

Dioxin '97, Indianapolis, Indiana, USA

Myotonic Dystrophy in Regions with Different Environment in Bashkortostan Republic (Russia)

Rim V. Magzhanov and Leila R. Akhmadeyeva, Department of Neurology and Medical Genetics, Bashkirian State Medical University, Revolutsionnaya St., 16 - 24, Ufa, 450015, Russia (Phone/fax: **7-3472-239579; E-mail: medic@bashinform.ru)

Myotonic Dystrophy (MD) is an inherited disorder altering many systems of human body¹⁾. It is one of the diseases which is considered to be a very serious medical and social problem because of its chronic and progressive development, shortening of the patients' uncomplicated life and high death rate. It is caused by the specific mutation which is the expansion of CTG trinucleotide repeats in the long arm of the 19th Chromosome^{2,3)}. The normal size of CTG repeats at this locus does not exceed 30. MD patients have more than 50 repeats. Those who have 30-50 CTG repeats (premutation) are called "intermediate" cases. These people are considered to be a reservoir for MD in the nature. Clinically they are not affected but the area with 30-50 CTG repeats is unstable and the influence of different (not known yet) factors can cause its widening which always leads to the disease⁴⁾.

Mutations are often induced by environmental mutagens and they could appear both in somatic and sex cells. These mutations cause many harmful genetic outcomes for a human being's health. Mutations in somatic cells cause a variety of illnesses including cancer, mutations in sex cells cause the risk of inherited disorders and congenital abnormalities.

For the last 20 years a new ecological danger was added to the list of those threatening the civilization - it is a possibility of whole-planet intoxication with dioxins and related compounds⁵⁾. Dioxin was identified in the 1970s as the most potent animal carcinogen ever tested. It is one of the most toxic chemicals known and is a general term that describes a group of hundreds of chemicals. They do not break down easily into less harmful substances. Dioxins resist degradation in the environment for decades or centuries. They are very soluble in oil but not in water and so are attached to living tissues which then can not excrete them. Dioxins move through the food chain and are magnified in concentrations, reaching levels in predator species (such as humans) that are millions of times greater than their concentrations in the ambient environment. There appears to be no safe dose of dioxin - no threshold below which effects do not occur. The main health impacts associated with dioxin include: reproductive disorders (reduced sperm count, testicular atrophy, abnormal testis structure, reduced testosterone levels in males, decreased fertility, inability to maintain pregnancy, ovarian dysfunction, endometriosis in females and changes in sexual behavior in both), birth defects, increased rates of cancer, impaired neurological development and related cognitive or behavioral deficits, immune suppression, diabetes, other effects on or injury to the liver, thymus, spleen, bone marrow, skin, etc.⁶⁾ In high concentrations they

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cause mutagenous, teratogenous and embriotoxic effects, disorders of nervous system, liver, alimentary tract, etc. ⁷⁾. Contaminated adults pass dioxin to the fetus while it is still in the womb and to the infant through mother's milk. The full health impact on the child may not be expressed until maturity. Dioxins are preserved in target-cells for a long time as they are metabolic inert and usually are deposited in lipoprotein globules. Binding of nAhR with a "dioxin-sensitive intensifier of transcription" activates descending transcription of adjoining genes ⁸⁾. The majority of biological effects begins with interaction with Ah-receptors. The mechanism of a transformed AhR-dioxin complex influences on transcription factor's function in target cells is similar to the mechanism of steroid hormones action ⁹⁾. But in contrast to hormones with a limited short life-period in a body and in target-cells, dioxins influence on transcription factor's function for many years after a single exposure. Dioxin itself is not genotoxic but it could cause genotoxic effects in combination with other substances ¹⁰⁾.

Bashkortostan Republic (BR) with more than 4 million inhabitants is situated at the very east of Europe and it belongs to Russia. The biggest industrial cities of BR are it's capital Ufa and it's former capital Sterlitamak. In both cities there are several chemical plants which manufacture a wide range of chlorinated organic chemicals including pesticides, solvents, chemical intermediates, plastic polyvinyl chloride and several recycling factories. In both cities hospitals are equiped with disposable PVC plastic products much better than in rural areas. Ufa and Sterlitamak are cities with the most intensive automobiles-traffic and chlorinated chemicals are deliberately added to fuels (we do not have vehicles burning chlorine-free fuels which do not emit dioxins).

The objective of our study was to study prevalence of MD as an inherited disorder in ecologically different regions of RB. The basic methods used in this study were epidemiological, clinical and genealogical. We formed a computerized MD register for RB. All diagnosed patients and their examined family members are recorded there. There are 116 alive MD patients in BR today. So the prevalence of MD is 2.84 for 100 000 citizens.

We formed two groups for the study: risk-group (Group 1) and controls (Group 2). Group 1 included Ufa and Sterlitamak, Group 2 included all other cities (Belebey, Beloretsk, Birsik, Ishimbay, Kumertau, Meleuz, Neftekamsk, Oktyabrsky, Salavat, Sibay, Tuimazy, Uchaly).

The results of our epidemiological study (we counted patients living in the mentioned cities for the 15th of April, 1997) are presented in the tables below:

CITY	POPULATION	PATIENTS	PREVALENCE OF MD	
UFA	1 079 765	27	1 : 39 991	2.50×10^{-5}
STERLITAMAK	247 736	4	1 : 61 934	1.61×10^{-5}
TOTAL (GR. 1)	1 327 501	31	1 : 42 823	2.34×10^{-5}

CITY	POPULATION	PATIENTS	PREVALENCE OF MD	
BELEBEY	75 573	5	1 : 15 115	6.62×10^{-5}
BELORETSK	88 370	2	1 : 44 185	2.26×10^{-5}

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BIRSK	34 735	1	1 : 34 735	2.88×10^{-5}
ISHIMBAY	70 175	1	1 : 70 175	1.43×10^{-5}
KUMERTAU	68 143	1	1 : 68 143	1.47×10^{-5}
MELEUZ	53 120	0	—	—
NEFTEKAMSK	114 768	0	—	—
OKTYABRSKY	104 536	0	—	—
SALAVAT	150 760	2	1 : 75 380	1.33×10^{-5}
SIBAY	49 412	1	1 : 49 412	2.02×10^{-5}
TUIMAZY	88 355	3	1 : 29 452	3.40×10^{-5}
UCHALY	35 330	1	1 : 35 330	2.83×10^{-5}
TOTAL (GR. 2)	933 277	17	1 : 54 899	1.82×10^{-5}

So there is a slight difference in MD prevalence in ecologically polluted and relatively clean cities of Bashkortostan, but statistically it occurred to be not significant.

We conclude that now it is impossible to prove or to exclude mutagenous influence of dioxins. This study is to be continued and molecular DNA diagnosis should be used to confirm the results.

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