Simposio 13

Nutrizione e disruptor endocrini

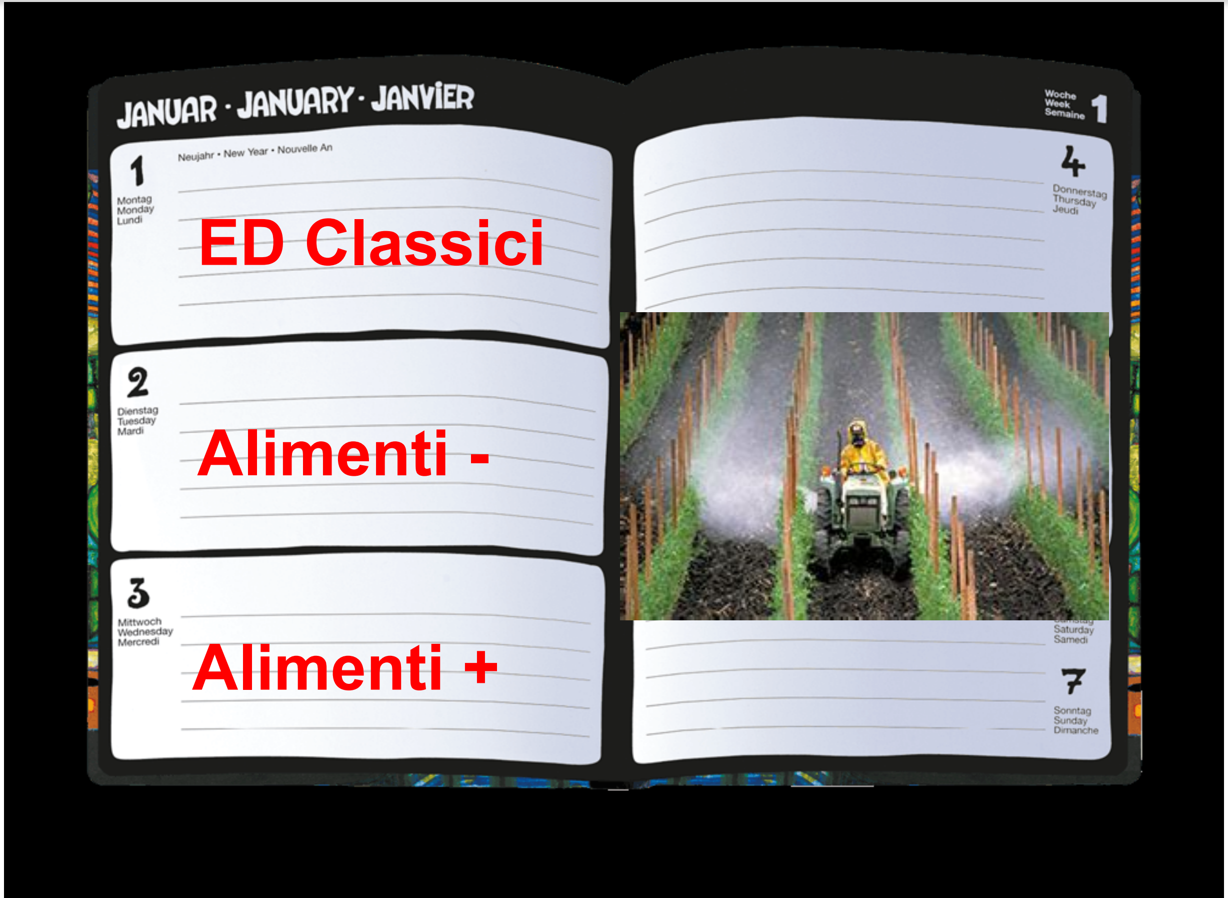
Testicolo

M.G. Schiesaro

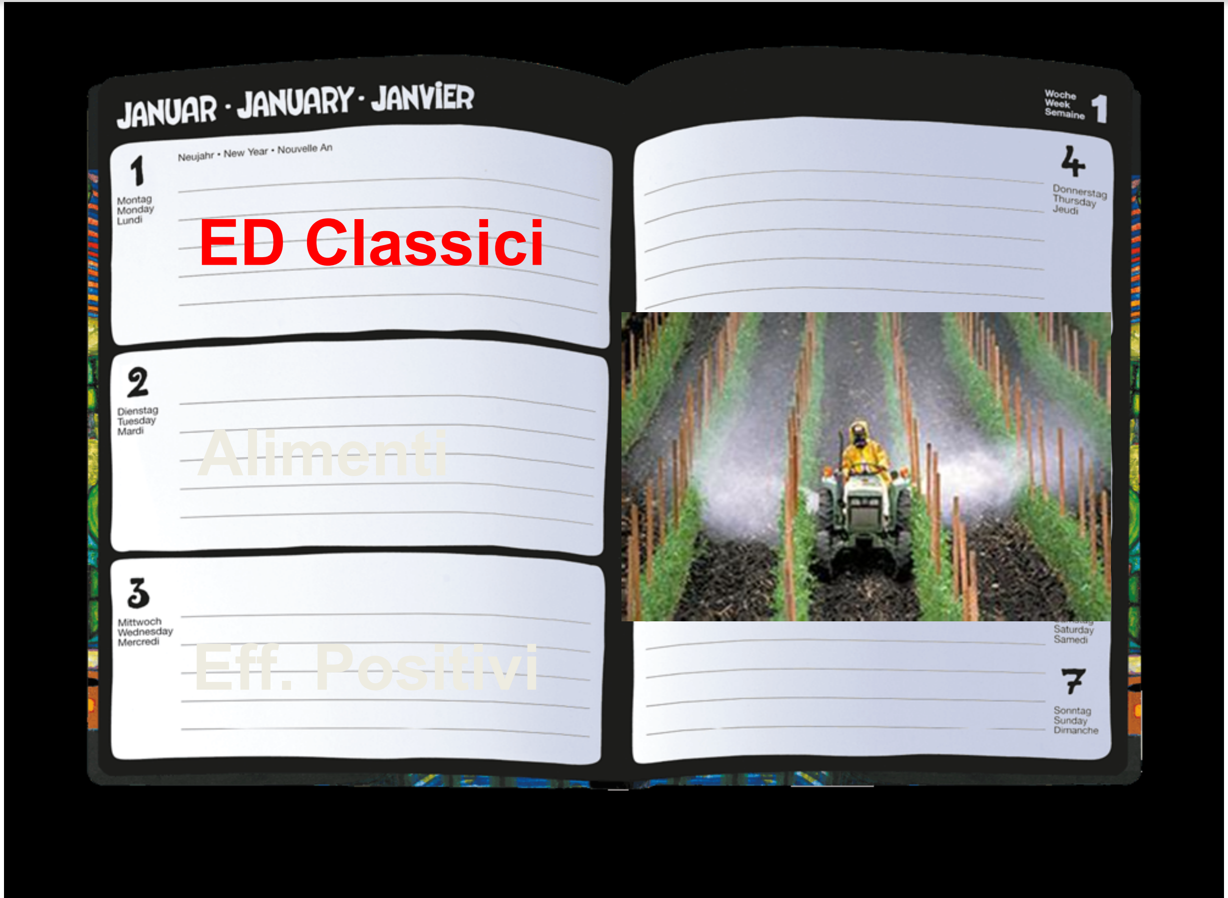
Conflitti di interesse

Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni non ho avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario.

Agenda


JANUAR · JANUARY · JANVIER
Woche Week Semaine 1
1 Montag Monday Lundi
Neujahr • New Year • Nouvelle An
ED Classici
2 Dienstag Tuesday Mardi
Alimenti -
3 Mittwoch Wednesday Mercredi
Alimenti +
4 Donnerstag Thursday Jeudi
Saturday Samedi
7 Sonntag Sunday Dimanche

Agenda



ED Classici

Alimenti

Eff. Positivi

Evidence for decreasing quality of semen during past 50 years

Elisabeth Carlsen, Aleksander Giwercman, Niels Keiding, Niels E Skakkebæk

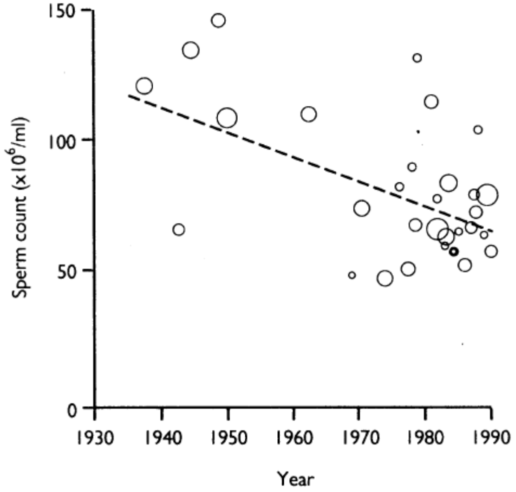


FIG 1—*Linear regression of mean sperm density reported in 61 publications (represented by circles whose area is proportional to the logarithm of the number of subjects in study) each weighted according to number of subjects, 1938-90*

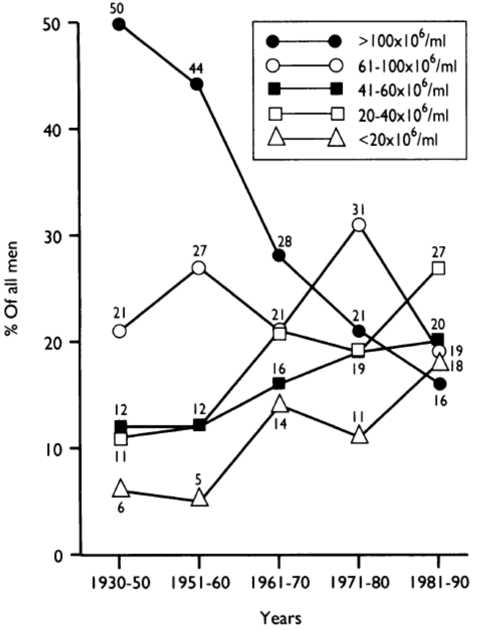
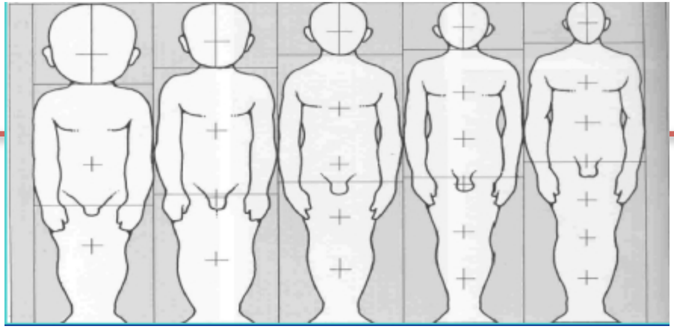


FIG 2—*Number (percentage) of men with sperm densities in the different concentration bands: <20×10⁶/ml, 20-40×10⁶/ml, 41-60×10⁶/ml, 61-100×10⁶/ml, >100×10⁶/ml (data from 27 publications)*

Sistema Endocrino



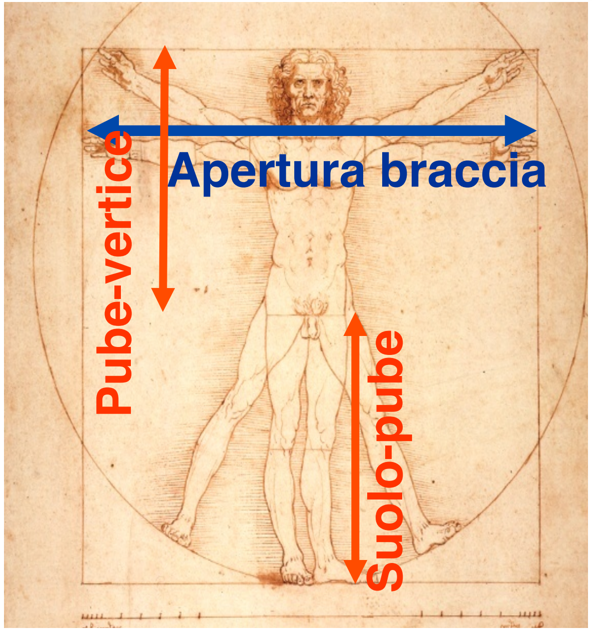
Androgeni condizionano l'accrescimento, le proporzioni corporee, i caratteri sessuali secondari, la distribuzione del grasso sottocutaneo e della massa muscolare

