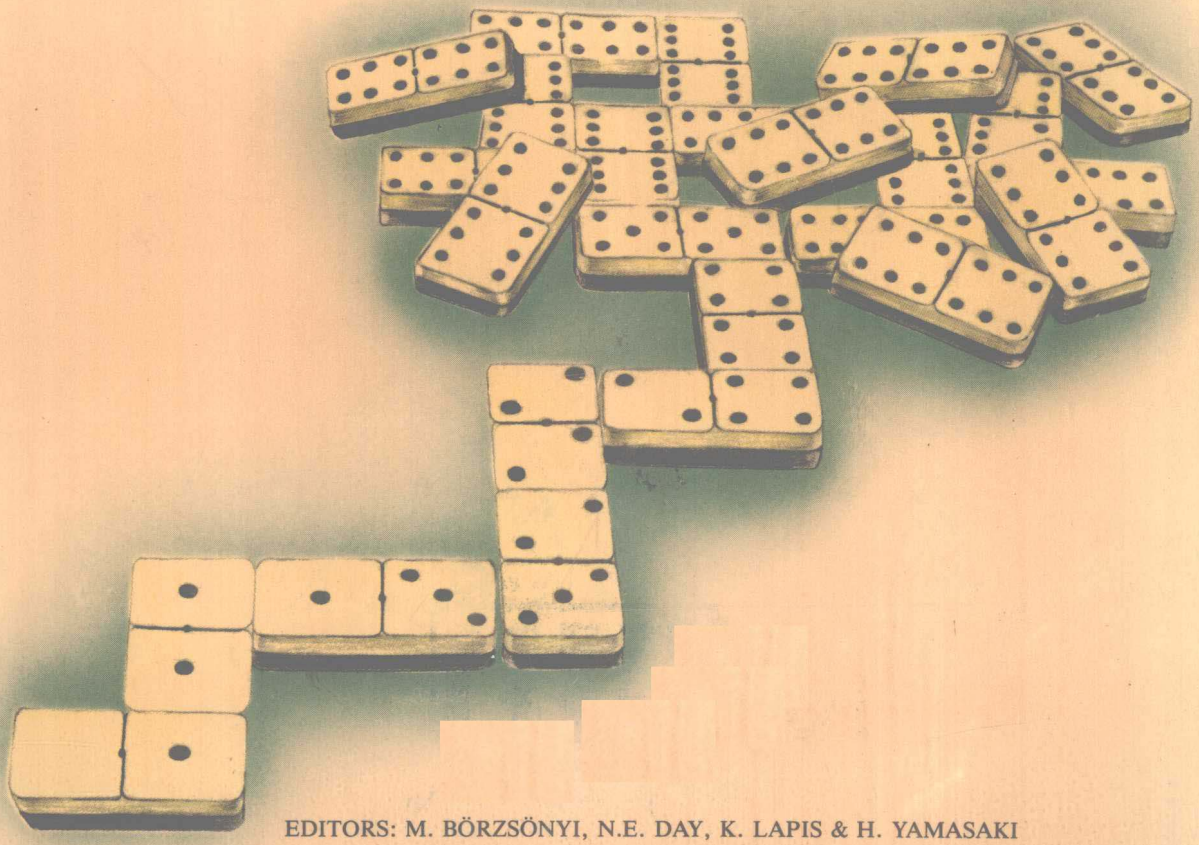
WORLD HEALTH ORGANIZATION

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

MODELS, MECHANISMS AND ETIOLOGY OF TUMOUR PROMOTION



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LYON 1984

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Proceedings of a Symposium organized by
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EDITORS

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The International Agency for Research on Cancer (IARC) was established in 1965 by the World Health Assembly, as an independently financed organization within the framework of the World Health Organization. The headquarters of the Agency are at Lyon, France.

The Agency conducts a programme of research concentrating particularly on the epidemiology of cancer and the study of potential carcinogens in the human environment. Its field studies are supplemented by biological and chemical research carried out in the Agency's laboratories in Lyon and, through collaborative research agreements, in national research institutions in many countries. The Agency also conducts a programme for the education and training of personnel for cancer research.

The publications of the Agency are intended to contribute to the dissemination of authoritative information on different aspects of cancer research.

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FOREWORD

Both epidemiological and laboratory studies indicate that most malignant tumours result from the interaction of target cells with multiple endogenous and exogenous factors and that their development is the result of a succession of steps occurring over a considerable part of the host's life span. Environmental factors are considered to play major roles at different stages during the development of human cancers.

One of the main goals of the research activities of the Agency is the primary prevention of human cancer, and the identification of environmental risk factors in carcinogenesis is an important aspect. In order to fulfill this goal, it is also essential to understand the mechanisms underlying different stages of carcinogenesis. Mechanisms of later stages of carcinogenesis – especially tumour promotion in two-stage models of carcinogenesis – are now being studied widely; however, much less is known about the later stages than about the earlier stage of carcinogenesis – including tumour initiation.

This volume is the first IARC publication devoted specifically to multi-stage carcinogenesis. It is my hope that it will not only summarize the state of present knowledge but also encourage further investigations for a better understanding of tumour promotion and multi-stage carcinogenesis.

The hospitality of the Hungarian Cancer Society, Budapest, is gratefully acknowledged. The meeting was cosponsored by the European Association for Cancer Research and was financed in part by donations made by a number of individual firms in the Federal Republic of Germany, France, Hungary, Italy, Switzerland, the UK and the USA.

L. Tomatis, MD
Director
International Agency for Research
on Cancer

INTRODUCTION

Following the first observation of two-stage carcinogenesis on mouse skin in the 1940s, many studies of tumour promotion were carried out, with mouse skin as the target organ and with phorbol esters as model tumour promoters. More recently, work with other species, at other sites and with other agents has led to acceptance that the multi-stage process is a general mechanism of carcinogenesis. In parallel, but almost independently, multi-stage models have been developed to explain a wide variety of epidemiological observations. An abundance of data has accumulated, both epidemiological and experimental, in support of the idea that the development of many cancers is multi-stage.

In order to understand the nature of the multi-stage process of carcinogenesis, and to identify risk factors involved in the causation of cancer, multi-disciplinary approaches are essential. However, epidemiologists and laboratory investigators often take separate and independent approaches to the very same problem. In the study of tumour promotion, cooperation between experimentalists and epidemiologists is especially desirable, since the elimination of risk factors that act in the later stages of carcinogenesis should lead to rapid reductions in human cancer mortality.

The present symposium was planned to stimulate a dialogue between epidemiologists and experimentalists in order to advance our knowledge of multi-stage carcinogenesis. Thus, this volume contains descriptions of human models of multi-stage carcinogenesis and models for possible identification of etiological factors in terms of multi-stage or multi-factorial carcinogenesis, as well as models and cellular and molecular mechanisms of experimental tumour promotion.

The interaction of epidemiologists and laboratory experimentalists in studies of the mechanism of multi-stage carcinogenesis and in the identification of environmental risk factors in terms of multi-stage carcinogenesis is still in an initial phase. It is our sincere hope that this volume will stimulate more such interaction in order to attain our mutual goal – cancer prevention.

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