11204 P

Factors Determining Frequency Distribution of Lesions Induced by Papilloma Protein and Vaccinia Virus.*

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Parker[1] has presented statistical evidence for the concept that the frequency distribution of lesions with vaccinia virus is related to the chance distribution of virus particles in the inocula. This was based on the resemblance of the observed frequency to the theoretical Poisson frequency to be expected if a single virus particle causes infection. Similar studies on the purified papilloma protein[2] have shown that results with this virus follow this theoretical expectation as well as did those with vaccinia virus. However, consistent deviations of observed from theoretical results at the extremes of the frequency distributions, and the finding of about 100,000,000 papilloma protein molecules in the dilution giving the 50% point (where only 0.69 particles should have been according to this concept) have led to critical examination of Parker's data and interpretations. Using the procedure recommended by Haldane[3] for determining χ^2, the fit of observed to theoretical frequencies in Parker's data was good in 2 experiments and improbable in 2.

On the basis of these inconsistencies other relations were sought to explain the character of results with vaccinia virus and the papilloma protein. It has seemed that a more logical interpretation and one more consistent with experimental results is that the observed frequency is an S shaped dose-response curve determined by variations in host resistance. If host variation follows a normal distribution, response to logarithmic doses will be S shaped and will be constant for a given material and population of test animals. Such a curve would represent an integrated frequency curve which can be placed in straight line form by plotting normal equivalent deviation against logarithm of dose.[4]

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The data of Parker's experiments[1] and those obtained in the present work with the papilloma protein have been analyzed from this point of view. It was found that in all 4 of Parker's experiments the observed points fell about a straight line with a high degree of probability. This is illustrated in Fig. 1 for which the data of Parker's Exp. 4 were used. In Fig. 1 (a) is shown the relation of the observed points to the straight line drawn by the method of least squares. The Poisson curve has been drawn from the theoretical values given by Parker, and the deviation of observed points from the curve is shown in Fig. 1 (b).

The response to the papilloma protein likewise is linear until the 22nd day of the incubation period (which usually lasts about 30 days). Due probably to acquired resistance developing at about this period, as shown by actual retrogression of warts in some animals, there occurs a break in the line increasing progressively to the 32nd day. The response at this time assumes a character compatible with the concept that it is determined by change in the level of host resistance, from that of natural resistance to that of the total of natural

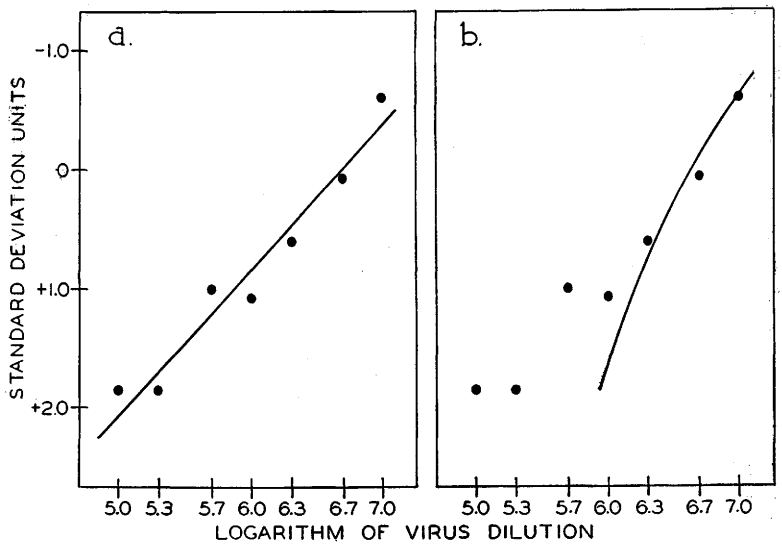

FIG. 1.

The points represent observed percentage response to vaccinia virus in Parker's Exp. 4 expressed as normal equivalent deviation, that is, the deviation on a normal frequency curve to which the percentage is equivalent. The deviation is given in standard deviation units.

(a) Comparison of observed points with the straight line drawn by the method of least squares.

(b) Comparison of observed points with the curve determined from theoretical values given by Parker on the assumption that a single virus particle infects.

plus acquired resistance. This possibility will be illustrated in detail in a forthcoming publication.

These results indicate that the character of the dose-response curves obtained with these viruses is determined, not by chance presence or absence of virus particles in inocula, but by variations in host resistance.

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Lack of Demonstrable Androgenic Activity of Desoxycorticosterone Acetate.*

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Crystalline desoxycorticosterone has been isolated from the adrenal cortex.[1] Manifold biological activities have been attributed to this substance. It has a potent cortinomimetic activity[2] and has been shown to be a fairly effective progestational substance.[2-5] Salmon[6] has stated that it has an estrogenic effect on the human vagina. Robson[4] has reported that desoxycorticosterone will directly antagonize and nullify the effects of simultaneously administered estrogen on the vagina of the castrate mouse. These last two observations are contradictory and could only be reconciled by the assumption that there is a marked difference between the human and the mouse in their reactions to this compound.

The present authors have offered direct evidence that the adrenals of immature castrate male rats, 26 to 31 days of age, are capable of producing an androgenic substance.[7, 8] In this paper it was noted that adrenosterone[9] and progesterone[10] had been isolated from the

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