

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2177: Wong WY, Zielhuis GA, Thomas CM, Merkus HM, Steegers-Theunissen RP. New evidence of the influence of exogenous and endogenous factors on sperm count in man. Eur J Obstet Gynecol Reprod Biol. 2003 Sep 10;110(1):49-54.	2003	The Netherlands	English	case-control	34.4 mean	infertility	semen	drugs for acid related disorders	A02	various	A02			92; 73	prevalence of oligozoospermia as compared to healthy men	OR 6.2 (95% CI 1.4-26.8)							
803: Gupta A, Gupta S, Tiwary AK. Spermicidal efficacy of H2-receptor antagonists and potentiation with 2', 4'-dichlorobenzamil hydrochloride: role of intrasperm Ca ²⁺ . Contraception. 2003 Jul;68(1):61-4.	2003	India	English	experimental	young	spermatozoa in vitro	Ca2+ influx	drugs for acid related disorders	A02	histamin-2 receptor antagonists	A02BA		in vitro		sperm cells, rise of Ca2+	faster with addition of H2 receptor antagonists						2+	
804: Van Thiel DH, Gavalier JS, Smith WI Jr, Paul G. Hypothalamic-pituitary-gonadal dysfunction in men using cimetidine. N Engl J Med. 1979 May 3;300(18):1012-5.	1979	USA	English	prospective	young	healthy	sperm count, hormones	drugs for acid related disorders	A02	cimetidine	A02BA01	1200mg/d	9w	7	sperm count, decrease; testosterone level, decrease	by 43%		no				3	
889: Knigge U, Dejgaard A, Wollesen F, Ingerslev O, Bennett P, Christiansen PM. The acute and long term effect of the H2-receptor antagonists cimetidine and ranitidine on the pituitary-gonadal axis in men. Clin Endocrinol (Oxf). 1983 Mar;18(3):307-13.	1983		English	retrospective	young	peptic ulcer	hormones	drugs for acid related disorders	A02	cimetidine	A02BA01	400 mg/d	6m		gonadotropin levels, increase			no				3	
888: Wang C, Wong KL, Lam KC, Lai CL. Ranitidine does not affect gonadal function in man. Br J Clin Pharmacol. 1983 Oct;16(4):430-2.	1983		English	retrospective	young	peptic ulcer	semen, hormones	drugs for acid related disorders	A02	ranitidine	A02BA02	300 mg/d	3m	20	sperm parameters, gonadotropin levels, testosterone level, alteration	no difference between exposed and control men		no	ranitidine	placebo		2-	
369: Savarino V, Giusti M, Scalabrini P, Bessarione D, Magnolia MR, Percario G, Celle G. Famotidine has no significant effect on gonadal function in man. Gastroenterol Clin Biol. 1988 Jan;12(1):19-22.	1988	Italy	English	prospective	young	peptic ulcer	semen	drugs for acid related disorders	A02	famotidine	A02BA03	40mg	4w	8	sperm parameters, impairment	none		no				3	
2143: Lindquist M, Edwards IR. Endocrine adverse effects of omeprazole. BMJ. 1992 Aug 22;305(6851):451-2	1992	Sweden	English	retrospective	52 mean	gastric hypersecretion	clinical reports	drugs for acid related disorders	A02	omeprazole	A02BC01	20-40mg/d	>8m	30	notifications of problems with male reproductive system	impotence 15 men; gynecomastia 15 men						3	
872: Dammann HG, Bethke T, Burkhardt F, Wolf N, Khalil H, Luehmann R. Effects of pantoprazole on endocrine function in healthy male volunteers. Aliment Pharmacol Ther. 1994 Oct;8(5):549-54.	1994	Germany	English	prospective, randomized	young	healthy	hormones	drugs for acid related disorders	A02	pantoprazole	A02BC02	40mg/d	2w	12	testosterone level and response to hCG, unaltered	no difference between groups		yes	pantoprazole	placebo		1-	
871: Gaetani M, De Giorgio R, Buratti P, Pasquali R, Capelli M, Stanghellini V, Corinaldesi R. Chronic oral administration of lansoprazole does not affect the hypothalamic pituitary gonadal axis in healthy young men. Eur J Gastroenterol Hepatol. 1995 Mar;7(3):211-3.	1995	Italy	English	prospective, randomized	young	healthy	hormones	drugs for acid related disorders	A02	lansoprazole	A02BC03	30mg/d	3w	11	LH pulsatility, unaltered	no difference between groups		yes	lansoprazole	placebo		1-	
786: Graf KJ, Schmidt-Gollwitzer M, Horowski R, Dorow R. Effect of metoclopramide and lisuride on hypophyseal and gonadal function in men. Clin Endocrinol (Oxf). 1982 Sep;17(3):243-51.	1982		English	prospective	young	healthy	sperm parameters, hormones	drugs for functional gastrointestinal disorders	A03	metoclopramide	A03FA01	10mg/4xd	3d	24	sperm parameters, unaltered			no				3	

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849: Ufearo CS, Orisakwe OE. Restoration of normal sperm characteristics in hypoprolactinemic infertile men treated with metoclopramide and exogenous human prolactin. Clin Pharmacol Ther. 1995 Sep;58(3):354-9.	1995	Nigeria	English	pro-spective	young	infertility	sperm parameters	drugs for functional gastrointestinal disorders	A03	metoclopramide	A03FA01	10mg/d	16w	20	sperm morphology, improvement	abormal sperm from 66.75% to 24.7% (prolactine) and 31% (metoclopramide)						3	
852: Spitz IM, Halperin Y, Zylber-Haran E, Shilo S, Leroith D, Liel Y, Livshin J, Laufer N, Schenker J. Prolactin response to metoclopramide and chlorpromazine in primary testicular failure and isolated gonadotrophin deficiency. Clin Endocrinol (Oxf). 1981 Apr;14(4):375-80.	1981		English	pro-spective	young	infertility	hormones	drugs for functional gastrointestinal disorders	A03	metoclopramide	A03FA01		single dose	17	prolactin response to metoclopramide	enhanced in low sperm count						3	
851: Baranowska B, Jeske W, Niewiadomska A, Rozbicka G, Walczak L, Zgliczynski S. Enhanced serum prolactin concentration after metoclopramide stimulation in idiopathic oligozoospermia and azoospermia. Andrologia. 1983;15 Spec No:554-9.	1983		English	pro-spective	21-34	infertility	hormones	drugs for functional gastrointestinal disorders	A03	metoclopramide	A03FA01		single dose	13	prolactin response to metoclopramide	enhanced in low sperm count						3	
787: Jecht E, Kleissl HP, Pache U. Short-term increase of sperm output under metoclopramide administration. Int J Androl. 1981 Feb;4(1):49-54.	1981		English	pro-spective	young	healthy	sperm count	drugs for functional gastrointestinal disorders	A03	metoclopramide	A03FA01	10mg/d	4w	9	sperm count and prolactin levels, increase	twofold		no				3	
850: Elias AN, Szekeres AV, Stone S, Valenta LJ, Haw T, Ascher MS. GABA-ergic and dopaminergic mechanisms in gonadotrophin secretion in males--effects of baclofen and metoclopramide. Acta Endocrinol (Copenh). 1983 Aug;103(4):451-6.	1983		English	pro-spective	young	healthy	hormones	drugs for functional gastrointestinal disorders	A03	metoclopramide +baclofen	A03FA01		single dose	6	GnRH-induced LH release	blunted in the baclofen group						2-	
788: Falaschi P, Frajese G, Sciarra F, Rocco A, Conti C. Influence of hyperprolactinaemia due to metoclopramide on gonadal function in men. Clin Endocrinol (Oxf). 1978 May;8(5):427-33.	1978	Italy	English	pro-spective	young	healthy	sperm parameters	drugs for functional gastrointestinal disorders	A03	metoclopramide	A03FA01			5	sperm count, seminal volume, decrease	in all participants		no				3	
896: Nakagawa K, Obara T, Matsubara M, Kubo M. Relationship of changes in serum concentrations of prolactin and testosterone during dopaminergic modulation in males. Clin Endocrinol (Oxf). 1982 Oct;17(4):345-52.	1982	Japan	English	pro-spective	young	healthy	hormones	drugs for functional gastrointestinal disorders	A03	metoclopramide	A03FA01	10mg/d	3d	n.g.	testosterone level and response to hCG, decrease	significant						3	
2141: Toovey S, Hudson E, Hendry WF, Levi AJ. Sulphasalazine and male infertility: reversibility and possible mechanism. Gut. 1981 Jun;22(6):445-51.	1981	UK	English	retrospective	young	inflammatory bowel disease	semen	antidiarrheals, antiinflammatory/antiinfective agents	A07	sulphasalazine	A07EC01	2-4g/d	1m	28	sperm parameters, impairment	Abnormalities in 18/28 patients. Improvement after discontinuation, 10 pregnancies reported		no				3	
533: Karbach U, Ewe K, Schramm P. Quality of semen in patients with Crohn's disease. Z Gastroenterol. 1982 Jun;20(6):314-20.	1982	Germany	German	retrospective	young	inflammatory bowel disease	semen	antidiarrheals, antiinflammatory/antiinfective agents	A07	sulfasalazopyridine	A07EC01			27	spermatogenesis, impairment	few patients		no	sulfasalazopyridine	sulfasalazopyridine + cortisone	untreated	2-	
548: Freeman JG, Reece VA, Venables CW. Sulphasalazine and spermatogenesis. Digestion. 1982;23(1):68-71.	1982		English	retrospective	young	inflammatory bowel disease	semen	antidiarrheals, antiinflammatory/antiinfective agents	A07	sulfasalazopyridine	A07EC01			17	spermatogenesis, impairment	in most men		no	sulfasalazopyridine	no sulfasalazopyridine		2-	
615: Levi AJ, Fisher AM, Hughes L, Hendry WF. Male infertility due to sulphasalazine. Lancet. 1979 Aug 11;2(8137):276-8.	1979	UK	English	retrospective	young	inflammatory bowel disease	semen	antidiarrheals, antiinflammatory/antiinfective agents	A07	sulfasalazopyridine	A07EC01			4	spermatogenesis, recovery	after withdrawal in 3 of 4, 3 pregnancies		no				3	

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458: Steeno OP. Side-effects of salazopyrin on male fertility. Eur J Obstet Gynecol Reprod Biol. 1984 Dec;18(5-6):361-4.	1984	Belgium	English	review	young	spermatogenic dysfunction	semen	antidiarrheals, antiinflammatory/antiinfective agents	A07	sulfasalazopyridine	A07EC01				spermatogenesis, impairment	none						4	
79: Niederberger C. The adverse effect of sulfasalazine on spermatogenesis and male reproductive potential. J Androl. 2002 Mar-Apr;23(2):180.	1995		English	retrospective	young	inflammatory bowel disease	semen	antidiarrheals, antiinflammatory/antiinfective agents	A07	sulfasalazopyridine	A07EC01		n.g.		spermatogenesis, impairment	none		no				3	Sulfasalazine seems to exert no direct effect on spermatogenesis. The deleterious effect might therefore occur only after ejaculation and result in asthenozoospermia
846: Riley SA, Lecarpentier J, Mani V, Goodman MJ, Mandal BK, Turnberg LA. Sulphasalazine induced seminal abnormalities in ulcerative colitis: results of mesalazine substitution. Gut. 1987 Aug;28(8):1008-12.	1987	UK	English	retrospective	young	inflammatory bowel disease	sperm parameters	antidiarrheals, antiinflammatory/antiinfective agents	A07	5-amino salicylic acid after sulfasalazine	A07EC02		4m	16	sperm parameters, improvement	3m after discontinuation of sulfosalazine, 4 pregnancies						3	
845: Zelissen PM, van Hattum J, Poen H, Scholten P, Gerritse R, te Velde ER. Influence of salazosulphapyridine and 5-aminosalicylic acid on seminal qualities and male sex hormones. Scand J Gastroenterol. 1988 Nov;23(9):1100-4.	1988	The Netherlands	English	retrospective	young	inflammatory bowel disease	sperm parameters	antidiarrheals, antiinflammatory/antiinfective agents	A07	5-amino salicylic acid after sulfasalazine	A07EC02		4m	11	sperm parameters, improvement	5m after discontinuation of sulfosalazine, 3 pregnancies						3	
843: Wu FC, Aitken RJ, Ferguson A. Inflammatory bowel disease and male infertility: effects of sulfasalazine and 5-aminosalicylic acid on sperm-fertilizing capacity and reactive oxygen species generation. Fertil Steril. 1989 Nov;52(5):842-5.	1989	UK	English	prospective	young	inflammatory bowel disease	sperm parameters	antidiarrheals, antiinflammatory/antiinfective agents	A07	5-amino salicylic acid after sulfasalazine	A07EC02		16w	6	sperm parameters, improvement	no change in ROS activity						3	
844: Delaere KP, Srijbos WE, Meuleman EJ. Sulphasalazine-induced reversible male infertility. Acta Urol Belg. 1989;57(1):29-33.	1989	Belgium	English	case report	young	inflammatory bowel disease	sperm parameters	antidiarrheals, antiinflammatory/antiinfective agents	A07	5-amino salicylic acid after sulfasalazine	A07EC02		3m	1	sperm parameters, improvement; pregnancy in the female partner	3m after discontinuation of sulfosalazine						3	
2140: Cann PA, Holdsworth CD. Reversal of male infertility on changing treatment from sulphasalazine to 5-aminosalicylic acid. Lancet. 1984 May 19;1(8386):1119.	1984	UK	English	retrospective	33	inflammatory bowel disease	semen	antidiarrheals, antiinflammatory/antiinfective agents	A07	5-amino salicylic acid after sulfasalazine	A07EC02	3x1g/d	12m	1	semen parameters, improvement	after change from sulphasalazine to 5-ASA						3	
2170: Sallmen M, Sandler DP, Hoppin JA, Blair A, Baird DD. Reduced fertility among overweight and obese men. Epidemiology. 2006 Sep;17(5):520-3.	2006	USA	English	retrospective, patients	young	obesity	semen	anti-obesity preparations	A08	anti-obesity preparations	A08		no treatment	2111	infertility associated with obesity	A 3-unit change in BMI was associated with adjusted ORs of 1.11 to 1.12						2+	
847: Ozata M, Oktenli C, Bingol N, Ozdemir IC. The effects of metformin and diet on plasma testosterone and leptin levels in obese men. Obes Res. 2001 Nov;9(11):662-7.	2001	Turkey	English	prospective	middle-aged	obesity and type-2 diabetes	hormones	drugs used in diabetes	A10	metformin	A10BA02	1700mg/d	3m	40	sex steroid hormones, decrease	significant in diabetic group		no				2-	
29. Akmal M, Qadri JQ, Al-Waili NS, Thangal S, Haq A, Saloom KY. Improvement in human semen quality after oral supplementation of vitamin C. J Med Food. 2006 Fall;9(3):440-2.	2006	Dubai	English	prospective	25-35	infertility	semen	vitamins	A11	vitamin C	A11GA01	2000mg/d	2m	13	sperm count, increase	14x10(6) to 32x10(6)		no				3	

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995: Ortiz-Perez D, Rodriguez-Martinez M, Martinez F, Borja-Aburto VH, Castelo J, Grimaldo JI, de la Cruz E, Carrizales L, Diaz-Barriga F. Fluoride-induced disruption of reproductive hormones in men. Environ Res. 2003 Sep;93(1):20-30.	2003	Mexico	English	retrospective	young	fluoride-exposed	semen	mineral supplements	A12	fluorides	A12CD	3-27mg/d		n.g.	sperm count, alteration	no difference to lower exposition		no				2-	
2301: Wong WY, Flik G, Groenen PM, Swinkels DW, Thomas CM, Copius-Peereboom JH, Merkus HM, Steegers-Theunissen RP. The impact of calcium, magnesium, zinc, and copper in blood and seminal plasma on semen parameters in men. Reprod Toxicol. 2001 Mar-Apr;15(2):131-6.	2001	The Netherlands	English	prospective	young	infertility	semen	mineral supplements	A12	zinc	A12CB			210	concentrations of calcium, magnesium, zinc, and copper in blood and seminal plasma	not different between the subfertile and fertile men. Weak correlations between blood plasma zinc concentrations and sperm count, sperm motility, abnormal sperm morphology.		no				2-	
2302: Chia SE, Ong CN, Chua LH, Ho LM, Tay SK. Comparison of zinc concentrations in blood and seminal plasma and the various sperm parameters between fertile and infertile men. J Androl. 2000 Jan-Feb;21(1):53-7.	2000	Singapore	English	prospective	young	infertility	semen	mineral supplements	A12	zinc	A12CB			210	zinc concentration in blood	no significant differences in the geometric means between the fertile and infertile men		no				2-	
2199: Ebisch IM, Pierik FH, DE Jong FH, Thomas CM, Steegers-Theunissen RP. Does folic acid and zinc sulphate intervention affect endocrine parameters and sperm characteristics in men? Int J Androl. 2006 Apr;29(2):339-45.	2006	The Netherlands	English	prospective, randomized	young	infertility	semen	mineral supplements	A12	zinc sulphate + folic acid	A12CB	66mg/d	26w	87	positive correlation between zinc levels and sperm count	disappearance after intervention		yes	zinc+folate	placebo		1-	
2303: Mohan H, Verma J, Singh I, Mohan P, Marwah S, Singh P. Inter-relationship of zinc levels in serum and semen in oligospermic infertile patients and fertile males. Indian J Pathol Microbiol. 1997 Oct;40(4):451-5.	1997	India	English	prospective	young	infertility	semen	mineral supplements	A12	zinc	A12CB			75	zinc concentration in blood	significantly lower in infertile than in fertile men		no				2-	
2300: Ali H, Baig M, Rana MF, Ali M, Qasim R, Khem AK. Relationship of serum and seminal plasma zinc levels and serum testosterone in oligospermic and azoospermic infertile men. J Coll Physicians Surg Pak. 2005 Nov;15(11):671-3	2005	Pakistan	English	prospective	20-40	infertility	semen	mineral supplements	A12	zinc	A12CB			58	zinc serum levels	lower in men with oligozoospermia than with normozoospermia		no				2-	
2305: Kynaston HG, Lewis-Jones DI, Lynch RV, Desmond AD. Changes in seminal quality following oral zinc therapy. Andrologia. 1988 Jan-Feb;20(1):21-2.	1988	UK	English	prospective	young	infertility	semen	mineral supplements	A12	zinc	A12CB	n.g.		33	sperm motility	increase after application		no				1-	
2306: Tikkiwal M, Ajmera RL, Mathur NK. Effect of zinc administration on seminal zinc and fertility of oligospermic males. Indian J Physiol Pharmacol. 1987 Jan-Mar;31(1):30-4.	1987	India	English	prospective	24-45	infertility	semen	mineral supplements	A12	zinc	A12CB	220mg/d	4m	14	sperm count, sperm motility, increase	significant		no				1-	
2304: Hunt CD, Johnson PE, Herbel J, Mullen LK. Effects of dietary zinc depletion on seminal volume and zinc loss, serum testosterone concentrations, and sperm morphology in young men. Am J Clin Nutr. 1992 Jul;56(1):148-57.	1992	USA	English	prospective	young	healthy	semen, hormones	mineral supplements	A12	zinc	A12CB	0.4, 2.5, 3.4, 4.4, or 10.4 mg/d	63	11	T levels, seminal volume	sensitive to zinc loss		no				1-	
632: Abbasi AA, Prasad AS, Rabbani PR. Experimental zinc deficiency in man: effect on spermatogenesis. Trans Assoc Am Physicians. 1979;92:292-302.	1979		English	prospective	51-65	healthy	semen	mineral supplements	A12	zinc restriction	A12CB		40w	5	spermatogenesis, impairment	all		no				3	

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9. Parkinson AB, Evans NA. Anabolic androgenic steroids: a survey of 500 users. Med Sci Sports Exerc. 2006 Apr;38(4):644-51. USA.	2006	USA	English	pro-spective	young	anabolic steroid abuse	abuse in body builders	anabolic agents for systemic use	A14	anabolic steroids, cessation	A14A		continuous	500	anabolic steroids, abuse	99.2% of bodybuilders		no				2-	
986. Knuth UA, Maniera H, Nieschlag E. Anabolic steroids and semen parameters in bodybuilders. Fertil Steril. 1989 Dec;52(6):1041-7.	1989	Germany	English	retro-spective	26.7 mean	anabolic steroid abuse	semen	anabolic agents for systemic use	A14	anabolic steroids, cessation	A14A	various	continuous	41;41	sperm count, depression	24/41 in abuse, 5/41 in normal controls		no	anabolic steroids	normal volunteers		2+	
985. Torres-Calleja J, Gonzalez-Unzaga M, DeCelis-Carrillo R, Calzada-Sanchez L, Pedron N. Effect of androgenic anabolic steroids on sperm quality and serum hormone levels in adult male bodybuilders. Life Sci. 2001 Mar 2;68(15):1769-74.	2001	USA	English	retro-spective	26 mean	anabolic steroid abuse	semen	anabolic agents for systemic use	A14	anabolic steroids, cessation	A14A	various	continuous	15;15	spermatogenesis, impairment	3 men had azoospermia,		no	anabolic steroids	no anabolic steroids		2-	
21: Karila T, Hovatta O, Seppala T. Concomitant abuse of anabolic androgenic steroids and human chorionic gonadotrophin impairs spermatogenesis in power athletes. Int J Sports Med. 2004 May;25(4):257-63.	2004	Finland	English	pro-spective	young	anabolic steroid abuse	semen	anabolic agents for systemic use	A14	anabolic steroids, cessation	A14A	various	continuous	18	spermatogenesis, improvement	in 18 patients		no	anabolic steroids	anabolic steroids + hCG		2-	
999: Salazar EL, Torres JA, Avila A, Andrade A. Hyperplastic changes and receptor status in the breast tissue of bodybuilders under anabolic-androgenic steroid stimulation. Arch Androl. 2000 Jul-Aug;45(1):1-7.	2000	Mexico	English	experimental	21-45	gynecomastia	receptor status	anabolic agents for systemic use	A14	anabolic steroids, cessation	A14A	various	continuous	8	receptor density	significantly higher than in non-anabolic induced gynecomastia		no				2-	
33. Gazvani MR, Buckett W, Luckas MJ, Aird IA, Hipkin LJ, Lewis-Jones DI. Conservative management of azoospermia following steroid abuse. Hum Reprod. 1997 Aug;12(8):1706-8.	1997	UK	English	retro-spective	27-33	anabolic steroid abuse	semen	anabolic agents for systemic use	A14	anabolic steroids, cessation	A14A	various	5y	4	azoospermia, reversal after cessation	spontaneously within 12m		no				3	
994. Tricker R, O'Neill MR, Cook D. The incidence of anabolic steroid use among competitive bodybuilders. J Drug Educ. 1989;19(4):313-25.	1989	USA	English	retro-spective	young	anabolic steroid abuse	abuse in body builders	anabolic agents for systemic use	A14	anabolic steroids, cessation	A14A		continuous	n.g.	anabolic steroids, abuse	in 54% of bodybuilders		no				2-	
676: Holma PK. Effects of anabolic steroid (metandienone) on spermatogenesis. Contraception. 1977 Feb;15(2):151-62.	1977		English	retro-spective	young	anabolic steroid abuse	semen	anabolic agents for systemic use	A14	metandienone	A14AA03	15mg/d	2m	15	sperm parameters, impairment	decrease of motility		no				3	
918: Dobs AS, Sarma PS, Guarnieri T, Griffith L. Testicular dysfunction with amiodarone use. J Am Coll Cardiol. 1991 Nov 1;18(5):1328-32.	1991	USA	English	retro-spective	old	cardiac disease	hormones	cardiac therapy	C01	amiodarone	C01BD01		continuous	44	gonadotropin levels, increase; testosterone level, unaltered	no effects		no				3	
55: Kovacic B, Vlaisavljevic V, Reljic M. Clinical use of pentoxifylline for activation of immotile testicular sperm before ICSI in patients with azoospermia. J Androl. 2006 Jan-Feb;27(1):45-52.	2006	Slovenija	English	retro-spective	young	infertility	sperm motility	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	1.76mmol	in-vitro	77 cycles	motility of frozen sperm, improvement; pregnancy rate, improvement	95%; no alteration		no	pentoxifylline	no addition in vitro		2-	
51: Griveau JF, Lobel B, Laurent MC, Michardiere L, Le Lannou D. Interest of pentoxifylline in ICSI with frozen-thawed testicular spermatozoa from patients with non-obstructive azoospermia. Reprod Biomed Online. 2006 Jan;12(1):14-8.	2006	France	English	pro-spective	young	infertility	sperm motility	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	1.5mmol	in-vitro	64 cycles	motility of frozen sperm, improvement	54% fertilisation rate	not mentioned	no				2-	

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101: Tasdemir M, Tasdemir I, Kodama H, Tanaka T. Pentoxifylline-enhanced acrosome reaction correlates with fertilization in vitro. Hum Reprod. 1993 Dec;8(12):2102-7.	1993	Japan	English	pro-spective	young	infertility	IVF outcome	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	3.6mmol	in-vitro	51	IVF outcome, improvement	parallel to increase of acro-some reaction		no	pentoxifylline	no addition in vitro		2-	
536: Schill WB. Therapy of idiopathic astheno- and oligo-zoospermia with pentoxifylline. Fortschr Med. 1982 Apr 22;100(15):696-700.	1982	Germany	German	pro-spective	young	spermato-genic dysfunc-tion	semen	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	1.2g/d		65	spermatogenesis, improvement	most		no				3	
78: Kolon TF, Philips KA, Buch JP. Pentoxifylline enhancement of post-thaw motility in cryopreserved semen of spinal cord-injured men. Int J Fertil Menopausal Stud. 1995 May-Jun;40(3):156-60	1995	USA	English	pro-spective	young	spinal cord injury	sperm motility	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	3.6mmol	in-vitro	36	motility of frozen sperm, improvement	no significant effect		no	pentoxifylline	no addition in vitro		2-	
80: Verheyen G, Tournaye H, Janssenswillen C, Henderix P, Devroey P, Van Steirteghem A. The effect of pentoxifylline on in-vitro fertilization in the presence of anti-sperm antibodies. J Reprod Immunol. 1994 Dec;27(3):187-97.	1994	Belgium	English	pro-spective	young	immune infertility	sperm motility	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	3.6mmol	in-vitro	28	motility of frozen sperm, improvement; ICSI outcome, improvement	no alteration		yes	pentoxifylline	no addition in vitro		1+	
93: Maier U, Szabo N, Ludvik G. Oral pentoxifylline in therapy-resistant idiopathic OAT syndrome. Arch Androl. 1994 Jul-Aug;33(1):59-62.,	1994	Austria	English	pro-spective	young	infertility	sperm parameters	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	1200mg/d	3m	25	sperm parameters, improvement	no alteration		no				3	
104: Marrama P, Baraghini GF, Carani C, Celani MF, Giovenco P, Grandi F, Montanini V. Further studies on the effects of pentoxifylline on sperm count and sperm motility in patients with idiopathic oligo-astheno-zoospermia. Andrologia. 1985 Nov-Dec;17(6):612-6.	1985	Italy	English	pro-spective	young	infertility	sperm parameters	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	1200mg/d	6m	22	sperm parameters, improvement	sperm count increased 2.0-fold, sperm motility increased 2.8-fold	none of patients	no				3	
105: Aparicio NJ, Schwarzstein L, de Turner EA. Pentoxifylline (BL 191) by oral administration in the treatment of astheno-zoospermia. Andrologia. 1980 May-Jun;12(3):228-31.	1980		English	pro-spective	young	infertility	sperm parameters	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	1200mg/d	6m	15	sperm parameters, improvement	percentage of forward progressive spermatozoa and of live and motile spermatozoa	Two patients reported mild gastrointestinal; routine laboratory not changed	no				3	
82: Faka B, Api M, Ficicioglu C, Gurbuz A, Oral O. Pentoxifylline in male-factor infertility: its therapeutic efficacy after oral administration. Acta Eur Fertil. 1994 Nov-Dec;25(6):351-3.	1994	Turkey	English	pro-spective	young	infertility	sperm parameters	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	1200mg/d	n.g.	14	sperm parameters, improvement	slight improvement of sperm count and motility		no				3	
70: Terriou P, Hans E, Giorgetti C, Spach JL, Salzmann J, Urrutia V, Roulier R. Pentoxifylline initiates motility in spontaneously im-motile epididymal and testicular spermatozoa and allows normal fertilization, pregnancy, and birth after intracytoplasmic sperm injection. J Assist Reprod Genet. 2000 Apr;17(4):194-9.	2000	France	English	pro-spective	young	infertility	sperm motility	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	3.6mmol	in-vitro	10	motility of frozen sperm, improvement; ICSI outcome, improvement	no alteration		no	pentoxifylline	no addition in vitro		2-	
103: Tournaye H, Janssens R, Camus M, Staessen C, Devroey P, Van Steirteghem A. Pentoxifylline is not useful in enhancing sperm function in cases with previous in vitro fertiliza-tion failure. Fertil Steril. 1993 Jan;59(1):210-5.	1993	Belgium	English	pro-spective	young	infertility	IVF outcome	peripheral vasodilators	C04	pentoxiphyllin	C04AD03	3.6mmol	in-vitro	n.g.	IVF outcome, improvement	no alteration		yes	pentoxifylline	no addition in vitro		1+	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
766: Cowart CL, London SN, Vernon MW, Pedigo NG. The effects of cyclic adenosine monophosphate, forskolin, and theophylline on motility parameters in gossypol-treated human sperm. Fertil Steril. 1994 May;61(5):929-34.	1994		English	pro-spective	sperm in vitro	healthy	gossypol induced motility inhibition	peripheral vasodilators	C04	forskolin, theophylline	not listed		in vitro		sperm motility, impaired, caused by inhibition of AMP formation			no				2-	
767: Magnus O, Abyholm T, Brekke I, Purvis K. Provocation testing of human sperm motility using energy substrates and activators of the cyclic nucleotide system: II. Studies on sperm from asthenozoospermic subjects. Int J Fertil. 1993 Mar-Apr;38(2):123-8.	1993		English	pro-spective	sperm in vitro	healthy	sperm motility	peripheral vasodilators	C04	deoxyadenosin	not listed		in vitro		sperm motility, impaired, caused by poor endogenous stimulation of adenylyl cyclase			no				2-	
886: Taylor RG, Crisp AJ, Hoffbrand BJ, Maguire A, Jacobs HS. Plasma sex hormone concentrations in men with hypertension treated with methyldopa and/or propranolol. Postgrad Med J. 1981 Jul;57(669):425-6.	1981	UK	English	retro-spective	middle-aged	hypertension	hormones	beta blocking agents	C07	propranolol	C07AA05		continuous	34	gonadotropin and testosterone levels	no difference between exposed and untreated men						2-	
885: White DR, Clarkson JS, Ratnasooriya WD, Aitken RJ. Complementary effects of propranolol and nonoxynol-9 upon human sperm motility. Contraception. 1995 Oct;52(4):241-7.	1995	UK	English	experimental	sperm in vitro	healthy	sperm motility	beta blocking agents	C07	propranolol	C07AA05		in vitro		sperm motility, impairment	complete immobilisation, not based on Ca2+ influx						1-	
867: Hershlag A, Cooper GW, Benoff S. Pregnancy following discontinuation of a calcium channel blocker in the male partner. Hum Reprod. 1995 Mar;10(3):599-606.	1995	UK	English	case report	30	infertility	conception	calcium channel blockers	C08	nifedipine	C08CA05		continuous	1	conception	3m after cessation of medication						3	
862: Kirkman-Brown JC, Barratt CL, Publicover SJ. Nifedipine reveals the existence of two discrete components of the progesterone-induced [Ca2+]i transient in human spermatozoa. Dev Biol. 2003 Jul 1;259(1):71-82.	2003	UK	English	experimental	sperm in vitro	healthy	Ca2+ influx	calcium channel blockers	C08	nifedipine	C08CA05		in vitro		acrosome reaction, inhibition	no influence of progesterone induced Ca2+ influx						2-	
865: Goodwin LO, Leeds NB, Hurley I, Mandel FS, Pergolizzi RG, Benoff S. Isolation and characterization of the primary structure of testis-specific L-type calcium channel: implications for contraception. Mol Hum Reprod. 1997 Mar;3(3):255-68.	1997	USA	English	experimental	sperm in vitro	healthy	progesterone-stimulated acrosome reaction	calcium channel blockers	C08	nifedipine	C08CA05		in vitro		calcium channel, voltage dependent, protein binding	inhibition of acrosome reaction by inhibition of Ca2+ influx						2-	unique target for the design of new male contraceptive agents
868: Kanwar U, Anand RJ, Sanyal SN. The effect of nifedipine, a calcium channel blocker, on human spermatozoal functions. Contraception. 1993 Nov;48(5):453-70.	1993	India	English	experimental	sperm in vitro	healthy	sperm motility	calcium channel blockers	C08	nifedipine	C08CA05		in vitro		sperm motility	dose-dependent influence						2-	
907: Anand RJ, Kanwar U, Sanyal SN. Calcium channel antagonist verapamil modulates human spermatozoal functions. Res Exp Med (Berl). 1994;194(3):165-78.	1994	India	English	experimental	sperm in vitro	healthy	motility, Ca2+ influx	calcium channel blockers	C08	verapamil	C08DA01	50mmol	in vitro		sperm motility, inhibition; Ca2+ influx, inhibition	significant						2-	
909: Roldan ER, Wramsby H, Yanagimachi R. Verapamil, a Ca2+ channel antagonist, accelerates the in vitro penetration of zona-free hamster eggs by human spermatozoa. Clin Reprod Fertil. 1987 Feb-Apr;5(1-2):1-4.	1987	USA	English	experimental	sperm in vitro	healthy	hamster oocyte penetration	calcium channel blockers	C08	verapamil	C08DA01	100mmol	in vitro		zona-free hamster oocyte test	increase by an acceleration of the acrosome reaction						2-	

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859: Kohn FM, Muller C, Drescher D, Neukamm C, el Mulla KF, Henkel R, Hagele W, Hinsch E, Habenicht UF, Schill WB. Effect of angiotensin converting enzyme (ACE) and angiotensins on human sperm functions. Andrologia. 1998 Aug-Sep;30(4-5):207-15.	1998	Germany	English	experimental	sperm in vitro	infertility	sperm functions	agents acting on the renin-angiotensin system	C09	captopril	C09AA01		in vitro		acrosome reaction, induction; oolemma binding, inhibition	not affected by incubation with captopril; significant inhibition						1-	
925: Foresta C, Mioni R, Rossato M, Varotto A, Zorzi M. Evidence for the involvement of sperm angiotensin converting enzyme in fertilization. Int J Androl. 1991 Oct;14(5):333-9.	1991	Italy	English	experimental	sperm in vitro	healthy	sperm paramters	agents acting on the renin-angiotensin system	C09	captopril	C09AA01	100nmol	in vitro		acrosome reaction, inhibition; HOS test, reduction	significant						2-	
834: Koshida H, Takeda R, Miyamori I. Lisinopril decreases plasma free testosterone in male hypertensive patients and increases sex hormone binding globulin in female hypertensive patients. Hypertens Res. 1998 Dec;21(4):279-82.	1998	Japan	English	pro-spective	young	hypertension	hormones	agents acting on the renin-angiotensin system	C09	lisinopril	C09AA03	5-20mg	6m	20	testosterone level, unaltered; free testosterone, increase	insignificant		no				3	
860: Vinson GP, Mehta J, Evans S, Matthews S, Puddefoot JR, Saridogan E, Holt WV, Djahanbakhch O. Angiotensin II stimulates sperm motility. Regul Pept. 1996 Dec 3;67(2):131-5.	1996	UK	English	experimental	sperm in vitro	infertility	sperm functions	agents acting on the renin-angiotensin system	C09	angiotensin II	not listed		in vitro		sperm motility, CASA parameters, alteration	several parameters						2-	
125: Dobs AS, Miller S, Neri G, Weiss S, Tate AC, Shapiro DR, Musliner TA. Effects of simvastatin and pravastatin on gonadal function in male hypercholesterolemic patients. Metabolism. 2000 Jan;49(1):115-21.	2000	USA	English	pro-spective, randomized	29-55	hypercholesterolemia	lipids in serum	lipid modifying agents	C10	simvastatin, pravastatin	C10AA01		n.g.	159	testosterone level, decline	no alteration	none	yes	simvastatin 20mg/die	simvastatin 40mg/die	pravastatin 40mg/die	1++	
840: Purvis K, Tollefsrud A, Rui H, Haug E, Norseth J, Viksmoen L, Ose L, Lund H. Short-term effects of treatment with simvastatin on testicular function in patients with heterozygous familial hypercholesterolaemia. Eur J Clin Pharmacol. 1992;42(1):61-4.	1992	Norway	English	pro-spective	young	familial hypercholesterolemia	hormones	lipid modifying agents	C10	simvastatin	C10AA01	40mg/d	14w	19	testosterone level, semen parameters, alteration	no change during treatment		no				3	
837: Azzarito C, Boiardi L, Vergoni W, Zini M, Portioli I. Testicular function in hypercholesterolemic male patients during prolonged simvastatin treatment. Horm Metab Res. 1996 Apr;28(4):193-8.	1996	Italy	English	pro-spective	middle-aged	hypercholesterolemia	hormones	lipid modifying agents	C10	simvastatin	C10AA01	20mg/d	continuous	8	testosterone level and response to hCG	no change during treatment						3	
842: Mastroberardino G, Costa C, Gavelli MS, Vitaliano E, Rossi F, Catalano A, Barletta R, Guarini G. Plasma cortisol and testosterone in hypercholesterolaemia treated with clofibrate and lovastatin. J Int Med Res. 1989 Jul-Aug;17(4):388-94.	1989	Italy	English	pro-spective	40-45	familial hypercholesterolemia	hormones	lipid modifying agents	C10	lovastatin	C10AA02	40mg/d	4w	32	testosterone level, alteration	no change during treatment with lovastatin, but decrease in clofibrate		yes	lovastatin	clofibrate		1+	
838: Segarra A, Chacon P, Vilardell M, Piera LL. Prospective case control study to determine the effect of lovastatin on serum testosterone and cortisol concentrations in hyperlipidemic nephrotic patients with chronic renal failure. Nephron. 1996;73(2):186-90.	1996	Spain	English	pro-spective	middle-aged	renal insufficiency	hormones	lipid modifying agents	C10	lovastatin	C10AA02		continuous	25	testosterone level and GnRH stimulation, alteration	no alteration						2-	

