

## THE DIOXIN POLLUTION AS A RISK OF DEVELOPMENT FEMALE BREAST CANCER. CHAPAEVSK STUDY, RUSSIA

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### Introduction

In recent years, many studies have in fact demonstrated small but statistically significant increases in the number of breast cancer cases in groups exposed many years ago to high doses of dioxins. Epidemiological evidence supports the link between exposure to organochlorines and breast cancer. The focus was made on chemical industry workers. The results of epidemiological research on environment risk factors and breast cancer vary, but in certain case - control studies the role of these factors has been confirmed.

Organochlorines simulate or mimic sex hormones that may be mentioned as causes of some types of cancer. They accumulate in breast milk, blood and adipose tissue. Natural estrogens are usually metabolized and excreted rapidly, but synthetic estrogens can have long half-lives and bioaccumulate in fat. However, one point on which all investigators agree at this time is that the greater the lifetime exposure to estradiol, the greater the risk of breast cancer developing. An increase in risk is seen if the estrogen exposure occurs during the fetal, rapid breast formation time, pregnancy or menopause periods [1-2].

### Object description

Chapayevsk was taken as the object of the study due to more than 30 years' production of organochlorine compounds was taken as the object of public health and environmental exposure' study [3, 4]. Comparisons of dioxin concentrations in blood and breast milk to available published data indicated that average levels may be substantially higher in Chapayevsk residents than in non-occupationally exposed populations of Russia, Europe and North America [4-5]. Chronic exposures (more than 30 years) of such magnitude may have appreciable effects on public health. It is unexplained that breast cancer incidence rates are much higher in all age groups especially from the age of 35 to 55 years. The observed number of deaths from breast cancer is significant, as it is two times greater than the expected number of deaths in Samara region. The aim of this study is to reveal the role of dioxin exposure in breast cancer development on the base of analytic epidemiological "case-control" study with questionnaire administration in case and two control groups.

### Methods and Materials

All alive breast cancer patients born after 1940 year were included in the case-control study to investigate the role of established breast cancer risk factors and to estimate the possible dioxin exposure. The number of cancers diagnosed among these subjects during the period 01 January 1985 through 31 December 2000 was 356. 144 patients (42 %) were young at the diagnosis moment (before

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55 years). We planned to interview 71 women. The response in case group was 65 persons. Three women left the city and one died. It is important that we have no refuse. The selection of controls was taken from the general medical insurance database. This group will be matched by age. For the higher reliability the ratio of number cases/controls was 2:1. A special questionnaire was developed and it included questions on birthplace, occupation and residence of women and their parents, diet, lifestyle, reproductive function, medical history.

## Methods of statistical analysis

The "SPSS 10.05" statistical software was used to develop a logistic regression model for evaluating the relationship between breast cancer and possible dioxins exposure, adjusted for confounders and other known breast cancer risk factors. Only those variables for which completeness of information was more than 50 % were included in the study.

## Results

Quality of medical care for breast cancer patients is characterized by high proportion of localized tumors (53.5 %) and stage T1 – T2 (70%). Morphological verification of the diagnosis is near 75 %. The disease was detected on screening in 22.5 %.

The first step was to evaluate the influence of non-exposure factors on the risk of breast cancer. These factors include: history of at least one full-term pregnancy; age at birth of first child; number of children; history of benign breast tumor; cancer among relatives (with a special regard for breast cancer among female relatives); age at menarche; age at menopause; educational level; type of professional activities; alcohol consumption and smoking. Information on these factors was abstracted from special developed questionnaire. The second step was to evaluate the potential contribution of dioxins exposure on the risk of breast cancer.

Age at menarche was less than 13 years among 13.8 percent of the breast cancer cases and 11.5 % of the controls. The usage of oral contraception was two much higher in cases than in controls.

The frequency of nulliparity was higher among cases than among controls, 10.8 % and 3.1%, respectively. Among 65 women with breast cancer, the proportion of those who gave birth to their first child up to 30 years old was 86.2 %, while the respective value for controls was 90.8 %. The proportion of women who gave birth to their first child at less than 25 years of age was higher for controls (77.7 %) compared with women who developed breast cancer (69.2 %).

Literature about the dependence of the number of children in a family on the subsequent risk of breast cancer is inconsistent. However, the number of children born in a family can indirectly indicate the total duration of women's lactation period. In our study women diagnosed with breast cancer tended to have 2 or fewer children more often than women without cancer, 93.1 % and 76.2 %, respectively.

A prior history of benign breast disease occurred 2 times more frequently among cases than among controls: 10.8 % and 6.9 %, respectively. A history of breast cancer in genetic relatives was observed among 16.9 % of cases and 1.5 % of controls.

Some studies have shown an increased breast cancer risk for women as a function of alcohol consumption (3 times a day or more often). In our study a slightly higher alcohol consumption in general was noted for cases compared to controls: 92.3 % and 84.6 %, respectively. It should be mentioned, however, that there were no cases of chronic alcoholism and alcohol abuse among either of cases or controls.

