Cancer Epidemiology and Prevention in Children and Adolescents – View Thesis

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Abstract: Growing up in the world of globalization and changes in families' structure generate noticeable health and psychosocial well-being threats in children and adolescents [167]. Civilization development, as well as technical, economic, and industrial progress, despite obvious positive changes they bring, have also become the reason for disorder of internal homeostasis of an organism due to continuous influence of various harmful external factors, and their existence is connected to civilization development. Due to civilization development human being in every stage of their life, from conception to adulthood, is exposed to carcinogenic factors that are responsible for malignant transformation of a cell that is formation of tumours.

Technological advance, modern methods of research, primary and secondary prophylaxis, do not stop the problem of growing tumors. Every year in Poland about 1,300 new cases of cancer appear in Poland, which are the cause of death in children, or cause permanent disability and mental strain. Today we know that the diseases of civilisation, including cancers, are curable, but the key to success is to reduce the risk of these diseases and early diagnosis. Statistics show that in the developed countries the detection of cancer in children happens already in stage I and II of the disease, while in Poland, the diagnosis is made most often in stage III and IV, which gives a much lower chance of recovery.

Therefore, the question appears: what action needs to be taken to change the current situation. Prevention, or in other words the reduction of occurance of such diseases by reducing the exposure to harmful factors, is very important, but so is early diagnosis, which includes screening and the increase of children's knowledge about health risks and healthy behaviors.

Keywords: Cancer, children, pidemiology, prevention.

CANCER EPIDEMIOLOGY

Growing up in the world of globalization and changes in families' structure generate noticeable health and psychosocial well–being threats in children and adolescents [1]. Civilization development, as well as technical, economic, and industrial progress, despite obvious positive changes they bring, have also become the reason for disorder of internal homeostasis of an organism due to continuous influence of various harmful external factors, and their existence is connected to civilization development. Due to civilization development human being in every stage of their life, from conception to adulthood, is exposed to carcinogenic factors that are responsible for malignant transformation of a cell that is formation of tumours [2-5].

Cancerous diseases classified as civilization diseases are the second (after poisoning and accidents) cause of death in children over 1 year old and it is predicted that within the first decade of the current century one person out of 900 adults aged 18–44 yrs will be a convalescent after a cancerous disease from childhood [6,7]. Most cases of cancerous diseases are observed in boys and children aged 0–4 yrs [8,9]. Incidence of childhood cancer is more frequently noted among children of urban origin, however, it has been observed that this difference is being slowly blurred, which is related to carcinogenic factors present in children's environment [10]. Incidence of cancer in developed countries ranges from 110 to 150 children per million, which means that from 1/600 to 1/450 children will suffer from cancer within first 15 years of their life [11]. Children's cancer makes up 1–1.5% of all cancers occurring in the whole population [12, 13]. Every year in Europe there are noted 15,000 of new cases of cancers among children aged 0–14 yrs, while among teenagers and young adults aged 15–24 yrs additional 20,000 cases. There are countries, where childhood cancer incidence rate exceeds 150 cases per 1 million children. These countries include: Nigeria, Brazil, New Zealand, Sweden, and Australia [13]. Due to different clinical symptomatology in comparison to adults' population, cancers that occur in children and adolescents have a very large variety of histological types, anatomical localization and incidence [12,14]. The most frequent childhood cancer is leukaemia. It makes up 24% of all childhood cancers. Acute lymphoblastic leukaemia (ALL) is the most common and makes up about 80% of all cases of leukaemia in population aged under 18 yrs, while acute non–lymphocytic leukaemia (ANLL) occur

