Table 2. Constants calculated from time courses. Values for H_{max} were obtained by successive approximation from the data.

Antibody (mg/ml)	H_{max} (10^{-9} mole)	t^*	k min^{-1}
0.004	13.5	102	0.00478
.008	11.0	75	.00637
.016	12.0	63	.00763
.032	11.5	40	.00798
.064	11.3	23	.00935

The butanolic phase was passed through columns packed with cotton acid-succinate (*5*), and the adsorbed histamine was liberated with 0.2*N* HCl, neutralized, and assayed on ileal strips obtained from normal guinea pigs according to the method used in this laboratory (*6*).

Curves of unit histamine release plotted against time are sigmoidal, the slope becoming steeper and the "lag" period shorter with increasing antibody concentration. The initial velocity constants for these curves were evaluated from the modified form of the first-order law as applied to growth data by Lotka (*7*) and Brody (*8*). In the present case the working expression can be written

$$1 - \frac{H}{H_{max}} = e^{-k(t-t^*)} \qquad (1)$$

in which H_{max} is the maximum unit histamine release, H is the release at time t, and t^* is the time at which the extrapolated curve crosses the time axis. The value for H_{max} was obtained graphically for each antibody concentration by successive approximations, differing in steps of 0.5 units, to reach that value which would linearize the curve of log $(1 - H/H_{max})$ plotted against $(t-t^*)$. The first-order constants were obtained by multiplying the slopes by -2.303. The values of H_{max}, t^*, and k for the respective systems are entered in Table 2.

The dependence of k upon antibody concentration (Fig. 1), is described by a curve which rises steeply from the origin and then becomes asymptotic to a line parallel to the x-axis. The curve evidently is an hyperbola since a plot of the reciprocals produces a straight line. Using the classical notation of Michaelis-Menten kinetics,

$$\frac{1}{V} = \left(\frac{1}{S} \cdot \frac{K_s}{V_{max}}\right) + \frac{1}{V_{max}} \qquad (2)$$

in which K_s/V_{max} is the slope of the reciprocal plot and $1/V_{max}$ its intercept, we can evaluate the limiting velocity, V_{max}, and the antibody concentration at which the velocity has one-half the maximum value, K_s. Putting k for V and the antibody concentration for S, and taking the intercept as 103 and the slope as 0.36, we obtain 0.0097 min^{-1} for the V_{max}, and 0.0035 mg/ml for K_s.

One of the features of passive sensitization is the so-called induction or "lag" period which elapses between the passive transfer of antibodies and the time at which a certain degree of reaction first becomes evident. Our experiments show this in the sigmoidal form of the function describing the time course of sensitization. The reduction of the "lag" period with increasing antibody concentration is quantitatively illustrated (Fig. 2) by the linear plot of t^* against antibody concentration on semilogarithmic coordinates. Assuming that the linear function continues to hold at antibody concentrations higher than those used in our study, we can see that the value of t^* approaches that of t_0 at about 0.15 mg of antibody per milliliter.

The sensitizing power of a particular antibody preparation often has been given in terms of the minimum sensitizing dose. For example, Kabat and Landow (*9*) found that 30 μg of antibody nitrogen was sufficient to sensitize a guinea pig in 48 hours; Brocklehurst *et al.* (*10*) reported positive Schultz-Dale reactions in tissues containing 0.02 μg of antibody per gram; and, more recently, Humphrey *et al.* (*11*) showed that histamine release by isolated mast cells was still possible under conditions in which the maximum antibody load was less than 10^6 molecules of γ-globulin per cell. Owing to the kinetic basis of the sensitization reaction suggested by our present work, the minimum sensitizing dose can have only a practical meaning; presumably, a vanishingly small dose ought to be sufficient if the time allotted for incubation were long enough and if the rate of antibody disappearance were negligibly small.

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Reversal in Tactile and Visual Learning

Moffett and Ettlinger (*1*) conclude from study of four monkeys that "tactile and visual learning take place in independent functional systems." Their conclusion, however, should be held in doubt since their procedure permitted the possible presence of a confounding phenomenon. It has been shown that, after such extensive discrimination training as that used by them, discrimination-reversal learning is retarded in nonvisual discrimination-learning tasks (*2*).

In order that Moffett and Ettlinger may legitimately derive their conclusion, they must be able to draw a meaningful performance baseline for each task in reversal. That is, reversal of a tactile discrimination must be meaningfully compared with reversal of the same discrimination in light. If the former reversal task is handicapped by the effect mentioned above, comparison of reversal in light and darkness has little utility.

The validity of Moffett and Ettlinger's conclusion, therefore, awaits experimental proof that their procedure did not fall prey to the overtraining effect that has been described in the literature dealing with discrimination reversal.

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