Long H, Jin Y, Lin M, Sun Y, Zhang L, Clinch CA. Fluoride Toxicity in the Male Reproductive System. Fluoride 42(4): 275-91. Available from:
http://www.fluorideresearch.org/424/files/FJ2009_v42_n4_p260-276.pdf

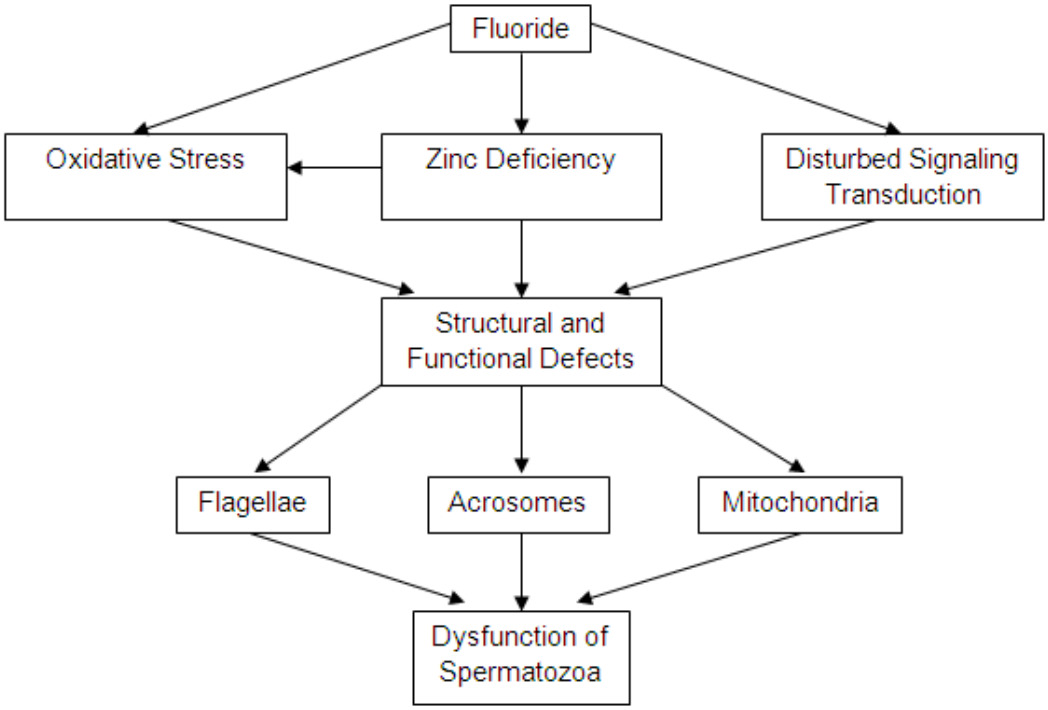

Figure 1. F causes dysfunction of spermatozoa by three mechanisms, i.e., oxidative stress, zinc deficiency, disturbed signaling transduction.

