Re: False-Positive Results in Cancer Epidemiology: A Plea for Epistemological Modesty

In their plea for epistemological modesty, Boffetta et al. (1) criticize overinterpretation of new epidemiological findings. They assert that this is a common problem and cite two International Agency for Research on Cancer (IARC) Monographs. A closer reading of these Monographs, however, provides reassurance that scientists on Monograph Working Groups are able to put new epidemiological findings in perspective by considering other lines of evidence. In addition, IARC’s use of interdisciplinary Working Groups reduces the risk that individuals or collaborators may overinterpret their own work.

In discussing acrylonitrile, Boffetta et al. suggest that IARC based its 1979 conclusion (2) on a single new epidemiological study without confirmatory evidence. In fact, that acrylonitrile Working Group characterized the human study as “preliminary” and based its conclusion primarily on multisite carcinogenicity in male and female rats by two exposure routes and on mutagenicity. IARC updates the Monographs as science evolves and newer studies become available, and acrylonitrile has since been classified as “probably carcinogenic” (3) and later as “possibly carcinogenic” (4).

In discussing formaldehyde, Boffetta et al. cite IARC’s TCDD Working Group. In fact, IARC’s TCDD Working Group modestly characterized the human evidence as “limited,” meaning that “chance, bias or confounding could not be ruled out with reasonable confidence” (5). IARC’s evaluation of TCDD as “carcinogenic to humans” considered additional strong evidence that TCDD is a multisite carcinogen in animals and acts through the aryl hydrocarbon receptor, which functions similarly in animals and humans.

The lesson we draw from these examples is the complementary value of findings from all lines of research. Consider the example of formaldehyde. The first formaldehyde Monograph (6) found “sufficient evidence” of respiratory tract cancer in animals, although the evidence in humans was “inadequate.” Subsequent Monographs concluded that the human evidence had increased to “limited” (7,8) and ultimately “sufficient” (9). Thus, it was appropriate to regard formaldehyde as “probably carcinogenic” well before the human evidence became “sufficient.”

Accordingly, our plea for modesty is not to let preliminary or inconclusive results from one’s own discipline outweigh strong findings from another. Hill (10) advised, “All scientific work is incomplete. . . . That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action it appears to demand at a given time.” It would be wrong to dismiss new epidemiological findings or studies that suggest small increases in risk without first considering additional lines of evidence, such as animal bioassays and mechanistic data from experimental models and from exposed humans.

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References

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Correspondence to: Vincent Cogliano, PhD, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France (e-mail: cogliano@iarc.fr). In October 2009, the most recent Monograph Working Group concluded that there is now “sufficient evidence” in humans for 2,3,7,8-tetrachlorodibenzo-p-dioxin and reaffirmed that there is “sufficient evidence” in humans for formaldehyde.

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