COMO APROFUNDAR A INVESTIGAÇÃO ?

Edson Borges Jr.

Fertility Medical Group
FERTGROUP
Instituto Sapientiae

FERTGROUP | FERTILITY

Associação Instituto Sapientiae

Declaração

Sem conflito de interesse para divulgar relacionado ao assunto desta palestra

Resolução do Conselho Federal de Medicina
nº 1.595/2.000

ANDROLOGIA BASEADA EM EVIDÊNCIAS

- Raros estudos prospectivos, randomizados
  Consequência: resultados inclusivos ou conflitivos

- Etiopatogenia não evidente em 30 – 40% das causas (idiopática)

- Estudos com pouco tempo de acompanhamento, falta de validação por outros grupos, seleção heterogênea de pacientes, grande variação natural da produção espermática

- Nenhum modelo experimental válido para infertilidade masculina

Category	Frequency
Immunological	-
Idiopathic	32.6%
Varicocele	26.6%
Obstruction	15.3%
Normal female factor (unexplained male infertility)	10.7%
Cryptorchidism	[illegible]
Ejaculatory failure	[illegible]
Endocrinologic	[illegible]
Drug/r[illegible]	[illegible]
[illegible]	1.2%
[illegible]	1.1%
[illegible]	0.7%
[illegible]ospermia	0.5%
Cancer	0.4%
Systemic disease	0.3%
Infection	0.2%
Torsion	0.1%
Ultrastructural	0.1%
Total	100.0%

Doença multifactorial com fenótipo heterogêneo

Larry I. Lipshultz. Office evaluation of the subfertile male. In: Larry I. Lipshultz SSH, Craig S. Niederberger, editor. Infertility in the Male. 4th ed: Cambridge university press 2009. p. 153 -76.

ANDROLOGIA BASEADA EM EVIDÊNCIAS

Consequência do tratamento convencional da infertilidade masculina: ***gestação e nascimento***

Interpretação extremamente difícil

Fatores fora do âmbito andrológico influenciam no resultado terapêutico!!


ONDE NASCE A VIOLÊNCIA
EU VOU FECUNDAR SOZINHO! SE ALGUÉM SE APROXIMAR EU ARRANCO A CABEÇA DELE!
amar@zaz.com.br
AMARILDO

FER

Análise Seminal

Não é um teste de fertilidade!

Avaliação do *status* funcional do testículo no momento da coleta

EDITOR'S CORNER

Evaluation of sperm damage: beyond the World Health Organization criteria

Nabil Aziz, M.R.C.O.G., M.D.,[a] and Ashok Agarwal, Ph.D., H.C.L.D.[b]

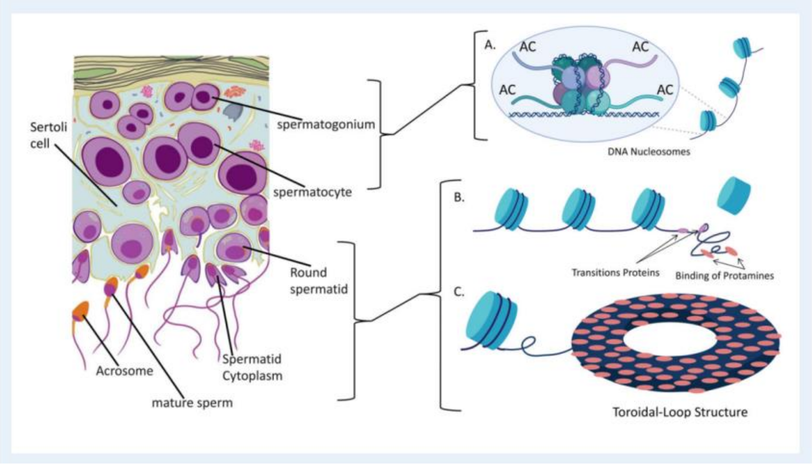
Fertility and Sterility® Vol. 90, No. 3, September 2008

- ✓ *grande flutuação na concentração, motilidade e morfologia;*
- ✓ *variação intra / inter observador;*
- ✓ *AS não investiga as propriedades biológicas e subcelulares do sptz;*
- ✓ *AS adequada para alterações seminais GRAVES;*
- ✓ *Para alterações leves/moderadas: INCONCLUSIVA*

☛ ***necessidade de outros testes funcionais mais específicos***

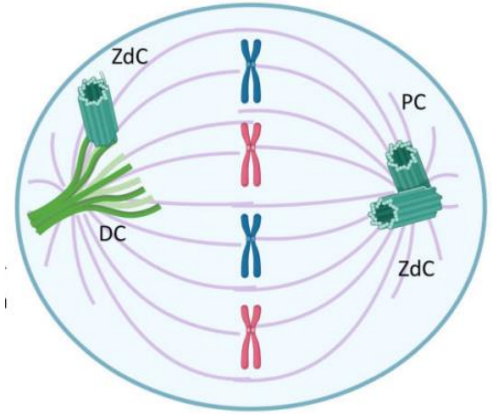
Contribuição do SÊMEN na fertilização e divisão embrionária

- ***Plasma seminal - vesículas extracelulares:*** epididimossomos e prostatossomos, com influência na gametogênese, fertilização, embriogênese e receptividade endometrial

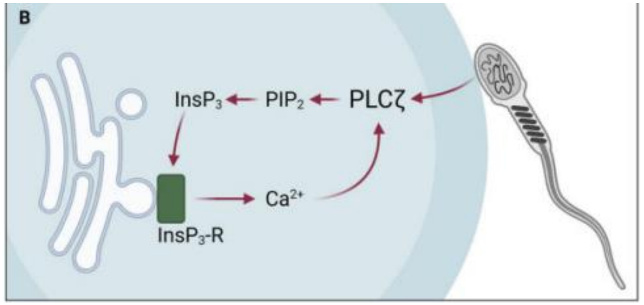


- ***Espermatogênese:*** material genético e influência epigenética (histonas/protaminas)

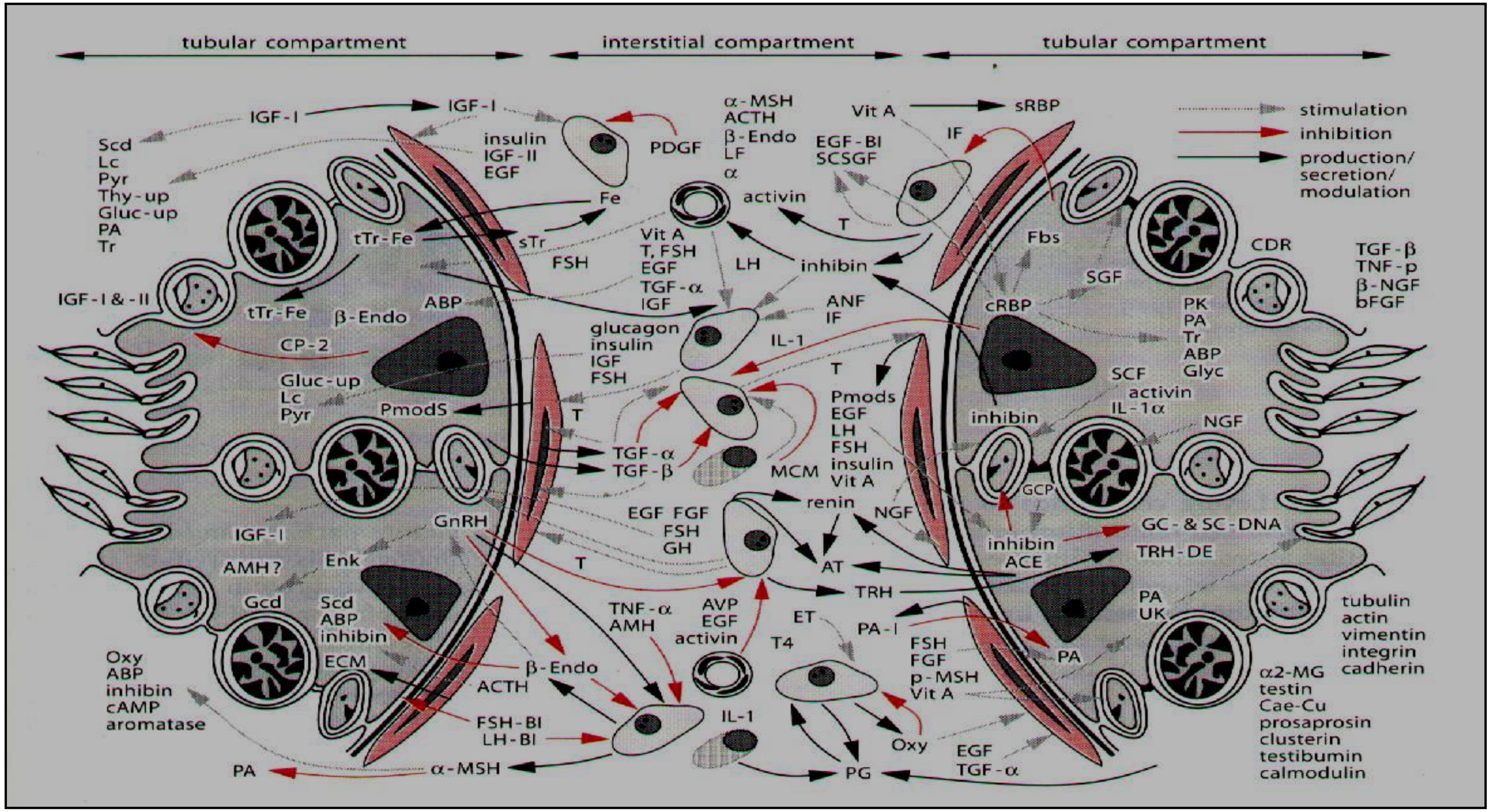
- ***Centríolos***: divisão embrionária



- ***Fertilização:*** PLC zeta



TÚBULO SEMINÍFERO



- 65-70 dias: espermatogônia - espermatozoide
- 3 mitoses + 2 meioses
- 10^{12} – 10^{13}: produção em vida
- 75% perda por apoptose

