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### Elevation of Peripheral Vascular Resistance in Renoprival Hypertension.\* (30450)

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Bilateral nephrectomy of the dog followed by dietary protein and parenteral sodium is associated with acute hypertensive cardiovascular disease (renoprival hypertension)(1,2). In mongrel dogs so treated, the renoprival hypertension is significant for 8 of 10 animals within 4 days, provided there is no major weight loss through vomiting and/or diarrhea. This communication records a concomitant significant elevation of the total peripheral vascular resistance (TPR) in this form of renoprival hypertension.

**Material and methods.** Mongrel dogs of either sex, weighing between 7 and 10.6 kg, were used. The arterial pressure was obtained by direct femoral artery puncture after the animal became accustomed to the procedure. It was recorded by means of a transducer and Sanborn Twin-Viso recorder. The control pressure was determined by averaging the readings for 4 to 7 days before the nephrectomies. After the nephrectomies, the pressure was taken daily for 4 days when the experiment was terminated. Bilateral nephrectomy was performed at one sitting under ether anesthesia, as previously described(1). Each day thereafter, the animal was fed a diet containing about 3 g of casein per kg

and infused with 16 ml per kg of physiologic saline as previously described(1). Total water intake by mouth amounted to 4.5 ml per kg. Under these conditions and without dialysis, nephrectomized dogs maintain a satisfactory clinical state for the 4 days of study.

Cardiac output was measured by the dye-dilution technic using cardio-green according to the procedure of Gilford(3). A Gilford cuvette-densitometer and attached Texas Instruments recorder with second timer were used. A polyethylene tube was threaded through the femoral artery to the lower abdominal aorta and a similar tube was threaded through a brachial vein to the superior vena cava to establish the circuit through the cuvette. The dye curve was analyzed according to Lilienfeld and Kovach(4).

The TPR was derived according to Bohr's recommendations(5) in which  $TPR = MAP \div CO/kg$ , when  $TPR = \text{total peripheral resistance in peripheral resistance units per kg}$ , MAP is mean arterial pressure in mmHg and CO/kg is cardiac output in ml per kg body weight. In determining TPR, the pressure and cardiac output were determined at the same sitting.

In 6 experiments, TPR was determined before the nephrectomies and on the fourth day

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TABLE I. Data Indicating an Increment in Total Peripheral Vascular Resistance on 4th Day of Canine Renoprival Hypertension. Note only minimal change in body weight during 4 days.

| Dog # | Body wt, kg |         | Mean BP, mmHg |         | Cardiac output, ml/kg/min |         | TPR, PRU/kg |         | $\Delta$ TPR % |
|-------|-------------|---------|---------------|---------|---------------------------|---------|-------------|---------|----------------|
|       | C           | 4th Day | C             | 4th Day | C                         | 4th Day | C           | 4th Day |                |
| 2294  | 10.6        | 11.0    | 113           | 130     | 194                       | 184     | .58         | .71     | + 22           |
| 2308  | 8.2         | 8.2     | 98            | 125     | 232                       | 256     | .42         | .48     | + 26           |
| 2326  | 8.2         | 8.2     | 113           | 140     | 268                       | 256     | .42         | .55     | + 31           |
| 2339  | 7.7         | 8.0     | 95            | 135     | 220                       | 223     | .43         | .61     | + 42           |
| 2349  | 8.2         | 8.0     | 79            | 105     | 293                       | 325     | .27         | .32     | + 18           |
| 2352  | 7.0         | 7.0     | 89            | 120     | 339                       | 274     | .26         | .44     | + 69           |
| 2418  | 9.7         | 9.1     | 105           | 135     | 227                       | 212     | .46         | .64     | + 40           |
| 2423  | 8.2         | 8.2     | 78            | 125     | 260                       | 209     | .28         | .60     | +114           |
| 2432  | 8.4         | 8.0     | 100           | 135     | 245                       | 258     | .39         | .52     | + 34           |
| 2436  | 10.5        | 10.5    | 96            | 130     | 152                       | 172     | .62         | .76     | + 23           |
| Avg   | 8.7         | 8.6     | 97            | 128     | 243                       | 237     | .41         | .56     | + 42           |

C = Control value before nephrectomies. 4th Day = Fourth day following nephrectomies.  
 TPR = Total peripheral vascular resistance. PRU = Peripheral resistance unit.  $\Delta$  TPR % =  
 % Change in TPR from control to 4th day.

after the nephrectomies. For the additional 4 experiments, TPR was derived before nephrectomy and each day for the subsequent four days.

