SEXUAL AND PHYSICAL MATURATION OF MALE ADOLESCENTS IN A DIOXIN CONTAMINATED REGION: CHAPAEVSK, RUSSIA.

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Introduction

Animal studies have shown effects of dioxins on sexual development, serum concentrations of sex hormones and gonadotropins, and developmental malformations[1,2,3]. However, the relationship between dioxin exposure and human sexual development has not been well studied[4]. There is epidemiological evidence of an association between dioxins and decreased levels of testosterone, as well as increased levels of LH and FSH in occupationally exposed adults[5].

We are conducting a collaborative investigation of the health of adolescent boys in the city of Chapaevsk (Samara region, Russia) where there is evidence of environmental contamination with dioxin.[6] This city, population of 83,000, is located in the central part of Russia. The main source of dioxin pollution is a chemical plant that previously produced hexachlorane, liquid chlorine, acids, vinyl chloride, and other chlorine containing chemical products. Residential neighborhoods are in close proximity to the chemical plant. The average dioxin level in blood samples collected in 1998 from six Chapaevsk residents living within 3 kilometers of the plant was 75 pg/TEQ/g lipid[6], which is higher than levels reported among general population samples in the U.S. [7]

The objectives of this pilot study were to evaluate physical and sexual maturation and the prevalence of minor urogenital abnormalities among a sample of adolescent boys (11-16 years old) residing in Chapaevsk.

Methods and Materials

Male children born between 1988 and 1982 were eligible for examination and were identified through their school. Among 3041 age-eligible boys (age 10-16 years), 2580 (84,9%) were examined, 129 boys (4,2%) were rejected because they moved to the region recently (mostly children of military servicemen). Twenty-four (0.8%) declined participation, 122 (4%) were sick and not in school at the time of examination, and 186 (6,1%) were absent from school at the time of examination for other reasons (e.g. were out of town).

A medical history questionnaire was administered by a trained nurse to both the mother and child. Questions included whether the child was ever diagnosed or treated for undescended testicles. As a validation, the child's pediatric record was checked for the diagnosis of cryptorchidism.

Physical examinations of the children were performed in 1999 by a pediatric endocrinologist and an urologist. Anthropometric measurements, including height, weight, hip and waist circumference, arm span, and arm and leg lengths, were performed using standard methods[8]. Pubertal maturation was graded according to Tanner Staging for genitalia and pubic hair [8]. The breast areolar diameter and penile length were measured using a firm straight edge, while testicle size was determined using an orchidometer (Prader beads). Testicular location and the presence of typical orchidopexy postoperative scars were noted. The presence of hypospadias was based on the location of the external urethral meatus. The diagnosis of phimosis was based on a history of therapeutic circumcision or the inability to completely retract the foreskin on examination. The presence of inguinal hernias, varicoceles and hydroceles was also noted.

Statistical analysis was performed using Statistica 5.0. Tanner stages and testicular volume were used to assess sexual maturity. Maturational categories were defined as follows: PS1 indicates absence of pubic hair and testicular volume <3 ml; PS2a indicated absent pubic hair, testicular volume >=3 ml; PS2b indicated Tanner stage 2 pubic hair; PS3-5 are Tanner pubic hair stages[8,9]. Delayed sexual maturation was defined as the onset of puberty onset (i.e. PS2a and PS2b) at an age that was greater than 2 standard deviations above the mean age of onset among the screened population.

Results and Discussion

For each six-month interval between ages 11 and 16 years, the mean (SD) and the lowest 5th percentile for weight, height and BMI are presented (Table 1). Note that the total number of children (N) in tables 1- 4 are less than 2580 because children with missing values for individual responses are excluded. In addition, Tables 1, 2 and 4 do not include 174 children between 10 and 11 years old.

For each one-year age interval, the mean Tanner stage, penile length, testicular volume, as well as areolar and breast tissue diameter are presented in Table 2.

Table 1. Parameters of physical development of Chapaevsk boys, ages 11-16 years (total N=2387).