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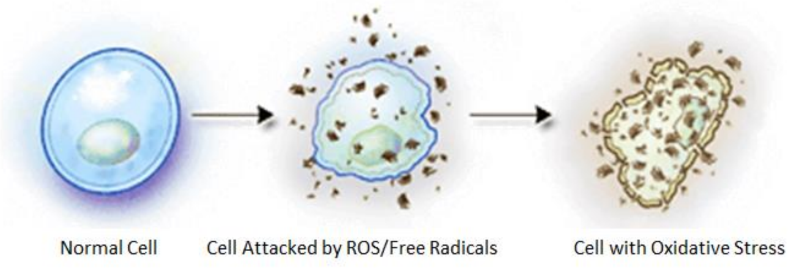
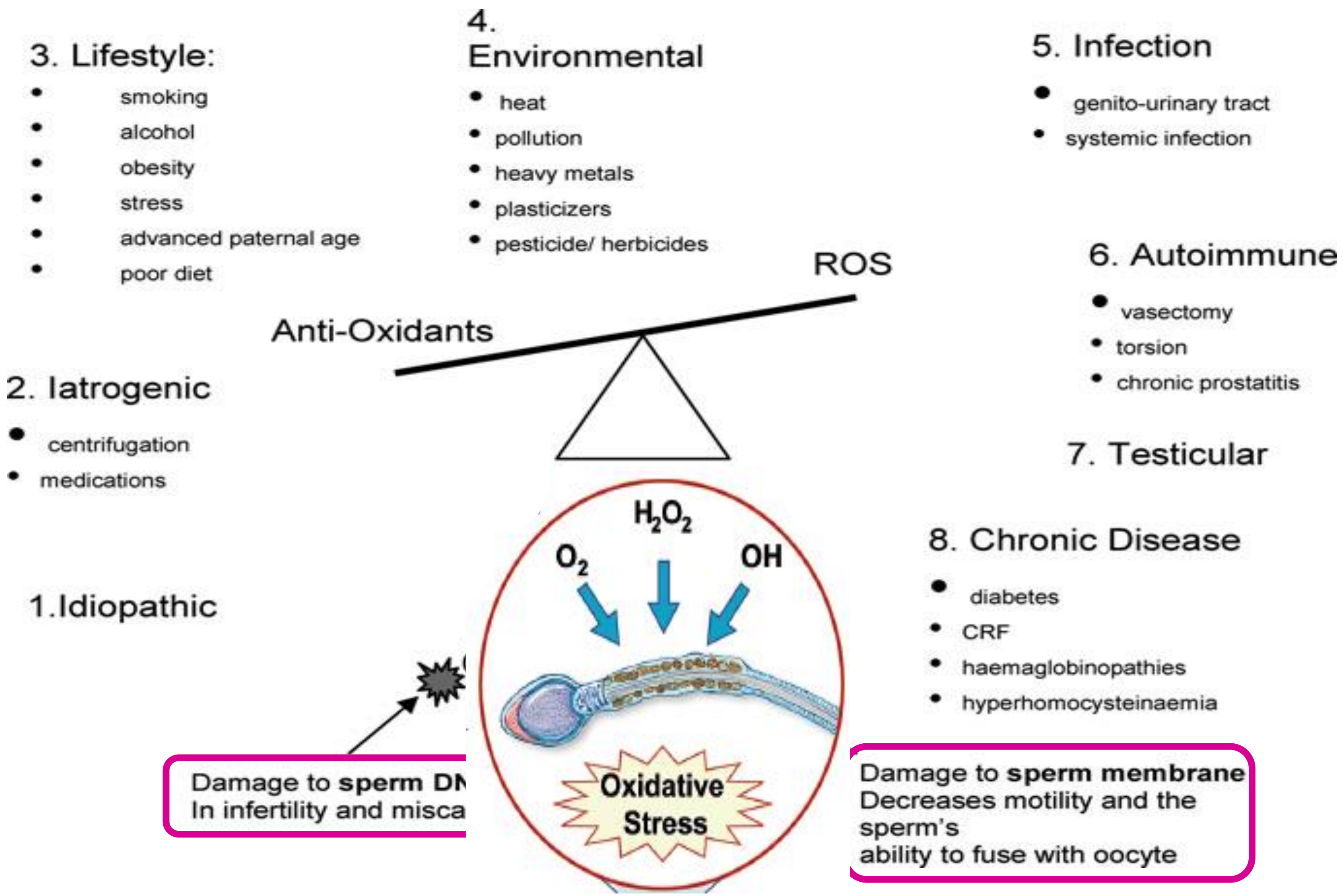
Mecanismos biológicos da Fragmentação do Espermatozoide