**Results.** Table I relates the results from 10 dogs with acute renoprival hypertension. During the 4 days of observation there was no change in body weight in 4 dogs, a slight gain in weight in 2 and a slight loss in weight in 4 dogs. Thus, the weight was virtually unaltered. This is an important feature of such experiments since renoprival dogs which lose more than 0.6 kg during a 4-day interval usually vomit and/or have diarrhea, two complications which may interfere with the expression of the hypertension(6).

All animals developed a significant elevation of the arterial pressure (diastolic, systolic and mean). The Table contains the mean pressure which was elevated an average of 31 mmHg (range 17-47 mmHg). In 5 cases, cardiac output was slightly elevated and in 5 it was lowered as renoprival hypertension became definite. The elevation of pressure was distinctly greater than the change in cardiac output; thus, the peripheral vascular resistance was elevated in each case, the average amounting to 42% of the control (range 22-114%).

Daily measurement of TPR (Fig. 1) indicated a progressive elevation of the resistance over the first 3 days as arterial pressure mounted. On the fourth day, the hypertension and elevated peripheral resistance re-

mained although there was a slight recession over the values for the third day. Thus, the pressure and resistant changes accompanied each other.

**Comment.** Significant elevation of the arterial pressure within 4 days following bilateral nephrectomy of the dog (renoprival hypertension) was reported by Grollman, Muirhead and Vanatta(7) (elevation from

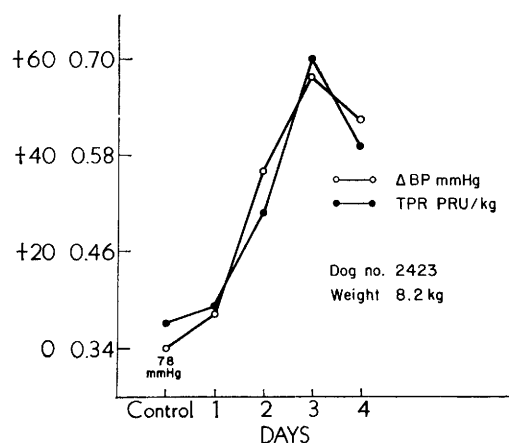


FIG. 1. Daily measurement of total peripheral resistance indicated its elevation as renoprival hypertension progressed over the first 3 days. Pressure and resistance remained elevated on 4th day although slightly lower than on 3rd day.

control averaged +31 mmHg) and by Grollman, Turner, Levitch and Hill(8) (elevation averaged +25 mmHg for 4 dogs, range +20 to +30 mmHg) when the animals were sustained by *in vivo* dialysis. Similar hyperten-

sion in the absence of dialysis was also reported by Muirhead, Grollman and Vanatta (9) (range +10 to +50 mmHg for 8 dogs, average +30 mmHg), Orbison, Christian and Peters(10) (average +37 mmHg for 7 dogs), and Muirhead, Stirman and Jones(1) (average +38 mmHg, for 8 dogs). These various results are comparable to those of the experiments herein reported.

Grollman *et al*(8) demonstrated no change in the cardiac index in canine renoprival hypertension of 8 to 59 days duration as derived in association with intermittent peritoneal lavage. The hypertension was interpreted as due to increased peripheral vascular resistance. The present experiments demonstrate that canine renoprival hypertension developing over 4 days time and in the absence of dialysis is also associated with elevated peripheral vascular resistance. Thus, acute renoprival hypertension of this type (in association with dietary protein and parenteral sodium) appears due to increased tone of resistance blood vessels (small arteries and arterioles), and as such, resembles the renal type of experimental hypertension.

**Summary.** Renoprival hypertension of the dog is definite within 4 days of bilateral nephrectomy when the animal is given dietary protein, parenteral sodium and does not exhibit excessive vomiting and diarrhea (weight

loss minimal). Ten dogs with renoprival hypertension also exhibited an elevation of the peripheral vascular resistance. In acute canine renoprival hypertension, increased tone of resistance vessels appears to contribute in a major way to the hypertensive state. In this respect, the hypertension resembles experimental hypertension of renal type.

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### Modification of Norepinephrine Tachyphylaxis by Guanethidine.\* (30451)

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Tachyphylaxis to norepinephrine and epinephrine, as gauged by a decreasing pressor response, has been demonstrated by several investigators(1,2). Rosenthale and DiPalma (1) for example reported that, in order to maintain the blood pressure in dogs 30 to

40 mmHg above control levels during a three-hour infusion of norepinephrine the rate of the infusion of norepinephrine has to be increased at least 5 times and in many animals more than 20 times the initial dose. Recently it was reported from this laboratory that guanethidine elicits a marked pressor response after tachyphylaxis to norepinephrine has developed and not only restores but seems to enhance the pressor effect of ad-

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