CF activity in normal blood by the methods now available.

Summary. Endogenous heparinemia produced during anaphylactoid shock in dogs is regularly accompanied by the appearance in the plasma of lipemia clearing factor identical to that produced by heparin injection. The significance of this finding is discussed in relation to the postulated role of heparin in lipid metabolism.

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Locus of Emetic Action Following Irradiation.* (20922)

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The central emetic mechanism has recently been resolved into 2 anatomically close but functionally distinct areas—a chemoceptive trigger zone and the vomiting center(1-3). The former structure is bilaterally situated at the surface of the medulla oblongata in the lateral region of the area postrema, and the vomiting center is located in the region of fasciculus solitarius and underlying reticular formation. Destruction of the trigger zone prevents vomiting from "central" acting drugs (apomorphine, morphine, Hydergine,‡ etc.) but does not affect vomiting after orally administered copper sulfate(4,5).

The observation that motion sickness in dogs(6) can also be prevented by destruction of the trigger zone raises the interesting possibility that certain apparently nonchemical emetic stimuli may actually have a chemical basis. It was of considerable interest, therefore, to determine whether the vomiting after irradiation might be similarly prevented by ablation of the trigger zone. Indirect evidence that this chemosensitive area is involved are the recent clinical reports on the relief of nausea and vomiting from irradiation with chlorpromazine(7), an apomorphine antagonist. The present experiments were designed to test the effect of surgical ablation of the trigger zone in preventing emesis in dogs after irradiation.

Methods. As controls, 33 normal mongrel dogs weighing 7 to 13 kg were fed commercial dog food and 30 minutes later irradiated with 300-800 r. A Picker deep therapy x-ray unit was employed with 260 KVP and 18 MA. The external filtration was 1 mm Al and 0.50

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‡ An equiproportional mixture of the methanesulfonates of dihydroergocornine, dihydroergocristine and dihydroergokryptine.

TABLE I. X-Radiation Doses Required to Produce Vomiting in Dogs.

Dose, r	Dogs vomiting/dogs tested	Latent vomiting period after radiation (min.)	Range latent vomiting period (min.)
300	1/ 6	120	120
400	1/ 5	210	210
600	6/10	48.8	25– 79
800	12/12	32.4	9–107

mm Cu plus 0.25 mm Cu inherent filtration. The target-to-object distance was 118 cm and the dose rate 13 r/min. in air. The dog received half the radiation dose on one side of the body, at which time he was turned and given the remainder of the dose. After irradiation the dogs were observed from 4 to 6 hours unless vomiting occurred earlier. In the experimental series 9 similarly selected dogs underwent surgical ablation of the emetic trigger zone, as previously described(3). The emetic responsiveness of these animals was tested with apomorphine and copper sulfate during observation periods of 6 to 8 months. They were fed, exposed to 800 r as already outlined, and observed for 4 to 6 hours. The animals were sacrificed 24 to 72 hours later, the brains perfused *in situ* with formalin, and the lesions examined histologically.

Results. Since no report could be found of the irradiation dose required for emesis in dogs, it was first necessary to establish this level. From Table I it is apparent that 800 r was adequate to cause vomiting in each of 12 control dogs. Using the method of Litchfield and Wilcoxen(8) the dose required to produce vomiting in 50% of the animals was calculated to be 540 r. The latent period between the completion of irradiation and the onset of vomiting decreased somewhat with increasing dose. However, since the irradiation time was greater for 800 r than for 600 r, the total time from start of irradiation to vomiting was almost identical at both dosage levels.

Nine dogs with surgically ablated trigger zones were exposed to 800 r, with no vomiting in any case. The destruction of the trigger zone was evident in every instance by the animal's resistance to large doses of intravenous apomorphine (1.0 mg/kg of body weight). The lesion was further confirmed by histological examination. That the vomiting center was not damaged by the surgical procedure in at least 7 of the 9 dogs is evident from their normal threshold to orally-administered copper sulfate (40 to 80 mg). In one dog 160 mg of copper sulfate was necessary to cause vomiting, and in the remaining animal vomiting could not be induced even with this dose. No gross or histological evidence of damage to the vomiting center was apparent.