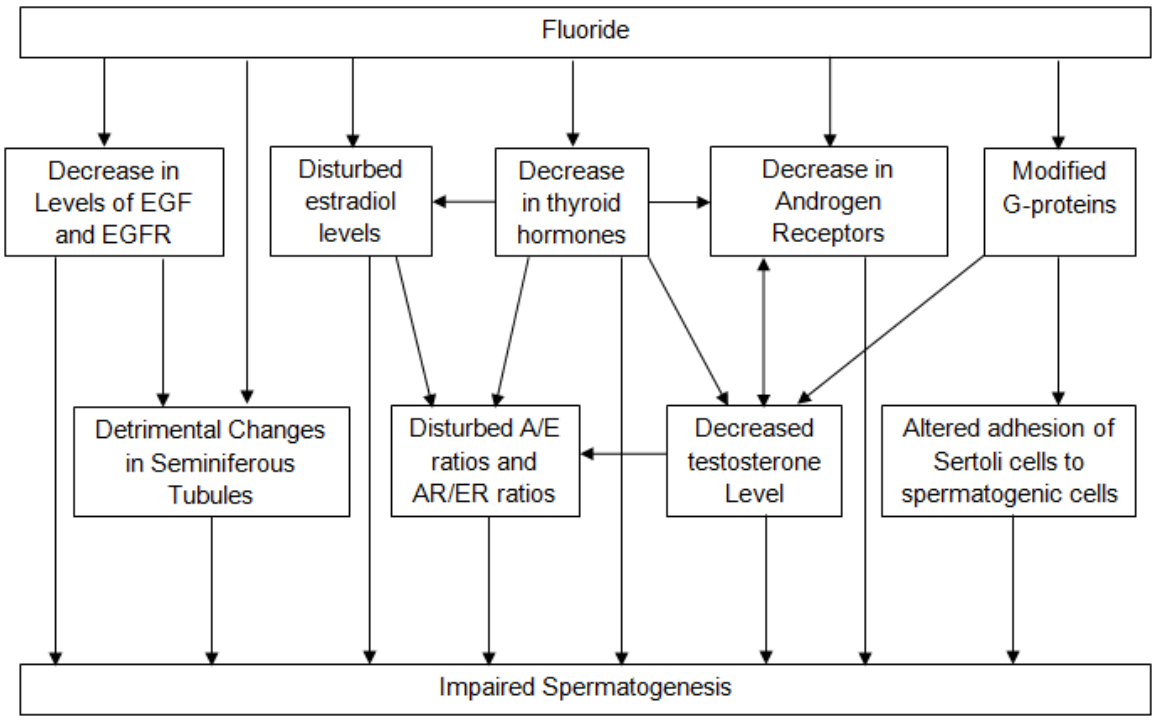

Figure 2. F interferes with spermatogenesis through five mechanisms.

No.	Species	Dose	Length of exposure	Effect	Reference
1	Rabbit	10 mg NaF/kg bw/day	18 mo	Structural defects in various organelles in spermatozoa e.g., flagella, acrosome, and mitochondria	6
2	Rat	4.5 ppm or 9 ppm NaF DW[a]	75 Days	Decrease in sperm motility and steroidogenic enzymes	4
3	Mouse	10 mg NaF/kg bw/day	?	A significant decline in sperm acrosomal acrosin and hyaluronidase	21
4	Rat	5 mg F/kg bw/day	8 Weeks	Altered plasma membrane, and deceased ability to undergo acrosome reaction and oocyte fertilization	22
5	Rat	10 mg NaF/kg bw/day	30 or 50 Days	Disturbances in energy metabolism in vas deferens and seminal vesicle	8
6	Rat	5 mg F/kg bw/day; F in serum: 0.263±0.024 ppm	8 Weeks	Oxidative stress and loss of mitochondrial transmembrane potential	25
7	Mouse	50, 100, 200, 300 mg NaF/L DW	8 Weeks	Reduced antioxidative defense and oxidative stress, in two high dose groups, distinct testis cell apoptosis	26
8	Rat	5 or 26 mg F/L DW	12 Weeks	Free radical toxicity in testis	27
9	Rat	100 or 200 ppm F DW	16 Weeks	Decreased zinc concentrations in testis	36
10	Bank Vole	200 mg F/mL DW	4 mo	Decreased testicular zinc concentration	37
11	Bank Vole	200 mg/mL F DW plus moderate photo period	4 mo	Decreased zinc concentration in testis	38
12	Mouse	10 or 100 ppm F DW	3 mo	Decreased sperm head tyrosine phosphorylation and actin polymerization	42
13	Mouse	150 mg NaF/L DW	7 Weeks	Decreased sperm hyperactivation and Catsper1 gene expression level	46
14	Rabbit	10 mg NaF/kg bw/day	18 or 29 mo	In 29-mo group, F crossed the blood-testis barrier; cessation of spermatogenesis.	49
15	Mouse	1000 ppm NaF DW	3 mo	Necrosis of seminiferous tubules, lack of maturation and differentiation of spermatocytes, and cessation of spermatogenesis.	50
16	Rabbit	10 mg NaF/kg	23 mo	Fragmentation of spermatozoa in	13