	Livi, anno 1896	*Costanzo anno 1948*	*Cappieri anno 1960*	*Grassivaro anno 1972*	*Istat, 1983*	*Istat, 1995*	*Istat, 2000*	*Progetto Andrologico anni 2005-2010*
Altezza	166,6	166,7	170	171,7	174,77	176,1	176,9	178.8±6.6

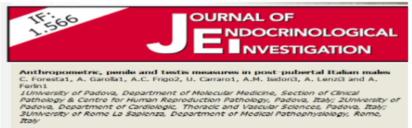
	Loeb et al. anno 1881	*Bondil et al. anno 1972*	*Ponchietti et al., 2001 anno 1999*	*Cacciari et al., anno 2002*	*Progetto Andrologico anni 2005-2010*
Peso	53,3	54,5	69,1	68,6	72.6±10.9
BMI	20,1	20,3	20,4	22	22.7±3.0

	Kinsey, anno 1948	*Ponchietti et al., 2001 anno 1999*	*Progetto Andrologico anni 2005-2010*
Lungh. Pene	9,7cm	9,0cm	8.9±1.4
Circ. Pene	10,6cm	10,0cm	9.5±1.0

Parametri androgeno-dipendenti



	n (%)
BMI (kg/m²)	
< 18.5 (underweight)	79 (3.9)
18.5 - 24.99 (normal)	1606 (79.5)
25 - 29.99 (overweight)	286 (14.2)
30 - 34.99 (obese)	37 (1.8)
≥ 35 (extreme obese)	11 (0.5)
Waist (cm)	
< 102 (normal)	1930 (95.6)
≥ 102 (pathological)	89 (4.4)
Arm span – height (cm)	
≤ 3 (normal)	1292 (64.0)
> 3 (pathological)	727 (36.0)
Crown-to-pubis/pubis-to-floor	
> 0.92 (normal)	1116 (55.3)
≤ 0.92 (pathological)	903 (44.7)
Mean testicular volume (mL)	
> 12 (normal)	596 (76.8)
≤ 12 (pathological)	180 (23.2)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JOURNAL OF ENDOCRINOLOGICAL INVESTIGATION

Anthropometric, penile and testis measures in post-pubertal Italian males

C. Foresta1, A. Garolla1, A.C. Frigo2, U. Carraro1, A.M. Isidori3, A. Lenzi3 and A. Ferlin1

1University of Padova, Department of Molecular Medicine, Section of Clinical Pathology & Centre for Human Reproduction Pathology, Padova, Italy; 2University of Padova, Department of Cardiologic, Thoracic and Vascular Sciences, Padova, Italy; 3University of Rome La Sapienza, Department of Medical Pathophysiology, Rome, Italy

Patologie andrologiche in aumento

- Infertilità
- Criptorchidismo
- Tumore del testicolo
- Ipospadia
- Ipogonadismo

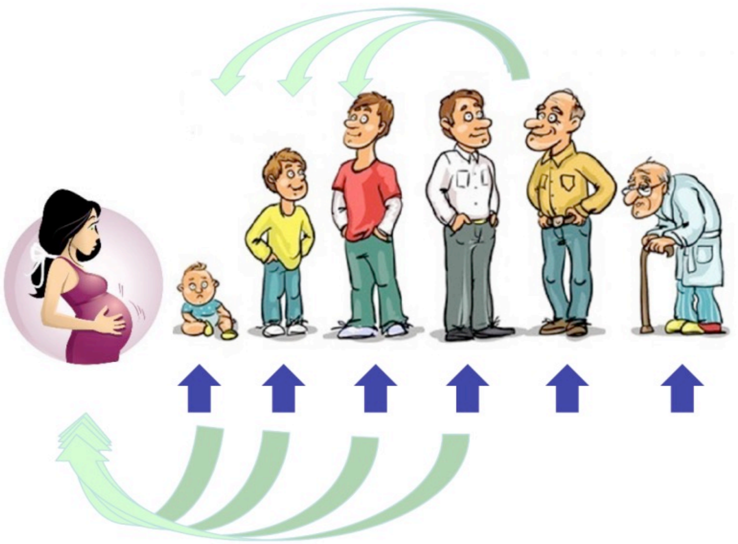
Patologie andrologiche in cui si suppone un impatto dell'ambiente

- Infertilità
- Criptorchidismo
- Tumore del testicolo
- Ipospadia

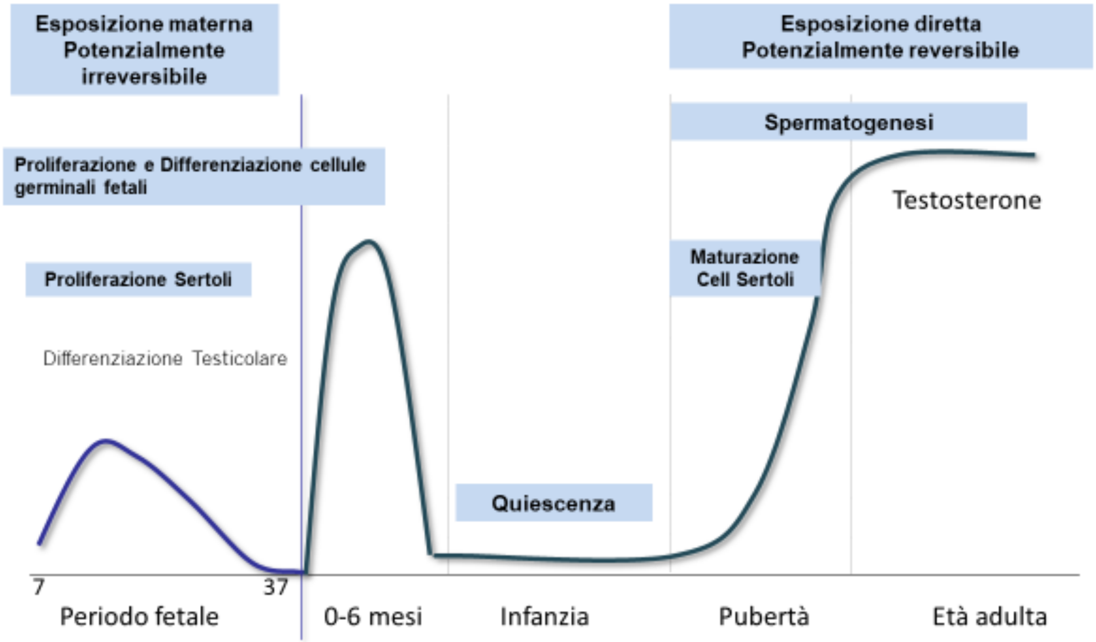
Patologie andrologiche che si sviluppano per effetto di endocrine disruptors in animali (esposizione in utero)

- Infertilità
- Criptorchidismo
- Tumore del testicolo
- Ipospadia
- Micropene
- Femminilizzazione

Vita andrologica



Abitudini voluttuarie/Endocrine Disruptors



ModifiedfromSharpe RM, 2010

Testicular dysgenesis syndrome

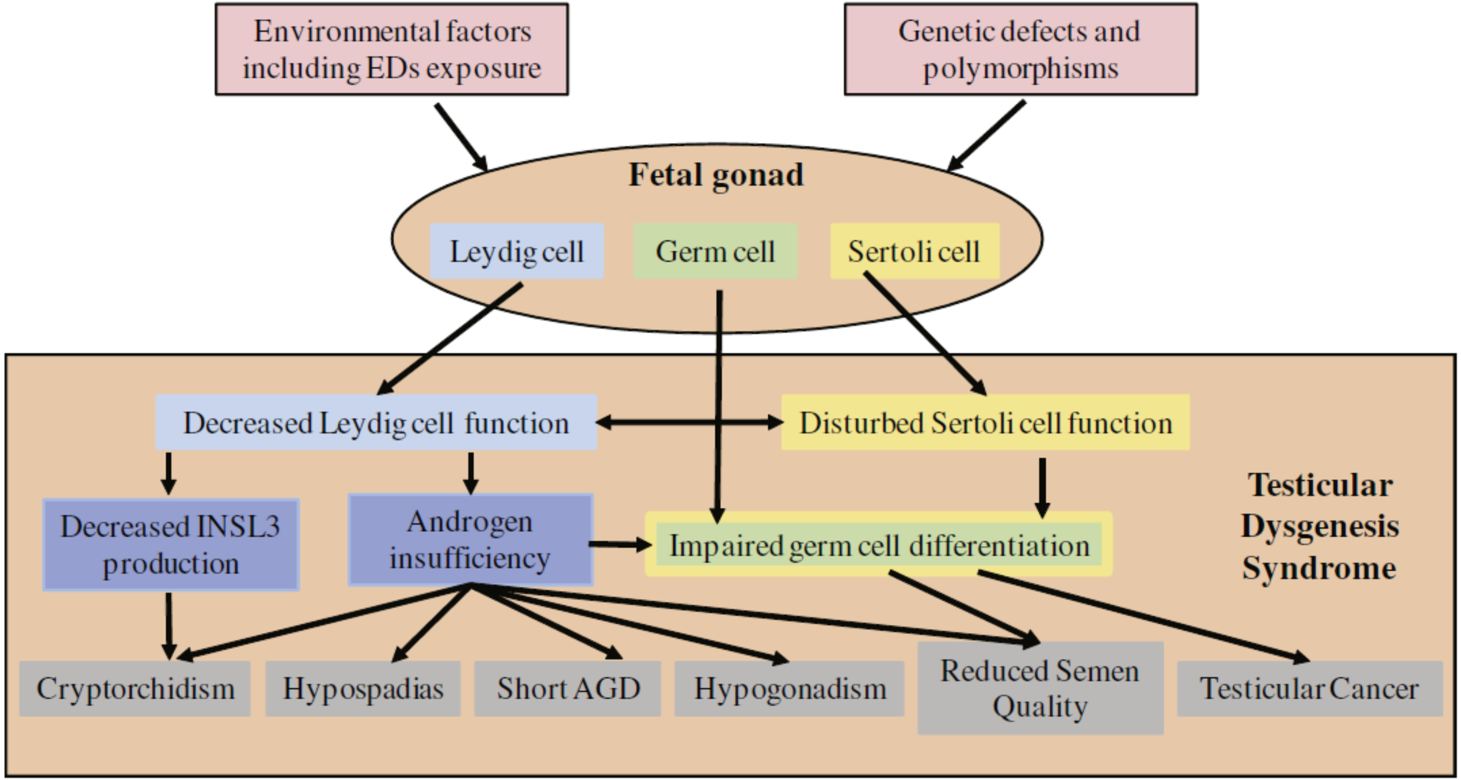
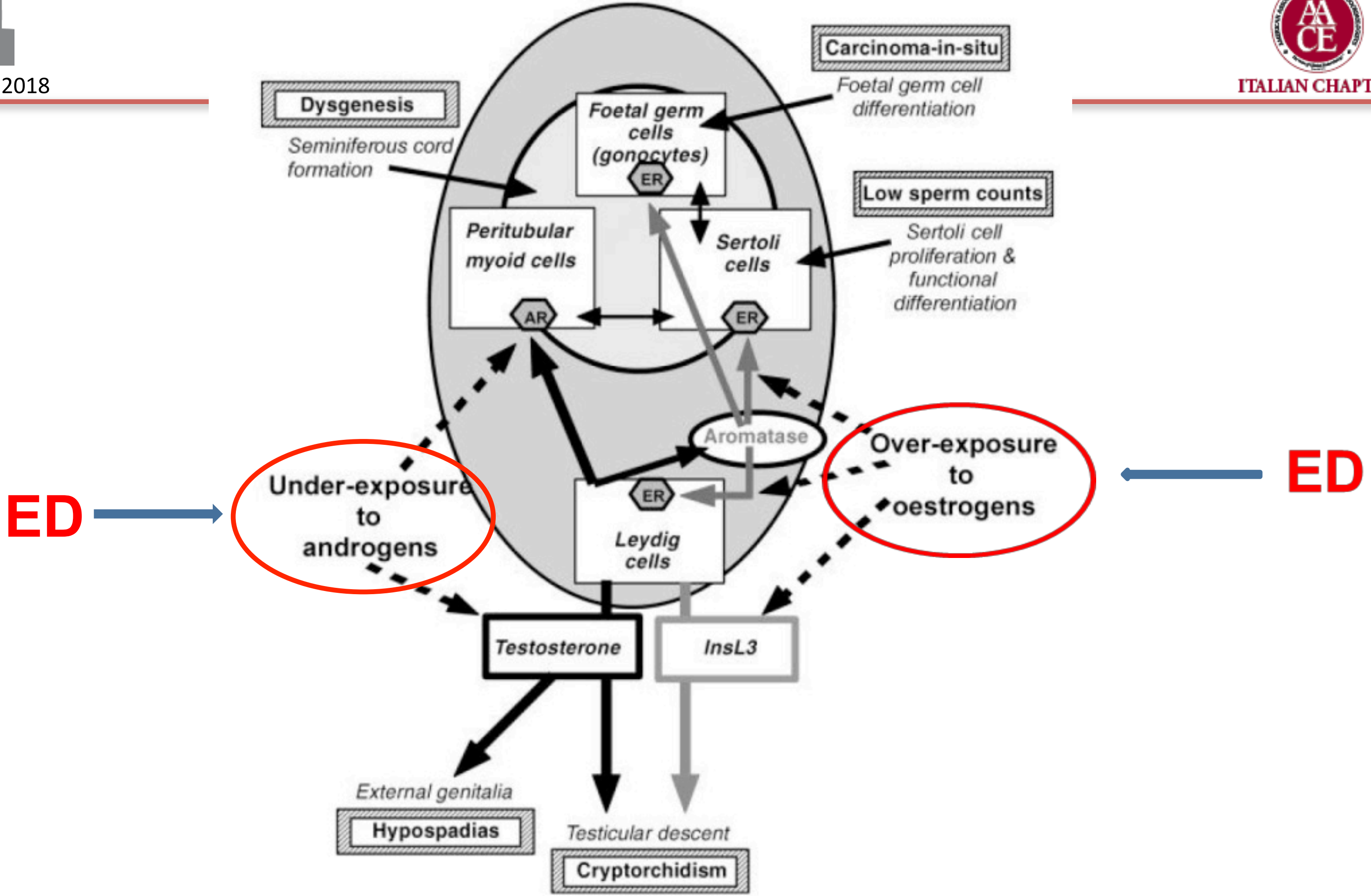


