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Carcinogenic agents and cancer treatment

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Abstract

A Carcinogen is defined as any substance, radionuclide, or radiation that is an agent directly involved in causing cancer. Several radioactive substances are considered carcinogens, but their carcinogenic activity is attributed to the radiation, for example gamma rays and alpha particles, these are the substances that even cause tumours. (oncology the study and treatment of tumours.)

Four substances have been added in the U.S. Department of Health and Human Services 13th Report on Carcinogens, a science-based document that identifies chemical, biological, and physical agents that are considered cancer hazards for people living in the United and rest world States. The new report now includes 243 listings.

Keywords: Carcinogen, radionuclide, radiation, radioactive, tumours, oncology, hazards

Introduction

Cancer ranks second only to heart disease in the United States as the leading cause of death. Over 1.6 million of new cases of cancer are diagnosed yearly with over a half a million world population dying of cancer, accounting for nearly 1 of every 4 deaths. This chapter provides an overview of the major concepts and topic areas associated with the induction of cancer and cancer biology. Additional details on particular topic areas are presented elsewhere in this volume [1] By the second half of the 1960s, it had become evident that several physical, chemical, and biological agents could cause cancer in humans. Epidemiology is based on direct evidence in humans, and hence it is the litmus test of carcinogenicity [2]

A carcinogen is an agent that causes neoplasia in a multicellular organism. Carcinogens can be chemicals, viruses, hormones, ionizing radiation, or solid materials. These agents all produce cancer by modifying genomic DNA in a cell and then causing these modified cells to proliferate rather than undergoing differentiation into normal functional cells. Carcinogens may be DNA reactive (genotoxic carcinogens), which is a classification for chemicals that interact with genomic DNA resulting in damage to or alteration of its structure resulting in a mutation. Other carcinogens may change how DNA expresses its information without directly modifying its structure, or may modify the environment within a cell or tissue, resulting in increased susceptibility to incur DNA damage from other sources. Agents that function in this manner are referred to as non-DNA-reactive (nongenotoxic) carcinogens [2].

Classification of carcinogenic agents by IARC

Agents classified by the IARC monographs

Table1: Carcinogenic agents classification

Group 1	Carcinogenic to humans	120 agents
Group 2A	Probably carcinogenic to humans	82
Group 2B	Possibly carcinogenic to humans	311
Group 3	Not classifiable as to its carcinogenicity to humans	499
Group 4	Probably not carcinogenic to humans	1 ^[3]

Cancer hotspots

A first type of epidemiological study consisted of building on the suggestions, often coming from clinical observations or crudely recorded data on a geographical basis, that there were hotspots of cancer incidence in areas where some characteristic exposure was reported as common. Most often this occurred in developing countries, and IARC established collaborations in those areas with local health professionals who provided, directly and via official government channels, scientific support to mount rigorous epidemiological and

laboratory investigations designed to put the suggestions to the test. Significant results were soon obtained, of value locally for the populations concerned and also of broader significance for the knowledge of new carcinogens [2]

Chemical names [3]

Table 2: Chemical names

4342-03-4	Dacarbazine	2B	26, Sup 7	1987	
4548-53-2	Ponceau SX	3	8, Sup 7	1987	
4549-40-0	Nitrosomethylvinylamine	2B	17, Sup 7	1987	
4657-93-6	5-Aminoacanthophenone	3	16, Sup 7	1987	
4680-78-8	Guinea Green B	3	16, Sup 7	1987	
5131-60-2	4-Chloro- <i>meta</i> -phenylene diamine	3	27, Sup 7	1987	
5141-20-8	Light Green SF	3	16, Sup 7	1987	

Tobacco and cancer

Evidence for causation by tobacco

Epidemiological studies from around the world have provided sufficient evidence that the smoking of tobacco as cigarettes and bidis causes cancer of the respiratory tract and the upper digestive tract (International Agency for Research on Cancer (IARC), 1986). Similarly, smokeless tobacco including the forms most commonly used in South Asia, has been demonstrated to cause oral cancer and other head and neck cancers (IARC, 1985). The risks of these cancers are substantially increased in tobacco users who have a high-level consumption of alcohol (IARC 1986). Since evidence up to 1985 has been extensively reviewed by the IARC, in this paper largely post-1985 studies are included. [4]

