Malignant neoplasms (MN) are one of the insidious diseases that occur in children of different ages, which accordingly determine the need for their study, especially in terms of epidemiology.

Depending on the type in the structure of the MN incidence in children, the leading positions are taken by leukemia, myeloproliferative and myelodysplastic diseases, which account for 34.1% (acute lymphoblastic leukemia (OLL) – 26.7%; acute myeloid leukemia (AML) – 4.6%; chronic myeloproliferative diseases – 0.5%; myelodysplastic syndrome – 2% are included as well). With regard to lymphomas and reticuloendothelial tumors, they account for 11.4% of the (in this case Hodgkin's lymphoma (HL) – 4.8%; non-Hodgkin's lymphoma (NHL) – 6.5%; a few rarer Burkitt's lymphoma - 2.1% is met).

Over the past decade, the increase tumors of the central nervous system (CNS) in the MN structure in children should be noted, accounting for 22% (astrocytoma – 11%; ependymomas – 2%; embryonal tumors - 5%, other gliomas – 2%); neuroblastoma, and retinoblastoma makes up respectively 7.4% and 2.3%, kidney tumor - 5.6%, liver tumors - 1.1%, bone sarcomas - 4.5% (osteosarcoma - 2.3%, Ewing's sarcoma - 2.1%), soft tissue sarcoma – 5.9%, germ cell tumors -2.5%, epithelial tumors - 1.6% [4,8,13].

According to many authors [3,4,6], epidemiology in pediatric oncology, unlike in adults, less considers the issues such as relationship of tumors with geographical and other environmental factors. Apparently, this is due to the errors in the statistical accounting of MNs in children, as well as the relative rarity of their occurrence in comparison with the regional population. Thus, in the US, according to statistics, no more than 8,000 children fall ill each year, and in Europe, about 21,000 cases are registered annually. Another reason is that the external environment, geographical, climatic conditions affect the child's body indirectly, through their mothers, so the epidemiology of tumors in children is the epidemiology of their parents, that is: the presence of occupational hazards, bad habits, the impact of physical, chemical, radioactive carcinogens that have a direct impact not only on the adult body, but also the developing fetus.

In this regard, numerous researchers imply the existence of a direct connection of their occurrence with a history of maternal obstetric pathology, viral infection during pregnancy, vaccination, as well as with congenital and family hereditary factors, age and sex, malformations under the epidemiology of tumors in children.

A leading epidemiologist A. Miller [4,10,11,14] gives a review of the epidemiological evaluation of the relationship between MN and birth defects. He conditionally divides tumors of children into three groups: the first – leukemia, the second - nephroblastoma, liver and adrenal cancer, the third - neuroblastoma. These tumors are most often combined with various congenital malformations – leukemia – Down's syndrome and other groups of the disease (except nephroblastoma) – with hemihypertrophy. In neuroblastoma aniridia (congenital absence of the iris) often occurs. The second group includes brain tumors, which are more often combined with CNS malformations. The third group includes tumors of the genitals, which are also often found simultaneously with other defects. According to the author, lymphomas are often combined with congenital A-gammaglobulinemia, bone tumors with multiple exostomes, enchondromas and osteogenesis imperfecta.
According to a number of researchers\textsuperscript{[11,18,19]} it is noted that in countries with a temperate climate leukemias occupy a leading place in the structure of pediatric oncology, and in tropical environment a leading place is occupied by lymphomas. In the study of A. Miller\textsuperscript{[4,9,11]} there were cases of group occurrence of these diseases in the same school, in the same quarter, which today is difficult to explain.

It should also be noted that MN is more common in boys and its frequency varies from country to country depending on socio-economic groups. The majority of the black population, due to low levels and unidentified ethnic factors, are more likely to have lymphomas, compared to the incidence of leukaemia, which is typical for children from the wealthiest segments of the population. The highest NHL index is recorded in Africa (due to Burkitt's lymphoma), while in Japan the incidence is twice lower compared to other countries.