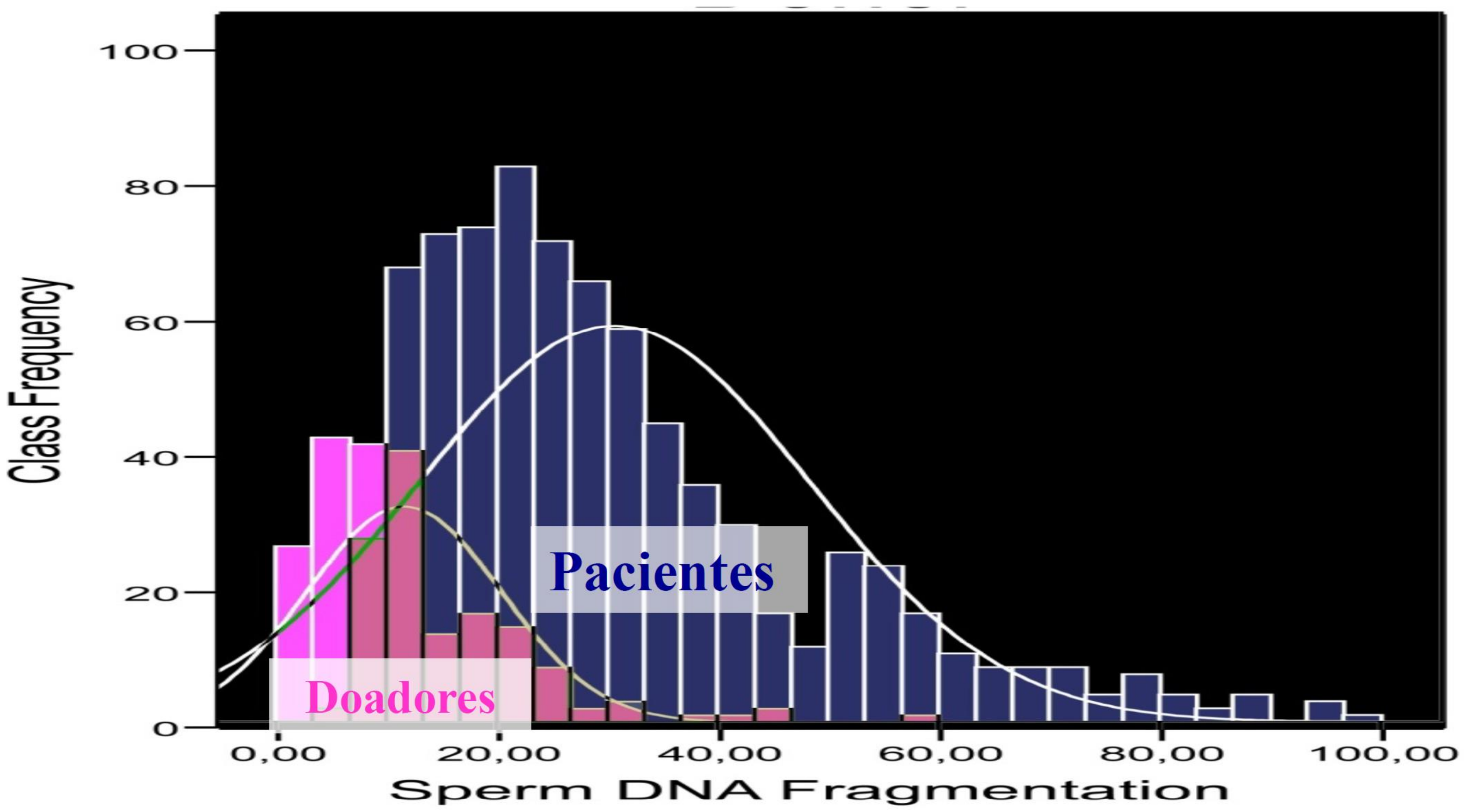
- *ALTERAÇÃO DA PROTAMINA*
- *APOPTOSE ABORTIVA*
- *ESTRESSE OXIDATIVO*





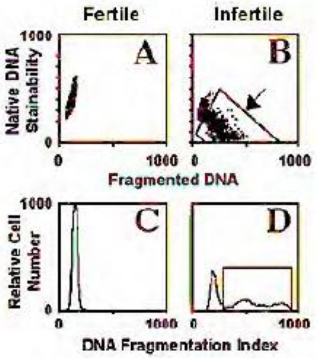
Kelton Tremellen; Human Reproduction Update, Vol.14, No.3 pp. 243–258, 2008

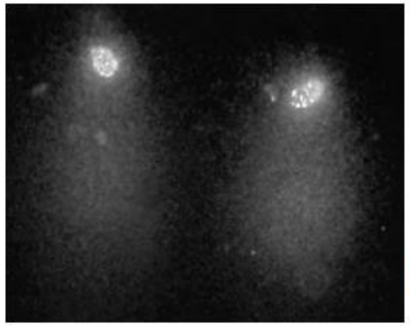
Taxa de Fragmentação do DNA espermático

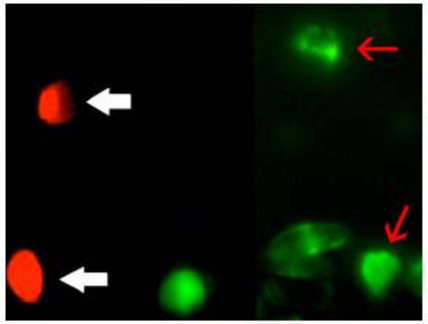


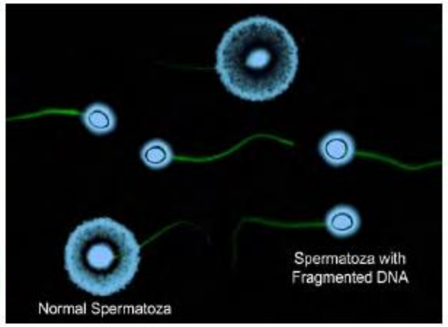
Gosalvez et al. J *Reprod Biotechnol Fertil*. 2015

	Labor-intensive	Expensive equipment	Analysis Subjectivity	Validation & Standardization
TUNEL	++++	+++	++	++
SCSA	++	++++	+	++++
Comet	++++	+++	+++	+
SCD	+	+	++	+++









Correlação e limiares semelhantes entre SCSA, TUNEL e SCD para o diagnóstico de Infertilidade Masculina

Ribas-Maynou *et al.* Andrology, 2013

- SCD e SCSA (r= 0,71; p < 0,001)
- SCD e TUNEL (r= 0,70; p < 0,001)
- SCSA e TUNEL (r= 0,79; p < 0,001)

Asian Journal of Andrology (2017) 19, 80–90

www.asiaandro.com; www.ajandrology.com

Open Access

ORIGINAL ARTICLE

Sperm Biology

A systematic review and meta-analysis to determine the effect of sperm DNA damage on *in vitro* fertilization and intracytoplasmic sperm injection outcome

Luke Simon[1,*], Armand Zini[2,*], Alina Dyachenko[2], Antonio Ciampi[2], Douglas T Carrell[1,3,4]

Table 3: Meta-analysis summary: Overall and subgroup odds ratios of studies on sperm DNA damage and pregnancy

Effect	*Number of studies*	*Fixed effects model*		*Random effects model*	
		OR (95% CI)	*P*	*OR (95% CI)*	*P*
Overall effect	56	1.68 (1.49–1.89)	0.0000*	1.84 (1.5–2.27)	<0.0001*
Sperm DNA damage assays					
SCSA	23	1.18 (0.96–1.44)	0.1115	1.22 (0.93–1.61)	0.1522
TUNEL	18	2.18 (1.75–2.72)	0.0000*	2.22 (1.61–3.05)	<0.0001*
Comet	7	3.34 (2.32–4.82)	0.0000*	3.56 (1.78–7.09)	0.0003*
SCD	8	1.51 (1.18–1.92)	0.0011*	1.98 (1.19–3.3)	0.0086*
Types of assisted treatment					
IVF	16	1.65 (1.34–2.04)	0.0000*	1.92 (1.33–2.77)	0.0005*
ICSI	24	1.31 (1.08–1.59)	0.0068*	1.49 (1.11–2.01)	0.0075*
Mixed	16	2.37 (1.89–2.97)	0.0000*	2.32 (1.54–3.5)	0.0001*

Asian Journal of Andrology (2017) 19, 80–90

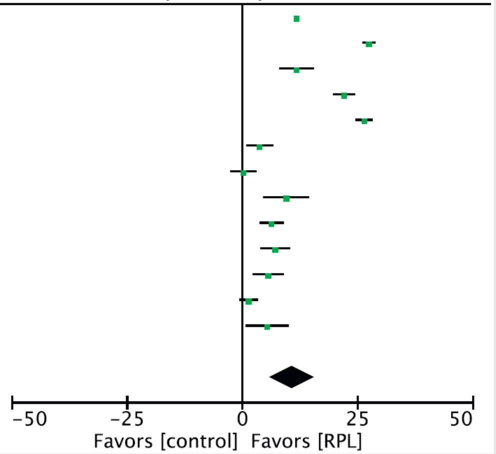
Sperm DNA fragmentation and recurrent pregnancy loss: a systematic review and meta-analysis

Dana B. McQueen, M.D., M.A.S., John Zhang, Ph.D., and Jared C. Robins, M.D.

Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Northwestern University, Chicago, Illinois

Study or Subgroup	Recurrent Pregnancy Loss Mean	SD	Total	Fertile Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Absalan 2012	23.3	1.1	30	11.6	0.5	30	7.9%	11.70 [11.27, 12.13]
Bareh 2016	36.8	2.7	26	9.4	2.7	31	7.9%	27.40 [25.99, 28.81]
Bhattachara 2008	18.1	16.1	74	6.4	3.6	65	7.6%	11.70 [7.93, 15.47]
Brahem 2011	32.2	6.1	31	10.2	2.1	20	7.8%	22.00 [19.66, 24.34]
Carrell 2003	38.3	4.2	21	11.9	1	26	7.8%	26.40 [24.56, 28.24]
Coughlan 2014	10.9	1.9	16	7.2	3.7	7	7.7%	3.70 [0.81, 6.59]
Esquerre–Lamare 2018	6.8	5.6	33	6.6	5.5	27	7.7%	0.20 [−2.62, 3.02]
Imam 2011	23.4	9.9	20	13.9	5.4	20	7.3%	9.50 [4.56, 14.44]
Kumar 2012	28.1	5	45	21.8	4.8	20	7.8%	6.30 [3.74, 8.86]
Ribas 2012	19.3	6.1	20	12.2	4.6	25	7.7%	7.10 [3.88, 10.32]
Ruixue 2013	25.6	11.5	68	20	7.7	63	7.6%	5.60 [2.27, 8.93]
Zhang 2012	15.2	6.4	111	13.9	4.4	30	7.8%	1.30 [−0.67, 3.27]
Zidi–Jrah 2016	17.1	9.3	22	11.8	5.7	20	7.4%	5.30 [0.68, 9.92]
Total (95% CI)			**517**			**384**	**100.0%**	**10.70 [5.82, 15.58]**

Heterogeneity: $Tau^2 = 78.10$, $Chi^2 = 1019.62$, df = 12 ($P < 0.00001$); $I^2 = 99\%$
Test for overall effect: Z = 4.30 ($P < 0.0001$)



Primary outcome in overall analysis.

McQueen. Sperm DNA fragmentation and RPL. Fertil Steril 2019.