Tobacco

Diseases related to the smoking of tobacco include lung cancer and cancer at other sites, coronary heart disease and stroke, chronic bronchitis and emphysema, and many other diseases, including peptic ulcers. Tobacco smoking "is the single most important preventable environmental factor contributing to illness, disability, and death in the United States" according to WHO. It states: Smoking-related diseases are such important causes of disability and premature death in developing countries that the control of cigarette smoking could do more to improve health and prolong life in these countries than any single action in the whole field of preventive medicine. The harmful effects of tobacco are greater when it is smoked as cigarettes than when consumed in other forms. This may be because acid cigarette smoke is less irritating than the alkaline smoke from pipes and cigars and, therefore, more easily inhaled. However, tobacco

consumption in any form appears to be accompanied by adverse effects, most recently demonstrated in a study showing that long-time snuff dippers experience a highly increased risk of oral cancer. The categories used are not necessarily "natural" assemblages, nor are they the only possible groupings of the components. [7] The discussion of each factor includes a description of important inclusions and exclusions. For instance, the "diet" section looks at all "foodstuffs," including naturally occurring and added contaminants. Drinking water, which is discussed under "pollution," and "alcohol," which is treated as a factor unto itself, is excluded from diet. All of the estimates considered in preparing the following discussion of factors are listed in table 2, at the end of this chapter. Only "best estimates," either point estimates or intervals, as presented by each author are included in the table. The primary references should be consulted for acceptable ranges and/or confidence limits, exact data sources and methods, and caveats. Tobacco is known to contribute more heavily to the number of cancer deaths than any other single substance. The relationship of cigarette smoking and cancer was first suggested in the 1920's. During the 1950's, results from many epidemiologic studies confirmed this association. Many carcinogens have been identified in cigarette smoke, and the differences consistently observed between rates of lung cancer among regular cigarette smokers and lifetime non-smokers is so extreme that it is not likely to be an artefact of the epidemiologic method. The 1964 Surgeon General's Report reached the following conclusion: 'Cigarette smoking is causally related to lung cancer in men and the data for women, though less extensive, points in the same direction.' Today, cigarette smoking is regarded as the major cause of lung cancer in both males and females and is largely responsible for the recent rapid rise in female lung cancer rates. The 1980 Surgeon General's report, The Health Consequences of Smoking for women, states the first signs of an epidemic of smoking-related disease among women are now appearing [7]

Foods that cause cancer

Certain components present in food items trigger reactions that lead to epigenetic modifications responsible for cancer. These components are present in our daily food items

Epigenetics

Epigenetics is the study of cellular and physiological traits that are not caused by changes in the DNA sequence but are still heritable by daughter cell. It's the study of stable and long-term alterations in the transcriptional potential of a cell. It comprises several components such as DNA methylation, covalent histone modifications, particularly histone acetylation and methylation, and non-coding RNA-related mechanisms. Epigenetics has shown that many forms of cancer are caused by the chemical modifications brought forth by the environmental factors and diet. Thus the cause of these cancers is not a genetic mutation but an alteration in gene function. As a result more research is now being directed towards finding cures by altering the gene function as opposed to mutating the whole gene. Researchers now know that epigenetic modifications influence gene expression. For example, silencing of a tumour suppressor gene, which normally regulates cell growth and death, by an epigenetic modification rather than by a mutation of the gene itself. Thus it can be said that these modifications play an important role in the development of diseases, including cancer. [5]

Table 3: Cancer causing components of food ^[5]

Foods	Components
French fries, potato chips, cornflakes	Acrylamide
Red meat	Neu5GC
Processed meat	Sodium nitrite i.e. nitrosamines
Microwave popcorn	PFOA(perfluorooctanoic acid)
Salted fish	Nitrosamines
Soft drinks (diet)	Aspartame
Butter/oil/milk	Saturated fats

Table 4: Diet, nutrition and cancer: levels of evidence ^[6]

Level of evidence	Decrease risk	Increase risk
Convincing	Physical activity (colon)	Overweight and obesity (oesophagus, colorectum, breast in postmenopausal women, endometrium, kidney) Alcohol (oral cavity, pharynx, larynx, oesophagus, liver, breast) Aflatoxin (liver) Chinese-style salted fish (nasopharynx)
Probable	Fruits and vegetables (Oral cavity, oesophagus, stomach, colorectum*) Physical activity (breast)	Preserved meat and red meat (colorectum) Salt preserved foods and salt (stomach) Very hot (thermally) drinks and food (oral cavity, pharynx, oesophagus)
Insufficient	Fibre, soya, fish, n-3 fatty acids, carotenoids, vitamins B2, B6, folate, B12, C, D, E, calcium, zinc, selenium, non-nutrient plant constituents (e.g. allium compounds, flavonoids, isoflavones, lignans)	Animal fats, heterocyclic amines, polycyclic aromatic hydrocarbons, nitrosamines

Other risk factors that cause cancer

- Age.
- Alcohol.
- Chronic Inflammation.
- Diet.
- Hormones.
- Immunosuppression.
- Infectious Agents

Treatments for cancer

Different cancers can require different treatments, like chemotherapy, radiation therapy, or immunotherapy. ^[8]

Chemotherapy

Chemotherapy is a type of cancer treatment that uses one or more anti-cancer drugs as part of a standardized

chemotherapy regimen. Chemotherapy may be given with a curative intent, or it may aim to prolong life or to reduce symptoms

Radiation therapy

Radiation therapy or radiotherapy, often abbreviated RT, RTx, or XRT, is therapy using ionizing radiation, generally as part of cancer treatment to control or kill malignant cells and normally delivered by a linear accelerator.