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883: Bohm M, Herrmann W, Wassmann S, Laufs U, Nickenig G. Does statin therapy influence steroid hormone synthesis? Z Kardiol. 2004 Jan;93(1):43-8.	2004	Germany	English	pro-spective, random-ized	young	hyperlip-idemia	hormones	lipid modifying agents	C10	pravastatin	C10AA03	40mg/d	continuous	15	steroid hormone levels, alteration	no alteration		yes				1+	
153: Bernini GP, Brogi G, Argenio GF, Moretti A, Salvetti A. Ef-fects of long-term pravastatin treatment on spermatogenesis and on adrenal and testicular steroidogenesis in male hy-percholesterolemic patients. J Endocrinol Invest. 1998 May;21(5):310-7.	1998	Italy	English	pro-spective	middle-aged	hypercho-lesterol-emia	semen, hormones	lipid modifying agents	C10	pravastatin	C10AA03	20mg/d	26w	8	spermatogenesis, alteration	8 of 8 unaltered	none	no				2-	
824: Torok L, Kadar L, Kasa M. Spermatological investigations in patients treated with etreti-nate and isotretinoin. Androlo-gia. 1987 Nov-Dec;19(6):629-33.	1987	Hungary	English	pro-spective	young	acne	sperm parameters	antipsoriatics	D05	etretinate, isotretinoin	D05BB01	etretinate: 50-75mg/d; isotretinoin 1mg/kg/d	16w	28	sperm parameters, alteration	unaltered during treatment						3	
2142: Coleman R, MacDonald D. Effects of isotretinoin on male reproductive system. Lancet. 1994 Jul 16;344(8916):198	1994	UK	English	retro-spective	young	acne	clinical reports	anti-acne preparations	D10	isotretinoin	D10AD04	various	6m	150	notifications of problems with male reproductive system	gynecomastia 48; discom-fort 38; impotence 32; reduced fertility 12; ejacu-latory failiure 2; others 20		no				3	
276: Hoting VE, Schutte B, Schir-ren C. [Isotretinoin treatment of acne conglobata. Andrologic follow-up] Fortschr Med. 1992 Aug 20;110(23):427-30.	1992	Germany	German	pro-spective	young	acne	semen	anti-acne preparations	D10	isotretinoin	D10AD04		12m	20	spermatogenesis, impairment	none		no				3	
448: Vogt HJ, Ewers R. 13-cis-Retinoic acid and spermatogen-esis. Spermatological and im-pulse cytophotometric studies. Hautarzt. 1985 May;36(5):281-6.	1985	Germany	German	pro-spective	young	acne	semen	anti-acne preparations	D10	isotretinoin	D10AD04	1mg/kg	12w	20	spermatogenesis, impairment	none		no				3	
311: Parsch EM, Ruzicka T, Przybilla B, Schill WB. Andrological investigations in men treated with acitretin (Ro 10-1670). Andrologia. 1990 Sep-Oct;22(5):479-82.	1990	Germany	English	pro-spective	young	infertility	semen	anti-acne preparations	D10	isotretinoin	D10AD04	n.g.	3m	10	spermatogenesis, impairment	none		no				3	
50: Hair WM, Wu FC, Lincoln GA. An investigation of the effectiveness of testosterone implants in combination with the prolactin inhibitor quina-golide in the suppression of spermatogenesis in men. Hum Reprod. 2003 Apr;18(4):749-55.	2003	UK	English	pro-spective, random-ized	young	contra-ception	semen, hormones	gynecologicals	G02	quinagolide	G02CB04	75mg/d	24w		azoospermia, induction	group 1: 11/13, group 2: 11/12, groups 3: 8/13		yes	T + placebo	T 1200mg/m + 75mg/d quinagolide	T 800mg/ m+75mg/d quinagolide	1-	
898: Uebelhart B, Herrmann F, Pavo I, Draper MW, Rizzoli R. Ra-loxifene treatment is associated with increased serum estradiol and decreased bone remodel-ing in healthy middle-aged men with low sex hormone levels. J Bone Miner Res. 2004 Sep;19(9):1518-24.	2004	Switzer-land	English	pro-spective, random-ized	49-70	healthy	hormones	gynecologicals	G02	raloxifen	G02CB04	120mg/d	6w	43	sex steroid hormone levels, increase	by 11-13%	decrease of os-teocalcin levels	yes	raloxifen	placebo		1-	
897: Duschek EJ, Gooren LJ, Netelenbos C. Comparison of effects of the rise in serum testosterone by raloxifene and oral testosterone on serum insulin-like growth factor-1 and insulin-like growth factor bind-ing protein-3. Maturitas. 2005 Jul 16;51(3):286-93.	2005	The Neth-erlands	English	pro-spective, random-ized	60-70	healthy	hormones	gynecologicals	G02	raloxifen	G02CB04	120mg/d	3m	30	testosterone level, increase	by 20%	decrease of IGF-1 levels	yes	raloxifen	placebo		1-	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
7: Meriggiola MC, Costantino A, Saad F, D'Emidio L, Morselli Labate AM, Bertaccini A, Bremner WJ, Rudolph I, Ernst M, Kirsch B, Martorana G, Pelusi G. Norethisterone enanthate plus testosterone undecanoate for male contraception: effects of various injection intervals on spermatogenesis, reproductive hormones, testis, and prostate. J Clin Endocrinol Metab. 2005 Apr;90(4):2005-14. Epub 2005 Jan 5.	2005	Italy	English	pro-spective, random-ized	young	contra-ception	semen	sex hormones and modulators of the genital system	G03	nor-ethisterone enanthate	G03AC01	200mg/w plus T 1000mg/12w	48w	40	azoospermia, induction	90% verum 37% placebo	n.g.	yes	NETE + T	NET + placebo		1-	
137: Anawalt BD, Bebb RA, Bremner WJ, Matsumoto AM. A lower dosage levonorgestrel and testosterone combination effectively suppresses spermatogenesis and circulating gonadotropin levels with fewer metabolic effects than higher dosage combinations. J Androl. 1999 May-Jun;20(3):407-14.	1999	USA	English	pro-spective, random-ized	young	contra-ception	semen	sex hormones and modulators of the genital system	G03	levonorgestrel	G03AC03			54	azoospermia, induction	severe oligoazoospermia in 89% of the LNG 125, 89% of the LNG 250,and 78% of the LNG 500 groups versus 56% of the men in no LNG.		no	T 100mg/w + 125mg/d levonorgestrel	T 100mg/w + 250mg/d levonorgestrel		2-	
18: Gui YL, He CH, Amory JK, Bremner WJ, Zheng EX, Yang J, Yang PJ, Gao ES. Male hormonal contraception: suppression of spermatogenesis by injectable testosterone undecanoate alone or with levonorgestrel implants in chinese men. J Androl. 2004 Sep-Oct;25(5):720-7.	2004	China	English	pro-spective, random-ized	young	contra-ception	semen, hormones	sex hormones and modulators of the genital system	G03	levonorg-estrel implants	G03AC03	300mg implant	24w	52	azoospermia, induction	62%	n.g.	yes	T 500mg/8w	T 500mg/8w + levonorgestrel	T 1000mg/8w	1-	
67: Gonzalo IT, Swerdloff RS, Nelson AL, Clevenger B, Garcia R, Berman N, Wang C. Levonorg-estrel implants (Norplant II) for male contraception clinical trials: combination with transdermal and injectable testosterone. J Clin Endocrinol Metab. 2002 Aug;87(8):3562-72.	2002	USA	English	pro-spective, random-ized	20-45	contra-ception	semen	sex hormones and modulators of the genital system	G03	levonorg-estrel implants	G03AC03	125mg/d	34w	39	azoospermia, induction	24, 35, 33, 93% dependent on dosis of levonorgestrel	none	yes	T patch	LNG 4 implants + T patch	LNG 125mg/d + T patch	1-	
205: Bebb RA, Anawalt BD, Christensen RB, Paulsen CA, Bremner WJ, Matsumoto AM. Combined administration of levonorgestrel and testosterone induces more rapid and effective suppression of spermatogenesis than testosterone alone: a promising male contraceptive approach. J Clin Endocrinol Metab. 1996 Feb;81(2):757-62.	1996	USA	English	pro-spective, random-ized	20-42	contra-ception	semen	sex hormones and modulators of the genital system	G03	levonorgestrel	G03AC03	500mg/d	6m	36	azoospermia, induction	33 and 67%	no serious	yes	T 100mg/w+ levonorgestrel	T 100mg/w alone		1-	
112: Kamischke A, Ploger D, Venherm S, von Eckardstein S, von Eckardstein A, Nieschlag E. Intramuscular testosterone undecanoate with or without oral levonorgestrel: a randomized placebo-controlled feasibility study for male contraception. Clin Endocrinol (Oxf). 2000 Jul;53(1):43-52.	2000	Germany	English	pro-spective, random-ized	young	contra-ception	semen	sex hormones and modulators of the genital system	G03	levonorgestrel	G03AC03		24w	28	azoospermia, induction	8 of 14; 7 of 14	decrease of high-density lipoprotein (HDL) levels	yes	T 1000mg/12w + 250mg/d levonorgestrel	T 1000mg/12 + placebo		1-	
15: Matthiesson KL, Amory JK, Berger R, Ugoni A, McLachlan RI, Bremner WJ. Novel male hormonal contraceptive combinations: the hormonal and spermatogenic effects of testosterone and levonorgestrel combined with a 5alpha-reductase inhibitor or gonadotropin-releasing hormone antagonist. J Clin Endocrinol Metab. 2005 Jan;90(1):91-7.	2005	Australia	English	pro-spective, random-ized	young	contra-ception	semen, hormones	sex hormones and modulators of the genital system	G03	levonorg-estrel + dutasteride	G03AC03	100mg/w T	8 wk	22	spermatogenesis, impairment	20/22, no improvement by dutasteride	n.g.	yes	T 100mg/w T+ 125mg/w levonorgestrel	100mg/w T + 125mg/w le- vonorgestrel + 0.5mg/d dutasteride		1-	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
26: Liu ST, Gui YL, Lin CH, He CH. Hormonal contraception in Chinese men: variations in suppression of spermatogenesis with injectable testosterone undecanoate and levonorgestrel implants. Asian J Androl. 2004 Mar;6(1):41-6.	2004	China	English	pro-spective	young	contra-ception	semen	sex hormones and modulators of the genital system	G03	levonorgestrel	G03AC03		18w	16	azoospermia, induction	6 of 16	not mentioned	no	low sperm count	normal sperm count		3	
579: Fogh M, Corker CS, McLean H, Hunter WM, Petersen IB, Philip J, Schou G, Skakkebaek NE. Clinical trial with levo-norgestrel and testosterone oenanthate for male fertility control. Acta Endocrinol (Copenh). 1980 Oct;95(2):251-7.	1980	Denmark	English	pro-spective	young	contra-ception	semen	sex hormones and modulators of the genital system	G03	levonorgestrel	G03AC03	250mg	6m	12	spermatogenesis, impairment	all	none	yes	T + 250mg/d levonorgestrel	T + 500mg/d levonorgestrel		1-	
16: Coviello AD, Bremner WJ, Matsumoto AM, Herbst KL, Amory JK, Anawalt BD, Yan X, Brown TR, Wright WW, Zirkin BR, Jarow JP. Intratesticular testosterone concentrations comparable with serum levels are not sufficient to maintain normal sperm production in men receiving a hormonal contraceptive regimen. J Androl. 2004 Nov-Dec;25(6):931-8.	2004	USA	English	pro-spective	n.g.	healthy	testosterone concentration intra-testicular fluid (ITT)	sex hormones and modulators of the genital system	G03	levonorgestrel	G03AC03		6m	7	intratesticular testosterone, decline	ITT (822 +/- 136 nmol/L) was approximately 40x higher than serum T at baseline. It was suppressed by 98% to 13.1 +/- 4.5 nmol/L.	n.g.	no	61mg/d LNG + 100mg/w T	31mg/d LNG + 100mg/w T		1-	
532: Brache V, Alvarez-Sanchez F, Leon P, Schmidt F, Faundes A. The effect of levonorgestrel and estrone rods on male reproductive function. Contraception. 1982 Jun;25(6):591-603.	1982		English	pro-spective	young	contra-ception	semen	sex hormones and modulators of the genital system	G03	levonorgestrel, oestrone	G03AC03	6 implants		7	sperm count, depression	in all men to 1*10(6)		no				3	
591: Foegh M, Damgaard-Pedersen F, Gormsen J, Knudsen JB, Schou G. Oral levo-norgestrel - testosterone effects on spermatogenesis, hormone levels, coagulation factors and lipoproteins in normal men. Contraception. 1980 Apr;21(4):381-91.	1980		English	pro-spective	young	contra-ception	hormones	sex hormones and modulators of the genital system	G03	levonorgestrel	G03AC03	250mg/d levonorgestrel + 400mg/w T	9m	4	spermatogenesis, impairment	most	hypercholesterinemia	no				3	
34: McLachlan RI, Robertson DM, Pruyers E, Ugoni A, Matsumoto AM, Anawalt BD, Bremner WJ, Meriggiola C. Relationship between serum gonadotropins and spermatogenic suppression in men undergoing steroidal contraceptive treatment. J Clin Endocrinol Metab. 2004 Jan;89(1):142-9.	2004	Australia	English	pro-spective	young	contra-ception	hormones	sex hormones and modulators of the genital system	G03	levonorgestrel, cyproterone, desogestrel	G03AC03	100/200mg/w	48w		spermatogenesis, impairment	via depression of gonadotropins		yes	T + levonorgestrel	T + cyproterone	T + desogestrel	1+	
23: Gu YQ, Tong JS, Ma DZ, Wang XH, Yuan D, Tang WH, Bremner WJ. Male hormonal contraception: effects of injections of testosterone undecanoate and depot medroxyprogesterone acetate at eight-week intervals in chinese men. J Clin Endocrinol Metab. 2004 May;89(5):2254-62.	2004	China	English	pro-spective, randomized	young	contra-ception	semen	sex hormones and modulators of the genital system	G03	medroxyprogesterone acetate	G03AC06	1000mg T/12w, 400mg DMPA/w	60 wk	30	spermatogenesis, impairment	100%	none	yes	T 1000mg/12w	T 1000mg/12 + 15mg/d DMPA	T 1000mg/12w + 30mg/d DMPA	1+	
188: Handelsman DJ, Conway AJ, Howe CJ, Turner L, Mackey MA. Establishing the minimum effective dose and additive effects of depot progestin in suppression of human spermatogenesis by a testosterone depot. J Clin Endocrinol Metab. 1996 Nov;81(11):4113-21.	1996	Australia	English	pro-spective, randomized	young	contra-ception	semen	sex hormones and modulators of the genital system	G03	medroxyprogesterone acetate	G03AC06			30	azoospermia, induction	4 of 10 with T alone, 8 of 10 with T+MPA	no	yes	T 2x200mg pellet	T 4x200mg pellet	T 4x200mg pellet + 300mg s.d. DMPA	1-	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
346: Fossa SD, Klepp O, Norman N. Lack of gonadal protection by medroxyprogesterone acetate-induced transient medical castration during chemotherapy for testicular cancer. Br J Urol. 1988 Nov;62(5):449-53.	1988	Norway	English	pro-spective	young	testicular cancer	hormones	sex hormones and modulators of the genital system	G03	medroxprogesterone acetate	G03AC06			24	spermatogenesis, impairment	no protection against cytotoxic therapy	"medical castration" (loss of libido and erections)	no				3	
592: Bain J, Rachlis V, Robert E, Khait Z. The combined use of oral medroxyprogesterone acetate and methyltestosterone in a male contraceptive trial programme. Contraception. 1980 Apr;21(4):365-79.	1980		English	pro-spective, randomized	young	contraception	semen	sex hormones and modulators of the genital system	G03	medroxprogesterone acetate	G03AC06		15m	23	spermatogenesis, impairment	most	acne, gynecomastia	no	different doses of MPA			2-	
332: Wu FC, Aitken RJ. Suppression of sperm function by depot medroxyprogesterone acetate and testosterone enanthate in steroid male contraception. Fertil Steril. 1989 Apr;51(4):691-8.	1989	UK	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	medroxprogesterone acetate	G03AC06		12m	10	spermatogenesis, impairment	hamster oocyte penetration, abolished		no				3	
616: Barfield A, Melo J, Coutinho E, Alvarez-Sanchez F, Faundes A, Brache V, Leon P, Frick J, Bartsch G, Weiske WH, Brenner P, Mishell D Jr, Bernstein G, Ortiz A. Pregnancies associated with sperm concentrations below 10 million/ml in clinical studies of a potential male contraceptive method, monthly depot medroxyprogesterone acetate and testosterone esters. Contraception. 1979 Aug;20(2):121-7.	1979		English	pro-spective, randomized	young	contraception	pregnancy rate	sex hormones and modulators of the genital system	G03	medroxprogesterone acetate	G03AC06	n.g.	12m	9	spermatogenesis, impairment	9 pregnancies in partners of men with sperm count <10mio, 5 of them in partners of men with <1mio/ml.		no	T implant + MPA	T i.m. + MPA		2-	
530: Frick J, Danner C, Kunit G, Joos H, Kohle R. Spermatogenesis in men treated with injections of medroxyprogesterone acetate combined with testosterone enanthate. Int J Androl. 1982 Jun;5(3):246-52.	1982		English	pro-spective, randomized	young	contraception	semen	sex hormones and modulators of the genital system	G03	medroxprogesterone acetate	G03AC06		8m	9	spermatogenesis, impairment	all		no	T 250/m + MPA 150mg/m	T 250mg/m + MPA 75mg/m		2-	
510: Soufir JC, Jouannet P, Marson J, Soumah A. Reversible inhibition of sperm production and gonadotrophin secretion in men following combined oral medroxyprogesterone acetate and percutaneous testosterone treatment. Acta Endocrinol (Copenh). 1983 Apr;102(4):625-32.	1983		English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	medroxprogesterone acetate	G03AC06	T 100mg/d percutaneous + medroxyprogesterone 20mg/d	12m	6	spermatogenesis, impairment	95% reduction in respect to pretreatment values	hyperglycemia	no				2	
66: Anderson RA, Kinniburgh D, Baird DT. Suppression of spermatogenesis by etonogestrel implants with depot testosterone: potential for long-acting male contraception. J Clin Endocrinol Metab. 2002 Aug;87(8):3640-9.	2002	UK	English	pro-spective, randomized	young	contraception	semen	sex hormones and modulators of the genital system	G03	etonogestrel implant	G03AC08		24w	28	azoospermia, induction	64% (group 1), 73% (group 2)	none	yes	T 400mg/w + 1x implant	T 400mg/w + 2x implant		1-	
57: Anderson RA, Zhu H, Cheng L, Baird DT. Investigation of a novel preparation of testosterone decanoate in men: pharmacokinetics and spermatogenic suppression with etonogestrel implants. Contraception. 2002 Nov;66(5):357-64.	2002	China	English	pro-spective, randomized	young	contraception	semen	sex hormones and modulators of the genital system	G03	etonogestrel implant	G03AC08		12m	20	azoospermia, induction	in 16 of 20 men	body weight increase	no	T implant + 1 implant etonogrestrel	T implant + 2 implants etonogrestrel		2-	
17: Brady BM, Walton M, Hollow N, Kicman AT, Baird DT, Anderson RA. Depot testosterone with etonogestrel implants result in induction of azoospermia in all men for long-term contraception. Hum Reprod. 2004 Nov;19(11):2658-67.	2004	UK	English	pro-spective	n.g.	contraception	semen, hormones	sex hormones and modulators of the genital system	G03	etonogestrel implant	G03AC08	T 400mg/12w + 3x68mg etonogestrel implants	48w	15	azoospermia, induction	15 of 15 men	no hypercholesterinemia	no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
72: Kinniburgh D, Zhu H, Cheng L, Kicman AT, Baird DT, Anderson RA. Oral desogestrel with testosterone pellets induces consistent suppression of spermatogenesis to azoospermia in both Caucasian and Chinese men. Hum Reprod. 2002 Jun;17(6):1490-501.	2002	UK	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	desogestrel	G03AC09		24w	66	azoospermia, induction	22 of 31 (group 1) and 28 of 28 (group 2)	body weight increase	yes	T 40mg/12w + 150mg/d desogestrel	T 400mg/12w+ 300mg desogesterel		1+	
59: Anderson RA, Van Der Spuy ZM, Dada OA, Tregoning SK, Zinn PM, Adeniji OA, Fakoya TA, Smith KB, Baird DT. Investigation of hormonal male contraception in African men: suppression of spermatogenesis by oral desogestrel with depot testosterone. Hum Reprod. 2002 Nov;17(11):2869-77.	2002	UK	English	pro-spective, randomized	young	contraception	semen	sex hormones and modulators of the genital system	G03	desogestrel	G03AC09		20w	52	azoospermia, induction	33 of 39 men	none	yes	T 400mg/12w + 150mg/d desogestrel	T 400mg/12w + 300mg/d desogestrel		1+	
108: Anawalt BD, Herbst KL, Matsumoto AM, Mulders TM, Coelingh-Bennink HJ, Bremner WJ. Desogestrel plus testosterone effectively suppresses spermatogenesis but also causes modest weight gain and high-density lipoprotein suppression. Fertil Steril. 2000 Oct;74(4):707-14.	2000	USA	English	pro-spective, randomized	20-49	contraception	semen	sex hormones and modulators of the genital system	G03	desogestrel	G03AC09			24	azoospermia, induction	7 of 8 men (group 2); 8 of 8 men (group 3)	body weight increase, decrease of high-density lipoprotein (HDL) levels	yes	T 50mg/w +desogestrel 150mg/d	T 100mg/w +desogestrel 150mg/d	T 100mg/w +desogestrel 300mg/d	1-	
141: Wu FC, Balasubramanian R, Mulders TM, Coelingh-Bennink HJ. Oral progestogen combined with testosterone as a potential male contraceptive: additive effects between desogestrel and testosterone enanthate in suppression of spermatogenesis, pituitary-testicular axis, and lipid metabolism. J Clin Endocrinol Metab. 1999 Jan;84(1):112-22.	1999	UK	English	pro-spective, randomized	young	contraception	semen	sex hormones and modulators of the genital system	G03	desogestrel	G03AC09			24	azoospermia, induction	78%		no	T 100mg/w + 300mg/d desogestrel	T 50mg/w + 300mg/d desogestrel	T 100mg/w + 150mg/d desogestrel	2-	
90: Hair WM, Kitteridge K, O'Connor DB, Wu FC. A novel male contraceptive pill-patch combination: oral desogestrel and transdermal testosterone in the suppression of spermatogenesis in normal men. J Clin Endocrinol Metab. 2001 Nov;86(11):5201-9. .	2001	UK	English	pro-spective, randomized	young	contraception	semen, hormones	sex hormones and modulators of the genital system	G03	desogestrel	G03AC09		32w	23	azoospermia, induction	57%in 300mg/d DSG	none	yes	T patch +75mg/d desogestrel	T patch +150mg/d desogestrel	T patch + 300mg/d desogestrel	1-	
102: Kinniburgh D, Anderson RA, Baird DT. Suppression of spermatogenesis with desogestrel and testosterone pellets is not enhanced by addition of finasteride. J Androl. 2001 Jan-Feb;22(1):88-95.	2001	UK	English	pro-spective, randomized	young	contraception	semen	sex hormones and modulators of the genital system	G03	desogestrel, finasteride	G03AC09		24w	16	azoospermia, induction	5 of 7 men (group 1); 6 of 8 men (group 2)		yes	T 400mg/12w + 150mg desogestrel + 5mg finasteride	T 400mg/12w + 150mg desogestrel		1-	
680: Jones TM, Fang VS, Landau RL, Rosenfield RL. The effects of fluoxymesterone administration on testicular function. J Clin Endocrinol Metab. 1977 Jan;44(1):121-9.	1977		English	pro-spective, randomized	young	contraception	semen	sex hormones and modulators of the genital system	G03	fluoxymesterone	G03BA01		12w	9	spermatogenesis, impairment	insignificantly lower sperm count		no	10mg/d	20mg/d	30mg/d	2-	
655: Charny CW, Gordon JA. Testosterone rebound therapy: a neglected modality. Fertil Steril. 1978 Jan;29(1):64-8.	1978		English	retrospective	young	infertility	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	3x50mg/	20w	225	pregnancy rate induced	60% of oligozoospermic patients improvement, 25% pregnancy rate	body weight gain in1 patient	no				3	4% continuous azoospermia
722: Lamensdorf H, Compere D, Begley G. Testosterone rebound therapy in the treatment of male infertility. Fertil Steril. 1975 May;26(5):469-72.	1975		English	pro-spective	young	infertility	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	100mg/w T	20w	131	pregnancy rate induced, increase in rebound phase	29% in partners of patients with oligozoospermia, 8% with azoospermia		no				3	

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589: Kloer H, Hoogen H, Nieschlag E. Trial of high-dose testosterone undecanoate in treatment of male infertility. Int J Androl. 1980 Apr;3(2):121-9.	1980	Germany	English	pro-spective	young	infertility	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	3x80mg/d	12w	5	spermatogenesis, impairment	in few men		no				3	
202: World Health Organization [No authors listed]. Contraceptive efficacy of testosterone-induced azoospermia and oligozoospermia in normal men. Fertil Steril. 1996 Apr;65(4):821-9.	1996	Switzerland	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	200mg/w		399	pregnancies induced	4 of 349 in oligozoospermic, none in azoospermic men		no				2-	
53: Gu YQ, Wang XH, Xu D, Peng L, Cheng LF, Huang MK, Huang ZJ, Zhang GY. A multicenter contraceptive efficacy study of injectable testosterone undecanoate in healthy Chinese men. J Clin Endocrinol Metab. 2003 Feb;88(2):562-8.	2003	China	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	500mg/m	12 m	308	azoospermia, induction	95%	no significant changes in serum chemistry	no				3	
184: Anderson RA, Wallace EM, Groome NP, Bellis AJ, Wu FC. Physiological relationships between inhibin B, follicle stimulating hormone secretion and spermatogenesis in normal men and response to gonadotrophin suppression by exogenous testosterone. Hum Reprod. 1997 Apr;12(4):746-51.	1997	UK	English	pro-spective	young	healthy	inhibin B	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	200mg/w	65w	56	inhibin B recovery after suppression	parallel to sperm count		no				3	
321: Matsumoto AM. Effects of chronic testosterone administration in normal men: safety and efficacy of high dosage testosterone and parallel dose-dependent suppression of luteinizing hormone, follicle-stimulating hormone, and sperm production. J Clin Endocrinol Metab. 1990 Jan;70(1):282-7.	1990	USA	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03		6m	51	spermatogenesis, impairment	not 100% azoospermia	acne	yes	300mg/w	100mg/w	placebo	1-	
273: Handelsman DJ, Conway AJ, Boylan LM. Suppression of human spermatogenesis by testosterone implants. J Clin Endocrinol Metab. 1992 Nov;75(5):1326-32.	1992	Australia	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03		6m	47	spermatogenesis, impairment	38% sperm decrease in T implants, 77% in T enanthate		no	T implant 1200mg	T enanthate 200mg/w		2-	
178: Anderson RA, Kelly RW, Wu FC. Comparison between testosterone enanthate-induced azoospermia and oligozoospermia in a male contraceptive study. V. Localization of higher 5 alpha-reductase activity to the reproductive tract in oligozoospermic men administered supraphysiological doses of testosterone. J Androl. 1997 Jul-Aug;18(4):366-71.	1997	UK	English	pro-spective	young	androgen receptor, type	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	200mg/w	16w	33	azoospermia, induction	18 of 33 men; activity of type 2 5a reductase in OAT increased	sebum decrease	no				2-	
235: Bagatell CJ, Heiman JR, Matsumoto AM, Rivier JE, Bremner WJ. Metabolic and behavioral effects of high-dose, exogenous testosterone in healthy men. J Clin Endocrinol Metab. 1994 Aug;79(2):561-7.	1994	USA	English	pro-spective	young	healthy	contraception	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	200mg/w	20w	19	spermatogenesis, impairment	most	body weight increase, decrease of HDL levels, increase of parathormone levels	no				3	
190: Aribarg A, Sukcharoen N, Chanprasit Y, Ngeamvijawat J, Kriangsinyos R. Suppression of spermatogenesis by testosterone enanthate in Thai men. J Med Assoc Thai. 1996 Oct;79(10):624-9.	1996	Thailand	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	200mg/w		17	spermatogenesis, recovery	to sperm count >20 x 10(6)/ml at a median time of 3.9 months, recovery to their own baseline in 13/17 (76.5%) at a median time of 4.9 months.		no				3	

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179: Wang C, Leung A, Superlano L, Steiner B, Swerdloff RS. Oligozoospermia induced by exogenous testosterone is associated with normal functioning residual spermatozoa. Fertil Steril. 1997 Jul;68(1):149-53.	1997	USA	English	pro-spective	young	contraception	sperm function test	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	200mg/w	15m	12	spermatogenesis, impairment	in 12 men sperm function unchanged		no				3	
213: Behre HM, Baus S, Kliesch S, Keck C, Simoni M, Nieschlag E. Potential of testosterone buciclate for male contraception: endocrine differences between responders and nonresponders. J Clin Endocrinol Metab. 1995 Aug;80(8):2394-403.	1995	Germany	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03		32w	12	azoospermia, induction	in 3 of 8 men with 1200mg T, in 0 of 4 men with 600mg T		no	1200mg/12w	600mg/12w		2-	
159: Zhengwei Y, Wreford NG, Royce P, de Kretser DM, McLachlan RI. Stereological evaluation of human spermatogenesis after suppression by testosterone treatment: heterogeneous pattern of spermatogenic impairment. J Clin Endocrinol Metab. 1998 Apr;83(4):1284-91.	1998	Australia	English	pro-spective, randomized	31-46	contraception	histology	sex hormones and modulators of the genital system	G03	testosterone	G03BA03			10	spermatogenesis, impairment	5 of 5	n.g.	yes	200mg/w	placebo		1-	
637: Nieschlag E, Hoogen H, Bolk M, Schuster H, Wickings EJ. Clinical trial with testosterone undecanoate for male fertility control. Contraception. 1978 Dec;18(6):607-14.	1978		English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	3x80mg/d	12w	8	azoospermia, induction	1 of 8 men		no				3	
649: Mauss J, Borsch G, Richter E, Bormacher K. Demonstration of the reversibility of spermatozoa suppression by testosterone oenanthate. Andrologia. 1978 Mar-Apr;10(2):149-53.	1978		English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03		long-term	7	spermatogenesis, impairment	all men, recovery after withdrawal		no				3	
733: Mauss J, Borsch G, Bormacher K, Richter E, Leyendecker G, Nocke W. Effect of long-term testosterone oenanthate administration on male reproductive function: clinical evaluation, serum FSH, LH, testosterone, and seminal fluid analyses in normal men. Acta Endocrinol (Copenh). 1975 Feb;78(2):373-84.	1975		English	pro-spective	20-27	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	250mg/w	21	7	spermatogenesis, impairment	to mean 3 mio/ml	weight gain, reversible	no				3	
445: Matsumoto AM, Bremner WJ. Stimulation of sperm production by human chorionic gonadotropin after prolonged gonadotropin suppression in normal men. J Androl. 1985 May-Jun;6(3):137-43.	1985	USA	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	200mg/w	4m	4	spermatogenesis, impairment	all, severe		no				3	
829: Hero M, Wickman S, Hanhijarvi R, Siimes MA, Dunkel L. Pubertal upregulation of erythropoiesis in boys is determined primarily by androgen. J Pediatr. 2005 Feb;146(2):245-52.	2005	Finland	English	pro-spective	pubertal	delayed puberty	erythropoiesis	sex hormones and modulators of the genital system	G03	testosterone + letrozole	G03BA03		12m	23	erythropoiesis, increase	better increase in T+L than in T+placebo		yes	T + letrozole	T + placebo		1-	
830: Dunkel L, Wickman S. Novel treatment of short stature with aromatase inhibitors. J Steroid Biochem Mol Biol. 2003 Sep;86(3-5):345-56.	2003	Finland	English	pro-spective	pubertal	delayed puberty	pubertal growth	sex hormones and modulators of the genital system	G03	testosterone + letrozole	G03BA03		12m	23	growth acceleration increase	in the T+L group, not in T+placebo group		yes	T + letrozole	T + placebo		1-	
35: Drincic A, Arseven OK, Sosa E, Mercado M, Kopp P, Molitch ME. Men with acquired hypogonadotropic hypogonadism treated with testosterone may be fertile. Pituitary. 2003;6(1):5-10.	2003	USA	English	pro-spective	young	hypogonadism, secondary	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03	200mg/w		16	spermatogenesis, recovery	in 12 men sperm function unchanged		no				3	Men with acquired HH treated with testosterone are not necessarily sterile in contrast to patients with IHH

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
572: Burger HG, de Kretser DM, Hudson B, Wilson JD. Effects of preceding androgen therapy on testicular response to human pituitary gonadotropin in hypogonadotropic hypogonadism: a study of three patients. Fertil Steril. 1981 Jan;35(1):64-8.	1981		English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	testosterone	G03BA03			3	spermatogenesis, recovery	no inhibition, if T is given prior to gonadotropins		no				3	
54: Caroppo E, Niederberger C, Iacovazzi PA, Correale M, Palagiano A, D'Amato G. Human chorionic gonadotropin free beta-subunit in the human seminal plasma: a new marker for spermatogenesis? Eur J Obstet Gynecol Reprod Biol. 2003 Feb 10;106(2):165-9.	2003	Italy	English	retrospective	young, inf	infertility	semen	sex hormones and modulators of the genital system	G03	mesterolone + tamoxifen	G03BB01	mesterolone 100mg/d + 20mg/d tamoxifen	6 m	79	sperm morphology, improvement	significant		no				3	
124: Handelsman DJ, Wishart S, Conway AJ. Oestradiol enhances testosterone-induced suppression of human spermatogenesis. Hum Reprod. 2000 Mar;15(3):672-9.	2000	Australia	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	estrogens	G03CA03			26	azoospermia, induction	in 6 of 26 men	gynecomastia, loss of libido	yes	implant of T 600mg +10mg estradiol	implant of 600mg T +20mg estradiol	implant of T 600mg alone	1-	
252: Chiu AW, Chen MT, Chiang H, Wu LH, Fang RH, Chang LS. Deoxyribonucleic acid histogram of testes in primary transsexualism. Br J Urol. 1993 Oct;72(4):495-7.	1993	China	English	pro-spective	24-32	transsexualism	DNA flow-cytometry of spermatozoa	sex hormones and modulators of the genital system	G03	estrogens	G03CA03			8	spermatogenesis, impairment	maturation arrest		no				3	
97: O'Donnell L, Robertson KM, Jones ME, Simpson ER. Estrogen and spermatogenesis. Endocr Rev. 2001 Jun;22(3):289-318.	2001	Australia	English	review animal		normal spermatogenesis	estrogen effects	sex hormones and modulators of the genital system	G03	estrogens	G03CA03				spermatogenesis, impairment	estrogen effects						4	
99: Sharpe RM. Hormones and testis development and the possible adverse effects of environmental chemicals. Toxicol Lett. 2001 Mar 31;120(1-3):221-32.	2001	UK	English	review	embryo	healthy, testicular physiology	estrogen effects	sex hormones and modulators of the genital system	G03	estrogens	G03CA03				antiandrogen effects	dose dependent						4	Disorders of male reproductive health in phenotypically normal males, such as cancer, oligozoospermia and failure of descent have a common origin.
284: Behre HM, Nashan D, Hubert W, Nieschlag E. Depot gonadotropin-releasing hormone agonist blunts the androgen-induced suppression of spermatogenesis in a clinical trial of male contraception. J Clin Endocrinol Metab. 1992 Jan;74(1):84-90.	1992	Germany	English	pro-spective, randomized	young	contraception	semen	sex hormones and modulators of the genital system	G03	19-nortestosterone hexyloxyphenylpropionate (19NT-HPP) + buserelin	G03FA05		30w	24	azoospermia, induction	4 of 8 men with nortestosterone alone, 4 of 16 men with buserelin added	hematokrit, increase	yes	nortestosterone 200mg/3w + GnRH implant 3.3mg	nortestosterone 200mg/3w + GnRH implant 6.6mg	nortestosterone 200mg/3w alone	1-	
473: Schurmeyer T, Knuth UA, Belkien L, Nieschlag E. Reversible azoospermia induced by the anabolic steroid 19-nortestosterone. Lancet. 1984 Feb 25;1(8374):417-20.	1984	Germany	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	19-nortestosterone	G03FA05	200mg/w	13w	5	azoospermia, induction	achieved at 7-13w of treatment		no				2-	
88: Behre HM, Kliesch S, Lemcke B, von Eckardstein S, Nieschlag E. Suppression of spermatogenesis to azoospermia by combined administration of GnRH antagonist and 19-nortestosterone cannot be maintained by this non-aromatizable androgen alone. Hum Reprod. 2001 Dec;16(12):2570-7.	2001	Germany	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	19-nortestosterone + cetorelix	G03FA05	200mg/w	26w	6	azoospermia, induction	1 of 6	n.g.	no	nortestosterone 200mg/3w + 100mg cetorelix	nortestosterone alone		2-	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
182: Burgues S, Calderon MD. Subcutaneous self-administration of highly purified follicle stimulating hormone and human chorionic gonadotrophin for the treatment of male hypogonadotropic hypogonadism. Spanish Collaborative Group on Male Hypogonadotropic Hypogonadism. Hum Reprod. 1997 May;12(5):980-6.	1997	Spain	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	hCG, FSH	G03GA01	FSH 450 IU/w + 5000IU/w hCG	6m	60	spermatogenesis, maturation	48 of 60 patients positive for spermatozoa in semen	gynecomastia	no				2-	
2: Miyagawa Y, Tsujimura A, Matsumiya K, Takao T, Tohda A, Koga M, Takeyama M, Outcome of gonadotropin therapy for male hypogonadotropic hypogonadism at university affiliated male infertility centers: a 30-year retrospective study. J Urol. 2005 Jun;173(6):2072-5.	2005	Japan	English	retrospective	11-42	idiopathic hypogonadotropic hypogonadism (IHH)	clinically, semen	sex hormones and modulators of the genital system	G03	hCG	G03GA01	n.g.	n.g.	36	spermatogenesis, maturation	36% (group1), 71% (group 2)	n.g.	no	small testis volume	normal testis volume		2-	
429: Finkel DM, Phillips JL, Snyder PJ. Stimulation of spermatogenesis by gonadotropins in men with hypogonadotropic hypogonadism. N Engl J Med. 1985 Sep 12;313(11):651-5.	1985	USA	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01			35	spermatogenesis, maturation	1 of 16 patients with hCG alone, 5 of 7 with hCG+hMG		n.g.	hCG alone	hCG+hMG		2-	
42: Bouloux PM, Nieschlag E, Burger HG, Skakkebaek NE, Wu FC, Handelsman DJ, Baker GH, Ochsenukuehn R, Syska A, McLachlan RI, Giwercman A, Conway AJ, Turner L, van Kuijk JH, Voortman G. Induction of spermatogenesis by recombinant follicle-stimulating hormone (puregon) in hypogonadotropic azoospermic men who failed to respond to human chorionic gonadotropin alone. J Androl. 2003 Jul-Aug;24(4):604-11.	2003	France	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen, hormones	sex hormones and modulators of the genital system	G03	hCG, rFSH	G03GA01		48w	30	spermatogenesis, maturation			yes	hCG 3000IU/w + FSH 2x225IU/w	hCG 3000IU/w + FSH 3x150IU/w		1-	
491: Okuyama A, Namiki M, Aono T, Matsumoto K, Utsunomiya M, Itoh H, Yoshioka T, Itatani H, Sonoda T. Improvement of spermatogenesis by hCG and hMG treatment in pubertal boys with history of orchiopexy at early childhood. Arch Androl. 1984;12 Suppl:29-33.	1984	Japan	English	pro-spective	young	orchidopexy	semen	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01		long-term	23	spermatogenesis, maturation	5 of 12 versus 9 of 11		no				3	
349: Burris AS, Rodbard HW, Winters SJ, Sherins RJ. Gonadotropin therapy in men with isolated hypogonadotropic hypogonadism: the response to human chorionic gonadotropin is predicted by initial testicular size. J Clin Endocrinol Metab. 1988 Jun;66(6):1144-51.	1988	USA	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen, testicular volume	sex hormones and modulators of the genital system	G03	hCG	G03GA01			22	spermatogenesis, maturation	6 of 11 with complete, 9 of 11with partial gonadotropin deficiency		no				3	
282: Okada Y, Kondo T, Okamoto S, Ogawa M. Induction of ovulation and spermatogenesis by hMG/hCG in hypogonadotropic GH-deficient patients. Endocrinol Jpn. 1992 Feb;39(1):31-43.	1992	Japan	English	pro-spective	23.8 mean	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01		5y	20	spermatogenesis, maturation	19 of 20 patients at 2.19y mean		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
277: Vicari E, Mongioi A, Calogero AE, Moncada ML, Sidoti G, Polosa P, D'Agata R. Therapy with human chorionic gonadotrophin alone induces spermatogenesis in men with isolated hypogonadotrophic hypogonadism--long-term follow-up. Int J Androl. 1992 Aug;15(4):320-9.	1992	Italy	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	T, semen, testicular volume	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01		14-120m	17	spermatogenesis, maturation	13 of 17 patients	n.g.	no				3	
232: Kung AW, Zhong YY, Lam KS, Wang C. Induction of spermatogenesis with gonadotrophins in Chinese men with hypogonadotrophic hypogonadism. Int J Androl. 1994 Oct;17(5):241-7.	1994	China	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01		52m	17	spermatogenesis, maturation	12 pregnancies		no	hCG 4000IU/w + FSH 225IU/w			3	
345: Liu L, Banks SM, Barnes KM, Sherins RJ. Two-year comparison of testicular responses to pulsatile gonadotropin-releasing hormone and exogenous gonadotropins from the inception of therapy in men with isolated hypogonadotropic hypogonadism. J Clin Endocrinol Metab. 1988 Dec;67(6):1140-5.	1988	USA	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	hormones	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01			16	spermatogenesis, maturation	none in both groups after 12 m, 2 in GNRH and 8 in gonadotropin group after 24m		yes	GnRH pulsatile	gonadotropins		1-	
140: Barrio R, de Luis D, Alonso M, Lamas A, Moreno JC. Induction of puberty with human chorionic gonadotropin and follicle-stimulating hormone in adolescent males with hypogonadotropic hypogonadism. Fertil Steril. 1999 Feb;71(2):244-8.	1999	Spain	English	pro-spective	14-17	idiopathic hypogonadotropic hypogonadism (IHH)	hormones, semen	sex hormones and modulators of the genital system	G03	hCG, FSH	G03GA01		n.g.	14	pubertal development	good effect		no				3	
56: Depenbusch M, von Eckardstein S, Simoni M, Nieschlag E. Maintenance of spermatogenesis in hypogonadotropic hypogonadal men with human chorionic gonadotropin alone. Eur J Endocrinol. 2002 Nov;147(5):617-24.	2002	Germany	English	case report	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen, hormones	sex hormones and modulators of the genital system	G03	hCG	G03GA01		12m	13	spermatogenesis, maturation	12 of 13 patients		no				3	
247: Schaison G, Young J, Pholsena M, Nahoul K, Couzinet B. Failure of combined follicle-stimulating hormone-testosterone administration to initiate and/or maintain spermatogenesis in men with hypogonadotropic hypogonadism. J Clin Endocrinol Metab. 1993 Dec;77(6):1545-9.	1993	France	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen, hormones	sex hormones and modulators of the genital system	G03	hCG, FSH	G03GA01		24m	10	spermatogenesis, maturation	in all men after 24m		no	hCG 4500IU/w + hMG 450IU/w	hMG450IU/w + T 250mg/w		2-	
234: Radicioni A, Paris E, Dondero F, Bonifacio V, Isidori A. Recombinant-growth hormone (rec-hGH) therapy in infertile men with idiopathic oligozoospermia. Acta Eur Fertil. 1994 Sep-Oct;25(5):311-7.	1994	Italy	English	pro-spective	young	spermatogenic dysfunction	semen	sex hormones and modulators of the genital system	G03	hCG	G03GA01		short-term	10	spermatogenesis, improvement	in 5 of 10 patients		no				3	
344: De Sanctis V, Vullo C, Katz M, Wonke B, Nannetti C, Bagni B. Induction of spermatogenesis in thalassaemia. Fertil Steril. 1988 Dec;50(6):969-75.	1988	Italy	English	pro-spective	15-23	thalassaemia	semen	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01			10	spermatogenesis, maturation	in 7 of 10 patients occurrence of sperm with hCG alone		no				3	
279: Shoham Z, Conway GS, Ostergaard H, Lahlou N, Bouchard P, Jacobs HS. Cotreatment with growth hormone for induction of spermatogenesis in patients with hypogonadotropic hypogonadism. Fertil Steril. 1992 May;57(5):1044-51.	1992	UK	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	hCG, somatotropin	G03GA01		24w	7	spermatogenesis, maturation	in 2 of 4 patients increase of sperm count, 1 pregnancy		no	somatotropin after unsuccessful stimulation			3	

