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Mercury content in healthy and cancerous tissues of human's large intestine

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Abstract
Mercury exposures in excess of dietary selenium intakes in young children can have severe neurological consequences, preventing nerve sheaths from forming properly. High mercury exposures deplete the amount of cellular selenium available for the biosynthesis of thioredoxin reductase and other selenoenzymes that prevent and reverse oxidative damage. The aim of our research was to determine the content of mercury both in cancerous and healthy tissues of the human large intestine and to compare how the levels of its accumulation depend on the location. Colon cancer tissues were taken during surgery (partial or total resection of organ) from the men and women of various age groups. The average content of mercury in the healthy tissues (control) was 0.0105 ± 0.009 ppm. The average mercury content in tissues away from the tumor was 0.0304 ± 0.047 ppm. The average mercury content in adjacent tissues was 0.037 ± 0.024 ppm. The tumor tissues of the colon had average mercury content 0.026 ± 0.018 ppm.

1. Toxicity of mercury

Mercury is highly reactive with selenium, an essential dietary element required by about 25 genetically distinct enzyme types (selenoenzymes) [1]. Among their numerous functions, selenoenzymes prevent and reverse oxidative damage in the brain and endocrine organs. The molecular mechanism of mercury toxicity involves its unique ability to irreversibly inhibit activities of selenoenzymes, such as thioredoxin reductase [2]. Although it has many additional functions, thioredoxin reductase restores vitamins C and E, as well as a number of other important antioxidant molecules, back into their reduced forms, enabling them to counteract oxidative damage within body cells [3]. Since the rate of oxygen consumption is particularly high in brain tissues, production of reactive oxygen species (ROS) is accentuated in these vital cells, making them particularly vulnerable to oxidative damage and especially dependent upon the antioxidant protection provided by selenoenzymes. High mercury exposures deplete the amount of cellular selenium available for the biosynthesis of thioredoxin reductase and other selenoenzymes that prevent and reverse oxidative damage [4], which, if the depletion is severe and long lasting, results in brain cell dysfunctions that can ultimately cause death.

High exposures to mercury in its various forms are particularly toxic to fetuses and infants. Women who have been exposed to mercury in substantial excess of dietary selenium intakes during pregnancy are at risk of giving birth to children with serious birth defects. Mercury exposures in excess of dietary selenium intakes in young children can have severe neurological consequences, preventing nerve sheaths from forming properly. Mercury inhibits the formation of myelin. According to some evidence, mercury poisoning may predispose to Young's syndrome (men with bronchiectasis and low sperm count) [5]. Because of differences in tissue distributions, mercury poisoning's effects will differ depending on whether it has been caused by exposure to elemental mercury, inorganic mercury compounds (as salts), or organomercury compounds.

Quicksilver (liquid metallic mercury) is poorly absorbed by ingestion and skin contact. It is hazardous due to its potential to release mercury vapor. Animal data indicate less than 0.01% of ingested mercury is absorbed through the intact gastrointestinal tract, though it may not be true for individuals suffering from ileus. Cases of systemic toxicity from accidental swallowing are rare, and attempted suicide via intravenous injection does not appear to result in systemic toxicity [6]. Though not studied quantitatively, the physical properties of liquid elemental mercury limit its absorption through intact skin and in light of its very low absorption rate from the gastrointestinal tract, skin absorption would not be high [7]. Some mercury vapor is absorbed dermally, but uptake by this route is only about 1% of that by inhalation [8]. In humans, approximately 80% of inhaled mercury vapor is absorbed via the respiratory tract, where it enters the circulatory system and is distributed throughout the body [9]. Chronic exposure by inhalation, even at low concentrations in the range 0.7–42 μg/m^3, has been shown in case control studies to cause effects such as tremors, impaired cognitive skills, and sleep disturbance in workers [10; 11].

Acute inhalation of high concentrations causes a wide variety of cognitive, personality, sensory, and motor disturbances. The most prominent symptoms include tremors (initially affecting the hands and sometimes spreading to other parts of the body), emotional lability (characterized by irritability, excessive shyness, confidence loss, and nervousness), insomnia, memory loss, neuromuscular changes (weakness, muscle atrophy, muscle twitching), headaches, polyneuropathy (paresthesia, stocking-glove sensory loss, hyperactive tendon reflexes, slowed sensory and motor nerve conduction velocities), and performance deficits in tests of cognitive function.

Mercury occurs inorganically as salts such as mercury(II) chloride. Mercury salts affect primarily the gastrointestinal tract and the kidneys, and can cause severe kidney damage; however, as they cannot cross the blood–brain barrier easily, mercury salts inflict little neurological damage without continuous or heavy exposure [12]. As two oxidation states of mercury form salts (Hg_2^{2+} and Hg^{2+}), mercury salts occur in both mercury(I) (or mercurous) and mercury(II) (mercuric) forms. Mercury(II) salts are usually more toxic than their mercury(I) counterparts because their solubility in water is greater; thus, they are more readily absorbed from the gastrointestinal tract.

