Title: RELATIONSHIP BETWEEN ADRENAL CATECHOLAMINE SECRETION AND MEDULLARY BLOOD FLOW

Authors: M. J. Breslow, M.D., and R. J. Traystman, Ph.D.

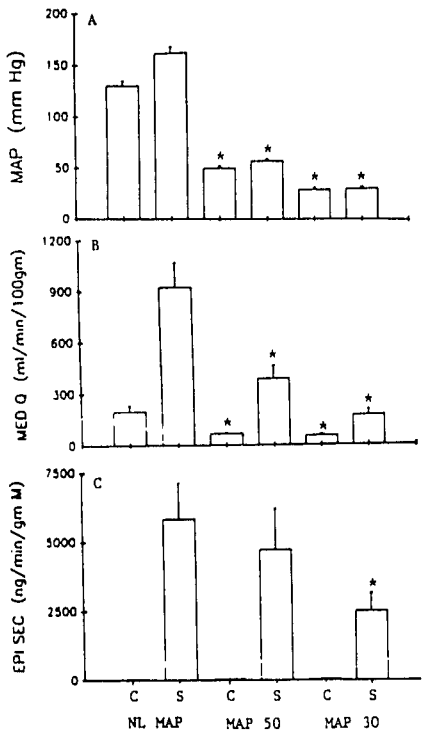
Affiliation: Department of Anesthesiology/Critical Care Medicine, The Johns Hopkins Medical Institutions, Baltimore, Maryland 21205

Introduction. Our laboratory has recently reported that both physiologic (1) and direct electrical (2) stimulation of adrenal catecholamine secretion are associated with 3-4 fold increases in blood flow to the adrenal medulla. We hypothesized that medullary vasodilation during catecholamine secretion may be an important component of the secretory response, necessary for maximal entry of adrenal catecholamines into the systemic circulation. This hypothesis was tested in the present study by comparing the catecholamine secretory response to electrical stimulation of the splanchnic nerve (NS) under control conditions with the response when the increase in medullary blood flow was sharply limited by reduction of arterial blood pressure.

Methods. Pentobarbital anesthetized, ventilated, adult male mongrel dogs (25-35 kg) underwent laparotomy, left adrenal denervation, left lumbo-adrenal vein cannulation and isolation of the left greater splanchnic nerve. After a 90 minute equilibration period, animals were subjected to three identical nerve stimulations (8 volts, 20 hz) lasting 3 minutes each and performed at 30 minute intervals. Control animals (Group 1, n=4) had each stimulation performed at normal arterial blood pressure, while experimental animals (Group 2, n=6) had mean arterial blood pressure (MAP) reduced to 50 and 30 mm Hg by controlled hemorrhage into a pressurized bottle system prior to the second and third stimulations, respectively. Regional adrenal blood flow was measured using radiolabeled microspheres as described previously (1) and adrenal vein catecholamine levels were determined by high pressure liquid chromatography.

Results. Control animals demonstrated similar 3-4 fold increases in adrenal medullary blood flow and 300 fold increases in adrenal catecholamine secretion with each NS. Adrenal cortical blood flow and contralateral medullary blood flow were unaffected by NS. The increases in adrenal medullary blood flow and catecholamine secretion in group 2 animals during NS at normal arterial blood pressure were similar to those observed in group 1 animals (fig. 1). Reduction of MAP to 51 $\pm$ 2 mm Hg prior to and during NS decreased medullary blood flow by 60% at both control and during NS, but had no effect on catecholamine secretion. Reduction of MAP to 29 $\pm$ 2 mm Hg reduced the medullary blood flow response to NS by 80% (compared to normal MAP) and decreased catecholamine secretion by 50%. Oxygen delivery to the adrenal medulla during NS decreased from 186 $\pm$ 31 at normal MAP to 76 $\pm$ 16 and 29 $\pm$ 6 ml O_2/min/100gm at MAP=50 and MAP=30, respectively.

Discussion. The results of the present study indicate that electrically stimulated catecholamine secretion is attenuated by profound hypotension. We attribute this effect of hypotension on catecholamine secretion to the markedly reduced levels of medullary blood flow which are observed when nerve stimulation is performed at reduced arterial blood pressure. Since these experiments were performed following adrenal denervation, it is unlikely that reflexes elicited by hemorrhage are responsible for altered secretion. The mechanism by which reduced blood flow affects secretion is unknown. Possible explanations include 1) reduction of oxygen delivery to levels which cannot support metabolic needs during chromaffin cell degranulation, or 2) increased chromaffin cell reuptake of catecholamines when blood flow is reduced.



Arterial blood pressure (A), adrenal medullary blood flow (B) and adrenal epinephrine secretion (C) prior to and during nerve stimulations performed at normal MAP, MAP-50 and MAP-30. C, control; S, stimulation, * = $P < 0.05$ compared to value at normal MAP.

References.

1. Breslow MJ, Mennen A, Koehler RC, et al: Adrenal medullary and cortical blood flow during hemorrhage. Amer J Physiol 250:H954-H960, 1986.

2. Breslow MJ, Jordan DA, Thellman ST, et al: Neural control of adrenal medullary and cortical blood flow during hemorrhage. Amer J physiol 252:H521-H528, 1987.