Immunotherapy

Immunotherapy is a type of cancer treatment that helps your immune system fight cancer. The immune system helps your body fight infections and other diseases. It is made up of white blood cells and organs and tissues of the lymph system. Immunotherapy is a type of biological therapy

Table 5: Classification of current anti - cancer drugs ^[9]

Class	Name of the drug	Type of cancer
Alkylating agents	Mechlorethamine	Hodgkin's disease and non-hodgkin's lymphoma
	Cyclophosphamide	Acute and chronic lymphocytic leukemia; Hodgkin's disease; non-Hodgkin's lymphoma; multiple myeloma; neuroblastoma; breast, ovary, lung cancer; Wilms' tumor; cervix, testis cancer; soft-tissue sarcoma
	Melphalan (L-sarcolysin) Chlorambucil A	Multiple myeloma; breast, ovarian cancer Chronic lymphocytic leukemia; primary macroglobulinemia; Hodgkin's disease; non-Hodgkin's lymphoma
	Altretamine	Ovarian cancer
	Thiotepa	Bladder, breast, ovarian cancer
	Procarbazine	Hodgkin's disease
	Busulfan	Chronic myelogenous leukemia
	Carmustine (BCNU)	Hodgkin's disease; non-Hodgkin's lymphoma; primary brain tumor; melanoma
	Streptozocin (streptozotocin)	Malignant pancreatic insulinoma; malignant carcinoid
	Dacarbazine (DTIC; dimethyltriazenoimidazole carboxamide), temozolomide	Malignant melanoma; Hodgkin's disease; soft-tissue sarcomas; glioma; melanoma
Antimetabolites	Cisplatin, carboplatin, oxaliplatin	Testicular, ovarian, bladder, oesophageal, lung, colon cancer
	Methotrexate (amethopterin)	Acute lymphocytic leukemia; choriocarcinoma; breast, head, neck, and lung cancer; osteogenic sarcoma; bladder cancer
	Pemetrexed Fluorouracil	Mesothelioma, lung cancer Breast, colon, esophageal, stomach, pancreas, head and neck; premalignant skin lesion (topical)
	Cytarabine (cytosine arabinoside)	Acute myelogenous and acute lymphocytic leukemia; non-Hodgkin's lymphoma

	Gemcitabine	Pancreatic, ovarian, lung cancer
	Mercaptopurine	Acute lymphocytic and myelogenous leukemia
	Pentostatin	Hairy cell leukemia; chronic lymphocytic leukemia; small cell non-Hodgkin's lymphoma
Natural products	Vinblastine, vinorelbine	Hodgkin's disease; non-Hodgkin's lymphoma: breast, lung, and testis cancer
	Vincristine	Acute lymphocytic leukemia; neuroblastoma; Wilms' tumor; rhabdomyosarcoma; Hodgkin's disease; non-Hodgkin's lymphoma
	Paclitaxel, docetaxel	Ovarian, breast, lung, bladder, head and neck cancer
	Etoposide	Testis, small-cell lung, and other lung cancer; breast cancer; Hodgkin's disease; non-Hodgkin's lymphomas; acute myelogenous leukemia; Kaposi's sarcoma
Miscellaneous agents	L-Asparaginase	Acute lymphocytic leukemia
	Hydroxyurea	Chronic myelogenous leukemia; polycythemia vera; essential thrombocytosis
	Imatinib	Chronic myelocytic leukemia; gastrointestinal stromal tumors; hyper eosinophilia syndrome
Hormones and antagonists	Prednisone	Acute and chronic lymphocytic leukemia; non-Hodgkin's lymphoma; Hodgkin's disease; breast cancer
	Hydroxyprogesterone caproate	Endometrial, breast cancer
	Tamoxifen	Breast cancer
	Leuprolide	Prostate cancer

Conclusion

Cancer has become a common disease that is increasing rapidly due to various reasons among which diet is thought to be partly responsible for about 30% to 40% of all cancers. Carcinogens are the substances that cause cancer of which some of them are insecticides, radiations (alpha, gamma rays), certain medicines like Azathioprine, Arsenic and inorganic arsenic compounds, Chlorambucil (though used for cancer), N'-Nitrosornicotine, etc.. The therapy of cancer has been improved during past half century. This improvement can be traced by number of factors: a better understanding of cancers causing and natural history, better technologies for earlier detection and diagnosis, improve control of primary tumours through better surgery and radiation therapy and more effective drugs.

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