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REVIEW

Preventable Exposures Associated With Human Cancers

Vincent James Cogliano, Robert Baan, Kurt Straif, Yann Grosse, Béatrice Lauby-Secretan, Fatiha El Ghissassi, Véronique Bouvard, Lamia Benbrahim-Tallaa, Neela Guha, Crystal Freeman, Laurent Galichet, Christopher P. Wild

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Correspondence to: Vincent James Cogliano, PhD, Section of IARC Monographs, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France (e-mail: imo@iarc.fr).

Information on the causes of cancer at specific sites is important to cancer control planners, cancer researchers, cancer patients, and the general public. The International Agency for Research on Cancer (IARC) Monograph series, which has classified human carcinogens for more than 40 years, recently completed a review to provide up-to-date information on the cancer sites associated with more than 100 carcinogenic agents. Based on IARC's review, we listed the cancer sites associated with each agent and then rearranged this information to list the known and suspected causes of cancer at each site. We also summarized the rationale for classifications that were based on mechanistic data. This information, based on the forthcoming IARC Monographs Volume 100, offers insights into the current state-of-the-science of carcinogen identification. Use of mechanistic data to identify carcinogens is increasing, and epidemiological research is identifying additional carcinogens and cancer sites or confirming carcinogenic potential under conditions of lower exposure. Nevertheless, some common human cancers still have few (or no) identified causal agents.

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Cancer includes many diseases, and the question often arises which exposures are associated with cancer of a specific organ or site. This information is important for rational planning of cancer control programs. It is also critical to the identification of potential confounding factors in the design and analysis of epidemiological studies and to the formulation of hypotheses concerning mechanistic pathways for experimental investigation. On a more personal level, patients and their families often wonder whether preventable environmental, occupational, dietary, or consumer exposures might have contributed to their disease. Information about exposures associated with cancer at specific sites is difficult to obtain because it is spread across hundreds of agent-specific assessments published by different health authorities at various times using different methods.

Recently, the International Agency for Research on Cancer (IARC) completed a review (1) of the more than 100 chemicals, occupations, physical agents, biological agents, and other agents that it has classified as carcinogenic to humans (Group 1; IARC classifies agents as carcinogenic to humans [Group 1], probably carcinogenic to humans [Group 2A], possibly carcinogenic to humans [Group 2B], not classifiable [Group 3], or probably not carcinogenic to humans [Group 4]) (2). To this end, IARC convened six Working Groups that included 160 scientists from 28 countries to critically review published epidemiological and experimental studies, to evaluate the carcinogenicity of each agent, to identify cancer sites where a causal association is established or credible, and to identify mechanistic events that are known or likely to be involved. This work will be published in 2011 as Volume 100 of the IARC Monographs (1), and summary information is already available (3–8). IARC's review provides up-to-date information on cancer sites associated with each human carcinogen.

There has been debate over the value of identifying cancer sites associated with an agent, with some scientists arguing that association with some cancer sites implies exclusion of a possible association with cancer at other sites (9,10). The crux of the matter is whether to regard a list of cancer sites restrictively, as a finite number of sites where carcinogenesis is possible, or expansively, as examples where strong evidence of an association exists at the time of evaluation (11). IARC has taken the expansive view, and its recent review provides information pertinent to this question.

In this article, we have brought together cancer site information on more than 100 human carcinogens identified through 40 years of IARC Monographs reviews, rearranged this information to list the known and suspected causes of cancer at various sites, and discussed some implications for the state-of-the-science of carcinogen identification. Other factors associated with an increased cancer risk not covered in the IARC Monographs, notably genetic traits, reproductive status, and some nutritional factors, are not included in this review.

Methods

For each agent that IARC classifies as carcinogenic to humans, we compiled lists of the cancer sites for which we have "sufficient evidence" or "limited evidence" of an association in humans. For the purposes of this analysis, sufficient evidence in humans means that a causal relationship has been established and that chance, bias, and confounding could be ruled out with reasonable confidence,