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in 15–20% of children and most frequently in infancy. Incidence of ALL is higher in white people than in black people population. The highest incidence is observed in the USA, Australia, Germany, Costa Rica and it makes up 32–44%, while in the majority of the European countries it is 23–29% of population. The lowest incidence is observed in China (19.6%), India (11%), Japan (21%), New Zealand (12%), and Brazil (11.4%). Occurrence of ANLL is similar in various geographical regions, except for Japan and some of African countries, where ANLL is more frequent than ALL. The second frequent type of cancer are brain tumours that make up about 22% of all cancers. In England and Wales they make up 16.21%, in France 16.85%, in Germany 20.0%, and in Hungary as much as 26.5%. Incidence of brain tumours in Poland is 29.8 per one million. The third frequent cancer that occurs in children is Lymphoma that makes up 15% of all cancers. Incidence of particular groups of childhood cancers varies in particular age groups. Incidence of acute lymphoblastic leukaemia is most frequent in children aged 2–5 yrs, while the highest incidence of ANLL is observed in infants. The highest incidence of embryonal tumours occurs in the very first years of life. Within the first year of life one diagnoses the highest number of cases of neuroblastoma, retinoblastoma, and hepatoblastoma. As for Hodgkin's lymphoma, Ewing's sarcoma, and osteosarcoma, they are most frequently diagnosed in adolescence. Gonadal tumours in boys are most frequently diagnosed in early childhood and by the age of 15, until the end of adolescence. As far as girls are concerned, higher incidence of these tumours is observed in adolescence. Sex of a child has a slight influence on occurrence of tumours. They occur little more frequently in males than in females, in relation 4:3. Incidence of ALL is higher in boys than in girls. The biggest difference concerns incidence of lymphomas; it is less visible in brain tumours, neuroblastoma, soft–tissue sarcoma and osteosarcoma. Girls more frequently suffer from germ cell tumours and adrenal cortex cancer as well as thyroid cancer. It has been observed that there are differences in incidence of particular types of tumours between the races. Ewing's sarcoma and malignant testicular tumours concern mainly white race, Wilms' tumour occurs more rarely in Asia than in Europe and in the USA, while more frequently in black race population. Acute lymphoblastic leukaemia is two times more often diagnosed in white race than in black race population. As it turns out, incidence of tumours is also influenced by a region of the world and living conditions. As an example, clinically most aggressive subtypes of Hodgkin lymphoma occur in countries with worse social and economic conditions. On this basis there are being made attempts to find the causes that could be etiologically linked with particular tumours in the particular region [13,15,16]. In population of children and adolescents one may observe the increased incidence of primary tumours of histological structure, typical of adults. These cases make up less than 10% of all cases belonging to a particular clinical group highlighted in the International Classification of Childhood Cancer (ICCC) [12,17,18].

Table 1: Number of Cases and Deaths from Cancer in Female and Male Children by Five Year Age Groups in Poland in 2002–2009 [327,328,329,330,331,332,333]

Year	Age group (yrs)	Number of cases		Number of deaths	
		W	M	W	M
2002	0 – 4	115	136	40	47
	5 – 9	84	108	35	53
	10 – 14	81	147	34	58
	15 – 19	207	243	56	98
2004	0 – 4	106	156	34	37
	5 – 9	78	123	29	42
	10 – 14	108	136	34	43
	15 – 19	191	228	48	67
2005	0 – 4	132	143	28	25
	5 – 9	90	128	26	31
	10 – 14	109	125	26	40
	15 – 19	207	251	30	76
2006	0 – 4	125	132	31	37
	5 – 9	83	118	35	38
	10 – 14	80	114	31	48
	15 – 19	198	249	53	80
2007	0 – 4	111	136	28	33
	5 – 9	82	97	18	27
	10 – 14	79	112	26	43
	15 – 19	184	237	42	76
2008	0 – 4	160	187	29	48
	5 – 9	84	86	19	28
	10 – 14	91	105	14	39
	15 – 19	176	220	38	62
2009	0 – 4	151	165	25	27
	5 – 9	78	112	25	28
	10 – 14	105	107	20	29
	15 – 19	162	234	27	59

Table 2: The Incidence Rate of Childhood Cancer in Poland [43]