Fig. 2. Schematic representation of testicular dysgenesis syndrome.


Dysgenesis
Seminiferous cord formation
Carcinoma-in-situ
Foetal germ cell differentiation
Foetal germ cells (gonocytes)
ER
Low sperm counts
Sertoli cell proliferation & functional differentiation
Peritubular myoid cells
AR
Sertoli cells
ER
Aromatase
ED
Under-exposure to androgens
Over-exposure to oestrogens
ED
ER
Leydig cells
Testosterone
InsL3
External genitalia
Hypospadias
Testicular descent
Cryptorchidism

Endocrine Disruptors

Table 1
Effects of EDs on male reproductive health.

ED	Mode of action	Impact on male reproduction health
Bisphenol A	Weak ER agonist	Decrease in the quantity and quality of sperm production [58,59], cryptorchidism, hypospadias [127], reduced AGD [148]
PCBs	ER agonist	Reduced penile length, delayed sexual maturation, reduced fertility [90,91,105]
Dioxin	AHR agonist	Altered serum testosterone levels and decline in sperm concentration [137], Reduced AGD [149]
Phthalate	Reduced testosterone synthesis in fetal testis	Reduced AGD [132,144], reduced semen parameters [63,71,72,79,82]
Pesticides and metabolites	ER agonist Weak AR antagonist	Decrease in the quantity and quality of sperm [90,96,98,165], cancer [118] genital dyformities [146], hypospadias, cryptorchidism [128,135]
DES	ER agonist	Hypospadias, cryptorchidism, micropenis, epididymal cysts [126]

ER: estrogen receptor, AGD: anogenital distance, PCBs: polychlorinated biphenyls, AHR: aryl hydrocarbon receptor, AR: androgen receptor, DES: Diethylstilbestrol.

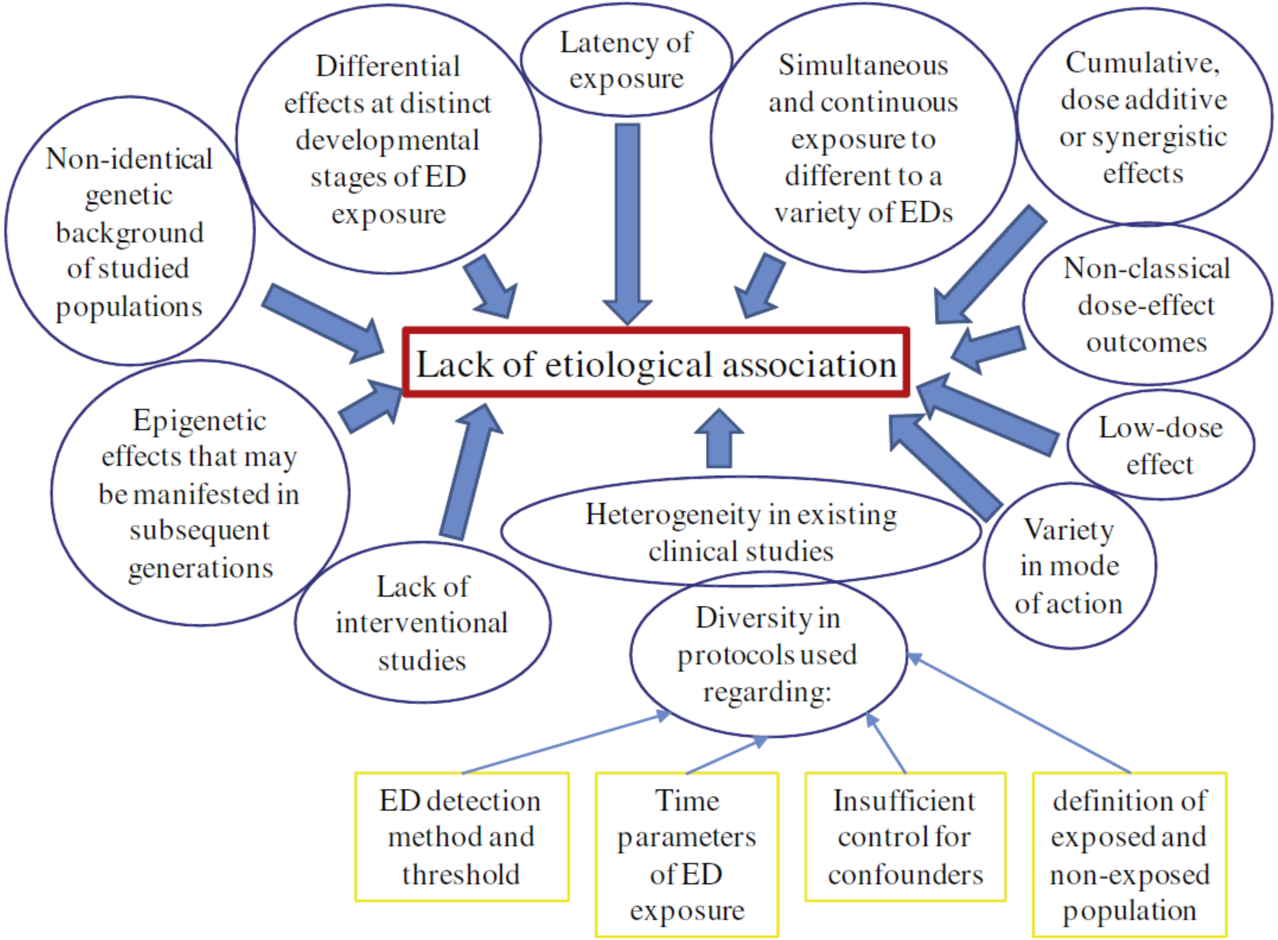


Fig. 5. Factors responsible for the lack of etiological association between ED exposure and male reproductive disorders.

Incidence of Breast, Prostate, Testicular, and Thyroid Cancer in Italian Contaminated Sites with Presence of Substances with Endocrine Disrupting Properties

Table 1. Environmental pollutants with endocrine disrupting properties considered to be carcinogenic by scientific institutions/advisory committees for the tumours studied.

Cancer Site	IARC [1]	WHO/UNEP [25]	European Commission [26]	European Environmental Agency [27]	The Endocrine Society [28]
Breast	PCB Ethylene oxide	Dioxins Furans PCBs Solvents	Cadmium Solvents	Oestrogenic EDs	Dioxins
Prostate	Arsenic Cadmium Rubber production industry	Arsenic Cadmium PCBs Pesticides	Arsenic Cadmium PCBs Pesticides	Pesticides	Cadmium Farming PCBs
Testis		Prenatal exposure to POPs Fungicides PBDE Pesticides	Organochlorine chemicals (including DDT and some pesticides) PCBs	DDE DDT PCBs	Arsenic Cadmium PCBs
Thyroid		Pesticides TCDD	PCBs Pesticides Solvents	PCBs	

DDE: Dichorodiphenyldichloroethylene; DDT: Dichlorodiphenyltrichloroethane; PBDE: Polybrominated Diphenyl Ethers; IARC: International Agency for the Research on Cancer; PCBs: Polychlorinated Biphenyls; POPs: Persistent organic pollutants; TCDD: 2,3,7,8-Tetrachlorodibenzo-p-dioxin; WHO/UNEP: World Health Organization/United Nations Environment Programme.

Int. J. Environ. Res. Public Health **2017**, *14*, 355

Table 2. National Priority Contaminated sites (NPCSs) information on pollution sources, and endocrine disruptors (EDs) of interest detected in environmental matrices, human biological samples, and food.

NPCS	Area Description		Other Data on EDs of Interest	
	Pollution Sources	EDs of Interest Detected in Environmental Matrices	Human Biomonitoring	Food
Bacino Chienti	Shoe factories	PCDDs/PCDFs, benzene, toluene, other solvents		
Brescia Caffaro	Chemical plants, landfill	As, PCBs, PCDDs/PCDFs, chlorobenzene	PCDDs/PCDFs, PCB (human serum)	PCB (food of animal and vegetal origin); PCDDs/PCDFs, PCB (cattle's meat, cow milk, forage)
Fidenza	Chemical plants, urban and hazardous waste landfills	As, PCBs, PCDDs, benzene, other solvents		
Litorale Domizio Flegreo	Urban waste landfill, illegal dumping sites, illegal burning of waste	As, PCBs, PCDDs, benzene, other solvents	PCDDs/PCDFs (breast milk)	PCDDs/PCDFs, (cow and buffalo's milk)
Laguna Grado Marano	Cellulose production plant, dockyard	As, PCDDs, benzene, other solvents		
Laghi Mantova	Metallurgy plants, paper plant, petrochemical plant, harbour area, industrial waste landfills, hazardous waste incinerator	As, Cd, PCDDs, ethylbenzene, other solvents		PCBs (fruit, vegetables)
Milazzo	Oil refinery, steel plant, thermal power plant, electrical equipment factories, illegal dumping site	PCDDs, heavy metals. Benzo(a)pyrene	Cd, As (serum)	
Porto Torres	Chemical plants, petrochemical plant, refinery, power plant, harbour area, illegal dumping site	As, Cd, chlorobenzene, other solvents		PCDDs (fish and other seafood)
Priolo	Chemical plants, petrochemical plant, refinery, harbour area, hazardous waste landfills	PCB, hexachlorobenzene	Dioxins, PCB, HCB (breast milk, and puerperal hair)	Cd, Pb, Hg, PCDDs, organochlorine compounds (fish and other seafood)
Sassuolo-Scandiano	Ceramic industries, industrial waste landfills	Heavy metals		
Taranto	Oil refinery, steel plant, harbour area, cement plant, controlled and illegal waste dumps	As, Cd, PCDDs, PCBs, benzene, xylene	As, Cd (serum and urine); PCDDs, PCBs (serum and milk)	PCDDs, PCB (sheep and cow's milk, clams); PCB, HCB, PAHs (clams)
Terni-Papigno	Steel plant, hazardous waste landfills	PCB		
Trento Nord	Chemical plant	Solvents		
Venezia Porto Marghera	Chemical plants, petrochemical plant, oil refinery, harbour area, illegal dumping sites	As, Cd, PCBs, PCDDs, solvents		As, Cd, PCDDs, PCDFs (shellfish)

NPCS: National Priority Contaminated site; As: Arsenic; Cd: Cadmium; EDs: Endocrine disruptors HCB: Hexachlorobenzene; PAHs: Polycyclic Aromatic Hydrocarbons; PCDDs: Polychlorinated dibenzo-p-dioxins; PCDFs: Polychlorinated dibenzofurans.

