \times 10^6 / \text{ml}$
 > 39 milhões / ejaculado
- Motilidade: $> 40\%$ (32% A+B)
 - A – progressão rápida
 - B – progressão lenta
 - C – sem progressão
 - D – imóveis
- Morfologia: $\geq 4\%$ Kruger
- Vitalidade: $> 58\%$
- Células redondas:
Leucócitos $\leq 10^6 / \text{ml}$
- Análise imunológica –
espermatozóides móveis aglutinados
com as partículas
MAR test / Imonobeads: positivo $\geq 50\%$

Fig. 2.1 Variation in total number of spermatozoa and sperm concentration over a one-and-a-half-year period



O.M.S. 1980/87/92/99/2010

Table 1. Cut-off values for semen variables as published in consecutive WHO manuals [6–9] and as proposed in the fifth World Health Organization (WHO) manual [1].

Semen variable	1980	1987	1992	1999	2010 ¹
Volume (mL)	–	≥ 2.0	≥ 2.0	≥ 2.0	1.5
Concentration (10 ⁶ mL ⁻¹)	20–200	≥ 20	≥ 20	≥ 20	15
Total sperm number (10 ⁶ /ejaculate)	–	≥ 40	≥ 40	≥ 40	39
Motility (% motile)	≥ 60	≥ 50 (a + b) ²	≥ 50 (a + b)	≥ 50 (a + b)	40 (a + b + c)
Forward progression (for 1980 only)	≥ 2 ³	≥ 25 (a)	≥ 25 (a)	≥ 25 (a)	32 (a + b)
Morphology (% normal)	80.5 ⁴	≥ 50	≥ 30 ⁵	(14) ⁶	4
Viability/vitality (% live)	–	≥ 50	≥ 75	≥ 75	58
White blood cells (10 ⁶ mL ⁻¹)	< 4.7	< 1.0	< 1.0	< 1.0	< 1.0

Abnormal sperm count and motility on semen analysis are not sufficiently predictive of abnormal Kruger morphology

Fertility and Sterility® Vol. 94, No. 7, December 2010

Sara S. Morelli, M.D.^a
 Aimee Seungdamrong, M.D.^{a,b}
 David H. McCulloh, Ph.D.^{a,b}
 Peter G. McGovern, M.D.^{a,b}

Abnormal morphology by Kruger's strict criteria cannot be predicted reliably by the presence of other abnormal parameters on semen analysis. Assessment of Kruger morphology therefore remains a necessary component of a complete semen analysis in the workup of the infertile couple. (Fertil Steril® 2010;94:2882-4. ©2010 by American Society for Reproductive Medicine.)

TABLE 1

Classification of semen analyses.

Count ($\geq 2 \times 10^7$ /mL)	Motility ($\geq 50\%$)	Kruger morphology ($> 4\%$)	No.	Percentage of total
Low	Low	Low	158	11
Low	Low	Normal	58	4
Low	Normal	Low	48	3
Low	Normal	Normal	41	3
Normal	Low	Low	69	5
Normal	Low	Normal	92	7
Normal	Normal	Low	187	14
Normal	Normal	Normal	731	53
Total			1,384	

Morelli. Correspondence. Fertil Steril 2010.

Propedêutica em infertilidade

*Espermograma com morfologia estrita
(OMS 2010)*

②

Mínimo de duas coletas seminais com intervalo igual a frequência ejaculatória do homem

Oligozoospermia / Azoospermia *Vale a pena tratamento?*

- 1. Tratamento medicamentoso**
- 2. Tratamento cirúrgico**

Drug Therapy for Idiopathic Male Infertility: Rationale Versus Evidence

Rajeev Kumar,* Gagan Gautam and Narmada P. Gupta



Material e Método: Pesquisa no MEDLINE/PubMed nos últimos 20 anos com foco nas publicações sobre tratamento medicamentoso para infertilidade masculina

Conclusão: Tratamento medicamentoso para infertilidade masculina idiopática é no mínimo empírico. Não existe benefício claro no uso de qualquer medicação nestes pacientes. Entretanto, andrógenos não devem ser usados devido a seu efeito supressório sobre a espermatogênese.

The role of sperm oxidative stress in male infertility and the significance of oral antioxidant therapy

Parviz Gharagozloo^{1,*} and R. John Aitken²

¹CellOxess LLC, 16 Blue Spruce Drive, Pennington, NJ 08534, USA ²Priority Research Centre in Reproductive Science, Discipline of Biological Sciences, University of Newcastle, Callaghan, NSW 2308, Australia

- ***Impacto dos antioxidantes orais no estresse oxidativo (EO) e DNA espermático***
- 19 / 20 estudos mostraram diminuição do ***EO***
- Forte evidência no *aumento da motilidade* (principalmente nos astenozoospermicos)
- 6 /10 estudos: aumento das taxas de gestação



Antioxidants for male subfertility

Showell MG, Brown J, Yazdani A, Stankiewicz MT, Hart RJ

Published Online: March 14, 2012

Oxidative stress may cause sperm cell damage. This damage can be reduced by the body's own natural antioxidant defences. Antioxidants can be part of our diet and taken as a supplement. It is believed that in many cases of unexplained subfertility, and also in instances where there may be a sperm-related problem, taking an oral antioxidant supplement may increase a couple's chance of conceiving when undergoing fertility treatment. This [review](#) identified 34 randomised controlled trials involving 2876 couples. Pooled findings from three small trials suggest an increase in live birth rates for the partners of subfertile men taking an antioxidant supplement as part of an assisted reproductive program. However, further well-designed large randomised [placebo](#)-controlled trials are needed to confirm these findings.

