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European Code against Cancer 4th Edition: Environment, occupation and cancer☆

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ABSTRACT

People are exposed throughout life to a wide range of environmental and occupational pollutants from different sources at home, in the workplace or in the general environment – exposures that normally cannot be directly controlled by the individual. Several chemicals, metals, dusts, fibres, and occupations have been established to be causally associated with an increased risk of specific cancers, such as cancers of the lung, skin and urinary bladder, and mesothelioma. Significant amounts of air pollutants – mainly from road transport and industry – continue to be emitted in the European Union (EU); an increased occurrence of lung cancer has been attributed to air pollution even in areas below the EU limits for daily air pollution. Additionally, a wide range of pesticides as well as industrial and household chemicals may lead to widespread human exposure, mainly through food and water. For most environmental pollutants, the most effective measures are regulations and community actions aimed at reducing and eliminating the exposures. Thus, it is imperative to raise awareness about environmental and occupational carcinogens in order to motivate individuals to be proactive in advocating protection and supporting initiatives aimed at reducing pollution. Regulations are not homogeneous across EU countries, and protective measures in the workplace are not used consistently by all workers all the time; compliance with regulations needs to be continuously monitored and enforced. Therefore, the recommendation on Environment and Occupation of the 4th edition of the European Code against Cancer, focusing on what individuals can do to reduce their cancer risk, reads: "*In the workplace, protect yourself against cancer-causing substances by following health and safety instructions.*"

1. Sources of environmental and occupational exposures: An overview

"Environment" is usually defined as the physical, chemical and biological conditions external to the human host, and all related behaviours. People are exposed to a wide range of pollutants from different sources through different pathways and exposure routes (such as inhalation, ingestion or dermal contact). Exposures occur throughout life on multiple occasions and in various settings: at home, at the workplace or in the general environment. There is some evidence that environmental exposures may be more hazardous during gestation and more in children than in adults [1]. Additionally, parental environmental or occupational exposures may increase the risk of cancer in the offspring [2–4]. Environmental contaminants typically affect the general population through exposures that normally cannot be directly controlled

Abbreviations: AF, attributable fraction; BFRs, brominated flame retardants; DDT, dichlorodiphenyltrichloroethane; ESCAPE, European Study of Cohorts for Air Pollution Effects; EU, European Union; HR, hazard ratio; IARC, International Agency for Research on Cancer; PM_{10}, particulate matter with diameter of 10 micrometres or less; $PM_{2.5}$, particulate matter with diameter of 2.5 micrometres or less; PAHs, polycyclic aromatic hydrocarbons; PBBs, polybrominated biphenyls; PBDEs, polybrominated diphenyl ethers; PCBs, polychlorinated biphenyls; PCDD/Fs, polychlorinated dibenzo-p-dioxins and -furans; POPs, persistent organic pollutants; REACH, Registration, Evaluation and Authorisation of Chemicals; TCDD, 2,3,7,8-tetrachlorodibenzo-para-dioxin; UK, United Kingdom; WHO, World Health Organization.

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by the individual. Some exposures are widespread (e.g. air pollution), whereas others are limited to small areas close to, for example, specific industrial sites.

Air pollution, especially outdoors, is a major environmental health problem in Europe [5,6]. Other environmental health exposures derive from consumer products (predominantly man-made) that people are exposed to involuntarily in their daily life: e.g. paints or building materials in households, pesticides applied in gardens or playgrounds, chemicals used for cleaning at home or in schools, and toys. Occupational health risks are directly related to agents occurring in the work environment. The specific types of cancer linked with occupational exposures are mainly cancers of the lung, skin (non-melanoma) and urinary bladder, and mesothelioma [7]. The harmful health effects of environmental exposures usually depend on the carcinogenic potential of the agent, the dose and duration of the exposure, and the susceptibility of the individual.

The International Agency for Research on Cancer (IARC) Monographs programme on the evaluation of carcinogenic risks to humans rigorously evaluates and classifies the carcinogenicity to humans of specific chemicals, groups of related chemicals, complex mixtures, occupational and environmental exposures, cultural or behavioural practices, biological organisms and physical agents [8] into: Group 1 (carcinogenic to humans), 2A (probably carcinogenic to humans), 2B (possibly carcinogenic to humans), 3 (not classifiable as to its carcinogenicity to humans), and 4 (probably not carcinogenic to humans) [9]. The Monographs programme is one of the major sources for the scientific justification of the recommendations related to environment and occupation.

In the framework of the European Code against Cancer [10], the Environment and Occupation Working Group aims to summarise below the current evidence on the main environmental and occupational carcinogens of a chemical nature to which the citizens of the European Union (EU) may be still exposed today.

