Book Reviews

K. Lapis and J. V. Johannessen (eds.) Liver Carcinogenesis

In this volume of the Journal of Toxicology and Environmental Health the authors deal with the present results and problems of liver carcinogenesis of humans, experimental animals and those of in vitro systems. The first part of this book sums up present knowledge about etiology, diagnosis of hepatocarcinogenesis and the chemotheraphy of human liver tumors. Whereas a large number of potential environmental chemical carcinogens for animals are known, only a few of them can be evaluated as contaminant agents for humans as well.

The naturally occurring and synthetic liver carcinogens have been appraised. The possible role of mycotoxins has been discussed in details; in particular the association between the aflatoxins and liver cancer of the populations in Africa and Far East (Linsell).

In the carcinogenicity of pesticides it was pointed out that although only a few pesticides were subjected to carcinogenicity tests, 16 of them have been identified as hepatocarcinogenic agents in animals. The herbicide, 2,4,5-trichlorophenoxycetanol (TCPE) containing different amounts of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) was tested for carcinogenicity in Swiss mice. TCPE enhanced liver tumors in males, but TCDD in the dose-range used failed to do so (Sugar, Toth, Csuka, Gdti, Somfai-Relle).

Hydrazine analogues occurring in two edible mushrooms (Gyro-mitra exculenta and Agaricus bisporus) were reported to induce high incidence of benign and malignant hepatocellular neoplasms and some other tumors, also in Swiss mice and Syrian hamsters when administered orally. Since these mushrooms are consumed on a large scale by humans in various parts of the world, it was recommended to consider their hazardous nature (Toth).

It was reported that the proliferation inhibitory effect of cortico-costerone can be inactivated by blocking its cytoplasmic receptors in liver cells with other steroids (Desser-Wiest).

Several contributors dealt with the possible role of oral contraceptives in the pathogenesis of liver tumors. On the basis of experiences on pathological material from 150 women with liver tumors (mostly ingesting steroids), further studies were recommended to clarify the possible association between estrogens and primary liver carcinomas (Christopherson, Mays). The inability of methanol demethylation resulted in a massive accumulation of oncogenic metabolites in the smooth endoplasmic reticulum of hepatocytes. This consequence of synthetic estrogens, together with others (cholestasis, hypervascularity, induction of intracellular enzyme systems, etc.), was reported to contribute to the pathogenesis of liver tumors (Nissen, Kent, Nissen).

The American College of Surgeons’ survey data on 378 female and 165 male cases of primary liver tumors were evaluated (Vana, Murphy, Aronoff, Baker). Among females, 43.9% of the tumors were malignant and 56% were benign. A positive history of oral contraceptive use was found in nearly half of all tumors. The suggested association between the use of oral contraceptives and hepatic cell adenomas and focal nodular hyperplasias (mainly in the age group 20–30 years) was confirmed.
An analysis of the role of hepatitis B virus in human liver cancers was given (Zuckermann). It was concluded that primary liver cancer is the cumulative result of several cofactors (infection with hepatitis B virus, genetic, immunologic, hormonal and nutritional factors and different carcinogenic environmental factors).

The post-alcoholic liver cirrhosis was pointed out as the main cause of primary liver cell carcinoma in the 403 clinically unselected patients in West Germany. HBs antigen-positive liver cirrhosis was more often associated with primary liver cell cancer than liver cirrhosis with HBs antigenemia. Combination of alcohol abuse and HBs anti-genemia and/or acute hepatitis were suggested to play a role in higher risk of developing primary liver cell carcinoma (Lehmann, Wegener).

Precancerous changes in the human liver were surveyed. Cirrhosis was mentioned as a common antecedent or accompaniment of liver cell carcinoma. Other cellular changes were observed in patients and among populations considered to be at risk: infestation with liver flukes and duct epithelial hyperplasia occurred before development of cancer. Angiosarcoma was often preceded by a peculiar fibrosis, vascular changes and Kupffer cell hyperplasia (Anthony).

A detailed description has been given about the macroscopic and microscopic features of human liver cancers as well as their association with cirrhosis. The ultrastructural features of liver cancers of various degrees of differentiation were also reported (Lapis, Johan-nessen).

The applicability of afetoprotein (AFP) to the early diagnosis of patients at carcinogenic risk was discussed. AFP was suggested to be linked to dividing hepatocytes at a certain step of cell differentiation regardless of the stages of precancerous development (Dolezalovd, Simickovd, Stratil).

An ordered pattern of enzymatic and biochemical imbalance of cancer cells was presented on the basis of the molecular correlation concept, of the concept of key enzymes and the use of biological model systems. It was pointed out that the observed pattern of biochemical imbalance was also applicable to human hepatocellular carcinomas. Thus this system is open for the development of sensitive assays for biochemical diagnosis of liver tumor and for enzyme-pattern targeted chemotherapy (Weber, Kizaki, Tzeng, Williams).