- 34 estudos randomizados - 2.876 casais
- Aumento da taxa gestação (OR=4,18)
- Aumento na taxa de nascidos vivos (OR=4,85)

The effect of sperm DNA fragmentation on miscarriage rates: a systematic review and meta-analysis

Lynne Robinson^{1,*}, Ioannis D. Gallos^{1,2}, Sarah J. Conner^{1,2},
Madhurima Rajkhowa¹, David Miller³, Sheena Lewis⁴,
Jackson Kirkman-Brown^{1,2}, and Arri Coomarasamy^{1,2}

- **16 estudos – 2969 casais**
- Aumento significativo de *abortamento* em homens com aumento da *fragDNA espermática*: RR = 2,16 (1,54 – 3,03)
- TUNEL: RR = 3,94 (2,45 – 6,32)

Tratamento Medicamentoso

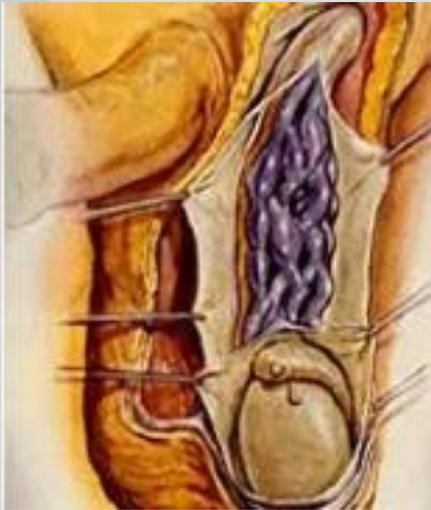
*Tratamento hormonal: sem eficácia
(algumas vezes prejudicial)*

- ③ *Uso de antioxidantes: efeito parcial em alguns casos*

FragDNA espermático: > abortamento

Tratamento Cirúrgico

- Cirurgia de Varicocele



Cirurgia de Varicocele

➤ *INCIDÊNCIA DE VARICOCELE EM HOMENS INFÉRTEIS*

5.228 homens / 1.803 com varicocele (35%)

➤ *MELHORA SEMINAL E % DE GESTAÇÕES APÓS VARICOCELECTOMIA*

- ✓ 3.507 pacientes operados
- ✓ Melhora seminal: 51 - 92%
- ✓ Gestação: 25 - 55% (média = 30%)

MALE FACTOR

Fertil Steril 88:639-48, 2007

**Reassessing the value of varicocelectomy
as a treatment for male subfertility
with a new meta-analysis**

*Joel L. Marmar, M.D.,^a Ashok Agarwal, Ph.D.,^b Sushil Prabakaran, M.D.,^b Rishi Agarwal,^b
Robert A. Short, Ph.D.,^c Susan Benoff, Ph.D.,^d and Anthony J. Thomas, Jr., M.D.^b*

**Aumento 2,8x chances
de gestação espontânea**

Cirurgia de Varicocele

- Principal causa conhecida de lesão testicular
- Melhora seminal após 2-3 ciclos da espermatogênese (6-9 meses)
- Melhores resultados em alterações seminais moderadas

④ *Casal tem de ter TEMPO!!*

AZOOSPERMIA

- 1% dos homens
- 10 -15% dos homens inférteis

AZOOSPERMIA

- **Obstrutiva:** espermatogênese normal
- **Não-Obstrutiva:** alteração da espermatogênese

The importance of semen analysis in the context of azoospermia

Nabil Aziz

Liverpool Women's Hospital & The University of Liverpool, Liverpool, United Kingdom

Reference	Recommended centrifugation
Mortimer (1994) (23)	1000 x g for 15 minutes
the Nordic Association for Andrology (24)	At least 1000 x g for 15 minutes
WHO manual (1999) (25)	600 x g for 15 minutes to concentrate samples with low sperm counts (less than 2 sperm per 400x field) Less than 3000 x g for 15 minutes for all samples in which spermatozoa are not detected
Corea et al. (2005) (20)	A minimum of 1000 x g for 15 minutes was adequate for the detection of azoospermia
WHO manual (2010) (2)	3000 x g for 15 minutes for all samples in which no spermatozoa are detected