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467: Levalle O, Bokser L, Pacenza N, Aszenmil G, Fiszlejder L, Chervin A, Guitelman A. Restoration and maintenance of spermatogenesis by HCG therapy in patients with hypothalamo-hypophyseal damage. Andrologia. 1984 Jul-Aug;16(4):303-9.	1984		English	pro-spective	young	hypogonadism, secondary	hormones	sex hormones and modulators of the genital system	G03	hCG	G03GA01	5000IU/w		3	spermatogenesis, recovery	only with hCG + T		no				3	
485: D'Agata R, Heindel JJ, Vicari E, Aliffi A, Gulizia S, Polosa P. hCG-induced maturation of the seminiferous epithelium in hypogonadotropic men. Horm Res. 1984;19(1):23-32.	1984	Italy	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	hCG	G03GA01		long-term	3	spermatogenesis, maturation	in 2 of 3		no				3	
320: Hammar M, Berg AA. Long term androgen replacement therapy does not preclude gonadotrophin-induced improvement on spermatogenesis. Scand J Urol Nephrol. 1990;24(1):17-9.	1990	Sweden	English	pro-spective	young	hypogonadism, secondary	semen	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01			1	spermatogenesis, recovery	also after testosterone pretreatment		no				3	
564: Luboshitzky R, Dickstein G, Barzilai D. Induction of spermatogenesis in isolated hypogonadotropic hypogonadism with exogenous human chorionic gonadotropin. J Endocrinol Invest. 1981 Apr-Jun;4(2):217-9.	1981		English	case report	21	idiopathic hypogonadotropic hypogonadism (IHH)	hormones	sex hormones and modulators of the genital system	G03	hCG	G03GA01		20m	1	spermatogenesis, maturation	complete						3	
181: Yong EL, Lee KO, Ng SC, Ratnam SS. Induction of spermatogenesis in isolated hypogonadotrophic hypogonadism with gonadotrophins and early intervention with intracytoplasmic sperm injection. Hum Reprod. 1997 Jun;12(6):1230-2.	1997	Singapur	English	case report	37	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	hCG, FSH	G03GA01	3x 150IU/w FSH, 5000IU/w hCG	19m	1	spermatogenesis, maturation	28.3x10(6)/ml spermatozoa after 16 months, natural conception		no				3	
636: Johnsen SG. Maintenance of spermatogenesis induced by HMG treatment by means of continuous HCG treatment in hypogonadotrophic men. Acta Endocrinol (Copenh). 1978 Dec;89(4):763-9.	1978		English	case report	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01			1	spermatogenesis, maturation	after induction with hCG/hMG maintenance with hCG alone						3	
638: Spitz IM, Schumert Z, Steiner J, Rosen E, Segal S, Slonim A, Rabinowitz D. Induction of spermatogenesis in hypogonadotrophic hypogonadism. Postgrad Med J. 1978 Oct;54(636):694-7.	1978		English	case report	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	hCG, hMG	G03GA01		n.g.	1	spermatogenesis, maturation	pregnancy induced						3	
342: Hammar M, Berg AA, Kjessler B. hCG-treatment alone is insufficient for restitution of spermatogenesis in a state with arrest at the spermatogonial level. Scand J Urol Nephrol. 1989;23(4):247-9.	1989	Sweden	English	case report	young	spermatogenic dysfunction	semen	sex hormones and modulators of the genital system	G03	hCG	G03GA01			1	spermatogenesis, maturation	only with combination of hMG		no	hCG alone	hCG+hMG		3	
117: Zarrilli S, Paesano L, Colao A, Mirone V, Lombardi G, De Rosa M. FSH treatment improves sperm function in patients after varicocelectomy. J Endocrinol Invest. 2000 Feb;23(2):68-73.	2000	Italy	English	pro-spective	18-45	varicocele	semen	sex hormones and modulators of the genital system	G03	FSH	G03GA04			183	spermatogenesis, improvement	clear-cut improvement		n.g.	high ligation + FSH 75IU/2d	high ligation alone		2-	
118: Foresta C, Bettella A, Merico M, Garolla A, Plebani M, Ferlin A, Rossato M. FSH in the treatment of oligozoospermia. Mol Cell Endocrinol. 2000 Mar 30;161(1-2):89-97.	2000	Italy	English	pro-spective	young	sperm parameters, impaired	semen	sex hormones and modulators of the genital system	G03	FSH	G03GA04			135	spermatogenesis, improvement	significant increase only in oligozoospermic subjects with normal basal FSH and inhibin B plasma levels		no	group A: normal FSH and inhibin B	group B: high FSH and normal inhibin B	group C: high FSH and low inhibin B	2-	

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998: Aydos K, Unlu C, Demirel LC, Evrigen O, Tolunay O. The effect of pure FSH administration in non-obstructive azoospermic men on testicular sperm retrieval. Eur J Obstet Gynecol Reprod Biol. 2003 May 1;108(1):54-8.	2003	Turkey	English	pro-spective	young	infertility	semen	sex hormones and modulators of the genital system	G03	FSH	G03GA04	3x75IU/w	3m	108	sperm retrieval by TESE	in 40/63 patients treated with rFSH and 15/45 patients not treated		no	FSH	no FSH		2-	
160: Foresta C, Bettella A, Ferlin A, Garolla A, Rossato M. Evidence for a stimulatory role of follicle-stimulating hormone on the spermatogonial population in adult males. Fertil Steril. 1998 Apr;69(4):636-42.	1998	Italy	English	pro-spective	young	infertility	semen	sex hormones and modulators of the genital system	G03	FSH	G03GA04	3x75IU/w	3m	90	spermatogenesis, maturation	in 20 of 60 patients		yes	FSH	placebo		1-	
30. Baccetti B, Piomboni P, Bruni E, Capitani S, Gambera L, Moretti E, Sterzik K, Strehler E. Effect of follicle-stimulating hormone on sperm quality and pregnancy rate. Asian J Androl. 2004 Jun;6(2):133-7. Italy	2004	Italy	English	pro-spective	28-45	infertility	semen	sex hormones and modulators of the genital system	G03	FSH	G03GA04	3x150IU/w	12w	44	pregnancy rate induced, increase	33 % in the treated group and 20 % in the control		yes	FSH	placebo		1-	
8. Paradisi R, Busacchi P, Seracchioli R, Porcu E, Venturoli S. Effects of high doses of recombinant human follicle-stimulating hormone in the treatment of male factor infertility: results of a pilot study. Fertil Steril. 2006 Sep;86(3):728-31.	2006	Italy	English	pro-spective, randomized	young	infertility	semen	sex hormones and modulators of the genital system	G03	FSH	G03GA04	300IU/2d	4m	30	sperm count, increase	significant		yes	FSH	placebo		1+	
150: Buchter D, Behre HM, Kliesch S, Nieschlag E. Pulsatile GnRH or human chorionic gonadotropin/human menopausal gonadotropin as effective treatment for men with hypogonadotropic hypogonadism: a review of 42 cases. Eur J Endocrinol. 1998 Sep;139(3):298-303.	1998	Germany	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	hormones, semen	sex hormones and modulators of the genital system	G03	FSH	G03GA04		12m	42	spermatogenesis, maturation	pregnancy in the partners of 36 of 42 patients		no	hCG+hMG	GnRH pulsatile		2-	
232: Kung AW, Zhong YY, Lam KS, Wang C. Induction of spermatogenesis with gonadotrophins in Chinese men with hypogonadotrophic hypogonadism. Int J Androl. 1994 Oct;17(5):241-7.	1994	Hong-kong	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	gonadotropins	G03GA04		52m	17	spermatogenesis, maturation	12 pregnancies		no	hCG 4000IU/w + FSH 225IU/w			3	
261: Jones TH, Darne JF. Self-administered subcutaneous human menopausal gonadotrophin for the stimulation of testicular growth and the initiation of spermatogenesis in hypogonadotrophic hypogonadism. Clin Endocrinol (Oxf). 1993 Feb;38(2):203-8.	1993	UK	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	FSH	G03GA04	525IU/w	12m	9	spermatogenesis, maturation	pregnancy in the partners of 3 of 9 patients	n.g.	no				3	
135: Giagulli VA. Absence of effect of recombinant growth hormone to classic gonadotropin treatment on spermatogenesis of patients with severe hypogonadotropic hypogonadism. Arch Androl. 1999 Jul-Aug;43(1):47-53.	1999	Italy	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	hormones	sex hormones and modulators of the genital system	G03	FSH	G03GA04		12m	4	spermatogenesis, maturation	All patients remained azoospermic after 6m gonadotropin treatment alone as well as after 6m subsequent addition of somatotropin.		no				3	
302: Jacobs HS, Bouchard P, Conway GS, Homburg R, Lahlou N, Mason B, Ostergaard H, Owen EJ, Shoham Z. Role of growth hormone in infertility. Horm Res. 1991;36 Suppl 1:61-5.	1991	France	English	review	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	sex hormones and modulators of the genital system	G03	gonadotropins	G03GA04			4	spermatogenesis, maturation	2x production of sperm, 1 pregnancy		no				4	addition of GH is suitable in induction of puberty, not in improving spermatogenesis in the adult

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204: Zalel Y, Draysen E, Goldschmit R, Zadik Z, Shoham Z. A prospective pilot study of co-treatment with growth hormone and gonadotropins for improving spermatogenesis in normogonadotropic patients with severe oligoteratoasthenospermia. Gynecol Endocrinol. 1996 Feb;10(1):23-8.	1996	Israel	English	pro-spective	young	spermatogenic dysfunction	semen	sex hormones and modulators of the genital system	G03	gonadotropins	G03GA04		24w	4	spermatogenesis, improvement	in 0 of 4		no				3	
217: Turek PJ, Williams RH, Gilbaugh JH 3rd, Lipshultz LI. The reversibility of anabolic steroid-induced azoospermia. J Urol. 1995 May;153(5):1628-30.	1995	USA	English	case report	young	anabolic steroid abuse	semen	sex hormones and modulators of the genital system	G03	gonadotropins	G03GA04		5y	1	azoospermia induced by anabolic steroids, reversal	conception after three months		no				3	
20: Selman HA, Cipollone G, Stuppia L, De Santo M, Sterzik K, El-Danasouri I. Gonadotropin treatment of an azoospermic patient with a Y-chromosome microdeletion. Fertil Steril. 2004 Jul;82(1):218-9.	2004	Italy	English	case report	32	Y-Deletion with azoospermia	semen	sex hormones and modulators of the genital system	G03	FSH	G03GA04			1	spermatogenesis, improvement	small number of spermatozoa						3	
77: Meriggiola MC, Bremner WJ, Costantino A, Bertaccini A, Morselli-Labate AM, Huebler D, Kaufmann G, Oettel M, Flamigni C. Twenty-one day administration of dienogest reversibly suppresses gonadotropins and testosterone in normal men. J Clin Endocrinol Metab. 2002 May;87(5):2107-13.	2002	Italy	English	pro-spective	young	contraception	hormones, semen	sex hormones and modulators of the genital system	G03	cyproterone acetate	G03HA01		21d	25	gonadotropin levels, decline	profound suppression	none	yes	10mg/d CPA + 10mg/d dienogest	10mg/d CPA + 5mg/d dienogest	10mg/d CPA + placebo	1-	
36: Meriggiola MC, Costantino A, Cerpolini S, Bremner WJ, Huebler D, Morselli-Labate AM, Kirsch B, Bertaccini A, Pelusi C, Pelusi G. Testosterone undecanoate maintains spermatogenic suppression induced by cyproterone acetate plus testosterone undecanoate in normal men. J Clin Endocrinol Metab. 2003 Dec;88(12):5818-26.	2003	Italy	English	pro-spective	young	contraception	semen, hormones	sex hormones and modulators of the genital system	G03	cyproterone acetate	G03HA01		32 wk	24	azoospermia, induction	in all men		yes	T 1000mg/6w + 2mg/d CPA	T 1000mg/6w + 20mg/d CPA	T 1000mg/6w + placebo	1-	
595: Wang C, Yeung KK. Use of low-dosage oral cyproterone acetate as a male contraceptive. Contraception. 1980 Mar;21(3):245-72.	1980		English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	cyproterone acetate	G03HA01		16w	23	azoospermia, induction	in only 1 of 12, but lower sperm count in all men		no	CPA 10mg/d	CPA 5mg/d	placebo	2-	
64: Meriggiola MC, Costantino A, Bremner WJ, Morselli-Labate AM. Higher testosterone dose impairs sperm suppression induced by a combined androgen-progestin regimen. J Androl. 2002 Sep-Oct;23(5):684-90.	2002	Italy	English	pro-spective	21-45	contraception	semen	sex hormones and modulators of the genital system	G03	cyproterone acetate	G03HA01		16w	18	azoospermia, induction	lower T dose leads to stronger suppression of sperm			T100mg/d + CPA 5mg/d	T200mg/d + CPA 5mg/d		2-	
154: Meriggiola MC, Bremner WJ, Costantino A, Di Cintio G, Flamigni C. Low dose of cyproterone acetate and testosterone enanthate for contraception in men. Hum Reprod. 1998 May;13(5):1225-9.	1998	Italy	English	pro-spective	young	contraception	semen	sex hormones and modulators of the genital system	G03	cyproterone acetate	G03HA01		16w	10	azoospermia, induction	in 10 of 10 men	hemoglobin, depression	yes	25 CPA+T	12,5 CPA+T		1-	
590: Moltz L, Rommler A, Post K, Schwartz U, Hammerstein J. Medium dose cyproterone acetate (CPA): effects on hormone secretion and on spermatogenesis in men. Contraception. 1980 Apr;21(4):393-413.	1980	Germany	English	pro-spective	young	contraception	hormones	sex hormones and modulators of the genital system	G03	cyproterone acetate	G03HA01	10mg/d	12w	10	gonadotropin levels, decline; sperm motility, impairment	suppression by 30-40%; inhibition	no serious	no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
618: Roy S, Chatterjee S. Studies with cyproterone acetate for male contraception. J Steroid Biochem. 1979 Jul;11(1B):675-80.	1979		English	pro-spective	young	contra-ception	semen	sex hormones and modulators of the genital system	G03	cyproterone acetate	G03HA01		28w	n.g.	spermatogenesis, impairment	all	testosterone levels decreased, libido and potency were not altered	yes	5mg/d CPA	10mg/d CPA		2-	
654: Fredricsson B. On the development of different morphologic abnormalities of human spermatozoa. Andrologia. 1978 Jan-Feb;10(1):43-8.	1978		English	review	young	infertility	semen	sex hormones and modulators of the genital system	G03	cyproterone acetate	G03HA01				spermatogenesis, impairment	morphologic anomalies of midpiece and tail after 2w, of heads after 4w		no				3	
565: Johnsen SG. Clomiphene stimulation test in men with idiopathic hypospermatogenesis. Acta Endocrinol (Copenh). 1981 Apr;96(4):557-63.	1981		English	pro-spective	young	spermato-genic dysfunction	semen	sex hormones and modulators of the genital system	G03	clomiphen	not listed			35	LH response to GnRH	increase during treatment		no	clomiphen in hypozoospermia	clomiphen in normozoospermia		2-	
696: Paulson DF, Wacksman J. Clomiphene citrate in the management of male infertility. J Urol. 1976 Jan;115(1):73-6.	1976		English	pro-spective	young	infertility	semen	sex hormones and modulators of the genital system	G03	clomiphen	not listed		9m	35	spermatogenesis, improvement	31 of 35 men, 8 pregnancies		no				3	
578: Ronnberg L. The effect of clomiphene citrate on different sperm parameters and serum hormone levels in preselected infertile men: a controlled double-blind cross-over study. Int J Androl. 1980 Oct;3(5):479-86.	1980		English	pro-spective	young	spermato-genic dysfunction	semen	sex hormones and modulators of the genital system	G03	clomiphen	not listed	50 mg/d	3m	30	spermatogenesis, improvement	13.3 to 28.7x10(6) sperm in the verum group, no change in placebo group	none	yes	clomiphen	placebo		1-	
625: Schill WB. Treatment of idiopathic oligozoospermia by kallikrein: results of a double-blind study. Arch Androl. 1979 Mar;2(2):163-70.	1979		English	pro-spective	young	infertility	semen	sex hormones and modulators of the genital system	G03	kallikrein	not listed	600U/d	7w	90	pregnancy induction	38% in kallikrein group, 16% in placebo group		yes	kallikrein 600U/d	placebo		1+	
666: Kienitz T, Schill WB. Oral kallikrein-therapy of asthenozoospermia. Fortschr Med. 1977 Sep 15;95(34):2102-5.	1977		German	pro-spective	young	infertility	semen	sex hormones and modulators of the genital system	G03	kallikrein	not listed	600U/d	7w	51	pregnancy induction	in partners of 31% of patients		no				3	
388: Giovenco P, Amodei M, Barbieri C, Fasani R, Carosi M, Dondero F. Effects of kallikrein on the male reproductive system and its use in the treatment of idiopathic oligozoospermia with impaired motility. Andrologia. 1987 Jun;19 Spec No:238-41.	1987	Italy	English	pro-spective	young	spermato-genic dysfunction	semen	sex hormones and modulators of the genital system	G03	kallikrein	not listed	600U/d	120d	16	spermatogenesis, improvement	significant		yes	kallikrein 200mg/d	vitamin E 200mg/d		1-	
685: Salat-Baroux J, Le Lorier G, Sakiz E, Rotman J, Piquet JM. Preliminary trials of an oral chemical contraceptive for men. J Gynecol Obstet Biol Reprod (Paris). 1976 Sep;5(6):831-42.	1976		French	pro-spective	25-35	contra-ception	semen	sex hormones and modulators of the genital system	G03	gestrinone	G03XA02		long-term	20	spermatogenesis, impairment	8 azoospermic with T+gestrinone, 7 with gestrinone alone	decrease of libido and other sexual functions	yes	T + 50mg/w	T + 100mg/d	placebo + 100mg/d	1-	
37: von Eckardstein S, Noe G, Brache V, Nieschlag E, Croxatto H, Alvarez F, Moo-Young A, Sivin I, Kumar N, Small M, Sundaram K; International Committee for Contraception Research, The Population Council. A clinical trial of 7 alpha-methyl-19-nortestosterone implants for possible use as a long-acting contraceptive for men. J Clin Endocrinol Metab. 2003 Nov;88(11):5232-9.	2003	Germany	English	pro-spective	young	contra-ception	semen, hormone	sex hormones and modulators of the genital system	G03	7α-methyl-nortestosterone (MENT)	not listed	MENT implants, releasing 400mg/d	6m	35	spermatogenesis, impairment	dose related depression of spermatogenesis		yes	MENT 1 implant	MENT 2 implants	MENT implants	1+	
138 Jones AR, Cooper TG. A re-appraisal of the post-testicular action and toxicity of chlorinated antifertility compounds. Intern J Androl 1999;22;130-138	1999	UK	English	review	rat	contra-ception	sperm motility	sex hormones and modulators of the genital system	G03	α-chlorohydrine	not listed				spermatogenesis, impairment	S-enantiomer is more effective	kidney toxicity by R-enantiomer	no				4	α-chlorohydrins are not harmful to animals (rat, hamster, guinea pig, ram, rhesus monkey), not tested in man

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518: Jones AR. Antifertility actions of alpha-chlorohydrin in the male. Aust J Biol Sci. 1983;36(4):333-50.	1983		English	review	men and animals	contraception	semen	sex hormones and modulators of the genital system	G03	α-chlorohydrine	not listed				spermatogenesis, impairment	recovery after withdrawal	neurotoxic	no				4	toxicity of α-chlorohydrin in humans is unknown
119: Coutinho EM, Athayde C, Atta G, Gu ZP, Chen ZW, Sang GW, Emuveyan E, Adekunle AO, Mati J, Otubu J, Reidenberg MM, Segal SJ. Gossypol blood levels and inhibition of spermatogenesis in men taking gossypol as a contraceptive. A multicenter, international, dose-finding study. Contraception. 2000 Jan;61(1):61-7.	2000	Brazil	English	prospective	young	contraception	semen	sex hormones and modulators of the genital system	G03	gossypol	not listed		56w	151	spermatogenesis, impairment	81 of 81	none	yes	gossypol 7.5mg/d	gossypol 10mg/d		1+	
360: Meng GD, Zhu JC, Chen ZW, Wong LT, Zhang GY, Hu YZ, Ding JH, Wang XH, Qian SZ, Wang C, et al. Recovery of sperm production following the cessation of gossypol treatment: a two-centre study in China. Int J Androl. 1988 Feb;11(1):1-11.	1988	China	English	prospective	young	contraception	semen	sex hormones and modulators of the genital system	G03	gossypol	not listed	total dose 8.5g mean (2.5 – 27.5g)	12m	46	spermatogenesis, recovery after cessation	61% in 1.1 years		no				3	
314: Gu ZP, Wang YX, Sang GW, Wang WC, Chen ZX, Zhao XJ, Shao QX, Jiang Y. Relationship between hormone profiles and the restoration of spermatogenesis in men treated with gossypol. Int J Androl. 1990 Aug;13(4):253-7.	1990	China	English	prospective	young	contraception	semen	sex hormones and modulators of the genital system	G03	gossypol	not listed	20mg	70d	35	azoospermia, induction	100%, after recovery 8 men azoospermic		no				3	
439: Zhang GY, Xiao B, Chen ZW, Zhu JC, Meng GD. Dynamic study of serum gonadotrophin and testosterone levels in gossypol-treated men. Long term follow-up study of 60 cases. Int J Androl. 1985 Jun;8(3):177-85.	1985	China	English	prospective	young	contraception	semen	sex hormones and modulators of the genital system	G03	gossypol	not listed		52w	26	spermatogenesis, impairment; FSH levels, increase	low sperm count after 3 months; FSH continuously elevated		no				3	elevated FSH levels may indicate permanent spermatogenic defect
885: White DR, Clarkson JS, Ratnasooriya WD, Aitken RJ. Complementary effects of propranolol and nonoxynol-9 upon human sperm motility. Contraception. 1995 Oct;52(4):241-7.	1995	UK	English	experimental	human sperm in vitro	healthy	sperm motility	sex hormones and modulators of the genital system	G03	nonoxinol	not listed		in vitro	50	sperm motility, decrease	complete, not based on Ca2+ influx						2-	
130: Aversa A, Mazzilli F, Rossi T, Delfino M, Isidori AM, Fabbri A. Effects of sildenafil (Viagra) administration on seminal parameters and post-ejaculatory refractory time in normal males. Hum Reprod. 2000 Jan;15(1):131-4.	2000	UK	English	prospective, randomized	32 mean	healthy	semen	urologicals	G04	sildenafil	G04BE03	100mg	single dose	20	sperm parameters, alteration	no changes in seminal parameters when compared to placebo	none	yes	sildenafil	placebo		1-	Interestingly, sildenafil administration led to a marked reduction of the post-ejaculatory refractory time
129: Purvis K, Muirhead GJ, Harness JA. The effects of sildenafil on human sperm function in healthy volunteers. Br J Clin Pharmacol. 2002;53 Suppl 1:53S-60S.	2002	Norway	English	prospective, randomized	19-34	healthy	semen	urologicals	G04	sildenafil	G04BE03	100mg	single dose	17	sperm parameters, alteration	no statistically significant effect	well tolerated	yes	sildenafil	placebo		1-	The amount of sildenafil in the ejaculate was < 2x10(-4)% of the administered dose at 1.5 h
40: Hellstrom WJ, Overstreet JW, Yu A, Saikali K, Shen W, Beasley CM Jr, Watkins VS. Tadalafil has no detrimental effect on human spermatogenesis or reproductive hormones. J Urol. 2003 Sep;170(3):887-91.	2003	USA	English	prospective, randomized	>45	erectile dysfunction	semen, hormones	urologicals	G04	tadalafil	G04BE08		6m	421	spermatogenesis, impairment	no effect	headache, dyspepsia and back pain	yes	tadalafil	placebo		1++	

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131: Overstreet JW, Fuh VL, Gould J, Howards SS, Lieber MM, Hellstrom W, Shapiro S, Carroll P, Corfman RS, Petrou S, Lewis R, Toth P, Shown T, Roy J, Jarow JP, Bonilla J, Jacobsen CA, Wang DZ, Kaufman KD. Chronic treatment with finasteride daily does not affect spermatogenesis or semen production in young men. J Urol. 1999 Oct;162(4):1295-300.	1999	USA	English	pro-spective, random-ized	19-41	healthy	semen	urologicals	G04	finasteride	G04CB01	1mg/d	48w	181	spermatogenesis, impairment	no effect	none	yes	finasteride	placebo		1++	
43: Jones HB, Betton GR, Bowdler AL, McFarquhar RL, Middleton BJ, Lunglmayr G. Pathological and morphometric assessment of testicular parameters in patients with metastatic prostate cancer following treatment with either the anti-androgen Casodex (ZM176,334) or bilateral orchidectomy. Urol Res. 1994;22(3):191-5.	1994	UK	English	pro-spective	old	prostate cancer	testicular histology	urologicals	G04	casodex	not listed	n.g.	n.g.	34	Leydig cells, hyperplasia	not increased in comparison to controls		no	casodex	orchidectomy		2-	
242: Bjerklund Johansen TE, Majak M, Nesland JM. Testicular histology after treatment with the new antiandrogen Casodex for carcinoma of the prostate. A preliminary report. Scand J Urol Nephrol. 1994 Mar;28(1):67-70.	1994	The Netherlands	English	pro-spective	55-78	prostate cancer	testicular histology	urologicals	G04	casodex	not listed	50mg/d	12m	5	spermatogenesis, impairment	not significant		no				3	
194: Ovesen P, Jorgensen JO, Ingerslev J, Ho KK, Orskov H, Christiansen JS. Growth hormone treatment of sub-fertile males. Fertil Steril. 1996 Aug;66(2):292-8.	1996	Denmark	English	pro-spective	young	spermatogenic dysfunction	semen, fertility	pituitary and hypothalamic hormones and analogues	H01	somatotropin	H01AC01	6U/d	12w	18	pregnancy induced	3 pregnancies in the nine couples from the asthenozoospermic group, 0 pregnancies in the oligozoospermic group		no	oligo-as-theno-terato-zoospermia	asthenozoospermia		3	
193: Ng SC, Lee KO. Treatment of male infertility with growth hormone. Clin Sci (Lond). 1996 Sep;91(3):254-5.	1996	Singapur	English	pro-spective	young	infertility	semen	pituitary and hypothalamic hormones and analogues	H01	somatotropin	H01AC01			15	spermatogenesis, improvement	not statistically significant						3	
201: Tato L, Zamboni G, Antoniazzi F, Piubello G. Gonadal function and response to growth hormone (GH) in boys with isolated GH deficiency and to GH and gonadotropins in boys with multiple pituitary hormone deficiencies. Fertil Steril. 1996 Apr;65(4):830-4.	1996	Italy	English	pro-spective	children	somatotropin deficiency	semen	pituitary and hypothalamic hormones and analogues	H01	somatotropin	H01AC01	0.7IU/kg/w	5.3m mean	15	spermatogenesis, maturation	in all patients	not mentioned	no	somatotropin deficiency	panhypopituitarism		2-	
139: Carani C, Granata AR, De Rosa M, Garau C, Zarrilli S, Paesano L, Colao A, Marrama P, Lombardi G. The effect of chronic treatment with GH on gonadal function in men with isolated GH deficiency. Eur J Endocrinol. 1999 Mar;140(3):224-30.	1999	Italy	English	pro-spective	33-54	hypogonadism, secondary	hormone	pituitary and hypothalamic hormones and analogues	H01	somatotropin	H01AC01	0.25IU/kg/w	12m	11	spermatogenesis, improvement	no effect		no				3	
38: Byrne MM, Rolf C, Depenbusch M, Cooper TG, Nieschlag E. Lack of effect of a single i.v. dose of oxytocin on sperm output in severely oligozoospermic men. Hum Reprod. 2003 Oct;18(10):2098-102.	2003	Germany	English	pro-spective	young	infertility	semen	pituitary and hypothalamic hormones and analogues	H01	oxytocin	H01BB02		single dose	49	sperm parameters, improvement	no effect		yes	oxytocin	placebo		1-	

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145: Grigoriou O, Konidaris S, Antonaki V, Papadias C, Antoniou G, Gargaropoulos A. Corticosteroid treatment does not improve the results of intrauterine insemination in male subfertility caused by antisperm antibodies. Eur. J. Obstet. Gynecol. Reprod. Biol. 1996;65:227-30.	1995	Greece	English	pro-spective	young	infertility, immune	semen	corticosteroids for systemic use	H02	glucocorticoids	H02AB	40mg/d	10d	36	sperm parameters, improvement	none	13 patients (42%) reported mild side effects; dyspepsia (10), acne (6), mood changes (5), weight gain (4) flushes (4).	no				2-	
147: Haas GG Jr, Manganiello P. A double-blind, placebo-controlled study of the use of methylprednisolone in infertile men with sperm-associated immunoglobulins. Fertil. Steril. 1987;47:295-301.	1987	USA	English	pro-spective, randomized	young	infertility, immune	semen	corticosteroids for systemic use	H02	methylprednisolon	H02AB04	96mg	7d	43	sperm parameters, improvement	none		yes	Methylprednisolon	placebo		1-	
161: Omu AE, al-Qattan F, Abdul Hamada B. Effect of low dose continuous corticosteroid therapy in men with antisperm antibodies on spermatozoal quality and conception rate. Eur. J. Obstet. Gynecol. Reprod. Biol. 1996;69:129-34.	1996	Arabia	English	pro-spective	young	infertility, immune	semen	corticosteroids for systemic use	H02	prednisolone	H02AB06	20mg	7d	77	sperm parameters, improvement	none		no				3	
156: Lahteenmaki A, Rasanen M, Hovatta O. Low-dose prednisolone does not improve the outcome of in-vitro fertilization in male immunological infertility. Hum. Reprod. 1995;10:3124-9.	1995	Finland	English	pro-spective	young	infertility, immune	in vitro fertilization	corticosteroids for systemic use	H02	prednisolone	H02AB06	20mg	7d	53	sperm parameters, improvement	none		no				3	
152: Hendry WF, Hughes L, Scammell G, Pryor JP, Hargreave TB. Comparison of prednisolone and placebo in subfertile men with antibodies to spermatozoa. Lancet 1990;335(8681):85-8.	1990	UK	English	pro-spective, randomized	young	infertility, immune	semen	corticosteroids for systemic use	H02	prednisolone	H02AB06	20mg	7d	43	sperm parameters, improvement	pregnancy rate, increase	mild	yes	prednisolone	placebo		1-	
132: Bals-Pratsch M, Doren M, Karbowski B, Schneider HP, Nieschlag E. Cyclic corticosteroid immunosuppression is unsuccessful in the treatment of sperm antibody-related male infertility: a controlled study. Hum. Reprod. 1992;7:99-104.	1992	Germany	English	pro-spective, randomized	young	infertility, immune	semen	corticosteroids for systemic use	H02	prednisolone	H02AB06	40mg/d	7d	20	sperm parameters, improvement	none	mild	yes	prednisolone	placebo		1-	
133: De Almeida M, Feneux D, Rigaud C, Jouannet P. Steroid therapy for male infertility associated with antisperm antibodies. Results of a small randomized clinical trial. Int. J. Androl. 1985;8:111-7.	1985	Spain	English	pro-spective, randomized	young	infertility, immune	semen	corticosteroids for systemic use	H02	prednisolone	H02AB06	1mg/kg/d	9d	10	sperm parameters, improvement	none		yes	prednisolone	placebo		1-	
164: Rasanen M, Lahteenmaki A, Agrawal YP, Saarikoski S, Hovatta O. A placebo-controlled flow cytometric study of the effect of low-dose prednisolone treatment on sperm-bound antibody levels. Int. J. Androl. 1996;19:150-4.	1996	Finland	English	pro-spective	young	infertility, immune	semen, flowcytometry	corticosteroids for systemic use	H02	prednisolone	H02AB06	20mg	7d	n.g.	sperm parameters, improvement	none		yes	prednisolone	placebo		1-	
610: Hendry WF, Stedronska J, Hughes L, Cameron KM, Pugh RC. Steroid treatment of male subfertility caused by antisperm antibodies. Lancet. 1979 Sep 8;2(8141):498-501.	1979	UK	English	pro-spective	young	infertility, immune	semen	corticosteroids for systemic use	H02	prednisone	H02AB07	5mg/d	12m	47	male accessory gland inflammation, improvement	decline of antibody titres, 3 pregnancies induced		no				3	