Type of Cancer	Standardised Incidence Rate
Leukaemia	35.4
Brain tumours	29.8
Lymphoma	21.2
Soft–tissue sarcoma	10.6
Neuroblastoma	9.3
Nephroblastoma	7.4
Germ cell tumours	6.3
Bone tumours	6.0
Retinoblastoma	3.7
Epithelial carcinoma	2.7
Hepatoblastoma	1.3
Other	0.4
Total	134.1

In cancer aetiology numerous scientific evidence indicates the role of common infections in early childhood and of immunological mechanisms even in aetiology of ALL, whereas in acute myeloid leukaemia (AML), exposure to ionizing radiation, chemotherapeutic agents and benzenes. In the case of lymphoma, incidence proportion has been identified in primary immunodeficiencies, as a result of ionizing radiation, pesticides, benzene derivatives, organochlorine substances, as well as as a result of Epstein–Barr virus. In the case of brain tumours, the causes are unknown; it is assumed that ionizing radiation may be a risk factor especially if it influences a woman during pregnancy period or has a direct effect on baby's head during treatment for leukaemia [7].

CANCER PREVENTION

Numerous studies worldwide have shown that reducing the risk of cancer is most effective by adopting a healthy lifestyle, avoiding exposure to carcinogens and regular screening tests [19]. Prevention and early detection of cancer at the developmental age became a priority for national health policy in many European countries [20], and in particular it seems significant to prevent cancer among young people, so that to take care of healthy society. On the one hand, it is possible thanks to systematically performed physical examinations, conducted en masse and best if in learning environment, and on the other hand, by increasing awareness of young people about cancer [8,21]. All preventive measures are only meaningful if they are executed continuously by people adequately prepared to carry them out, especially in contact with healthy young people.

Preventive medicine consists in "actions that are aimed at prevention of disease by promoting healthy lifestyles and health education, promotion of preventive examinations and early detection of diseases and their treatment. Oncology aims at preventing and reducing incidence of cancer, as well as at early detection and prompt and effective treatment" [22,23]. Prevention of cancer is traditionally divided into primary and secondary prevention [24].

Primary prevention aims at decrease of cancer incidence and mortality by eliminated or reduced exposure to risk factors and promotion of protective factors [22,25]. More than 80% of cancers are connected to lifestyle, that is why health behaviours are extremely important in cancer prevention and are a significant part of preventive measures. Pro–health behaviours are influenced by pro–health knowledge and use of this knowledge in everyday life as well as effective motivation. It is important to remember to adjust the knowledge passed on to a child to their age, needs, attitude and skills. Promotion of pro–health behaviours should concern as well or especially women in child–bearing age, pregnant women and, finally, parents of all children, not only of those children in which anomalies were diagnosed after birth

Table 3: Incidence of Particular Types of Childhood Cancers [12]

	Poland	Europe	United States of America
Leukaemia	28.7%	33.5%	30%
Lymphoma	14.3%	9.9%	13%
Brain tumours	16.3%	22.6%	19%
Sympathetic nervous system	6.6%	6.8%	7%
Retinoblastoma	2.7%	3.3%	1%
Kidneys	6.5%	6.9%	7%
Liver	1.5%	0.9%	1%

[8,21,23]. Knowledge of cancer risk factors enables people to take preventive measures that must involve the whole society to bring measurable and intended effect. These preventive measures should be planned for the period of a few decades and should be consistently executed throughout the whole period. Without such determination in execution, hope placed on preventive measures will never be possible to pursue [22].

