Cardiovascular Reflexes

THE IMPORTANCE of cardiovascular reflexes in maintaining systemic arterial pressure has been known for decades. The baroreceptors in the arterial walls, the afferent neural pathways, the integrating areas of the central nervous system, and the effector systems are all components of this negative feedback servo control system which maintains arterial pressure around a set point. These elements have been well characterized, and this work has been the subject of several recent reviews.2,3 Furthermore, mathematical models have been developed to define this system and to demonstrate the manner in which perturbations alter this responsiveness.4 Another important cardiovascular reflex, which has received recent attention, is that responsible for controlling vascular volume.5,6 Atrial and ventricular receptors which respond to stretch and thus cavity volumes have been demonstrated. The effector limb of this system has direct effects on renal function thereby regulating vascular volume. Thus, under physiologic conditions, systemic arterial pressure is maintained around a set point and deviations from this pressure induced by postural changes, level of activity, etc. are rapidly corrected by a well-defined system. Likewise, vascular volume is regulated by stretch receptors in the vasculature and deviations from its set point are regulated through diuresis or fluid retention by the kidney.

James et al.,7 elsewhere in this issue, have carefully characterized a cardiovascular reflex which originates in chemoreceptors located in coronary arteries and produces arterial hypertension. The authors have compared this chemoreceptor-initiated reflex with the well known Bezold Jarish reflex which produces arterial hypotension and bradycardia. The cardiovascular responses to these chemoreceptors, as well as to myocardial mechanoreceptors, are certainly dramatic (increase in arterial pressure of 100 mm Hg in the present study), but the role of these receptors in homeostasis under physiologic conditions is not at all clear. However, as pointed out by James et al.,7 the potent responses initiated by these chemical and mechanical receptors may well be operative in the response to pathophysiologic states.

Indeed, it is becoming increasingly evident that the cardiovascular reflexes are not only important in maintaining homeostasis under physiologic conditions, but are also critical in the organism's responses to disease and to drugs. For example, Quest and Gillis,8,9 in several series of experiments, have demonstrated an important interaction of digitalis and the arterial baroreceptors. Digitalis produces a dose-dependent increase in the carotid sinus nerve activity at a given carotid sinus pressure. Furthermore, digitalis potentiates the fall in systemic arterial pressure as carotid sinus pressure is raised. These investigators have also shown that at a constant carotid sinus pressure digitalis administration produces carotid sinus nerve activity identical to that produced by an increase in carotid sinus pressure. These important experimental findings suggest that the organism's response to digitalis is dependent not only on the direct cardiac and vascular actions of the drug, but also on the effect of the drug on the baroreceptor reflex. The functional significance of this interaction of digitalis and the baroreceptors has been demonstrated by Gillis et al.10 in that when afferent neural pathways of the baroreceptors are sectioned, the toxic arrhythmic effects of digitalis are observed earlier and at smaller doses.

The important clinical syndrome of bradycardia and hypotension which occurs during the early phase of acute myocardial infarction in man is due to an alteration of the homeostatic systems which, under physiologic conditions, maintain arterial pressure. In experimental myocardial infarction, the hemodynamic response to coronary occlusion is greatly influenced by the experimental preparation, anesthesia, and the site of occlusion. However, Constantin11 demonstrated that circumflex coronary occlusion

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produces a fall in systemic arterial pressure which is accompanied not by the expected vasoconstriction of the peripheral vessels in an attempt to return arterial pressure to its set point, but by vasodilation which, of course, aggravates the arterial hypotension. Hanley et al.\textsuperscript{12} have demonstrated that the peripheral vessels respond in a complex manner to experimental coronary occlusion, which produces vasodilation in the cutaneous tissues of the hindlimb, but directionally opposite responses occur in the skeletal muscle, namely vasoconstriction. Furthermore, coronary occlusion produces vasoconstriction in adipose tissue and vasodilation in the renal vessels.\textsuperscript{13, 14} The renal vasodilation coincided with a decrease in efferent sympathetic nerve activity to the kidney as noted by Kezdi et al.\textsuperscript{15} Thus, a fall in peripheral resistance following experimental coronary occlusion reflects the net effects of vasomotion occurring in the various arterial beds.

These findings have raised the question of how coronary occlusion alters the homeostatic systems and prevents these systems from maintaining homeostasis. Instead of the expected vasoconstriction accompanying the fall in arterial pressure after coronary occlusion, vasodilation occurs in many peripheral vascular beds. Enhanced vagal afferent activity produced by coronary occlusion appears to be responsible for this altered response to hypotension since the paradoxic response of vasodilation can be abolished, and the expected vasoconstriction restored, if the vagus nerves are sectioned.\textsuperscript{11, 12, 15, 16} Since atropine does not abolish the vasodilation,\textsuperscript{13, 16} the efferent vagal pathways do not mediate this paradoxic response in experimental coronary occlusion. The receptors which initiate this paradoxic vasodilation are found in the left ventricular myocardium.\textsuperscript{17} Ventricular receptors which demonstrate increased activity after coronary artery occlusion have been identified.\textsuperscript{18-20} Furthermore, it appears that there are at least two types of sensory receptors in the left ventricular wall, namely those that respond to chemical stimuli and those that respond to mechanical stimulation. Thus, coronary occlusion either a) excites chemical receptors in the left ventricular wall by local hypoxia, acidsosis, accumulated metabolites and, perhaps, serotonin or b) excites mechanical receptors by systolic bulging of the akinetic area, or both. The increased activity of these receptors is transmitted, primarily through vagal afferents and perhaps also through sympathetic afferents,\textsuperscript{18, 20} to the integrating areas of the central nervous system, and change the expected cardiovascular response to arterial hypotension, for some peripheral vascular beds, from vasoconstriction to vasodilation.

Thus, the organism’s response to an important cardiovascular drug, digitalis, and an important clinical condition, acute myocardial infarction, is greatly determined by altered cardiovascular reflexes. Further understanding of the interaction of pathologic conditions and drugs with the cardiovascular reflexes is necessary for the proper approach to these important clinical problems.

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