Interpretation of Virus-induced Changes in the Shape of Hemagglutination-Inhibition Curves with Egg-White Inhibitor

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The authors have recently presented a hypothesis to account for the striking changes that occur in the shape of the hemagglutination-inhibition curve when egg-white inhibitor is treated with certain active influenza viruses (*1–3*). The basic postulate of this hypothesis is that inhibitor is inactivated in a progressive rather than all-or-none manner by virus, with a resultant progressive decrease in its affinity for virus. In certain situations (*2*) the inhibition curve of partially modified inhibitor presented a two-step character, which appeared to necessitate the auxiliary postulate that the virus employed in the titrations was heterogeneous with respect to affinity for modified inhibitor. In this interpretation the plateau which occurred at intermediate levels of inhibition was taken as a measure of the fraction of the total virus which was poorly inhibited. Occasionally, there was observed a dip in the inhibition curve, occurring immediately before the steep terminal rise (*2*). Because of the usually small magnitude of this effect in relation to the experimental error, no explanation of it was attempted.

Studies now in progress have confirmed thus far the basic notion of a progressive action, but have cut away the foundation for the auxiliary postulate. A slight increase in the precision of measurement, gained through several technical refinements, which included the substitution of a photoelectric densitometer (modeled after that of Hirst and Pickels [*4*]) for the visual method of reading previously employed, has enabled us to demonstrate that the dip is a real experimental feature, although it may not always appear. From Fig. 1, which illustrates results of titrations carried out with the densitometer, it is easy to see how a slight loss of precision could lead to the erroneous interpretation of a shallow optimum as a plateau.

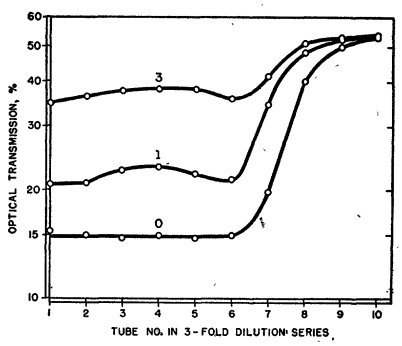

FIG. 1. Hemagglutination-inhibition curves of semipurified egg-white inhibitor after treatment for 0 (control), 1, or 3 hr at 26° C with dialyzed active swine influenza virus in allantoic fluid. The virus-inhibitor mixtures were heated (2 min, 100° C) to destroy the virus and titrated by the method of inhibitor-dilution against 3.5 hemagglutinating doses of heated (30 min, 53° C) virus. A transmission of 15% corresponds to that of a 1% suspension of chicken erythrocytes and denotes complete inhibition of the titrating virus. A transmission of 55% is the maximal value, obtained in the absence of inhibitor. For details of methods, reference is made to previous reports (*1, 2*).

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In experiments stimulated by these findings, the controllable factors have been manipulated in an effort to delineate the origin and evolution of the phenomena under discussion. The available results point to the optimum and the dip as the consequences of the operation of several processes which differ in direction (for or against hemagglutination) and rate; however, no completely satisfactory explanation has as yet emerged.

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Fundamental Role of the Tone and Resistance to Stretch of the Carotid Sinus Arteries in the Reflex Regulation of Blood Pressure[1]

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It has been shown (*1*) that external local application to the arteries of the carotid sinus areas of epinephrine, norepinephrine or pitressin induces a stimulation of the carotid sinus pressoreceptors and thus a marked and prolonged reflex fall of the systemic arterial pressure and a suppression of the normal hypertensive response to decrease of pressure in the carotid sinus. Local application of drugs such as papaverine or Priscoline provokes, on the contrary, a decrease of stimulation of the carotid sinus pressoreceptors and thus a reflex rise of the systemic arterial pressure. From these experiments it has been concluded that drugs contracting the arterial wall where the pressoreceptors are located stimulate these receptors, whereas drugs relaxing the arterial wall of the carotid sinus induce a decrease of stimulation of the pressoreceptors and thus a decrease of the activity of the carotid sinus nerves which by reflex action moderate the systemic arterial pressure. These experiments also show that the tone and resistance to stretch of the arterial wall where the pressorecep-