NPCS (Geographical Area)	Thyroid Cancer				Testicular Cancer	
	Males		Females			
	obs.	SIR * (90% CI)	obs.	SIR * (90% CI)	obs.	SIR * (90% CI)
Basso Bacino Fiume Chienti (Central Italy)	6	83 (36–163)	21	85 (57–122)	11	148 (83–245)
Brescia Caffaro (Northern Italy)	47	170 (132–217)	131	156 (134–180)	31	102 (74–137)
Fidenza (Northern Italy)	18	145 (94–215)	32	88 (64–118)	15	134 (83–207)
Litorale Domizio Flegreo and Agro Aversano (Southern Italy)	54	95 (75–119)	147	69 (60–79)	70	108 (87–131)
Laguna Grado Marano (Northern Italy)	3	33 (9–86)	15	57 (35–88)	15	176 (109–272)
Laghi Mantova (Northern Italy)	21	174 (117–251)	58	155 (123–193)	17	141 (90–211)
Milazzo (Southern Italy)	6	124 (54–245)	24	140 (96–196)	4	98 (34–225)
Porto Torres (Southern Italy)	30	69 (50–94)	155	97 (84–111)	51	135 (105–170)
Priolo (Southern Italy)	34	89 (66–119)	132	94 (81–109)	37	103 (77–136)
Sassuolo Scandiano (Northern Italy)	41	146 (111–190)	106	130 (110–152)	39	121 (91–159)
Taranto (Southern Italy)	34	158 (116–210)	98	120 (101–142)	20	108 (72–158)
Terni Papigno (Central Italy)	32	106 (77–142)	67	66 (53–81)	32	121 (88–163)
Trento Nord (Northern Italy)	20	71 (47–103)	71	70 (57–85)	32	104 (76–140)
Venezia Porto Marghera (Northern Italy)	57	74 (59–92)	165	71 (62–81)	76	94 (77–114)

Geographic association between abnormalities in male reproductive health

Denmark

- High incidence of testicular cancer
- High prevalence of cryptorchidism
- High prevalence of hypospadias
- Low sperm counts
- Smaller testes as newborns and lower inhibin-Blevels

Finland

- Low incidence of testicular cancer
- Low prevalence of cryptorchidism
- Low prevalence of hypospadias
- High sperm counts
- Bigger testes as newborns and higher inhibin-Blevels

ORIGINAL ARTICLE

2009 European Academy of Andrology • *International Journal of Andrology* **32,** 1–9

Roma, 8-11

ER

Country-specific chemical signatures of persistent environmental compounds in breast milk

K. Krysiak-Baltyn,*† J. Toppari,‡ N. E. Skakkebaek,† T. S. Jensen,* H. E. Virtanen,‡ K.-W. Schramm,§¶ H. Shen,§ T. Vartiainen,** H. Kiviranta,** O. Taboureau,* S. Brunak* and K. M. Main†

Table 1 Chemicals with significantly higher concentrations in Danish than in Finnish breast milk samples in a linear multiple regression analysis after correction for multiple testing. Percentiles show unadjusted concentrations

	Percentile, Denmark			Percentile, Finland				
Chemical	25th	50th	75th	25th	50th	75th	*p*-value	Higher in
1,2,3,4,7,8-HCDD	2.39e-3	3.32e-3	4.76e-3	0.78e-3	1.06e-3	1.28e-3	2.18e-4	Denmark
PCB 209	0.088	0.11	0.16	0.045	0.061	0.092	3.27e-5	Denmark
PCB 156	4.21	5.66	8.62	2.83	3.59	4.83	1.07e-2	Denmark
PCB 157	0.70	0.86	1.27	0.44	0.60	0.80	2.25e-2	Denmark
Dieldrin	3.06	4.66	5.98	1.86	2.21	3.10	2.30e-4	Denmark
Hexachlorobenzene	8.80	11.78	14.16	6.87	7.60	8.55	1.32e-4	Denmark

Levels below LOQ were assigned the value 0. Data are given as mean ± SD. LOQ, Limit of Quantification.

Roma, 8-1

Testicular Cancer Risk in First- and Second-Generation Immigrants to Denmark

Charlotte Myrup, Tine Westergaard, Tine Schnack, Anna Oudin, Christian Ritz, Jan Wohlfahrt, Mads Melbye

J Natl Cancer Inst 2008;100:41–47

Table 1. Rate ratio of testicular cancer in men living in Denmark according to birthplace and parental birthplace, 1968–2003*

Parental birthplace		Risk in parental birthplace†	Birthplace						
			DK			FC			
Mother	Father		No. of cases	PYRS	RR_{DK}‡ (95% CI)	No. of cases	PYRS	RR_{FC}‡ (95% CI)	RR_{DK}/RR_{FC}§ (95% CI)
DK	DK		3853	37 883	1 (reference)	23	275	1.03 (0.68 to 1.55)	0.98 (0.65 to 1.47)
DK	FC		60	825	1.00 (0.77 to 1.29)	9	63	1.71 (0.89 to 3.29)	0.59 (0.29 to 1.20)
FC	DK		81	919	0.97 (0.78 to 1.21)	11	95	1.19 (0.66 to 2.15)	0.79 (0.42 to 1.49)
FC	FC	All	13	542	0.88 (0.51 to 1.53)	166	2681	0.37 (0.31 to 0.43)	2.48 (1.41 to 4.38)
		Low	7	478	0.65 (0.31 to 1.36)	59	1887	0.19 (0.14 to 0.24)	3.62 (1.64 to 7.97)
		High	6	63	1.50 (0.68 to 3.35)	107	795	0.80 (0.66 to 0.97)	1.86 (0.81 to 4.24)

The testicular cancer risk in first-generation immigrants was lower than that in native-born Danes and reflected that in the countries of origin, whereas the risk in second-generation immigrants was similar to that in natives of Denmark. Together these findings argue for a substantial influence of environmental factors limited to the period early in life, most probably to the period in utero.

Perfluorochemicals and Human Semen Quality: The LIFE Study

Table 1. Description of male partners in the cohort by study site: the LIFE Study.

Characteristic	Michigan (*n* = 96)	Texas (*n* = 366)	Total (*n* = 462)
Nonwhite race/ethnicity	9 (9)	42 (12)	51 (11)
≤ High school education	8 (8)	28 (8)	36 (8)
No health insurance	10 (10)	28 (8)	38 (8)
Never fathered a pregnancy	47 (49)	193 (53)	240 (52)
Current smoker (cotinine > 40.35 ng/mL)	18 (19)	66 (18)	84 (18)
Age (years)	32.1 ± 4.5	31.7 ± 4.9	31.8 ± 4.9
BMI (kg/m^2)	29.7 ± 5.4	29.9 ± 5.8	29.8 ± 5.7
Abstinence time (days)	4.4 ± 4.0	4.0 ± 5.2	4.1 ± 5.0
Sample age (hours)	28.5 ± 10.0	27.8 ± 8.2	28.0 ± 8.6

Data are *n* (%) or mean ± SD. None of the values were statistically significant; all *p*-values (from chi-square test for categorical characteristics and Wilcoxon rank sum test for continuous characteristics) comparing the two sites were > 0.05.

Table 2. Distribution of serum PFC concentrations in male partners by availability of semen samples: the LIFE Study.

PFC (ng/mL)	Percent < LOD	Michigan (*n* = 96) GM (95% CI)	Michigan (*n* = 96) Median (IQR)	Texas (*n* = 366) GM (95% CI)	Texas (*n* = 366) Median (IQR)
Et-PFOSA-AcOH	97	0.12 (0.10, 0.14)	0 (0, 0.1)	0.12 (0.10, 0.13)	0 (0, 0)
Me-PFOSA-AcOH	22	0.47 (0.40, 0.54)	0.4 (0.3, 0.7)	0.29 (0.26, 0.31)	0.25 (0.1, 0.5)
PFDeA	5	0.31 (0.28, 0.35)	0.3 (0.2, 0.4)	0.47 (0.45, 0.50)	0.5 (0.3, 0.6)
PFNA	1	0.96 (0.84, 1.11)	1.0 (0.75, 1.35)	1.68 (1.61, 1.76)	1.65 (1.2, 2.2)
PFOA	< 1	4.29 (3.86, 4.77)	4.6 (3.0, 6.05)	5.09 (4.86, 5.33)	5.3 (4.1, 6.6)
PFOS	< 1	17.39 (14.94, 20.24)	19.15 (14.65, 25.7)	21.23 (20.07, 22.46)	21.6 (15.8, 29.9)
PFOSA	84	0.13 (0.11, 0.15)	0 (0, 0.1)	0.11 (0.10, 0.12)	0 (0, 0)

IQR, interquartile range. All differences were statistically significant ($p \leq 0.02$), comparing the two sites. Thirty-nine men were excluded because of missing PFC measurements (*n* = 13) or semen samples (*n* = 2).