		bw/day		epididymis	
17	Rat	20 mg NaF/kg bw/day	28 Days	Inhibition of spermatogenesis and significant diminution in steroidogenic enzymes (3β-HSD, 17βHSD)	51
18	Rat	50 mg/50 mL NaF into vas deferens	Single injection	Arrest of spermatogenesis and absence of spermatozoa in ST[b]	52
19	Rat	150 mg NaF/L DW	10 Days	Decreased expression of EGF & EGFR in spermatogenic and Leydig cells	53
20	Rat	4.5 mg NaF/kg bw/day	60 Days	Decreased diameter of ST	19
21	Rat	150 mg NaF/L DW	50, 100 or 120 Days	Decrease in diameter of ST and number of seminiferous epithelial cell layers	59
22	Mouse	10 or 20 mg NaF/kg bw/day	30 Days	Severe disorganization and denudation of germinal epithelial cells in ST	11
23	Human	3-27 mg F/day bw/day or 2-13 mg F/day bw/day	Long Time	A significant reduction in T[c] and increase in FSH	12
24	Human	Fluorosis	Long Time	Decrease in T, increase in FSH and LH	66
25	Rat	Subcutaneous injection of NaF solution	28 or 38 Days	Decrease in serum estradiol level and apoptosis of spermatogenic cells	67
26	Human	1.52-6.95 mg NaF/L DW; F in serum: 0.216±0.060 ppm	Long Time	Altered conversion of testosterone into potent metabolite	68
27	Rat	0.1 or 1.0 mg F daily	2 mo	Decrease in T4 and T3 level in plasma	69
28	Human	122±5 mumol/L or 52±5 mumol/L F DW	Long Time	Elevated TSH, decrease in T3	70
29	Rat	30 mg F/L DW	?	Decrease in T3,T4, and thyroid peroxidase	71
30	Rat	150 mg F/L DW	120 Days	Decrease in T3 andT4; flattened follicular epithelial cells	72
31	Rat	20 mg NaF/kg bw/day	29 Days	Oxidative stress; decrease in T and steroidogenic enzymes	9
32	Human	Skeletal fluorosis	Long Time	A significant reduction in T	82
33	Mouse	200 or 300 mg NaF/L DW	8 Weeks	Decrease in AR expression	84
34	Rat	10 mg NaF/kg bw/day	50 Days	Significant change in diameter of Leydig cells, reduced steroidogenic enzymes, and disturbance in steroidogenesis	85
35	Rabbit	4.5 mg/kg bw/day	?	Degenerative changes in Leydig cells	86
36	Rat	30 or 100 mg F/L DW	8 Weeks	Disturbed hormone levels of each layer of the hypothalamus-	88

				hypophysis-testis axis	
37	Human	F in pineal gland: 297±257 mg F/kg	Long Time	Accumulation of F in pineal gland	89
38	Gerbil	HiF[d]: 37 mg F/kg bw/day in food. LF[e]: 7 mg F/kg bw/day in food	7, 9, 11.5, 16 Weeks	Depressed pineal melatonin output	3
39	Human	1.52-6.95 mg NaF/L DW; F in serum:0.216±0.060 ppm	Long Time	Fluorosis, significant increase in serum catecholamines, and stimulatory effect on sympathetic nervous system.	5
40	Chick	500, 1000, 1500, 2000 mg F/kg in food	150 Days	Karyopyknosis, decreased microvilli and swollen vacuoles in epithelial follicular cells	110
41	Mouse	500 ppm NaF DW to mother mice	Duration [f]	For the suckling pups: decreased colloid volume	111
42	Pig	100, 250 or 400 mg F/kg in food	50 Days	Decrease in activities of Na/K-ATPase and thyroid peroxidase (TPO)	114

[a]DW: drinking water; [b]ST: seminiferous tubules; [c]T: testosterone; [d]HiF: high F; [e]LF: low F; [f]Duration: from 15th day of pregnancy to 4th or 14th day after parturition.

Definitions:

Acrosome: A caplike structure at the anterior end of a spermatozoon that produces enzymes (acrosin and hyaluronidase[21]) aiding in dissolution of the zona pellucida of an ovum in order to facilitate the fusion of two gametes.

Capacitation:changes made by sperm which enable them to penetrate eggs

EGF: Epidermal Growth Factor

Karyopyknosis: shrinkage of the nucleus of a cell with the condensation of the chromatin into structureless masses