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11: Rees DA, Dodds AL, Rathbone N, Davies JS, Scanlon MF. Azoospermia in testicular sarcoidosis is an indication for corticosteroid therapy. Fertil Steril. 2004 Dec;82(6):1672-4.	2004	UK	English	case report	27	sarcoidosis, testicular	semen	corticosteroids for systemic use	H02	cortisone	H02AB10	60 down to 15mg/d	5m	1	spermatogenesis, improvement	good effect		case report				3	
71: Tiitinen A, Valimaki M. Primary infertility in 45-year-old man with untreated 21-hydroxylase deficiency: successful outcome with glucocorticoid therapy. J Clin Endocrinol Metab. 2002 Jun;87(6):2442-5.	2002	Finland	English	case report	45	hydroxylase deficiency	semen	corticosteroids for systemic use	H02	cortisone	H02AB10		6m	1	spermatogenesis, improvement	good effect	not mentioned	case report				3	
753: Toth A, Lesser ML. Ureaplasma urealyticum and infertility: the effect of different antibiotic regimens on the semen quality. J Urol. 1982 Oct;128(4):705-7.	1982		English	prospective	young	male accessory gland infection	sperm motility	antibacterials for systemic use	J01	tetracycline	J01AA07		2w	243	sperm motility, increase	by 80%		no				3	
745: Hargreaves CA, Rogers S, Hills F, Rahman F, Howell RJ, Homa ST. Effects of co-trimoxazole, erythromycin, amoxycillin, tetracycline and chloroquine on sperm function in vitro. Hum Reprod. 1998 Jul;13(7):1878-86.	1997		English	prospective	young	male accessory gland infection	sperm functions in vitro	antibacterials for systemic use	J01	tetracycline	J01AA07	50mg/ml	24h		sperm motility, decrease	dose-dependent		no				2-	
2179: Rolf C, Kenkel S, Nieschlag E. Age-related disease pattern in infertile men: increasing incidence of infections in older patients. Andrologia. 2002 Sep;34(4):209-17	2002	Germany	English	retrospective, patients	20-55	infertility	semen	antibacterial for systemic use	J01	various	J01			3698	history of infection	incidence increasing with age						3	
2175: Bayasgalan G, Naranbat D, Radnaabazar J, Lhagvasuren T, Rowe PJ. Male infertility: risk factors in Mongolian men. Asian J Androl. 2004 Dec;6(4):305-11.	2004	Mongolia	English	case-control	31.2 mean	infertility	history, semen	antibacterial for systemic use	J01	none				430	history urinary infection	79 cases men with in abnormal semen parameters, 63 in men with normal semen parameters; P<0.01						2-	
2173: Okonofua F, Menakaya U, Onemu SO, Omo-Aghoja LO, Bergstrom S. A case-control study of risk factors for male infertility in Nigeria. Asian J Androl. 2005 Dec;7(4):351-61.	2005	Nigeria	English	case-control	30-50	infertility	history, semen	antibacterial for systemic use	J01	none				150; 150	STD as risk factors	significant more urethritis, genital ulcer, testicular swelling infertile patients than in fertile men						2-	
2177: Wong WY, Zielhuis GA, Thomas CM, Merkus HM, Steegers-Theunissen RP. New evidence of the influence of exogenous and endogenous factors on sperm count in man. Eur J Obstet Gynecol Reprod Biol. 2003 Sep 10;110(1):49-54.	2003	The Netherlands	English	case-control	34.4 mean	infertility	semen	antibacterial for systemic use	J01	none				92; 73	oligozoospermia	OR 8.0 (95% CI 1.7–37.3), 0.002							
745: Hargreaves CA, Rogers S, Hills F, Rahman F, Howell RJ, Homa ST. Effects of co-trimoxazole, erythromycin, amoxycillin, tetracycline and chloroquine on sperm function in vitro. Hum Reprod. 1998 Jul;13(7):1878-86.	1997		English	prospective	young	male accessory gland infection	sperm functions in vitro	antibacterial for systemic use	J01	amoxycillin	J01CA04	500mg/ml	24h		sperm motility, alteration	no effect		no				2-	
745: Hargreaves CA, Rogers S, Hills F, Rahman F, Howell RJ, Homa ST. Effects of co-trimoxazole, erythromycin, amoxycillin, tetracycline and chloroquine on sperm function in vitro. Hum Reprod. 1998 Jul;13(7):1878-86.	1997		English	prospective	young	male accessory gland infection	sperm functions in vitro	antibacterial for systemic use	J01	co-trimoxazole	J01EE01	96mg/ml	24h		sperm motility, alteration	no effect		no				2-	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
745: Hargreaves CA, Rogers S, Hills F, Rahman F, Howell RJ, Homa ST. Effects of co-trimoxazole, erythromycin, amoxycillin, tetracycline and chloroquine on sperm function in vitro. Hum Reprod. 1998 Jul;13(7):1878-86.	1997		English	pro-spective	young	male accessory gland infection	sperm functions in vitro	antibacterial for systemic use	J01	erythromycin	J01FA01	50mg/ml	24h		sperm motility, alteration	significant decrease		no				2-	
751: Vicari E. Effectiveness and limits of antimicrobial treatment on seminal leukocyte concentration and related reactive oxygen species production in patients with male accessory gland infection. Hum Reprod. 2000 Dec;15(12):2536-44.	2000		English	pro-spective	young	male accessory gland infection	leukocyte count, sperm parameter	antibacterial for systemic use	J01	ofloxacin	J01MA01		3m	122	leukocytes in semen decrease; sperm parameters, increase	positive effects		no				2-	
926: Waite NM, Edwards DJ, Arnott WS, Warbasse LH. Effects of ciprofloxacin on testosterone and cortisol concentrations in healthy males. Antimicrob Agents Chemother. 1989 Nov;33(11):1875-7.	1989	USA	English	pro-spective	young	healthy	hormones	antibacterial for systemic use	J01	ciprofloxacin	J01AM02	500mg/d	4d	8	testosterone level, alteration	no effect						3	
323: Giorgi PM, Giorgi P, Canale D, Turchi P, Poggi MS, Di Coscio M, Bartelloni M, Meschini P, Andreini F, Campa M, et al. Treatment of male genital infections with enoxacin. Arch Ital Urol Nefrol Androl. 1989 Sep;61(3):235-41.	1989	Italy	Italian	pro-spective	32 mean	male accessory gland infection	semen	antibacterial for systemic use	J01	enoxacin	J01MA04	600 mg/d	10w	30	sperm parameters, impairment	50% hyperviscosity of semen		no				3	
214: Barletta D, Monzani F, Gasperi M, Caraccio N, Maccanti O, Bellitti P, Bonadio M, Pucci E. Efficacy of enoxacin in the treatment of prostatitis-vesiculitis: its absence of toxicity on spermatogenesis. Presse Med. 1995 Jun 17;24(22):1025-7.	1995	Italy	English	pro-spective	young	spermatogenic dysfunction	semen	antibacterial for systemic use	J01	enoxacin	J01MA04		7d	20	spermatogenesis, impairment	no effect		no				3	
855: Foote RH. Effects of metronidazole, ipronidazole, and dibromochloropropane on rabbit and human sperm motility and fertility. Reprod Toxicol. 2002 Nov-Dec;16(6):749-55.	2002	USA	English	experimental	human sperm in vitro	healthy	sperm parameters	antibacterial for systemic use	J01	metronidazol	J01XD01		in vitro		sperm motility, depression; hamster oocyte test, unaltered	significant						3	
949: Nashan D, Knuth UA, Weidinger G, Nieschlag E. The antimycotic drug terbinafine in contrast to ketoconazole lacks acute effects on the pituitary-testicular function of healthy men: a placebo-controlled double-blind trial. Acta Endocrinol (Copenh). 1989 May;120(5):677-81.	1989	Germany	English	pro-spective, randomized	young	healthy	hormones	antimycotics for systemic use	J02	ketoconazole, terbinafine	J02AB02	n.g.	3 times	n.g. (low)	testosterone level decreased, LH pulse unaltered	marginally		cross-over	ketoconazole 200mg/3times	terbinafine 500gm/3 times	placebo	1-	
940: Touchette MA, Chandrasekar PH, Milad MA, Edwards DJ. Contrasting effects of fluconazole and ketoconazole on phenytoin and testosterone disposition in man. Br J Clin Pharmacol. 1992 Jul;34(1):75-8.	1992	USA	English	pro-spective, randomized	young	healthy	hormones	antimycotics for systemic use	J02	fluconazole, ketoconazole	J02AC01	400mg/200mg	5d	9	testosterone level	increase after fluconazol, decrease after ketoconazole		cross-over	fluconazole 400mg/d	ketoconazole 200mg/d		1-	
904: Rieth H, Sauerbrey N. Interaction studies with fluconazole, a new triazole antifungal drug. Wien Med Wochenschr. 1989 Aug 31;139(15-16):370-4.	1989	Germany	German	review	young	healthy	hormones	antimycotics for systemic use	J02	fluconazol	J02AC01				cytochrome-P-450-dependent enzymes of steroid hormone synthesis	no influences in male						4	

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826: Queiroz-Telles F, Purim KS, Boguszewski CL, Afonso FC, Graf H. Adrenal response to corticotrophin and testosterone during long-term therapy with itraconazole in patients with chromoblastomycosis. J Antimicrob Chemother. 1997 Dec;40(6):899-902.	1997	Brazil	English	retro-spective	young	mycosis	hormones	antimycotics for systemic use	J02	itraconazol	J02AC02	200-400mg/d	12m	15	testerone level, alteration	none						3	
877: Bammel A, van der Mee K, Ohnhaus EE, Kirch W. Divergent effects of different enzyme-inducing agents on endogenous and exogenous testosterone. Eur J Clin Pharmacol. 1992;42(6):641-4.	1992	Germany	English	pro-spective	young	healthy	hormones	antimycotics for systemic use	J04	rifampicin	J04AB02	600mg/d	7d	18	testosterone level and response to hCG, alteration	significant						3	
65: Kul'chavenia EV, Brizhitiuk EV, Medvedev SA. Toxic effect of antituberculous drugs on spermatogenesis. Probl Tuberk. 2002;(5):29-32..	2002	Russia	Russian	retro-spective	n.g.	spermatogenic dysfunction	semen	antimycotics for systemic use	J04	isoniazide	J04AC01			n.g.	spermatogenesis, impairment	no effect of combined antituberculous therapy						3	
916: Douglas JM Jr, Davis LG, Remington ML, Paulsen CA, Perrin EB, Goodman P, Conner JD, King D, Corey L. A double-blind, placebo-controlled trial of the effect of chronically administered oral acyclovir on sperm production in men with frequently recurrent genital herpes. J Infect Dis. 1988 Mar;157(3):588-93. Original	1988	USA	English	pro-spective, randomized	19-35	herpes simplex recurrent	semen	antivirals for systemic use	J05	aciclovir	J05AB01		6m	33	sperm parameters, impairment	no difference between treated and control men	none	yes	aciclovir 1000mg/d	placebo		1-	
4: Wyrobek AJ, Schmid TE, Marchetti F. Relative susceptibilities of male germ cells to genetic defects induced by cancer chemotherapies. J Natl Cancer Inst Monogr. 2005;(34):31-5	2005	USA	English	review	young	spermatogenic dysfunction	sperm chromosomes	antineoplastic agents	L01	antineoplastic agents in general					germ cells, chromosomal abnormalities, induction	highest in the first weeks after treatment		no				4	
2044: Hales BF, Robaire B. Paternal exposure to drugs and environmental chemicals: effects on progeny outcome. J Androl. 2001 Nov-Dec;22(6):927-36.	2001	Canada	English	review	all	infertility	progeny outcome	antineoplastic agents	L01	antineoplastic agents in general					alteration of number and quality of progeny	within the first cycle of spermatogenesis						4	
2175: Bayasgalan G, Naranbat D, Radnaabazar J, Lhagvasuren T, Rowe PJ. Male infertility: risk factors in Mongolian men. Asian J Androl. 2004 Dec;6(4):305-11.	2004	Mongolia	English	case-control	31.2 mean	infertility	history, semen	antineoplastic agents	L01	antineoplastic agents in general				430	history of systemic disease	84 cases in men with abnormal semen parameters, 91 cases in men with normal semen parameters; P>0.05						2-	
550: Maguire LC, Dick FR, Sherman BM. The effects of anti-leukemic therapy on gonadal histology in adult males. Cancer. 1981 Nov 1;48(9):1967-71.	1981		English	retro-spective	young	cancer, leukemia	testicular histology	antineoplastic agents	L01	antineoplastic agents in general			post mortem	29	spermatogenesis, impairment	in longer treatment		no	various treatment periods			2-	
122: Lopez Andreu JA, Fernandez PJ, Ferris i Tortajada J, Navarro I, Rodriguez-Ineba A, Antonio P, Muro MD, Romeu A. Persistent altered spermatogenesis in long-term childhood cancer survivors. Pediatr Hematol Oncol. 2000 Jan-Feb;17(1):21-30.	2000	Spain	English	retro-spective	young	cancer, in childhood	semen	antineoplastic agents	L01	cyclophosphamide	L01AA01			43	sperm parameters after puberty, impairment	8 of 43 patients azoospermia, 16 of 43 patients normospermia						3	
716: Buchanan JD, Fairley KF, Barrie JU. Return of spermatogenesis after stopping cyclophosphamide therapy. Lancet. 1975 Jul 26;2(7926):156-7.	1975		English	retro-spective	young	cancer	semen	antineoplastic agents	L01	cyclophosphamide	L01AA01		31m	26	spermatogenesis, recovery after treatment	31m after cessation of therapy despite >100mg/d		no				3	

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562: Trompeter RS, Evans PR, Barratt TM. Gonadal function in boys with steroid-responsive nephrotic syndrome treated with cyclophosphamide for short periods. Lancet. 1981 May 30;1(8231):1177-9.	1981	UK	English	retrospective	young	nephrotic syndrome in childhood	semen	antineoplastic agents	L01	cyclophosphamide	L01AA01		8w	19	spermatogenesis, impairment	most		no				3	
668: Lentz RD, Bergstein J, Steffes MW, Brown DR, Prem K, Michael AF, Vernier RL. Postpubertal evaluation of gonadal function following cyclophosphamide therapy before and during puberty. J Pediatr. 1977 Sep;91(3):385-94.	1977		English	retrospective	children	nephrotic syndrome	hormones	antineoplastic agents	L01	cyclophosphamide	L01AA01			19	spermatogenesis, impairment	in all boys		no				3	
310: Bogdanovic R, Banicevic M, Cvoric A. Testicular function following cyclophosphamide treatment for childhood nephritic syndrome: long-term follow-up study. Pediatr Nephrol. 1990 Sep;4(5):451-4.	1990	Yugoslavia	English	retrospective	children	nephrotic syndrome	semen	antineoplastic agents	L01	cyclophosphamide	L01AA01	640 mg/kg		17	spermatogenesis, impairment	5 azoo-, 1 oligo-, 11 normozoospermic		no				3	
731: Pennisi AJ, Grushkin CM, Lieberman E. Gonadal function in children with nephrosis treated with cyclophosphamide. Am J Dis Child. 1975 Mar;129(3):315-8.	1975		English	retrospective	children	nephrotic syndrome	semen	antineoplastic agents	L01	cyclophosphamide	L01AA01	5 mg/kg	6m	16	spermatogenesis, impairment	no effect		no				3	
801. Masala A, Faedda R, Alagna S et al: Use of testosterone to prevent cyclophosphamide-induced azoospermia. Ann Int Med 1997;126: 292-295	1997	USA	English	prospective	young	cancer	semen	antineoplastic agents	L01	cyclophosphamide	L01AA01			15	spermatogenesis, recovery after treatment	1/10 without T, 5/5 with T		yes	cyclophosphamide daily	cyclophosphamide bolus monthly	cyclophosphamide monthly + T	1-	
694: Etteldorf JN, West CD, Pitcock JA, Williams DL. Gonadal function, testicular histology, and meiosis following cyclophosphamide therapy in patients with nephrotic syndrome. J Pediatr. 1976 Feb;88(2):206-12.	1976		English	retrospective	children	nephrotic syndrome	testicular histology	antineoplastic agents	L01	cyclophosphamide	L01AA01		up to 489d	8	azoospermia, induction	in all after puberty		no	2 to 4 mg/d	2 to 5 mg/d		1-	
652: Guesry P, Lenoir G, Broyer M. Gonadal effects of chlorambucil given to prepubertal and pubertal boys for nephrotic syndrome. J Pediatr. 1978 Feb;92(2):299-303.	1978		English	retrospective	children	nephrotic syndrome	semen	antineoplastic agents	L01	chlorambucil	L01AA02		long-term	21	azoospermia, induction	in 17 of 21 patients		no				3	
577: Callis L, Nieto J, Vila A, Rende J. Chlorambucil treatment in minimal lesion nephrotic syndrome: a reappraisal of its gonadal toxicity. J Pediatr. 1980 Oct;97(4):653-6.	1980	USA	English	retrospective	prepuberal	nephrotic syndrome	semen	antineoplastic agents	L01	chlorambucil	L01AA02			16	spermatogenesis, impairment	total safe dosis < 8.2 mg/kg		no				3	
634: Calamera JC, Morgenfeld MC, Mancini RE, Vilar O. Biochemical changes of the human semen produced by chlorambucil, testosterone propionate and human chorionic gonadotropin administration. Andrologia. 1979 Jan;11(1):43-50.	1979		English	retrospective	young	lymphoma	semen	antineoplastic agents	L01	chlorambucil	L01AA02			6	spermatogenesis, impairment	in all men, treatment with T improved only fructose concentration		no				3	
275: Marmor D, Grob-Menendez F, Duyck F, Delafontaine D. Very late return of spermatogenesis after chlorambucil therapy: case reports. Fertil Steril. 1992 Oct;58(4):845-6.	1992	France	English	case report	young	nephrotic syndrome.	semen	antineoplastic agents	L01	chlorambucil	L01AA02	3,000-6,500mg cumulative	14y	2	spermatogenesis, recovery after treatment	after 19 years		no				3	

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69: Thomson AB, Anderson RA, Irvine DS, Kelnar CJ, Sharpe RM, Wallace WH. Investigation of suppression of the hypothalamic-pituitary-gonadal axis to restore spermatogenesis in azoospermic men treated for childhood cancer. Hum Reprod. 2002 Jul;17(7):1715-23.	2002	UK	English	pro-spective	young	cancer, in childhood	semen	antineoplastic agents	L01	dacarbazine	L01AX04		24w	7	spermatogenesis, recovery after treatment	azoospermia in all men		no				3	
633: El-Beheiry A, El-Mansy E, Kamel N, Salama N. Methotrexate and fertility in men. Arch Androl. 1979;3(2):177-9.	1979		English	retro-spective	young	psoriasis	semen	antineoplastic agents	L01	methotrexate	L01BA01			26	spermatogenesis, impairment	none		no				3	
250: Morris LF, Harrod MJ, Menter MA, Silverman AK. Methotrexate and reproduction in men: case report and recommendations. J Am Acad Dermatol. 1993 Nov;29(5 Pt 2):913-6.	1993	USA	English	case report	26	psoriasis arthritis	semen	antineoplastic agents	L01	methotrexate	L01BA01	228mg cumulative		1	spermatogenesis, impairment	partial		no				3	avoid conception for at least 90 days
981: Jenderny J, Jacobi ML, Ruger A, Rohrborn G. Chromosome aberrations in 450 sperm complements from eight controls and lack of increase after chemotherapy in two patients. Hum Genet. 1992 Sep-Oct;90(1-2):151-4.	1992	USA	English	retro-spective	36	chronic hepatitis	semen, sperm chromosomes	antineoplastic agents	L01	6-mercaptopurine	L01BB02	50-70mg/d	4y	1	sperm parameters, impairment	no difference against controls		no				3	
980: Cohen RD. Sperm, sex, and 6-MP: the perception on conception. Gastroenterology. 2004 Oct;127(4):1263-4.	2004	USA	English	hypothesis	young	inflammatory bowel disease	offspring	antineoplastic agents	L01	6-mercaptopurine	L01BB02	all doses			malformations in the children fathered	no more frequent than in controls						3	The risk/benefit ratio still weighs heavily in favor of continuing therapy in men attempting conception in their female partners.
493: Da Cunha MF, Meistrich ML, Ried HL, Gordon LA, Watchmaker G, WYROBEK AJ. Active sperm production after cancer chemotherapy with doxorubicin. J Urol. 1983 Nov;130(5):927-30.	1983		English	retro-spective	young	cancer	semen	antineoplastic agents	L01	doxorubicine	L01DB01			14	spermatogenesis, impairment	In contrast to protocols with mechlorethamine, vincristine, procarbazine and prednisone sperm production after short-time recovery is possible after treatment with protocols that include doxorubicin.		no				3	
2113: Berger CC, Bokemeyer C, Schuppert F, Schmoll HJ. Endocrinological late effects after chemotherapy for testicular cancer. Br J Cancer. 1996 May;73(9):1108-14	1996	Germany	English	retro-spective	19-53	cancer, testicular	hormones	antineoplastic agents	L01	cisplatin	L01XA01			63	hormone levels, impairment	Elevated FSH levels in 63% of patients, elevated LH levels in 24%, subnormal T levels in 10%. Gonadotropin elevation was highly significantly correlated with the cumulative platinum dose.		no				3	
32: Ishikawa T, Kamidono S, Fujisawa M. Fertility after high-dose chemotherapy for testicular cancer. Urology. 2004 Jan;63(1):137-40.	2004	Japan	English	retro-spective	young	cancer, testicular	semen	antineoplastic agents	L01	cisplatin	L01XA01	1250 mg/cm²		27	spermatogenesis, impairment	in all 27 men		no				3	
262: Fossa SD, Aabyholm T, Vespestad S, Norman N, Ous S. Semen quality after treatment for testicular cancer. Eur Urol. 1993;23(1):172-6.	1993	Norway	English	retro-spective	young	cancer, testicular	semen	antineoplastic agents	L01	cisplatin	L01XA01			n.g	spermatogenesis, recovery after treatment	2-3 y after chemotherapy		no				3	
180: Pont J, Albrecht W. Fertility after chemotherapy for testicular germ cell cancer. Fertil Steril. 1997 Jul;68(1):1-5.	1997	Austria	English	review	young	cancer	semen	antineoplastic agents	L01	cisplatin	L01XA01				azoospermia, induction	>400 mg/cm² cisplatin irreversible		no				4	
5: Boekelheide K. Mechanisms of toxic damage to spermatogenesis. J Natl Cancer Inst Monogr. 2005;(34):6-8.	2005	USA	English	review	young	cancer, testicular	semen, histology	antineoplastic agents	L01	cisplatin	L01XA01				spermatogenesis, increase of apoptosis	increase of apoptosis		no				4	cisplatin induces leakage of blood-testis barrier and germ cell apoptosis

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87: Schrader M, Muller M, Straub B, Miller K. The impact of chemotherapy on male fertility: a survey of the biologic basis and clinical aspects. Reprod Toxicol. 2001 Nov-Dec;15(6):611-7.	2001	Germany	English	review	young	spermatogenic dysfunction	semen	antineoplastic agents	L01	cisplatin	L01XA01				azoospermia, induction	in 50% of patients		no				4	Hormonal protection of spermatogenesis so far succeeded only in animals. The mechanism is unclear, since there are no changes in number of spermatogonia.
268: Hansen PV, Hansen SW. Gonadal function in men with testicular germ cell cancer: the influence of cisplatin-based chemotherapy. Eur Urol. 1993;23(1):153-6.	1993	Denmark	English	review	young	cancer, testicular	semen	antineoplastic agents	L01	cisplatin	L01XA01				spermatogenesis, recovery after treatment	most in the following years	persisting Leydig cell dysfunction	no				4	
94: Howell SJ, Shalet SM. Testicular function following chemotherapy. Hum Reprod Update. 2001 Jul-Aug;7(4):363-9.	2001	UK	English	review	young	cancer	semen	antineoplastic agents	L01	procarbazine	L01XB01				spermatogenesis, recovery after treatment	80% by 5 y		review				4	Permanent azoospermia suggests that all spermatogonia may be eradicated, in these cases there is no possibility of recovery.
492: Bonadonna G, Santoro A, Viviani S, Lombardi C, Ragni G. Gonadal damage in Hodgkin's disease from cancer chemotherapeutic regimens. Arch Toxicol Suppl. 1984;7:140-5.	1984	Italy	English	retrospective	young	Hodgkin disease	semen	antineoplastic agents	L01	not procarbazine	L01XB01				spermatogenesis, impairment	less and transient gonadal failure		no				2-	
476: Evenson DP, Arlin Z, Welt S, Claps ML, Melamed MR. Male reproductive capacity may recover following drug treatment with the L-10 protocol for acute lymphocytic leukemia. Cancer. 1984 Jan 1;53(1):30-6.	1984	USA	English	prospective	young	cancer, lymphoma	semen, flowcytometry	antineoplastic agents	L01	asparaginase, prednisolon, vincristine	L01XX02		42m	6	sperm chromosomes, impairment	none as determined by flow cytometry		no				3	
818: Gambacorti-Passerini C, Tornaghi L, Cavagnini F, Rossi P, Pecori-Giraldi F, Mariani L, Cambiaghi N, Pogliani E, Corneo G, Gnessi L. Gynaecomastia in men with chronic myeloid leukaemia after imatinib. Lancet. 2003 Jun 7;361(9373):1954-6.	2003	Italy	English	retrospective	old	cancer, chronic myeloid leukemia	hormones	antineoplastic agents	L01	imatinib	L01XX28		23m	38	testosterone synthesis, inhibition	observed in 7 men with gynecomastia						3	
301: Viviani S, Ragni G, Santoro A, Perotti L, Caccamo E, Negretti E, Valagussa P, Bonadonna G. Testicular dysfunction in Hodgkin's disease before and after treatment. Eur J Cancer. 1991;27(11):1389-92.	1991	Italy	English	retrospective	young	Hodgkin disease	semen	antineoplastic agents	L01	MOPP/ABVD	L01XY			92	spermatogenesis, impairment	87% azoospermic, recovery in 27 of 42 patients		no				3	
391: Redman JR, Bajorunas DR, Goldstein MC, Evenson DP, Gralla RJ, Lacher MJ, Koziner B, Lee BJ, Straus DJ, Clarkson BD, et al. Semen cryopreservation and artificial insemination for Hodgkin's disease. J Clin Oncol. 1987 Feb;5(2):233-8.	1987	USA	English	retrospective	young	Hodgkin disease	semen	antineoplastic agents	L01	combinations	L01XY			79	spermatogenesis, impairment	in 80% azoospermia		no				3	
298: Fossa SD, Melvik JE, Juul NO, Pettersen EO, Amellem O, Theodorsen L. DNA flow cytometry in sperm cells from testicular cancer patients. Impact of different treatment modalities on spermatogenesis. Eur Urol. 1991;19(2):125-31.	1991	Norway	English	prospective	young	cancer, testicular	semen, flowcytometry	antineoplastic agents	L01	combinations	L01XY			77	spermatogenesis, impairment	useful information by flow cytometry		no				3	

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318: Bramswig JH, Heimes U, Heiermann E, Schlegel W, Nieschlag E, Schellong G. The effects of different cumulative doses of chemotherapy on testicular function. Results in 75 patients treated for Hodgkin's disease during childhood or adolescence. Cancer. 1990 Mar 15;65(6):1298-302.	1990	Germany	English	retro-spective	young	cancer, in childhood	semen	antineoplastic agents	L01	OPPA and COPP	L01XY			75	gonadotropin levels, increase	18 of 75 (24.0%) elevated basal and 65/74 (87.8%) elevated stimulated LH levels		no				3	procarbazine is the major gonadotoxic agent
630: Chapman RM, Sutcliffe SB, Rees LH, Edwards CR, Malpas JS. Cyclical combination chemotherapy and gonadal function. Retrospective study in males. Lancet. 1979 Feb 10;1(8111):285-9.	1979	UK	English	retro-spective	young	Hodgkin disease	semen	antineoplastic agents	L01	combinations	L01XY			74	spermatogenesis, recovery after treatment	4 of 74 recovered after mean 27m		no				3	
24. Pectasides D, Pectasides M, Farmakis D, Nikolaou M, Koumpou M, Kostopoulou V, Mylonakis N. Testicular function in patients with testicular cancer treated with bleomycin-etoposide-carboplatin (BEC(90)) combination chemotherapy. Eur Urol. 2004 Feb;45(2):187-93.	2004	Greece	English	retro-spective	young	cancer, testicular	semen	antineoplastic agents	L01	BEC (bleomycin, ectoposide, carboplatine)	L01XY			69	spermatogenesis, impairment	93% remained normo-zoosperm following chemotherapy		no				2-	
317: Siimes MA, Rautonen J. Small testicles with impaired production of sperm in adult male survivors of childhood malignancies. Cancer. 1990 Mar 15;65(6):1303-6.	1990	Finland	English	retro-spective	young	cancer, in childhood	semen, testicular volume	antineoplastic agents	L01	combinations	L01XY			66	spermatogenesis, impairment	51 of 66 patients had small testis volume; cyclophosphamide most toxic		no				3	
394: Rustin GJ, Pektasides D, Bagshawe KD, Newlands ES, Begent RH. Fertility after chemotherapy for male and female germ cell tumours. Int J Androl. 1987 Feb;10(1):389-92.	1987		English	retro-spective	young	cancer, testicular	semen	antineoplastic agents	L01	POMB-ACE	L01XY			59	spermatogenesis, recovery after treatment	in 81% without radiation, in 32% with radiation		no				3	
172: Meistrich ML, Wilson G, Mathur K, Fuller LM, Rodriguez MA, McLaughlin P, Romaguera JE, Cabanillas FF, Ha CS, Lipshultz LI, Hagemeister FB. Rapid recovery of spermatogenesis after mitoxantrone, vincristine, vinblastine, and prednisone chemotherapy for Hodgkin's disease. J Clin Oncol. 1997 Dec;15(12):3488-95.	1997	USA	English	retro-spective	young	Hodgkin disease	semen	antineoplastic agents	L01	NOVP	L01XY			58	azoospermia, induction	100% in month 1, 0% after 1 year		no				3	
2070: Rautonen J, Koskimies AI, Siimes MA. Vincristine is associated with the risk of azoospermia in adult male survivors of childhood malignancies. Eur J Cancer. 1992;28A(11):1837-41.	1992	Finland	English	retro-spective	>18	cancer, in childhood	semen	antineoplastic agents	L01	combination	L01XY			55	azoospermia, induction	In multivariate analysis, RR of azoospermia after vincristine 5 (95% CI 1.3-18.8), after cyclophosphamide 3.4-fold (0.95-12.3), after testicular irradiation it was 8.2-fold.		no	radiation	protocol including vincristine	protocol including cyclophosphamide	2+	
219: Marmor D, Duyck F. Male reproductive potential after MOPP therapy for Hodgkin's disease: a long-term survey. Andrologia. 1995 Mar-Apr;27(2):99-106.	1995	France	English	retro-spective	young	Hodgkin disease	semen	antineoplastic agents	L01	MOPP	L01XY			47	spermatogenesis, impairment	azoospermia in 26 of47 patients after 89.4m		no				3	
331: Kreuser ED, Kurrle E, Hetzel WD, Heymer B, Porzsolt F, Hautmann R, Gaus W, Schlipf U, Pfeiffer EF, Heimpel H. Reversible germ cell toxicity following aggressive chemotherapy in patients with testicular tumors: results of a prospective study. Klin Wochenschr. 1989 Apr 3;67(7):367-78.	1990	Germany	German	retro-spective	young	cancer, testicular	semen	antineoplastic agents	L01	combinations	L01XY			44	spermatogenesis, recovery after treatment	in 77% of patients 25-60m after treatment		no				3	