Recommendations in primary prevention include above all nutritional factors, which have been proved to be an important part of preventive measures, however, still many questions on roles of a particular nutrient or a combination of nutrients remain unexplained. Epidemiological studies have proved that in populations whose diet contains large amounts of vegetables and fruit as well as little amounts of animal fats, meat and calories, one may observe reduced cancer risk. Undoubtedly, in cancer prevention antioxidants, such as vitamin E and β–carotene, are of great importance, which has been proved in numerous studies worldwide [21,26,27,28,29,30,31]. Risk of oesophageal cancer, stomach, colorectal, anal, breast, and cervical cancer is reduced by consumption of products containing vitamin C. Protective effect of ascorbic acid is shown mainly by the ability of vitamin C to capture the oxygen free radicals and block the nitrosation process as well as maintain homeostasis of the intracellular environment [32]. Regular consumption of vegetables and fruit significantly contributes to reduced risk of stomach cancer, colorectal, anal, and breast cancer. Vegetables and fruit are the source of carotenoids, folic and ascorbic acid as well as bioactive components such as phenols, flavonoids, isothiocyanate and indoles, dietary fibre and vegetable fibres, that have anti–cancerogenic effect. Legumes, especially cooked beans, have a protective effect and reduce the risk of colorectal cancer due to the presence of saponin, oligosaccharides, phenolic compounds, and isoflavonoids [33,34]. Anti–cancer effect has been proved also in garlic, onion, leek, chives, and chlorophyll present in green parts of the plants probably has anti–cancer effect due to binding cancerogenic substances [33]. Unsaturated fatty acids omega–3 have been also proved to have a positive effect on human organism, especially those long–chain polyunsaturated fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). In the Inuit population, whose diet is based on marine fish rich in fatty acids, there has been observed rare occurrence of the incidence of various types of cancer [33]. Currently, it is recommended to follow a diet based mainly on vegetable products that include at least five portions of vegetables and fruit per day; diet should contain whole grain products that would replace the source of carbohydrates. The child should be fed food free from biological contamination, so fresh and the most natural, derived from reliable sources [21,26-29,31]. Prevention should also include avoiding exposure to carcinogens that can be found in food. Since nitrosamines that are formed during frying food have been proved to have a carcinogenic effect, such form of preparing a meal should be avoided. It is also important to exclude from the diet too hot, not crumbled and too caloric meals that exceed the energy requirement of the body. It is necessary to remember that harmful factors, both biological and physical or chemical contained in a diet may have an influence on a child in each stage of life: also before birth, during foetal life, even before conception. That is why the principles of healthy diet should be followed as well by the parents of a child [21,26-29,31].

Potential environmental risk factors identified for childhood leukaemia include exposure to magnetic fields of more than 0.4 micro T, exposure to pesticides, solvents, benzene and other hydrocarbons, maternal alcohol consumption, contaminated drinking water, infections, and high birth weight. The finding of space–time clustering and seasonal variation also supports a role for infections. Breast–feeding, consumption of fresh fruit and vegetables and having allergies all appear to be protective.

Undoubtedly, an important factor in cancer prevention is physical activity that trough a variety of mechanisms may influence the risk of cancer, although to this day a lot of questions about the role of physical activity in cancer prevention remains unanswered. Physical activity helps to maintain proper body weight, so indirectly, prevents cancer, in which obesity is a risk factor, for example, cancers of the gall bladder, breast, cervical, endometrial, ovarian, colorectal and prostate. Currently, it is recommended to do moderate physical activity for 30 minutes, five times a week. Moderate or intense physical activity performed for at least 45 minutes at least five days per week may reduce the risk of breast and colorectal cancer to a great extent as well as reduce risk of kidney tumours, endometrial cancer, and oesophageal cancer [7,35,36]. In the age of computerization, common access to media and freedom in using them, such recommendations for adolescents are neither surprising nor unnecessary, and on the contrary, they have become the basic element of promotion activities and health education at schools [60,61].

An important issue in primary prevention of cancer is to reduce active and passive exposure to tobacco smoke, which is a single and main cause of cancers [28]. Nowadays, there are many strategies and programs that may prevent young people from starting to use tobacco, such as limited advertisements and promotion, increase of excise taxes, other measures aimed at restricted access of the under aged to tobacco, education and anti–promotion. Preventive measures, mainly in the form of health education should involve children, young people, who in the near future will become parents and the health of their child will depend on them [35, 36]. Epidemiological data show the effectiveness of primary prevention in the fight against smoking, which is the motivation to continue in this direction and create effective control programs [37].

