

HUMAN CARCINOGENS

Identified by the IARC Monographs Program

The International Agency for Research on Cancer (IARC) Monographs (www.monographs.iarc.fr) identify environmental and occupational causes of human cancer. Sometimes called the WHO “Encyclopedia of Carcinogens,” the IARC Monographs are critical reviews and evaluations of the weight of the evidence that an agent can increase the risk of cancer in humans. Since the program’s inception in 1971, over 1000 agents have been evaluated, including individual chemicals, complex mixtures, physical agents, biological agents, personal habits, and occupational exposures.

The agents are classified as “carcinogenic to humans” (Group 1), “probably carcinogenic to humans” (Group 2A), “possibly carcinogenic to humans” (Group 2B), “not classifiable as to their carcinogenicity to humans” (Group 3), or as “probably not carcinogenic to humans” (Group 4). This classification, based on all published scientific literature, reflects the strength of the evidence derived from epidemiological studies in humans, cancer bioassays in experimental animals, and in-vivo and in-vitro studies on the mechanisms of carcinogenicity. Evidence from studies in humans and animals is considered to be sufficient, limited, inadequate, or suggesting lack of carcinogenicity. Data from mechanistic studies are considered as providing strong, moderate, or weak evidence for a given mechanism. To date, 120 agents have been classified in Group 1, the vast majority on the basis of sufficient evidence from epidemiological studies that the agent can cause cancer at one or several sites in humans. Some important risk factors known to cause cancer in humans have however not been covered in the IARC Monographs

HAZARD VS. RISK

The classification indicates the strength of the evidence that a substance or agent causes cancer. The Monographs Programme seeks to identify cancer hazards. An agent is considered a cancer hazard if it is capable of causing cancer under some circumstances. However, it does not indicate

the level of risk associated with exposure. The cancer risk associated with substances or agents assigned the same classification may be very different, depending on factors such as the type and extent of exposure and the strength of the effect of the agent.

program, notably genetic traits, reproductive status, and some nutritional factors. Other factors, such as weight control or physical activity, have been evaluated by the IARC Handbooks for their preventive effects.

The main figure shows, for each organ or group of organs in the human body, which agent(s) can cause an increased risk of cancer at a given site.

FIGURE 9.1 Over 40 agents have more than one target organ site, with up to 17 sites for tobacco smoking and 14 sites for X-radiation and gamma-radiation.

FIGURE 9.2 Some agents have been classified in Group 1 with less than sufficient evidence from epidemiological studies, often on the basis of sufficient evidence of carcinogenicity in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity. It is noteworthy that a few agents have been shown to cause cancer in the offspring of the person exposed.