Limitations of current treatment methods for primary carcinoma of the liver were discussed. Treatment regimens of patients with stage II liver cancer were compared. The survival rates for these increased in the following manner: systemic chemotherapy < surgical resection < dearterialization (McBride).

Considering the perspectives of the chemotherapy of primary liver cancer, the present results were reviewed. The importance of initiation

of polychemotherapy trials in surgically treated patients, the necessity and possibilities of designing new agents were pointed out (Eckhardt).

The second part of this book deals with some interesting experimental results of in vivo and in vitro carcinogenesis.

The ultrastructural characterization of transplantable hepatomas was given. The lesions appearing during hepatocarcinogenesis were separated into morphologically different entities. Similarly, the primary and transplantable hepatocellular carcinomas were arranged into a sequence of stages (Hruban).

The development, growth rate, degree of malignancy and chromosome pattern of Morris transplantable hepatomas were evaluated (Morris, Slaughter).
Hepatomas induced in inbred animals were characterized by new individual cell surface antigens which may offer a target for tumor immunotherapy. The cell surface fetal antigens were common for different hepatomas. The possible practical exploitation of these antigens in therapy and diagnosis of tumors were discussed (Embleton).

A comprehensive picture was given about MC-29 virus-induced liver cancer in chickens. The macroscopic, light and electron microscopic features and biological properties of this hepatoma and of its transplantable, virus-producing hepatoma were reported (Lapis).

Most of the enzymatic imbalances elucidated in chemically induced rat hepatomas were also applicable to this MC-29 virus-induced hepatoma, independent from the nature of the oncogenic agent and from the species (Prajda, Eckhardt, Suba, Lapis).

Observations on enzyme inducibility by glucocorticoids and on the mechanism of the deficient binding of 3H-hydrocortisone to DNA furnished evidences for the disorder of gene expression in MC-29 virus-induced transplantable hepatoma of chickens (Jeney, Kovalszky, Gyapay, Lapis, Suba).

Both humoral and cellular immunological reactions have a role in the pathogenesis of this virus-induced tumors, and the hepatomas may be influenced by nonspecific immunostimulation (Foldes). Just as common tumor-specific transplantation antigens of MC-29 hepatoma and Rous sarcoma were suggested (Elek, Lapis, Foldes).

The advantage of using a medaca (Oryzas latipes) in hepatocarcinogenesis studies was evaluated (Ishikawa, Takayama). A two-step perfusion method of the isolated liver was described for isolation of hepatocytes (Seglen). It was elucidated that corticosterone blocks the Fu 5a clone of the Reuber hepatoma cells in the late G1 phase of the cell cycle, resulting in the synchronization of the population (Vetterlein, Desser-Wiest). Finally, Kupffer cell suspension and cultures as a tool in experimental carcinogenesis were evaluated (Munthe-Kaas).

Overall, this book is a very valuable source of data about the actual problems of liver carcinogenesis.

E. Olah
L. Fishbein

Potential Industrial Carcinogens and Mutagens
This book provides detailed information on reported 167 industrial carcinogens and mutagens, arranged in 21 major groups by chemical structure. CAS #, major impurities, US production volume, number of workers potentially exposed, in what industries, national permissible exposure levels, e.g., OSHA and ACGIH standards, are included.

There is a detailed introductory chapter discussing the currently available screening test systems for the detection of carcinogenic and/or mutagenic chemicals covering their different advantages and limitations. To help to predict hazards from new agents considered for introduction in the environment and to avoid false-negative results, the application of a combination of screening tests is recommended. These include submammalian indicator organisms, such as the Salmonella/microsome test as an initial screen, followed by studies for DNA damage and repair in cultured mammalian cells; as the third phase, in vivo assays for gene mutations in rodents are suggested. Finally, long-term animal tests in one or two species should be done.

In another chapter, ‘combination effects in chemical carcinogenesis’, major aspects of epidemiology and problems associated with ‘risk assessment’ and ‘threshold doses’ are discussed.
Despite some errors in the illustrations and in the chemical formulae, this book is a good reference for scientists involved in genetic toxicology, carcinogenesis and mutagenesis studies, as the bibliography is extensive and current. It may also provide valuable assistance to industrial hygienists or officials working in public health and environmental protection agencies, as concise chapters on one particular compound or specific classes or chemicals are available for those wishing to be brought up to date in this rapidly moving field.