The proportion of women with complete secondary, technical secondary and higher education was the same – 86.2 %.

The 14 breast cancer cases (22 %) versus 15 controls (11.5 %) had chronic long-term exposure. They were occupied at Chapaevsk chemical plant. Mean time of occupation at chemical plant was 20.4 and 12.1 years in cases and controls respectively. It is important that there were no another established professional risk factors in both groups. Not only breast cancer patients themselves were significantly more occupied in chemical production but their parents too comparing with the controls (27.7 % and 19.7 %).

Low migration level is well illustrated by the fact that more than a half of respondents were born in Chapaevsk. Mean residence time in the city was the same for 95 % cases and controls – near 40 years. The most significant persistent pollutants are characterized not only by toxicity and stability, but also by ability to bioaccumulation. In Chapaevsk City the people often use vegetables, meat, eggs and milk from the local sources – from the farms or gardens in the Chapaevsk region. The analysis of questions about diet habits shows that breast cancer patients use more than 50 % of all food types from farms in the Chapaevsk region. In the case group the usage of pork, fish and pork fat for cooking is significantly higher compared to controls. The risk of breast cancer development is 3.8 times higher for women who have never had a full-term normal pregnancy than for those who have given birth to at least 1 child. The presence of breast cancer in genetic relatives increases the risk of breast cancer in 9 times among cases versus controls. In future, we will standardize risks of breast cancer with respect to genetic factors. Diet habits seem to be related for breast cancer development. Usage more than 50 % of pork from farms in the Chapaevsk region increases risk 5.7-fold, usage more than 50 % of fish from the nearest lakes or rivers – in 2.3 times.

Odds Ratios (OR)\* for breast cancer risk factors

Risk factor	OR	p
<b>Nulliparity</b>	3.8 [1.1 – 13.5]	0.038
<b>Oral contraception</b>	2.4 [1.03 – 5.5]	0.042
<b>Breast cancers in relatives</b>	9.0 [1.85 – 43.6]	0.006
Usage more than 50% of pork from farms in the Chapaevsk region	5.7 [1.3 – 25.5]	0.021
Usage more than 50% of fish from the nearest lakes or rivers	2.3 [1.13 – 4.80]	0.022
Parents worked at Chemical plant	1.8 [0.80 – 4.00]	0.16
Occupation at Chemical plant	2.1 [0.95 – 4.68]	0.07
Age at menarche < 13 years	0.82 [0.34 – 1.97]	0.64

\* Crude odds ratios

Oral contraception is also significant factor for development of breast cancer OR=2.4. Some increase in breast cancer risk was determined for a group of women occupied at chemical plant. However, the influence of this factor is statistically insignificant, p=0.07. Effect of occupation of woman's parents at chemical plant before her birth had a slight increase in cases, the risk value did not reach statistical significance.

## Conclusions

Thus, as a result of the case-control study conducted with the aim to estimate the risk of breast cancer development for women exposed to dioxins in Chapaevsk City the effect of the following factors was noted:

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- Type of occupational activities - a significantly higher risk was observed among women mostly engaged in chemical plant, OR =2.1.
- The presence of at least one full-time pregnancy during lifetime - for childless women the risk of breast cancer development is in 3.8 times higher than for women who have at least one child, p= 0.04.
- Presence of breast cancer in genetic relatives increases the subsequent risk of breast cancer development 9-fold, p= 0.006.
- Our study demonstrated strong effects of diet habits. Risk increased for women who use more than 50 % of pork from farms in the Chapaevsk region (OR=5.7), more than 50 % of fish from the nearest lakes or rivers – OR= 2.3.

This project has scientific and practical importance. For the first time the role of food with dioxins was associated as breast cancer risk factor. This factor has the same significance as other established risk factors, for example, presence of breast cancer in genetic relatives and null parity. This may define the future directions for investigation of relation of dioxin exposure and women breast cancer. We suggest that Chapaevsk is an incredibly interesting site for further environmental-epidemiological research to estimate the impact of dioxins on human health.

Social significance of the project has three important directions. First of all, the danger of environment of cities with former military chemistry plants for human health was shown. The occupational risk for breast cancer was much higher for chemical plant workers compared with controls. The second important side of the problem is chronic environmental pollution. As was shown in the results of the project in Chapaevsk City the residents often use vegetables, meat, eggs and milk from the local sources – from the farms or gardens in the Chapaevsk region. The analysis of questions about diet habits shows that breast cancer patients use more than 50 % of all food types from farms in the Chapaevsk region. In the case group the usage of pork, fish and pork fat for cooking is significantly higher compared with controls. Citizens prefer to use more than a half of consumed fish from the nearest lakes or rivers. This fact indicates the necessity of informational distribution of danger of local food.

## References

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