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Relationship of Carotid and Aortic Mechanisms to Digitalis Emesis.*

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The site of the emetic action of digitalis and related compounds has been a subject of considerable research and controversy over a period of more than 30 years. The initial conclusions of Hatcher and Eggleston,[1,2,3] that the effect was of central rather than peripheral origin, were not borne out by later studies.[4,5] Hatcher and Weiss[4,6,7] and Hatcher and French[8] suggested that the emetic response to digitalis was of a reflex nature initiated by afferent impulses arising in the heart. This was later questioned by Dresbach and Waddell,[9,10,11] and by Haney and Lindgren.[12] The latter authors conclude that the mechanism must lie either in a direct action on the medullary center, as originally suggested, or "on other structures from which impulses pass to the center via nerves other than those eliminated in the experiments described." The liver, as a possible source of such impulses, has been eliminated by Dresbach.[13] Hanzlik and Wood concluded that, in spite of the fact that digitalis emesis occurred in their dehepatized pigeons, the liver is still the primary source of the reflex.[14] The gastro-intestinal tract was eliminated by Hatcher and Eggleston.[1]

It is well known the muscles of respiration are definitely concerned with vomiting[15] and that excitation of the mechanisms located in the carotid and aortic bodies and indirectly through the carotid sinus and arch of the aorta may, under proper circumstances, result in respiratory stimulation. It has also been noted[9] that in cases where emesis does not result from digitalis administration *rapid respiration* frequently occurs. The present study was undertaken in order to determine whether or not the surgical elimination of the carotid and aortic mechanisms or their nervous pathways might result in abolishing the emetic response. An abstract of the work herein reported appeared recently.[16]

Method. A single intravenous dose of digitoxin, which would produce emesis within 30 minutes, was established. Three dogs were given 0.09 mg/kg digitoxin. At the end of one hour, none of the animals having vomited, each dog was given one-half of its original dosage. Emesis occurred in all animals within 30 minutes. Three dogs were, therefore, given the approximate sum of these doses (0.15 mg/kg). Emesis occurred in all animals within 30 minutes. Hence, in all subsequent experiments this was the vomiting dose employed.

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TABLE I.
Effect of Removal of Carotid Bodies and Sinuses and Denervation of the Aortic Regulators on the Emetic Response to 0.15 mg/kg Digitoxin on Dogs.

Dog No.	Date	Treatment	Emesis after digitoxin in
1 ♂	4-12		22 minutes
	20	Carotids removed	
	26		24 "
2 ♀	5-24		18 "
	29	Carotids removed	
	6-3		6 "
	9	Right vagus cut	
	12		17 "
3 ♀	5-29		20 "
	6-5	Carotids removed	
	12		16 "
	19	Right vagus cut	
	23		15 "
4 ♀	12-18		16 "
	21	Carotids removed, left vagus cut	
	27		25 "
	1-10	Right vagus cut	
	11		25 "
5 ♂	12-27		12 "
	28	Carotids removed, left vagus cut	
	1-3		12 "
6 ♀	12-29		6 "
	30	Carotids removed, left vagus cut	
	1-13		22 "
7 ♂	12-30		15 "
	31	Carotids removed, left vagus cut	
	1-6		27 "
	11	Right vagus cut	
	13		16 "

Seven dogs (4 females, 3 males) were each checked for the normal emetic response to 0.15 mg/kg digitoxin. After allowing a minimum of 24 hours for recovery, the animals underwent the following operations in 2 or more steps as indicated by Table I: (a) removal of the carotid bodies and sinuses by extirpation of segments of the carotid arteries from points just caudal to the origin of the superior thyroid artery to points slightly cephalic to the origin of the lingual artery, (b) sectioning of one or both vagal trunks (in the neck region) thus interrupting the nervous pathways from the aorta.[17] All operations were performed under ether anesthesia.

Each animal was given a minimum of 24 hours to recover from operation and at least 7 days to recover from the previous dose of digitoxin. The dog was then given 0.15 mg/kg digitoxin and watched for 30 minutes for emesis. This was repeated after each phase of the operation.

The results are shown in Table I. In every case vomiting was as prompt and typical after operation as before. Six of these dogs survived sectioning of one vagus and 2 survived sectioning of both vagi without change in their vomiting response to digitoxin. This is contrary to the experience of Hanzlik and Wood[14] who found that double vagotomy abolished digitalis emesis in pigeons. It is in agreement, however, with the results of Haney and Lindgren[13] on dogs.

Conclusion. Vomiting initiated by digitoxin is not abolished by removal of the carotid bodies and sinuses and by denervation of the

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aortic mechanisms. Assuming the mechanism to be reflex in nature, the site of origin of the impulses causing digitalis vomiting is still undetermined. The possibility remains that afferent impulses may be set up in a structure or structures not yet eliminated. It is perhaps more probable that impulses may arise from any one of several structures all of which would have to be denervated in the same animal to abolish the emetic response to digitalis.

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The Electron Micrography of Plant Virus-Antibody Mixtures.

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Electron microscopy is a promising new way of studying the interaction between an antigen and its specific antibody. Such a study is of practical importance because the minute amounts of required material make possible the development of unusually sensitive tests for antigen and antibody. From a more fundamental standpoint the ability of the microscope to record particles comparable in size to antibody molecules may provide a way of checking directly the several hypotheses that have been developed to explain the nature and specificity of the immune reaction.

Very few papers dealing with the electron microscopy of antigen-antibody mixtures have thus far been published. In two[1,2] the antigens are bacteria; another[3] describes the apparent swelling of tobacco mosaic virus particles when mixed with antibody. The published pictures of sensitized typhoid and paratyphoid bacilli give clear evidence of the adsorption of antibody onto both the cell walls and the flagella. In the tobacco mosaic-serum photographs isolated fibers show the same kind of thickening as these bacterial flagella. It was suggested[3] this broadening of the tobacco mosaic particles, from a normal 150A to *ca.* 600A, was due to each being coated with a single layer of antibody molecules arranged with their long axes at right angles to the axis of the virus particle.

The visibility of viruses[4] and other objects of macromolecular dimensions[5] is improved by the oblique evaporation upon the preparation of a very thin metallic film.[6] We are using this "shadow" technic to see what new information it will give concerning the reaction between certain plant viruses and sera prepared against them. Preliminary photographs are reproduced in this note.

Antigens used were tomato bushy stunt and southern bean mosaic viruses purified by means of a preliminary clarification with $(NH_4)_2SO_4$ followed by fractionation in a high speed centrifuge. Antisera for the bushy stunt virus and for the bean virus[7] were prepared by intraperitoneal injection of rabbits with puri-

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