Nowadays, a lot of attention is paid to the role of electromagnetic field in tumours as well as to reduction of its impact on human body. Regardless of the size of acceptable exposure limits to electromagnetic field, it is recommended to apply the principle of prudent avoidance and to reduce one's exposure at home, at work and in environment. This can easily be achieved by reducing staying close to electrical wires, household electrical appliances that are on, office equipment, televisions or computers, especially by avoiding these devices in the vicinity of rest and sleep area [38]. It is also being considered if to reduce the impact of waves produced by mobile phones and microwave ovens, especially in children [11].

Prevention of skin cancer includes reduced exposure to ultraviolet radiation, which is extremely important in childhood and adolescence. The best method to reduce exposure to ultraviolet radiation is to avoid the sun in the hours of its greatest activity between 10.00AM and 3.00PM as well as wear adequate clothes (long sleeves, covering the head). Additionally, when exposed to ultraviolet radiation, children should use creams with UV filter that absorb more than 15 (SPF> 15) [7,21,28]. In modern sunscreen formulations, in order to increase the protection, there are usually used multiple chemical filters and physical filter. Chemical filters penetrate the superficial layers of the epidermis, which undergo isomerisation and absorb radiant energy and change it into heat energy. Modern chemical filters that are used in sunscreens with proven effectiveness and high safety profile are: camphor derivatives (Mexoryl), avebenzones, and benzotriazoles (Tinosorb).Physical filters reflect and scatter radiation A and B and this way protect from radiation. Physical protectors that are used are as follows: titanium dioxide, zinc oxide and iron oxide. It is also important to pay attention to the recommendations how the product should be applied, which has a large influence on product's effectiveness. This concerns the amount of product used and its durability. It is assumed that the right application would be about 2 mg of the product on 1 cm^2 of skin, which gives about 2–3 g on an adult's face and about 10 g on a child's body. However, it is significant to note that there are factors that potentially reduce the durability of the product on the skin and weaken its effect: mechanical removal during physical activity, due to friction between skin and clothing, use of towel or contact with water. Appropriate sunscreen is characterized by: broad spectrum photo protection, photo stability, long–lasting protection, waterproofness and good quality [39].

It has been proved that contamination of environment and work environment is the cause of cancers that is hard to be avoided, however, it is possible to take preventive actions at least on a smaller scale. Actions that should be taken are commonly known: reduced emission of smoke and dust coming from factories, cars, natural fertilization on farms, proper treatment of drinking water, application of safety standards that protect pregnant women and nursing mothers from exposure to chemicals in work environment [26,31]. An important element is also limited exposure of children and pregnant women as well as nursing mothers to detergents used in households, pesticides, smoke coming from incenses and hair dyes [26].

Due to increased role of infectious agents in creation of tumours, it is important to reduce one's exposure to biological factors such as: viruses, bacteria, fungi, protozoa. Preventive measures include taking care of adequate living conditions of a child (dry and no fungi), reducing possibilities of infections, avoiding early infections in infants under 3 months. Children with cases of liver cancer or liver diseases in family should be tested for HBV and HCV. Children whose mothers are carriers of HBV or HCV should receive after birth antibodies. Women who are carriers of HTLV–1 should not breast feed. What is more, children with cases of stomach cancer in their family should be tested for Helicobacter pylori [7,37].