18,6% Azoo Ob
22,8% Azoo
NOB



Sptz
móveis/imóveis

RECUPERAÇÃO DE
ESPERMATOZÓIDES
NÃO EJACULADOS

ESPERMATOZÓIDES
ESPIDIDIMÁRIOS

PERCUTANEOUS
EPIDYDIMAL
SPERM
ASPIRATION

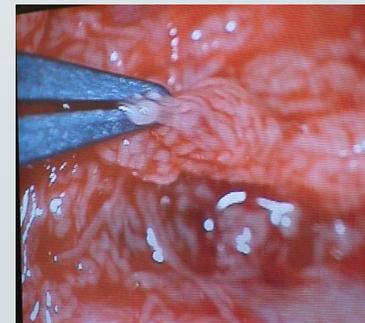


ESPERMATOZÓIDES
TESTICULARES

TESTICULAR
SPERM
ASPIRATION

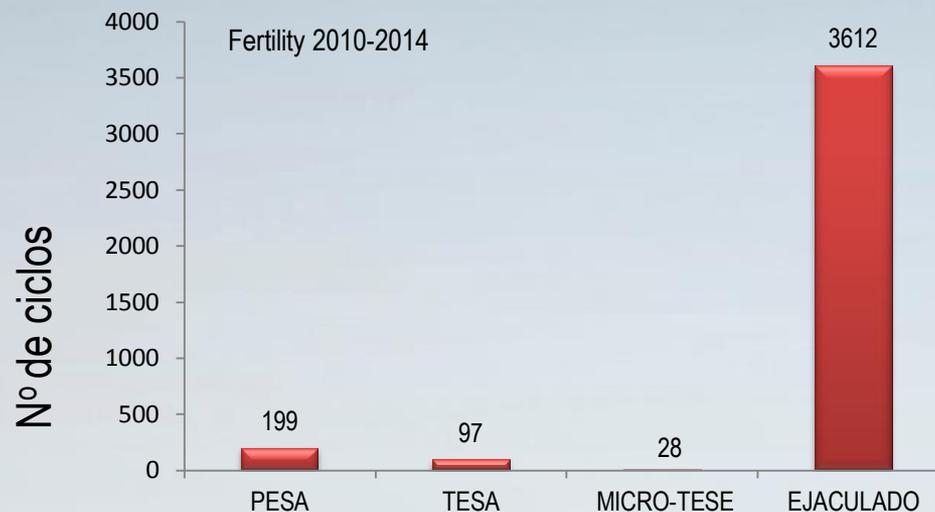


Micro
TESTICULAR
SPERM
EXTRACTION



Características gerais dos ciclos de ICSI – *Fertility* (2010-2014)

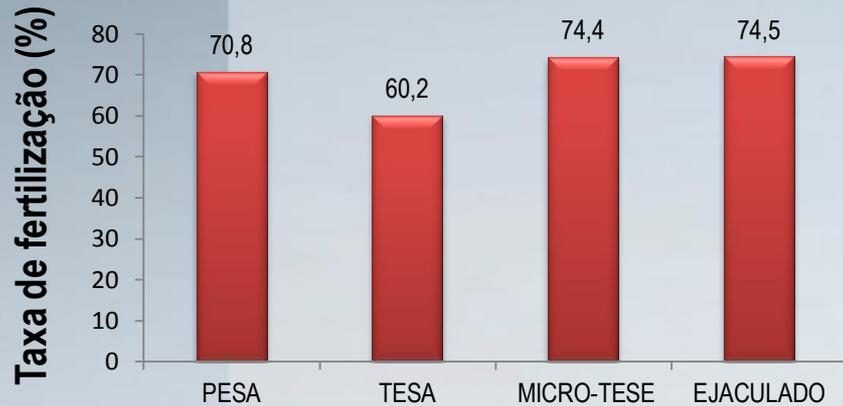
“Origem do espermatozoide”



Características	PESA	TESA	MICRO-TESE	EJACULADO
Nº de ciclos	199	97	28	3612
Idade média \pm DP	34.9 \pm 4.6	34.8 \pm 5.4	32.2 \pm 2.7	35.8 \pm 4.7
Nº de folículos aspirados \pm DP	20.4 \pm 15.4	18.1 \pm 11.3	15.9 \pm 14.4	15.8 \pm 12.4
Nº de oócitos recuperados \pm DP	14.2 \pm 10.8	13.3 \pm 9.3	11.0 \pm 11.4	11.0 \pm 9.0
Nº de oócitos micromanipulados \pm DP	9.8 \pm 6.4	8.9 \pm 5.1	8.0 \pm 6.9	7.8 \pm 5.8

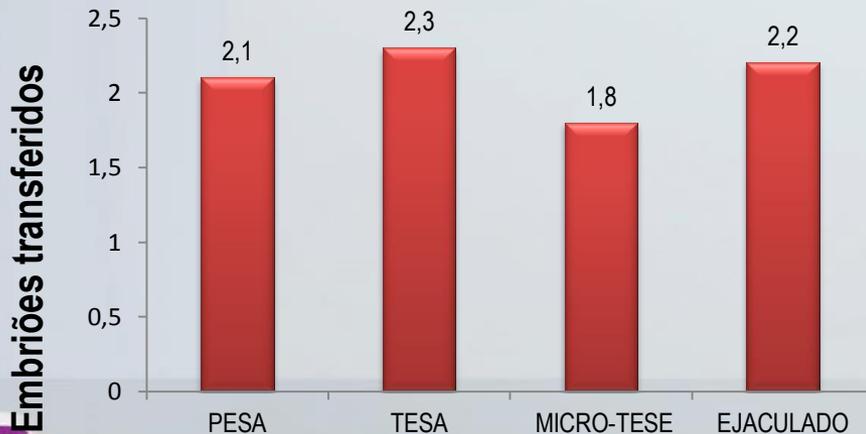
Resultados clínicos e laboratoriais – *Fertility* (2010-2014)

“Origem do espermatozoide”



COMPARAÇÃO	VALOR DE P
PESA VS TESA	< 0.001
PESA VS MICRO-TESE	> 0.05
PESA VS EJACULADO	> 0.05
TESA VS MICRO-TESE	> 0.05
TESA VS EJACUALDO	< 0.001
MICRO-TESE VS EJACULADO	> 0.05

ANOVA



COMPARAÇÃO	VALOR DE P
PESA VS TESA	> 0.05
PESA VS MICRO-TESE	> 0.05
PESA VS EJACULADO	> 0.05
TESA VS MICRO-TESE	> 0.05
TESA VS EJACUALDO	> 0.05
MICRO-TESE VS EJACULADO	> 0.05

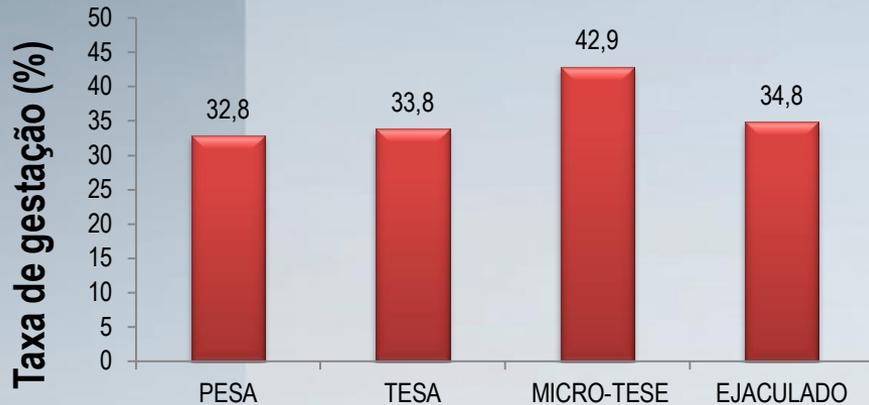
ANOVA

Embrões transferidos

FERTILITY

Resultados clínicos e laboratoriais – *Fertility* (2010-2014)