ANDROLOGY

ISSN: 2047-2919

ANDROLOGY

ORIGINAL ARTICLE

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

Received: 13-Jul-2018
Revised: 4-Oct-2018
Accepted: 7-Nov-2018

doi: 10.1111/andr.12572

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

[1,2]E. Borges Jr., [1,2]D. P. A. F. Braga, [2]B. F. Zanetti, [1,2]A. Iaconelli Jr. and [1,2]A. S. Setti

[1]Fertility Medical Group, Sao Paulo, Brazil, and [2]Sapientiae Institute, Sao Paulo, Brazil

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Linear model analysis of the association between sperm parameters and EA length (n = 818)

SEMEN PARAMETER	R	SLOPE	R^2 (%)	P-VALUE
Semen volume (mL)	0.1405	1.62102	5.28	<0.001
Sperm count ($x10^6$/mL)	3.1261	52.2206	2.59	<0.001
Total sperm count ($x10^6$)	18.941	170.650	8.37	<0.001
Total sperm motility (%)	-0.3355	19.0885	0.23	0.212
Progressive sperm motility (%)	-0.1895	19.1802	0.07	0.483
TMSC ($x10^6$)	9.6396	102.629	6.14	<0.001
Morphology (%)	0.0227	1.29926	0.23	0.215
SDF (%)	0.5355	9.34201	2.57	<0.001

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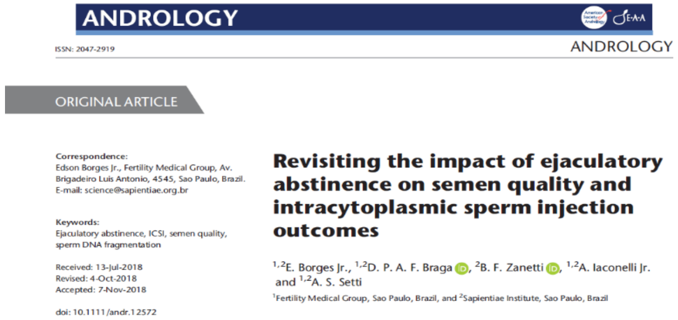

ANDROLOGY
ISSN: 2047-2919
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ORIGINAL ARTICLE

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[1]Fertility Medical Group, Sao Paulo, Brazil, and [2]Sapientiae Institute, Sao Paulo, Brazil

Abstinência ejaculatória ≤ 4 dias:

- Frag DNA espermático significativamente menor, maiores taxas de fertilização, embriões de alta qualidade no dia 3, desenvolvimento a blastocisto, implantação e gestação quandocomparados ao grupo de abstinência ejaculatória ≥ 4 dias.

- Taxas de implantação significativamente maiores e taxas de gestação tendendo a serem maiores com ***um dia de abstinência ejaculatória***, comparado a 2 – 4 de abstinência ejaculatória.

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DOI: 10.1111/and.13090

ORIGINAL ARTICLE

WILEY andrologia

Paternal lifestyle factors in relation to semen quality and in vitro reproductive outcomes

Edson Borges Jr[1,2] | Daniela Paes de Almeida Ferreira Braga[1,2] | Rodrigo R. Provenza[1] | Rita de Cassia Savio Figueira[1] | Assumpto Iaconelli Jr[1,2] | Amanda Souza Setti[1,2]

- Fator masculino isolado
- 1º. ciclo de tratamento
- Idade mulher < 36 anos
- 233 ciclos ICSI

1. Quantos cigarros/dia?
2. Consumo semanal de álcool?
3. Frequência de exercícios ?
4. Medicações nos últimos 3 meses? Qual?
5. Exposição a agentes tóxicos, pesticidas, radiação etc..

Linear regression analyses' results for the influence of paternal lifestyle factors on semen quality (n=965)

	Cigarette smoking		Alcohol consumption	
	B	p	B	p
Semen volume	-0.417	0.047	-0.1363	0.592
Sperm count/mL	-7.363	0.014	-12.527	0.040
Total sperm count	-4.43	0.023	-34.91	0.156
Total sperm motility	2.316	0.347	0.342	0.895
Progressive sperm motility	-0.369	0.887	2.547	0.240
TMSC	- 1.38	0.045	-16.33	0.278
Sperm morphology	-0.0563	0.779	0.3751	0.180
SDF	0.014	0.033	5.833	0.002

Sperm DNA fragmentation is correlated with poor embryo development, lower implantation rate, and higher miscarriage rate in reproductive cycles of non–male factor infertility

Edson Borges Jr., M.D., Ph.D.,[a,b] Bianca Ferrarini Zanetti, Ph.D.,[a,b] Amanda Souza Setti, M.Sc.,[a,b] Daniela Paes de Almeida Ferreira Braga, Ph.D.,[a,b] Rodrigo Rosa Provenza, B.Sc.,[a] and Assumpto Iaconelli Jr., M.D.[a,b]

[a] Fertility Medical Group and [b] Instituto Sapientiae, Centro de Estudos e Pesquisa em Reprodução Humana Assistida, São Paulo, Brazil

Descriptive analysis of seminal parameters according to SDF groups.

Parameter	< 30% SDF (n = 433)	≥30% SDF (n = 42)	*P* value
Paternal age, y	38.68 ± 5.65	41.19 ± 6.35	.009
Ejaculatory abstinence, d	3.92 ± 2.42	5.51 ± 5.46	.002
Seminal volume, mL	2.94 ± 0.50	3.79 ± 1.09	.001
Seminal concentration, $\times 10^6$/mL	77.70 ± 29.83	81.09 ± 33.23	.677
Total sperm count, $\times 10^6$	214.58 ± 72.95	303.71 ± 78.80	.003
Total sperm motility, %	63.45 ± 12.75	55.52 ± 17.55	< .001
Progressive sperm motility, %	54.90 ± 14.27	46.50 ± 16.77	< .001
Total motile sperm count	121.11 ± 98.24	146.89 ± 139.09	.120
SDF, %	17.48 ± 8.70	37.67 ± 6.39	< .001

Borges. Sperm DNA fragmentation and ICSI outcomes. Fertil Steril 2019.

ORIGINAL ARTICLE: ANDROLOGY

Check for updates

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Edson Borges Jr., M.D., Ph.D.,[a,b] Bianca Ferrarini Zanetti, Ph.D.,[a,b] Amanda Souza Setti, M.Sc.,[a,b] Daniela Paes de Almeida Ferreira Braga, Ph.D.,[a,b] Rodrigo Rosa Provenza, B.Sc.,[a] and Assumpto Iaconelli Jr., M.D.[a,b]

[a] Fertility Medical Group and [b] Instituto Sapientiae, Centro de Estudos e Pesquisa em Reprodução Humana Assistida, São Paulo, Brazil

Effect of SDF on laboratory and clinical outcomes.

Variable	< 30% SDF (n = 433)	≥30% SDF (n = 42)	*P* value
Laboratory outcomes[a]			
Fertilization rate	90.10 ± 3.50	85.67 ± 1.03	.226
Normal cleavage speed rate	72.16 ± 1.30	61.56 ± 4.40	.010
High-quality embryos at day 3 rate	36.47 ± 1.51	23.89 ± 5.51	.021
Blastocyst rate	56.25 ± 2.01	39.01 ± 1.40	.016
Blastocyst quality rate	30.54 ± 2.27	11.32 ± 7.72	< .001
Clinical outcomes[b]			
Implantation rate	46.09 ± 0.55	33.21 ± 1.96	< .001
Chemical pregnancy rate	34.99	33.11	.940
Clinical pregnancy rate	32.42	30.33	.774
Miscarriage rate	17.8	39.9	.018

[a] Adjusted for maternal age, maternal BMI, total FSH dose, number of retrieved oocytes, and paternal age.
[b] Adjusted for maternal age, maternal BMI, total FSH dose, number of retrieved oocytes, paternal age, number of transferred embryos, endometrial thickness.

Borges. Sperm DNA fragmentation and ICSI outcomes. Fertil Steril 2019.

