

LETTERS TO THE EDITOR

Histamine Releasers and Histamine Sensitivity

SIR,—Harvey (1961) reported a decreased sensitivity to histamine 6 hr. after 48/80 administration. This present report is to confirm and extend her results using different animals and methods.

Normal female guinea-pigs and those desensitized to histamine by daily injection of progressively higher doses of histamine until the original LD 95 (4.0 mg./kg. subcutaneously) was tolerated were subjected to histamine aerosol before and after the administration of n-octylamine (0.3 mg./kg. subcutaneously) and 48/80 (4.0 mg./kg. subcutaneously).

The Aerosol Reaction Time (A.R.T.) was determined by averaging the durations of exposure to histamine aerosol before (a) cough, and (b) dyspnoea, according

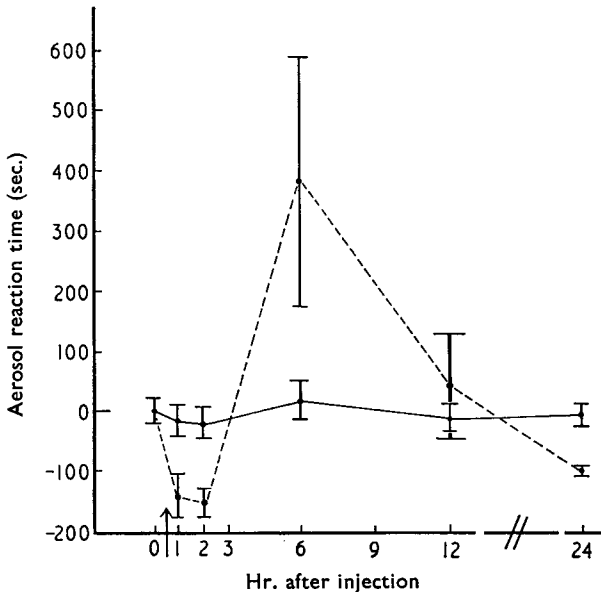


Fig. 1. The effect of n-octylamine on normal guinea-pigs. n-Octylamine given at arrow.—control --- experimental.

to Kallos and Pagel (1937). Each point on the curves represents the mean of at least 5 determinations on 5 animals. The scatter for each point is quite wide, nevertheless all curves drawn from determinations on single animals have the same general shape, indicating significant differences from point to point. The actual A.R.T.s were adjusted arithmetically so that the "0" hour pre-injection A.R.T. coincides with zero on the Y-axis.

It can be seen that the curves (Figs. 1 and 2) are biphasic. A period of increased sensitivity to histamine aerosol occurs 1 to 3 hr. after n-octylamine injection, while 6 hr. after injection the animals are less sensitive, than in the pre-injection period. Similar, though not as well defined, biphasic curves are produced by 48/80 injection.

The inverse relationship between tissue content of histamine and that tissue's tolerance to histamine as suggested by Harvey (1961), several authors quoted by her, and Ambrus, Ambrus and Harrison (1951) would seem to be borne out. Initially, when the releasers lower the tissue content of histamine, the sensitivity of the guinea-pig to histamine (aerosol) increases. Perhaps the mechanism is

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similar to that suggested by Straub (1907) whereby the amount of a particular drug crossing the cell membrane is inversely related to the intracellular concentration of that drug. This possibility was suggested by Ambrus and others (1951).

The secondary decrease in sensitivity to histamine at 6 hr. and more after injection to the releaser is more difficult to explain although it agrees with Miss Harvey's (1961) findings and the findings of several authors quoted by her. The secondary decrease in sensitivity might depend on the increased ability of

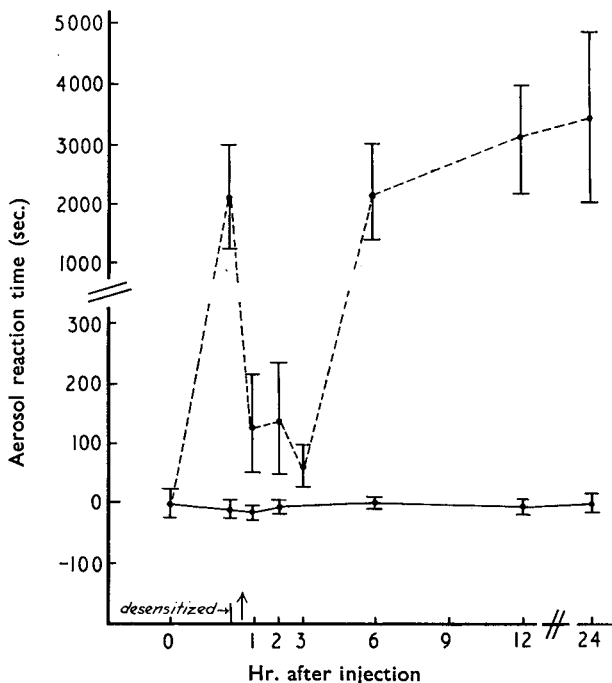


Fig. 2. The effect of n-octylamine on histamine-tolerant guinea-pigs. n-Octylamine given at arrow.—control --- experimental.

histamine-depleted tissues to bind histamine (Schayer, Davis and Smiley, 1955). The period of maximum sensitivity reflects the time of lowest tissue histamine concentration. After this maximally-sensitive period the tissues gradually replenish their histamine store both by synthesis and binding of exogenous histamine. This replenishment is reflected in the return to normal A.R.T. The secondary decrease in sensitivity (higher A.R.T.) indicates that the tissues have bound more histamine than in the normal state. This explanation is purely conjectural and is subject to confirmatory tissue histamine determinations.

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Carcinoid Tumours and Pineapples

SIR,—In a letter to the Editor in this Journal, West (1960) claims that he has found only traces of indole derivatives in pineapples, and that Foy and Parratt (1960) found likewise. In fact, Foy and Parratt claim that they found none. I find quite high levels in Australian pineapples (25 $\mu\text{g./ml.}$ in canned juice) and have the confirming finding of raised indole excretion after the ingestion of pineapple juice (Bruce, 1960). My result is confirmed by Sjoerdsma (personal communication) working with canned pineapple juice available in Maryland, and in which he claims to have detected 35 $\mu\text{g./ml.}$

The possible reasons for this discrepancy seem to be twofold:

- (1) the geographical or ripeness differences in the fruit, and
- (2) differences in extraction procedures or in chromatographic, bioassay or colorimetric methods.

I have written to Dr. West with a view to resolving the differences, and suggesting the exchange of samples and assay methods. I shall communicate my result to this Journal as soon as possible.

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