HEAD AND NECK OCCUPATIONAL CANCER 
ETHYOPATHOGENIC ASPECTS

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Abstract: The environmental factors are directly or indirectly responsible for a large percentage (80-90%) of all cancers and at least 90% of these factors are chemical. The number and the quantity of chemical substances present in the environment and especially in the working environment, has increased significantly and, at the same time, so has the number of “carcinogenic chemicals”; according to their mechanism of action, they are divided into three categories: primary carcinogens, procarcinogens and cocarcinogens. The occupational cancer of the ORL sphere includes a group of neoplasms originating from the upper aerodigestive tract. It is an etiogenus group of tumours with different risk factors. Occupational exposure to oncogenic chemical agents determines the location of the neoplastic process, with a clear predilection for the nasal fossa, the sinuses and the larynx.

Rezumat: O mare proporţie (80 - 90 %) din toate cancerele depinde direct sau indirect de factorii de mediu şi cel puţin 90% din aceşti factori sunt de natură chimică. Numărul şi cantitatea substanţelor chimice din mediul inco�ator şi în special din mediul de muncă, a crescut foarte mult si o dată cu aceasta şi cel al substanţelor “chimice cancerigene”; după mecanismul de acţiune se împart în trei categorii: cancerigeni primari, procarcancerigeni şi cocancerigeni. Cancerul sferei O.R.L. include un grup de neoplasme cu originea la nivelul căilor aero-digestive superioare. Reprezintă un grup etiogen de tumori cu factori de risc diferiţi. Exemplul profesională la agenţii chimici oncojeni determina localizarea procesului neoplazic, cu o predilectie evidentă, la nivelul foselor nazale, sinusurilor şi laringelui.

The environmental factors are directly or indirectly responsible for 80-90% of all cancers and at least 90% of these factors are chemical. According to other opinions, 90% of all cancers are induced or promoted by specific environmental factors and are directly related to industry and diseases generated by occupational noxious factors. Most of these factors in the environment are the result of human activity and can be prevented.

Thousands of chemicals were tested, hundreds of them have been proven to be carcinogenic, but only a small amount of them are used in industry. Carcinogenic agents are not only very different, but they are also very widespread.

Chemical substances range from complex organic structures up to chemical elements, being widespread in both the working environment and outside it, in the everyday life. So far, 20 chemical substances or mixtures have been proven to cause cancer.(1) Clinical observations were followed by attempts to produce experimental cancer, in animals, with different chemicals. Only in 1915, the results were satisfactory, repeatedly painting tar on the inner face of the ear in the rabbit. The results were confirmed and also extended in other animals with tars, heavy mineral oils, etc and it was noticed that carcinogenic tars could be obtained from substances containing only C and H. Further research has led to the conclusion that the noxious principles of tars were the polycyclic aromatic hydrocarbons. Besides polycyclic aromatic hydrocarbons, that are the most active carcinogenic substances, other compounds, particularly some coloring matter like para-dimethyl-azonobenzene and amino-azo-toluene, are also known. Possible pollution with carcinogen chemicals, noticed in recent years, raises serious public health problems in many countries.(2) At present, the main issue is to know them and to develop control measures that must be just as rigorous as those adopted against the microbiological noxious agents.

In terms of determining the occupational risk of cancer, this one is being complicated by a series of factors: irritation of the occupational etiological factors with the nonoccupational ones (smoking for lung cancer); long period of latency for cancer; individual sensibility in carcinogens, lack of difference between occupational and nonoccupational cancer; low value of experimental data upscaling from laboratory animals to human. Due to these inherent difficulties in determining the occupational etiological factor, the diagnosis of occupational cancer is reduced in number as compared to all cancers in the general population.(3) The percentage of cancers that can be the cause of an occupational exposure is only of 1-5% of all cancers.

OCCUPATIONAL CARCINOGENS MECHANISMS

The mechanism of occupational carcinogenesis is a complex one. All carcinogenic chemicals, their large majority, require prior metabolic activation. Initial wounds resemble those produced by radiations and viruses. After a biochemical transformation that results in electrophilic reactants, DNA adducts are formed (DNA carcinogen) that, if not repaired, lead to genetic mutations and eventually to cancer. Ionizing

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radiations produce specific DNA injuries that, when they do not cause the death of the cell, lead to neoplasia. These injuries consist of chromosomal translocations, punctiform mutations, deletions or error repairs that alter the transmission of genetic information.

The emergence of neoplasia requires an exposure period of 15–20 years, in extreme cases up to 50 years. The exposure period does not match the latency period. The longer the latency period and the exposure period, the higher the risk of carcinogenesis. Research in recent years has brought new elements regarding cancerogenesis. Today, it is assumed the existence of a multistage process, that can be divided in three evolutionary stages: initiation, promotion and progression. Occupational neoplasia does not have a carcinogenic mechanism different from that of general neoplasia, being a genetic disease in essence, irreversible, induced in somatic cells, as a result of a clonal expansion of the initiated cell. Initiation can be subject to a primary prophylaxis by avoiding exposure to occupational carcinogens.