FERTGR

Fertility and Sterility® Vol. 112, No. 3, September 2019

Review Article

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World J Mens Health 2019 Sep 37(3): 296-312
https://doi.org/10.5534/wjmh.190055

The World Journal of MEN's HEALTH

Male Oxidative Stress Infertility (MOSI): Proposed Terminology and Clinical Practice Guidelines for Management of Idiopathic Male Infertility

Ashok Agarwal[1,2], Neel Parekh[2], Manesh Kumar Panner Selvam[1,2], Ralf Henkel[1,3], Rupin Shah[4], Sheryl T. Homa[5], Ranjith Ramasamy[6], Edmund Ko[7], Kelton Tremellen[8], Sandro Esteves[9,10], Ahmad Majzoub[1,11], Juan G. Alvarez[12], David K. Gardner[13], Channa N. Jayasena[14,15], Jonathan W. Ramsay[15], Chak-Lam Cho[16], Ramadan Saleh[17], Denny Sakkas[18], James M. Hotaling[19], Scott D. Lundy[2], Sarah Vij[2], Joel Marmar[20], Jaime Gosalvez[21], Edmund Sabanegh[2], Hyun Jun Park[22,23], Armand Zini[24], Parviz Kavoussi[25], Sava Micic[26], Ryan Smith[27], Gian Maria Busetto[28], Mustafa Emre Bakırcıoğlu[29], Gerhard Haidl[30], Giancarlo Balercia[31], Nicolás Garrido Puchalt[32], Moncef Ben-Khalifa[33], Nicholas Tadros[34], Jackson Kirkman-Browne[35,36], Sergey Moskovtsev[37], Xuefeng Huang[38], Edson Borges Jr[39], Daniel Franken[40], Natan Bar-Chama[41], Yoshiharu Morimoto[42], Kazuhisa Tomita[42], Vasan Satya Srini[43], Willem Ombelet[44,45], Elisabetta Baldi[46], Monica Muratori[47], Yasushi Yumura[48], Sandro La Vignera[49], Raghavender Kosgi[50], Marlon P. Martinez[51], Donald P. Evenson[52], Daniel Suslik Zylbersztejn[53], Matheus Roque[54], Marcello Cocuzza[55], Marcelo Vieira[56,57], Assaf Ben-Meir[58], Raoul Orvieto[59,60], Eliahu Levitas[61], Amir Wiser[62,63], Mohamed Arafa[64], Vineet Malhotra[65], Sijo Joseph Parekattil[66,67], Haitham Elbardisi[64], Luiz Carvalho[68,69], Rima Dada[70], Christophe Sifer[71], Pankaj Talwar[72], Ahmet Gudeloglu[73], Ahmed M.A. Mahmoud[74], Khaled Terras[75], Chadi Yazbeck[76], Bojanic Nebojsa[77], Damayanthi Durairajanayagam[78], Ajina Mounir[79], Linda G. Kahn[80], Saradha Baskaran[1], Rishma Dhillon Pai[81], Donatella Paoli[82], Kristian Leisegang[83], Mohamed-Reza Moein[84], Sonia Malik[85], Onder Yaman[86], Luna Samanta[87], Fouad Bayane[88], Sunil K. Jindal[89], Muammer Kendirci[90], Baris Altay[91], Dragoljub Perovic[92], Avi Harlev[93]

Male Infertility

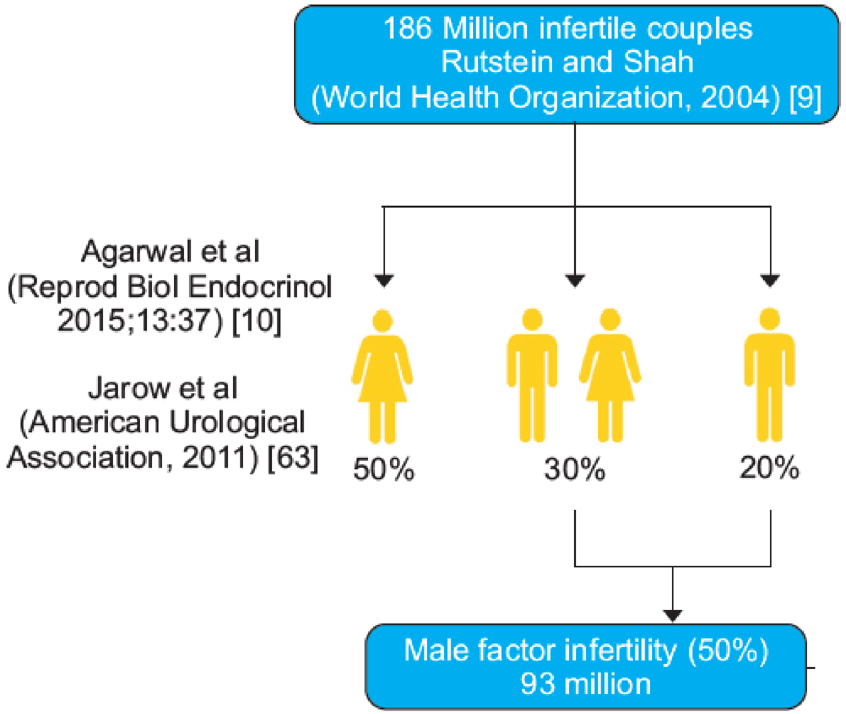
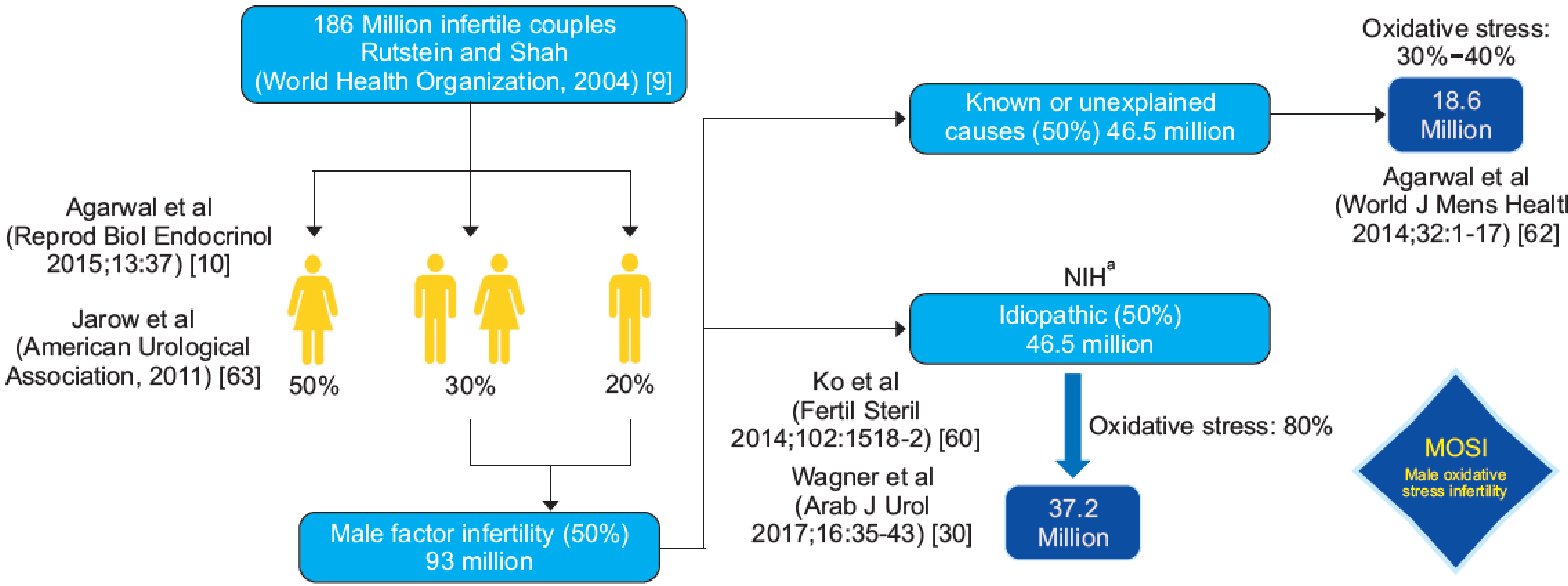


Fig. 3. Worldwide incidence of MOSI in infertile men. [a]National Institutes of Health (NIH) (https://www.nichd.nih.gov/health/topics/menshealth/conditioninfo/infertility) [61], Agarwal et al (2014) [62], Jarow et al (2011) [63].