“Origem do espermatozoide”



COMPARAÇÃO	VALOR DE P
PESA VS TESA	> 0.05
PESA VS MICRO-TESE	> 0.05
PESA VS EJACULADO	> 0.05
TESA VS MICRO-TESE	> 0.05
TESA VS EJACULADO	> 0.05
MICRO-TESE VS EJACULADO	> 0.05

QUI-QUADRO

COMPARAÇÃO	VALOR DE P
PESA VS TESA	> 0.05
PESA VS MICRO-TESE	> 0.05
PESA VS EJACULADO	> 0.05
TESA VS MICRO-TESE	> 0.05
TESA VS EJACULADO	> 0.05
MICRO-TESE VS EJACULADO	> 0.05

ANOVA



Falha na recuperação do espermatozoide *Fertility* (2010-2014)

Técnica	Nº Ciclos	Ciclos com ausência de espermatozóide	% de falha
PESA	230	31*	13.5
TESA	85	19	22.3
microTESE	28	12	42.9



* 100% após TESA

5

Azoospermia

Obstrutiva

Recuperação
espermática na
maioria dos casos

PESA

Não
obstrutiva

Recuperação
espermática em
50% dos casos

TESA
microTESE

The prevalence of chromosomal abnormalities in subgroups of infertile men[†]

E.C. Dul^{1,*}, H. Groen², C.M.A. van Ravenswaaij-Arts³, T. Dijkhuizen³, J. van Echten-Arends¹, and J.A. Land¹

- ✓ 1.223 homens candidatos ICSI: 79 azoospérmicos (6,5%)
- ✓ 3,1% com anormalidades cromossômicas
- ✓ 15,2% dos azoo (OR=7,70 - p<0,001)
- ✓ FSH alto e anormalidade cromossômica (OR=2,96 - p=0,013)
- ✓ Azoospérmicos com história andrológica positiva < incidência de anormalidade cromossômica (OR=0,28 - p=0,047)

The genetic causes of male factor infertility: A review

Katherine L. O'Flynn O'Brien, B.A.,^a Alex C. Varghese, Ph.D.,^b and Ashok Agarwal, Ph.D.^a

Prevalence and phenotypes of common chromosomal abnormalities associated with male infertility.

Genetic abnormality	Phenotype	Prevalence, %
Chromosomal abnormalities	Azoospermia to normozoospermia	5 (total infertile population); 15 (azoospermic)
Klinefelter syndrome	Azoospermia to severe oligozoospermia	5 (severe oligozoospermia); 10 (azoospermic)
Robertsonian translocation	Azoospermia to normozoospermia	0.8 (total infertile population); 1.6 (oligozoospermic); 0.09 (azoospermic)
Y chromosome microdeletions	Azoospermia to oligozoospermia	10–15 (azoospermic); 5–10 (oligozoospermic)
AZFa deletion	Azoospermia, Sertoli cell-only syndrome	0.5–1.0 (2)
AZFb deletion	Azoospermia, spermatogenic arrest	0.5–1.0 (2)
AZFc deletion	Severe oligozoospermia to nonobstructive azoospermia	6–12
Partial AZF-c deletions	From azoospermia to normozoospermia	3–5 (2)

- *Klinefelter:* 7 - 13% azoospermicos
- *MicroDeleção Y:* 2 - 20% oligo grave / azoospermicos
- *CBAVD:* 1 - 2% homens inférteis
10% azoospermias obstrutivas

Alteração Seminal Grave (oligo/azoospermia)

⑥

*SEMPRE PENSAR EM DOENÇA
GENÉTICA ASSOCIADA*

"Considerações"

- Envolvimento do homem
- A.S. (OMS 2010) com morfologia estrita
- fragDNA espermático: > abortamento
- Tratamento medicamentoso: AO
- Varicocelelectomia: casal com "tempo"
- Azoospermia obstrutiva: recuperação maioria dos casos
- Azoospermia não-obstrutiva: ~ 50%
- Alteração seminal grave: doença genética

DESAFIOS NA MEDICINA REPRODUTIVA

Podem as condições da "vida moderna" interferirem na fertilidade masculina?

- Alimentação / Peso
- Queda da qualidade seminal com o tempo

Food intake and social habits in male patients and its relationship to intracytoplasmic sperm injection outcomes

Fertility and Sterility® Vol. 97, No. 1, January 2012

Daniela Paes de Almeida Ferreira Braga, D.V.M., M.Sc.,^{a,b} Gabriela Halpern, M.Sc.,^a Rita de Cássia S. Figueira, M.Sc.,^a Amanda S. Setti, B.Sc.,^b Assumpto Iaconelli Jr., M.D.,^a and Edson Borges Jr., M.D., Ph.D.^{a,b}

Objective: To investigate the influence of the male partner's lifestyle, including eating and social habits, on semen quality and intracytoplasmic sperm injection (ICSI) success.

Design: Observational study.

Setting: Private fertility clinic.

Patient(s): Two hundred fifty male patients undergoing ICSI cycles.

Intervention(s): We recorded dietary and social habits using a food frequency questionnaire adapted to meet specific study objectives. Evaluation of semen parameters and ICSI outcomes were performed.