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248: Shafford EA, Kingston JE, Malpas JS, Plowman PN, Pritchard J, Savage MO, Eden OB. Testicular function following the treatment of Hodgkin's disease in childhood. Br J Cancer. 1993 Dec;68(6):1199-204.	1993	UK	English	retrospective	prepuberal	cancer	semen	antineoplastic agents	L01	CIVPP	L01XY		n.g.	40	spermatogenesis, recovery after treatment	none when FSH levels were elevated		no				3	
2064: Kulkarni SS, Sastry PS, Saikia TK, Parikh PM, Gopal R, Advani SH. Gonadal function following ABVD therapy for Hodgkin's disease. Am J Clin Oncol. 1997 Aug;20(4):354-7.	1997	India	English	retrospective	young	Hodgkin disease	semen	antineoplastic agents	L01	combination	L01XY			38	spermatogenesis, impairment	Azoospermia was seen in one patient from theABVD group and 10 patients from the COPP/ABVD group		no				3	
121: Dubey P, Wilson G, Mathur KK, Hagemeister FB, Fuller LM, Ha CS, Cox JD, Meistrich ML. Recovery of sperm production following radiation therapy for Hodgkin's disease after induction chemotherapy with mitoxantrone, vincristine, vinblastine, and prednisone (NOVP). Int J Radiat Oncol Biol Phys. 2000 Feb 1;46(3):609-17.	2000	USA	English	prospective	young	Hodgkin disease	semen	antineoplastic agents	L01	NOVP	L01XY		8w	34	spermatogenesis, impairment	at 4.5m to nadir of sperm		no	additionally various doses of radiation			2-	
236: Meistrich ML, Chawla SP, Da Cunha MF, Johnson SL, Plager C, Papadopoulos NE, Lipshultz LI, Benjamin RS. Recovery of sperm production after chemotherapy for osteosarcoma. Cancer. 1989 Jun 1;63(11):2115-23.	1989	USA	English	retrospective	young	ostosarcoma	semen	antineoplastic agents	L01	PADIC	L01XY			32	spermatogenesis, recovery after treatment	in 78% after 2y, lower in cisplatin >600mg/m²		no				3	
647: Roeser HP, Stocks AE, Smith AJ. Testicular damage due to cytotoxic drugs and recovery after cessation of therapy. Aust N Z J Med. 1978 Jun;8(3):250-4.	1978		English	retro	young	cancer, lymphoma	semen	antineoplastic agents	L01	combinations	L01XY			32	spermatogenesis, recovery after treatment	70% in group1, 17% in group 2		no	cyclophosphamide / vincristine / prednisone	mustine / procarbazine / vincristine / prednisone		2-	
2135: Shamberger RC, Sherins RJ, Rosenberg SA. The effects of postoperative adjuvant chemotherapy and radiotherapy on testicular function in men undergoing treatment for soft tissue sarcoma. Cancer. 1981 May 15;47(10):2368-74.	1981		English	retrospective	young	sarcoma	hormones	antineoplastic agents	L01	combination	L01XY			26	hormone levels, impairment	FSH and LH levels increased, T levels normal; 8 of 12 patients low sperm count		no	chemotherapy	chemotherapy + radiation		3	
324: Hansen PV, Trykker H, Helkjoer PE, Andersen J. Testicular function in patients with testicular cancer treated with orchiectomy alone or orchiectomy plus cisplatin-based chemotherapy. J Natl Cancer Inst. 1989 Aug 16;81(16):1246-50.	1989	Denmark	English	prospective	young	cancer, testicular	semen	antineoplastic agents	L01	CVB	L01XY			25	spermatogenesis, recovery after treatment	in 46% after 5y		no				3	
468: da Cunha MF, Meistrich ML, Fuller LM, Cundiff JH, Hagemeister FB, Velasquez WS, McLaughlin P, Riggs SA, Cabanillas FF, Salvador PG. Recovery of spermatogenesis after treatment for Hodgkin's disease: limiting dose of MOPP chemotherapy. J Clin Oncol. 1984 Jun;2(6):571-7.	1984	USA	English	retrospective	young	Hodgkin disease	semen	antineoplastic agents	L01	MOPP	L01XY			25	spermatogenesis, recovery after treatment	better after only 2 cycles than after 5 cycles		no	2 cycles MOPP	5 cycles MOPP		2-	
2065: Naccache P, Decaudin D, Koscielny S, Bendahmane B, Auger J, Munck JN. Semen preservation and gonadal toxicity in the treatment of non Hodgkin lymphoma. Experience at the Gustave-Roussy Institute from 1980 to 1993. Bull Cancer. 1996 Apr;83(4):307-14.	1996	France	French	retrospective	30 mean	non-Hodgkin lymphoma		antineoplastic agents	L01	combination	L01XY			24	spermatogenesis, impairment	in 3 of 9 patients return to pretherapeutic status		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
300: Kader HA, Rostom AY. Follicle stimulating hormone levels as a predictor of recovery of spermatogenesis following cancer therapy. Clin Oncol (R Coll Radiol). 1991 Jan;3(1):37-40.	1991	UK	English	pro-spective	young	cancer, testicular	FSH	antineoplastic agents	L01	combinations	L01XY			20	spermatogenesis, recovery after treatment	reduction of FSH preceeds recovery		no				3	
490: Johnson DH, Hainsworth JD, Linde RB, Greco FA. Testicular function following combination chemotherapy with cis-platin, vinblastine, and bleomycin. Med Pediatr Oncol. 1984;12(4):233-8.	1984		English	retro-spective	young	cancer, testicular	semen	antineoplastic agents	L01	VBP +/- A	L01XY			18	spermatogenesis, recovery after treatment	in 5 of 6 patients spermaozoa after 24m		no				3	
374: Tsatsoulis A, Whitehead E, St John J, Shalet SM, Robertson WR. The pituitary-Leydig cell axis in men with severe damage to the germinal epithelium. Clin Endocrinol (Oxf). 1987 Dec;27(6):683-9.	1987	UK	English	retro-spective	18-30	Hodgkin disease	hormones	antineoplastic agents	L01	MVPP	L01XY			18	Leydig cell function, alteration	identical stimulability by hCG in comparison to controls		no	MVPP	healthy		2-	
790. Chan PTK, Palermo GD, Veeck LL, Rosenwaks Z, Schlegel PN: Testicular sperm extraction combined with intracytoplasmatic sperm injection in the treatment of men with persistent azoospermia porstchemotherapy. Cancer 2001, 166: 45-50	2001	USA	English	retro-spective	28-54	cancer	ICSI-TESE outcome	antineoplastic agents	L01	combinations	L01XY	n.g.	n.g.	17	interval chemotherapy to ICSI 16 years	9 of 20 patients positive for TESE, 3 pregnancies in 9 successful egg fertilisations		no				3	
2136: Wang C, Ng RP, Chan TK, Todd D. Effect of combination chemotherapy on pituitary-gonadal function in patients with lymphoma and leukemia. Cancer. 1980 Apr 15;45(8):2030-7.	1980		English	retro-spective	young	lymphoma and leukemia	hormones	antineoplastic agents	L01	combination	L01XY			15	hormone levels, impairment	elevated FSH in 14 of 15, elevated LH levels in 7 of 15, low T in 2 of 15 patients		no				3	
695: Asbjornsen G, Molne K, Klepp O, Aakvaag A. Testicular function after combination chemotherapy for Hodgkin's disease. Scand J Haematol. 1976 Jan;16(1):66-9.	1976		English	retro-spective	young	Hodgkin disease	semen	antineoplastic agents	L01	combinations	L01XY			8	spermatogenesis, impairment	in 7 of 8 patients azoospermia after 24m		no				3	
2090: Robbins WA, Meistrich ML, Moore D, Hagemeister FB, Weier HU, Cassel MJ, Wilson G, Eskenazi B, Wyrobek AJ. Chemotherapy induces transient sex chromosomal and autosomal aneuploidy in human sperm. Nat Genet. 1997 May;16(1):74-8.	1997	USA	English	retro-spective	young	Hodgkin disease	FISH of sperm chromosomes	antineoplastic agents	L01	NOVP	L01XY			8	Sperm aneuploidy rates of chromosomes X, Y, 8, increased	5-fold increases in sperm with disomies, diploidies and complex genotypes involving chromosome X, Y and 8.		no				3	
27: Puscheck E, Philip PA, Jeyendran RS. Male fertility preservation and cancer treatment. Cancer Treat Rev. 2004 Apr;30(2):173-80.	2004	USA	English	review	young	cancer	semen	antineoplastic agents	L01	combinations	L01XY				spermatogenesis, impairment	various according to regimen						4	there is no pharmacologically prohibiton against cytotoxic damage of spermatogenesis
584: Schilsky RL, Lewis BJ, Sherins RJ, Young RC. Gonadal dysfunction in patients receiving chemotherapy for cancer. Ann Intern Med. 1980 Jul;93(1):109-14.	1980		English	review	young	cancer	semen	antineoplastic agents	L01	combinations	L01XY				spermatogenesis, impairment	most		no				4	
223: Azizi F, Keshavarz A, Roshanzamir F, Nafarabadi M. Reproductive function in men following exposure to chemical warfare with sulphur mustard. Med War. 1995 Jan-Mar;11(1):34-44.	1995	Iran	English	retro-spective	young	poisoning	hormones	antineoplastic agents	L01	mustard gas	not listed			42	testosterone level, decrease	three months after exposition		no				3	
744: Friedman G, Freeman R, Bookchin R, Boyar R, Murthy G, Hellman L. Testicular function in sickle cell disease. Fertil Steril. 1974 Dec;25(12):1018-21.	1974		English	retro-spective	young	sickle cell anemia	semen	antineoplastic agents	L01	hydroxyurea	not listed			8	spermatogenesis, impairment	all patients had OAT syndrome		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
529: da Cunha MF, Meistrich ML, Haq MM, Gordon LA, Wyrobek AJ. Temporary effects of AMSA (4'-(9-acridinylamino) methanesulfon-m-aniside) chemotherapy on spermatogenesis. Cancer. 1982 Jun 15;49(12):2459-62.	1982		English	case report	young	melanoma	semen	antineoplastic agents	L01	acridinyl anisideide	not listed			1	azoospermia, induction	after 6 courses		no				3	no further references with this compound
2055: Huyghe E, Matsuda T, Daudin M, Chevreau C, Bachaud JM, Plante P, Bujan L, Thonneau P. Fertility after testicular cancer treatments: results of a large multicenter study. Cancer. 2004 Feb 15;100(4):732-7.	2004	France	English	retrospective, multicenter	young	cancer, testicular	fertility	physical therapy		radiation		various		446	children fathered	Before diagnosis of testicular cancer, 91.2% of patients who had tried to get their partners pregnant had succeeded, compared with 67.1% of patients after treatment. Radiotherapy much more deleterious effect on fertility than chemotherapy alone.		no	radiation	no radiation		2-	
2085: Gandini L, Lombardo F, Salacone P, Paoli D, Anselmo AP, Culasso F, Dondero F, Lenzi A. Testicular cancer and Hodgkin's disease: evaluation of semen quality. Hum Reprod. 2003 Apr;18(4):796-801	2003	Italy	English	retrospective	young	cancer, testicular	semen	physical therapy		radiation		before treatment		232	sperm parameters, impairment	normal mean of the semen parameters, but 35% below the lower limit of sperm count		no				3	
2075: Fossa SD, Almaas B, Jetne V, Bjerkedal T. Paternity after irradiation for testicular cancer. Acta Radiol Oncol. 1986 Jan-Feb;25(1):33-6.	1986	Norway	English	retrospective	29.7 mean	cancer, testicular	pregnancy in the female partner	physical therapy		radiation		50Gy inguinal		172	pregnancies induced	sex ratio, weight, height and malformation of children not different from control group		no				2+	
2050: Huddart RA, Norman A, Moynihan C, Horwich A, Parker C, Nicholls E, Dearnaley DP. Fertility, gonadal and sexual function in survivors of testicular cancer. Br J Cancer. 2005 Jul 25;93(2):200-7.	2005	UK	English	retrospective	young	cancer, testicular	semen, hormones	physical therapy		radiation		various		158	hormone levels; fertility	decrease of T, increase of gonadotropin levels, fertility in 67% of patients compared to wait-and-see 85%		no	chemotherapy	radiation	surveillance	2-	
2079: Meyer A, Greiner R. Fertility of semi-castrated and irradiated patients with testicular tumors. Schweiz Med Wochenschr. 1977 Sep 3;107(35):1225-8. [Article in German]	1977	Switzerland	German	retrospective	18-54	cancer, testicular	semen	physical therapy		radiation		inverted Y field 6000rad		62	sperm parameters, impairment	17 normozoospermia, 28 azoospermia		no				3	
2062: Sedlmayer F, Joos H, Deutschmann H, Rahim H, Merz F, Kogelnik HD. Long-term tumor control and fertility after para-aortic limited radiotherapy of stage I seminoma. Strahlenther Onkol. 1999 Jul;175(7):320-4.	1999	Germany	German	retrospective	young	cancer, testicular + radiotherapy of paraaortal lymph nodes	FSH levels	physical therapy		radiation		28.07 Gy, mean testicular scatter dose 0.22 Gy		58	FSH levels, increase	transient in 27%		no				3	
2104: Petersen PM, Giwercman A, Daugaard G, Rorth M, Petersen JH, Skakkeak NE, Hansen SW, von der Maase H. Effect of graded testicular doses of radiotherapy in patients treated for carcinoma-in-situ in the testis. J Clin Oncol. 2002 Mar 15;20(6):1537-43.	2002	Denmark	English	prospective	young	testicular intraepithelial neoplasia (TIN)	hormones	physical therapy		radiation		14-20Gy		48	hormone levels, impairment	T level showed a stable decrease for more than 5 years after treatment (3.6% per year) without dose dependency. The levels of LH and FSH were increased after radiotherapy.		no				3	
2083: Thomas C, Cans C, Pelletier R, De Robertis C, Hazzouri M, Sele B, Rousseaux S, Hennebicq S. No long-term increase in sperm aneuploidy rates after anticancer therapy: sperm fluorescence in situ hybridization analysis in 26 patients treated for testicular cancer or lymphoma. Clin Cancer Res. 2004 Oct 1;10(19):6535-43.	2004	France	English	retrospective	young	cancer, testicular	FISH of sperm chromosomes	physical therapy		radiation				38	sperm aneuploidy rates of chromosomes X, Y, 13, 18, and 21, increased	no significant alterations		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2110: Brennemann W, Stoffel-Wagner B, Wichers M, Helmers A, Albers P, Mezger J, Klingmuller D. Pretreatment follicle-stimulating hormone: a prognostic serum marker of spermatogenesis status in patients treated for germ cell cancer. J Urol. 1998 Jun;159(6):1942-6.	1998	Germany	English	retrospective	young	cancer, testicular	hormones	physical therapy		radiation		infradiaphragmatic		38	pretreatment FSH level	normal levels (12 patients) associated with lower increase after radiation than high levels (8 patients)		no	normal FSH levels	high FSH levels		2-	
2073: Fossa SD, Abyholm T, Normann N, Jetne V. Post-treatment fertility in patients with testicular cancer. III. Influence of radiotherapy in seminoma patients. Br J Urol. 1986 Jun;58(3):315-9	1986	Norway	English	retrospective	young	cancer, testicular	semen	physical therapy		radiation				29	sperm parameters, impairment	improvement up to 2 years, FSH levels increased in 50% up to three years		no				3	
2058: Panidis D, Rousso D, Matalliotakis I, Kourtis A, Mavromatidis G, Mamopoulos M, Koumantakis E. Do characteristic spermatozoal morphological abnormalities exist in patients whom have undergone unilateral orchiectomy and preventive radiotherapy? Int J Fertil Womens Med. 2003 Mar-Apr;48(2):83-7.	2003	Greece	English	retrospective	young	cancer, testicular	semen	physical therapy		radiation		various		16	sperm morphology, impairment	morphologic abnormalities of sperm head and neck identical to fertile men, but in higher percentage		no				3	
2068: Malas S, Levin V, Sur RK, Donde B, Krawitz HE, Pacella JA. Fertility in patients treated with radiotherapy following orchidectomy for testicular seminoma. Clin Oncol (R Coll Radiol). 1994;6(6):377-80.	1994	South Africa	English	retrospective	young	cancer, testicular	fertility	physical therapy		radiation		<2 Gy		16	pregnancy in the female partner	11/16 pregnancies if the dose to the remaining testis was <2 Gy. No genetic abnormalities in the offspring.		no				3	
2089: Panidis D, Matalliotakis I, Papathanasiou K, Roussos C, Koumantakis E. The sperm deformity and the sperm multiple anomalies indexes in patients who underwent unilateral orchectomy and preventive radiotherapy. Eur J Obstet Gynecol Reprod Biol. 1998 Oct;80(2):247-50.	1998	Greece	English	retrospective	young	cancer, testicular	sperm morphology	physical therapy		radiation				16	sperm deformity and the sperm multiple anomalies index, impairment	no alteration		no	radiation	no tumor		2-	
2076: Hahn EW, Feingold SM, Simpson L, Batata M. Recovery from aspermia induced by low-dose radiation in seminoma patients. Cancer. 1982 Jul 15;50(2):337-40.	1982	USA	English	retrospective	young	cancer, testicular	semen	physical therapy		radiation		mean: 78.4 +/- 7.4 rad		14	azoospermia, induction	10 of 14 patients, if >65 rad; recovery after 30-80w		no				3	
2071: Martin RH, Hildebrand K, Yamamoto J, Rademaker A, Barnes M, Douglas G, Arthur K, Ringrose T, Brown IS. An increased frequency of human sperm chromosomal abnormalities after radiotherapy. Mutat Res. 1986 Jul;174(3):219-25	1986	USA	English	retrospective	19-47	cancer, testicular	sperm chromosomes	physical therapy		radiation		0.4-5.0 Gy		13	sperm chromosome abnormalities, increase	from 0 to 13%, significantly correlated to testicular radiation dose		no				3	
2129: Nader S, Schultz PN, Cundiff JH, Hussey DH, Samaan NA. Endocrine profiles of patients with testicular tumors treated with radiotherapy. Int J Radiat Oncol Biol Phys. 1983 Nov;9(11):1723-6.	1983		English	retrospective	young	cancer, testicular	hormones	physical therapy		radiation			20y ago	12	hormone levels, impairment	in 9 of 12 patients levels of FSH and LH, in 1 of 12 patients T level outside the normal ranges.		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2087: Sedlmayer F, Holtl W, Kozak W, Hawliczek R, Gebhart F, Gerber E, Joos H, Albrecht W, Pummer K, Kogelnik HD; Australian Uro-Oncology Group (AUO). Radiotherapy of testicular intraepithelial neoplasia (TIN): a novel treatment regimen for a rare disease. Int J Radiat Oncol Biol Phys. 2001 Jul 15;50(4):909-13.	2001	Austria	English	retrospective	young	testicular intraepithelial neoplasia (TIN)	hormones	physical therapy		radiation		13 Gy		9	hormone levels, impairment	FSH levels continued to increase 1 year after radiotherapy		no				3	
2067: Centola GM, Keller JW, Henzler M, Rubin P. Effect of low-dose testicular irradiation on sperm count and fertility in patients with testicular seminoma. J Androl. 1994 Nov-Dec;15(6):608-13.	1994	USA	English	retrospective	32.9 mean	cancer, testicular	semen	physical therapy		radiation		44 cGy		8	sperm parameters, impairment	At 3 months sperm count decreased to <10x10(6)/ml (range 4.4- 8.6x10(6) in all except one, who decreased from 189x10(6)/ml to 58x10(6)/ml.		no				3	
2093: Freund I, Zenzes MT, Muller RP, Potter R, Knuth UA, Nieschlag E. Testicular function in eight patients with seminoma after unilateral orchidectomy and radiotherapy. Int J Androl. 1987 Apr;10(2):447-55.	1987	Germany	English	retrospective	young	cancer, testicular	semen, hormones	physical therapy		radiation		15 to 157.5 rad		8	sperm parameters, impairment	decrease of sperm count, hamster-oocyte-penetration test normal		no				3	
2102: Pickles T, Graham P; Members of the British Columbia Cancer Agency Prostate Cohort Outcomes Initiative. What happens to testosterone after prostate radiation monotherapy and does it matter? J Urol. 2002 Jun;167(6):2448-52.	2002	Canada	English	retrospective	old	cancer, prostate	hormones	physical therapy		radiation		external beam radiation without neoadjuvant or adjuvant androgen ablation		666	testosterone level, decline	At 6 months decreased to 83% of baseline. Only 60% had recovery to their individual pretreatment level. Nadir dependent on radiation volume.		no				2+	
2112: Zagars GK, Pollack A. Serum testosterone levels after external beam radiation for clinically localized prostate cancer. Int J Radiat Oncol Biol Phys. 1997 Aug 1;39(1):85-9.	1997	USA	English	retrospective	old	cancer, prostate	hormones	physical therapy		radiation		external beam radiation		85	hormone levels, impairment	Pretreatment T levels 185 to 783 ng/dl. Postradiation 3-month T 163 ng/dl to 796 ng/dl (significant mean difference)		no				3	
2101: Basaria S, Lieb J 2nd, Tang AM, DeWeese T, Carducci M, Eisenberger M, Dobs AS. Long-term effects of androgen deprivation therapy in prostate cancer patients. Clin Endocrinol (Oxf). 2002 Jun;56(6):779-86.	2002	USA	English	prospective	old	cancer, prostate	hormones	physical therapy		radiation				58	hormone levels, impairment	severe by GnRH, lesser by radiotherapy, none in healthy men		no	radiation	GnRH agonist	healthy	2-	
2107: Daniell HW, Clark JC, Pereira SE, Niazi ZA, Ferguson DW, Dunn SR, Figueroa ML, Stratte PT. Hypogonadism following prostate-bed radiation therapy for prostate carcinoma. Cancer. 2001 May 15;91(10):1889-95.	2001	USA	English	retrospective	>70	cancer, prostate	hormones	physical therapy		radiation				33	hormone levels, impairment, 3 to 8y post treatment	decline of testosterone levels 27.3%, increase of LH levels 52.7% greater, increase of FSH levels 100%		no				3	
2130: Tomic R, Bergman B, Damber JE, Littbrand B, Lofroth PO. Effects of external radiation therapy for cancer of the prostate on the serum concentrations of testosterone, follicle-stimulating hormone, luteinizing hormone and prolactin. J Urol. 1983 Aug;130(2):287-9.	1983		English	retrospective	old	cancer, prostate	hormones	physical therapy		radiation		total tumor dose 63.5Gy		17	hormone levels, impairment	T levels lower, LH and FSH levels higher than in controls.T levels decreased 3 months after treatment, but pre-treatment values again 6 and 12 months after treatment.		no				3	
2134: Fleck H, Stahl F, Mau S. Suppression of testicular testosterone production by irradiation of the testis in prostatic cancer. Z Urol Nephrol. 1981 Jun;74(6):443-6.	1981	Germany	German	retrospective	68-78	cancer, prostate	hormones	physical therapy		radiation		20Gy		11	hormone levels, impairment	decrease of T levels to an average of 70,3% of the initial values		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2084: Mydlo JH, Lebed B. Does brachytherapy of the prostate affect sperm quality and/or fertility in younger men? Scand J Urol Nephrol. 2004;38(3):221-4	2004	USA	English	retro-spective	young	cancer, prostate	semen	physical therapy		radiation		total dose to the testis 18.88 cGy (125)I		4	sperm parameters, impairment	no significant alterations		no				3	This value is considered too low to have any significant effect on testicular tissues
2137: Seal US. FSH and LH elevation after radiation for treatment of cancer of the prostate. Invest Urol. 1979 Jan;16(4):278-80.	1979		English	retro-spective	old	cancer, prostate	hormones	physical therapy		radiation		n.g.		n.g.	hormone levels, impairment	increase of FSH and LH levels, no alteration of T levels at 3 and 12m		no				3	
2099: Dueland S, Guren MG, Olsen DR, Poulsen JP, Magne Tveit K. Radiation therapy induced changes in male sex hormone levels in rectal cancer patients. Radiother Oncol. 2003 Sep;68(3):249-53.	2003	Norway	English	retro-spective	65 mean	cancer, rectum	hormones	physical therapy		radiation		testicular dose 8.4 Gy		25	hormone levels, impairment	100% increase in serum FSH, 70% increase in LH, 25% reduction in testosterone levels.		no				3	
2097: Hermann RM, Henkel K, Christiansen H, Vorwerk H, Hille A, Hess CF, Schmidberger H. Testicular dose and hormonal changes after radiotherapy of rectal cancer. Radiother Oncol. 2005 Apr;75(1):83-8.	2005	Germany	English	pro-spective	55.2 mean	cancer, rectum	hormones	physical therapy		radiation		testicular dose 3.56 Gy (0.7-8.4 Gy)		11	hormone levels, impairment	Levels of LH increased to 350%, of FSH levels to 185%, of testosterone decreased to 78%.		no				3	
2082: Rosario PW, Barroso AL, Rezende LL, Padrao EL, Borges MA, Guimaraes VC, Purisch S. Testicular function after radioiodine therapy in patients with thyroid cancer. Thyroid. 2006 Jul;16(7):667-70.	2006	Brazil	English	retro-spective	all ages	cancer, thyroid	hormones	physical therapy		radiation		3.7-5.5 GBq (131)I		52	hormone levels, impairment	FSH levels increased in 31 of 52 patients, testosterone levels unaltered		no				3	
2088: Wichers M, Benz E, Palm- edo H, Biersack HJ, Grunwald F, Klingmuller D. Testicular function after radioiodine therapy for thyroid carcinoma. Eur J Nucl Med. 2000 May;27(5):503-7.	2000	Germany	English	retro-spective	23-73	cancer, thyroid	hormones	physical therapy		radiation		radioiodine dose 9.8+/- 0.89 GBq		25	hormone levels, impairment	FSH increased significantly to 21.32.4 IU/l after 6 months, decreased to 7.41.3 IU/l after 18 months. Inhibin B significantly decreased to 29.4 pg/ml after 6 months,increased to 154 pg/ml after 18 months. LH and testosterone were within the normal range during the whole study.		no				3	
2133: Handelsman DJ, Turtle JR. Testicular damage after radioactive iodine (I-131) therapy for thyroid cancer. Clin Endocrinol (Oxf). 1983 May;18(5):465-72.	1983	Australia	English	retro-spective	young	cancer, thyroid	hormones	physical therapy		radiation		(131)I		12	hormone levels, impairment	dose-dependent elevation of serum FSH levels		no				3	
2077: Handelsman DJ, Conway AJ, Donnelly PE, Turtle JR. Azoospermia after iodine-131 treatment for thyroid carcinoma. Br Med J. 1980 Dec 6;281(6254):1527.	1980	Australia	English	retro-spective	32	cancer, thyroid	semen	physical therapy		radiation		350mCi (131)I	single dose	1	spermatogenesis, impairment	azoospermia						3	
2108: Howell SJ, Radford JA, Smets EM, Shalet SM. Fatigue, sexual function and mood following treatment for haematological malignancy: the impact of mild Leydig cell dysfunction. Br J Cancer. 2000 Feb;82(4):789-93	2000		English	retro-spective	all ages	lymphoma and leukemia	hormones	physical therapy		radiation				66	fatigue, mood and sexual function by questionnaire; decrease	no significant differences between men with normal and low T levels							
2119: Feyer P, Tittlbach O, Hoffmann FA, Kubel M, Helbig W. Endocrine dysfunction after total body irradiation and bone marrow transplantation. Folia Haematol Int Mag Klin Morphol Blutforsch. 1989;116(3-4):547-52.	1989	Germany	English	retro-spective	young	lymphoma and leukemia	hormones	physical therapy		radiation		total body irradiation and bone marrow transplantation		16	hormone levels, impairment	T and LH low levels, in the posttransplant period return of LH levels to the normal range, but not the sexual steroids.		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2118: Kinsella TJ, Trivette G, Rowland J, Sorace R, Miller R, Fraass B, Steinberg SM, Glatstein E, Sherins RJ. Long-term follow-up of testicular function following radiation therapy for early-stage Hodgkin's disease. J Clin Oncol. 1989 Jun;7(6):718-24.	1989	USA	English	retrospective	young	Hodgkin disease	hormones	physical therapy		radiation		testicular dose 6-70cGy		17	hormone levels, impairment	In patients receiving more than 20 cGy, increase in serum FSH values following up to 6m, return to normal within 24m. No significant changes in LH and T. 2 patients transient oligospermia with complete recovery by 18 months following treatment		no				3	
2091: Monteil M, Rousseaux S, Chevrete E, Pelletier R, Cozzi J, Sele B. Increased aneuploid frequency in spermatozoa from a Hodgkin's disease patient after chemotherapy and radiotherapy. Cytogenet Cell Genet. 1997;76(3-4):134-8	1997	France	English	retrospective	young	Hodgkin disease	FISH of sperm chromosomes	physical therapy		radiation				1	sperm aneuploidy rates of chromosomes X, Y, 1, 6, 11, increased	day 0 as well as at day 38		no				3	Lymphoma itself affect spermatogenic cell divisions
2081: Asbjornsen G, Molne K, Klepp O, Aakvaag A. Testicular function after radiotherapy to inverted,Y' field for malignant lymphoma. Scand J Haematol. 1976 Aug;17(2):96-100.	1976	Sweden	English	retrospective	young	lymphoma, malignant	semen	physical therapy		radiation		inverted Y field, mantle field		9	sperm count, decrease	8 men sperm count zero or low. FSH levels elevated, 3 pregnancies in the female partner		no				3	
2069: Pryzant RM, Meistrich ML, Wilson G, Brown B, McLaughlin P. Long-term reduction in sperm count after chemotherapy with and without radiation therapy for non-Hodgkin's lymphomas. J Clin Oncol. 1993 Feb;11(2):239-47. Houston	1993	USA	English	retrospective	29 median	non-Hodgkin lymphoma	semen	physical therapy		radiation		2.46-5.3 Gy + cyclophosphamide, doxorubicine, vincristine, bleomycin		7	sperm parameters, impairment	0-44x10(6)		no				3	
2124: Shapiro E, Kinsella TJ, Makuch RW, Fraass BA, Glatstein E, Rosenberg SA, Sherins RJ. Effects of fractionated irradiation of endocrine aspects of testicular function. J Clin Oncol. 1985 Sep;3(9):1232-9.	1985	USA	English	retrospective	14-67	soft tissue sarcoma	hormones	physical therapy		radiation		testicular dose 1 to 2,500 rad		27	hormone levels, impairment	Only patients receiving more than 200 rad significant LH changes. No significant changes in total testosterone levels.		no				3	
2094: Martin RH, Rademaker A, Barnes M, Arthur K, Ringrose T, Douglas G. A prospective serial study of the effects of radiotherapy on semen parameters, and hamster egg penetration rates. Clin Invest Med. 1985;8(3):239-43.	1985	USA	English	retrospective	young	cancer	semen	physical therapy		radiation		0.4 to 5.0 Gy		11	sperm parameters, impairment	At 3 and 12 months post-radiotherapy 8/11 men were azoospermic, by 24 months 8/11 were producing sperm. Hamster-oocyte-penetration >15%.		no				3	
2121: Snyder PJ, Fowble BF, Schatz NJ, Savino PJ, Gennarelli TA. Hypopituitarism following radiation therapy of pituitary adenomas. Am J Med. 1986 Sep;81(3):457-62.	1986	USA	English	retrospective	young	pituitary adenoma	hormones	physical therapy		radiation				35	hormone levels, impairment	deficiencies of adrenal, thyroid, and gonadal function in 67, 55, and 67% of the patients; in patients only surgically treated deficiencies in 13, 13, and 0%.		no	pituitary radiation	surgical intervention		2-	
2139: Aloia JF, Archambeau JO. Hypopituitarism following pituitary irradiation for acromegaly. Horm Res. 1978;9(4):201-7.	1978		English	retrospective	young	acromegaly	hormones	physical therapy		radiation		pituitary dose 5,500 rad		8	hormone levels, impairment	low T levels in 1/6 patients		no				3	
2061: Ramsewak S, Naraynsingh A, Kuruvilla A, Duffy S. Successful pregnancy by intracytoplasmic sperm injection after radiotherapy-induced azoospermia. West Indian Med J. 1999 Dec;48(4):240-1.	1999	Trinidad	English	retrospective	young	pineal gland germinoma	IVF outcome	physical therapy		radiation		n.g.		1	pregnancy in the female partner	ICSI was successful						3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2054: Byrne J, Fears TR, Mills JL, Zeltzer LK, Sklar C, Meadows AT, Reaman GH, Robison LL. Fertility of long-term male survivors of acute lymphoblastic leukemia diagnosed during childhood. <i>Pediatr Blood Cancer</i> . 2004 Apr;42(4):364-72.	2004	USA	English	retrospective	young	acute lymphoblastic leukemia (ALL) in childhood	fertility	physical therapy		radiation		various		213; 145	fertility disorders, increased	relative fertility (RF) = 0.95, 95% (CI 0.63-1.43), with high dose (24 cGy) cranial radiotherapy reduced fertility RR = 0.09, 95% (CI 0.01-0.82)		no	radiation	no radiation		2++	
2122: Voorhess ML, Brecher ML, Glicksman AS, Jones B, Harris M, Krischer J, Boyett J, Forman E, Freeman AI. Hypothalamic-pituitary function of children with acute lymphocytic leukemia after three forms of central nervous system prophylaxis. A retrospective study. <i>Cancer</i> . 1986 Apr 1;57(7):1287-91.	1986		English	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	hormones	physical therapy		radiation		2400 rad cranial + methotrexate intrathecal		93	hormone levels, impairment	no significant alterations		no	radiation +methotrexate	methotrexate		2-	
2115: Siimes MA, Lie SO, Andersen O, Marky I, Rautonen J, Hertz H. Prophylactic cranial irradiation increases the risk of testicular damage in adult males surviving ALL in childhood. <i>Med Pediatr Oncol</i> . 1993;21(2):117-21. Finland	1993	Finland	English	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	pubertal maturation	physical therapy		radiation		prophylactic cranial radiation		41	pubertal stages, development	decrease of 5.7 (95% CI 1.5-9.9) cm in height, decrease of 4.8 (95% CI 0.3-9.2) ml in testicle size. No loss in sexual activity.		no				3	
2127: Carrascosa A, Audi L, Ortega JJ, Javier G, Toran N. Hypothalamo-hypophyseal-testicular function in prepubertal boys with acute lymphoblastic leukemia following chemotherapy and testicular radiotherapy. <i>Acta Paediatr Scand</i> . 1984 May;73(3):364-71.	1984		English	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	hormones	physical therapy		radiation		testicular dose 2,000 rad		28	hormone levels, impairment	basal and stimulated FSH and LH levels increased, T response to hCG low.		no	radiation	radiation +chemotherapy		2-	
2120: Brauner R, Caltabiano P, Rappaport R, Leverger G, Schaison G. Leydig cell insufficiency after testicular irradiation for acute lymphoblastic leukemia. <i>Horm Res</i> . 1988;30(2-3):111-4.	1988	France	English	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	hormones	physical therapy		radiation		testicular irradiation 24 Gy		21	hormone levels, impairment	low T levels and response to hCG, increase in LH levels in 19/21 patients		no				3	
2098: Frisk P, Arvidson J, Gustafsson J, Lonnerholm G. Pubertal development and final height after autologous bone marrow transplantation for acute lymphoblastic leukemia. <i>Bone Marrow Transplant</i> . 2004 Jan;33(2):205-10.	2004	Sweden	English	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	pubertal maturation	physical therapy		radiation		bone marrow transplantation + total body irradiation		17	pubertal stages, development	hypogonadism in all boys		no				3	
2117: Castillo LA, Craft AW, Kernahan J, Evans RG, Aynsley-Green A. Gonadal function after 12-Gy testicular irradiation in childhood acute lymphoblastic leukaemia. <i>Med Pediatr Oncol</i> . 1990;18(3):185-9.	1990	UK	English	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	hormones, semen	physical therapy		radiation		testicular dose 12-24Gy		15	hormone levels, impairment	normal in all boys. Azospermia in all boys		no				3	
2131: Brauner R, Czernichow P, Cramer P, Schaison G, Rappaport R. Leydig-cell function in children after direct testicular irradiation for acute lymphoblastic leukemia. <i>N Engl J Med</i> . 1983 Jul 7;309(1):25-8.	1983		English	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	hormones	physical therapy		radiation				12	hormone levels, impairment	T levels low more than four years after testicular irradiation, diminished testicular volume		no				3	
2128: Leiper AD, Grant DB, Chessells JM. The effect of testicular irradiation on Leydig cell function in prepubertal boys with acute lymphoblastic leukaemia. <i>Arch Dis Child</i> . 1983 Nov;58(11):906-10.	1983		English	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	hormones	physical therapy		radiation		testicular dose 2,400-rad		11	hormone levels, impairment	stimulated FSH and LH levels increased, T basal and response to hCG low.		no				3	

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2132: Bramswig JH, Schellong G, Nieschlag E. Pituitary-gonadal function following therapy of testicular relapse in boys with acute lymphoblastic leukemia, Klin Padiatr. 1983 May-Jun;195(3):176-80.	1983	Germany	German	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	hormones	physical therapy		radiation		1,100-3,000 rad		9	hormone levels, impairment	In the age of 12 years, elevated basal and/or stimulatedLH- and FSH-values were elevated. T response to HCG-test only in patients with gonadal dose of 1,100 and 1,500 rads. No response in doses of 2,400 and 3,000 rads.		no				3	
2125: Blatt J, Sherins RJ, Niebrugge D, Bleyer WA, Poplack DG. Leydig cell function in boys following treatment for testicular relapse of acute lymphoblastic leukemia. J Clin Oncol. 1985 Sep;3(9):1227-31.	1985		English	retrospective	young	acute lymphoblastic leukemia (ALL) in childhood	hormones	physical therapy		radiation		testicular dose 2,400-rad		7	hormone levels, impairment	3/4 boys with bilateral lesion had delayed sexual maturation, elevated FSH and LH levels, low testosterone levels.		no				3	
2126: Shalet SM, Horner A, Ahmed SR, Morris-Jones PH. Leydig cell damage after testicular irradiation for lymphoblastic leukaemia. Med Pediatr Oncol. 1985;13(2):65-8.	1985	UK	English	retrospective	prepuberal	acute lymphoblastic leukemia (ALL) in childhood	hormones	physical therapy		radiation		testicular radiation		7	hormone levels, impairment	T response to hCG low, but normal basal T levels		no				3	
2106: Schmiegelow M, Lassen S, Poulsen HS, Schmiegelow K, Hertz H, Andersson AM, Skakkebaek NE, Muller J. Gonadal status in male survivors following childhood brain tumors. J Clin Endocrinol Metab. 2001 Jun;86(6):2446-52.	2001	Denmark	English	retrospective	9 mean	cancer, brain, not including hypothalamohypophyseal region, in childhood	hormones	physical therapy		radiation				30	hormone levels, impairment in age >18y	FSH significantly higher than in controls, inhibin significantly lower, testicular volume lower		no				3	
2111: Lannering B, Jansson C, Rosberg S, Albertsson-Wikland K. Increased LH and FSH secretion after cranial irradiation in boys. Med Pediatr Oncol. 1997 Oct;29(4):280-7.	1997	Sweden	English	retrospective	prepuberal	cancer, brain, not including hypothalamohypophyseal region, in childhood	hormones	physical therapy		radiation		cranial		13	hormone levels, impairment in puberty	FSH and LH levels increased, T levels normal		no				3	
2078: Shalet SM, Beardwell CG, Jacobs HS, Pearson D. Testicular function following irradiation of the human prepubertal testis. Clin Endocrinol (Oxf). 1978 Dec;9(6):483-90.	1978	UK	English	retrospective	17-36	nephroblastoma during childhood	semen	physical therapy		radiation		testes: 268 to 983 rad		10	sperm parameters, impairment	8 men sperm count 0 to 5.6 million/ml, 7 of them seven of whom elevated FSH level.		no				3	
2138: Shalet SM, Beardwell CG, Jacobs HS, Pearson D. Testicular function following irradiation of the human prepubertal testis. Clin Endocrinol (Oxf). 1978 Dec;9(6):483-90.	1978	UK	English	retrospective	prepuberal	nephroblastoma during childhood	hormones	physical therapy		radiation				10	hormone levels, impairment	8 men had low sperm count (0 to 5.6 million/ml), 7 had elevated FSH level. 1 men showed raised LH level and low T level.		no				3	
2059: Thomson AB, Campbell AJ, Irvine DC, Anderson RA, Kelnar CJ, Wallace WH. Semen quality and spermatozoal DNA integrity in survivors of childhood cancer: a case-control study. Lancet. 2002 Aug 3;360(9330):361-7.	2002	UK	English	retrospective	young	cancer, in childhood	semen	physical therapy		radiation		various		33;66	sperm parameters, impairment	sperm count significantly lower than in controls, no differences in DNA integrity, FSH levels higher,		no	radiation	no radiation		2+	
2114: Didi M, Morris-Jones PH, Gattamaneni HR, Shalet SM. Pubertal growth in response to testosterone replacement therapy for radiation-induced Leydig cell failure. Med Pediatr Oncol. 1994;22(4):250-4.	1994	UK	English	retrospective	prepuberal	cancer, in childhood	pubertal maturation	physical therapy		radiation				8	pubertal stages, development	mean adult standing height, 167.5 +/- 9.9 cm, mean adult leg length, 80.8 +/- 6.2cm not significantly different from the normal boys, mean adult sitting height, 86.7+/.4.8 cm shorter than in normals boys		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2051: Ronckers CM, Verduijn PG, Land CE, Hayes RB, Stovall M, van Leeuwen FE. No convincing evidence for a causal relationship between childhood nasopharyngeal radium irradiation and head-neck tumors or hormone-related disorders later in life; a retrospective cohort study. Ned Tijdschr Geneeskd. 2004 Sep 4;148(36):1775-80.	2004	The Netherlands	Dutch	retrospective	young	nasopharyngeal radium irradiation for hypertrophic adenoid or otitis media serosa	fertility	physical therapy		radiation		2.75Gy for nasopharynx		5358; 5265	fertility disorders, increased	slightly more fertility disorders than men in the control group (OR: 1.4; 1.0-2.1)		no	radiation	no radiation		2++	
357: Hembree WC, Nagler HM, Fang JS, Myles EL, Jagiello GM. Infertility in a patient with abnormal spermatogenesis and in utero DES exposure. Int J Fertil. 1988 May-Jun;33(3):173-7.	1988	USA	English	case report	young	spermatogenic dysfunction	histology, chromosome synapsis	endocrine therapy	L02	diethylstilbestrol in utero	L02AA01			1	spermatogenesis, impairment	meiotic dysruption		no				3	
798. Toppari J, Larsen JC, Christianse P et al: Male reproductive health and environmental xenoestrogens. Environ Health Perspect 1996;104 (Suppl. 4), 741-803	1996	Finland	English	review	young	abortion, threatening in the mother	genital malformations in the sons	endocrine therapy	L02	diethylstilbestrol	L02AA01				testicular cancer, hypospadias, cryptorchidism	significant increase		no				3	
257: Delemarre-Van de Waal HA. Induction of testicular growth and spermatogenesis by pulsatile, intravenous administration of gonadotrophin-releasing hormone in patients with hypogonadotrophic hypogonadism. Clin Endocrinol (Oxf). 1993 May;38(5):473-80.	1998	The Netherlands	English	prospective	young	idiopathic hypogonadotropic hypogonadism (IHH)	sperm, testicular volume	endocrine therapy	L02	GnRH + hCG	L02AE	2-20 mg GnRH puls	12m	38	gonadotropin levels, increase	in 35 of 38 patients		no				3	
400: Spratt DJ, Finkelstein JS, O'Dea LS, Badger TM, Rao PN, Campbell JD, Crowley WF Jr. Long-term administration of gonadotropin-releasing hormone in men with idiopathic hypogonadotropic hypogonadism. A model for studies of the hormone's physiologic effects. Ann Intern Med. 1986 Dec;105(6):848-55.	1986	USA	English	prospective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	endocrine therapy	L02	GnRH pulsatile	L02AE		36m	23	spermatogenesis, maturation	in 20 of 23 patients mature spermatozoa in semen		no				3	
76: Christiansen P, Skakkebaek NE. Pulsatile gonadotropin-releasing hormone treatment of men with idiopathic hypogonadotropic hypogonadism. Horm Res. 2002;57(1-2):32-6.	2002	Denmark	English	prospective	young	idiopathic hypogonadotropic hypogonadism (IHH)	hormones	endocrine therapy	L02	GnRH pulsatile	L02AE		24m	11	pregnancy induction	7 of 11 patients induced pregnancy		no				3	
398: Niles NL, McCorkell SJ, Woodhouse NJ. Male hypothalamic hypogonadism: induction of spermatogenesis by subcutaneous pulsatile gonadotrophin-releasing hormone. Horm Res. 1987;25(3):152-9.	1987		English	prospective	young	idiopathic hypogonadotropic hypogonadism (IHH)	hormones	endocrine therapy	L02	GnRH pulsatile	L02AE		74w	6	spermatogenesis, maturation	in 3 of 6 patients		no				3	
524: Hoffman AR, Crowley WF Jr. Induction of puberty in men by long-term pulsatile administration of low-dose gonadotropin-releasing hormone. N Engl J Med. 1982 Nov 11;307(20):1237-41.	1982		English	prospective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen, hormones	endocrine therapy	L02	GnRH pulsatile	L02AE		43w	6	spermatogenesis, maturation	in all patients		no				3	
426: Klingmüller D, Schweikert HU. Maintenance of spermatogenesis by intranasal administration of gonadotropin-releasing hormone in patients with hypothalamic hypogonadism. J Clin Endocrinol Metab. 1985 Nov;61(5):868-72.	1985	Germany	English	prospective	young	idiopathic hypogonadotropic hypogonadism (IHH)	hormones	endocrine therapy	L02	GnRH	L02AE		6m	3	spermatogenesis, maturation	in all patients after 161 days		no				3	

