MATHEMATICAL MODELS OF CHEMOTHERAPY

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1. Introduction

Suppose one injects a drug into an animal. What is the time course of the drug concentration in the blood and in the various organs of the body? Although preliminary attempts to set up mathematical models of this problem were made by Teorell [1], [2] and models of certain special cases have been considered by von Schrotter [3], Smith and Morales [4], and Morales and Smith [5], [6], it continues to challenge the biologist and mathematician. Much of the recent theoretical work in this area has been concerned with the analysis of radioactive tracer experiments on compartmentalized systems assumed to be in a steady state [7], [8]. This leads to the usual sets of simultaneous linear differential equations. We wish to consider the more complex kinetic problem. In particular, we wish to consider the kinetics of distribution of an injected compound assuming that it exchanges between capillary plasma and extracellular space by diffusion, enters the intracellular space by diffusion and perhaps by some active transport process and can react with some constituent (say an enzyme) of the intracellular space. Although the motivation for studying this problem was the desire to obtain a theoretical framework for the analysis of results with various agents used in cancer chemotherapy, the problem is of more general importance for physiology and pharmacology.

2. Anatomical and physiological considerations

Any mathematical model of such a complex process must be firmly imbedded in the known anatomical and physiological background if it is to approach