Perfluorocarburi ➡ Packaging + Acqua

- Riduzione di forme normali
- Alterazioni della testa
- Alterazioni integrità DNA

Environmental Health Perspectives • VOLUME 123 | NUMBER 1 | January 2015

Steroidogenesis in Leydig Cells: Effects of Aging and Environmental Factors

Environmental factors affecting LHR-cAMP and mitochondrial cholesterol cascades

Toxin	Animal Cell	Age	Dose (/kgBW) Duration	Effects on (LC or Testis)	Mechanisms Sensitive Targets	Reference
BDE-47	MA10		1μM; 24h	P4 production↓	cAMP↓; Cyp11a1↓	Han, 2012
TCDD	mice	Adult	100μg; once	Testicular T↓	LHR↓; Cyp11a1↓	Fukuzawa, 2004
Permethrin	mice	Adult	35mg; 6w	Serum T↓ Testicular T↓	TSPO↓; STAR↓; Cyp11a1↓	Zhang, 2007
Atrazine	rat	Pnd23–50	200mg; 4w	T+DHT productions↓	cAMP↓; LHR↓; SR-B1↓ SF-1↓; STAR↓; Cyp17a1↓; Hsd17b3↓	Pogrmic, 2009
Triclosan	rat LCs	Adult	0.01μM; 2h	T production↓	cAMP↓; STAR↓; Cyp17a1↓ Cyp11a1↓; Hsd17b3↓; Hsd3b1↓ Preventable by forskolin	Kumar, 2008
Lindane	rat LCs	Adult	10μg/ml; 3h	T production↓	cAMP↓	Ronco, 2001
PFDoA	mLTC-1/rat LCs		10μM; 24h	P4 production ↓ T production↓	STAR↓	Shi, 2010
Salinomycin	mice	Adult	3mg; 4w	Testicular T↓ Testis W↓ Vesicles W↓ Epididymis W↓	STAR↓; Cyp11a1↓	Ojo, 2013
Quinalphos	mice	Adult	7.5 mg; 7d	Serum T↓ Testis W↓ Vesicles W↓ Epididymis W Prostrate W↓	STAR↓; Cyp11a1↓	Kokilavani, 2014
MEHP	MA-10		200μM; 24h	P4 production↓	cAMP↓; STAR↓	Zhou, 2013
Cobalt	MA10		100μM; 24h	P4 production↓	Cyp11a1	Kumar, 2014
Dimethoate	rat	Adult	15mg; 5w	Serum T↓ LH↑ FSH↑	STAR↓ Hsd17b3↓; Hsd3b1↓	Astiz, 2009
Dimethoate	rat LCs		1ppm; 24h	T production↓	STAR↓ Hsd17b3↓; Hsd3b1↓	Astiz, 2012

BDE-47: 2,2',4,4'-Tetrabromodiphenyl Ether;Cyp11a1: Cholesterol side-chain cleavage;Cyp17a1: Cytochrome P450 17a1 (Steroid 17α-hydroxylase/17,20 lyase);DEHP: Diethylhexyl Phthalate;DHT: Dihydrotestosterone;Hsd17b3: Hydroxysteroid 17-Beta Dehydrogenase 3;LHR: Luteinizing Hormone/choriogonadotropin Receptor;MEHP: Monoethylhexyl phthalic acid;P4: Progesterone;PFDoA: Perfluorododecanoic acid;Pnd: Postnatal day;SF-1: Steroidogenic Factor 1 (NR5A1);SR-B1: Scavenger Receptor class B member 1 ;STAR: Steroidogenic Acute Regulatory protein,;T: Testosterone;TCDD: 2,3,7,8-Tetrachlorodibenzodioxin;TSPO: Translocator Protein

Reproduction. 2017 October ; 154(4): R111–R122.

Environmental factors affecting redox environment of Leydig cells

Toxin	Animal Cell	Age	Dose (/kgBW); Duration	Effects on (LC or Testis)	Mechanisms Sensitive Targets	Reference
Lindane	rat	Adult	5mg; 12h	StAR↓ Hsd17b3↓; Hsd3b1↓	H_2O_2↑	Saradha, 2008
PFDoA	mLTC-1/rat LCs		10μM; 24h	P4 production ↓ T production↓	StAR↓; H_2O_2↑ Preventable by MnTMPyP	Shi, 2010
Aroclor1254 rat LCs		Adult	10^{-8}M; 6h	T production ↓ Cyp11a1↓ Hsd17b3↓ Hsd3b1↓	H_2O_2↑; LPO↑ Hydroxyl radical↑; SOD↓ CAT↓; GPx↓; γ-GT↓; GR↓ GST↓; Vitamin C and E↓	Murugesan, 2008
Salinomycin	mice	Adult	3mg; 4w	Testicular T↓ StAR↓ Cyp11a1↓	LPO↑ GSH↓; CAT↓; LDH↓; SOD↓	Ojo, 2013
Quinalphos	rat	Adult	250μg; 3d	Serum T↓ Testis W↓ Germ cell loss↑	LPO↑; SOD↑; GPx ↑ CAT↓; GSH↓	Debnath, 2000
Quinalphos	mice	Adult	7.5 mg; 7d	Serum T↓ StAR↓; Cyp11a1↓ Hsd17b3↓ Hsd3b1↓	SOD↓; CAT↓; GPx↓ Vitamin C↓ Preventable by antioxidant *Cissus quadrangularis*	Kokilavani, 2014
DEHP	rat	Pnd21	1000mg; 10d	Serum T↓	Serum LH↓; Serum FSH↓ Preventable by selenium diet;	Erkekoglu, 2011
DEHP	rat	Pnd21	1000mg; 10d	GSH/GSSG↓ TBARS↑	Cu,Zn-SOD↓; CAT↑ GSH/GSSG↓; GPx4↓ Preventable by selenium diet	Erkekoglu, 2014
MEHP/ DEHP	MA-10		200μM; 24h	P4 production↓ cAMP↓; StAR↓	ROS↑ GSH depended Vitamin E protective	Zhou, 2013
MEHP	MA-10		1μM; 48h	P4 production↓ T production↓	ROS↑; Cyp1a1 network↑	Fan, 2010
MEHP	MA-10		200μM; 24h	P4 production↓ cAMP↓; StAR↓	ROS↑ GSH depended Vitamin E protective	Zhou, 2013
Mercury	rat	Adult	50ppm; 90d	Serum T↓ Sperm count↓	LPO↑; TBARS↑ SOD↓; CAT↓	Boujbiha, 2009
Lead	rat	Adult	25μg; 15d	Serum T↓ Hsd17b3↓ Hsd3b1↓	LPO↑; GSH↓; GST↓; SOD↓ CAT↓; GPx↓; TBARS↑ Preventable by Vitamin C	Pandya, 2012
Cadmium	rat	Adult	25μg; 15d	Serum T↓ Hsd17b3↓ Hsd3b1↓	LPO↑; GSH↓; GST↓; SOD↓ CAT↓; GPx↓; TBARS↑ Preventable by Vitamin C	Pandya, 2012
Cobalt	MA10		100μM; 24h	P4 production↓ Cyp11a1↓	ROS↑ HIF-1a activity↑	Kumar, 2014
Arsenite	mice	Adult	11.5ppm; 36d	Serum T↓ Hsd17b3↓ Hsd3b1↓	GSH↓ Preventable by Vitamin C	Chang, 2007
BPA	R2C		0.1nM; 24h	T production↓ Aromatase↑ EP2↑; EP4↑; CREB↑	COX2↑; PGE2↑ Preventable by inhibitions of PKA/ Akt/ ERK/ JNK/ p38	Kim, 2010
Dimethoate	rat	Adult	15mg; 5w	Serum T↓ StAR↓ LH↑	LPO↑; PGE2↑; PGF2α↑ COX2↑; α-tocopherol↓ Preventable by TROLOX or rofecoxib	Astiz, 2009
Dimethoate	rat LCs		1ppm; 24h	T production↓ StAR↓	LPO↑; COX2↑ Preventable by PUFA	Astiz, 2012

BPA: Bisphenol A CAT: Catalase COX2: Cyclooxygenase-2 CREB: cAMP Response Element Binding protein EP2: Prostaglandin E2 receptor 2 EP4: Prostaglandin E2 receptor 4 GPx: Glutathione Peroxidase GR: Glutathione Reductase GST: Glutathione-S-Transferase γ-GT: γ-Glutamyl Transpeptidase HIF-1a: Hypoxia Inducible Factor 1, alpha subunit LDH: Lactate Dehydrogenase LPO: Lipid

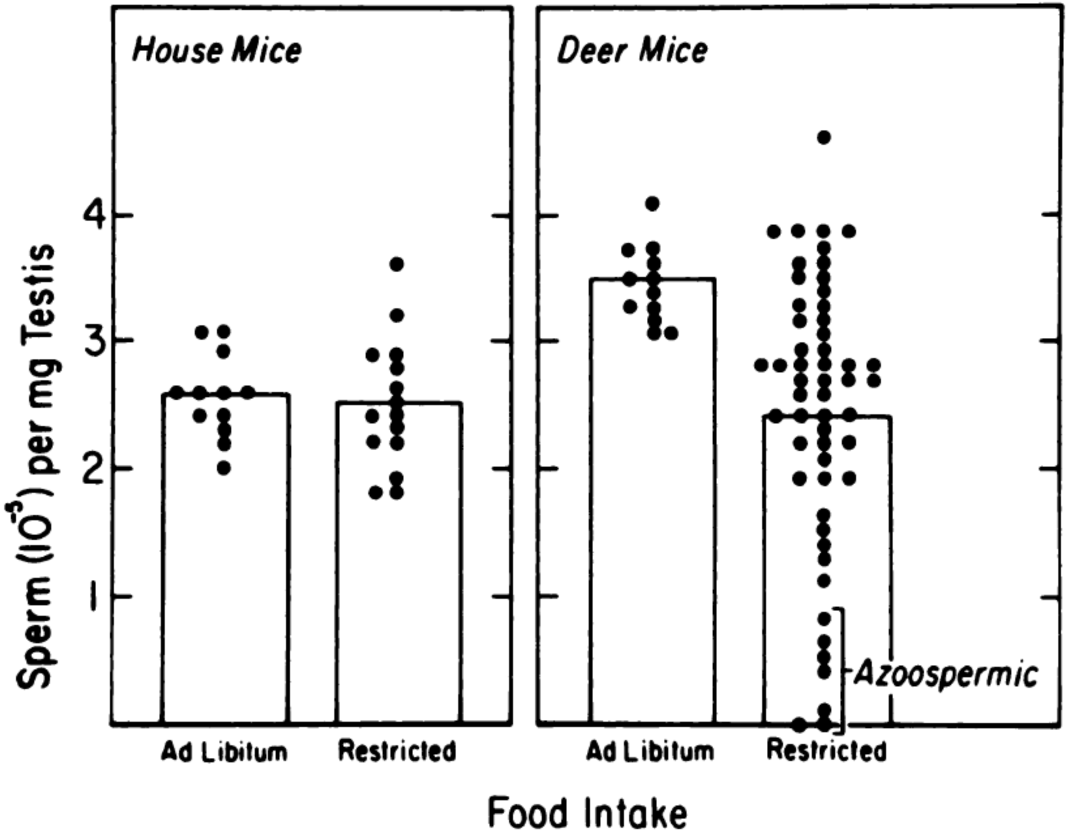
Roma, 8-11 novembre 2018

Agenda

ITALIAN CHAPTER

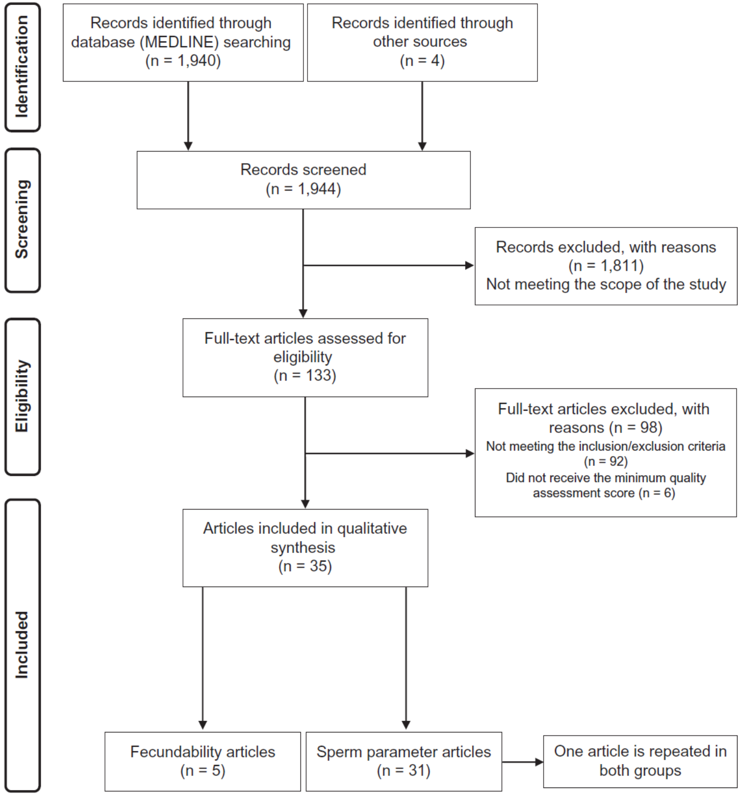
BIOLOGY OF REPRODUCTION 30, 410–415 (1984)

Spermatogenesis is Modified by Food Intake in Mice



Roma, 8-11 novembre 2018

Dietary patterns, foods and nutrients in male fertility parameters and fecundability: a systematic review of observational studies



Human Reproduction Update, Vol.23, No.4 pp. 371–389, 2017

Dietary fatty acid intakes and asthenozoospermia: a case-control study

Main dietary sources and description of fatty acid subclasses for cases and matched controls.