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489: Skarin G, Nillius SJ, Wide L. Long-term subcutaneous pulsatile low dose LH-RH administration for treatment of infertile men with secondary hypogonadotropic hypogonadism. Ups J Med Sci. 1984;89(1):81-90.	1984		English	pro-spective	young	hypogonadism, secondary	semen	endocrine therapy	L02	GnRH pulsatile	L02AE		250d	3	pregnancy, induction	2 of 3 patients induced pregnancies after 181d		no				3	
351: Blumenfeld Z, Makler A, Frisch L, Brandes JM. Induction of spermatogenesis and fertility in hypogonadotropic azoospermic men by intravenous pulsatile gonadotropin-releasing hormone (GnRH). Gynecol Endocrinol. 1988 Jun;2(2):151-64.	1988	Israel	English	pro-spective	young	idiopathic hypogonadotropic hypogonadism (IHH)	semen	endocrine therapy	L02	GnRH pulsatile	L02AE		6m	2	spermatogenesis, maturation	after 42 days		no				3	
377: Oppermann D, Happ J, Mayr WR. Stimulation of spermatogenesis and biological paternity by intranasal (low dose) gonadotropin-releasing hormone (GnRH) in a male with Kallmann's syndrome: intraindividual comparison of GnRH and gonadotropins for stimulation of spermatogenesis. J Clin Endocrinol Metab. 1987 Nov;65(5):1060-6.	1987	Germany	English	case report	28	idiopathic hypogonadotropic hypogonadism (IHH)	hormones	endocrine therapy	L02	GnRH pulsatile	L02AE			1	spermatogenesis, recovery	conception on day 162		no				3	
325: Fok AC, Tsakok FH, Sum CF, Cheah JS. Restoration of spermatogenesis with pulsatile gonadotrophin releasing hormone therapy in hypogonadotropic hypogonadism of traumatic etiology. Aust N Z J Med. 1989 Aug;19(4):354-7.	1989	Australia	English	case report	36	hypogonadism, traumatic	semen	endocrine therapy	L02	GnRH pulsatile	L02AE		15m	1	spermatogenesis, recovery	complete		no				3	
728: Schwarzstein L, Aparicio NJ, Turner D, Calamera JC, Mancini R, Schally AV. Use of synthetic luteinizing hormone-releasing hormone in treatment of oligospermic men: a preliminary report. Fertil Steril. 1975 Apr;26(4):331-6.	1975		English	pro-spective	24-39	infertility	semen	endocrine therapy	L02	GnRH pulsatile	L02AE	500 mg/d	135d	4	spermatogenesis, improvement	in 2 of 4 patients		no				3	
2105: Shahidi M, Norman AR, Gadd J, Huddart RA, Horwich A, Dearnaley DP. Recovery of serum testosterone, LH and FSH levels following neoadjuvant hormone cytoreduction and radical radiotherapy in localized prostate cancer. Clin Oncol (R Coll Radiol). 2001;13(4):291-5.	2001	UK	English	retro-spective	old	prostate cancer	hormones	endocrine therapy	L02	GnRH agonist	L02AE		6m	419	hormone levels, impairment	T levels return to normal after cessation, LH levels remain increased		no				3	
2103: Pickles T, Agranovich A, Berthelet E, Duncan GG, Keyes M, Kwan W, McKenzie MR, Morris WJ; British Columbia Cancer Agency, Prostate Cohort Outcomes Initiative. Testosterone recovery following prolonged adjuvant androgen ablation for prostate carcinoma. Cancer. 2002 Jan 15;94(2):362-7.	2002	Canada	English	retro-spective	old	prostate cancer	hormones	endocrine therapy	L02	GnRH agonist	L02AE		3y	276	testosterone level, increase after cessation	97% recovered normal testosterone levels (10nmol/L), and 93% recovered levels of at least 5nmol/L. Median time to testosterone recovery was 10 months.		no	GnRH 1m depot	GnRH 3m depot		2+	
230: Brennemann W, Brensing KA, Leipner N, Boldt I, Klingmuller D. Attempted protection of spermatogenesis from irradiation in patients with seminoma by D-Tryptophan-6 luteinizing hormone releasing hormone. Clin Investig. 1994 Nov;72(11):838-42.	1994	Germany	English	pro-spective	young	testicular cancer, radiation therapy	hormones, semen	endocrine therapy	L02	GnRH agonist	L02AE		6w	20	gonadotropin levels, decrease	total suppression, recovery independent of GnRH treatment		no	GnRH agonist	no hormonal therapy		3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
371: Lunglmayr G, Girsch E, Meixner EM, Viehberger G, Bieglmayer C. Effects of long term GnRH analogue treatment on hormone levels and spermatogenesis in patients with carcinoma of the prostate. Urol Res. 1988;16(4):315-9.	1988	Austria	English	pro-spective	old	prostate cancer	testicular histology	endocrine therapy	L02	GnRH agonist	L02AE		10m	16	spermatogenesis, impairment and maturation arrest	in all patients		no				3	
378: Huhtaniemi I, Nikula H, Parvinen M, Rannikko S. Pituitary-testicular function of prostatic cancer patients during treatment with a gonadotropin-releasing hormone agonist analog. II. Endocrinology and histology of the testis. J Androl. 1987 Nov-Dec;8(6):363-73.	1987	Finland	English	pro-spective	old	prostate cancer	T production in-vitro	endocrine therapy	L02	GnRH agonist	L02AE			14	testosterone production, decrease	by 94%		no				3	
370: Giberti C, Barreca T, Martorana G, Truini M, Franceschini R, Rolandi E, Giuliani L. Hormonal pattern and testicular histology in patients with prostatic cancer after long-term treatment with a gonadotropin-releasing hormone agonist analogue. Eur Urol. 1988;15(1-2):125-7.	1988	Italy	English	pro-spective	old	prostate cancer	testicular histology	endocrine therapy	L02	GnRH agonist	L02AE		32m	7	spermatogenesis, impairment	in all men		no				3	
162: Meistrich ML. Hormonal stimulation of the recovery of spermatogenesis following chemo- or radiotherapy. Review article. APMIS. 1998 Jan;106(1):37-45; discussion 45-6.	1998	USA	English	review	young	cancer	semen	endocrine therapy	L02	GnRH	L02AE				spermatogenesis, recovery after cancer therapy	no improvement by GnRH						4	
255: Bagatell CJ, Matsumoto AM, Christensen RB, Rivier JE, Bremner WJ. Comparison of a gonadotropin releasing-hormone antagonist plus testosterone (T) versus T alone as potential male contraceptive regimens. J Clin Endocrinol Metab. 1993 Aug;77(2):427-32.	1993	USA	English	pro-spective	young	contraception	azoospermic	endocrine therapy	L02	GnRH antagonist + T	L02AE		20w	19	azoospermia, induction	in 7 of 10 men		no	T 200mg/w + GnRH 100mg/kg/d	T alone		2-	
148: Swerdloff RS, Bagatell CJ, Wang C, Anawalt BD, Berman N, Steiner B, Bremner WJ. Suppression of spermatogenesis in man induced by Nal-Glu gonadotropin releasing hormone antagonist and testosterone enanthate (TE) is maintained by TE alone. J Clin Endocrinol Metab. 1998 Oct;83(10):3527-33.	1998	USA	English	pro-spective	21-41	contraception	semen	endocrine therapy	L02	GnRH antagonist + T	L02AE	T 100mg/w + GnRH 10mg/w	24w	15	azoospermia, induction	in 10 of 15 men		no				3	
472: Rabin D, Evans RM, Alexander AN, Doelle GC, Rivier J, Vale W, Liddle GW. Heterogeneity of sperm density profiles following 20-week therapy with high-dose LHRH analog plus testosterone. J Androl. 1984 May-Jun;5(3):176-80.	1984	USA	English	pro-spective	young	contraception	semen, hormones	endocrine therapy	L02	GnRH agonist + T	L02AE		20w	8	spermatogenesis, impairment	in all men		no				3	
553: Linde R, Doelle GC, Alexander N, Kirchner F, Vale W, Rivier J, Rabin D. Reversible inhibition of testicular steroidogenesis and spermatogenesis by a potent gonadotropin-releasing hormone agonist in normal men: an approach toward the development of a male contraceptive. N Engl J Med. 1981 Sep 17;305(12):663-7.	1981		English	pro-spective	young	contraception	semen	endocrine therapy	L02	GnRH agonist	L02AE		10w	8	sperm count, decrease	to 70% of basal sperm count		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
383: Bhasin S, Yuan QX, Steiner BS, Swerdloff RS. Hormonal effects of gonadotropin-releasing hormone (GnRH) agonist in men: effects of long term treatment with GnRH agonist infusion and androgen. J Clin Endocrinol Metab. 1987 Sep;65(3):568-74.	1987	USA	English	pro-spective	young	contra-ception	semen	endocrine therapy	L02	GnRH agonist + T	L02AE		16w	7	sperm count, decrease	by 93% in week 16		no				3	
447: Bhasin S, Heber D, Steiner BS, Handelsman DJ, Swerdloff RS. Hormonal effects of gonadotropin-releasing hormone (GnRH) agonist in the human male. III. Effects of long term combined treatment with GnRH agonist and androgen. J Clin Endocrinol Metab. 1985 May;60(5):998-1003.	1985	USA	English	pro-spective	young	contra-ception	semen	endocrine therapy	L02	GnRH agonist + T	L02AE	200mg/d	16w	7	sperm count, decrease	by 83%		no				3	
498: Doelle GC, Alexander AN, Evans RM, Linde R, Rivier J, Vale W, Rabin D. Combined treatment with an LHRH agonist and testosterone in man. Reversible oligozoospermia without impotence. J Androl. 1983 Sep-Oct;4(5):298-302.	1983	The Netherlands	English	pro-spective	young	contra-ception	semen	endocrine therapy	L02	GnRH agonist + T	L02AE		20w	6	sperm count, decrease	from 76.7 x 10(6)/ml to a mean nadir of 12.3 x 10(6)/ml		no				3	
256: Bastias MC, Kamijo H, Pavlou SN. Sperm motion parameters after suppression of spermatogenesis with a gonadotropin-releasing hormone antagonist plus testosterone supplementation. Fertil Steril. 1993 Jun;59(6):1261-5.	1993	USA	English	pro-spective	young	contra-ception	semen, evaluation by CASA	endocrine therapy	L02	GnRH antagonist	L02AE		20w	6	sperm motility, CASA parameters, alteration	no significant alteration of motility parameters		no				3	
329: Krause W, Pfluger KH. Treatment with the gonadotropin-releasinghormone agonist busere- lin to protect spermatogenesis against cytotoxic treatment in young men. Andrologia. 1989 May-Jun;21(3):265-70.	1989	Germany	English	pro-spective	young	cancer	semen	endocrine therapy	L02	buserelin	L02AE01		7d prior to cytotoxic therapy	20	azoospermia, induction	all but one like in cytotoxic therapy alone		no				3	
381: Hadziselimovic F, Senn E, Bandhauer K. Effect of treatment with chronic gonadotro- pin releasing hormone agonist on human testis. J Urol. 1987 Oct;138(4 Pt 2):1048-50.	1987	Switzer-land	English	retro-spective	old	prostate cancer	testicular histology	endocrine therapy	L02	buserelin	L02AE01		138m	12	spermatogenesis, impairment	in 50% SCOS, in 92% Leydig cell atrophy		no	buserelin alone	buserelin + flutamide		2-	
341: Properzi G, Francavilla S, Vicentini C, Cordeschi G, Galassi P, Paradiso Galatioto G, Miano L. Testicular changes after treatment with a GnRH analog (buserelin) in association with cyproterone acetate in men with prostatic cancer. Eur Urol. 1989;16(6):426-32.	1989	Italy	English	pro-spective	53-78	prostate cancer	testicular histology	endocrine therapy	L02	buserelin	L02AE01		96w	12	spermatogenesis, impairment	11 of 12		no				3	
44: Huhtaniemi I, Nikula H, Parvinen M, Rannikko S. Pituitary-testicular function of prostatic cancer patients during treatment with a gonadotro- pin-releasing hormone agonist analog. II. Endocrinology and histology of the testis. J Androl. 1987 Nov-Dec;8(6):363-73.	1987	Finland	English	retro-spective	old	prostate cancer	testicular histology	endocrine therapy	L02	buserelin	L02AE01	1800mg/d	6m	7	spermatogenesis, suppression	highly in all patients		no				3	
416: Frick J, Aulitzky W. Effects of a potent LHRH-agonist on the pituitary gonadal axis with and without testosterone substitu- tion. Urol Res. 1986;14(5):261-4.	1986	Austria	English	pro-spective	young	contra-ception	semen	endocrine therapy	L02	buserelin	L02AE01		5m	15	sperm count, decrease	in all men		yes	3x50mg/w	3x100mg/w	3x200mg/w + 5mg fluoxymester- one	1-	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
399: Bouchard P, Garcia E. Influence of testosterone substitution on sperm suppression by LHRH agonists. Horm Res. 1987;28(2-4):175-80.	1987	Finland	English	pro-spective	young	contraception	sperm	endocrine therapy	L02	buserelin	L02AE01		30w	10	spermatogenesis, impairment	4x azoospermia in group with oral T		yes	buserelin depot + 125mg/m T i.m.	buserelin depot + 120mg/d T orally		1-	
49. Smith JA Jr, Urry RL. Testicular histology after prolonged treatment with a gonadotropin-releasing hormone analogue. J Urol. 1985 Apr;133(4):612-4	1985	USA	English	retrospective	46-82	prostate cancer	testicular histology	endocrine therapy	L02	leuprolide	L02AE02	1-10mg/d	24m	12	spermatogenesis, impairment; Leydig cell, hypoplasia	in all patients		no				3	
461: Rajfer J, Swerdloff RS, Heber DM. Testicular histology following chronic gonadotropin-releasing hormone agonist treatment. Fertil Steril. 1984 Nov;42(5):765-71.	1984	USA	English	pro-spective	old	prostate cancer	testicular histology	endocrine therapy	L02	leuprolide	L02AE02		12m	4	spermatogenesis, impairment; Leydig cell, hypoplasia	in all patients after 1 year of treatment		no				3	
46: Johansen TE, Og Reid P, Kjellevoid K, Blom P. Testicular histology after treatment with LH-RH analogue for carcinoma of the prostate. Br J Urol. 1990 Apr;65(4):376-8.	1990	Norway	English	retrospective	old	prostate cancer	testicular histology	endocrine therapy	L02	goserelin	L02AE03	n.g.	17m	16	spermatogenesis, suppression	tubular atrophy in all patients		no				3	
931: Boccardo F, Rubagotti A, Battaglia M, Di Tonno P, Selvaggi FP, Conti G, Comeri G, Bertacchini A, Martorana G, Galassi P, Zattoni F, Macchiarella A, Siragusa A, Muscas G, Durand F, Potenzoni D, Manganelli A, Ferraris V, Montefiore F. Evaluation of tamoxifen and anastrozole in the prevention of gynecomastia and breast pain induced by bicalutamide monotherapy of prostate cancer. J Clin Oncol. 2005 Feb 1;23(4):808-15.	2005	Italy	English	pro-spective, randomized	old	prostate cancer, treatment with bicalutamide	breast swelling	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	48w	114	gynecomastia and breast pain, development	10% of men treated with tamoxifen + bicalutamide, 73% of placebo + bicalutamide	no differences in sexual function	yes	tamoxifen 20mg/d + bicalutamide 150mg/d	astronazol 1mg/d + bicalutamide 150mg/d	placebo + bicalutamide 150mg/d	1+	
930: Saltzstein D, Sieber P, Morris T, Gallo J. Prevention and management of bicalutamide-induced gynecomastia and breast pain: randomized endocrinologic and clinical studies with tamoxifen and anastrozole. Prostate Cancer Prostatic Dis. 2005;8(1):75-83.	2005	USA	English	pro-spective, randomized	old	prostate cancer, treatment with bicalutamide	breast swelling	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d		107	gynecomastia and breast pain, development	reduction in tamoxifen co-treated groups		yes	tamoxifen 20mg/d + bicalutamide 150mg/d	astronazol 1mg/d + bicalutamide 150mg/d	placebo + bicalutamide 150mg/d	1+	
932: Derman O, Kanbur NO, Kutluk T. Tamoxifen treatment for pubertal gynecomastia. Int J Adolesc Med Health. 2003 Oct-Dec;15(4):359-63.	2003	Turkey	English	retrospective	young	gynecomastia	breast swelling	endocrine therapy	L02	tamoxifen	L02BA01	n.g.	n.g.	37	gynecomastia, reduction	in all patients	no side effects	no				3	
934: Li CP, Lee FY, Hwang SJ, Chang FY, Lin HC, Kuo BI, Chu CJ, Lee SD. Treatment of mastalgia with tamoxifen in male patients with liver cirrhosis: a randomized crossover study. Am J Gastroenterol. 2000 Apr;95(4):1051-5.	2000	China	English	pro-spective, crossover	old	liver cirrhosis	breast swelling	endocrine therapy	L02	tamoxifen	L02BA01	2x20mg/d	1m	16	gynecomastia and breast pain, reduction	in 14 of 16 patients	no side effects	yes	tamoxifen 2X20mg/d	placebo		1-	
933: Novoa FJ, Boronat M, Carrillo A, Tapia M, Diaz-Cremades J, Chirino R. Effects of tamoxifen on lipid profile and coagulation parameters in male patients with pubertal gynecomastia. Horm Res. 2002;57(5-6):187-91.	2002	Spain	English	retrospective	young	gynecomastia	serum lipids	endocrine therapy	L02	tamoxifen	L02BA01	10mg/d	3m	15	serum lipid proteins, alteration	none in all patients		no				3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
900: Spijkstra JJ, Spinder T, Gooren L, van Kessel H. Divergent effects of the antiestrogen tamoxifen and of estrogens on luteinizing hormone (LH) pulse frequency, but not on basal LH levels and LH pulse amplitude in men. Clin Endocrinol Metab. 1988 Feb;66(2):355-60.	1988	The Netherlands	English	pro-spective	young	healthy	hormones	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	6w	13	LH pulsatility, increase	levels and pulse frequency		no				3	
902: van Bergeijk L, Gooren LJ, van Kessel H, Sassen AM. Effects of continuous LHRH infusion on plasma levels of LH and FSH in males, before and after oestrogen or anti-oestrogen treatment. Horm Metab Res. 1986 Aug;18(8):558-64.	1986	The Netherlands	English	pro-spective	young	healthy	hormones	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	3m	7	gonadotropin and testosterone levels, increase	in tamoxifen group		no	tamoxifen	placebo		2-	
935: Staiman VR, Lowe FC. Tamoxifen for flutamide/finasteride-induced gynecomastia. Urology. 1997 Dec;50(6):929-33.	1997	USA	English	retro-spective	old	prostate cancer, treatment with flutamide	breast swelling	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	1m	6	gynecomastia and breast pain, reduction	in 5 of 6 patients	no side effects	no				3	
936: McDermott MT, Hofeldt FD, Kidd GS. Tamoxifen therapy for painful idiopathic gynecomastia. South Med J. 1990 Nov;83(11):1283-5.	1990	USA	English	pro-spective, crossover	old	gynecomastia, idiopathic	breast swelling	endocrine therapy	L02	tamoxifen	L02BA01	n.g.	1m	6	gynecomastia and breast pain, reduction	in 5 of 6 patients	no side effects	yes	tamoxifen	placebo		1-	
903: Fauser BC, Dony JM, Doesburg WH, Thomas CM, Rolland R. Short- and long-term hormonal effects of a single dose of 50 mg tamoxifen administered to normal males. Andrologia. 1984 Sep-Oct;16(5):465-70.	1984	The Netherlands	English	pro-spective	young	healthy	hormones	endocrine therapy	L02	tamoxifen	L02BA01	50mg	1time	5	gonadotropin and testosterone levels, alteration	no consistent effects						3	
327: Gooren L. Improvement of spermatogenesis after treatment with the antiestrogen tamoxifen in a man with the incomplete androgen insensitivity syndrome. J Clin Endocrinol Metab. 1989 Jun;68(6):1207-10.	1989	The Netherlands	English	case report	young	androgen receptor pathology	fertility	endocrine therapy	L02	tamoxifen	L02BA01		20w	1	gonadotropin levels, increase	each time after tamoxifen application		no				3	
166: Adamopoulos DA, Pappa A, Billa E, Nicopoulou S, Koukkou E, Michopoulos J. Effectiveness of combined tamoxifen citrate and testosterone undecanoate treatment in men with idiopathic oligozoospermia. Fertil Steril. 2003 Oct;80(4):914-20. Greece	2003	Greece	English	pro-spective, randomized	young	infertiliy	semen	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	6m	212	sperm parameters, improvement	increase of sperm count and sperm motility in verum group, not in placebo group; pregnancies 33.9% in verum group, 10.3% in placebo group		yes	tamoxifen	placebo		1+	
174: Krause W, Holland-Moritz H, Schramm P. Treatment of idiopathic oligozoospermia with tamoxifen--a randomized controlled study. Int J Androl. 1992 Feb;15(1):14-8.	1992	Germany	English	pro-spective, randomized	young	infertiliy	semen	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	6m	77	sperm parameters, improvement	sperm count increased, testosterone levels increased	none	yes	tamaxifen	placebo		1-	
171: Bartsch G, Scheiber K. Tamoxifen treatment in oligozoospermia. Eur Urol. 1981;7(5):283-7.	1981	Austria	English	pro-spective	young	infertiliy	semen	endocrine therapy	L02	tamoxifen	L02BA01	30mg/d	long-term	56	sperm parameters, improvement	32 of 56 patients reached normal sperm density		no				3	
554: Traub AI, Thompson W. The effect of tamoxifen on spermatogenesis in subfertile men. Andrologia. 1981 Sep-Oct;13(5):486-90.	1981		English	pro-spective	young	spermatogenic dysfunction	semen	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	6m	43	spermatogenesis, improvement	most pronounced in men with initial sperm count < 5.10(6)		no				3	
173: Schill WB, Landthaler M. Tamoxifen treatment of oligozoospermia. Andrologia. 1980 Nov-Dec;12(6):546-8.	1980	Germany	English	pro-spective	young	infertility	semen, hormones	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	long-term	33	sperm parameters, improvement	significant increase of sperm count, sperm motility and morphology		no				3	

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167: Sterzik K, Rosenbusch B, Mogck J, Heyden M, Lichtenberger K. Tamoxifen treatment of oligozoospermia: a re-evaluation of its effects including additional sperm function tests. Arch Gynecol Obstet. 1993;252(3):143-7.	1993	Germany	English	pro-spective	young	infertiliy	semen	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	3m	29	sperm parameters, improvement	no significant improvement seminal volume, sperm count, sperm motility, morphology, and of hamster-oocyte penetration test results	n.g.	no				3	
170: Damber JE, Abramsson L, Duchek M. Tamoxifen treatment of idiopathic oligozoospermia: effect on hCG-induced testicular steroidogenesis and semen variables. Scand J Urol Nephrol. 1989;23(4):241-6.	1989	Sweden	English	retro-spective	young	infertiliy	hormones	endocrine therapy	L02	tamoxifen	L02BA01	20mg/d	3m	n.g.	hormone levels, increase	LH, FSH, progesterone, 17 alpha-progesterone, testosterone and oestradiol-17 beta		no				3	
2096: Di Lorenzo G, Perdona S, De Placido S, D'Armiento M, Gallo A, Damiano R, Pingitore D, Gallo L, De Sio M, Autorino R. Gynecomastia and breast pain induced by adjuvant therapy with bicalutamide after radical prostatectomy in patients with prostate cancer: the role of tamoxifen and radiotherapy J Urol. 2005 Dec;174(6):2197-203.	2005	Italy	English	pro-spective	old	prostate cancer	gynecomastia	endocrine therapy	L02	bicalutamide	L02BB03	150mg/d		102	gynecomastia, breast pain, development	67% (no additional treatment), 8% (tamoxifen), 34% (radiotherapy)		no	bicalutamide alone	b + tamoxifen 10mg/d	b + radiation	1-	
45: Morgante E, Gradini R, Realacci M, Sale P, D'Eramo G, Perrone GA, Cardillo MR, Petrangeli E, Russo M, Di Silverio F. Effects of long-term treatment with the anti-androgen bicalutamide on human testis: an ultrastructural and morphometric study. Histopathology. 2001 Mar;38(3):195-201.	2001	Italy	English	case report	old	prostate cancer	testicular histology	endocrine therapy	L02	bicalutamide	L02BB03	50mg/d	4y	2	testicular morphology, alterations	unexpectedly well preserved; normal organization of seminiferous tubules, mature spermatozoa present		no				3	
828: de Boer H, Verschoor L, Ruinemans-Koerts J, Jansen M. Letrozole normalizes serum testosterone in severely obese men with hypogonadotropic hypogonadism. Diabetes Obes Metab. 2005 May;7(3):211-5.	2005	The Netherlands	English	pro-spective	48.2 mean	obesity, severe	hormones	endocrine therapy	L02	letrozole	L02BG04	7.5-17.5 mg/w	6w	10	testosterone level increase, SHBG level unaltered	in all men		no				3	
928. Skrzypek J, Krause W. Sirolimus and spermatogenesis. Abstract DGA-Congress 2006 Düsseldorf	2006	Germany	German	case report	young	renal transplantation	semen	immunosuppressive agents	L04	sirolimus	L04AA10	8y	8mg/d	1	azoospermia, continuous	increase after cessation						3	
822: Said TM, Agarwal A, Falcone T, Sharma RK, Bedaiwy MA, Li L. Infliximab may reverse the toxic effects induced by tumor necrosis factor alpha in human spermatozoa: an in vitro model. Fertil Steril. 2005 Jun;83(6):1665-73.	2005	USA	English	pro-spective, randomized	young	healthy	sperm in vitro	immunosuppressive agents	L04	infliximab + TNFa	L04AA12		in vitro	31	sperm parameters, decrease	lesser decrease by TNFa in the presence of infliximab						2-	
823: Mahadevan U, Terdiman JP, Aron J, Jacobsohn S, Turek P. Infliximab and semen quality in men with inflammatory bowel disease. Inflamm Bowel Dis. 2005 Apr;11(4):395-9.	2005	USA	English	pro-spective	young	inflammatory bowel disease	sperm parameters	immunosuppressive agents	L04	infliximab	L04AA12		2w	10	sperm motility and morphology, impairment	In longer treatment with infliximab more pronounced decrease in sperm progression		cross-over				1-	
643: Lange D, Henning H, Schirren C. Andrologic study in immunosuppressive treatment of chronic aggressive hepatitis. Andrologia. 1978 Sep-Oct;10(5):373-9.	1978		German	retro-spective	young	chronic aggressive hepatitis	semen	Immunosuppressive drugs	L04	azathioprine	L04AX01		1720 d	few	spermatogenesis, impairment	none below a dose of 150mg/d		no				3	

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2306: Cavallini G, Biagiotti G, Ferraretti AP, Gianaroli L, Vitali G. Medical therapy of oligoas-thenospermia associated with left varicocele. BJU Int. 2003 Apr;91(6):513-8.	2003	Italy	English	pro-spective, random-ized	young	infertilityin varicocele	semen	antiinflammatory and antirheumatic products	M01	cinnoxicam	M01AC	30mg/4d	12m	155	sperm parameters, improvement	at 2m, best at 4m, decline to baseline after cessation of treatment		yes	cinnoxicam	varicocele surgery		2-	
2197: Gambera L, Serafini F, Morgante G, Focarelli R, De Leo V, Piomboni P. Sperm quality and pregnancy rate after COX-2 inhibitor therapy of infertile males with abacterial leukocyto-spermia. Human Reprod 2007; 22 (4), 1047–1051	2007	Italy	English	pro-spective	young	infertility	semen	antiinflammatory and antirheumatic products	M01	rofecoxib	M01AH02	25mg/d	30d	47	sperm parameters, improvement	sperm motility and morphology		no				3	
917: Graef V, Zubrzycki Z, Jarrar K. The effect of allopurinol on testosterone metabo-lism. Arzneimittelforschung. 1984;34(12):1760-2.	1984	Germany	German	retro-spective	young	kidney stone patients	testoster-one levels	antigout preparations	M04	allopurinol	M04AA01		n.g.	n.g.	testosterone level, decrease	significant		no				3	
795. Sarica K, Suzer O, Gurler A et al. Urological evaluation of Behcet patients and the effect of colchicine on fertility. Eur Urol 1995;27: 39-42	1995	Turkey	English	pro-spective	young	Behcet syndrom	clinical	antigout preparations	M04	colchicine	M04AC01	n.g.		62	spermatogenesis, impairment	23 of 67 patients (37.1%) had oligonecrozoospermia, 2 of 67 patients (3.2%) had azoospermia		no				3	
560: Fukutani K, Ishida H, Shinohara M, Minowada S, Nijijima T, Hijikata K, Izawa Y. Suppression of spermatogenesis in patients with Behcet’s disease treated with cyclophosphamide and colchicine. Fertil Steril. 1981 Jul;36(1):76-80.	1981		English	pro-spective	young	Behcet syndrom	semen	antigout preparations	M04	colchicine, cyclophos-phamide	M04AC01		64m	27	azoospermia, induction	13 of 17 patients receiving cyclophosphamide, none of patients receiving colchicine		no				2-	
802. Merlin HE: Azoospermia caused by colchicines. A case report. Fertil Steril 1972;23: 180-181	1972		English	case report	young	Behcet syndrom	semen	antigout preparations	M04	colchicine	M04AC01	2 grains	n.g.	1	azoospermia, induction	with treatment; normal sperm count without treatment						3	
158: Haimov-Kochman R, Ben-Chetrit E. The effect of colchicine treatment on sperm production and function: a review. Hum Reprod. 1998 Feb;13(2):360-2.	1998	Israel	English	review	young	Behcet syndrom	semen	antigout preparations	M04	colchicine	M04AC01			131	spermatogenesis, impairment	no effect		no				4	in prospective studies no effect of colchicine on spermatogenesis
175: Wyrobek AJ, Brodsky J, Gordon L, Moore DH 2nd, Watchmaker G, Cohen EN. Sperm studies in anesthesi-ologists. Anesthesiology. 1981 Nov;55(5):527-32.	1981	USA	English	retro-spective	young	anaesthe-sia	semen	anaesthetics	N01	anaethetics, general	N01A		continu-ous, pro-fessionals	46	spermatogenesis, impairment	no effect		no				2-	
283: Andersen BN, Mortensen JT, Hansen P, Jakobsen J, Johansen JP. The influence of halothane on spermatogen-esis in surgical patients. Acta Anaesthesiol Scand. 1992 Feb;36(2):125-7.	1992	Denmark	English	pro-spective	young	anaesthe-sia	semen	anaesthetics	N01	halothane	N01AB01		1x	17	spermatogenesis, impairment	no effect		no				3	
2026: Bracken MB, Eskenazi B, Sachse K, McSharry JE, Hel-lenbrand K, Leo-Summers L. Association of cocaine use with sperm concentration, motility, and morphology. Fertil Steril. 1990 Feb;53(2):315-22. USA	1990	USA	English	retro-spective	31-35	cocaine use	semen	anaesthetics	N01	cocaine	N01BC01	more than 1 dose/m	2-5y	39	sperm count, impairment	OR 2.3 (95% CI 1.0-5.4) in comparison to non-users		yes	cocaine users	cocaine non-users		2+	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
857: Abs R, Verhelst J, Maeyaert J, Van Buyten JP, Opsomer F, Adriaensen H, Verlooy J, Van Havenbergh T, Smet M, Van Acker K. Endocrine consequences of long-term intrathecal administration of opioids. J Clin Endocrinol Metab. 2000 Jun;85(6):2215-22.	2000	Belgium	English	retrospective	49.2 mean	intractable pain	hormones	analgesics	N02	opioids intrathecally	N02A		26m	29	FSH, LH, testosterone levels, unaltered	levels unaltered, hormone substitution not necessary						2-	
858: Paice JA, Penn RD, Ryan WG. Altered sexual function and decreased testosterone in patients receiving intraspinal opioids. J Pain Symptom Manage. 1994 Feb;9(2):126-31.	1994	USA	English	retrospective	middle-aged	intractable pain	hormones	analgesics	N02	opioids intrathecally	N02A		continuous	6	testosterone level, decline	decrease of libido and sexual functions						3	
948: Conte D, Nordio M, Fillo S, De Giorgio G, Isidori A, Romanelli F. Aspirin inhibition of naloxone-induced luteinizing hormone secretion in man. J Clin Endocrinol Metab. 1996 May;81(5):1772-5.	1996	Italy	English	prospective	20-38	healthy	LH response to naloxon	analgesics	N02	aspirin	N02BA01	650mg	single dose	16	stimulatory activity of naloxone on LH release, inhibited	by 80%		yes	aspirin	placebo		1-	
921: Conte D, Romanelli F, Fillo S, Guidetti L, Isidori A, Franceschi F, Latini M, di Luigi L. Aspirin inhibits androgen response to chorionic gonadotropin in humans. Am J Physiol. 1999 Dec;277(6 Pt 1):E1032-7.	1999	Italy	English	prospective	young	healthy	hormones	analgesics	N02	aspirin	N02BA01		2w	16	steroid hormone, response to hCG, decrease	significant		yes	aspirin	placebo		1-	
967: Bauer J, Blumenthal S, Reuber M, Stoffel-Wagner B. Epilepsy syndrome, focus location, and treatment choice affect testicular function in men with epilepsy. Neurology. 2004 Jan 27;62(2):243-6.	2004	Germany	English	retrospective	young	epilepsy	hormones	antiepileptics	N03	antiepileptics	N03A	n.g.	continuous	275	testosterone level, decrease; LH level, increase	mean values						3	
966: Mikkonen K, Tapanainen P, Pakarinen AJ, Paivansalo M, Isojarvi JI, Vainionpaa LK. Serum androgen levels and testicular structure during pubertal maturation in male subjects with epilepsy. Epilepsia. 2004 Jul;45(7):769-76.	2004	Finland	English	retrospective	young	epilepsy	hormones	antiepileptics	N03	antiepileptics	N03A	n.g.	continuous	140	testosterone level, decrease; SHBG level, increase	mean values			valproat	carbamazepin	age-matched controls	2-	
956: Roste LS, Tauboll E, Morkrid L, Bjornenak T, Saetre ER, Morland T, Gjerstad L. Antiepileptic drugs alter reproductive endocrine hormones in men with epilepsy. Eur J Neurol. 2005 Feb;12(2):118-24.	2005	Norway	English	prospective	young	epilepsy	hormones	antiepileptics	N03	antiepileptics	N03A	n.g.	2y	70	testosterone level, unaltered; SHBG level, decrease	mean values			valproat	carbamazepin	age-matched controls	2-	
977: Nalin A, Galli V, Ciccarone V, Grandi F, Baraldi E, Carani C. Antiepileptic drugs and puberty. Brain Dev. 1988;10(3):192-4.	1988	Italy	English	retrospective	puberal	epilepsy	pubertal development	antiepileptics	N03	antiepileptics	N03A	n.g.	continuous	57	puberty stage II earlier, in puberty stage III lower FSH levels	mean values						2-	
955: Barragry JM, Makin HL, Trafford DJ, Scott DF. Effect of anticonvulsants on plasma testosterone and sex hormone binding globulin levels. J Neurol Neurosurg Psychiatry. 1978 Oct;41(10):913-4.	1978		English	retrospective	young	epilepsy	hormones	antiepileptics	N03	antiepileptics	N03A	n.g.	continuous	16	testosterone level, increase; SHBG level, increased	mean values						3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
952: Murialdo G, Galimberti CA, Fonzi S, Manni R, Costelli P, Parodi C, Torre F, Solinas GP, Pol-leri A, Tartara A. Sex hormones, gonadotropins and prolactin in male epileptic subjects in remission: role of the epileptic syndrome and of antiepileptic drugs. Neuropsychobiology. 1994;30(1):29-36.	1994	Italy	English	retro-spective	young	epilepsy	hormones	antiepileptics	N03	phenobarbital	N03AA02	n.g.	continuous	70	LH response to GnRH, decrease	significant changes in SHBG, testosterone, andro-stendione independent of the epileptic syndrome						2-	
876: Murialdo G, Galimberti CA, Fonzi S, Manni R, Costelli P, Parodi C, Torre F, Solinas GP, Pol-leri A, Tartara A. Sex hormones, gonadotropins and prolactin in male epileptic subjects in remission: role of the epileptic syndrome and of antiepileptic drugs. Neuropsychobiology. 1994;30(1):29-36.	1994	Italy	English	retro-spective	young	epilepsy	hormones	antiepileptics	N03	phenobarbital	N03AA02		continuous	35	sex steroid hormones and LH pulsatility, lower response to GnRH	significant						3	
877: Bammel A, van der Mee K, Ohnhaus EE, Kirch W. Divergent effects of different enzyme-in-ducing agents on endogenous and exogenous testoster-one. Eur J Clin Pharmacol. 1992;42(6):641-4.	1992	Germany	English	pro-spective	young	healthy	hormones	antiepileptics	N03	phenobarbital	N03AA02	100mg/d	7d	18	testosterone level, alteration	none						2-	
881: Murialdo G, Manni R, De Maria A, Bonura ML, Polleri A, Tartara A. Luteinizing hormone pulsatile secretion and pituitary response to gonadotropin releasing hormone and to thyrotropin releasing hormone in male epileptic subjects on chronic phenobarbital treat-ment. J Endocrinol Invest. 1987 Feb;10(1):27-31.	1987	Italy	English	retro-spective	young	epilepsy	hormones	antiepileptics	N03	phenobarbital	N03AA02		continuous	8	GnRH-induced LH release	blunted in comparison to control subjects						2-	
244: Taneja N, Kucheria K, Jain S, Maheshwari MC. Effect of phenytoin on semen. Epilepsia. 1994 Jan-Feb;35(1):136-40.	1994	India	English	pro-spective	young	epilepsy	semen, hormones	antiepileptics	N03	phenytoin	N03AB02		12m	55; 28	spermatogenesis, impairment	not significant		no	epilepsy and no PTH	PTH		2-	
939: Taneja N, Kucheria K, Jain S, Maheshwari MC. Effect of phenytoin on semen. Epilepsia. 1994 Jan-Feb;35(1):136-40.	1994	India	English	retro-spective	young	epilepsy	semen, hormones	antiepileptics	N03	phenytoin	N03AB02		continuous	55	spermatogenesis, impair-ment; testosterone levels, decrease	clear						3	
945: Heroz AG, Levesque LA, Drislane FW, Ronthal M, Schomer DL. Phenytoin-induced elevation of serum estradiol and reproductive dysfunction in men with epilepsy. Epilepsia. 1991 Jul-Aug;32(4):550-3.	1991	Israel	English	retro-spective	young	epilepsy	hormones	antiepileptics	N03	phenytoin	N03AB02	n.g.		41	estradiol levels, increase; SHBG levels, increase	significant			phenytoin	placebo		2-	
876: Murialdo G, Galimberti CA, Fonzi S, Manni R, Costelli P, Parodi C, Torre F, Solinas GP, Pol-leri A, Tartara A. Sex hormones, gonadotropins and prolactin in male epileptic subjects in remission: role of the epileptic syndrome and of antiepileptic drugs. Neuropsychobiology. 1994;30(1):29-36.	1994	Italy	English	retro-spective	young	epilepsy	hormones	antiepileptics	N03	phenytoin	N03AB02		continuous	35	sex steroid hormones and LH pulsatility, decrease; SHBG levels, increase	significant						3	
969: Brunet M, Rodamilans M, Martinez-Osaba MJ, Santamaria J, To-Figueras J, Torra M, Corbella J, Rivera F. Effects of long-term antiepileptic therapy on the catabolism of testoster-one. Pharmacol Toxicol. 1995 Jun;76(6):371-5.	1995	Spain	English	retro-spective	young	epilepsy	hormones	antiepileptics	N03	phenytoin	N03AB02	n.g.	continuous	29	testosterone level, increase; SHBG level, increase	lower androgenicity due to increased SHBG levels						2-	