Main Outcome Measure(s): Frequency of intake of food items and social habits were registered on a scale with five categories ranging from no consumption to repeated daily consumption.

Food intake and social habits in male patients and its relationship to intracytoplasmic sperm injection outcomes

Fertility and Sterility® Vol. 97, No. 1, January 2012

Daniela Paes de Almeida Ferreira Braga, D.V.M., M.Sc.,^{a,b} Gabriela Halpern, M.Sc.,^a Rita de Cássia S. Figueira, M.Sc.,^a Amanda S. Setti, B.Sc.,^b Assumpto Iaconelli Jr., M.D.,^a and Edson Borges Jr., M.D., Ph.D.^{a,b}

Xenobióticos

- Concentração: negativamente influenciada pelo IMC e álcool; positivamente influenciada pelo consumo de cereal e no. refeições/dia
- Motilidade: negativamente influenciada pelo IMC, álcool e cigarro; positivamente influenciada pelo consumo de cereal e frutas

Food intake and social habits in male patients and its relationship to intracytoplasmic sperm injection outcomes

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Xenobióticos

- Álcool: impacto negativo na fertilização
- Carne vermelha e dieta (perda peso): impacto negativo na implantação / diminui as chances de gestação



ELSEVIER

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www.rbmonline.com



ARTICLE

The impact of food intake and social habits on embryo quality and the likelihood of blastocyst formation



Daniela Paes Almeida Ferreira Braga ^{a,*}, Gabriela Halpern ^a, Amanda S Setti ^b, Rita Cássia S Figueira ^a, Assumpto Iaconelli Jr ^a, Edson Borges Jr ^a

- *2659 embriões - 269 pacientes submetidas a ICSI*
- Qualidade embrionária em estágio de clivagem: negativamente influenciada pelo álcool e cigarro; positivamente influenciada pelo consumo de cereal, vegetais e frutas
- Formação de blastocisto: negativamente influenciada pelo consumo de carne vermelha, perda de peso (dieta), álcool e cigarro; positivamente influenciada pelo consumo frutas e peixes



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ARTICLE

The impact of food intake and social habits on embryo quality and the likelihood of blastocyst formation



Daniela Paes Almeida Ferreira Braga ^{a,*}, Gabriela Halpern ^a, Amanda S Setti ^b, Rita Cássia S Figueira ^a, Assumpto Iaconelli Jr ^a, Edson Borges Jr ^a

- Carne vermelha e IMC: impacto negativo na implantação e gestação
- Perda de peso (dieta): impacto negativo na implantação

BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis

N. Sermondade^{1,2}, C. Faure^{1,2}, L. Fezeu², A.G. Shayeb³, J.P. Bonde⁴,
T.K. Jensen⁵, M. Van Wely⁶, J. Cao⁷, A.C. Martini⁸, M. Eskandar⁹,
J.E. Chavarro^{10,11}, S. Koloszar¹², J.M. Twigt¹³, C.H. Ramlau-Hansen¹⁴,
E. Borges Jr¹⁵, F. Lotti¹⁶, R.P.M. Steegers-Theunissen¹³, B. Zorn¹⁷,
A.J. Polotsky¹⁸, S. La Vignera¹⁹, B. Eskenazi²⁰, K. Tremellen²¹,
E.V. Magnusdottir²², I. Fejes²³, S. Hercberg^{2,24}, R. Lévy^{1,2†},
and S. Czernichow^{25,26,*†}

- **21 estudos, 13.077 homens da população geral e em investigação de infertilidade**
- **Estudo da relação entre BMI e incidência de oligozoospermia / azoospermia**
- **Comparados com homens com peso normal:**
 - ❖ Sobpeso: OR= 1,15 (0,93-1,43)
 - ❖ Sobrepeso: OR= 1,11 (1,01-1,21)
 - ❖ Obeso: OR= 1,28 (1,06-1,55)
 - ❖ Obeso mórbido: OR= 2,04 (1,59-2,62)