Fatty acid subclass and main sources (% of total daily intake among participants)	Asthenozoospermic cases		Normospermic controls		
	Median	IQR	Median	IQR	*P* value
Total fatty acids (g/d)	85.3	75.9–92.6	82.3	72.6–89.8	.002
Meat and meat products (18.1)					
Spreads[a] and cooking oils (13.7)					
Confectionary and savory snacks (8.9)					
Milk and milk products (7.6)					
Biscuits (6.3)					
Saturated fatty acids (g/d)	33.1	29.3–42.7	31.1	28.8–40.9	.001
Meat and meat products (17.3)					
Spreads and cooking oils (14.1)					
Milk and milk products (10.3)					
Milk (9.3)					
Biscuits (6.5)					
Monounsaturated fatty acids (g/d)	31.7	27.8–35.9	30.5	26.9–34.3	.122
Meat and meat products (19.1)					
Olive and olive oil (9.3)					
Fish and fish dishes (8.3)					
Spreads and other cooking oils (5.1)					
Confectionary and savory snacks (7.1)					
Biscuits (6.3)					
Polyunsaturated fatty acids (g/d)	13.9	10.9–15.3	15.1	12.3–16.9	< .001
Meat and meat products (14.9)					
Spreads and cooking oils (13.8)					
Confectionary and savory snacks (11.2)					
Fish and fish dishes (9.8)					
Vegetables[b] (9.5)					
Omega-6 polyunsaturated fatty acids (g/d)	10.3	8.7–13.1	10.9	8.9–13.6	.359
Spreads and cooking oils (15.3)					
Meat and meat products (14.5)					
Confectionary and savory snacks (9.8)					
Vegetables (6.5)					
Omega-3 polyunsaturated fatty acids (g/d)	2.1	1.8–2.6	2.5	1.9–3.9	< .001
Fish and fish dishes (33.9)					
Spreads and cooking oils (15.5)					
Vegetables (13.2)					
Meat and meat products (11.1)					
Savory foods, soups, and sauces (7.5)					
Trans-fatty acids (g/d)	3.8	3.1–4.4	3.2	2.9–4.1	.041
Spreads and cooking oils (21.3)					
Confectionary and savory snacks (16.8)					
Meat and meat products (15.1)					
Milk and milk products (10.1)					
Savory foods, soups, and sauces (5.1)					
Palmitic acid (g/d)	18.7	16.3–21.5	18.1	15.6–21.2	.003
Meat and meat products (20.3)					
Spreads and cooking oils (13.1)					
Milk and milk products (9.3)					
Confectionary and savory snacks (6.3)					
Biscuits (6.1)					
Stearic acid (g/d)	8.8	7.5–10.1	8.1	7.3–9.7	.002
Meat and meat products (26.1)					
Spreads and cooking oils (13.3)					
Biscuits (8.1)					
Confectionary and savory snacks (8.0)					
Milk and milk products (8.0)					
Oleic acid (g/d)	24.3	28.9–28.3	23.2	21.1–27.6	.098
Meat and meat products (20.8)					
Olive and olive oil (9.1)					
Confectionary and savory snacks (8.8)					
Biscuits (7.3)					
Spreads and cooking oils (5.9)					
Fish and fish dishes (5.1)					

Fertility and Sterility® Vol. 103, No. 1, January 2015

Trans fatty acid intake is inversely related to total sperm count in young healthy men

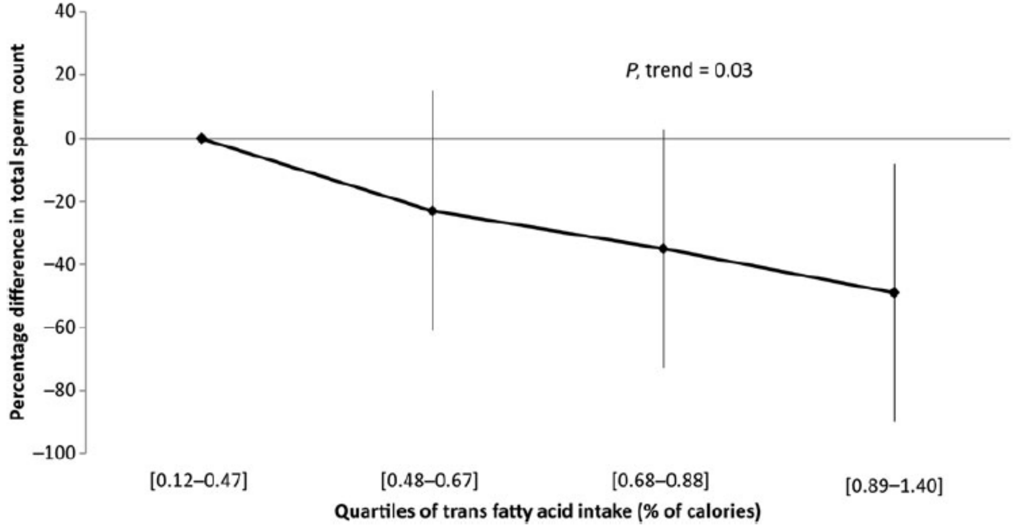


Figure 1 Relative difference in total sperm count in young men by increasing quartiles of *trans* fatty acid intake. Values represent the percentual (relative) difference and 95% confidence interval in total sperm count for men in the 2nd, 3rd and 4th quartile of *trans* fat intake when compared with men in the first quartile of intake. Models are adjusted for BMI (kg/m^2), smoking (current smoker versus not current smoker), ejaculation abstinence time (hours), alcohol intake (g/day), caffeine intake (mg/day), total caloric intake (kcal/day), fiber intake (%calories), protein intake (%calories), intakes of the remaining fatty acids (% calories), vitamin C (mg/day), β-cryptoxantine (μg/day), lycopene (μg/day) and β-carotene (μg/day).

Human Reproduction, Vol.29, No.3 pp. 429–440, 2014

Roma, 8-11 novembre 2018

Dietary fat and semen quality among men attending a fertility clinic

ITALIAN CHAPTER

BACKGROUND: The objective of this study was to examine the relation between dietary fats and semen quality parameters.

METHODS: Data from 99 men with complete dietary and semen quality data were analyzed. Fatty acid levels in sperm and seminal plasma were measured using gas chromatography in a subgroup of men ($n = 23$). Linear regression was used to determine associations while adjusting for potential confounders.

Table II Semen quality parameters (mean (95% CI)) of men by intake of total fat and major fatty acid groups.

Intake median, % of calories	*n*	Total sperm count (millions)	Sperm concentration (millions/ml)	Sperm motility (% motile)	Sperm morphology (% normal)
Total fat					
26	32	211 (158–283)	81 (61–107)	47 (39–55)	6.0 (5.0–7.1)
32	34	113 (85–150)*	49 (38–65)*	48 (41–56)	5.9 (5.0–7.0)
37	33	125 (94–166)*	51 (39–67)*	46 (38–54)	5.9 (4.8–6.9)
P_{trend}**		0.01	0.01	0.86	0.84
Saturated					
8	32	209 (156–280)	85 (65–112)	52 (44–59)	6.6 (5.5–7.6)
10	35	116 (88–155)*	48 (37–63)*	46 (38–53)	5.9 (4.9–6.9)
13	32	122 (91–164)*	50 (38–65)*	44 (36–51)	5.4 (4.4–6.5)
P_{trend}**		0.02	0.01	0.15	0.12
Monounsaturated					
10	32	201 (150–270)	84 (64–111)	47 (39–55)	5.5 (4.5–6.6)
12	33	119 (89–159)*	46 (35–60)*	48 (41–56)	6.4 (5.4–7.4)
15	34	124 (93–165)*	52 (40–68)*	46 (39–54)	5.9 (4.9–6.7)
P_{trend}**		0.03	0.02	0.83	0.62

Human Reproduction, Vol.27, No.5 pp. 1466–1474, 2012

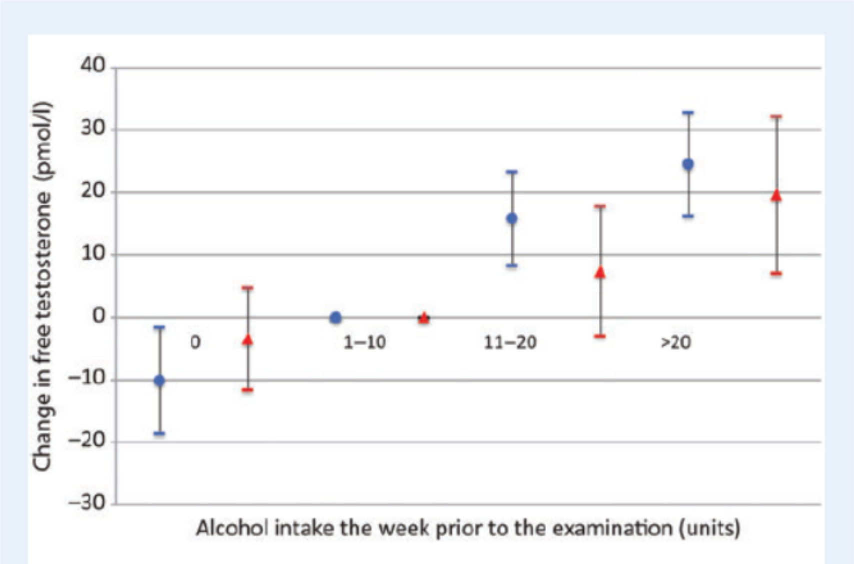
		Sp. Totali	Sp. Conc.	Motilità	Morfologia
Polyunsaturated					
4.2	33	165 (122–222)	73 (55–95)	45 (38–53)	5.4 (4.4–6.4)
5.6	33	135 (100–183)	54 (41–72)	47 (39–54)	5.8 (4.8–6.9)
7.3	33	132 (98–178)	50 (38–67)	49 (42–57)	6.6 (5.6–7.7)
P_{trend}**		0.31	0.07	0.50	0.09
Omega-6					
3.8	32	164 (121–222)	73 (55–97)	45 (37–53)	5.1 (4.1–6.1)
4.8	34	134 (100–180)	53 (41–71)	46 (39–54)	6.2 (5.2–7.2)
6.0	33	134 (100–182)	52 (39–68)	50 (42–58)	6.5 (5.5–7.6)
P_{trend}**		0.37	0.09	0.32	0.05
Omega-3					
0.4	34	132 (99–178)	62 (47–82)	45 (37–52)	5.0 (4.0–6.0)
0.5	35	163 (122–218)	60 (46–79)	50 (24–57)	5.8 (4.9–6.8)
0.8	30	135 (98–185)	53 (39–71)	47 (39–55)	7.2 (6.1–8.2)*
P_{trend}**		0.93	0.41	0.77	0.003

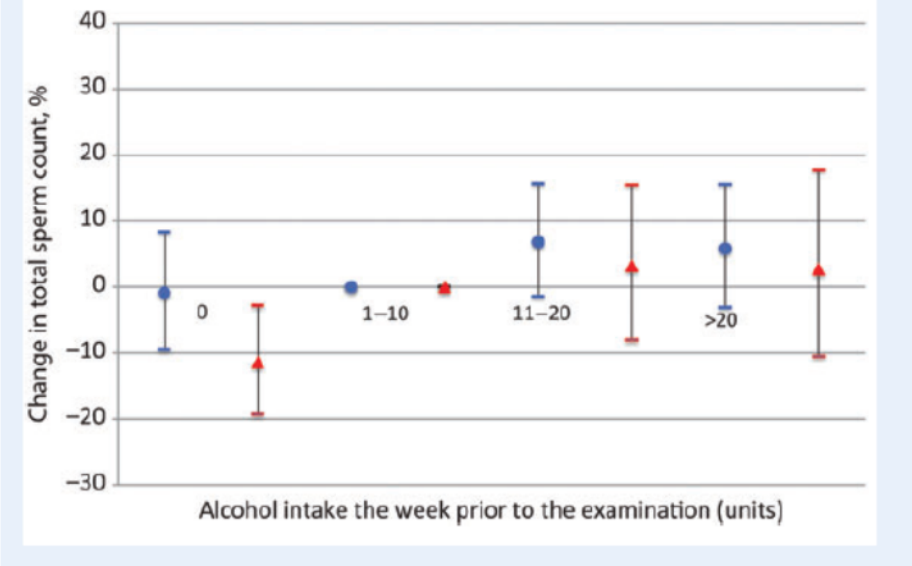
*Significantly different from men in the lowest tertile of intake at $P < 0.05$.