Male Infertility



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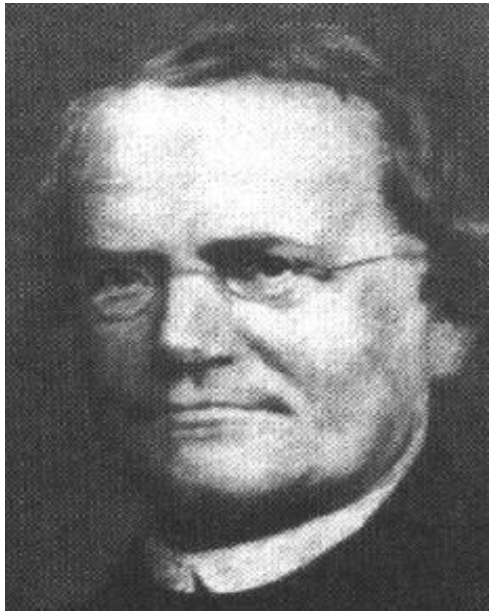
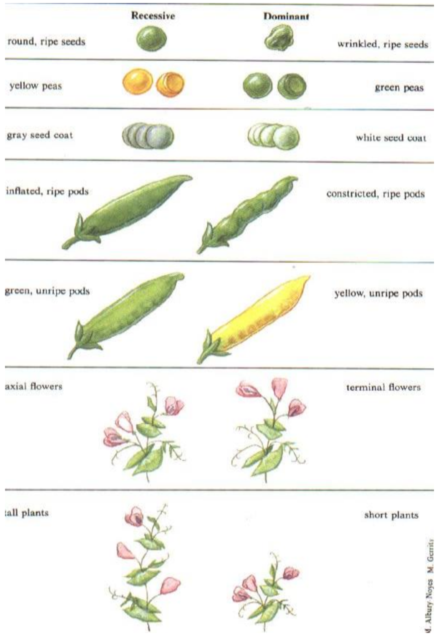
Genética e Infertilidade Masculina

GENÉTICA ⟺ FERTILIDADE



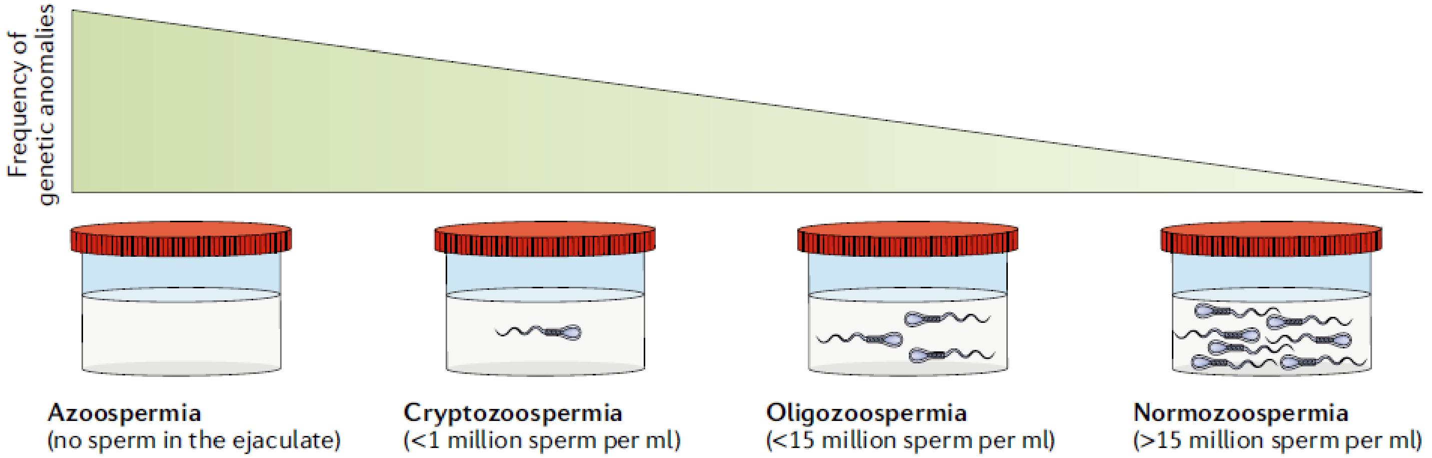
Gregor Mendel



ANORMALIDADES CROMOSSÔMICAS EM HOMENS INFÉRTEIS

REFERÊNCIAS	Nº	CROMOSSÔMOS SEXUAIS	AUTOSSÔMOS	TOTAL
KOULISCHER E SCHOYSMAN (1974)	1000	27 (2.7)	6 (0.6)	33 (3.3)
CHANDLEY (1979)	2372	33 (1.4)	18 (0.7)	51 (2.1)
ZUFFARDI E TIEPOLO (1982)	2542	175 (6.9)	40 (1.6)	215 (8.6)
ABRAMSSON *et al* (1982)	342	6 (1.8)	4 (1.2)	10 (2.9)
de GARDELLE *et al* (1983)	318	13 (4.1)	7 (2.2)	20 (6.3)
MATSUDA *et al* (1989)	295	0 (0)	5 (1.7)	5 (1.7)
YOSHIDA et al (1995)	1007	41 (4.1)	24 (2.4)	65 (6.5)
TOTAL	**7876**	**295 (3.8)**	**104 (1.3)**	**399 (5.1)**
NASCIDOS	**94.465**	**131 (0.14)**	**232 (0.25)**	**366 (0.38)**

Alterações cromossômicas maiores
&
densidade espermática



Gekas et al. Human Reprod 16:82-90, 2001
Crausz et al. Nat Ver Urol, 15:369-84, 2018

MODERN TRENDS
Edward E. Wallach, M.D.
Associate Editor
Fertility and Sterility® Vol. 93, No. 1, January 2010

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% azoospérmicos

MicroDeleleção Y: 2 - 20% oligo grave / azoospérmicos

CBAVD: 1 - 2% homens inférteis
10% azoospermias obstrutivas

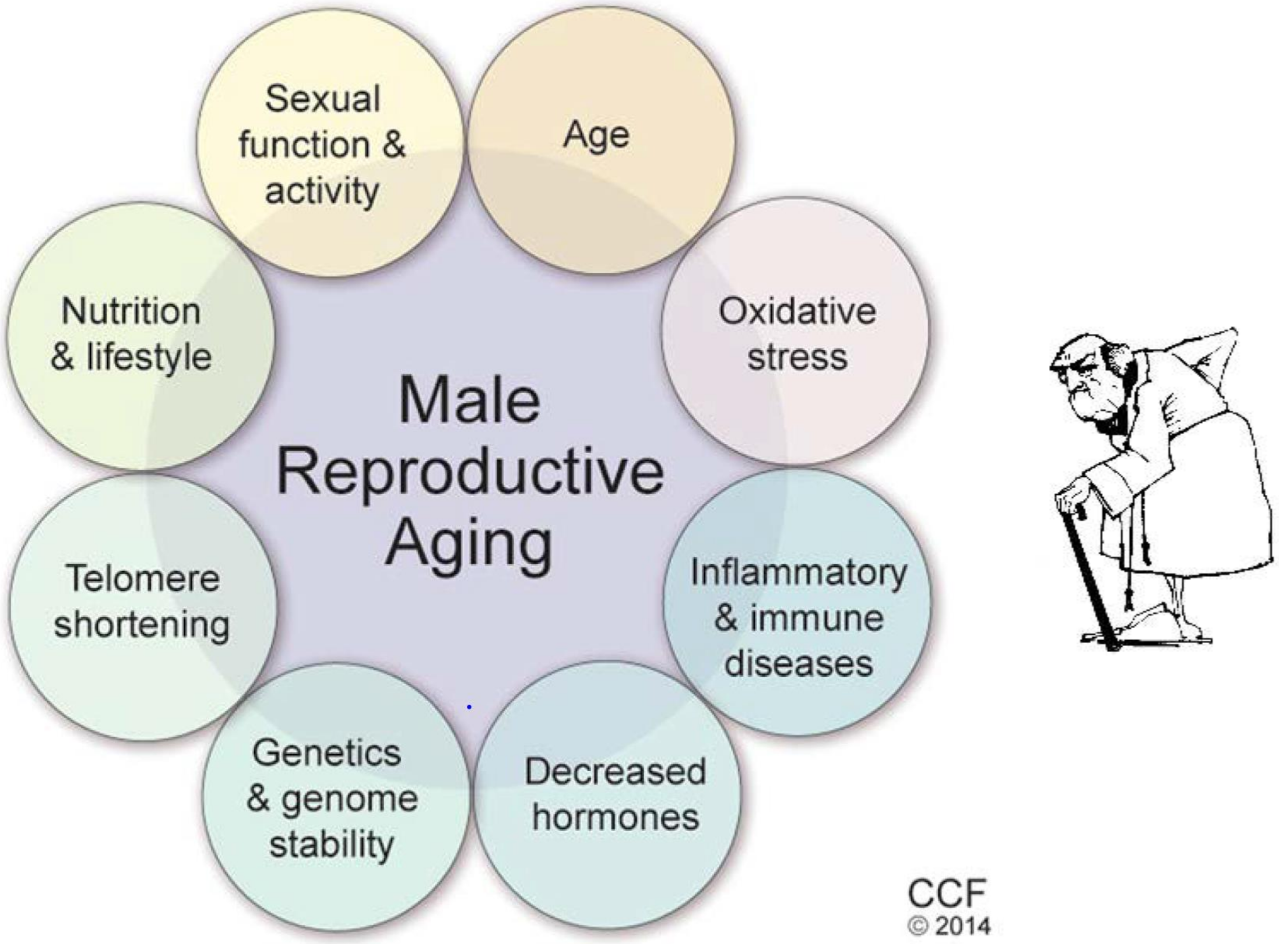


Figure 1 Main factors involved in impaired male infertility due to reproductive aging.