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970: Macphee GJ, Larkin JG, Butler E, Beastall GH, Brodie MJ. Circulating hormones and pituitary responsiveness in young epileptic men receiving long-term antiepileptic medication. Epilepsia. 1988 Jul-Aug;29(4):468-75.	1988	UK	English	retrospective	32 mean	epilepsy	hormones	antiepileptics	N03	phenytoin	N03AB02	various	continuous	13	hormone levels, alteration	SHBG levels increased		no	phenytoin	no treatment		2-	
952: Murialdo G, Galimberti CA, Fonzi S, Manni R, Costelli P, Parodi C, Torre F, Solinas GP, Polleri A, Tartara A. Sex hormones, gonadotropins and prolactin in male epileptic subjects in remission: role of the epileptic syndrome and of antiepileptic drugs. Neuropsychobiology. 1994;30(1):29-36.	1994	Italy	English	retrospective	young	epilepsy	hormones	antiepileptics	N03	carbamazepine	N03AF01	n.g.	continuous	70	LH response to GnRH, decreased	significant						3	
968: Rattya J, Turkka J, Pakarinen AJ, Knip M, Kotila MA, Lukkarinen O, Myllyla VV, Isojarvi JI. Reproductive effects of valproate, carbamazepine, and oxcarbazepine in men with epilepsy. Neurology. 2001 Jan 9;56(1):31-6.	2001	Finland	English	retrospective	young	epilepsy	hormones	antiepileptics	N03	carbamazepine	N03AF01	n.g.	continuous	65	testosterone level, unaltered; SHBG level, increase	significant						3	
876: Murialdo G, Galimberti CA, Fonzi S, Manni R, Costelli P, Parodi C, Torre F, Solinas GP, Polleri A, Tartara A. Sex hormones, gonadotropins and prolactin in male epileptic subjects in remission: role of the epileptic syndrome and of antiepileptic drugs. Neuropsychobiology. 1994;30(1):29-36.	1994	Italy	English	retrospective	young	epilepsy	hormones	antiepileptics	N03	carbamazepin	N03AF01		continuous	35	sex steroid hormones, LH pulsatility and response to GnRH, lower	significant						3	
746: Isojarvi JI, Lofgren E, Juntunen KS, Pakarinen AJ, Paivansalo M, Rautakorpi I, Tuomivaara L. Effect of epilepsy and antiepileptic drugs on male reproductive health. Neurology. 2004 Jan 27;62(2):247-53.	2004		English	retrospective	young	epilepsy	sperm motility, hormones	antiepileptics	N03	carbamazepin	N03AF01		long-term	33	DHEA levels, decrease; sperm motility, decrease			no				3	
969: Brunet M, Rodamilans M, Martinez-Osaba MJ, Santamaria J, To-Figueras J, Torra M, Corbella J, Rivera F. Effects of long-term antiepileptic therapy on the catabolism of testosterone. Pharmacol Toxicol. 1995 Jun;76(6):371-5.	1995	Spain	English	retrospective	young	epilepsy	hormones	antiepileptics	N03	carbamazepine	N03AF01	n.g.	continuous	28	testosterone level, increase; SHBG level, increase	lower androgenicity due to increased SHBG levels	lower androgenicity due to increased SHBG levels					3	
950: Isojarvi JI, Pakarinen AJ, Myllyla VV. Effects of carbamazepine on the hypothalamic-pituitary-gonadal axis in male patients with epilepsy: a prospective study. Epilepsia. 1989 Jul-Aug;30(4):446-52.	1989	Finland	English	prospective	young	epilepsy	hormones	antiepileptics	N03	carbamazepine	N03AF01	n.g.	2m	21	estradiol levels, increase, PRL response to metoclopramide, increase	significant						3	
970: Macphee GJ, Larkin JG, Butler E, Beastall GH, Brodie MJ. Circulating hormones and pituitary responsiveness in young epileptic men receiving long-term antiepileptic medication. Epilepsia. 1988 Jul-Aug;29(4):468-75.	1988	UK	English	retrospective	29 mean	epilepsy	hormones	antiepileptics	N03	carbamazepine	N03AF01	various	continuous	18	hormone levels, alteration	LH and prolactin levels enhanced		no	carbamazepin	no treatment		2-	
984: Isojarvi JI, Lofgren E, Juntunen KS, Pakarinen AJ, Paivansalo M, Rautakorpi I, Tuomivaara L. Effect of epilepsy and antiepileptic drugs on male reproductive health. Neurology. 2004 Jan 27;62(2):247-53.	2004	Finland	English	retrospective	young	epilepsy	semen, hormones, testicular volume	antiepileptics	N03	carbamazepine	N03AF01	n.g.	continuous	15	DHEA levels decreased, abnormal sperm increased, testicular volume unaltered	significant						3	

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978: Connell JM, Rapeport WG, Beastall GH, Brodie MJ. Changes in circulating androgens during short term carbamazepine therapy. Br J Clin Pharmacol. 1984 Mar;17(3):347-51.	1984		English	pro-spective	young	healthy	sexual function scale; hormones	antiepileptics	N03	carbamazepine	N03AF01	400mg	21d	6	sexual function, depression; testosterone level, increase	various						2-	
968: Rattya J, Turkka J, Pakarinen AJ, Knip M, Kotila MA, Lukkarinen O, Myllyla VV, Isojarvi JI. Reproductive effects of valproate, carbamazepine, and oxcarbazepine in men with epilepsy. Neurology. 2001 Jan 9;56(1):31-6.	2001	Finland	English	retrospective	young	epilepsy	hormones	antiepileptics	N03	valproate	N03AG01	n.g.	continuous	115	testosterone level, decrease; SHBG level, unaltered	moderate						3	
976: Stephen LJ, Kwan P, Shapiro D, Dominiczak M, Brodie MJ. Hormone profiles in young adults with epilepsy treated with sodium valproate or lamotrigine monotherapy. Epilepsia. 2001 Aug;42(8):1002-6.	2001	UK	English	retrospective	young	epilepsy	hormones	antiepileptics	N03	valproate, lamotrigine	N03AG01	n.g.	continuous	76	testosterone level, unaltered; gonadotropin level, unaltered	no effect						3	
747: Roste LS, Tauboll E, Haugen TB, Bjornenak T, Saetre ER, Gjerstad L. Alterations in semen parameters in men with epilepsy treated with valproate or carbamazepine monotherapy. Eur J Neurol. 2003 Sep;10(5):501-6.	2003		English	retrospective	young	epilepsy	sperm motility	antiepileptics	N03	valproate, carbamazepin	N03AG01			36	sperm motility, unaltered; testicular volume, decrease	significant		no				2-	
746: Isojarvi JI, Lofgren E, Juntunen KS, Pakarinen AJ, Paivansalo M, Rautakorpi I, Tuomivaara L. Effect of epilepsy and antiepileptic drugs on male reproductive health. Neurology. 2004 Jan 27;62(2):247-53.	2004		English	retrospective	young	epilepsy	sperm motility	antiepileptics	N03	valproate	N03AG01		long-term	27	androstendione levels, increase; sperm motility, decreased	significant		no				2-	
970: Macphee GJ, Larkin JG, Butler E, Beastall GH, Brodie MJ. Circulating hormones and pituitary responsiveness in young epileptic men receiving long-term antiepileptic medication. Epilepsia. 1988 Jul-Aug;29(4):468-75.	1988	UK	English	retrospective	young	epilepsy	hormones	antiepileptics	N03	valproate	N03AG01	various	continuous	10	hormone levels, alteration	no difference to control patients	negative correlation between free T and circulating CBZ	no	valproate	no treatment		2-	
947: Elias AN, Pahl M, Stone S, Vaziri ND, Valenta LJ. Modulatory role of gamma-aminobutyric acid (GABA) in the regulation of gonadotropin secretion in patients with chronic renal failure. Int J Artif Organs. 1982 Jan;5(1):13-6.	1982		English	pro-spective	young	terminal renal insufficiency	hormones	antiepileptics	N03	valproate	N03AG01	n.g.	2w	5	gonadotropin levels, unaltered; response to GnRH, increase	significant						3	
653: Lavieri JC, Pierini AA. L-dopa and oligozoospermia. Andrologia. 1978 Jan-Feb;10(1):74-9.	1978		English	pro-spective	young	infertility	semen	anti-Parkinson drugs	N04	L-DOPA	N04BA02	500mg/d	2m	39	spermatogenesis, improvement	14 of 25 patients in group 1; 8 of 14 patients in group 2		yes	500mg/d	750mg/d		1-	
2187: Lunglmayr G, Maier U, Spona J. [Therapy of idiopathic oligozoospermia with bromicriptine. Results of a prospective controlled study] Andrologia. 1983;15 Spec No:548-53.	1983	Austria	English	pro-spective	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	n.g.	n.g.	50	sperm parameters, alteration; pregnancy rate, increase	no effect		no				1-	
2189: Szollosi J, Szilagyi I, Sas M. Parlodel treatment of patients with pathospermia. Int Urol Nephrol. 1982;14(3):307-12.	1982		English	pro-spective	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	n.g.	n.g.	42	sperm parameters, alteration	no effect							

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2192: Hovatta O, Koskimies AI, Ranta T, Stenman UH, Seppala M. Bromocriptine treatment of oligospermia: a double blind study. Clin Endocrinol (Oxf). 1979 Oct;11(4):377-82.	1979		English	pro-spective, random-ized	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	n.g.	12w	40	sperm parameters, alteration	no significant effect superior to placebo on sperm volume, motility and morphology		yes	bromocryptin	placebo		1-	
2184: Merino G, Carranza-Lira S, Martinez-Chequer JC, Barahona E, Moran C, Bermudez JA. Hyperprolactinemia in men with asthenozoospermia, oligozoospermia, or azoospermia. Arch Androl. 1997 May-Jun;38(3):201-6.	1997	Mexico	English	pro-spective	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	2.5mg/d	6m	21	sperm parameters, alteration	no effect						3	
2188: AinMelk Y, Belisle S, Kandalaft N, McClure D, Tetreault L, Elhilali M. Bromocriptine therapy in oligozoospermic infertile men. Arch Androl. 1982 Mar;8(2):135-41.	1982		English	pro-spective, random-ized	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	5mg/d	4m	17	sperm parameters, alteration; pregnancy rate, increase	no effect		yes	bromocryptin	placebo		1-	
420: Ermolenko VM, Kukhtevich AV, Dedov II, Bunatian AF, Melnichenko GA, Gitel EP. Parlodel treatment of uremic hypogonadism in men. Nephron. 1986;42(1):19-22.	1986		English	pro-spective	young	uremia	hormones	anti-Parkinson drugs	N04	bromocriptine	N04BC01		3m	14	gonadotropin levels, unaltered	normalisation of spermatogenesis	erectile function, increase	no				3	
126: Nishimura K, Matsumiya K, Tsuboniwa N, Yamanaka M, Koga M, Miura H, Tsujimura A, Uchida K, Kondoh N, Kitamura M, Okuyama A. Bromocriptine for infertile males with mild hyperprolactinemia: hormonal and spermatogenic effects. Arch Androl. 1999 Nov-Dec;43(3):207-13.	1999	Japan	English	pro-spective	young	prolactinoma	semen, hormones	anti-Parkinson drugs	N04	bromocriptine	N04BC01		n.g.	10	testosterone level, alteration; sperm parameters, alteration	no alteration of hormone and semen parameters		no				3	
2183: Nishimura K, Matsumiya K, Tsuboniwa N, Yamanaka M, Koga M, Miura H, Tsujimura A, Uchida K, Kondoh N, Kitamura M, Okuyama A. Bromocriptine for infertile males with mild hyperprolactinemia: hormonal and spermatogenic effects. Arch Androl. 1999 Nov-Dec;43(3):207-13.	1999	Japan	English	pro-spective	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	n.g.	n.g.	10	sperm parameters, alteration; hormone parameters, alteration	no effect, only decrease of prolactin levels		no				3	
2186: Mancini A, Guitelman A, Levalle O, Aparicio N, Aszenmil G. Bromocriptine in the management of infertile men after surgery of prolactin secreting adenomas. J Androl. 1984 Jul-Aug;5(4):294-6.	1984	Argentina	English	pro-spective	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	7.5mg/d	6m	9	sperm parameters, alteration	significant increase of sperm count		no	bromocryptin	placebo		3	
2191: Madsen H, Andersen O, Hansen P. Bromocriptine treatment for male infertility. Andrologia. 1980 Jul-Aug;12(4):379-80.	1980		English	pro-spective	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	n.g.	90d	4	sperm parameters, alteration	no effect						3	
2185: Okada H, Iwamoto T, Fujioka H, Shirakawa T, Tatsumi N, Kanzaki M, Minayoshi K, Ohya K, Fujisawa M, Arakawa S, Kamidono S, Ishigami J. Hyperprolactinaemia among infertile patients and its effect on sperm functions. Andrologia. 1996 Jul-Aug;28(4):197-202.	1996	Japan	English	pro-spective	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	n.g.	10m	3	sperm parameters, alteration	no effect						3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2190: Laufer N, Yaffe H, Margalioth EJ, Livshin J, Ben-David M, Schenker JG. Effect of bromocriptine treatment on male infertility associated with hyperprolactinemia. Arch Androl. 1981 Jun;6(4):343-6.	1981		English	pro-spective	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	2.5-7.5mg/d	16w	3	sperm parameters, alteration	increase of sperm motility		no				3	
588: Fraioli F, Paolucci D, Dondero F, Spera G, Isidori A. Prolactin secreting adenoma in man and the role of prolactin in spermatogenesis. J Endocrinol Invest. 1980 Apr-Jun;3(2):155-61.	1980	Italy	English	case report	23	prolactinoma	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01	5mg/d	120d	1	spermatogenesis, recovery	after normalisation of prolactin levels		CR				3	
896: Nakagawa K, Obara T, Matsubara M, Kubo M. Relationship of changes in serum concentrations of prolactin and testosterone during dopaminergic modulation in males. Clin Endocrinol (Oxf). 1982 Oct;17(4):345-52.	1982	Japan	English	pro-spective	young	healthy	hormones	anti-Parkinson drugs	N04	bromocriptin	N04BC01	2,5mg/d	3d	n.g.	testosterone level and response to hCG, increase	significant						2-	
2182: Vandekerckhove P, Lilford R, Vail A, Hughes E. Bromocriptine for idiopathic oligo/asthenospermia. Cochrane Database Syst Rev. 2000;(2):CD000152.	2000	UK	English	cochrane review	young	infertility	semen	anti-Parkinson drugs	N04	bromocriptine	N04BC01				sperm parameters, alteration; pregnancy rate, increase	no effect, OR for pregnancy rate 0.70 (95% CI 0.15 to 3.24)		yes				1-	
972: Brown WA, Laughren TP, Williams B. Differential effects of neuroleptic agents on the pituitary-gonadal axis in men. Arch Gen Psychiatry. 1981 Nov;38(11):1270-2.	1981		English	retrospective	young	schizophrenia	hormones	psycholeptics	N05	thioridazine, trifluoperazine, chlorpromazine	N05AC02	n.g.	continuous	42	testosterone level, decrease; LH level, decrease	lower in thioridazine patients						2-	
951: Brambilla F, Guerrini A, Guastalla A, Rovere C, Riggi F. Neuroendocrine effects of haloperidol therapy in chronic schizophrenia. Psychopharmacologia. 1975 Oct 14;44(1):17-22.	1975		English	retrospective	19-62	schizophrenia	hormones	psycholeptics	N05	haloperidol	N05AD01	6mg/d	30d	62	gonadotropin and 17-keto-steroid urinary excretion, increase	as compared to subnormal levels before treatment						3	
817: Rinieris P, Hatzimanolis J, Markianos M, Stefanis C. Effects of treatment with various doses of haloperidol on the pituitary-gonadal axis in male schizophrenic patients. Neuropsychobiology. 1989;22(3):146-9.	1989	Greece	English	retrospective	young	schizophrenia	hormones	psycholeptics	N05	haloperidol	N05AD01	15-60mg/d	4+4w	30	testosterone level, alteration	decrease with higher dose of haloperidol	increase in prolactin levels					2-	
892: Nakano R, Yagi S, Nishi T. Pituitary and testicular response to luteinizing hormone releasing hormone in normal and sulpiride-induced hyperprolactinaemic men. Exp Clin Endocrinol. 1988 May;91(2):191-6.	1988	Japan	English	pro-spective	young	healthy	hormones	psycholeptics	N05	sulpiride	N05AL01	150mg/d	14d	8	gonadotropins and response to GnRH, alteration	no effect						2-	
895: Bernini GP, Gasperi M, Franchi F, Luisi M. Effects of sulpiride induced hyperprolactinemia on testosterone secretion and metabolism before and after HCG in normal men. J Endocrinol Invest. 1983 Aug;6(4):287-91.	1983	Italy	English	pro-spective	young	healthy	hormones	psycholeptics	N05	sulpiride	N05AL01	150mg/d	14d	7	testosterone level and response to hCG, increase	significant						2-	
890: von Bahr C, Wiesel FA, Movin G, Eneroth P, Jansson P, Nilsson L, Ogenstad S. Neuroendocrine responses to single oral doses of remoxipride and sulpiride in healthy female and male volunteers. Psychopharmacology (Berl). 1991;103(4):443-8.	1991	Sweden	English	pro-spective	young	healthy	hormones	psycholeptics	N05	sulpiride	N05AL01	200mg	1time	6	gonadotropin levels, alteration; sex steroid levels, alteration	none						2-	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
891: Oseko F, Oka N, Furuya H, Morikawa K. Effects of chronic sulpiride-induced hyperprolactinemia on plasma testosterone and its responses to hCG in normal men. J Androl. 1988 Jul-Aug;9(4):231-3.	1988	Japan	English	pro-spective	young	healthy	hormones	psycholeptics	N05	sulpiride	N05AL01	300mg/d	64d	5	testosterone level and response to hCG, alteration	no consistent effects						2-	
929: Kaneda Y, Fujii A. Gynecomastia with sulpiride. J Clin Pharm Ther. 2002 Feb;27(1):75-7.	2002	Japan	English	case report	38	psychosis	breast swelling	psycholeptics	N05	sulpiride	N05AL01	100mg/d	5m	1	gynecomastia	slow development						3	
896: Nakagawa K, Obara T, Matsubara M, Kubo M. Relationship of changes in serum concentrations of prolactin and testosterone during dopaminergic modulation in males. Clin Endocrinol (Oxf). 1982 Oct;17(4):345-52.	1982	Japan	English	pro-spective	young	healthy	hormones	psycholeptics	N05	sulpiride	N05AL01	50mg/d	3d	n.g.	testosterone level and response to hCG, alteration	no effect						2-	
890: von Bahr C, Wiesel FA, Movin G, Eneroth P, Jansson P, Nilsson L, Ogenstad S. Neuroendocrine responses to single oral doses of remoxipride and sulpiride in healthy female and male volunteers. Psychopharmacology (Berl). 1991;103(4):443-8.	1991	Sweden	English	pro-spective	young	healthy	hormones	psycholeptics	N05	remoxipride	N05AL04	100mg	1time	6	gonadotropin levels, alteration; sex steroid levels, alteration	no effect						2-	
755: Levin RM, Amsterdam JD, Winokur A, Wein AJ. Effects of psychotropic drugs on human sperm motility. Fertil Steril. 1981 Oct;36(4):503-6.	1981		English	pro-spective	young	depression	sperm functions in-vitro	psycholeptics	N05	lithium	N05AN01	25mM	in vitro	36	sperm motility, unaltered			no				3	
974: Hunter R, Christie JE, Whalley LJ, Bennie J, Carroll S, Dick H, Goodwin GM, Wilson H, Fink G. Luteinizing hormone responses to luteinizing hormone releasing hormone (LHRH) in acute mania and the effects of lithium on LHRH and thyrotrophin releasing hormone tests in volunteers. Psychol Med. 1989 Feb;19(1):69-77.	1989	UK	English	pro-spective	young	bipolar psychosis	hormones	psycholeptics	N05	lithium	N05AN01	below 1mmol Li+		14	testosterone level, alteration	none			drug-free mania	lithium		2-	
337: Tollefson G, Garvey MJ. Spermatogenesis during extended lithium treatment. Hillside J Clin Psychiatry. 1989;11(1):35-41.	1989	USA	English	pro-spective	young	psychosis	semen	psycholeptics	N05	lithium	N05AN01		10w	10	spermatogenesis, impairment	no effect		no				3	
953: Sheard MH, Marini JL, Giddings SS. The effect of lithium on luteinizing hormone and testosterone in man. Dis Nerv Syst. 1977 Oct;38(10):765-9.	1977		English	pro-spective	16-24	bipolar psychosis	hormones	psycholeptics	N05	lithium	N05AN01	n.g.	3m	n.g.	testosterone level, alteration	none						3	
973: Baptista T, Alastre T, Contreras Q, Martinez JL, Araujo de Baptista E, Burguera JL, de Burguera M, Hernandez L. Effects of lithium carbonate on reproductive hormones in healthy men: relationship with body weight regulation—a pilot study. Prog Neuropsychopharmacol Biol Psychiatry. 1997 Aug;21(6):937-50.	1993	Venezuela	English	retrospective	young	healthy	hormones	psycholeptics	N05	lithium	N05AN01	900mg/d	1m	n.g.	testosterone level, alteration; estradiol level, alteration	none			lithium 900mg/d	placebo		2-	
805: Baumgartner A, Schmid TE, Schuetz CG, Adler ID. Detection of aneuploidy in rodent and human sperm by multicolor FISH after chronic exposure to diazepam. Mutat Res. 2001 Jan 25;490(1):11-9.	2001	Germany	English	retrospective	young	diazepam addiction	sperm chromosomes	psycholeptics	N05	diazepam	N05BA01	0.3 mg/kg/d	6m	3	sperm aneuploidy	sperm number with disomy 13, disomy X, and total sex-chromosomal disomies enhanced as compared to controls						2-	

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870: Adler ID, Schmid TE, Baumgartner A. Induction of aneuploidy in male mouse germ cells detected by the sperm-FISH assay: a review of the present data base. Mutat Res. 2002 Jul 25;504(1-2):173-82.	2002	Germany	English	retrospective	young	diazepam addiction	DNA probes specific for certain chromosomes	psycholeptics	N05	diazepam	N05BA01		in vitro		sperm chromosomes	aberrations as analysed by FISH						3	
905: Olubodun JO, Ochs HR, von Moltke LL, Roubenoff R, Hesse LM, Harmatz JS, Shader RI, Greenblatt DJ. Pharmacokinetic properties of zolpidem in elderly and young adults: possible modulation by testosterone in men. Br J Clin Pharmacol. 2003 Sep;56(3):297-304.	2003	USA	English	prospective	61-85	healthy	clearance of zolipem as influenced by testosterone	psycholeptics	N05	zolpidem	N05CF02	5mg	single dose	16	clearance of zolpidem	decreased in elderly men, greater relative contribution of serum testosterone than age						2-	
755: Levin RM, Amsterdam JD, Winokur A, Wein AJ. Effects of psychotropic drugs on human sperm motility. Fertil Steril. 1981 Oct;36(4):503-6.	1981		English	prospective	young	depression	sperm functions	psychoanaleptics	N06	imipramine	N06AA02		3w		sperm motility in vitro, decrease	significant		no				3	
919: Padron RS, Nodarse M. Effects of amitriptyline on semen of infertile men. Br J Urol. 1980 Jun;52(3):226-8.	1980	UK	English	prospective	young	infertility	sperm parameters	psychoanaleptics	N06	amitryptilin	N06AA09		n.g.	20	sperm count and sperm morphology, increase	after treatment						3	
975: Bell S, Shipman M. Reduced testosterone level in a venlafaxine treated patient. Ann Clin Psychiatry. 2000 Sep;12(3):171-3.	2000		English	case report	26	paraphilia	hormones	psychoanaleptics	N06	venlafaxine	N06AX16	112mg/d	13w	1	testosterone level, decreased	increase after cessation						3	
968: Rattya J, Turkka J, Pakarinen AJ, Knip M, Kotila MA, Lukkarinen O, Myllyla VV, Isojarvi JI. Reproductive effects of valproate, carbamazepine, and oxcarbazepine in men with epilepsy. Neurology. 2001 Jan 9;56(1):31-6.	2001	Finland	English	retrospective	young	epilepsy	hormones	psychoanaleptics	N06	oxycarbazepine	not listed	n.g.	continuous	29	testosterone level, alteration; SHBG level, alteration	none						2-	
746: Isojarvi JI, Lofgren E, Juntunen KS, Pakarinen AJ, Paivansalo M, Rautakorpi I, Tuomivaara L. Effect of epilepsy and antiepileptic drugs on male reproductive health. Neurology. 2004 Jan 27;62(2):247-53.	2004	Finland	English	retrospective	young	epilepsy	semen, hormones, testicular volume	psychoanaleptics	N06	oxycarbazepine	not listed	n.g.	continuous	58	DHEA levels alteration, abnormal sperm alteration, testicular volume alteration	none							3
28. Trummer H, Habermann H, Haas J, Pummer K. The impact of cigarette smoking on human semen parameters and hormones. Hum Reprod. 2002 Jun;17(6):1554-9.	2002	Austria	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	1104	sperm parameters, decrease	no differences between non-smokers and ex-smokers		no				3	
2022: Hughes EG, Yeo J, Claman P, YoungLai EV, Sagle MA, Daya S, Collins JA. Cigarette smoking and the outcomes of in vitro fertilization: measurement of effect size and levels of action. Fertil Steril. 1994 Oct;62(4):807-14.	1994	Canada	English	retrospective	young	infertility	IVF outcome	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	462 cycles	sperm parameters, impairment	significant reduction of sperm count, fertilisation rate unaffected		no	smokers	non-smokers		2-	
2027: Oldereid NB, Rui H, Clausen OP, Purvis K. Cigarette smoking and human sperm quality assessed by laser-Doppler spectroscopy and DNA flow cytometry. J Reprod Fertil. 1989 Jul;86(2):731-6.	1989	Norway	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	350	sperm parameters, impairment	no significant differences in any aspect of sperm quality including DNA distribution between non-smokers, moderate smokers and heavy smokers		no	smokers	non-smokers		2+	
2030: Vogt HJ, Heller WD, Borelli S. Sperm quality of healthy smokers, ex-smokers, and never-smokers. Fertil Steril. 1986 Jan;45(1):106-10.	1986	Germany	English	retrospective	19-40	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	333	sperm parameters, impairment	no statistically significant effect of smoking habits on sperm density, motility, and morphologic features		no	smokers	non-smokers		2+	

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2009: Zhang JP, Meng QY, Wang Q, Zhang LJ, Mao YL, Sun ZX. Effect of smoking on semen quality of infertile men in Shandong, China. Asian J Androl. 2000 Jun;2(2):143-6.	2000	China	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	191; 110	sperm parameters, impairment	sperm density, viability and motility smokers than in the non-smokers and negatively correlated with pack-years.		no	smokers	non-smokers		2+	
2003: Ozgur K, Isikoglu M, Seleker M, Donmez L. Semen quality of smoking and non-smoking men in infertile couples in a Turkish population. Arch Gynecol Obstet. 2005 Feb;271(2):109-12. Epub 2003 Dec 18. Turkey.	2003	Turkey	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	290	sperm parameters, impairment	heavy smokers sperm motility decrease		no	heavy smokers	light smokers		2-	
2024: Oldereid NB, Rui H, Purvis K. Life styles of men in barren couples and their relationship to sperm quality. Int J Fertil. 1992 Nov-Dec;37(6):343-9. Norway.	1992	Norway	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	252	sperm parameters, impairment	no association to smoking habits		no	smokers	non-smokers		2-	
2031: Kulikauskas V, Blaustein D, Ablin RJ. Cigarette smoking and its possible effects on sperm. Fertil Steril. 1985 Oct;44(4):526-8.	1985	UK	English	retrospective	young	healthy	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	238	sperm parameters, impairment	Morphologic abnormalities did not differ significantly between smokers and non-smokers.		no	smokers	non-smokers		2+	
2025: Gerhard I, Lenhard K, Eggert-Kruse W, Runnebaum B. Clinical data which influence semen parameters in infertile men. Hum Reprod. 1992 Jul;7(6):830-7.	1992	Germany	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	225	sperm parameters, impairment	no significant changes in the spermiogram		no	smokers	non-smokers		2-	
2000: Hassa H, Yildirim A, Can C, Turgut M, Tanir HM, Senses T, Sahin-Mutlu F. Effect of smoking on semen parameters of men attending an infertility clinic. Clin Exp Obstet Gynecol. 2006;33(1):19-22. Turkey.	2006	Turkey	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various pack-years	continuous	223	sperm parameters, impairment	smoking was negatively correlated with sperm motility, not with sperm count and morphology		no	smokers	non-smokers		2-	
2017: Figa-Talamanca I, Cini C, Varricchio GC, Dondero F, Gandini L, Lenzi A, Lombardo F, Angelucci L, Di Grezia R, Patacchioli FR. Effects of prolonged automobile driving on male reproduction function: a study among taxi drivers. Am J Ind Med. 1996 Dec;30(6):750-8.	1996	Italy	English	retrospective	young	healthy	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	201	sperm parameters, impairment	smoking associated with poorer morphology		no	smokers	non-smokers		2+	
2033: Rodriguez-Rigau LJ, Smith KD, Steinberger E. Cigarette smoking and semen quality. Fertil Steril. 1982 Jul;38(1):115-6.	1982	USA	English	retrospective	31 mean	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	58;101	sperm parameters, impairment	sperm count, motility, morphology not different between smokers and non-smokers		no	smokers	non-smokers		2-	
2032: Handelsman DJ, Conway AJ, Boylan LM, Turtle JR. Testicular function in potential sperm donors: normal ranges and the effects of smoking and varicocele. Int J Androl. 1984 Oct;7(5):369-82.	1984	Australia	English	retrospective	young	healthy	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	119	sperm parameters, impairment	no significant differences in hormones and sperm count, but significantly lower motility (67 as compared to 72%), lower number of total oval sperm (120 as compared to 251x106) in smokers as compared to non-smokers.		no	smokers	non-smokers		2+	
2020: Goverde HJ, Dekker HS, Janssen HJ, Bastiaans BA, Rolland R, Zielhuis GA. Semen quality and frequency of smoking and alcohol consumption--an explorative study. Int J Fertil Menopausal Stud. 1995 May-Jun;40(3):135-8.	1995	The Netherlands	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	115	sperm parameters, impairment	insignificant higher proportion of smokers in group with poor semen quality		no	smokers	non-smokers		2-	

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2029: Rantala ML, Koskimies AI. Semen quality of infertile couples--comparison between smokers and non-smokers. Andrologia. 1987 Jan-Feb;19(1):42-6.	1987		English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	110	sperm parameters, impairment	Non-smokers sperm count 74.3, motility 65%. Smokers sperm count 67, motility 62%;significant lower. Sperm morphology no difference.		no	smokers	non-smokers		2-	
2010: Sergerie M, Ouhilal S, Bissonnette F, Brodeur J, Bleau G. Lack of association between smoking and DNA fragmentation in the spermatozoa of normal men. Hum Reprod. 2000 Jun;15(6):1314-21.	2000	Canada	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	90	sperm parameters, impairment	Percentages of DNA fragmentation in spermatozoa not statistically different in the heavy smokers (12.11%), light smokers (11.66%) and non-smokers (20.41%).		no	smokers	non-smokers		2-	
2016: Vine MF, Setzer RW Jr, Everson RB, Wyrobek AJ. Human sperm morphometry and smoking, caffeine, and alcohol consumption. Reprod Toxicol. 1997 Mar-Jun;11(2-3):179-84.	1997	USA	English	retrospective	18-35	healthy	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	86	sperm parameters, impairment	no significant effect on sperm nuclear size,shape, or chromatin texture		no	smokers	non-smokers		2+	
2034: Evans HJ, Fletcher J, Torrance M, Hargreave TB. Sperm abnormalities and cigarette smoking. Lancet. 1981 Mar 21;1(8221):627-9	1981	UK	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	43;43	sperm parameters, impairment	greater percentage of abnormal forms in smokers		no	smokers	non-smokers		2+	
2019: Sofikitis N, Miyagawa I, Dimitriadis D, Zavos P, Sikka S, Hellstrom W. Effects of smoking on testicular function, semen quality and sperm fertilizing capacity. J Urol. 1995 Sep;154(3):1030-4.	1995	Japan	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	49;28	sperm parameters, impairment	no significant differences in semen volume and sperm count, significantly lower motility, morphology, and hamster-oocyte-penetration test		no	smokers	non-smokers		2-	
2005: Saleh RA, Agarwal A, Sharma RK, Nelson DR, Thomas AJ Jr. Effect of cigarette smoking on levels of seminal oxidative stress in infertile men: a prospective study. Fertil Steril. 2002 Sep;78(3):491-9.	2003	USA	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	20;45	sperm parameters, impairment	Leukocyte count and ROS significantly higher in smokers. Differences in standard sperm variables and DNA damage indices not significant.		no	smokers	non-smokers		2-	
991. Shaarawy M, Mahmoud KZ. Endocrine profile and semen characteristics in male smokers. Fertil Steril. 1982 Aug;38(2):255-7.	1982	India	English	retrospective	25-35	smoking	semen	other nervous system drugs	N07	nicotine	N07BA01	>20 cigarettes/day	continuous	25;20	sperm motility, decrease	significant as compared to non-smokers		no				2-	
2008: Shi Q, Ko E, Barclay L, Hoang T, Rademaker A, Martin R. Cigarette smoking and aneuploidy in human sperm. Mol Reprod Dev. 2001 Aug;59(4):417-21.	2001	Canada	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	31	sperm parameters, impairment	no significant differences in semen parameters or in age across groups. Frequency of disomy 13 was significantly higher in light and heavy smokers than in non-smokers.		no	smokers	non-smokers		2-	
2014: Rubes J, Lowe X, Moore D 2nd, Perreault S, Slott V, Evenson D, Selevan SG, Wyrobek AJ. Smoking cigarettes is associated with increased sperm disomy in teenage men. Fertil Steril. 1998 Oct;70(4):715-23.	1998	USA	English	retrospective	exact 18	healthy	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	10;15	sperm parameters, impairment	sperm count and motility significantly lower; elevated frequencies of sperm aneuploidy in smokers		no	smokers	non-smokers		2-	
2001: Arabi M, Moshtaghi H. Influence of cigarette smoking on spermatozoa via seminal plasma. Andrologia. 2005 Aug;37(4):119-24. Iran.	2005	Iran	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	spermatozoa of nonsmokers in seminal plasma of smokers	in-vitro	n.g.	sperm parameters, impairment	by exposure to seminal plasma from smokers		no	smokers	non-smokers		2-	
2013: Potts RJ, Newbury CJ, Smith G, Notarianni LJ, Jeffries TM. Sperm chromatin damage associated with male smoking. Mutat Res. 1999 Jan 25;423(1-2):103-11	1999	UK	English	retrospective	young	infertility	semen	other nervous system drugs	N07	nicotine	N07BA01	various	continuous	n.g.	sperm parameters, impairment	higher levels of DNA strand breaks in spermatozoa of smokers		no	smokers	non-smokers		2-	

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799: Robbins WA, Vine MF, Truong KY, Everson RB. Use of fluorescence in situ hybridization (FISH) to assess effects of smoking, caffeine, and alcohol on aneuploidy load in sperm of healthy men. Environ Mol Mutagen. 1997;30(2):175-83.	1997	USA	English	pro-spective	19-35	spermatogenic dysfunction	FISH analysis	other nervous system drugs	N07	narcomania	N07BB			45	sperm aneuploidy of XX18 and YY18, increase	significant		no				3	
941: Ragni G, De Lauretis L, Bestetti O, Sghedoni D, Gambaro V. Gonadal function in male heroin and methadone addicts. Int J Androl. 1988 Apr;11(2):93-100.	1988	Italy	English	retro-spective	young	opiate addiction	semen, hormones	other nervous system drugs	N07	methadone, heroin	N07BC02		continuous	80	spermatogenesis, impairment; testosterone levels, unaltered	all men		no	heroin	methadone		2-	
979: Cicero TJ, Bell RD, Wiest WG, Allison JH, Polakoski K, Robins E. Function of the male sex organs in heroin and methadone users. N Engl J Med. 1975 Apr 24;292(17):882-7.	1975		English	retro-spective	young	opiate addiction	sexual function	other nervous system drugs	N07	methadone	N07BC02	n.g.	continuous	29	sexual function, alteration	ejaculate volume reduced by over 50%		no				3	
942: Lafisca S, Bolelli G, Franceschetti F, Filicori M, Flamigni C, Marigo M. Hormone levels in methadone-treated drug addicts. Drug Alcohol Depend. 1981 Nov;8(3):229-34.	1981		English	retro-spective	young	opiate addiction	hormones	other nervous system drugs	N07	methadone	N07BC02	30mg/d	2m	25	gonadotropin levels, decrease; sex steroid levels, increase	significant						3	
756: Ragni G, De Lauretis L, Gambaro V, Di Pietro R, Bestetti O, Recalcati F, Papetti C. Semen evaluation in heroin and methadone addicts. Acta Eur Fertil. 1985 Jul-Aug;16(4):245-9.	1985		English	retro-spective	young	heroin addiction	sperm functions	other nervous system drugs	N07	methadone, heroin	N07BC02		continuous	n.g.	sperm parameters, deterioration	clear		no				3	
943: Mendelson JH, Meyer RE, Ellingboe J, Mirin SM, McDouggle M. Effects of heroin and methadone on plasma cortisol and testosterone. J Pharmacol Exp Ther. 1975 Nov;195(2):296-302.	1975		English	retro-spective	young	opiate addiction	hormones	other nervous system drugs	N07	methadone, heroin	N07BC02	45mg/d	7d	n.g.	testosterone level, unaltered; cortisol level, unaltered	also after change to methadone		no	heroin	methadone		2-	
779: Whan LB, West MC, McClure N, Lewis SE. Effects of delta-9-tetrahydrocannabinol, the primary psychoactive cannabinoid in marijuana, on human sperm function in vitro. Fertil Steril. 2006 Mar;85(3):653-60.	2006		English	pro-spective	sperm in vitro	healthy	sperm motility and acrosome reaction	other nervous system drugs	N07	tetrahydrocannabinol	not listed	4.8 umol			sperm motility and acrosome reaction, reduction			no				2-	
379: Singer R, Segenreich E, Sagiv M, Shohat B, Livni E, Bartoov B, Zukerman Z, Leiba S, Servadio C. Decreased semen quality in a male infected with malaria. Int J Androl. 1987 Oct;10(5):685-9.	1987	Israel	English	case report	33	malaria	semen	protozoal agents	P01	malaria toxin	not listed			1	azoospermia or oligo-as-theno-teratozoospermia, induction	during 2 years		no				3	
531: El-Beheiry AH, Kamel MN, Gad A. Niridazole and fertility in bilharzial men. Arch Androl. 1982 Jun;8(4):297-300.	1982		English	pro-spective	young	bilharziosis	semen	anthelmintics	P02	niridazol	P02BX02		n.g.	20	spermatogenesis, impairment	all, recovery 3m after therapy		no				3	
52: Pages N, Sauviat MP, Bouvet S, Goudey-Perriere F. Reproductive toxicity of lindane. J Soc Biol. 2002;196(4):325-38.	2002	France	French	review	mammals	genital malformation	malformation	ectoparasiticides	P03	lindane	P03AB02				azoospermia, induction	in 94.8% of exposed men	none	no				4	Lindane is accumulated in the testis and induces hypoproduction of testosterone
911: Comhaire FH, Christophe AB, Zalata AA, Dhooge WS, Mahmoud AM, Depuydt CE. The effects of combined conventional treatment, oral antioxidants and essential fatty acids on sperm biology in subfertile men. Prostaglandins Leukot Essent Fatty Acids. 2000 Sep;63(3):159-65.	2000	Belgium	English	pro-spective	young	infertility	sperm paramters	cough and cold preparations	R05	N-acetyl-cysteine or vitamins A plus E + essential fatty acids	R05CB01		n.g.	27	sperm parameters, unaltered; ROS, decrease; acrosome reaction, increase	no alteration, decrease, increase		no				3	