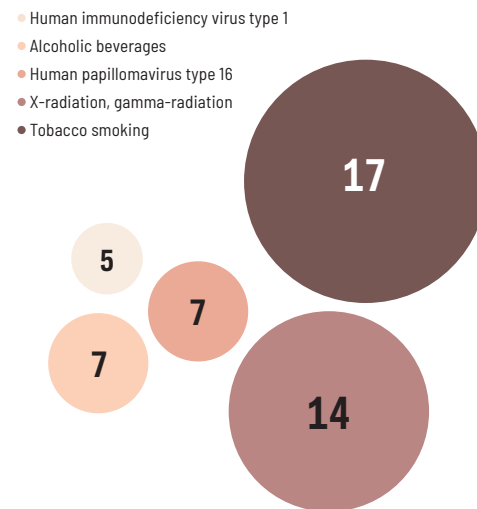
FIGURE 9.1

Group 1 carcinogenic agents by target site

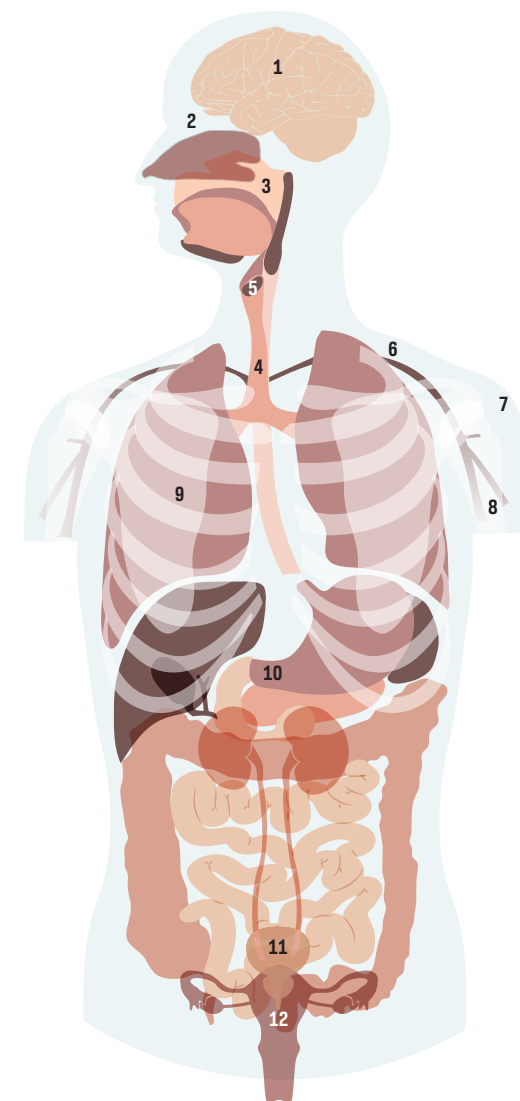
1 Brain and Central Nervous System	• X-radiation, gamma-radiation		
2 Eye	• Human immunodeficiency virus type 1 (HIV)	Ultraviolet-emitting tanning devices	Welding
3 Oral Cavity and Pharynx	ORAL CAVITY • Alcoholic beverages Betel quid with tobacco Betel quid without tobacco • Human papillomavirus type 16 Smokeless tobacco • Tobacco smoking	PHARYNX (ORO-, HYPO- AND/OR NOT OTHERWISE SPECIFIED) • Alcoholic beverages Betel quid with tobacco • Human papillomavirus type 16 • Tobacco smoking SALIVARY GLAND • X-radiation, gamma-radiation	NASOPHARYNX Epstein-Barr virus Formaldehyde Salted fish, Chinese-style Wood dust TONSIL • Human papillomavirus type 16
4 Respiratory System	NASAL CAVITY AND PARANASAL SINUS Isopropyl alcohol manufacture using strong acids Leather dust Nickel compounds Radium-226 and its decay products Radium-228 and its decay products • Tobacco smoking Wood dust LARYNX Acid mists, strong inorganic • Alcoholic beverages Asbestos (all forms) • Tobacco smoking LUNG Acheson process (occupational exposures associated with)	Aluminium production Arsenic and inorganic arsenic compounds Asbestos (all forms) Beryllium and beryllium compounds Bis(chloromethyl)ether; chloromethyl methyl ether (technical grade) Cadmium and cadmium compounds Chromium (VI) compounds Coal, indoor emissions from household combustion Coal gasification Coal-tar pitch Coke production Diesel engine exhausts Hematite mining (underground) Iron and steel founding	MOPP (vincristine-prednisone-nitrogen mustard-procarbazine mixture) Nickel compounds Outdoor air pollution Outdoor air pollution, particulate matter in Painter (occupational exposure as) Plutonium Radon-222 and its decay products Rubber production industry Silica dust, crystalline Soot Sulfur mustard Tobacco smoke, secondhand • Tobacco smoking • X-radiation, gamma-radiation Welding fumes
Mesothelium	Asbestos (all forms) Erionite	Fluoro-edenite Painter (occupational exposure as)	
5 Thyroid	Radioiodines, including iodine-131 (exposure during childhood and adolescence)	• X-radiation, gamma-radiation	

FIGURE 9.2

Carcinogenic agents associated with five or more cancer sites as listed here



To date, IARC has classified 120 agents as carcinogenic to humans.



Multiple Sites (Partly Unspecified)	Cyclosporine Fission products, including Strontium-90 • X-radiation, gamma-radiation (exposure in utero)
All Cancers Combined	2,3,7,8-Tetrachlorodibenzo-para-dioxin
Endothelium (Kaposi Sarcoma)	HIV type 1 • Kaposi sarcoma herpes virus
Less Than Sufficient Evidence in Humans*	N'-Nitrosonornicotine, (NNN) and 4-(N-nitro-methyl-amino-1-(3-pyridyl)-1-but none (NNK) 2,3,4,5,8-Pentachlorodibenzofuran 3,4,5,3',4'-Pentachlorobiphenyl (PCB-126) Polychlorinated biphenyls dioxin like, with a Toxic Equivalent Factor according to WHO (PCBs 77, 81, 105, 114, 118, 123, 126, 156, 167, 169, 189) Radionuclides, alpha-particle emitting, internally deposited Radionuclides, beta-particle emitting, internally deposited Ultraviolet radiation *Mechanistic upgrades to Group 1
Areca nut Aristolochic Acid Benzidine, dyes metabolized to Benzo[a]pyrene Ethanol in alcoholic beverages Ethylene oxide Etoposide Ionizing radiation (all types) 4,4'-Methylenebis (1-chloroaniline) (MOCA) Neutron radiation	