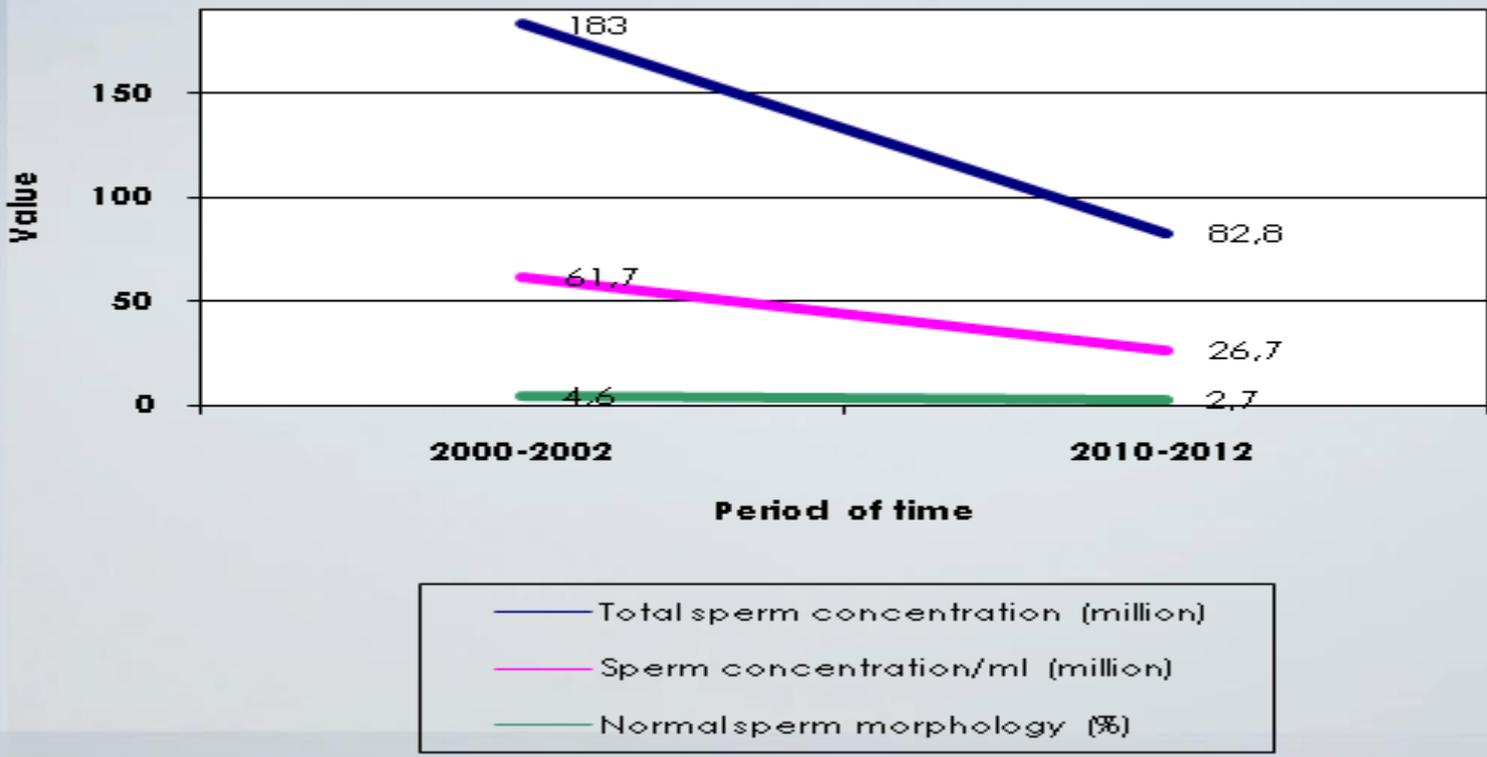
Decline in semen quality among infertile men in Brazil during the past 10 years

Edson Borges Jr.^{1,2}, Amanda Souza Setti^{1,2}, Daniela Paes de Almeida Ferreira Braga^{1,2}, Rita de Cassia Savio Figueira¹, Assumpto Iaconelli Jr.^{1,2}

Table 1 - General characteristics of analyzed semen samples (n=2300).

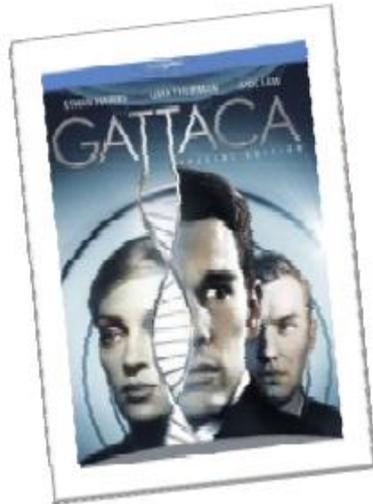
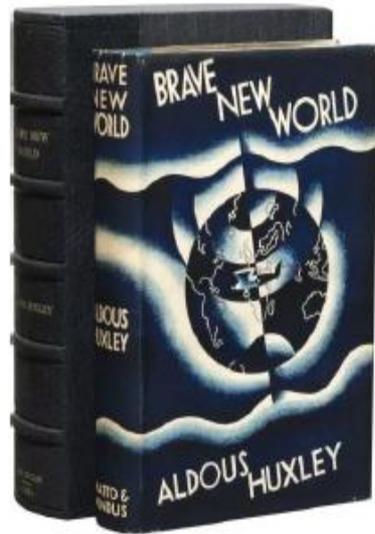
Variable	Mean	SD	Min	Max
Male age (y-old)	35.7	7.8	15.0	71.0
Days of abstinence	4.2	2.8	0.0	30.0
Semen sample volume (ml)	3.3	1.7	0.1	11.3
Sperm concentration/ml (million)	38.3	46.7	0.0	540.0
Total sperm concentration (million)	116.0	143.0	0.0	984.0
Progressive sperm motility (%)	36.9	18.9	0.0	84.0
Sperm morphology	3.4	2.9	0.0	16.0

values are mean \pm SD, unless otherwise noticed. **SD**= standard deviation; **Min**= minimum; **Max**= maximum.



Variável	2000-2002 (n=764)	2010-2012 (n=1536)	p
Idade masculina (anos)	35.0 ± 8.6	35.3 ± 8.1	0.318
Dias de abstinência	4.2 ± 3.1	4.2 ± 2.7	0.777
Volume da amostra (ml)	3.4 ± 1.8	3.3 ± 1.6	0.473
Concentração/ml (milhão)	61.7 ± 69.4	26.7 ± 27.3	<0.001
Concentração total (milhão)	183.0 ± 197.0	82.8 ± 89.5	<0.001
Motilidade progressiva (%)	36.4 ± 18.3	36.5 ± 19.2	0.812
Morfologia normal (%)	4.6	2.7	<0.001
Azoospermia (%)	38/764 (4.9)	131/1536 (8.5)	0.001
Oligozoospermia grave (%)	114/726 (15.7)	426/1405 (30.3)	<0.001

Fertilização	2000-2002 (n=315)	2010-2012 (n=842)	<i>p</i>
Taxa de fertilização total (%)	82.5	81.3	0.619
Taxa de fertilização anormal (1PN + 3PN) (%)	12.2	7.8	<0.001



Stem cells in reproductive medicine: ready for the patient?