Methylmercury is the major source of organic mercury for all individuals [13]. It works its way up the food chain through bioaccumulation in the environment, reaching high concentrations among populations of some species. Larger species of fish, such as tuna or swordfish, are usually of greater concern than smaller species. A 2006 review of the risks and benefits of fish consumption found, for adults, the benefits of one to two servings of fish per week outweigh the risks, even (except for a few fish species) for women of childbearing age, and that avoidance of fish consumption could result in significant excess coronary heart disease deaths and suboptimal neural development in children [14]. The period between exposure to methylmercury and the appearance of symptoms in adult poisoning cases is long. When the first symptom appears, typically paresthesia (a tingling or numbness in the skin), it is followed rapidly by more severe effects, sometimes ending in coma and death. The toxic damage appears to be determined by the peak value of mercury, not the length of the exposure [6].

1.1. The aim of the study, material and methods

The aim of our research was to determine the content of mercury both in cancerous and healthy tissues of the human large intestine and to compare how the levels of its accumulation depend on the location.

Tested samples were taken from the human colon from 163 patients of 5th Military Hospital with Policlinic in Cracow, Nonpublic Healthcare PROSMED in Cracow and from the Oncology Centre of Maria Skłodowska-Curie in Cracow. Healthy tissues of the colon (n=25 tissues) were collected during autopsy of men and women of various age groups (18-90 years old). The average weight of each tissue was between 0.5-2 g. Colon cancer tissues were taken during surgery (partial or total resection of organ) from the men and women of various age groups. Tissues from each patient with cancer were taken from 3 different places:

1. Cancerous tissue of the colon (n = 138 tissues).
2. Adjacent to colon tumor tissue healthy tissue (n = 138 tissues).
3. Tissue located away from the colon tumor tissue (n = 138 tissues).

Mercury content was measured by cold vapor atomic absorption spectrometry method (CVAAS). This method does not require pre-digestion and enables accurate measurements of the mercury level directly in the tissue. Small fragments of tissues were placed into the special crucible directly after defrosting and weighing. The results of weighing were inserted into the computer program which operated the spectrophotometer MA2. Due to this the automatically calculated outcome was given immediately after the end of the measuring cycle. The measurement was repeated three times for each sample. The results are expressed in ppm.

1.2. Results

The results were analyzed statistically using Statistica programm 10.0. In the description of the statistical characteristics of the respondents the arithmetic mean and standard deviation were used. The Shapiro-Wilk test for normality of distribution was performed. For independent samples Kruskal-Wallis test and multiple comparisons test were used.

The average content of mercury in the healthy tissues (control) was 0.0105 ± 0.009 ppm. The average mercury content in tissues away from the tumor was 0.0304 ± 0.047 ppm. The average mercury content in adjacent tissues was 0.037 ± 0.024 ppm. The tumor tissues of the colon had average mercury content 0.026 ± 0.018 ppm.

Multiple comparison analysis showed an average ranks showed statistically significant differences between the levels of mercury in the colon and:

1. Control tissues and tissue away from the tumor (p=0,000).

2. Control tissues and adjacent to the tumor tissues (p=0,000).

3. Control tissues and tumor tissues (p=0.000).

4. Tissues located away from the tumor and tumor tissues (p=0.002).

5. Adjacent to the tumor and tumor tissues (p=0.0006).

Discussed results illustrated in Figure 1.

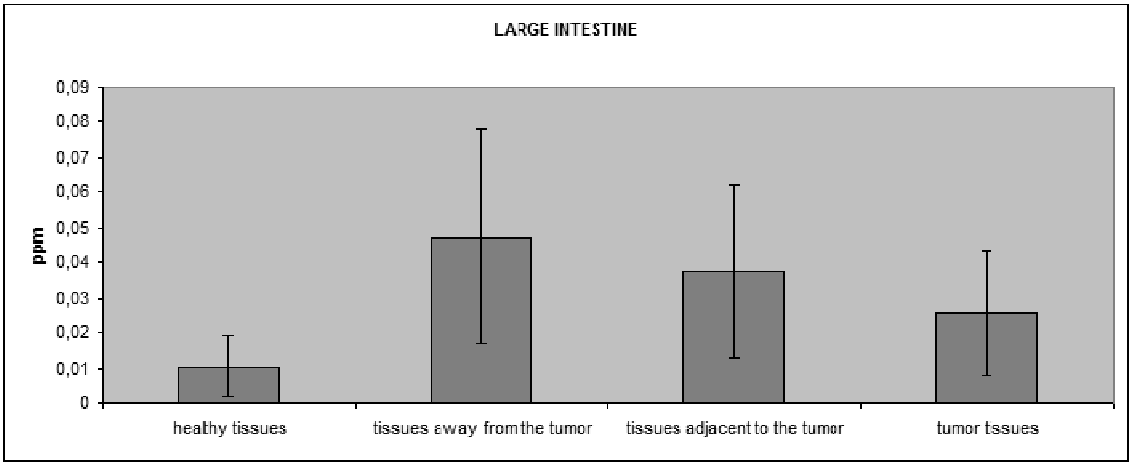

Fig. 1. The average content of mercury in healthy and cancerous tissues of human large intestine.

2. Conclusion

In the case of colorectal cancer the largest mercury content was detected in tissues located away from the tumor (0.047 ppm), while the lowest content of mercury was found in healthy tissues (control) of large intestine (0.010 ppm). The results suggest that the tumor tissue of the colon, in a sense, to defend themselves from an accumulation of mercury, because they have the lowest contents (0.025 ppm). However, studies show, that human exposure to inorganic mercury is not associated with the risk of cancer, with one exception, on the liver cancer [15].

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