All this dictates the need for in-depth epidemiological studies and the study of etiological risk factors for the occurrence of MN in children.

To explain the causes of tumors in children, there are various theories, one of which is the theory of Kohnheim, proposed in the 70-ies of the last century. According to this theory, tumors originate from persistent embryonic rudiments that occur during embryogenesis and its disorders. In the period of fetal development of embryonic tissue rudiments that are not used for their full formation, shifted and can be attached (to ectoparase) for a long time, not showing its properties. But, when exposed to any internal and external stimuli, ectopic areas of tissue can give tumor growth, in the place where they were originally fixed.

There are factors that contradict the theory of Kohnheim: the occurrence of tumors in the elderly, not in children; the prevalence of tumors in organs where there are no special difficulties in the formation of embryonic development. Thus, tumors in adults are relatively rare occur from the Gill arches, embryonic ducts, and more often - from the epithelium of the gastrointestinal tract. At the same time, the most common tumors in children (nephroblastoma, neuroblastoma, medulloblastoma, hepatoblastoma, retinoblastoma) develop during the embryonic or early postnatal periods from immature organs and tissues. The theory of Kohnheim also explains the combination of tumors with malformations prevailing in children under the age of 4 years, the predominant connective tissue genesis of tumors and the absence of precancerous diseases. Experimental evidence indicating the possibility of "spontaneous" malignancy of ectopic embryonic cells is also important. This same theory can explain the origin of many benign tumors in children (a tumor-like congenital abnormalities of tissue development, consisting of local tissues and of tissues, foreign to the given localization) - hamartoma.

There is also a theory of Fisher-Wasels, which was developed in the 20-s. In the occurrence of tumor growth it gives much importance to the conditions under which the tissue for a long time receives powerful physiological or pathological impulses to growth. They can occur as a result of repeated death or tissue regeneration (frequent exposure to x-rays), or under the influence of rapid tissue growth in certain age periods.

Kohnheim’s and Fisher-Wasels’s theories in some cases are consistent: we can assume that early determination of unused embryonic rudiments in the presence of some realizing factors leads to the development of tumors of them.

There is also a viral theory of the occurrence of tumors in children. Thus, in connection with the endemic distribution of African lymphoma (Burkitt's lymphoma), mainly in children aged 4-8 years, there is a lot of data indicating the involvement of the virus in the occurrence of this tumor. Viral theory also explains the occurrence of systemic tumors, in particular, leukemia, while lymphogranulomatosis is associated with the infectious nature of this tumor.

Currently, the immunological theory, according to which every healthy person can be exposed to any factors that contribute to the violation of immunological supervision in the body, which will further lead to the emergence of MN is of great interest. This theory finds its confirmation in the fact that in children with the breakdowns of the immune system most malignant tumors occur.

A theory of the origin of tumors associated with transplacental blastomogenesis is also of interest in terms of the occurrence of MNs in children. According to this theory, most tumors in children occur when carcinogens pass through the placenta (almost all drugs used in obstetric practice). The experiment has proved the permeability of the placenta for strontium-98, which has caused osteosarcoma in rats born at parenteral nutrition of the mother.\textsuperscript{[12,6,9,17]}

There are works\textsuperscript{[12,15,20]}, based on a large statistical material, indicating the transplacental effects of tobacco and alcohol on offspring. So, in smoking women children get sick twice as often as in non-smokers. Some drugs used in agriculture (pesticides) act transplacentarily, which is of particular importance in our country, where more people are involved in agricultural work in the fields, which directly implies contact with various chemical carcinogens, as well as UV irradiation (high solar insoluation). In this regard, it is necessary to carry out measures to limit the contact of a pregnant woman with highly active chemical and physical carcinogens.

The main factors involved in the theories of the origin of tumors in children:

2. Relationship of malignant tumors with developmental disabilities.
4. Immunological insufficiency in some tumors in children.
5. Spontaneous regression of some tumors in children.
6. Transplacental blastomogenesis.
7. Exposure during pregnancy and tumor in the fetus.
8. Mother's age and baby's tumor. The age factor is especially significant for mothers over 40 years, due to the increase of spontaneous mutations in germinogenic cells, with the aging of the oocytes, as well as the age of the father.

