

## REPRODUCTIVE HEALTH STATUS IN BOYS LIVING IN A DIOXIN POLLUTED AREA

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### Introduction

A number of research groups have published their results during the last few years related to growing frequency of reproductive system dysfunctions in humans and in animals. Cryptorchism and testes cancer are among them<sup>1,2</sup>. It is possible that the main causes of such diseases might be deteriorating ecological situation, and pollution of the environment with various toxic compounds<sup>3</sup>. Dioxins (TCDDs and TCDFs) and polychlorinated biphenyls (PCBs) can be considered as the most dangerous ecological toxicants.

In Samara region of Russia there is a town Chapaevsk which is heavily contaminated with dioxins<sup>4</sup>. High dioxin concentrations were found there in soil, drinking water, breast milk, and in the blood (plasma) of chemical factory workers<sup>5</sup>. For this reason we have chosen Chapaevsk as a model to study the possible dysfunctions of reproductive system in boys at the critical stage of development (puberty). The present material summarizes our previously published data<sup>6-8</sup>.

### Methods and Materials

Selected parameters of physical and reproductive health development were studied in a group of boys aged 11-15 years, living in the town Chapaevsk, Samara region, Russia. A total of 1525 boys were examined. The control group consisted of 574 age-matched boys living in Samara.

Studied parameters in this investigation were antropometric sizes of boys, evaluation of testes volume and penis size, screening for cryptorchism, varicocele, and inguinal hernia.

Assays of LH, FSH, prolactin, cortisol, and testosterone were performed by RIA using standardized WHO reagents<sup>9</sup>. DHEA and DHEA-S were assayed by RIA using highly specific antisera<sup>10</sup>.

Statistical analysis of data was done using variation statistics methods.

### Results and Discussion

The comparison of antropometric data showed that mean height of Chapaevsk boys aged 11, 13 and 15 years is significantly lower than in control group, whereas mean weight of Chapaevsk boys at the age of 12 is significantly higher.

It was also found that penis size in boys aged 11 and 13 living in Chapaevsk is significantly smaller than in the same age boys in Samara (Table 1). Our data match well the results of other researchers who investigated the children born from mothers who were poisoned by PCB – contaminated oil<sup>11,12</sup>. The authors found that the children of these poisoned mothers had also smaller penis size. The reason of such phenomenon was explained by the anti-androgenic effect of polychlorinated biphenyls.

**Table 1. Selected parameters of reproductive development (M±m)**

	Age	n	Testes volume, ml		Penis size, cm
			right	left	
Chapaevsk	11	318	2.34±0.09	2.34±0.09	4.18±0.05
	12	363	4.45±0.18	4.47±0.18	4.65±0.07
	13	326	7.20±0.26	7.23±0.26	5.61±0.10
	14	312	11.81±0.33	11.89±0.33	7.33±0.12
	15	206	14.34±0.43	14.54±0.43	7.74±0.12
Samara	11	111	2.69±0.26	2.63±0.26	4.67±0.13
	12	135	3.59±0.28	3.57±0.27	4.87±0.11
	13	136	6.68±0.39	6.65±0.40	5.98±0.16
	14	113	12.36±1.20	11.16±0.54	7.37±0.19
	15	79	11.67±0.50	11.60±0.50	7.98±0.21

It was shown that the boys of higher ages (13, 15 years) in Chapaevsk had significantly higher volume of testes in comparison with the control group.

True cryptorchism in Chapaevsk was found in 21 boy (1.38%) as compared to only 3 cases (0.52%) in Samara (Table 2).

It is well known that migration of testes into the scrotum takes place during the prenatal period. And a number of chemical compounds can interfere into this delicate process. As an example, it was shown that female rats treated with nanogram quantities of TCDD on 15th day of pregnancy gave rise to cryptorchism percentage in delivered male breed<sup>13</sup>.