H. Bartsch

IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans
Some Monomers, Plastics and Synthetic Elastomers, and Acrolein,
vol. 19

International Agency for Research on Cancer, Lyon 1979

WHO 1979. 512 pp.; sFr. 60.-
ISBN 92-832-1219-3

Volume 19 of the series of monographs of the IARC was published according to the views and expert opinions of the Working Group on the evaluation of carcinogenic risk of some monomers, plastic, synthetic elastomers and acrolein. Some of these substances had been considered on the previous meetings (see volumes 7 and 11 of this series).

The range of application of the polymers, their quantity and variety are truly gigantic, so the contact of humans with these substances is practically constant both in everyday life and in industry. The yearly production of polymers in highly developed countries is being estimated in thousands of millions of kilograms (e.g., in 1976 it was produced in all the countries about 30,000 tons of polyethylene alone).

At first, these compounds were accounted for as inert ones which contribute greatly to their adoption and use everywhere, including medicine, food industry and pharmacology, i.e., in fields where everybody contacts these chemicals one way or another. However, as early as 1941 Turner described the appearance of local sarcomas after subcutaneous implantation of Bakelite disks to rats. Nowadays, the main principles of 'plastic' carcinogenesis are formed.

Unfortunately, it is too difficult to evaluate its results because there are no absolutely inert materials and, practically, any implanted solid body of an appropriate size and form seems to be carcinogenic. So it is not easy to find a proper control in such experiments.

Nevertheless, the Working Group declared the carcinogenicity, in animals, of acrylonitrile, polymethyl metacrylate, polypropylene, polytetrafluoroethylene, polyurethane, polyvinyl, vinyl bromide, vinyl chloride und polyvinylpyrrolidone. Except acrylonitrile, all these substances caused local sarcomas after subcutaneous, intramuscular or intraperitoneal implantation of disks, laminas or sponges, powder or suspensions. Acrylonitrile produces tumours of forestomach, brain and Zymbal gland.

As for chloroprene, styrene oxide and vinylidene chloride, there are some data on their mutagenic activity and, besides, on their teratogenic and embryotoxic activity.

There is unequivocal evidence of carcinogenicity of vinyl chloride in humans: it increased the frequency of tumours of liver, brain, lung and the haemopoietic system. There are some epidemiological data on increased mortality of the fetus in women whose husbands were engaged in the production of the above-mentioned substance. This points to its mutagenic and, perhaps, teratogenic activity. The data on the increased frequency of stomach cancer in men and women engaged in the production of polyvinyl chloride is insufficient for a conclusion. Due to some solitary information concerning the carcinogenicity of acrylonitrile in
humans which raises the frequency of lung and intestinal tumours, the Working Group inclined to consider this preparation conditionally carcinogenic.

The necessity to continue the epidemiological investigations was stressed by the Working Group because the data got from the experiments makes one think of a probable carcinogenicity of the compounds considered in humans too.

One of the main difficulties for the experts was a bulk of commercial terms for the same substance. Besides, a lot of products constantly enter in everyday life. And that is why all the terms used for every substance considered are given in the reviewed volume.

The volume is supplied with detailed reference on physical and chemical properties of the substance production, usage and their presence in the environment, methods of analysis, etc. A lot of original literature and reviews are listed. Thus, in general, the 19th volume may be a good manual for oncologists and industry physicians.

N.P. Napalkov,
A. G. Huvos (ed.)
Bone Tumors: Diagnosis, Treatment and Prognosis

It is extremely rare, these days in age, to find single-author books or even single-author articles. No one person can now claim to be an expert in more than one field. The current practice is to invite other experts to join hands and put together various aspects of any subject. Dr. Huvos has achieved a great feat in writing 28 chapters in this almost 500-page book single-handedly. The author’s goal was to make the book lucid, well balanced and authoritative. He succeeded. He has made the classification of bone tumors incredibly simple and easy to understand even by those not engaged in the field. Generally, the book is well balanced although some of the chapters, especially the chapters on osteogenic sarcoma, Ewing’s sarcoma and multiple myeloma, have been extensively covered and are, therefore, more authoritative than the rest. Every chapter opens with an attempt to define the tumor to be discussed and is followed by a brief historical review.

The authority of the book is derived from the extensive literature review. The list of references number well over 3,500 and the stronger the chapter the longer the list of references. Because of the obvious delay from manuscript to publication Dr. Huvos’ book might be regarded as an excellent ‘state of the art’ on bone tumors as of 1977-1978. Although Dr. Huvos is a pathologist he has not shied away from treatment of the various bone tumors. For obvious reasons the sections on pathology and diagnosis are stronger than those on treatment. As would be expected of a single-author book, some of the sections, such as those on Burkitt’s lymphoma and Kaposi’s sarcoma, are inadequately covered and are not as well illustrated as the rest of the chapters.

On the whole, the book is well written, easy to read, and inundated with excellent illustrations. This book is a must as a reference manual for every practicing pathologist, radiologist, orthopedic surgeon, or oncologist.

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