tions generally prevailed in underground mines where the association between radon and lung cancer was first detected, therefore, dust per se does not necessarily block the detection of radon effects.

Like Upfal and colleagues, we were also concerned about the appropriateness of the alpha-track measurements as indicators of long-term exposure. We, thus, placed the detectors in homes for a full year, which eliminated seasonal effects and produced more precise exposure estimates than available from short-term monitors. The detectors were inserted in areas where residents spent most of their time at home. Perhaps most important, the women typically had lived in these homes for many years (median, 24). Because few homes had any renovations, it is likely that our exposure estimates reflect actual radon levels during the time period most critical to radon lung carcinogenesis. Indeed, the National Academy of Sciences (2) risk models assume that the effects of radon occur primarily within 25 years of exposure.

The findings of the Shenyang study must be interpreted very cautiously, but they do suggest that projections of low-dose home radon exposure based on information from high-dose exposures in underground mines do not fit the observed data well in this industrial city. Our findings by themselves do not suggest that the remedial action level of 4 pCi/L suggested by the Environmental Protection Agency is the correct one. Rather, they do suggest that projections of dose exposures in underground mines must be interpreted very cautiously, primarily within 25 years of exposure.

Academy of Sciences (2) risk models have the biologically plausible interpretation of radon effects.

WILLIAM J. BLOT
JOHN D. BOICE, JR.
JOSEPH F. FRAUMENI, JR.
Epidemiology and Biostatistics Program
Division of Cancer Etiology
National Cancer Institute
Bethesda, Md

References


CKM Carcinogenesis Models

Bogen wrote an article on cell-kinetic multistage (CKM) models of carcinogenesis (1). I would like to make three points relating to the subsequent letter by Keller and Whittemore (2) and the response to that letter by Bogen regarding his earlier article (3).

First, it is biologically plausible to assume that the rate of new cells in a precancerous stage \( i \) clone at time \( t \) is proportional to \( t^{n-1} \). For example, \( n = 2 \) if the clone grows as an expanding disk at a constant rate. Consequently, the total number of target cells in the clone at time \( t \) is given by: \( W^*_i(t) = 1 + b_i t^n \), where \( b_i \) is a constant and \( W^*_i(0) = 1 \) is the initial condition of the single cell progenitor of the clone. Clearly, if the stage \( i \) cell growth rate is important to the kinetics, i.e., \( n \) contributes to the exponent of age in the cancer incidence curve, then \( W^*_i(t) = b_i t^n \), which leads to the cancer incidence formula given correctly by Keller and Whittemore (4).

Second, as an alternative to \( W^*_i(t) \), Bogen proposes \( W_i(t) = (1 + a_i t) \). However, for the two dimension example, the rate of new cells to the clone at time \( t \) in this model is \( 2a_i + 2a_i t \), which, due to the constant, no longer has the biologically plausible interpretation given in point 1.

Third, if clonal growth contributes to the high exponent of time seen in cancer incidence curves, then the \( t^n \) term dominates both models of clonal growth and thus from this perspective the difference between \( W^*_i(t) \) and \( W_i(t) \) is irrelevant. This perspective is important. Gaffney and Altshuler (5) used a geometric CKM model for lung carcinogenesis and pointed out that if clonal growth does contribute to the high exponent seen in cancer incidence, then the chance of at least one normal cell proceeding to complete transformation without clonal growth would be very improbable. Consequently, a method that would eliminate or decrease clonal growth would be most effective in preventing tumors.

These three points should give a proper perspective to the implications in Bogen's paper that all of the previous CKM models must be erroneous, that he provided a "corrected" mathematical treatment, and that geometric CKM models are not being used in environmental risk assessment.

MICHAEL GAFFNEY*
Department of Clinical and Scientific Affairs
Pfizer Pharmaceuticals
New York, NY

References


Response

Although my paper (1) was submitted prior to the publication of Gaffney and Altshuler's (2), I regret that I did not, during the time my paper was in review and in press, learn of and properly reference their paper, which indeed contains a very interesting and valid geometric cell-kinetic multistage (CKM) analysis. I do, however, take issue with two points raised by Gaffney.

I agree that a \( 1 + bt^n \) model of premalignant clone growth (PCG) — which model, I note, was not explicitly stated by Gaffney and Altshuler (2) — is indeed perfectly reasonable, but this in no way validates the geometric CKM formula for cancer incidence given by Keller and Whittemore (3). That formula, based on mutation/growth terms of the form \( \lambda t^n \) with \( \lambda t << 1 \) and \( \lambda \) equal to a constant, was used to

*Correspondence to: William J. Blot, Ph.D., Division of Cancer Etiology, Executive Plaza North, Rm. 431, National Institutes of Health, Bethesda, MD 20892.

*Correspondence to: Michael Gaffney, Clinical and Scientific Affairs, Pfizer Pharmaceuticals, Pfizer, Inc., 235 E. 42nd St., New York, NY 10017.