# Heparin Suppression of Gastric Acid Secretion.* (28153)

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During gastric secretory studies in dogs designed to test the effect of cross-transfusion of a proposed antral chalone, we noted inhibition of gastric secretion following intravenous administration of heparin(1).

The following experiments were designed to study the effect of this inhibition on gastric secretion stimulated by food (antral phase) and by histamine.

*Materials and methods.* Thirteen adult female mongrel dogs weighing approximately 20 kg were used in this study. Denervated pouches of the gastric fundus (Heidenhain) were prepared in the usual fashion, and a stainless steel cannula was used to drain the pouch to the outside. During the 30 or more days which elapsed between the operation and onset of testing, the dogs were trained in the Pavlov stand. The animals were fasted for 18 or more hours prior to testing. In all studies, gastric pouch secretion was measured every 30 minutes and the acidity determined by using Töpfer's reagent, titrating with N/10 NaOH. Specimens of less than 1 cc were discarded. All animals were in a basal secretory state prior to testing.

1. *Antral phase, food stimulus.* Twenty-one paired control and test studies were performed on 5 dogs. The antral phase of gastric secretion was stimulated by feeding a standard test meal of 400 g of Pard. In control studies, 1 cc of physiologic saline solution was given intravenously at time of feeding. In test studies, 100 mg (1 cc) of aqueous heparin‡ was given intravenously at time of feeding. Control and test studies were otherwise identical and were performed on alternate days. The sequence of control-test experiments was varied. Pouch secretions were collected for 4 hours following feeding of standard meal.

2. *Histamine stimulus.* Fifty-one paired control-test studies were performed on 8 dogs. One mg histamine base was injected subcutaneously and gastric secretions were collected from the Heidenhain pouch for 3 hours. In control studies, 1 cc of sterile saline solution was given intravenously at time of histamine administration, and in test studies, 100 mg (1 cc) of aqueous heparin was given intravenously at time of histamine administration.

*Results.* 1. *Antral phase, food stimulus.* Intravenous administration of 100 mg of heparin resulted in uniform inhibition of Heidenhain pouch gastric secretion following the stimulus of a test meal. The average percentage inhibition of free hydrochloric acid output was 79%. This difference has a $P$ value of $<0.01$ (Table I). There was 56% reduction in volume of gastric juice and 55% diminution in acid concentration.

2. *Histamine stimulus.* Intravenous administration of 100 mg of aqueous heparin resulted in uniform inhibition of histamine-stimulated Heidenhain pouch gastric secretion. The average percentage inhibition of free hydrochloric acid output was 33%. This difference has a $P$ value of $<0.01$ (Table II). There was 26% reduction in volume of gastric juice and 18% diminution in acid concentration.

Benzyl alcohol was used as a preservative in the heparin solution. A solution of the same concentration of benzyl alcohol (9 mg/ml) in water was found to have no effect on gastric secretion stimulated by food or by histamine.

*Discussion.* Dragstedt, Wells, and Rocha e Silva(2) noted that heparin inhibited the release of histamine in antigen-antibody reactions. Parrot and Laborde(3) demonstrated

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‡ Generously supplied by Upjohn Co.

that heparin diminished the biologic activity of histamine on isolated guinea pig ileum while Gerendás *et al.*(4) showed that the *in vitro* anticoagulant action of heparin was suppressed by histamine. Other studies have confirmed the capacity of heparin to combine with histamine *in vitro*(5,6,7,8). The binding of histamine and other biologically active

TABLE I. Effect of Heparin on Antral Phase of Gastric Secretion (Food Stimulus).

| Dog No. | No. of studies | Periods (30-min) 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 4-hr total | % inhibition |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | | | | | | | | | | | |
| T- 3 | 5 | .04 | .03 | .10 | .27 | .43 | .58 | .52 | .39 | 2.36 | |
| T- 6 | 5 | .00 | .00 | .01 | .10 | .11 | .10 | .13 | .05 | .50 | |
| T- 47 | 2 | .00 | .02 | .16 | .43 | .60 | .36 | .45 | .09 | 2.11 | |
| T-103 | 5 | .00 | .01 | .03 | .07 | .20 | .32 | .32 | .36 | 1.31 | |
| T-117 | 4 | .00 | .01 | .16 | .32 | .39 | .36 | .43 | .35 | 2.02 | |
| Total | 21 | .04 | .07 | .46 | 1.19 | 1.73 | 1.72 | 1.85 | 1.24 | 8.30 | |
| Avg | | .01 | .01 | .09 | .24 | .35 | .34 | .37 | .25 | 1.66 | |
| Test | | | | | | | | | | | |
| T- 3 | 5 | .06 | .00 | .01 | .03 | .07 | .18 | .24 | .28 | .87 | 63.1 |
| T- 6 | 5 | .00 | .00 | .00 | .00 | .00 | .00 | .00 | .00 | .00 | 100 |
| T- 47 | 2 | .00 | .00 | .00 | .00 | .12 | .07 | .03 | .31 | .53 | 74.8 |
| T-103 | 5 | .00 | .00 | .00 | .00 | .00 | .07 | .17 | .12 | .36 | 72.5 |
| T-117 | 4 | .00 | .00 | .00 | .00 | .03 | .05 | .11 | .13 | .32 | 84.1 |
| Total | 21 | .06 | .00 | .01 | .03 | .22 | .37 | .55 | .84 | 2.08 | |
| Avg | | .01 | .00 | .00 | .01 | .04 | .07 | .11 | .17 | .42 | 78.9 |
| | | | | | $P = < .01$ | | | | | | |

Effect of heparin on antral phase of gastric secretion (food stimulus). Heidenhain pouch acid output in milliequivalents. *P* value given for average 3-hr difference. Figures represent average output of multiple studies performed on each animal.