RB&E REPRODUCTIVE BIOLOGY AND ENDOCRINOLOGY

Sharma *et al. Reproductive Biology and Endocrinology* (2015) 13:35
DOI 10.1186/s12958-015-0028-x

Human Reproduction Update, Vol.16, No.1 pp. 65–79, 2010
Advanced Access publication on August 20, 2009 doi:10.1093/humupd/dmp027

human reproduction update

Paternal age and reproduction

Gideon A. Sartorius[1,2] and Eberhard Nieschlag[1,3]

[1]Centre of Reproductive Medicine and Andrology of the University, Domagkstrasse 11, D-48149 Muenster, Germany [2]Present address:

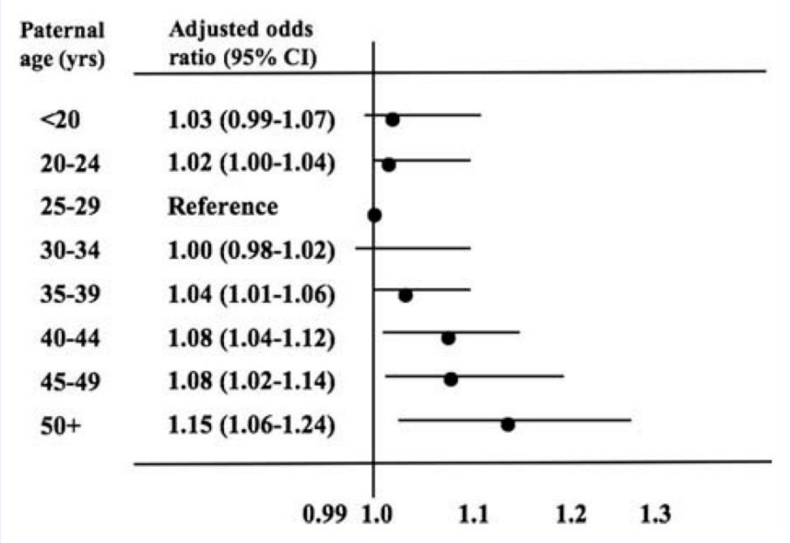


Figure 4 Relative risk of birth defects depending on paternal age.

Retrospective analysis of 5 213 248 subjects in the USA. Increased risk for heart defects, circulatory/respiratory defects, diaphragmatic hernia, tracheo-oesophageal fistulas, musculo-sceletal anomalies (data extracted from Yang *et al.*, 2007).

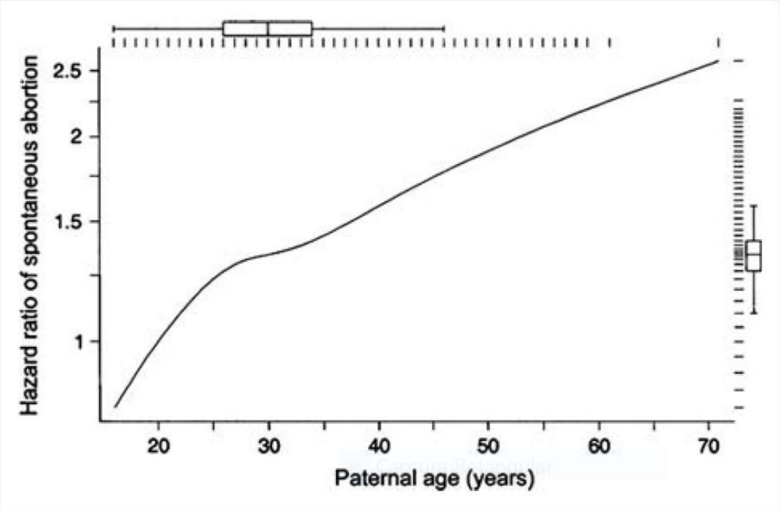


Figure 3 Hazard ratios of spontaneous miscarriages between 6 and 20 weeks according to paternal age adjusted for different confounders including maternal age (using prospective data from 5121 Californian women, men aged 20 years as referent).

Boxplots along the top and right side indicate data distribution according to each axis (with permission from Slama *et al.*, 2005).

Table XI Summary results of the meta-analyses of the association between paternal factors and perinatal and paediatric outcomes.

Exposure	Outcome	Pooled estimate (with 95% CI)	Certainty of evidence GRADE
Paternal age	PTB	1.02 (1.00–1.05)	⊕⊕○○
	Low BW	1.00 (0.97–1.03)	⊕⊕○○
	Stillbirth	1.19 (1.10–1.30)	⊕⊕○○
	★ Children with any birth defects	1.05 (1.02–1.07)	⊕⊕⊕○
	★ CHDs	1.03 (0.99–1.06)	⊕⊕⊕○
	Orofacial clefts	0.99 (0.95–1.04) 1.14 (1.02–1.29)*	⊕⊕○○
	★ Gastroschisis	0.88 (0.78–1.00)	⊕⊕⊕○
	★ Spina bifida	0.97 (0.90–1.04)	⊕⊕⊕○
	★ Trisomy 21	1.13 (1.05–1.23)	⊕⊕⊕○
	★ Acute lymphoblastic leukaemia	1.08 (0.96–1.21)	⊕⊕⊕○
	★ Autism and ASDs	1.25 (1.20–1.30)	⊕⊕⊕○
	★ Schizophrenia	1.31 (1.23–1.38)	⊕⊕⊕○
Paternal BMI	No meta-analysis		
Paternal smoking	PTB	1.16 (1.00–1.35)	⊕⊕○○
	Low BW	1.10 (1.00–1.21)	⊕⊕○○
	SGA	1.22 (1.03–1.44)	⊕⊕○○
	CHDs	1.75 (1.25–2.44)	⊕⊕○○
	Orofacial clefts	1.51 (1.16–1.97)	⊕⊕○○
	Brain tumours	1.12 (1.03–1.22)	⊕⊕○○

*Exposure: Paternal age >45 years.

AZOOSPERMIA

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

CLINICS

REVIEW

CLINICS 2013;68(S1):35-38

The importance of semen analysis in the context of azoospermia

Nabil Aziz

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

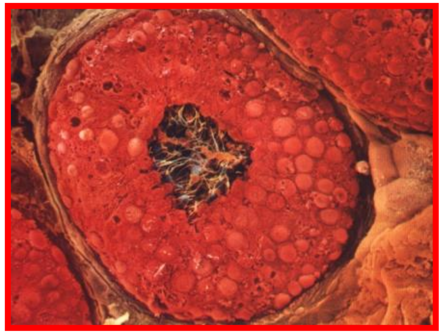
Reference	Recommended centrifugation
Mortimer (1994) (23)	1000 x *g* for 15 minutes
the Nordic Association for Andrology (24)	*At least* 1000 x *g* for 15 minutes
WHO manual (1999) (25)	600 x *g* for 15 minutes to concentrate samples with low sperm counts (less than 2 sperm per 400x field) *Less than* 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

AZOOSPERMIA OBSTRUTIVA (excretora)

- ***CONGÊNITA***
  - Agenesia congênita bilateral dos ductos deferentes



- ***ADQUIRIDA***
  - Processos inflamatórios-infecciosos dos epidídimos / traumas
  - Vasectomia
  - Neurológica
  - Obstrução ductos ejaculatórios

AZOOSPERMIA NÃO-OBSTRUTIVA

- ***CONGÊNITA***
  - Klinefelter, Noonan
  - Deleção Y
  - 47,XYY, anomalias estruturais
  - Insensibilidade androgênica
  - Disgenesia gonadal

- ***VARICOCELE***
- ***AMBIENTAL***
- ***IDIOPÁTICA***

- **ADQUIRIDA**
  - Orquite
  - Radiação
  - Medicamentosa (quimioterapia)
  - Anabolizantes esteroides
  - Torção testicular
  - Distopia testicular (criptorquidia)
  - Tumores

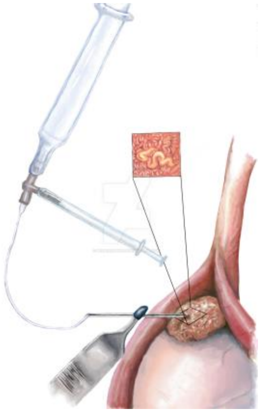
Falência Testicular !!