R. Vassena^{1,*}, C. Eguizabal², B. Heindryckx³, K. Sermon⁴, C. Simon^{5,6},
A.M.M. van Pelt⁷, A. Veiga^{8,9}, and F. Zambelli^{4,10} on behalf of the ESHRE
special interest group Stem Cells[†]

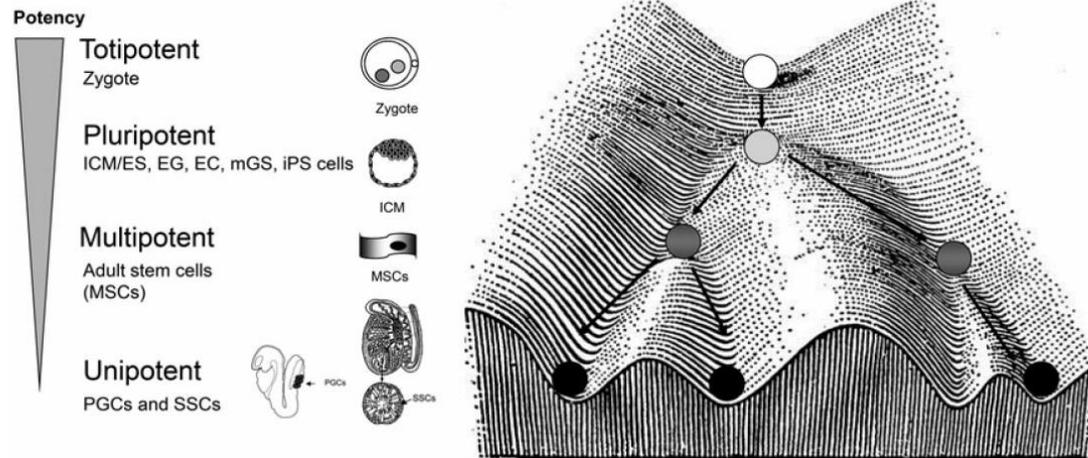


Figure 1 Schematic representation of the loss of potency as development and cell differentiation occurs. ICM, inner cell mass; ES, embryonic stem; MSC, mesenchymal stem cells; PGC, primordial stem cells; SSC, spermatogonia stem cell. Adapted from [Eguizabal et al. \(2013\)](#).

Stem cells in reproductive medicine: ready for the patient?

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Recently, human iPSCs (hiPSC) from azoospermic and normospermic males were transplanted into sterile mouse testis, partially colonizing the testicular niche and showing signs of early stage spermatogenesis (Ramathal *et al.*, 2014), raising the question of whether an initial *in vitro* differentiation step is needed at all. It has been recently shown that transplanting *in vitro* produced PGC-like cells into the mouse testis could be used to obtain functional mouse sperm, capable of producing healthy and fertile offspring (Hayashi *et al.*, 2011). From the recent scientific literature, it seems that so far there is still the need of a natural testicular niche in order to obtain mature functional spermatozoa, and that *in vitro* production of spermatozoa is currently not possible.

Artificial Sperm and Egg Cells Created From Skin Cells

December 24, 2014 | by Janet Fang

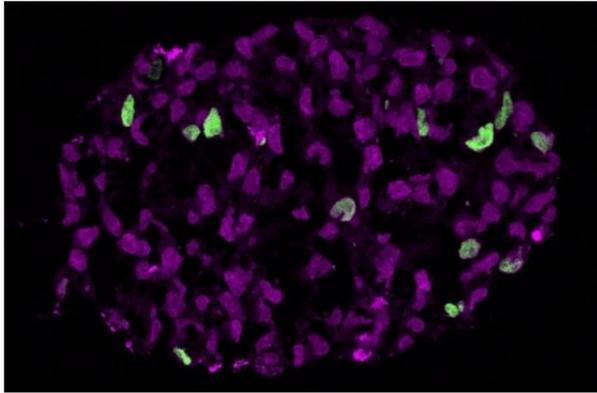


photo credit: This is an "embryoid" at the start of the appearance of SOX17 positive cells (green), which depict birth of the human germ cell lineage / Walfred Tang, University of Cambridge

A group of scientists has created artificial human sperm and eggs using human embryonic stem cells and skin cells. While researchers have already previously accomplished this using rodents, this is the first time they were able to replicate the process with human cells.

Their final products were not actually working sperm and eggs, but rather germ cells that potentially could mature and become viable for fertility. The study's findings were published Wednesday in the journal *Cell*.

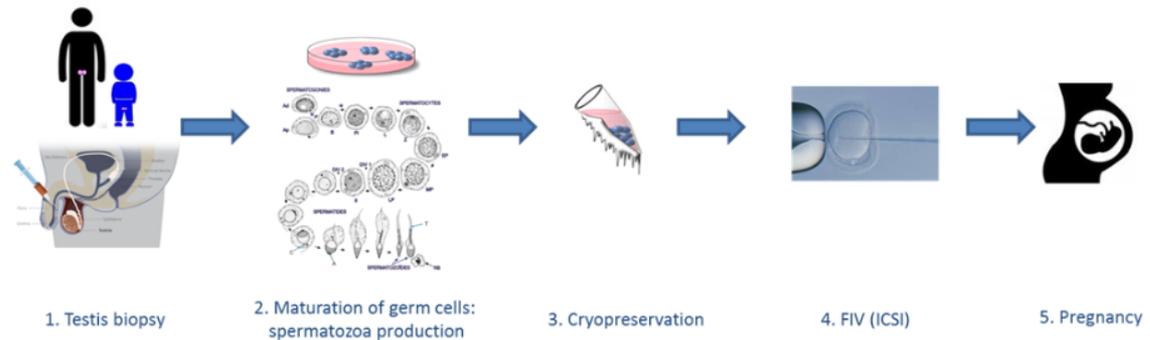
World first as SPERM is grown in a lab for the first time: Scientists claim breakthrough could give hope to infertile men

- Scientists: We have made 'fully-functioning' semen from genetic material
- Kallistem laboratory in France says it will soon carry out human trials
- Breakthrough could help thousands of men who cannot produce sperm
- Experts met claims with scepticism, as findings have not been verified

By BEN SPENCER SCIENCE REPORTER FOR THE DAILY MAIL

Technique

A testicular biopsy is achieved in boys, before treatment for cancer, or in adult men. The stem cells are then cryopreserved or directly cultivated with Artistem technology in order to mature cells into fully functional spermatozoa. The aim is to produce ex vivo spermatozoa. Then, in vitro fecondation will be performed by ICSI (intra cytoplasmique sperm injection).