**Genetic features of tumors in children**

There are about 100 genetically determined syndromes that predispose to the development of neoplastic processes in childhood. It is proved that genetic factors play the main role in the etiology of a number of congenital tumors in children. This is primarily typical for retinoblastoma and nephroblastoma. Thus, the hereditary nature of retinoblastoma is confirmed by the following factors: family cases with bilateral lesions, and the disease is inherited by half of the offspring regardless of gender. Spontaneous bilateral retinoblastoma is also characterized by inheritance in 50% of the offspring. Unilateral sporadic retinoblastoma is inherited in 8-25% of children. Retinoblastoma develops in relatives of the patient, although the parents are healthy.

The development of the most common embryonic tumors is associated with structural changes in the chromosomal apparatus, in particular, with the deletion (loss) of certain areas of the chromosome, as a result of which the action of suppressor tissue-specific mechanisms is activated and, possibly, certain oncogens are activated.

The most fundamental discovery in this area the mapping of suppressor genes in retinoblastoma, nephroblastoma and neuroblastoma should be considered. These mutational changes can occur both in germinal (germ) cells (then they are considered hereditary and are transmitted by autosomal dominant type of offspring) and in the somatic cells of the child (in these cases, the tumor is not inherited). For the transformation of a mutant cell into a cancer cell, it is necessary to have another event, most often a mutation, in the same cell. The probability of the second event determines the penetrance (probability of manifestation) of the tumor.

The result of medical genetic counseling is the allocation of two groups - with high and low risk of tumor - with appropriate recommendations to parents and the need for medical examination of children, if they belong to a high risk group. The obtained data allow to create a methodological basis of medical genetic counseling in pediatric oncology.

Embryonic tumors are a heterogeneous group. More than 40% of them should be attributed to genetically determined autosomal dominant states in which mutation occurs in germinal cells. In 60% of children, tumor development is due to mutation in somatic cells, which is not transmitted to offspring.

The criteria of belonging of the individual to a genetically-determined group is the twosideness, politeconomy of the process and the presence of another patient in the family. These children account for 12 - 25%, depending on the type of tumor. The risk of repeated cases in families of such patients reaches 30-40%. [6,7,17]

Unilateral sporadic tumors are a significant difficulty for medical genetic counseling, as they can be caused by mutations in both germinal and somatic cells. Different approaches are used to differentiate these phenomena: phenotypic identification, search for biochemical markers and adhesion groups. [5,14,15]

Medical and genetic counseling is the basis for the creation of a system for MNS prevention in children by their medical examination, to exclude persons who have a high risk of developing a tumor.

Prevention of the birth of a sick child can be performed by probabilistic prognosis (at a risk above 25% it is recommended to refrain from childbirth). The use of intrauterine diagnosis should be considered more effective. [14,18,19]

**Features of tumors diagnosis in children**

Diagnosis of tumors in children is represented by the following difficulties:

1. The difficulties associated with obtaining a history in children of younger age, absence or vagueness of the complaints. The child's relatives sometimes impose their point of view on the doctor, which is due to the fear of cancer diagnosis - carcinophobia, in which the child's parents come up with symptoms that seem to be characteristic of cancer. In this regard, the doctor is forced to actively "look for" signs of the disease, to assume possible complaints of the patient. It is important to pay attention to the behavior of the child. Changing the appearance and behavior of the child is particularly well seen by the doctor, constantly observing the child. In this regard, it is desirable to have contact with the patient's doctor, if examined by another doctor. It should be noted that children are dominated by a certain localization of the most common tumors: retroperitoneal space, mediastinum, axillary, inguinal, cervical and supraclavicular lymph nodes, soft tissues of the limbs. Unfortunately, the examination of a little child it is necessary to be guided by his/her behavior, appearance, body position, to build much on assumptions, as there are no specific complaints from the child, the ambiguity of the complaints, absence of their localization, if any, they extremely complicate the diagnosis. The diagnosis of brain tumors is especially difficult.
In older children in collecting history you have to consider the desire of the child to hide some of the symptoms because of the fear of pain during the examination and the reluctance of hospitalization.