RECUPERAÇÃO DE ESPERMATOZÓIDES NÃO EJACULADOS

ESPERMATOZÓIDES ESPIDIDIMÁRIOS

PERCUTANEOUS
EPIDYDIMAL
SPERM
ASPIRATION

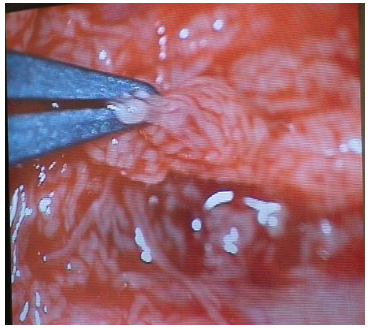
MICROSURGICAL
EPIDYDIMAL
SPERM
ASPIRATION



ESPERMATOZÓIDES TESTICULARES

TESTICULAR
SPERM
ASPIRATION

Micro
TESTICULAR
SPERM
EXTRACTION

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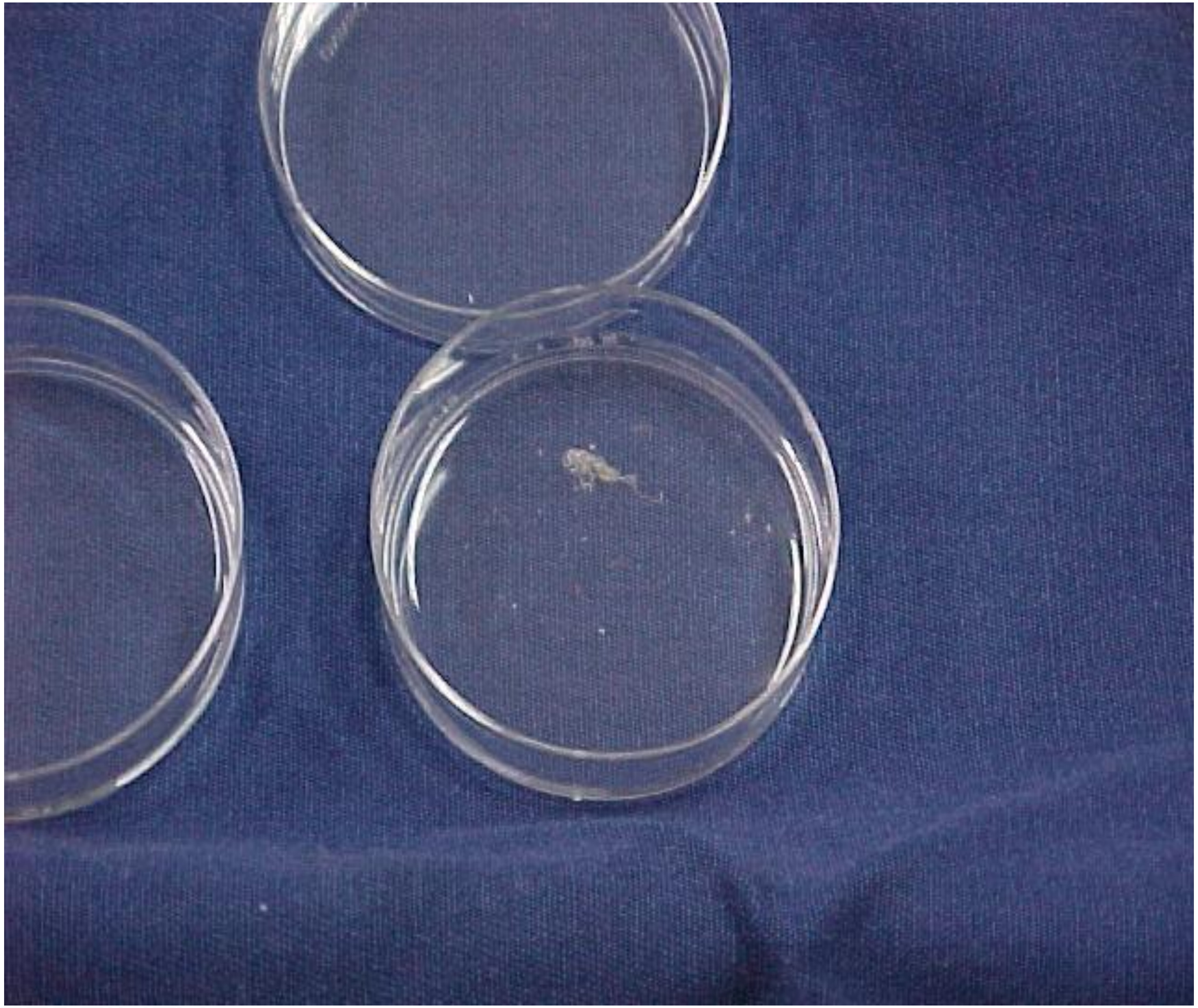
TESA / PESA


5
10
15

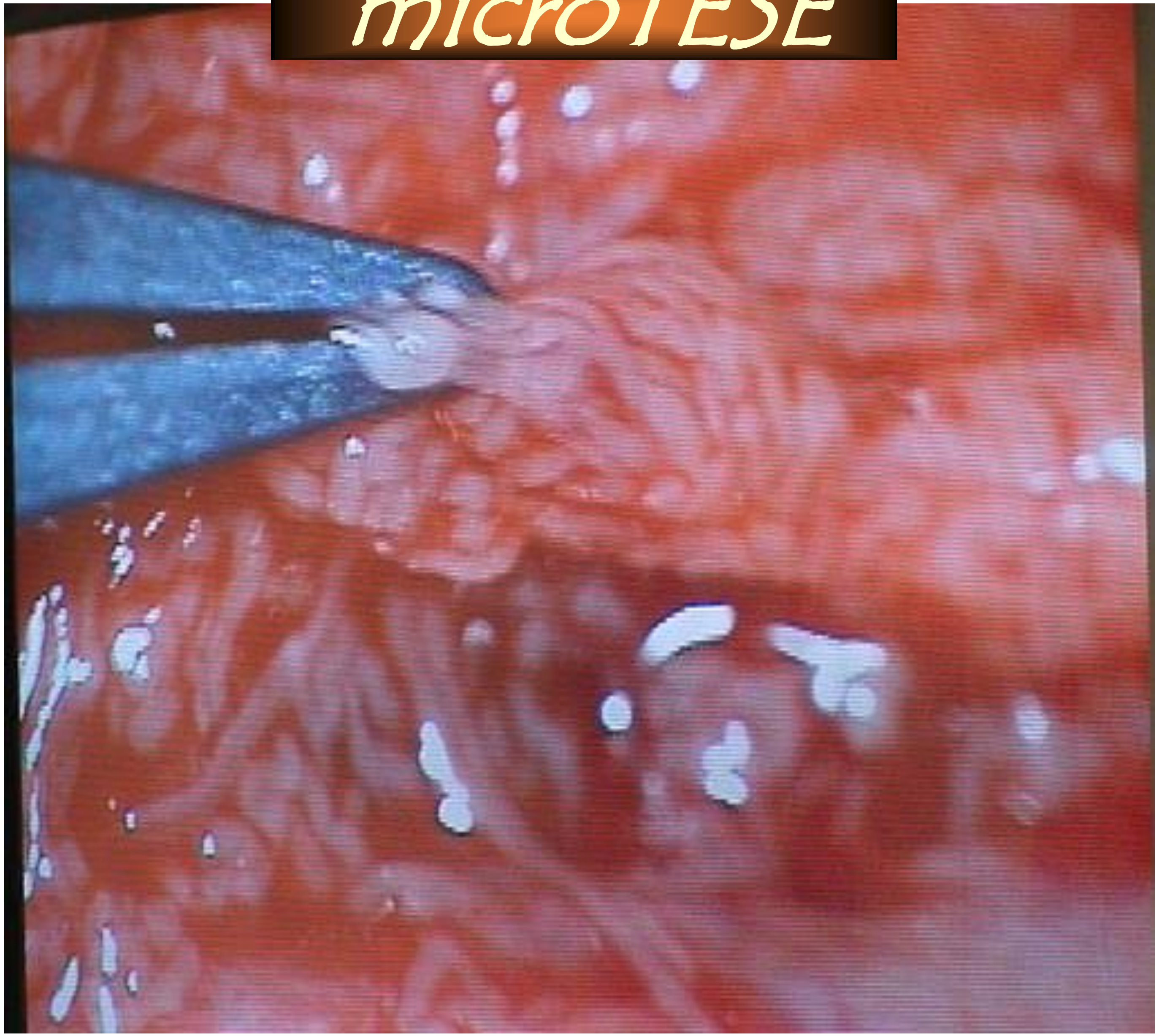


TESE MICROCIRURGICA
MicroTESE

PETER SCHLEGEL. *HUMAN REPROD*, 14: 131-135, 1999

SHERMAN J. SILBER. *HUMAN REPROD*, 15: 2278-2284, 2000

microTESE



microTESE

Take home message - 1

- Análise seminal da OMS: não é um teste de fertilidade;
- fragDNA espermático: importante na avaliação da capacidade fértil do homem;
- Infertilidade por estresse oxidativo masculino (MOSI): novo diagnóstico de infertilidade masculina;
- Quanto maior a alteração seminal: maior a possibilidade de alteração genética;

Take home message - 2

- **Idade masculina:** relação direta com malformações na prole e maiores chances de perda da gravidez;
- Azoospermia obstrutiva: **PESA;**
- Azoospermia não-obstrutiva **microTESE.**

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