Title: ENFLURANE ALTERS COMPENSATORY HUMORAL AND HEMODYNAMIC RESPONSES TO HEMORRHAGE

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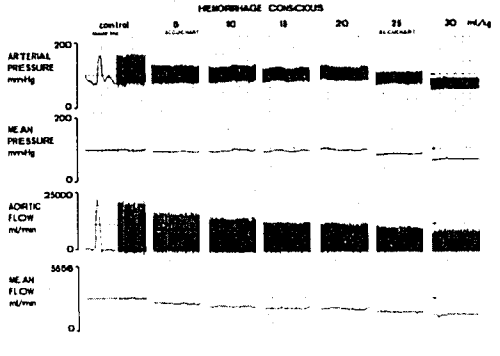
Introduction. Both the sympatho-adrenal system and the renin-angiotensin system are part of the cardiovascular defense against hypotension. The goal of this study was to determine (1) the extent to which enflurane affects the activity of these two systems in response to hemorrhage and (2) the effects of this anesthetic on hemodynamic responses to hemorrhage.

Methods. Aortic pressure catheters and electromagnetic flow transducers for measurements of cardiac output (CO) were inserted in nine healthy, trained mongrel dogs. Experiments were conducted after the animals had fully recovered from operation. Hemorrhage, at a constant rate of 1 ml/s, up to a total blood loss of 30 ml/kg or until mean arterial pressure (MAP) fell below 30 mmHg, was carried out in the conscious dogs on one day, and in the same dogs, anesthetized with enflurane (3%,O_2,N_2;FiO_2=0.25), on a separate day. The shed blood was reinfused after each experiment. Plasma renin activity and plasma catecholamines were determined using sensitive radiometric assays. Responses in the conscious and anesthetized states were compared using Student's t-test for unpaired data.

Results. In the conscious dogs both plasma norepinephrine (PNE) and epinephrine (PE) rose markedly with hemorrhage, while mean arterial pressure was well maintained (Fig.1). The anesthetized dogs responded with significantly smaller rises in catecholamines while the plasma renin-activity (PRA) rose more than it did in the conscious states. In contrast to the results obtained in the conscious animals, mean arterial pressure fell strikingly with hemorrhage in the anesthetized animals while the increases in heart rate (HR) and total peripheral resistance (TPR) were blunted (Fig.2).



Discussion. The present data suggest that the sympatho-adrenal and renin-angiotensin systems act reciprocally in response to hemorrhage in the conscious and anesthetized states. In the conscious dogs the sympatho-adrenal system predominated, whereas in the anesthetized state the renin-angiotensin system prevailed. Thus, enflurane blunted the response of plasma catecholamines to hemorrhage but augmented the response of plasma renin. The latter effect could be explained by the more severe hypotension incurred by the anesthetized dogs with hemorrhage. Nonetheless, despite the striking activation of the renin-angiotensin system, peripheral vasoconstriction was not powerful enough to maintain arterial pressure with hemorrhage in dogs under enflurane anesthesia.

	CONTROL	CHANGE WITH HEMORRHAGE
PRA (ng/ml/h)		
Conscious	0.61 ± 0.08	4.00 ± 0.60
Anesthetized	3.70 ± 0.50**	5.80 ± 0.30*
PNE (pg/ml)		
Conscious	126 ± 33	463 ± 75
Anesthetized	164 ± 41	190 ± 51*
PE (pg/ml)		
Conscious	163 ± 59	609 ± 157
Anesthetized	163 ± 57	106 ± 43*
CO (l/min)		
Conscious	2.72 ± 0.13	-1.91 ± 0.10
Anesthetized	2.15 ± 0.25**	-1.49 ± 0.10*
MAP (mmHg)		
Conscious	99 ± 3	-28 ± 4
Anesthetized	80 ± 3**	-50 ± 3**
TPR (mmHg/l/min)		
Conscious	36.5 ± 3.0	52.3 ± 4.0
Anesthetized	37.2 ± 2.4	8.3 ± 2.0**
HR (beats/min)		
Conscious	93 ± 3	65 ± 2
Anesthetized	131 ± 6**	15 ± 7**

Mean values ± S.E.M.; * p<0.05, ** p<0.01

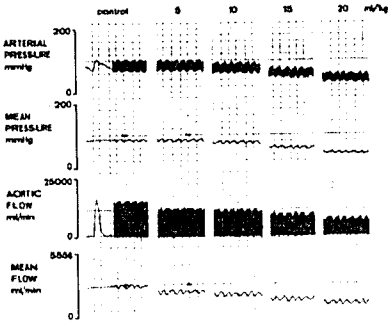


Fig. 2 Example of the response to hemorrhage for the same dog shown in Fig.1. The protocol was discontinued after a total blood loss of 23 ml/kg since MAP fell below 30 mmHg.