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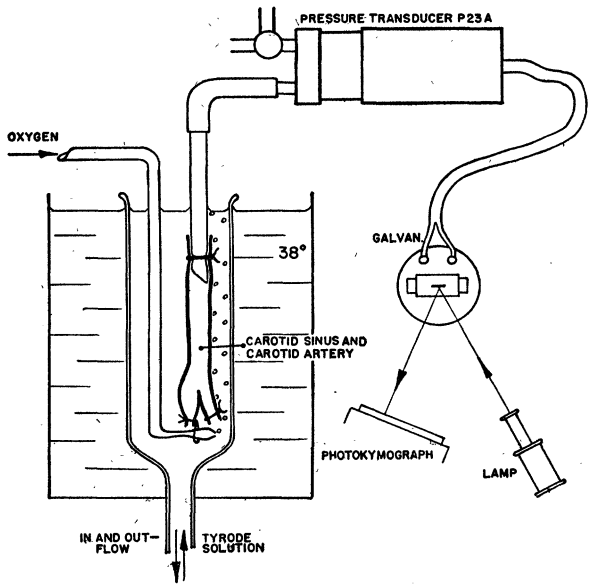

FIG. 1. Arrangement of the measuring technique used in the experiments. The Statham pressure transducer type P 23 A with Control Box CB 7 are used. The galvanometer is the Micromoll Kipp.

tors are located are the fundamental factors for the reflex automatic regulation of the systemic arterial pressure.

Experiments have been performed in order to investigate more directly the action of epinephrine and norepinephrine on the tone of the arterial wall of the carotid sinus area.

The efferent arteries of the carotid sinus are ligated, and the cephalic end of the corresponding common carotid artery is connected with a Statham pressure transducer. The blinded carotid sinus, the segment of common carotid artery, and the pressure transducer are filled with Tyrode solution at an internal pressure of about 10 mm Hg. The internal pressure variations are registered by means of a mirror galvanometer connected with the pressure transducer (Fig. 1).

Solutions of pure l-epinephrine or l-norepinephrine bitartrate were applied *in situ* on the carotid sinus area or added to the Tyrode solution in which the carotid sinus preparation was immersed.

As shown in Fig. 2, l-norepinephrine bitartrate in concentrations of 2.10^{-6}, acting on the arterial wall of the carotid sinus area, induces a rise of intra-

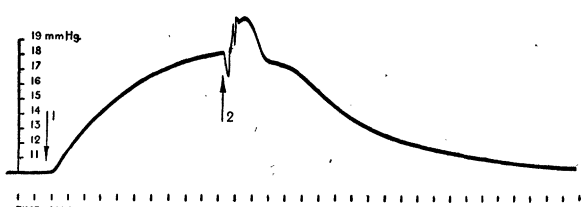

FIG. 2. Registration of the internal pressure recorded during an experiment. The pressure scale represents mm mercury of internal pressure. At 1 addition of l-norepinephrine, in concentration 2.10^{-6} followed by a rise of internal pressure. At 2 washing out with Tyrode solution, and return to previous levels of the internal pressure.

carotid sinus pressure up to 8–10 mm Hg. After removal of the norepinephrine, the internal pressure returns progressively to previous levels. The same observations have been made with l-epinephrine.

These experiments show that l-norepinephrine and l-epinephrine applied to the carotid sinus induce a contraction of the arterial wall of this area. This contraction of the arterial wall provokes the stimulation of the carotid sinus pressoreceptors and thus the reflex fall of the systemic arterial pressure observed in previous experiments (*1*).

These findings emphasize the fundamental importance of the tone and resistance to stretch (distensibility) of the arterial wall of the carotid sinus in the reflex automatic regulation of blood pressure.

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The Red Cloud Sand and Gravel, a New Pleistocene Formation in Nebraska

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Recent studies of the stratigraphy and paleontology of the Pleistocene of Nebraska have resulted in additional data that require further clarification and partial revision of the Grand Island sand and gravel formation (*1, 2*) in order that there may be no confusion as the result of varying usage of the term.

Lugn's type locality of the Grand Island formation is situated southeast of Grand Island, Nebraska, in the lower slopes of the bluffs of the Platte River Valley, where it is overlain conformably by the silts of the Sappa formation (*3*)—equal to Upland as formerly used by Lugn (*1*)—with a comparatively transitional contact. Only the upper part of the sand and gravel sequence is exposed above valley level, however. Lugn included in the Grand Island all the sand and gravel between the Sappa above and the Fullerton silts below, in part exposed at the type locality and in part encountered in test holes in the Platte River Valley to the northwest. The Grand Island was classified as essentially a time equivalent to the Kansan till of the glaciated area. Lugn (*1*) also correlated as uppermost Grand Island the sands and gravels in northeastern Seward County which rest above a comparatively thin Kansan till and are overlain by the Sappa formation.

Condra, Reed, and Gordon (*4*), as a result of extensive subsurface studies, continued the usage of Grand Island according to Lugn's conception and applied the name early Kansan sand and gravel to post-Aftonian sands and gravels deposited ahead of the