2. Cancer associated with environmental and occupational chemical exposures

Table 1 presents an overview of chemicals and mixtures, metals, dust and fibres, and occupations classified as carcinogenic (Group 1) to humans, and the cancer sites with sufficient or limited evidence for carcinogenicity. Environmental exposures and occupations with carcinogenetic potential may be related to specific compounds, mixtures of exposures, or exposure scenarios where specific carcinogenic agents have not yet been identified. Some environmental and work-related exposures with carcinogenic potential are presented elsewhere in the 4th edition of the European Code against Cancer (Box 1), including second-hand tobacco smoke [11], ionising radiation (radon, radiation-exposed workers) [12] and ultraviolet radiation in outdoor workers [13].

2.1. Environmental exposures

Recently, both outdoor air pollution *per se* and particulate matter (PM) from outdoor air pollution have been classified as carcinogenic to humans (Group 1) [6]. Outdoor air pollution is a mixture of multiple pollutants originating from a myriad natural and anthropogenic sources such as transport, power generation, industrial activity, biomass burning, and domestic heating and cooking. Exposure levels and contributions from the individual sources of outdoor air pollution vary substantially geographically and over time. Volatile organic compounds, nitrogen-containing and halogenated organic compounds, polycyclic aromatic hydrocarbons (PAHs), toxic metals, and many by-products of incomplete combustion (e.g. dioxins) are all carcinogenic air pollutants. An important contribution to the body of evidence for an association between PM and lung cancer was provided by the European Study of Cohorts for Air Pollution Effects (ESCAPE) – a pooled analysis of data from 17 European countries [14]. ESCAPE reported an increased risk for lung cancer associated with 10 $\mu g/m^3$ increments of PM_{10} (hazard ratio (HR): 1.22; 95% CI: 1.03–1.45) and $PM_{2.5}$ (HR: 1.40; 95% CI: 0.92–2.13). These results were apparent even for exposure levels below current European guidelines. The IARC Working Group concluded also that the existing studies have provided some evidence of an increased risk of bladder cancer associated with outdoor air pollution, including occupational and residential exposures to traffic emissions [6], after adjustment for tobacco smoking. Other substances or mixtures contributing to outdoor air pollution have also been classified or reconfirmed as Group 1 by the IARC, including diesel engine exhaust [15], benzene and PAHs [2]. Humans are usually exposed simultaneously to a variety of PAHs which include several potent carcinogens, such as benzo[*a*]pyrene. Urban populations with high ambient levels of PAHs and other pollutants have exhibited higher rates of lung cancer than rural populations which are independent of tobacco smoking [16]. Benzene is found in refuelling emissions near petrol filling stations and inside vehicles. In occupational studies, sufficient evidence has been established for the association between benzene and acute non-lymphocytic leukaemia, and potentially other haematopoietic malignancies, including acute lymphocytic leukaemia, chronic lymphocytic leukaemia, multiple myeloma and non-Hodgkin lymphoma [2].

In recent decades the European Union has significantly reduced emissions of several air pollutants, such as SO_2, CO, benzene and lead [5]. Emissions of primary PM_{10} and $PM_{2.5}$ decreased by 14% and 16%, respectively, between 2002 and 2011. Despite these improvements, road transport, industry, power plants, household and agricultural activities continue to emit significant amounts of air pollutants. During 2002–2011, 22–44% of the EU urban population was exposed to concentrations of PM_{10} above the EU limit for daily air quality, and the PM_{10} 24-h limit was exceeded in 22 European countries in 2011. Fig. 1 shows the attainment of the PM_{10} 24-h limit value for all EU member states in 2011. Cross-border pollution – e.g. from intercontinental transport – constitutes a particularly challenging issue since, in many EU countries, more than 50% of the observed $PM_{2.5}$ concentrations derive from outside-border emissions.

Furthermore, overall combustion of fuels for domestic needs has not decreased in the EU in the last decade [5]. Indoor emissions from household combustion of coal, an important source of PM and PAHs, have been classified as carcinogenic to humans with sufficient evidence for increased risk of lung cancer [17]. Another established carcinogen, formaldehyde (Group 1), is also released in combustion processes, and may also be released from particle boards and similar building materials, carpets, paints and varnishes, and during its use as a disinfectant [2]. Second-hand smoke, containing most of the constituents of tobacco smoke including 69 known carcinogens, also contributes to both indoor and outdoor air pollution, as reported elsewhere [11].

Other environmental contaminants are found in water and food. A wide range of compounds – including pesticides, industrial and household chemicals, metals and pharmaceutical products – can reach freshwater bodies in Europe. For instance, non-occupational exposure to arsenic in the general EU population is mainly through contaminated food [18] and water [19], as was shown in a study conducted in Hungary, Romania and Slovakia. Of particular concern are chemical contaminants with persistent and bio-accumulative properties, as well as potentially endocrine-disrupting properties which alter the hormonal and homeostatic systems and thus may be associated with an array of diseases and disorders. Many of these chemicals are used in plastics, textiles,