Discussion. This report indicates that the chemoceptive trigger zone is essential for the emetic effect of irradiation. The data suggest that the vomiting after irradiation and after apomorphine may have the same general etiology and may, in fact, depend upon identical or closely related chemical mediators, *e.g.*, acetylcholine. In support of such a concept is the effectiveness of chlorpromazine in preventing the vomiting in dogs(9) and humans(7) after irradiation, and after apomorphine injection in dogs(10,11). The possibility that ionizing radiation may have a direct rather than a mediated influence on the emetic trigger zone is deemed unlikely since shielding this area did not prevent vomiting when the rest of the body was irradiated(7).

Summary. The incidence of vomiting among 33 dogs receiving from 300 to 800 r is reported. All 12 dogs exposed to 800 r vomited within 2 hours after completion of the irradiation. The 50% vomiting dose was 540 r. No dog subjected to bilateral destruction of the emetic chemoreceptor zone vomited after 800 r exposure. The significance of these findings is discussed.

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Effect of Hypothalamic Lesions on Canine Neurogenic Arterial Hypertension.* (20923)

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That the hypothalamus plays a role in the regulation of the arterial tension has long been recognized, but it has also been known that it is not essential for the production of temporary hypertension by reflex or direct stimulation of the medulla oblongata. Its importance in the maintenance of chronic states of arterial hypertension has never been determined. The present study is concerned with the effect of lesions of the hypothalamus and its descending pathways upon chronic neurogenic hypertension in dogs. This type of hypertension is characterized by a marked increase in the cardiac output occasioned by the tachycardia which results when medullary cardiovascular centers are released from the inhibitory influence of stretch receptors in the carotid sinus and certain other arterial walls. According to some investigators, a polycythemia(3) and a peripheral vasoconstriction(1) are present as well. Nevertheless the present study concerns primarily the influence of the hypothalamus upon the raised central excitatory state of medullary cardiovascular centers which results subsequent to their release from peripheral inhibitory influences.

Methods. Twenty-four stock dogs were used in these experiments. They were rendered hypertensive by bilateral resection of the carotid sinuses, section of the vagosympathetic trunk on one side and a section of the aortic depressor nerve on the other. All

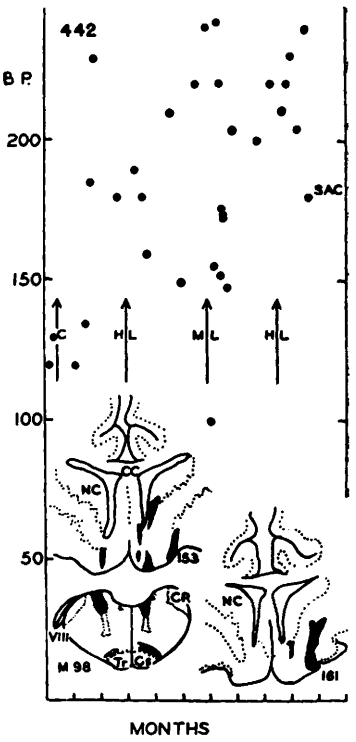

FIG. 1. (Dog 442). Indicates systolic blood pressures (ordinates) at intervals after excision of carotid sinus and partial vagectomy (C), and effect of bilateral hypothalamic lesions in septal region (Section 153), later medullary reticular lesions (Section 98) and finally larger lesions on the right side of anterior hypothalamus (Section 161). Although the pressures vary considerably, there was no consistent change following any of these procedures. Abbreviations used in the illustrations are as follows: C—moderator nerve section. CC—corpus callosum. CP—peduncularis cerebri. CR—corpus restiforme. HL—hypothalamic lesions. LG—corpus geniculatum laterale. M—corpus mammillare. MD—nucleus medialis dorsalis.

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