**P for trend from a linear regression model where the semen quality parameter was the outcome of interest and a variable with the median intake in each intake category was the predictor.

Alcohol and male reproductive health: a cross-sectional study of 8344 healthy men from Europe and the USA

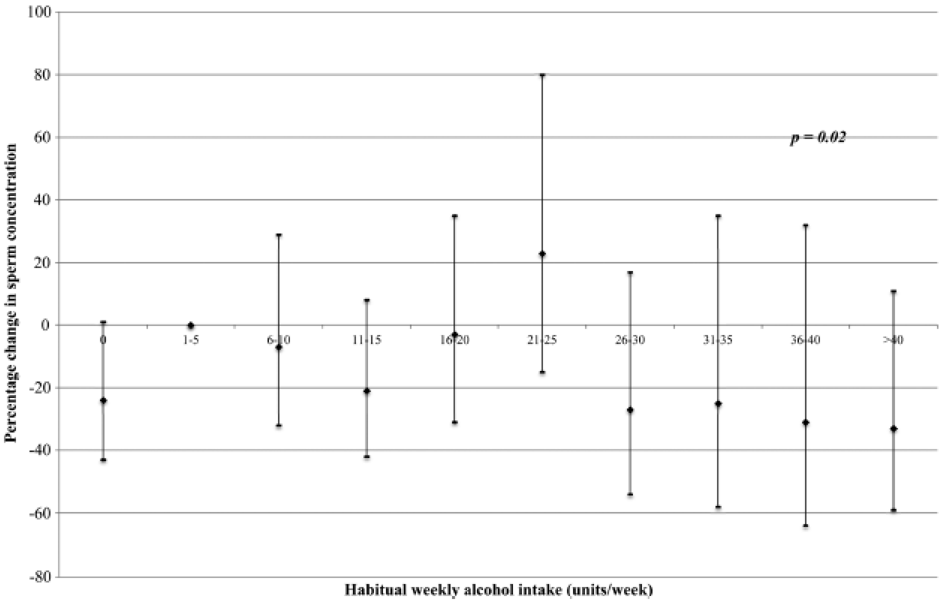
STUDY DESIGN, SIZE, DURATION: A coordinated international cross-sectional study among 8344 healthy men. A total of 1872 fertile men aged 18–45 years (with pregnant partners) from four European cities and four US states, and 6472 young men (most with unknown fertility) aged 18–28 years from the general population in six European countries were recruited.

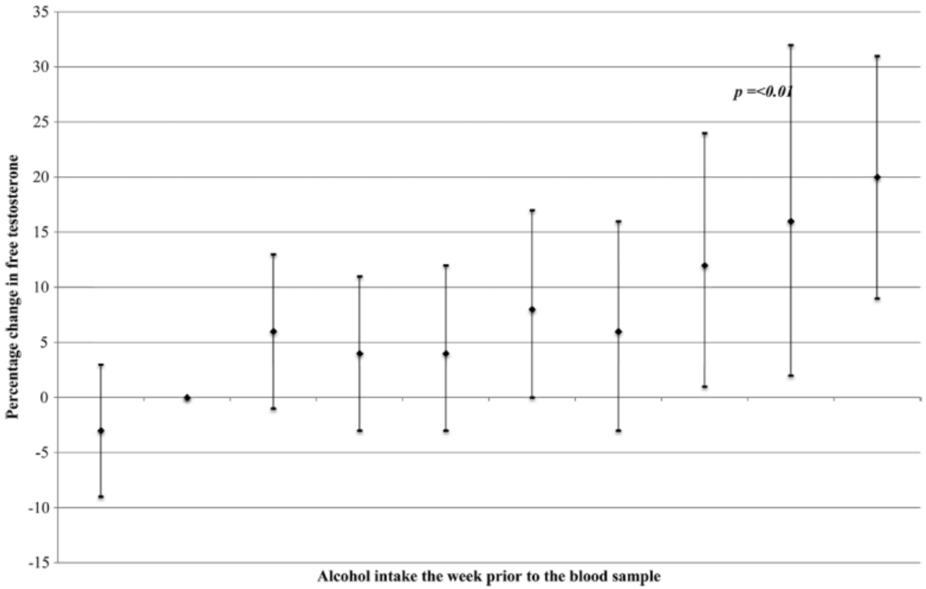




Human Reproduction, Vol.29, No.8 pp. 1801–1809, 2014

Habitual alcohol consumption associated with reduced semen quality and changes in reproductive hormones; a cross-sectional study among 1221 young Danish men

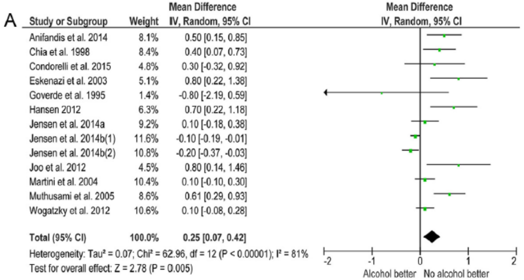




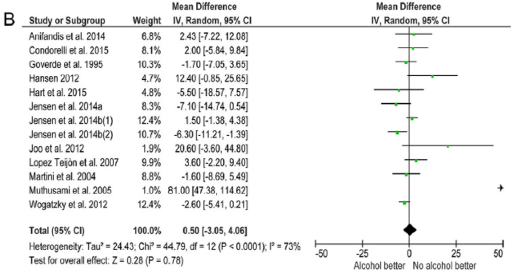
Semen quality and alcohol intake: a systematic review and meta-analysis

REPRODUCTIVE BIOMEDICINE ONLINE 34 (2017) 38–47

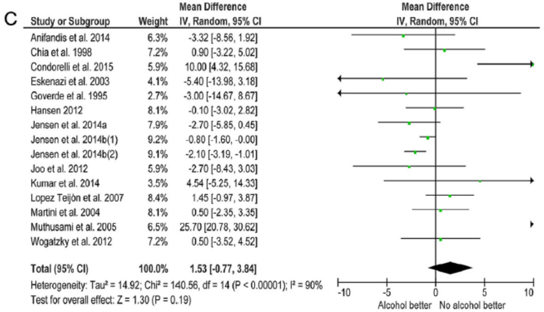
Volume



Concentrazione



Motilità



Morfologia

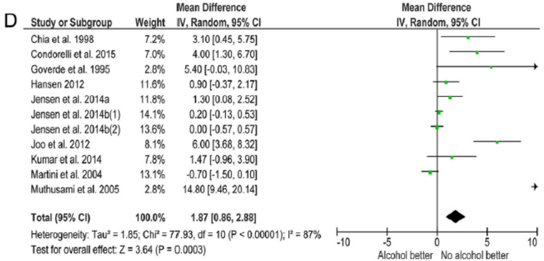


Table 3 – Subgroup analyses (if mean > 0 then no/occasional alcohol intake was better than any/daily alcohol intake).

	Volume, ml Mean (95% CI)	Concentration*, 10^6/ml Mean (95% CI)	Motility, % Mean (95% CI)	Normal morphology, % Mean (95% CI)
Overall	0.25 (0.07 to 0.42)	0.50 (−3.05 to 4.06)	1.53 (−0.77 to 3.84)	1.87 (0.86 to 2.88)
Unselected for semen quality and alcohol intake	0.22 (0.05 to 0.39)	−0.51 (−3.37 to 2.34)	−0.33 (−1.57 to 0.92)	1.20 (0.36 to 2.04)
Fertile men	0.13 (−0.33 to 0.60)	−2.74 (−10.79 to 5.31)	2.39 (−3.74 to 8.52)	2.13 (−0.73 to 4.99)
Unknown fertility	0.38 (0.00 to 0.76)	1.44 (−3.54 to 6.42)	−0.69 (−1.85 to 0.47)	1.75 (0.12 to 3.38)
Fertility clinics-infertile	0.18 (−0.01 to 0.38)	−2.13 (−4.65 to 0.39)	0.08 (−2.00 to 2.16)	0.07 (−1.96 to 2.11)
Occasional vs never drinkers	0.18 (0.01 to 0.35)	−1.51 (−4.78 to 1.76)	−1.11 (−1.92 to −0.30)	0.93 (0.04 to 1.82)
Daily vs occasional drinkers*	0.30 (−0.39 to 1.00)	1.75 (−2.72 to 6.23)	2.02 (−3.24 to 7.28)	5.17 (3.50 to 6.85)

* excluding Muthusami and Chinnaswamy (2005); 95% CI = 95% confidence interval (if it excludes 0, the estimate is statistically significant).

Alcool

- Consumo eccessivo: fattore di rischio per infertilità
- Blocco della secrezione di GnRH e della sua produzione da pre-pro-GnRH
- Azione diretta su LH
- Effetto negativo sulle cellule del Sertoli
- Dose-dipendenza: 40 g/die alterano parametri seminali; 160 g/die: OSCS

Sugar-sweetened beverage intake in relation to semen quality and reproductive hormone levels in young men

STUDY DESIGN, SIZE, DURATION: The Rochester Young Men's Study; a cross-sectional study of 189 healthy young men carried out at the University of Rochester during 2009–2010.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Men aged 18–22 years provided semen and blood samples, underwent a physical examination and completed a previously validated food frequency questionnaire (FFQ). Linear regression was used to analyze the association of SSBs with sperm parameters and reproductive hormone levels while adjusting for potential confounders.

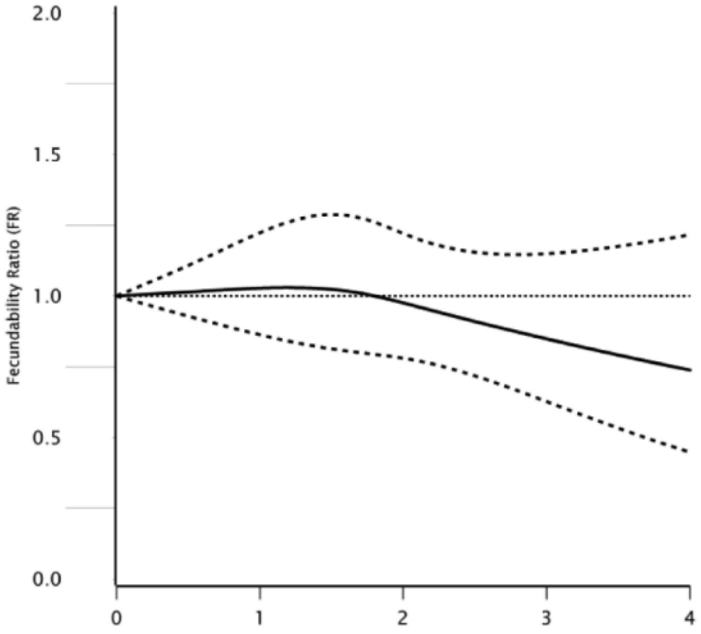
Table II **Directly measured semen quality parameters [mean (95% CI)] according to the intake of sugar-sweetened beverages (SSB).**