TABLE II. Effect of Heparin on Histamine-Stimulated Gastric Secretion.

| Dog No. | No. of studies | Periods (30-min) 1 | 2 | 3 | 4 | 5 | 6 | 3-hr total | % inhibition |
|---|---|---|---|---|---|---|---|---|---|
| Control | | | | | | | | | |
| T- 93 | 7 | .65 | 1.12 | .53 | .13 | .00 | .00 | 2.43 | |
| T-113 | 4 | 1.05 | 1.87 | .59 | .16 | .00 | .00 | 3.67 | |
| T-117 | 5 | .56 | 1.05 | .30 | .30 | .00 | .00 | 1.94 | |
| T-123 | 8 | .14 | .34 | .09 | .00 | .00 | .00 | .57 | |
| T-140 | 7 | .80 | 1.20 | .17 | .00 | .00 | .00 | 2.17 | |
| T-150 | 5 | .39 | .65 | .25 | .02 | .00 | .00 | 1.31 | |
| T-156 | 9 | 1.57 | 2.36 | 1.07 | .17 | .08 | .04 | 5.29 | |
| T-167 | 6 | .76 | .79 | .04 | .00 | .00 | .00 | 1.59 | |
| Total | 51 | 5.92 | 9.38 | 3.04 | .51 | .08 | .04 | 18.97 | |
| Avg | 6 | .74 | 1.17 | .38 | .06 | .01 | .01 | 2.37 | |
| Test | | | | | | | | | |
| T- 93 | 7 | .59 | .67 | .22 | .02 | .00 | .00 | 1.50 | 38 |
| T-113 | 4 | .86 | 1.13 | .04 | .00 | .00 | .00 | 2.30 | 37 |
| T-117 | 5 | .26 | .92 | .05 | .00 | .00 | .00 | 1.23 | 37 |
| T-123 | 8 | .17 | .09 | .04 | .00 | .00 | .00 | .30 | 47 |
| T-140 | 7 | .67 | .87 | .13 | .00 | .00 | .00 | 1.67 | 25 |
| T-150 | 5 | .15 | .26 | .20 | .21 | .00 | .00 | .82 | 37 |
| T-156 | 9 | 1.32 | 1.95 | .44 | .22 | .05 | .00 | 3.98 | 25 |
| T-167 | 6 | .84 | .42 | .00 | .00 | .00 | .00 | 1.26 | 21 |
| Total | 51 | 4.86 | 6.51 | 1.12 | .45 | .05 | .00 | 13.06 | |
| Avg | 6 | .61 | .81 | .14 | .06 | .01 | .00 | 1.63 | 33 |
| | | | | | $P = < .01$ | | | | |

Effect of heparin on histamine-stimulated gastric secretion. Heidenhain pouch acid output in milliequivalents. *P* value given for average 3-hr difference. Figures represent average output of multiple studies performed on each animal.

amines by heparin and other substances has been reviewed(9). Dolowitz and Dougherty (10) reported the clinical use of heparin in treatment of patients with allergic inflammation and suggested that the prompt relief of symptoms in such cases was due to the *in vivo* binding and inactivation of histamine by heparin.

Studies reported above indicate that heparin is capable of suppressing gastric secretion stimulated by food or by exogenously administered histamine. The mechanism for this action may be the *in vivo* binding of histamine by heparin. If this is the case, the suppression of food-stimulated gastric secretion would support the concept(11) of histamine as the final common pathway in the stimulation of gastric secretion.

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## Effect of X-Rays on Cultured Monkey Kidney Cells Infected with a Myxovirus.* (28154)

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The effect of x-rays on the susceptibility of cells to several animal viruses has been studied by various investigators using different systems. The results have varied greatly but several reports indicate that irradiation can increase the cellular susceptibility to certain virus infections(1-6).

The present study is concerned with the effects of x-irradiation on rhesus monkey kidney cells infected with a recently isolated myxovirus, the DA virus(7). This agent regularly multiplies in monkey kidney cultures but produces no distinct cytopathic effect. Its presence can be demonstrated, however, by the agar overlay plaque technic(8) or by the hemadsorption method described by Vogel and Shelokov(9).

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*Materials and methods. Virus.* "DA", a myxovirus originally isolated from human blood(7), was used after 95 serial transfers in rhesus kidney cultures. This agent is serologically indistinguishable from the simian myxovirus $SV_5$ which is considered to be a parainfluenza virus(10).†

*Cell cultures.* Suspensions of trypsinized rhesus (Rh) monkey kidney cells were prepared according to standard methods. Hanks' balanced salt solution, containing 0.5% lactalbumin hydrolysate and 2% calf serum, was used for growth medium. *For infected cells,* 1 ml of infected tissue culture fluid containing approximately $2 \times 10^7$ PFU of DA virus was added to 9 ml of freshly trypsinized cell

† The designation of parainfluenza virus type 5 has been proposed for the DA-$SV_5$ group of viruses at the VIII International Congress for Microbiology, Montreal, 1962.