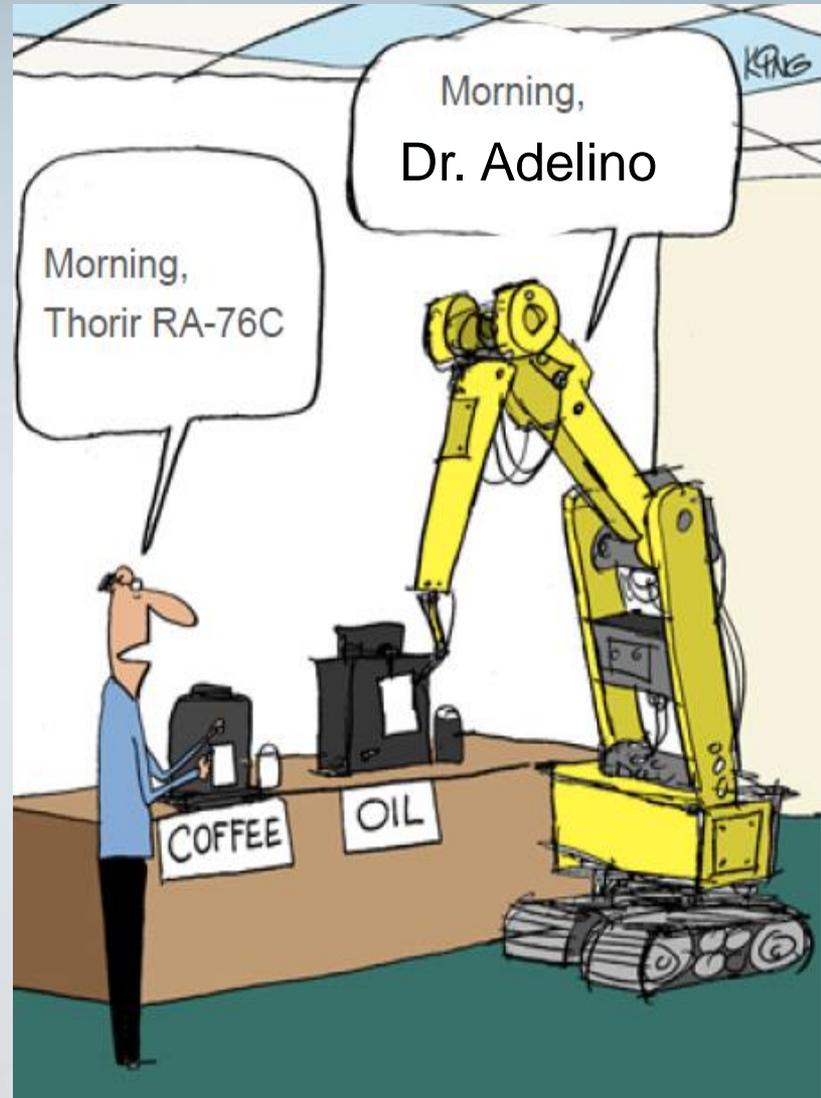
REVIEW

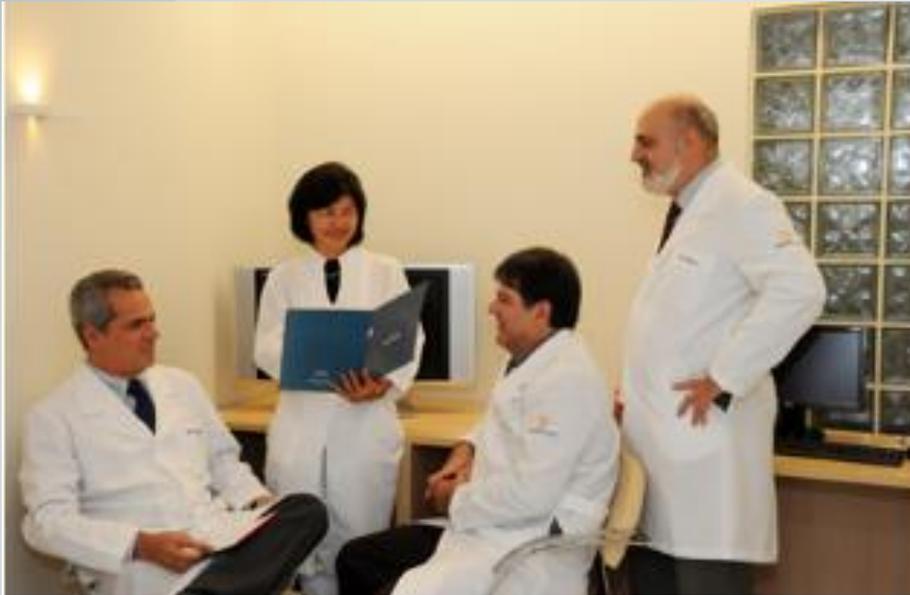
Full in vitro fertilization laboratory mechanization: toward robotic assisted reproduction?

Marcos Meseguer, Ph.D.,^a Ulrich Kruhne, Ph.D.,^b and Steen Laursen, Ph.D.^c

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Parabéns!!!!

Obrigado !

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