Based on the above, the doctor, taking into account, should strive to a greater extent to an objective examination, which is especially important in pediatric oncology, but never discount even a grain of knowledge obtained in the collection of anamnesis.

2. A relatively small number of visually observed tumors. Unlike adults, who have many visually observable forms of tumors (breast cancer, cancer of the esophagus, stomach, rectum, oropharynx, skin), which are available for simple or endoscopic examination, in children such tumors are extremely rare. However, a number of tumors in children (leukemia, malignant lymphomas) can be the object of visual observation, so the increase in lymph nodes of different localization in these tumors should alert the doctor. Mandatory help in this case is cytological and histological examination, which allows you to make a timely correct diagnosis.

3. The most common tumors in children are located in hard-to-reach areas. Unfortunately, a common tumor, especially in the youngest children, is located in areas inaccessible for direct study: the skull – CNS tumors; mediastinum - neuroblastoma, tumor of the thymus gland, malignant lymphoma; retroperitoneal space - nephroblastoma, neuroblastoma, teratoid tumors. Tumors located in these areas can grow for a long time without causing subjective sensations, without leading to visible objective changes (of course, we are not talking about those cases where, for example, a brain tumor affects vital centers). In some cases, tumors can cause pain or discomfort, squeezing nerves or blood vessels, but they usually grow, pushing the surrounding organs and tissues, especially since the anatomical and physiological data of the child's body allow it. Gradually, tumors located in hard-to-reach areas increase in size and are often found when they become very large. Often they are discovered by the mother of the child when dressing or bathing. In other cases, the primary tumor itself is not detected, but metastases attract the attention. Brain tumors are very difficult in terms of diagnosis as their manifestation (dizziness, headaches, nausea, changes in vision and others) are objectively recorded with difficulty, and it is difficult or impossible to question a child, especially a small one.

4. Most tumors in children are hidden under "masks". Diagnosis of tumors in childhood is complicated by the fact that most tumors in children are hidden under various "masks". Almost any disease in childhood, especially early, and some physiological processes can resemble a tumor in their manifestations, as well as a tumor can be taken for a physiological process or any non-oncological disease. The situation is aggravated by the fact that quite often, along with the tumor, other diseases occur simultaneously, there are physiological processes that can cover the tumor (teething, puberty, etc.). It is necessary to remember the frequent combination of tumors with malformations, which can also "cover" it by its manifestation. Unfortunately, usually the doctor stops at the diagnosis of the diseases well-known in the childhood, to which he/she has sufficient experience, so in terms of diagnosing of MN in children, oncological alertness is important.

5. Prevalence of the general symptoms over the local ones. The clinical picture of most tumors in children often seems the same, as the general symptoms come to the fore. In the vast majority of cases, all MNs are characterized by paleness of the skin of varying severity degrees, weight loss to one degree or another (or stop in weight gain), changes in behavior, fatigue, gastrointestinal tract insufficiencies (nausea, vomiting, constipation, diarrhea, pain), subfebrile temperature, anemia, increased ESR. In general, the doctor often observes the clinical picture typical for any child disease, for any child infection. The doctor should be aware of the typical MN in children and when detecting common symptoms, he/she should investigate the most common localization of tumors in childhood.

6. The need for anesthetic support. When carrying out diagnostic studies in children, it is necessary to provide them with anesthetic, especially in small children, to obtain quality information and maintain contact with the examined child (overcoming child fear, unpleasant sensations of pain, immobilization). Only complete exclusion of discomfort, fear, anxiety and pain in the child will allow to conduct a full study for diagnosis and further treatment.

BIBLIOGRAPHY


