ANALYSIS OF HEALTH EFFECTS CAUSED BY MULTIPLE INSULTS

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ABSTRACT

A method is presented for the analysis of the risk of health effects caused by a combination of insults. The approach is entirely phenomenological and has no built-in restrictions. Also, interactions between the effects of various toxicants are treated in a general manner. The only restrictions arise from the finite set of functions relating exposure parameters and the risk of health effects. As an example, the incidences of oral and esophageal cancer in man are analyzed as a function of alcohol and tobacco consumption. The properties of the solutions obtained are discussed, together with conclusions about the processes involved in the etiology of these cancers.

KEY WORDS: Multiple Insults, Synergism, Antagonism, Data Analysis.

INTRODUCTION

In the environment, no toxicant can act on an organism all by itself, there is always a mixture of many agents acting in combination. In order to study the health effects of multiple insults, the investigation of exposures to only one and two toxicants provides the basic information needed for a theoretical approach. At present, experiments involving two toxicants are being planned with increasing frequency both in chemical and in radiological toxicology, because the presence of other toxic agents can enhance or diminish the effects of a toxicant and yield results which are significantly different from those expected for an additivity of damages.

Most of the data available involve the exposure to a dose of either toxic agent alone, followed by an exposure to the combination of the doses. A simple comparison then shows whether the effects are at, above or below additivity (Reif, 1984). However, a measurement at a single dose combination does not allow a detailed study of the interaction between the effects of the two toxicants. For such an analysis, more elaborate data sets are needed. At present, sufficiently large sets are available only from epidemiological studies (Tuyns et al., 1977; Walter, 1980; Whittemore and McMillan, 1983) but corresponding experiments both in vitro and in vivo are being planned by many experimenters.

In the absence of sufficient experimental data, a multitude of mathematical forms can be constructed for the interaction of two toxicants. It is, therefore, important to approach the analysis without preconceived notions as to the nature of the interaction and to rely on a phenomenological approach to reach conclusions which are, as far as