	Sugar-sweetened beverage				
	Q1	Q2	Q3	Q4	P^{a}_{trend}
Sperm motility (% motile A+B+C)[e]					
Crude	63.0 (59.1, 66.8)	66.3 (62.4, 70.3)	63.6 (59.8, 67.4)	58.2 (54.4, 62.1)	0.01
Model 1[b]	63.9 (60.1, 67.8)	66.3 (62.3, 70.2)	63.8 (60.0, 67.6)	57.1 (53.1, 61.1)*	0.002
Model 2[c]	63.5 (59.5, 67.6)	65.3 (61.4, 69.2)	63.7 (59.9, 67.5)	58.5 (54.4, 62.7)	0.03
Model 3[d]	63.9 (59.7, 68.1)	65.4 (61.5, 69.3)	63.7 (59.9, 67.4)	58.0 (53.6, 62.5)	0.03
Progressive motility (% motile A+B)[e]					
Crude	58.5 (54.4, 62.5)	61.8 (57.7, 66.0)	59.8 (55.8, 63.8)	53.6 (49.6, 57.7)	0.01
Model 1[b]	59.6 (55.5, 63.6)	61.8 (57.7, 65.9)	60.0 (56.1, 64.0)	52.3 (48.2, 56.5)*	0.002
Model 2[c]	58.9 (54.7, 63.2)	60.8 (56.7, 64.9)	60.0 (56.0, 64.0)	54.0 (49.6, 58.4)	0.04
Model 3[d]	59.3 (54.8, 63.8)	60.9 (56.8, 65.0)	60.0 (56.0, 64.0)	53.5 (48.8, 58.2)	0.03

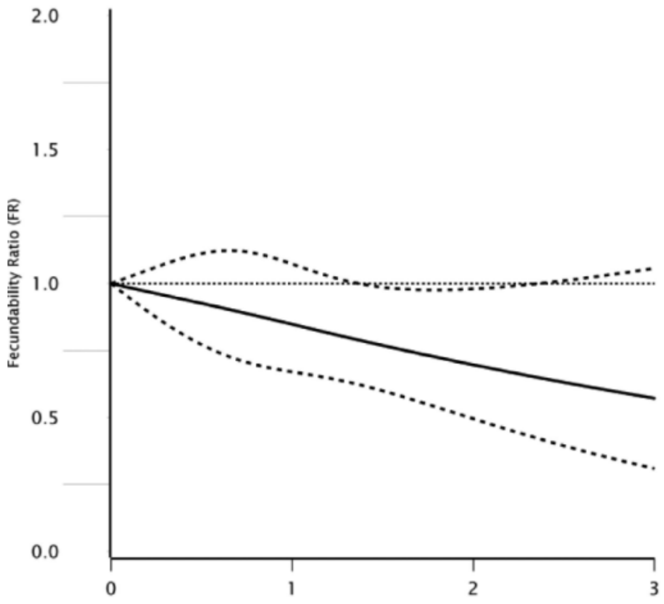
Human Reproduction, Vol.29, No.7 pp. 1575–1584, 2014

Caffeine and caffeinated beverage consumption and fecundability in a preconception cohort

662 maschi



Tazzine di caffè



Bevande energizzanti

Reprod Toxicol. 2016 July ; 62: 39–45.

Phthalates and heavy metals as endocrine disruptors in food: A study on pre-packed coffee products

Table 1
Detection of phthalates plasticizers in espresso coffee surrogates from pre-packed coffee products.

		DEP (μg/mL) (r.t. 27.11; *m/z* 149)	DiBP (μg/mL) (r.t. 33.72; *m/z* 149)	DBP (μg/mL) (r.t. 35.93; *m/z* 149)	DEHP (μg/mL) (r.t. 45.56; *m/z* 149)
M	mean	0.23	0.24	0.04	0.22
	st.dev	0.02	0.02	0.01	0.04
BD	mean	N/D	0.33	0.12	0.83
	st.dev		0.02	0.01	0.03
P1	mean	N/D	0.07	N/D	0.36
	st.dev		0.02		0.03
P2	mean	N/D	0.07	0.07	1.56
	st.dev		0.01	0.02	0.37

Abbreviations: DMP: Dimethyl-phthalate, DEP: Diethyl-phthalate, DiBP: Diisobuthyl-pthalate, DBP: Di-*n*-buthyl-phthalate, DEHP: Di(2-ethyl-hexyl)-phthalate, M: metal capsule, BD: bio-degradable capsule, P1-2: plastic capsule, r.t.: retention time, *m/z*: mass/ion charge ratio, st.dev: standard deviation, N/D: not detectable.

Table 3
Detection of heavy metals in espresso coffee surrogates and capsules from pre-packed coffe products.

		Pb (μg)		Cd (μg)		Ni (μg)	
		surrogate	capsule	surrogate	capsule	surrogate	capsule
M	mean	107.57	11.09	0.15	N/D	186.93	N/D
	st.dev	4.45	0.35	0.05	–	10.34	
BD	mean	0.48	N/D	0.63	N/D	940.32	N/D
	st.dev	0.08	–	0.09	–	12.54	
P1	mean	189.17	92.24	2.05	N/D	864.44	N/D
	st.dev	11.20	2.12	0.34	–	11.65	
P2	mean	80.14	N/D	0.78	N/D	1914.70	N/D
	st.dev	3.23	–	0.07	–	17.78	

Abbreviations: Pb: Lead, Cd: Cadmium, Ni: Nickel, N/D: not detectable, st.dev.: standard deviation.

Contribution of heavy metals found in espresso coffee surrogates to achievement of the daily tolerable intake.

	Pb [PTWI 25 μg/kg bw]	Cd [PTWI 7 μg/kg bw]	Ni [PTWI 35 μg/kg bw]
M	65%	0.2%	57%
BD	N/A	1.0%	317%
P1	79%	3.0%	267%
P2	42%	1.0%	633%

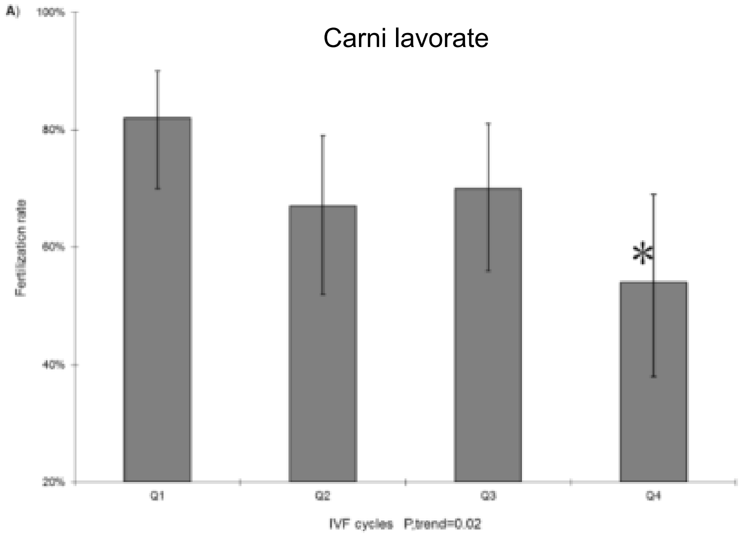
Abbreviations: Pb: Lead, Cd: Cadmium, Ni: Nickel, N/D: not detectable, PTWI: Provisional Tolerable Weekly Intake, bw: body weight.

Toxicology Reports 4 (2017) 234–239

Men's meat intake and treatment outcomes among couples undergoing assisted reproduction

Patient(s)—A total of 141 men whose female partners underwent 246 ART cycles from 2007 to 2014.

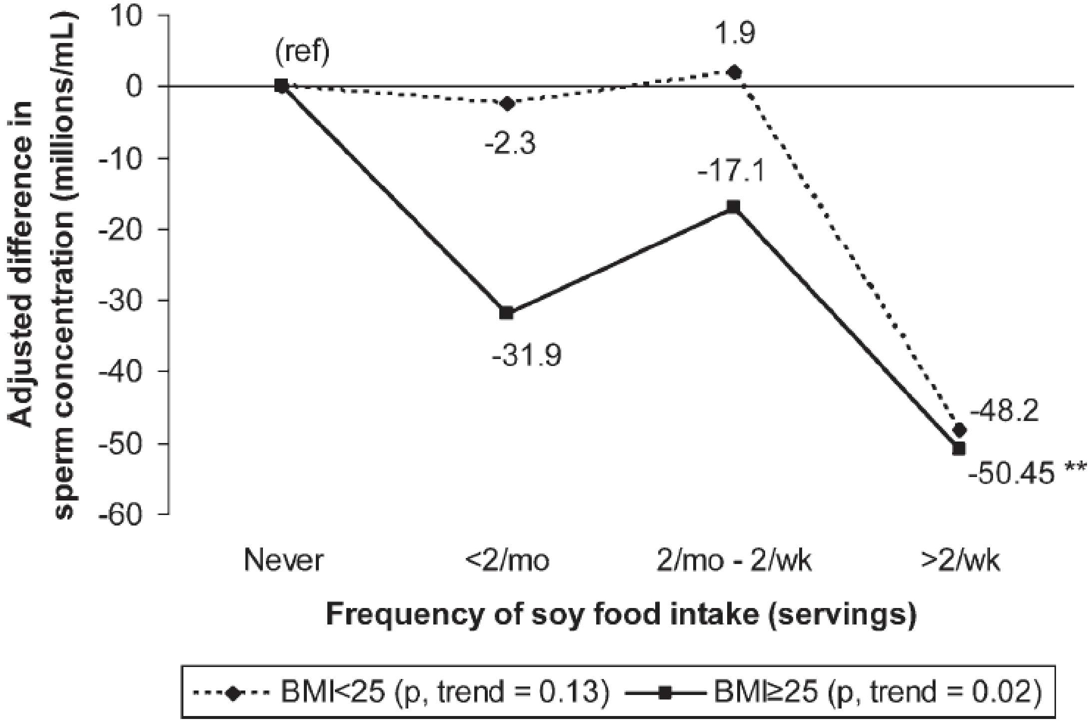
	Adjusted mean fertilization rate (95% Confidence Interval)			
MODEL	**Model 1**	**Model 2**	**Model 3**	**Model 4**
Total number of cycles	**206**	**206**	**206**	**183**
Quartile intake of poultry				
Q1 [0.00-0.18] (N=54)	0.66 (0.58 -0.72)	0.65 (0.57 -0.72)	0.65 (0.56- 0.72)	0.65 (0.56 -0.73)
Q2 [0.18-0.42] (N=45)	0.72 (0.65 -0.79)	0.72 (0.65- 0.78)	0.71 (0.62- 0.78)	0.73 (0.64- 0.80)
Q3 [0.45-0.71] (N=52)	0.74 (0.68- 0.80)	0.75 (0.68- 0.80)	0.74 (0.66- 0.80)	0.75 (0.68- 0.81)
Q4 [0.71-2.82] (N=55)	0.76 (0.70- 0.81)*	0.77 (0.70- 0.82)*	0.76 (0.69 -0.82)*	0.78 (0.71 -0.84)*
***P* trend**	.05	.03	.03	.04



Fertil Steril. 2015 October ; 104(4): 972–979.

Soy food and isoflavone intake in relation to semen quality parameters among men from an infertility clinic

99 soggetti con problematiche di infertilità di coppia, indagati per assunzione di 15 pietanze a base di soia



Roma, 8-11 novembre 2018

Agenda

ITALIAN CHAPTER


Male infertility
(abnormal sperm parameters or hormone levels)
High intake of coffee and alcohol
High consumption of sweets and sugar-sweetened beverages
High intake of total fat, saturated fatty acids and trans-fat
High intake of total proteins through processed meat, and processed red meat
High consumption of soy foods
High consumption of potatoes
High consumption of cheese, full-fat dairy, and total dairy products
Low consumption of low-fat dairy products, and skimmed milk
Low intake of antioxidants (vitamin E and C, β-carotene, selenium, zinc, cryptoxanthin, lycopene, vitamin D) and folate
Low consumption of poultry
Low intake of PUFAs (specially omega-3) mainly through fish, shellfish and sea food
Low intake of dietary fiber mainly through cereals
Low consumption of vegetables and fruits