6 Hematopoietic System	Azathioprine Benzene Busulfan 1,3-Butadiene Chlorambucil Cyclophosphamide Cyclosporine Epstein-Barr virus Etoposide with cisplatin and bleomycin Fission products, including Strontium-90	Formaldehyde <i>Helicobacter pylori</i> Hepatitis C virus • HIV type 1 Human T-cell lymphotropic virus type 1 Kaposi sarcoma herpes virus Lindane Melphalan MOPP (vincristine-prednisone-nitrogen mustard-procarbazine mixture)	Pentachlorophenol Phosphorus-32, as phosphate Rubber production industry Semustine [1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea, or methyl-CCNU] Thiotepa Thorium-232 and its decay products • Tobacco smoking Treoosulfan • X-radiation, gamma-radiation
7 Skin	MELANOMA Solar radiation Polychlorinated biphenyls Ultraviolet-emitting tanning devices	OTHER MALIGNANT NEOPLASMS Arsenic and inorganic arsenic compounds Azathioprine Coal-tar distillation Coal-tar pitch Cyclosporine	Methoxsalen plus ultraviolet A Mineral oils, untreated or mildly treated Shale oils Solar radiation Soot • X-radiation, gamma-radiation
8 Bone	Plutonium Radium-224 and its decay products	Radium-226 and its decay products Radium-228 and its decay products	• X-radiation, gamma-radiation
9 Breast	Alcoholic beverages Diethylstilbestrol	Estrogen-progestogen contraceptives Estrogen-progestogen menopausal therapy	• X-radiation, gamma-radiation
10 Digestive System	ESOPHAGUS Acetaldehyde associated with consumption of alcoholic beverages • Alcoholic beverages Betel quid with tobacco Betel quid without tobacco Smokeless tobacco • Tobacco smoking • X-radiation, gamma-radiation UPPER AERODIGESTIVE TRACT Acetaldehyde associated with consumption of alcoholic beverages STOMACH <i>Helicobacter pylori</i> Rubber production industry • Tobacco smoking • X-radiation, gamma-radiation	LIVER (ANGIOSARCOMA) Vinyl chloride LIVER (HEPATOCELLULAR CARCINOMA) Aflatoxins • Alcoholic beverages Estrogen-progestogen contraceptives Hepatitis B virus Hepatitis C virus Plutonium Thorium-232 and its decay products • Tobacco smoking (in smokers and in smokers' children) GALLBLADDER Thorium-232 and its decay products	BILIARY TRACT <i>Chlonorchis sinensis</i> 1,2-Dichloropropane <i>Opisthorchis viverrini</i> PANCREAS Smokeless tobacco • Tobacco smoking COLON AND RECTUM • Alcoholic beverages Processed meat (consumption of) • Tobacco smoking • X-radiation, gamma-radiation ANUS • HIV type 1 • Human papillomavirus type 16
11 Urinary System	KIDNEY • Tobacco smoking Trichloroethylene • X-radiation, gamma-radiation RENAL PELVIS Aristolochic acid, plants containing Phenacetin Phenacetin, analgesic mixtures containing • Tobacco smoking	URINARY BLADDER Aluminum production 4-Aminobiphenyl Arsenic and inorganic arsenic compounds Auramine production Benzidine Chlornaphazine Cyclophosphamide Magenta production 2-Naphthylamine Painter (occupational exposure as)	Rubber production industry <i>Schistosoma haematobium</i> • Tobacco smoking <i>ortho</i> -Toluidine • X-radiation, gamma-radiation URETER Aristolochic acid, plants containing Phenacetin Phenacetin, analgesic mixtures containing • Tobacco smoking
12 Genital System	UTERINE CERVIX Diethylstilbestrol (exposure in utero) Estrogen-progestogen contraceptives • HIV type 1 Human papillomavirus type 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 • Tobacco smoking	ENDOMETRIUM Estrogen menopausal therapy Estrogen-progestogen menopausal therapy Tamoxifen OVARY Asbestos (all forms) Estrogen menopausal therapy	• Tobacco smoking VAGINA Diethylstilbestrol (exposure in utero) • Human papillomavirus type 16 VULVA • Human papillomavirus type 16 PENIS • Human papillomavirus type 16