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759: Gupta A, Khosla R, Gupta S, Tiwary AK. Influence of histamine and H1-receptor antagonists on ejaculated human spermatozoa: role of intrasperm Ca2+. Indian J Exp Biol. 2004 May;42(5):481-5.	2004		English	pro-spective	sperm in vitro	healthy	histamine induced rise of sperm Ca	antihistamines for systemic use	R06	Antihistamines for systemic use	R06A	not mentioned		not mentioned	sperm Ca2+, histamin induced rise, no prevention by famotidine	significant		no				2-	
827: Oliva A, Multigner L. Ketotifen improves sperm motility and sperm morphology in male patients with leukocytospermia and unexplained infertility. Fertil Steril. 2006 Jan;85(1):240-3.	2006	Argentina	English	pro-spective	young	leukocytospermia	sperm parameters	antihistamines for systemic use	R06	ketotifen	R06AX17	2mg/d	12w	55	sperm parameters, improvement; leucocyte count, decrease	during treatment		no				3	
115: Matsuki S, Sasagawa I, Suzuki Y, Yazawa H, Tateno T, Hashimoto T, Nakada T, Saito H, Hiroi M. The use of ebastine, a mast cell blocker, for treatment of oligozoospermia. Arch Androl. 2000 Mar-Apr;44(2):129-32.	2000	Japan	English	pro-spective	young	infertility	semen	antihistamines for systemic use	R06	ebastine	R06AX22	10mg/d	3m	15	sperm parameters, improvement	in 9/15 patients		no				3	
107: Hayashi T, Yoshida S, Ohno R, Ishii N, Terao T, Yamada T. Asthenospermia in hay fever patients improved by stopping treatment with histamine H1 receptor antagonists. Int J Urol. 2006 Jul;13(7):1028-30.	2006	Japan	English	retrospective	35, 44	infertility	semen	antihistamines for systemic use	R06	fexofenadine	R06AX26	120mg/d	continuous	2	sperm motility, decrease	improvement after cessation		no				3	
111: Cayan S, Apa DD, Akbay E. Effect of fexofenadine, a mast cell blocker, in infertile men with significant increased testicular mast cells. Asian J Androl. 2002 Dec;4(4):291-4. Turkey	2002	Turkey	English	pro-spective	young	infertility, testicular histology with mast cells	semen	antihistamines for systemic use	R06	fexofenadine	R06AX26	180mg/d	9m	16	sperm parameters, improvement	no significant effect		no				2-	
113: Yamamoto M, Hibi H, Miyake K. New treatment of idiopathic severe oligozoospermia with mast cell blocker: results of a single-blind study. Fertil Steril. 1995 Dec;64(6):1221-3. Japan.	1995	Japan	English	pro-spective	young	infertility	semen	antihistamines for systemic use	R06	tranilast	not listed	300mg/d	12w	50	sperm parameters, improvement	significant in verum group		yes	tranilast	placebo		1-	
100: Hibi H, Kato K, Mitsui K, Taki T, Yamada Y, Honda N, Fukatsu H, Yamamoto M. The treatment with tranilast, a mast cell blocker, for idiopathic oligozoospermia. Arch Androl. 2001 Apr-Jun;47(2):107-11. Japan.	2001	Japan	English	pro-spective	young	infertility	semen	antihistamines for systemic use	R06	tranilast	not listed	300mg/d	12w	17	sperm count, increase	in 41% of patients		no				3	
237: Yamamoto M, Hibi H, Miyake K. Appearance of spermatozoon after administration of mast cell blocker to a patient with azoospermia. Hinyokika Kiyo. 1994 Jun;40(6):541-3.	1994	Japan	English	case report	young	infertility	semen	antihistamines for systemic use	R06	tranilast	not listed		1y	1	spermatogenesis, recovery	after azoospermia		no				3	
198: Pajarinen J, Savolainen V, Perola M, Penttila A, Karhunen PJ. Glutathione S-transferase-M1 ,null' genotype and alcohol-induced disorders of human spermatogenesis. Int J Androl. 1996 Jun;19(3):155-63.	1996	Finland	English	retrospective	young	spermatogenic dysfunction	molecular biology	all other therapeutic products	V03	alcohol	V03AZ01	various	continuous	271	alcohol-induced impairment of spermatogenesis	Of 212 men with mean daily alcohol consumption > 80 g), 21.2%) had normal spermatogenesis. Of these, 27 (60%) men had GST M1 'null' genotype (OR 2.7; 95% CI 1.0-4.0, compared to those with disorders of spermatogenesis)		no				2-	
2043: Dunphy BC, Barratt CL, Cooke ID. Male alcohol consumption and fecundity in couples attending an infertility clinic. Andrologia. 1991 May-Jun;23(3):219-21	1991	UK	English	retrospective	young	infertility	semen	all other therapeutic products	V03	alcohol	V03AZ01	0-20*8g/w	continuous	258	sperm parameters, impairment	no significant association between alcohol consumption and any semen parameter		no	various doses of alcohol			2-	

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191: Pajarinen J, Savolainen V, Perola M, Penttila A, Karhunen PJ. Polymorphism in the cytochrome P450 2E1 gene and alcohol-induced disorders of human spermatogenesis. Int J Androl. 1996 Oct;19(5):314-22.	1996	Finland	English	retrospective	n.g.	alcohol disease	amount per lifetime	all other therapeutic products	V03	alcohol	V03AZ01			204	cytochrome gene type, spermatogenesis, depression in alcohol disease	no association		no	various genetic polymorphism			2-	
2042: Figa-Talamanca I, Cini C, Varricchio GC, Dondero F, Gandini L, Lenzi A, Lombardo F, Angelucci L, Di Grezia R, Patacchioli FR. Effects of prolonged automobile driving on male reproduction function: a study among taxi drivers. Am J Ind Med. 1996 Dec;30(6):750-8.	1996	Italy	English	retrospective	young	healthy	semen	all other therapeutic products	V03	alcohol	V03AZ01	various	continuous	201	sperm parameters, impairment	moderate alcohol consumption associated with a better seminologic profile		no	alcohol	no alcohol		2-	
200: Pajarinen J, Karhunen PJ, Savolainen V, Lalu K, Penttila A, Laippala P. Moderate alcohol consumption and disorders of human spermatogenesis. Alcohol Clin Exp Res. 1996 Apr;20(2):332-7.	1996	Finland	English	retrospective	36-69	spermatogenic dysfunction	histology	all other therapeutic products	V03	alcohol	V03AZ01	22-260g/d	continuous	195	spermatogenesis, impairment	significant dependent on daily dose			<40g	40-80g	80-160g	2-	
19. Muthusami KR, Chinnaswamy P. Effect of chronic alcoholism on male fertility hormones and semen quality. Fertil Steril. 2005 Oct;84(4):919-24. India.	2005	India	English	retrospective	all ages	alcohol disease	semen, hormones	all other therapeutic products	V03	alcohol	V03AZ01	>180ml/day	1y	66;30	sperm parameters, impairment	significant for sperm count, motility, normal sperm		no	alcohol, non-smokers	non-exposed		2-	
186: Villalta J, Balleasca JL, Nicolas JM, Martinez de Osaba MJ, Antunez E, Pimentel C. Testicular function in asymptomatic chronic alcoholics: relation to ethanol intake. Alcohol Clin Exp Res. 1997 Feb;21(1):128-33.	1997	Spain	English	retrospective	39 mean	alcohol disease	hormones	all other therapeutic products	V03	alcohol	V03AZ01	100-350g/d	continuous	57	sperm parameters, impairment	39.4% of patients reduced sperm count, 44.7% reduced morphology, 50% reduced motility; correlation with life-time dose of alcohol		no	alcohol	no alcohol		2-	
39: Dmitrieva OA. Morphological changes in genesial system of men: medico-legal aspects. Leg Med (Tokyo). 2003 Mar;5 Suppl 1:S228-32.	2003	Russia	English	retrospective	18-35	alcohol disease	testicular histology	all other therapeutic products	V03	alcohol	V03AZ01	various	lifelong	50	spermatogenesis, impairment	depression of cell count in chronic alcohol intoxication		no				3	
2038: Stutz G, Zamudio J, Santillan ME, Vincenti L, de Cuneo MF, Ruiz RD. The effect of alcohol, tobacco, and aspirin consumption on seminal quality among healthy young men. Arch Environ Health. 2004 Nov;59(11):548-52.	2004	Argentina	English	retrospective	young	infertility	semen	all other therapeutic products	V03	alcohol	V03AZ01	various	continuous	34	sperm parameters, impairment	nonsignificant reduction in sperm concentration, motility, viability, and normal morphology in men with drinking habits		no	alcohol	no alcohol		2-	
2144: Mendelson JH, Mello NK, Ellingboe J. Effects of acute alcohol intake on pituitary-gonadal hormones in normal human males. J Pharmacol Exp Ther. 1977 Sep;202(3):676-82.	1977	USA	English	prospective	young	healthy	hormones	all other therapeutic products	V03	alcohol	V03AZ01	acute intoxication	single dose	16	hormone levels, alteration	At peak blood alcohol levels [109 +/- 4.6 mg/100 ml] T levels were significantly depressed, LH levels significantly increased. During descending phase of the blood alcohol curve, T levels remained depressed and LH levels decreased again.		no				3	
2037: Marinelli D, Gaspari L, Pedotti P, Taioli E. Mini-review of studies on the effect of smoking and drinking habits on semen parameters. Int J Hyg Environ Health. 2004 Jul;207(3):185-92.	2004	Italy	English	review	young	infertility	semen	all other therapeutic products	V03	alcohol	V03AZ01	various	continuous	n.g.	sperm parameters, impairment	apparent protective effect of moderate alcohol drinking on sperm parameters		no	alcohol	no alcohol		4	
516: Gavalier JS, Urso T, Van Thiel DH. Ethanol: its adverse effects upon the hypothalamic-pituitary-gonadal axis. Subst Alcohol Actions Misuse. 1983;4(2-3):97-110.	1983		English	review	all men	poisoning	hormones	all other therapeutic products	V03	alcohol	V03AZ01			review	spermatogenesis, impairment	recovery possible		no				4	

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1: Mkrtchyan A, Panosyan V, Panossian A, Wikman G, Wagner H. A phase I clinical study of Andrographis paniculata fixed combination Kan Jang versus ginseng and valerian on the semen quality of healthy male subjects. Phytomedicine. 2005 Jun;12(6-7):403-9.	2005	Armenia	English	pro-spective	n.g.	infertility	semen	medical plants		Kan Yang, Valeriana, Ginseng	not listed	n.g.	n.g.	n.g.	spermatogenesis, improvement	n.g.	n.g.	no				3	small effects in a accurate study
992. Gonzales GF, Cordova A, Gonzales C, Chung A, Vega K, Villena A. Lepidium meyenii (Maca) improved semen parameters in adult men Asian J Androl. 2001 Dec;3(4):301-3.	2001	Peru	English	pro-spective	24-44	infertility	semen	medical plants		Lepidium meyenii		3000mg/d	4m	9	sperm count, increase	increase of sperm count not related to dose of Maca		no				3	
504: Wyrobek AJ, Gordon LA, Burkhart JG, Francis MW, Kapp RW Jr, Letz G, Malling HV, Topham JC, Whorton MD. An evaluation of human sperm as indicators of chemically induced alterations of spermatogenic function. A report of the U.S. Environmental Protection Agency Gene-Tox Program. Mutat Res. 1983 May;115(1):73-148.	1983	USA	English	review	youg	spermatogenic dysfunction	semen	environmental toxicants		Environmen-tal toxicants in general	not listed			review	spermatogenesis, impairment	as an indicator of toxicants		no				4	
2048: Wyrobek AJ. Methods and concepts in detecting abnormal reproductive outcomes of paternal origin. Reprod Toxicol. 1993;7 Suppl 1:3-16.	1993	USA	English	review	all	paternal exposure to toxicants	gonadal dysfunction	environmental toxicants		Environmen-tal toxicants in general					the father's role in abnormal reproductive outcomes	(i) Insufficient number of functional sperm; (ii) Transmitted genetic defects; (iii) non-mutational changes of DNA; (iv) Possible source of toxic or infectious agents that negatively affect pregnancy; (v) Postnatal toxic exposure of the offspring. (vi) Bridging biomarkers for comparisons between exposed men and laboratory animals, i.e. biomarkers that can be measured in men and animals in response to damaging agents.						4	D
136: Ben-Jonathan N, Cooper RL, Foster P, Hughes CL, Hoyer PB, Klotz D, Kohn M, Lamb DJ, Stancel GM. An approach to the development of quantitative models to assess the effects of exposure to environmentally relevant levels of endocrine disruptors on homeostasis in adults. Environ Health Perspect. 1999 Aug;107 Suppl 4:605-11.	1999	USA	English	cell culture	testis in vitro	genital malformation	methods of homeostasis	environmental toxicants		endocrine disruptors	not listed				genital malformation	various modes of action and points of effect		no				4	testicular function as an integrated biologic read-out is well suited to assess the effects
151: Spira A, Multigner L. The effect of industrial and agricultural pollution on human spermatogenesis. Hum Reprod. 1998 Aug;13(8):2041-2.	1998	France	English	review	young	spermatogenesis	histology, semen	environmental toxicants		endocrine disruptors	not listed				spermatogenesis, impairment	as an effect of endocrine disruptors in the environment		no				4	the„endocrine disruptor hypothesis“ is unproven
176: Swan SH. Semen quality in fertile US men in relation to geographical area and pesticide exposure. Int J Androl. 2006 Feb;29(1):62-8; discussion 105-8. USA	2006	USA	English	retrospective	young	infertility	semen	environmental toxicants		alachlor	not listed	various	continuous	25;24	sperm parameters, impairment	in higher urinary concentrations more likely (OR 6.3 and 30.0)		no				2+	
800. Tates AD, van Dam JJ, de Zwart FA et al.: Biological effect monitoring in industrial workers from the Czech Repudblic exposed to low levels of butadiens. Toxicology 1996;113: 91-99	1996	Czechia	English	retrospective	young	healthy, hpert mutant frequency	molecular biology	environmental toxicants		butadiene	not listed			38	sperm parameters, unaltered	no significant differences between gene types		no				2-	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
106: Adler ID. Spermatogenesis and mutagenicity of environmental hazards: extrapolation of genetic risk from mouse to man. Andrologia. 2000 Sep;32(4-5):233-7.	2000	Germany	English	review, animal	young	infertility	spermatogenesis	environmental toxicants		butadiene	not listed		320-380 ppmh exposure time		spermatogonial cytogenesis, alteration	none		no				4	categories for germ cell mutagens of the MAK
775: Adler ID, Cochrane J, Osterman-Golkar S, Skopek TR, Sorsa M, Vogel E. 1,3- butadiene working group report. Mutat Res. 1995 Aug;330(1-2):101-14.	1995		English	review	young	poisoning	germinal cell DNA	environmental toxicants		butadiene	not listed				genotoxic effect	none		no				4	
2044: Hales BF, Robaire B. Paternal exposure to drugs and environmental chemicals: effects on progeny outcome. J Androl. 2001 Nov-Dec;22(6):927-36.	2001	Canada	English	review	all	infertility	progeny outcome	environmental toxicants		butadiene, organic solvents	not listed				alteration of number and quality of progeny	no effect						4	
231: Moseman RF. Chemical disposition of boron in animals and humans. Environ Health Perspect. 1994 Nov;102 Suppl 7:113-7.	1994	USA	English	review	all	poisoning	concentration of boron	environmental toxicants		boron	not listed				fertility, decrease	in wild rodents; in humans not proven		no				4	no further references of this compound
285: Potashnik G, Carel R, Belmaker I, Levine M. Spermatogenesis and reproductive performance following human accidental exposure to bromine vapor. Reprod Toxicol. 1992;6(2):171-4.	1992	Israel	English	retrospective	young	poisoning	semen	environmental toxicants		bromine vapor	not listed		accidental	8	spermatogenesis, impairment	no effect		no				3	
114: Djemek J, Jelinek R, Solansky' I, Benes I, Sram RJ. Fecundability and parental exposure to ambient sulfur dioxide. Environ Health Perspect. 2000 Jul;108(7):647-54.	2000	Czechia	English	retrospective	young	infertility	time to pregnancy	environmental toxicants		carbon disulfide	not listed			2585	spermatogenesis, impairment	OR of conception 0.57 as compared to low exposed men		no	40ug/m ³	40-80	>80	3	
2002: Meeker JD, Singh NP, Ryan L, Duty SM, Barr DB, Herrick RF, Bennett DH, Hauser R. Urinary levels of insecticide metabolites and DNA damage in human sperm. Hum Reprod. 2004 Nov;19(11):2573-80. Epub 2004 Aug 27. USA.	2004	USA	English	retrospective	young	infertility	semen	environmental toxicants		chlorpyrifos	not listed		continuous	260	sperm parameters, impairment	significant increase in DNA damages		no				3	
626: Whorton D, Milby TH, Krauss RM, Stubbs HA. Testicular function in DBCP exposed pesticide workers. J Occup Med. 1979 Mar;21(3):161-6.	1979	USA	English	retrospective	young	infertility	semen	environmental toxicants		dibromochloropropane	not listed			142	azoospermia, induction	13% versus 2.9% in control group		no	exposed	non-exposed		2-	
308: Olsen GW, Lanham JM, Bodner KM, Hylton DB, Bond GG. Determinants of spermatogenesis recovery among workers exposed to 1,2-dibromo-3-chloropropane. J Occup Med. 1990 Oct;32(10):979-84.	1990	Denmark	English	retrospective	young	poisoning	semen	environmental toxicants		dibromochloropropane	not listed	high/low	18m	47	spermatogenesis, recovery	complete		no	various jobs with DBCP			3	
471: Potashnik G, Goldsmith J, Insler V. Dibromochloropropane-induced reduction of the sex-ratio in man. Andrologia. 1984 May-Jun;16(3):213-8.	1984	Israel	English	retrospective	young	offspring of exposed fathers	sex ratio of offspring	environmental toxicants		dibromochloropropane	not listed			30	offspring, sex rate (b:g)	52.9% boys in non-exposed versus 35.2% in exposed period		no				2-	
393: Potashnik G, Yanai-Inbar I. Dibromochloropropane (DBCP): an 8-year reevaluation of testicular function and reproductive performance. Fertil Steril. 1987 Feb;47(2):317-23.	1987	Israel	English	retrospective	young	poisoning	semen	environmental toxicants		dibromochloropropane	not listed			15	spermatogenesis, recovery	after up to 8 years		no				3	

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639: Potashnik G, Ben-Aderet N, Israeli R, Yanai-Inbar I, Sober I. Suppressive effect of 1,2-dibromo-3-chloropropane on human spermatogenesis. Fertil Steril. 1978 Oct;30(4):444-7.	1978		English	retrospective	young	infertility	semen	environmental toxicants		dibromochloropropane	not listed		n.g.	6	spermatogenesis, impairment	in 2 of 6 men		no				3	
607: Sandifer SH, Wilkins RT, Loadholt CB, Lane LG, Eldridge JC. Spermatogenesis in agricultural workers exposed to dibromochloropropane (DBCP). Bull Environ Contam Toxicol. 1979 Nov;23(4-5):703-10.	1980		English	retrospective	young	infertility	semen	environmental toxicants		dibromochloropropane	not listed		n.g.	n.g.	spermatogenesis, impairment	most		no				3	
635: Biava CG, Smuckler EA, Whorton D. The testicular morphology of individuals exposed to dibromochloropropane. Exp Mol Pathol. 1978 Dec;29(3):448-58.	1978		English	retrospective	young	infertility	testicular histology	environmental toxicants		dibromochloropropane	not listed			n.g.	spermatogenesis, impairment	most		no				3	
627: Glass RI, Lyness RN, Mengle DC, Powell KE, Kahn E. Sperm count depression in pesticide applicators exposed to dibromochloropropane. Am J Epidemiol. 1979 Mar;109(3):346-51.	1979	USA	English	retrospective	young	infertility	semen	environmental toxicants		dibromochloropropane	not listed			n.g.	spermatogenesis, impairment	most, associated with duration of exposition		no				3	
444: Potashnik G, Abeliovich D. Chromosomal analysis and health status of children conceived to men during or following dibromochloropropane-induced spermatogenic suppression. Andrologia. 1985 May-Jun;17(3):291-6.	1985	Israel	English	retrospective	young	offspring of exposed fathers	health	environmental toxicants		dibromochloropropane	not listed				children fathered; genital malformation	none		no				3	
2177: Wong WY, Zielhuis GA, Thomas CM, Merkus HM, Steegers-Theunissen RP. New evidence of the influence of exogenous and endogenous factors on sperm count in man. Eur J Obstet Gynecol Reprod Biol. 2003 Sep 10;110(1):49-54.	2003	The Netherlands	English	case-control	34.4 mean	infertility	semen	environmental toxicants		fungicides	not listed			92; 73	spermatogenesis, impairment	OR 8.3 (95% CI 1.0–71.0) as compared to non-exposed men, p0.02							
267: Veulemans H, Steeno O, Masschelein R, Groeseneken D. Exposure to ethylene glycol ethers and spermatogenic disorders in man: a case-control study. Br J Ind Med. 1993 Jan;50(1):71-8.	1992	Belgium	English	case-control-study	young	poisoning	semen	environmental toxicants		glycol ethers	not listed			1019 cases, 475 controls	spermatogenesis, impairment	no correlation to urinary excretion		no				2-	
2177: Wong WY, Zielhuis GA, Thomas CM, Merkus HM, Steegers-Theunissen RP. New evidence of the influence of exogenous and endogenous factors on sperm count in man. Eur J Obstet Gynecol Reprod Biol. 2003 Sep 10;110(1):49-54.	2003	The Netherlands	English	case-control	34.4 mean	infertility	semen	environmental toxicants		heavy metals	not listed			92; 73	spermatogenesis, impairment	OR 2.6 (95% CI 1.1–6.2) as compared to non-exposed men, p0.03							
667: Ruse M, Suciú L, Zegreanu O. Participation of gonads in chronic poisonings with heavy metals. Z Gesamte Inn Med. 1977 Sep 15;32(18):469-70.	1977		German	retrospective	young	infertility	semen	environmental toxicants		heavy metals	not listed			37	spermatogenesis, impairment	improvement by gonadotropins		no	lead	hydrargirum	copper	3	no data on kind and duration of exposure; no data on disturbances of other organs
2044: Hales BF, Robaire B. Paternal exposure to drugs and environmental chemicals: effects on progeny outcome. J Androl. 2001 Nov-Dec;22(6):927-36.	2001	Canada	English	review	all	infertility	progeny outcome	environmental toxicants		heavy metals	not listed				number and quality of progeny, alteration	no effect						4	

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176: Swan SH. Semen quality in fertile US men in relation to geographical area and pesticide exposure. Int J Androl. 2006 Feb;29(1):62-8; discussion 105-8. USA	2006	USA	English	retro-spective	young	infertility	semen	environmental toxicants		isopropoxy-4-methylpyrimidinol	not listed	various	continuous	25;25	sperm parameters, impairment	in higher urinary concentrations more likely (OR 10 and 16.7)		no				2+	
169: Bonde JP, Kolstad H. Fertility of Danish battery workers exposed to lead. Int J Epidemiol. 1997 Dec;26(6):1281-8.	1997	Denmark	English	retro-spective	<60	infertility	birth rate	environmental toxicants		lead	not listed			1349	birth rate, alteration	none		no	38,9 ug/ml lead			2-	
2036: Lancranjan I, Popescu HI, GAvanescu O, Klepsch I, Serbanescu M. Reproductive ability of workmen occupationally exposed to lead. Arch Environ Health. 1975 Aug;30(8):396-401	1975		English	retro-spective	young	infertility	semen	environmental toxicants		lead	not listed		workplace	150	sperm parameters, alteration	increased frequency of asthenospermia, hypospermia, and teratospermia as compared to non-exposed men		no	lead exposed	not lead exposed		2-	
165: Alexander BH, Checkoway H, Costa-Mallen P, Faustman EM, Woods JS, Kelsey KT, van Netten C, Costa LG. Interaction of blood lead and delta-aminolevulinic acid dehydratase genotype on markers of heme synthesis and sperm production in lead smelter workers. Environ Health Perspect. 1998 Apr;106(4):213-6.	1998	USA	English	pro-spective	<60	lead exposure	semen, genotype	environmental toxicants		lead	not listed			134	spermatogenesis, impairment	lead different effective per gene type		no				2-	
288: Lerda D. Study of sperm characteristics in persons occupationally exposed to lead. Am J Ind Med. 1992;22(4):567-71.	1992	Argentina	English	retro-spective	young	poisoning	semen	environmental toxicants		lead	not listed		workplace	38	spermatogenesis, impairment	correlation to uptake of lead		no				3	
401: Assennato G, Paci C, Baser ME, Molinini R, Candela RG, Altamura BM, Giorgino R. Sperm count suppression without endocrine dysfunction in lead-exposed men. Arch Environ Health. 1986 Nov-Dec;41(6):387-90.	1986	Italy	English	case-control	young	lead exposure	semen	environmental toxicants		lead	not listed		n.g.	36	spermatogenesis, impairment	lower sperm count in lead exposed		no	lead exposed	not lead exposed		2-	
149: Apostoli P, Kiss P, Porru S, Bonde JP, Vanhoorne M. Male reproductive toxicity of lead in animals and humans. ASCLEPIOS Study Group. Occup Environ Med. 1998 Jun;55(6):364-74.	1998	Italy	English	meta-analysis	young	infertility	fertility	environmental toxicants		lead	not listed	>40ug /ml blood	lifelong		spermatogenesis, impairment			no				2+	
617: Rosenman KD, Anderson HA, Selikoff IJ, Wolff MS, Holstein E. Spermatogenesis in men exposed to polybrominated biphenyl (PBB). Fertil Steril. 1979 Aug;32(2):209-13.	1979		English	retro-spective	young	poisoning	semen	environmental toxicants		polybromebisphenyl (PBB)	not listed		work place	104	spermatogenesis, impairment	no difference between exposed and control men		no	exposed	non-exposed		2-	no further references of this compound
22. Hauser R, Altshul L, Chen Z, Ryan L, Overstreet J, Schiff I, Christiani DC. Environmental organochlorines and semen quality: results of a pilot study. Environ Health Perspect. 2002 Mar;110(3):229-33. USA.	2002	USA	English	retro-spective	young	healthy	semen	environmental toxicants		polychlorinated bisphenyls	not listed		work place	29	sperm count, decrease	no significant difference between groups		no	exposed	non-exposed		2-	
2044: Hales BF, Robaire B. Paternal exposure to drugs and environmental chemicals: effects on progeny outcome. J Androl. 2001 Nov-Dec;22(6):927-36.	2001		English	review	young	infertility	progeny outcome	environmental toxicants		polychlorinated bisphenyls	not listed				number and quality of progeny, alteration	reduced fecundity						4	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2174: Shin D, Lipshultz LI, Goldstein M, Barne GA, Fuchs EF, Nagler HM, McCallum SW, Niederberger CS, Schoor RA, Brugh VM 3rd, Honig SC. Herni-orrhaphy with polypropylene mesh causing inguinal vasal ob-struction: a preventable cause of obstructive azoospermia. Ann Surg. 2005 Apr;241(4):553-8	2005	USA	English	retro-spective	35.5 mean	hernia inguinalis	history, semen	environmental toxicants		polypropyl-ene mesh for herniorraphia	not listed		6.3y after surgery	14	azoospermia	obstruction after herniorraphy						3	
2152: Bonde JP, Olsen JH, Hansen KS. Adverse pregnancy outcome and childhood malignancy with reference to paternal welding exposure. Scand J Work Environ Health. 1992 Jun;18(3):169-77.	1992	Denmark	English	retro-spective	young	infertility	offspring health	environmental toxicants		stainless steel, welding	not listed		work place	23264	childhood malignancies in the offspring	The overall incidence of childhood malignancies was equal to national rates (RR 0.97, 95% CI 0.63-1.42)		no	exposed	non-exposed		2++	
2148: Hjollund NH, Bonde JP, Jensen TK, Ernst E, Henriksen TB, Kolstad HA, Giwercman A, Skakkebaek NE, Olsen J. Semen quality and sex hormones with reference to metal welding. Reprod Toxicol. 1998 Mar-Apr;12(2):91-5.	1998	Denmark	English	pro-spective	young	infertility	semen	environmental toxicants		stainless steel, welding	not listed		work place	430	sperm parameters, impairment	Median sperm density for welders 56 x 10(6)/mL and 52.5 x 10(6)/mL and 50.0 x 10(6)/mL in two reference groups		no	exposed	non-exposed		2-	
2149: Hjollund NH, Bonde JP, Jensen TK, Henriksen TB, Kolstad HA, Ernst E, Giwercman A, Pritzl G, Skakkebaek NE, Olsen J. A follow-up study of male exposure to welding and time to pregnancy. Reprod Toxicol. 1998 Jan-Feb;12(1):29-37.	1998	Denmark	English	pro-spective	young	infertility	concep-tions	environmental toxicants		stainless steel, welding	not listed		work place	430	fecundity, decreased	fecundability of male exposure to welding OR of 0.86 (95% CI 0.58-1.28)		no	exposed	non-exposed		2-	
2146: Hjollund NH, Bonde JP, Ernst E, Lindenberg S, Andersen AN, Olsen J. Spontaneous abortion in IVF couples--a role of male welding exposure. Hum Reprod. 2005 Jul;20(7):1793-7.	2005	Denmark	English	retro-spective	young	infertility	abortion rate after IVF	environmental toxicants		stainless steel, welding	not listed		work place	319	proportion of pregnan-cies terminated by spon-taneous abortion before gestational week 28	18% in pregnancies with paternal exposure to stain-less steel welding, 25% with mild steel welding, 28% in reference group		no	stainless steel welding	mild steel welding	reference group	2+	
2147: Hjollund NH, Bonde JP, Jensen TK, Henriksen TB, Ander-sson AM, Kolstad HA, Ernst E, Giwercman A, Skakkebaek NE, Olsen J. Male-mediated sponta-neous abortion among spouses of stainless steel welders. Scand J Work Environ Health. 2000 Jun;26(3):187-92. Denmark. akh-hhj@aaa.dk	2000	Denmark	English	pro-spective	young	infertility	abortion rate after sponta-neous conception	environmental toxicants		stainless steel, welding	not listed		work place	245	risk of spontaneous abor-tion, increased	with paternal exposure to stainless-steel welding, RR 3.5 (95% CI 1.3-9.1)		no	exposed	non-exposed		2-	
2151: Bonde JP, Ernst E. Sex hormones and semen quality in welders exposed to hexavalent chromium. Hum Exp Toxicol. 1992 Jul;11(4):259-63.	1992	Denmark	English	retro-spective	young	healthy	semen	environmental toxicants		stainless steel, welding	not listed		work place	77	chromium in urine, increase; semen param-eters, impairment	no association of semen parameters with increasing level of internal exposure to chromium		no	exposed	non-exposed		2-	
2153: Bonde JP. Semen quality in welders before and after three weeks of non-exposure. Br J Ind Med. 1990 Aug;47(8):515-8.	1990	Denmark	English	retro-spective	young	healthy	semen	environmental toxicants		stainless steel, welding	not listed		work place; after 3w break of exposure	53	semen parameters, improvement	no consistent alteration		no	exposed	non-exposed		2-	
322: Taskinen H, Anttila A, Lindbohm ML, Sallmen M, Hem-minki K. Spontaneous abortions and congenital malformations among the wives of men oc-cupationally exposed to organic solvents. Scand J Work Environ Health. 1989 Oct;15(5):345-52.	1989	Finland	English	retro-spective	young	infertility	pregnancy induction	environmental toxicants		styrene, tolu-ene, xylene, tetrachlo-roethylene, trichloroeth-ylen, and 1,1,1-trichlo-roethane	not listed			n.g.	abortion rate, increase	no significant association between different degrees of paternal or maternal exposure		case control	exposed	unexposed		2-	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
2197: Bundschu HD, Rager K, Heller S, Hayduk K, Pfeiffer EH, Luders G, Liebau G. Effects of longterm HCG administration on testicular function in hemodialysis patients. Klin Wochenschr. 1976 Nov 1;54(21):1039-46.	1976	Germany	German	retrospective	young	renal insufficiency	hormones	renal dialysis		dialysis				13	hCG-induced rise of testosterone levels, impairment	significant as compared to normal men						3	
129: Akbari F, Alavi M, Esteghamati A, Mehraei A, Djaladat H, Zohrevand R, Pourmand G. Effect of renal transplantation on sperm quality and sex hormone levels. BJU Int. 2003 Aug;92(3):281-3.,	2003	Iran	English	retrospective	young	renal insufficiency	semen	surgery		renal transplantation				30	sperm parameters, improvement	sperm motility, significant		no				3	
2195: Akbari F, Alavi M, Esteghamati A, Mehraei A, Djaladat H, Zohrevand R, Pourmand G. Effect of renal transplantation on sperm quality and sex hormone levels. BJU Int. 2003 Aug;92(3):281-3.	2003	Iran	English	retrospective	young	renal insufficiency	semen	surgery		renal transplantation				30	sperm parameters, improvement	Sperm motility improved significantly, but there were no significant changes in morphology or density.						3	
2196: Prem AR, Puneekar SV, Kalpana M, Kelkar AR, Acharya VN. Male reproductive function in uraemia: efficacy of haemodialysis and renal transplantation. Br J Urol. 1996 Oct;78(4):635-8.	1996	India	English	retrospective	22-41	renal insufficiency	semen, hormones	surgery		renal transplantation			6m	19	sperm parameters, improvement	After renal transplantation, testosterone and LH levels returned to normal in most patients, while FSH levels became normal in only two patients. Semen quality improved in 13 patients, the improvement in sperm density and motility was statistically significant.						3	
130: Prem AR, Puneekar SV, Kalpana M, Kelkar AR, Acharya VN. Male reproductive function in uraemia: efficacy of haemodialysis and renal transplantation. Br J Urol. 1996 Oct;78(4):635-8.	1996	India	English	retrospective	22-41	renal insufficiency	semen	surgery		renal transplantation				18	sperm parameters, improvement	In 13 patients, for sperm density and motility being significant		no				3	
990. Inci K, Duzova A, Aki FT, Bilginer Y, Erkan I, Tasar C, Bakaloglu A, Bakkaloglu M. Semen variables and hormone profiles after kidney transplantation during adolescence. Transplant Proc. 2006 Mar;38(2):541-2.	2006	Turkey	English	retrospective	13-19	renal insufficiency	semen	surgery		renal transplantation				7	sperm parameters, improvement	Only one patient had normal sperm parameters, 6/7 had oligo-asthenoteratozoospermia.		no				3	
663: Baumgarten SR, Lindsay GK, Wise GJ. Fertility problems in the renal transplant patient. J Urol. 1977 Dec;118(6):991-3.	1978		English	retrospective	young	renal insufficiency	semen	surgery		renal transplantation				7	sperm parameters, impairment	improvement after renal transplantation		no				3	
110: Xu LG, Shi SF, Qi XP, Huang XF, Xu HM, Song QZ, Wang XH, Shao ZF, Zhang JR. Morphological characteristics of spermatozoa before and after renal transplantation. Asian J Androl. 2005 Mar;7(1):81-5	2005	China	English	retrospective	n.g.	renal insufficiency	semen	surgery		renal transplantation				5	sperm parameters, improvement	return to normal values after transplantation		no				3	
2194: Xu LG, Shi SF, Qi XP, Huang XF, Xu HM, Song QZ, Wang XH, Shao ZF, Zhang JR. Morphological characteristics of spermatozoa before and after renal transplantation. Asian J Androl. 2005 Mar;7(1):81-5.	2005	China	English	retrospective	young	renal insufficiency	semen	surgery		renal transplantation				5	sperm parameters, improvement	After renal transplantation, most of the spermatozoa became normal						3	
2193: Lim VS, Fang VS. Gonadal dysfunction in uremic men. A study of the hypothalamo-pituitary-testicular axis before and after renal transplantation. Am J Med. 1975 May;58(5):655-62.	1975	China	English	retrospective	young	renal insufficiency	semen, hormones	surgery		renal transplantation			12m	4	sperm parameters, improvement	after transplantation from azoospermia to 20 to 40 million/ml, sperm motility 40 to 90 per cent						3	

Reference	year	country	language	type of study	age group	dysfunction	quantification	treatment class	ATC 2nd level	treatment substance	ATC code	dose	treatment period	patient number	treatment consequences	efficacy	side effects	randomization	dose arm 1	dose arm 2	dose arm 3	study quality	remarks
993. Chou FF, Lee CH, Lee CT, Huang FJ, Hsu KL. Spermatogenesis after parathyroidectomy in patients with symptomatic secondary hyperparathyroidism. J Am Coll Surg. 2003 Jun;196(6):854-8.	2003	Taiwan	English	retrospective	29-50	secondary hyperparathyroidism in renal insufficiency	semen	surgery		parathyroidectomy			3m	19	spermatogenesis, impairment	ten patients improved to normal sperm density (> or =20 x 106/mL), 9 had oligospermia or remained azoospermic		no				3	