

information. Using the same classification, the hypothesis of hormesis falls in identical classes, and is at least as plausible as the LNT hypothesis for the following reasons:

1. A stimulatory response induced by exposure to low doses has been observed in a wide variety of organisms, ranging from bacteria to mammals, and in different tissues of an individual, suggesting that the mechanism responsible for the stimulatory response has been evolutionary conserved (Makinodan and James 1990). As suggested by Alberts et al. (1989) in their widely used textbook, the problem of cancer seems to be not why it occurs, but why it occurs so infrequently.
2. Superoxide dismutase activities in living bodies decrease for increasing concentrations of active oxygen generated by high dose irradiation. However, in the case of low dose irradiation, superoxide dismutase activities increase resulting in a U-shaped response curve (Yamaoka 1991).
3. Canadian women who received repeated fluoroscopic examinations during therapeutic pneumothoraxes show a U-shaped response curve in breast cancer mortality (Miller et al. 1989).
4. Bogen (1997) developed a biologically plausible, mechanistically-based cytodynamic 2-stage (CD2) model predicting a U-shaped response curve for radon. As shown by Bogen, this model fits the observed uranium miner data as well as the hormesis reported by Cohen (1995).

Apparently, the participants in the controversy were unaware of key scientific information or chose to disregard it.

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RESPONSE TO STRAJA AND MOGHISSI

Dear Editors:

STRAJA and Moghissi recognize the focus of our recent exchange (Cohen 1998; Field et al. 1998; Lubin 1998a; Lubin 1998b; Smith et al. 1998), namely, ecologic regression is not informative about the relationship between lung cancer risk and individual exposure. This is because—here Cohen's response misses the point entirely—given two counties in which the higher lung cancer mortality rate occurs with the lower mean radon concentration, it is possible to construct correlations for radon and other lung cancer risk factors within each county that results in a higher "risk-adjusted" mean radon concentration in the higher rate county. Since the correlations between radon and the myriad lung cancer risk factors may differ within each county, one can never be certain that county-level regression

factors or *ad hoc* adjustments fully account for the effects of those correlates. My paper demonstrates that this bias is potentially unbounded and can occur with weak risk factors and small correlations (Lubin 1998a).

While the BEIR VI Committee acknowledges that a curvilinear effect or even a threshold effect at very low exposures cannot be ruled out with certainty, they provide a mechanistic basis for the existence of some risk at low exposures (NRC 1998). The main points are as follows. At residential exposures, most epithelial cells will never experience even one transversal by an alpha particle. Reducing exposure thus reduces the proportion of cells traversed, but does not alter the insult. Since evidence indicates that a single alpha particle can cause substantial and irreparable genomic damage among those cells not killed, including mutations and transformations, and since most cancers are

monoclonal, low radon exposure should cause some increased lung cancer risk. This mechanistic basis is directly supported by epidemiologic case-control and cohort studies that are based on radon exposures to individuals. Those studies are fully consistent with each other and with a significant lung cancer excess at residential radon levels.

Straja and Moghissi raise several points that may be relevant to low LET radiation; however, there is scant evidence of adaptive effects at low doses of high LET alpha particles from radon (NRC 1998). The fact that Bogen (1997) creates a "biologically plausible" model that fits ecologic data and the Colorado miner data has little significance, since ecologic data have little validity and since the Colorado study, the only one considered, has very extreme exposures and no non-exposed. The Colorado study has mean exposure and mean exposure rate 100 and 2,000 times greater than experienced by an average resident, respectively. The issue is whether the Bogan model fits data from epidemiologic studies of indoor radon and from miner studies more generally and whether there is biological evidence for the assumptions. Results from 11 studies of miners and, now, 13 indoor radon studies fail to support even the suggestion of a protective effect at low radon exposure.

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COMMENT ON LETTER BY STRAJA AND MOGHISSI

Dear Editors:

I HAVE never claimed that our studies support hormesis, since such an interpretation suffers from "the ecological fallacy." Our studies are designed to test the linear no-threshold theory, as we have shown by a rigorous mathematical analysis that this goal is not affected by the ecological fallacy.

I do report strong *negative* slopes in plots of lung cancer rates vs. average radon exposures in U.S. counties (as might be expected from hormesis), and show that these negative slopes

persist in spite of extensive attempts to eliminate them by consideration of possible uncertainties in our data by treating effects of over 500 potential confounding factors, etc. But my reason for doing this is only to make it clear that there is a huge discrepancy between these findings and the strong *positive* slopes predicted by linear no-threshold theory.

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RESPONSE TO STRAJA AND MOGHISSI

Dear Editors:

WE welcome the opportunity to briefly comment on the observations of Straja and Moghissi concerning our Forum article and rejoinder (Smith et al. 1998; Field et al. 1998). We heartily agree with Straja's and Moghissi's assertion that our publications centered on the validity of using an ecologic study to test the linear no-threshold theory. As the title of our Forum article stated (Smith et al. 1998), the focus of our paper was to

examine the validity of testing the linear no-threshold theory with ecologic data. In this case, the ecologic data were supplied by Cohen. The Forum article reveals that Cohen (1995) erroneously used the wrong model, based on faulty assumptions, to test the linear no-threshold theory. The invalidation of his model places his study in the domain of other ecologic studies.

We disagree with Straja's and Moghissi's assertion that Cohen's (1995) findings represent hormesis. Cohen (1990) admits that an ecologic study cannot determine whether or not radon causes lung cancer. Following the same logic, an