LETTERS

Carcinogen Risk Assessment

The action of the Environmental Protection Agency (EPA) Carcinogen Assessment Group on alternative approaches to carcinogen risk assessment is an important undertaking which has generated a considerable response (News and Comment, 3 Dec., p. 975; Letters, 18 Feb., p. 794). Some essential facts not considered and relating to carcinogenic hazards should be noted.

Available evidence relating to the mechanisms of carcinogenesis indicates that there are two distinct classes of carcinogens: (i) genotoxic carcinogens that have the ability to react with and alter genetic material and (ii) epigenetic agents that lack genotoxicity but are involved in the carcinogenic process through other biological effects (*1*). This now widely accepted fact (*2*) that there are different kinds of carcinogens necessarily implies that the extent of the human risk may not be the same for all agents.

The process of extrapolation from animal studies to human cancer risk is complex. No scientific basis exists for determining a priori which set of animal data is most appropriate for extrapolation (*3*). Moreover, the effects of genotoxic agents are cumulative, additive, or even multiplicative, are affected by age and sex as well as genetic factors, and are enhanced by cocarcinogenic and promoting elements. Thus these agents should be regarded generally, unless proved otherwise, as qualitative hazards, regardless of calculated risks from mathematical formulations.

In contrast, epigenetic agents generally lack the characteristics of genotoxins. In particular, the apparent mode of action of certain synthetic chemicals of environmental concern, involving effects such as cytotoxicity, prolonged endocrine imbalance, and tumor promotion, suggests a qualitatively different kind of hazard. In long-term bioassays, the carcinogenicity of many epigenetic agents declines sharply or even disappears when the maximum tolerated dose is reduced by one-half or three-quarters. Likewise, in nutritionally linked human cancers, such as colon or breast cancer, similar sharp changes in risk occur as a function of dietary levels of fat or fiber (*4*). Because of the diversity of epigenetic agents, their dose-response characteristics will have to be established individually. Nevertheless, the application of linear extrapolation in the low-dose range for such agents is not mandated by scientific facts.

Thus mechanistic considerations and available facts suggest that health risk analysis must include consideration of genotoxic and epigenetic effects. This does not imply that nongenotoxic agents are of lesser concern and, obviously, the most prudent approach for ensuring human safety is to eliminate exposure to all known carcinogens. While this must be the objective for genotoxic agents because of the reasons cited, it appears likely that epigenetic agents may display safe thresholds.

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Interpreting Quantum Mechanics

Arthur L. Robinson's article describing the recent "quantum mechanics test" by Alain Aspect and his co-workers (Research News, 7 Jan., p. 40) provides a good overview of complex ideas and intricate experiments. It highlights the dilemma of quantum mechanical interpretation after Bell's inequality: either quantum mechanics is not "realistic" (in the sense of describing systems with definite objective properties, whether they can be measured or not) or it is not "local" (in the sense of permitting enforcement of correlations between subsystems only when such subsystems are in speed-of-light contact). Among that minority of physicists who concern themselves with this dilemma at all, the prevailing view seems to be that one must give up "realism," since the alternative of allowing nonlocality leads to unacceptable conflicts with causality and special relativity.

I would like to advocate the alternative solution of retaining "realism" by providing an explicitly nonlocal description of quantum mechanical processes, as the results of Aspect *et al.* suggest. The intrinsic nonlocality of the quantum mechanical formalism is not difficult to identify; it lies in the requirement that separated measurements (like those of Aspect *et al.*) must be treated as parts of the *same* quantum mechanical state, no matter how large is the spatial separation between the measurements.

The interpretational problems of this manifest nonlocality of the formalism have long been recognized. The Copenhagen interpretation (the orthodox view) deals with these problems by asserting that the quantum mechanical state vector describing a given system is only a mathematical representation of "our knowledge of the system." As such, it does not have objective reality and is permitted to change instantaneously over all space whenever "our knowledge" changes (for example, whenever a measurement is made). This maneuver, originally devised by Heisenberg, is able to neutralize the simple nonlocality "paradoxes" that are implicit in the formalism if the state vector has objective reality. The "cost" of this maneuver is the acceptance of the premise that the solution of a simple second-order differential equation relating mass, energy, and momentum has somehow become a representation of "our knowledge."

It has taken five decades since the Copenhagen interpretation for compelling experimental evidence to emerge showing that the "our knowledge" maneuver cannot completely rid the formalism of its nonlocal characteristics. The results of Aspect *et al.* call for a reexamination of the way in which we interpret the quantum mechanical formalism. What seems to be required is a new and explicitly nonlocal interpretation that is consistent with causality and relativity (*1*).

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Erratum. The National Academy of Sciences elected 12, not 6, new foreign associates (News and Comment, 3 June, p. 1028). The remaining six are **Kimishige Ishizaka** (Japan), medicine and microbiology, Johns Hopkins University School of Medicine; **Ikuo Kushiro**, petrology, University of Tokyo, Tokyo, Japan; **Guido Pontecorvo** (Italy), geneticist, Imperial Cancer Research Fund Laboratories, London, United Kingdom; **Kai M. Siegbahn**, University of Uppsala, Uppsala, Sweden; **John R. Vane**, research and development, Wellcome Research Laboratories, Kent, United Kingdom; **Douglas F. Waterhouse** (retired), entomology, CSIRO, Deakin, Australia.