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From mouse-to-man: The quantitative assessment of cancer risks. With comments and a rejoinder by the authors. (English) Zbl 0955.62637

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Summary: Results from animal experiments are often used to assess cancer risks to humans from low doses of chemicals. This involves two extrapolations: from high dose to low dose and from animals to humans. This paper reviews the logic of both. In general, absent other information, we think that a chemical that is carcinogenic in a well-run animal experiment should be viewed with some suspicion. However, there are real problems with most animal experiments as they are currently done, and there are serious inconsistencies in the results. One probable cause is poorly defined end points, and another is uncontrolled variation. A number of suggestions are made for improvement, including proper randomization, 'blinding' the necropsy work and use of statistical techniques appropriate to multiple end points. Numerical assessments of human risk, even if based on good animal data, seem well beyond the scope of the scientifically possible. There are substantial differences in sensitivity between species, strains, sexes and individuals. Experimental work is needed to quantify these differences and explore their biological bases. The dose-response models now used in numerical extrapolation are quite far removed from the biology. At present there seems to be no sound way to choose a model on either biological or statistical grounds, and different models give substantially different disk estimates. On this score, there is little hope for progress until the biology of cancer is better understood. The paper is organized as follows. The issues are set out in the first section. Then the one-hit model is introduced in the context of a stylized risk assessment for DDT. Next the main generalizations of the one-hit model are explained: the multihit, Weibull and multistage. The biological foundations for these models are reviewed, and the impact of model selection on low-dose risk estimates is stressed. Dose scales and biological scaling factors are discussed, and then the conventional arguments for the mouse-to-man extrapolation. The DDT carcinogenesis literature is surveyed to show the quality of animal experiments. Opinions by others are cited, and conclusions are drawn.

MSC:

62P10 Applications of statistics to biology and medical sciences; meta analysis
92C50 Medical applications (general)

Full Text: DOI