Multistage theory of carcinogenesis is now unanimously accepted and supported by the results of some specific tests: in vitro tests, animal experiments and epidemiological studies. The control of cell proliferation and differentiation takes place at several points of the cellular cycle. Mutations in oncogenes determine the promotion to activate itself, while mutations in suppressor genes inactivate the inhibitor function of tumour growth. Proteins induced by oncogenes affect carcinogenesis in many stages, from initiation to progression. The proteins encoded by oncogenes are: growth factors, tyrosine kinases, G proteins, nuclear proteins, etc. Cellular balance in a tissue is determined by the increase in cell number, due to proliferation (apoptosis) and the decrease in cell number, both caused by the cell death (proapoptosis). Imbalance occurs either in the levels of protein, in cell proliferation or due to an insufficient number of cell deaths. Chemical carcinogens can be aliphatic or aromatic compounds, straight chains or branched, saturated or unsaturated, homo or heterocyclic, as well as in organic chemicals. They can be gasses, liquids or solids. According to their mechanism of action, carcinogenic chemicals are divided into three categories: primary carcinogens, procarcinogens, cocarcinogens. A modified DNA can be repaired using a complex multienzymatic system, but the cell that contains a DNA altered and that persists for a long time cannot be repaired. The enzymatic repair system can no longer recognize normal DNA and thus it is inefficient in restoring its function and its normal structure. The injury is transmitted to daughter cells, becoming irreversible and allowing the malignant tumour process to carry on.

Primary carcinogens. Their chemical structure is of such nature, so that they can induce the neoplasm without causing changes in any enzyme of the host. Primary carcinogen is a molecule that reacts with DNA, leading to a change in its structure. Procarcinogens. They represent the majority of chemical carcinogens that require biochemical activation mediated by the host. Thus, the action of this type of carcinogen is determined, to a great extent, by the host’s ability to perform this reaction.

This category of chemical carcinogens includes, for example: organic aromatic hydrocarbons, that have a special affinity for nucleic acids, the maximum interaction taking place within 24 hours after inserting the carcinogen (this period is explained by the formation of electrophilic metabolites under the enzymatic activity of the host); organic aromatic hydrocarbons act on target cells after transforming them into alchilant agents – metabolites named “last carcinogens”;

Cocarcinogens form another class of chemicals that interfere with the carcinogen process. These chemical compounds do not have the property to induce cancer by themselves, but they sometimes intensify the carcinogenic effect quite dramatically. Unlike carcinogens, this group does not act irreversibly. In order for them to be active, they must be present in a larger quantity and for a longer period of time. That is why removing them from the working environment or from the mixtures containing them, or reducing their quantity, would lead to a delay or prevention of cancer development.

DIAGNOSIS OF OCCUPATIONAL CANCER

Considered isolated, diagnosis in any case of occupational tumour is more difficult to make than in other occupational diseases, since occupational cancer does not differ clinically and anatomo-histologically from “spontaneous” tumours with the same starting point. Regardless of the causal agent that generates them, their clinical shape or position, malignant occupational tumours have, however, certain common characteristics that represent the basic elements of the etiological diagnosis(4):

- tumour location is remarkably constant for each carcinogenic agent and for that specific occupation (coal carriers’ skin cancer, spinners’ scrotal cancer, the cancer caused by raw isopropyl affect the ethmoid, the maxillary and frontal sinuses, etc).
- unlike common forms of cancer, tumours are often multiple.
- contact with the carcinogen agent is significant both in intensity and duration.
- in some cases, the tumour is followed by or coexists with noncarcinogenic manifestations that prove the exposure to the particular agent, or to the chronic occupational disease this is producing (respiratory tract tumours due to chromates are followed or accompanied by chronic irritation of the respiratory system, ulcerations of the nasal mucous membranes and the skin, lung cancer due to asbestos, always grafts on asbestosis pulmonary fibrosis).
- the chemical carcinogenic agent can be revealed most often in the patient’ s blood, tissues or the tumour (arsenic, chromium, asbestos fibbers).
- neoplasms occur after a long period of working time in high risk occupation (latency period is usually between 10 and 25 years). If exposure was intense enough or extended, the tumour can appear when the contact with that particular agent ends, even several years after.
- the tumour can be reproduced experimentally by applying the carcinogen agent found at the working place on animals.

HEAD AND NECK OCCUPATIONAL CANCER

Head and neck cancer includes a group of neoplasms originating from the upper aerodigestive tract. It is an eutrophic group of tumours with different risk factors. Occupational exposure to oncogenic chemical agents determines the location of the neoplastic process, with a clear predilection for the nasal fossas, the sinuses and the larynx. The oncogenic agents from the occupational environment incriminated in the etiology of cancer by nasal fossas and paranasal sinuses, are (5,6):

- wood dust for nasal cancer – although all types of wood can be incriminated, the incidence is higher for the exotic wood processing
- ethyl and methyl alcohol – an excess of cancers of the aerodigestive tract was noticed in places where these types of alcohol are made
- flour dust, coal dust, textile dust, printing ink
- nickel – causes the formation of malpighian epitheliums in
the nasal fossas (especially on the middle concha, the latency period is higher, 10-40 years).

- chromium and particularly its hexavalent derivates are incriminated in the etiology of cancer of nasal fossas in the workers with significant exposure (metallurgy of chromium, electrolytic chromium plate sections, chemical industry, fabrication of electric batteries).

REFERENCES