Book Review

Robert C. Jackson
The Theoretical Foundations of Cancer Chemotherapy

This is a unique monograph characterised by mathematical modelling as a means of teaching and research.

The first chapter, ‘Cell Cycle Effects of Drugs’, analyzes the biological properties of tumor cells and monoclonal or polyclonal character of individual tumors. It emphasizes the importance of stimulation or inhibition of peptide growth factors and deals with problems of protooncogenesis and of antioncogenesis. Tumor growth, expressed by Gompertz’s equation, could be mathematically modelled. It is hardly possible to perform cytotoxic therapy adequately without understanding the effects of drugs on individual phases of cell growth. The importance of flow cytometry for prediction of chemosensitivity of a tumor to individual cytotoxic drugs is stressed. The dose-response phenomenon of some cytotoxic drugs is analyzed. The curve which characterizes this relation is sharply ascending, which points to the necessity of high-dose therapy. The author also discusses the complexity of this relation in frequently used combination chemotherapy. To some extent, the cytotoxic effect seems to be proportional to the concentration of the cytotoxic drug and to the time of exposure.

In the second chapter, ‘Anticancer Drug Selectivity’, the author deals with experimental approaches and stresses the blastotrophy of individual cytostatics and their organ toxicity. From the pharmacological point of view, he emphasizes the importance of the therapeutic index of cytostatics and possibilities of its increase. The relation of tumor response to the tumor burden, i.e. the number of clonal cells of the tumor, is evident.

The third chapter, ‘Quiescent Cells, Differentiated Cells and Lost Cells’, which is especially valuable, analyzes the kinetics of bone marrow cells in relation to myelotoxicity. In response to cytotoxic drugs, the mobilization of the cells from the Go compartment to the proliferation compartment is significant. It demonstrates the great variability of the growing fraction of tumors (20-70%). The author stresses the importance of the combination of cytotoxic drugs without cross-resistance and overlapping toxicity. The process of differentiation of tumor cells after chemotherapy is also important. He analyzes the significance of the so-called cell loss factor (10-90%) in relation to the difference between the double-volume interval, which can be clinically recorded, and the potential doubling time.

The fourth chapter, ‘Pharmacokinetic Models’, presents one-, two- and three-compartment models and demonstrates the importance of a-, fS- and y-plas-matic half-time when chemotherapy is to be designed.
‘Invasion and Metastasis’, the fifth chapter, presents a model of metastatic cascade. The author analyzes several antimetastatic agents (ICFR-157, estra-mustine, vinblastine, anticoagulants, calcium channel blockers, retinoids).

The sixth chapter, ‘The Blood-Brain Barrier’, analyses the liposoluble cytostatics that pass through the hematoencephalic barrier, and deals with peripheral and central neurotoxicity of cytostatics.

The seventh chapter, ‘Cancer Treatment and the Immune Response’, deals with the significance of the immune response for the outcome of chemotherapy. A cancer patient, in whom the ‘supervision of immunity’ failed, is even more immunocompromised by chemotherapy itself, by radiotherapy and by surgical intervention). The immunosuppressive effect of cytostatics is individual and variable. The significance of cytokines is also dealt with.

In the eighth chapter, ‘Drug Resistance and Its Implications for Treatment Strategy’, the author analyzes mechanisms of the primary (type) and secondary (acquired) chemoresistance according to models of Gol-die and Coldman and of Skipper and Lloyd. From the practical point of view, it also contains data on cross-resistance of cytostatics, on the heterogeneity of the cell population of tumors, on the genetic instability of tumor cells and on multiple drug resistance.

The ninth chapter of the book, entitled “The Growth Kinetics of Large Tumors’ demonstrates the Gompertz equation and curve. For the growth of tumors, antiangiogenetic agents are important (anti-

TAF – Folkman). Special emphasis is put on the idea of dose intensity of chemotherapy, i.e. mg/m2/week or /cycle.


The last chapter, ‘Cytokinetics, Pharmacokinetics and Inhibition Kinetics: A Unified Model’ uses biochemical models to predict the ‘intrinsic sensitivity’ of cytostatics. The model of methotrexate inhibition is an ideal example for dihydrofolate reductase. The closing remarks contain critical comments on the limits of mathematical modelling in chemotherapy. Similarly, as with other mathematical models in biology and medicine, they cannot take into account all the complexity of a situation, but they, undoubtedly, represent a support in designing and performing the therapy, in teaching and in the research. A useful supplement is a diskette which contains computer systems analyzed in the text.

The book is an extraordinary and progressive monograph. Its study will contribute to the understanding of the experimental basis of tumor chemotherapy. It can, therefore, be recommended to all che-motherapeutists, clinical oncologists and radiothera-peutists.

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