AGE-DEPENDENCE IN A STOCHASTIC MODEL OF CARCINOGENESIS

W. A. O'N. WAUGH
MCGILL UNIVERSITY

1. Introduction

This paper is concerned with a two-hit model for the initiation of neoplasia. The model is related to those discussed by H. G. Tucker [5], and by J. Neyman and E. L. Scott [4] in this Symposium, and also in recent papers by D. G. Kendall [1] and J. Neyman [3]. I should like to take the opportunity to thank Mr. Kendall for drawing my attention to these problems. The papers just mentioned all treat Markovian models, and this requires that the life lengths of cells be random variables with a negative exponential distribution. The main purpose of this paper is to discuss a model in which the probabilities for reproduction, mutation, and death of individual cells are supposed to have a general distribution, that is, to be functions of the ages of the cells, so that the process is non-Markovian.

2. Description of the model

We shall suppose that there are three types of cells, and for convenience we shall call them normal, gray, and black. Clones of black cells form malignant growths, while the gray cells are supposed to represent an intermediate stage between normality and malignancy. By mutation, a normal cell can be converted into a gray one, or a gray cell into a black one. We suppose that the population of normal cells is so large that its fluctuations can be ignored. The incidence of first-order mutations, from normal to gray, produces during a time interval (t_1,t_2) a number of gray cells which is a Poisson variable of expectation

$$\int_{t_1}^{t_2} f(t)\,dt, \tag{2.1}$$

where $f(t)$ is a function expressing the intensity of the carcinogenic action which causes the first-order mutations.

A gray cell will generate a clone of gray cells developing independently of one another according to the following age-dependent birth, death, and mutation process. Any individual when newly born has probability $1 - G(t)$ to live for a time longer than t, where $0 \leqq G(t) \leqq 1$ and $G(t) \uparrow 1$. Its life will be considered to end when it reproduces by binary fission, or ceases to be a gray cell as a result of mutation, or dies. Note that the probability for a cell's life to end is treated