

Biological effects of dietary restriction.

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This book constitutes the proceedings of a conference organized by the International Life Sciences Institute in Washington, DC in March 1990. The title should perhaps have been "biological effects of overnutrition", since the premature ageing and high incidence of disease and cancer seen in laboratory rodents fed *ad lib.* are 'adverse effects' caused by overnutrition, while the effects of dietary restriction are apparently beneficial. Be that as it may, the book is of considerable importance because it brings together three disciplines—nutrition, toxicology and gerontology—which all too often paddle their own canoes on separate waters. Traditionally, the nutritionist is obsessed by the need for nutritional adequacy, while the toxicologist worries about the possible contamination of food by toxins and/or carcinogens, and it is only the gerontologists who concerns themselves with the importance of caloric intake *per se.*

Perhaps the most important question raised in this book concerns the relevance to man of the benefits of diet restriction in laboratory rodents. Clearly, different spectra of debilitating and life-shortening diseases afflict different species. Thus, in humans, heart disease, cerebrovascular disease, diabetes and cancer are prominent; whereas in rats, progressive nephritis, polyarteritis, chronic myocarditis, endocrine disturbances and cancer are centre stage. The difficulty of measuring and controlling how much people eat over periods of several years makes it difficult to obtain hard data for humans. Nevertheless, there are several examples given of an association between caloric restriction and improved survival and better health in humans.

Diet restriction in laboratory rodents is associated with reduced cell-turnover rates and with reduced liver weight relative to body weight. Phenobarbitone-induced sleeping times are longer in diet-restricted

rats than in those fed *ad lib.* The first of these observations is almost certainly relevant to the subsequent risk of developing cancer, and the second should warn the toxicologist that overnutrition can alter the way in which xenobiotics are detoxified or metabolically activated.

Those responsible for running the National Toxicology Program in the USA, and most industrial and contract research laboratories worldwide, are reluctant to undertake chronic bioassays under conditions of reduced caloric intake. They give a string of reasons for this including expense, prolongation of studies and fear of non-acceptance of findings by regulatory authorities. However, over-valuation of the databases built up from studies conducted under *ad lib.* feeding conditions is also a factor, even though it can be argued that data from overfed, endocrine-disturbed rodents are of dubious relevance for man anyway! Against this background, it is good news that, in the USA, the National Center for Toxicological Research and the National Institute on Aging have begun a joint investigation of the influence of diet restriction in gerontological and toxicity/carcinogenicity studies.

Other topics that are dealt with in the book include: the relationship between ageing, dietary restriction and glucocorticoids; and effects of caloric restriction on endocrine control and reproduction, behaviour, neurobiological endpoints, immune function, DNA-repair, and free radical damage. A report of findings in the so-called 1200 rat Biosure study indicates the extent to which the benefits of rationing caloric intake can be achieved in rats fed a low energy (high-fibre) diet *ad lib.* Initial findings in diet-restriction studies on monkeys, and the effects of caloric restriction in autoimmune-prone mice and germ-free animals are also discussed.

Somewhat buried in the volume (chapter 22) is a potentially important section in which the author points out that diet restriction does not affect equally all age-related phenomena. Consequently, it is likely that diet restriction will not only delay the onset of age-related diseases, but also alter the spectrum of them.

This well produced, carefully edited and valuable book ends with a 16-page record of a lively panel discussion that brought the conference to an end. In my opinion, this book should be regarded as essential reading for all toxicologists and nutritionists.

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