Primary prevention also consists in vaccination, which should not be limited only to those obligatory ones, but especially supplementary immunization, that

is against hepatitis A and B, Haemophilus influenzae type B, chickenpox, mumps, flu, and pneumococcus. Recently, one may observe much higher number of children vaccinated against these diseases, which obviously has an influence on better health of children, and therefore reduces the cancer risk [40,41]. Vaccinations as preventive measures have led to decrease of incidence rate of hepatitis type B in Poland. According to the epidemiological data, introduction of vaccinations for all of the babies in 1994–1996 has contributed to improvement of health condition among the youngest children. Incidence rate of hepatitis type B in 1997 for children aged 0–3 yrs was on average 2.5/100 thousand. At present, obligatory and free vaccinations concern newborns and infants as well as adolescent aged 14 yrs [42]. According to WHO guidelines, in the primary prevention of benign and cancerous changes caused by genital types of human papillomavirus (HPV), preventive vaccines are of groundbreaking importance [143]. In 2006 European Medicines Evaluation Agency allowed two vaccines which have shown effectiveness to be applied in Europe, reducing the risk of developing cervical precancerous condition. Mass vaccinations should take place in girls aged between 12 and 15 yrs, which creates a real opportunity to prevent cervical cancer [44-50].

Cancer secondary prevention consists in mass screening aimed at early detection of cancer in people without symptoms of the disease and decrease of mortality [28,51]. For years, in population of children and adolescents there have been functioning balance studies, so it would seem that cancer detection in adolescence is much more common when we take into consideration non–complexity of balance studies. However, it has turned out that balance studies are not entirely used for monitoring and securing correct development of a child and data collected are not used for analyses in a given region in wider range so that to take preventive actions [40]. Screening tests organized within the framework of secondary prevention have a positive influence on decrease of mortality due to cancer. An example of early detection of cancer by use of screening tests in cervical cancer prevention are pap smear and gynaecological exam, microbiological test, and virological test and concern adolescent girls [21,31,37,49,52,53]. Pap smear should be regarded as current form of screening test for intraepithelial neoplasia. American Society for Colposcopy and Cervical Pathology (ASCCP) together with American Cancer Society (ACS) recommend to perform pap smear test since the age of 21 or 3 years after start of sexual activity. Pap smear tests still remain the best form of screening tests [54-56].

Secondary prevention of ovarian cancers includes diagnosis of gonadal dysgenesis and androgen insensitivity syndrome, assessment of Barr body in all female newborns as well as ultrasound screening in order to establish the occurrence of follicular apparatus in gonads [57]. Other examples of screening tests in secondary prevention are ultrasonography and breast self–exam in breast cancer prevention, determining the level of secretion of catecholamines in the urine for the detection of neuroblastoma, screening and CT scans that allow the diagnosis of lung cancer, frequent physical examination and ultrasonography of the abdomen in children with congenital anomalies to detect Wilms' tumour [21,31,37,53,58]. Undoubtedly, the future of secondary prevention will be genetic tests that currently occupy a key position in determining the risk of developing a hereditary form of cancer. An example would be the analysis of the BRCA1 and BRCA2 genes, which aims at defining hereditary predisposition to ovarian cancer, breast cancer, and cancer of other organs. Researches on the BRCA2 gene have shown that mutations in this gene are responsible for 35–45% of hereditary condition of breast cancer in women. They also increase the risk of breast cancer up to 85%, of ovarian cancer 15–20%, and the risk of developing breast cancer in men 5–10% [59]. Also knowledge of early symptoms of cancer allows children and parents their self–observation, self–examination, as well as observation of a child in the direction of distressing symptoms and going for check–ups, which will allow early detection of the disease.

CONCLUSIONS

1. Cancerous diseases are the second (after poisoning and accidents) cause of death in children over 1 year old.
2. The highest incidence rate is observed in boys and children aged 0–4 yrs.
3. Incidence of childhood cancer is more frequently noted among children of urban origin.
4. Numerous studies worldwide have shown that reducing the risk of cancer is most effective by adopting a healthy lifestyle, avoiding exposure to carcinogens and regular screening tests.
5. All preventive measures are only meaningful if they are executed continuously by people adequately prepared to carry them out.

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