**Table 2. Frequency of cases with true cryptorchism and with retractible testes.**

	n	True cryptorchism		Retractible testes	
		Number of cases	%	Number of cases	%
Chapavesk	1525	21	1.38	34	2.23
Samara	574	3	0.52	2	0.35

We found higher percentage of cases with retractible testes in Chapaevsk boys in comparison with the controls. The ratio of cases with retractible testes had a tendency to fall with age.

Besides this we discovered significantly higher percentage of varicocele (3 times higher) and inguinal hernia in Chapaevsk boys living on the PCB – polluted area (Table 3).

**Table 3. Frequency of varicocele and inguinal hernia**

	Varicocele		Inguinal hernia	
	Number of cases	%	Number of cases	%
Chapaevsk(n=1525)	56	3.67	11	0.72
Samara (n=574)	7	1.22	2	0.35

The development of blood vessels, supplying blood to the testes takes place along with the migration of testes into the scrotum. And the fact that both the frequency of varicocele and cryptorchism in teenagers living on the polluted area is elevated in a similar manner allows us to suggest that both these defects might have a common mechanism.

## ENDOCRINE DISRUPTORS

Levels of hormones were determined in the peripheral blood of 47 Chapaevsk boys and in 40 boys from Samara control group. Testosterone level in Chapaevsk boys was significantly lower than in controls. We think that the main reason of this "testosterone fall" is the effect of PCBs, including TCDD. In animal experiments the administration of high TCDD doses resulted in a 90% fall in testosterone concentration, probably as a result of testosterone biosynthesis suppression<sup>14</sup>. According to the feedback mechanism the low level of testosterone should activate the synthesis of gonadotropic hormones. And our results illustrate it well (Table 4). Concentrations of LH and FSH in Chapaevsk boys were significantly higher than in controls.

Table 4. Levels of hormones in peripheral blood of boys in Chapaevsk and in Samara ( $M \pm m$ )

Parameter	Chapaevsk (n=47)	Samara (n=40)
Age, years	12.48±0.2	12.8±0.22
Testosterone, nmol/L	2.56±0.55	6.97±0.93
LH, mIU/L	1.96±0.24	0.92±0.16
FSH, mIU/L	2.63±0.50	0.89±0.07
Cortisol, nmol/L	196.5±13.86	214.63±17.68
DHEA, nmol/L	7.47±0.76	9.63±0.95

Our hormonal data go well in accord with the results of hormonal shifts found in factory workers who contacted PCDDs<sup>15</sup>. Low testosterone and high LH and FSH levels correlated reliably with dioxin concentration in these workers.

Our results of hormonal measurements: low testosterone and high level of gonadotropins are an unequivocal evidence of marked hormonal disbalances in boys of pubertal age living in PCB polluted region. Low testosterone concentration in Chapaevsk boys of this age results in reduced growth rate and in reduced penis size (at the age 11, 13 years). It is a known fact that androgenic deficiency interferes into the process of normal penis development and finally results in reduced penis size<sup>16</sup>.

One more evidence of hormonal disbalance is higher testes size in Chapaevsk boys aged 13 and 15 years. Prolonged hyperstimulation of testes tissues by gonadotropins induces them to grow more rapidly and results in bigger testes.

Table 5. Concentrations of hormones in peripheral blood of boys with true cryptorchism in Chapaevsk ( $M \pm m$ )

Parameter	Chapaevsk boys with cryptorchism (n=17)	Samara boys, control (n=40)
Age, years	13.12±0.28	12.9±0.29
Testosterone, nmol/L	3.7±1.02	6.97±0.93
LH, mIU/L	2.3±0.4	0.92±0.16
FSH, mIU/L	3.03±0.6	0.89±0.07
Cortisol, nmol/L	186.12±22.6	214.63±17.68
DHEA, nmol/L	8.4±1.5	9.63±0.95

We also studied the levels of reproductive hormones (testosterone, LH, FSH) in a subgroup of boys with true cryptorchism and found quite similar hormonal disbalances (Table 5) to those in the whole Chapaevsk group.

# ENDOCRINE DISRUPTORS

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