EFFECTS OF URETHANE DOSE AND TIME PATTERNS ON TUMOR FORMATION

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1. Introduction

The carcinogenic action of urethane on the lungs of mice was first noted by Nettleship, Henshaw, and Meyer [1] in 1943. The effect of this chemical is to produce multiple tumors of apparently discrete origin, visible as pearly white nodules on the surface of the lung. Although the quantitative relation between dose and number of tumors (herein termed the dose-effect relation) has been studied by a number of investigators, the available data were not sufficient to test the mathematical model of a two stage mechanism of tumor formation developed by Neyman and Scott [2]. It was apparent from the model that, if the hypothesis is correct, the needed constants might be determined from suitable studies of the changes in the dose-effect relation produced by variation in the time interval between doses.

Henshaw and Meyer [3] and Rogers [4] administered urethane with various time intervals between doses, but their results were not conclusive with respect to the effect of fractionating the dose. Shimkin, Wieder, Marzi, Gubareff, and Suntzeff [5] are presenting a paper in this session concerning their efforts to test Neyman's model. The work reported here was undertaken to supplement the previous data and, by covering a broader pattern of urethane administration, with respect to both quantity and time interval, hopefully to include the particular patterns that would critically test the hypothesis. Additionally, since tumors take time to develop to recognizable size, the effect of time interval from initial injection to sacrifice was introduced as a factor to be studied.

2. Material and methods

The animals used were female, strain A/Jackson mice which were 8½ to 10½ weeks old at the beginning of the experiment. It is to be noted that this is the same strain as used by Shimkin and Gubareff, but that only females were used

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