Age, year	N	Height,cm			Weight, kg			BMI, kg/m^2		
		Mean	SD	Lowest 5%	Mean	SD	Lowest 5%	Mean	SD	Lowest 5%
11	238	144,3	7,1	133,0	34,9	7,4	26,3	16,63	2,43	14,01
11,5	246	146,3	7,9	133,2	36,5	7,6	27,4	16,89	2,27	14,26
12	231	148,8	7,7	135,9	38,6	7,7	28,7	17,32	2,42	14,68
12,5	272	152,1	8,0	139,5	40,5	8,7	29,8	17,37	2,56	14,41
13	237	156,7	9,4	142,0	43,7	9,3	31,5	17,70	2,59	14,55
13,5	238	159,1	8,9	145,5	46,2	10,0	33,6	18,09	2,49	14,98
14	232	164,2	8,7	150,3	50,1	10,1	34,8	18,45	2,48	15,06
14,5	225	166,3	9,6	150,0	51,5	10,0	36,9	18,49	2,44	15,22
15	219	168,8	9,0	154,0	53,7	11,3	38,0	18,71	2,90	15,17
15,5	134	172,6	8,1	158,4	58,6	11,5	41,3	19,53	2,88	15,81
16	115	175,0	10,4	158,7	61,0	10,4	45,1	19,84	2,45	15,73

Table 2. Description of sexual maturation parameters of Chapaevsk boys by one-year age intervals (total N=2345).

Age, year	N	Genital stage (mean)	Puber-tal stage (mean)	Penile length, cm	Left testicle volume, ml	Right testicle Volume, ml	Areolar diameter, cm	Breast tissue width, cm
11	477	2,0	1,4	4,56	4,3	4,4	1,74	0,37
12	496	2,5	1,8	5,20	7,1	7,4	1,84	0,50
13	461	3,0	2,4	6,21	11,1	11,4	1,95	0,68
14	440	3,7	3,1	7,32	15,4	15,7	2,11	0,72
15	341	4,0	3,7	7,97	18,2	18,6	2,19	0,77
16	130	4,2	4,1	8,33	20,4	20,4	2,32	0,84

Table 3. Mean values of physical and sexual parameters in Chapaevsk (total N=2446).

Pu-bertal stage	N (%)	Age, year	Height ,cm	Weight kg	BMI, kg/m^2	Penile length, cm	Left testicle vol-ume, ml	Right testicle vol-ume, ml	Are-ola, cm
PS1	153 (6,3)	11,49	140,88	31,39	15,75	4,18	1,0	1,9	1,66
PS2a	568 (23,2)	12,16	146,39	36,05	16,72	4,55	4,9	5,0	1,73
PS2b	685 (28,0)	12,77	152,20	40,07	17,20	5,31	7,2	7,5	1,85
PS3	442 (18,1)	14,06	162,93	48,99	18,40	7,21	14,6	14,9	2,09
PS4	510 (20,8)	15,01	171,60	57,25	19,37	8,33	19,4	19,7	2,24
PS5	88 (3,6)	15,55	175,27	65,08	21,17	8,46	22,6	22,8	2,41

Table 4 shows the number of children with cryptorchidism, hypospadias, phimosis, varicocele, delayed sexual maturation and short stature.

Table 4. Frequency of minor urogenital abnormalities and delayed sexual maturation in male adolescents (11-16 years old) in Chapaevsk.

Age, year	N	Cryptor-chidism	Hypospa-dias	Phimosis	Delayed Sexual Development	Varico-cele	Short stature
11	*484*	7	2	57	-	78	8
12	*503*	13	4	44	-	111	13
13	*475*	10	2	25	-	126	9
14	*457*	7	5	29	32	95	14
15	*353*	2	3	14	32	59	12
16	*132*	4	2	6	18	16	6
Total	**2404**	**43**	**18**	**175**	**82**	**485**	**62**

Among 2404 children screened for minor urogenital abnormalities and delayed sexual maturation, 43 (2%) had cryptorchidism, 18 (0.8%) had hypospadias, 175 (7%) had phimosis, 485 (20%) had varicoceles, and, within this population, 82 (3%) met our definition of delayed sexual development.

An investigation of the potential association of dioxin exposure with the genital and maturational abnormalities observed in these boys is underway. We are currently collecting blood samples on boys (and their mothers) with cryptorchidism, hypospadias, and delayed sexual maturation. Blood samples from these boys and age-matched controls will be analyzed for dioxins.

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