Role of arterial baroreceptor reflex in controlling circulation

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The baroreceptor heart rate reflex was examined during acute occlusion of left anterior descending coronary artery in anesthetized, artificially ventilated, and thoracotomized dogs. During occlusion of LAD, baroreflex-heart rate response to changes in arterial pressure was attenuated in the animals with intact autonomic nervous system (ANS). In ANS and beta blocked (propanolal 1 mg/kg) animals, heart rate increased with the duration of occlusion of coronary artery, whereas in atropinized and vagotomized animals, LAD occlusion did not produce any significant change in the heart rate. In ANS animals, the baroreflex mediated tachycardia response to fall in blood pressure and bradycardia response to increase in blood pressure following four hours of LAD response after LAD occlusion. Whereas baroreflex mediated-bradycardia response was reduced in atropinized and vagotomized animals. The results demonstrated that acute occlusion of LAD attenuated arterial baroreflex control of heart rate and the reduction in the sensitivity of baroreflex due to LAD occlusion is mediated primarily by sympathetic limb of the autonomic nervous system. Acute normovolemic haemodilution in anesthetized animals produced an increase in cardiac output primarily by increasing the heart rate in ANS and beta-blocked animals, whereas, the compensatory increase in cardiac output on haemodilution in atropinized or vagotomized animals was by an increase in stroke volume. Baroreflex response was observed to be attenuated during acute haemodilution. The peripheral resetting in relation to increase in arterial pressure involves reduced activity of baroreceptors at equivalent pressure and vascular stretch. Like in acute hypoxia the altered responsiveness of baroreceptor-heart rate reflex during oxygen deficiency due to acute occlusion of LAD or acute normovolemic haemodilution may involve peripheral and central components.

THE role of cardiovascular sensory receptors in the regulation of cardiovascular system is well established[1–6]. The arterial baroreceptors are involved in the regulation of arterial pressure by reflex changes in heart rate and vascular tone[4,5,7–12]. The arterial receptors with vagal afferents are known to participate primarily in reflex regulation of blood volume[6,13–16]. Stimulation of cardiopulmonary receptors produces reflexly induced positive chronotropic effect[1,2,15,17]. Therefore, both arterial baroreceptors and cardiopulmonary receptors reflexly influence the cardiovascular system and are involved in blood pressure and volume control[16,18–26]. The modulatory role of one type of receptors on the reflex regulation of cardiovascular parameters by other types is well documented[16,19,23,27–29].

A number of stress-induced disturbances alter blood flow to various organs resulting in production of a chronotropic effect and changes in cardiac output[30–34]. The cardiovascular responses produced by a particular disturbance are usually specific, resulting from interaction between various cardiovascular sensory receptors and their reflex autonomic effects. The effects could also be nonautonomic, humoral and act directly on the heart and blood vessels[35]. The autonomic nervous system (ANS) circulatory responses to stress involve changes in sympathetic neural activity to various organs, with increased vascular constrictor tone in some areas and decreased tone in other vascular beds[1,2,35–41]. Parasympathetic efferents also play an important role in regulation of the cardiovascular parameters[1,2]. Sympathetic neural discharge is known to be influenced by emotional stimuli and by muscle exercise[33,34,40,42–44]. Besides aortic arch and carotid sinus arterial baroreceptors, other main cardiovascular receptors which influence heart rate, blood pressure and peripheral resistance, include atrial receptors and ventricular receptors[6,45,46]. Since heart and peripheral vessels of several regions are connected in series and parallel, any circulatory disturbance will tend to altered pressure in different regions of the body by changing inputs from various cardiovascular sensory receptors to the central nervous system (CNS). The resulting autonomic effector responses will depend on the interactions among the contributions of various receptor types (Figure 1). It is likely that depending on the circulatory disturbance at a particular time, one type of receptor may play a dominant role compared to others in bringing cardiovascular changes through autonomic effectors. The possibility of sensory receptors other than those located in the circulatory system influencing the cardiovascular parameters under certain environmental changes, also exists. Chemoreceptors, pulmonary stretch receptors and receptors located in skin and muscle are known to modulate the reflex cardiovascular effects of arterial pressure changes. Possible sensory inputs to the

CNS during circulatory disturbance and contributing autonomic effectors are illustrated in Figure 1.

Resetting of arterial baroreceptors

Increase in arterial pressure stimulates the arterial baroreceptors located in the aortic arch and carotid sinus regions. This leads to reflex inhibition of sympathetic efferent nerve activity[2,47] and excitation of parasympathetic efferent nerve activity[2]. A change in relationship between arterial pressure and heart rate or sympathetic efferent nerve activity is termed as resetting of the baroreceptor reflex[48]. The resetting of baroreceptor reflex may occur at the baroreceptor level, which is called peripheral resetting. Resetting within the CNS is called central resetting.

Peripheral resetting

An increase in the arterial pressure causes an increase in the threshold pressure required for activation of the baroreceptors[49–53]. This is accompanied by a rightward shift in the arterial pressure–baroreceptor activity curve. This shift in the pressure–baroreceptor activity relationship is known as resetting. It increases the threshold level for stimulation of arterial baroreceptors and maintains the arterial pressure at an elevated level. The slope of the pressure–response curve may decrease and there may be a decrease in maximum activity of the baroreceptors. In baroreceptor resetting, lower activity of arterial baroreceptors at an equivalent pressure may reduce the strain on the blood vessel, or fall in activity may produce unaltered or even greater deformity of the blood vessel. However, the baroreceptor resetting during fall in arterial pressure may result in the opposite responses, i.e. threshold pressure of arterial baroreceptors is decreased on exposure to low pressure and arterial pressure–receptor activity curve is shifted to the left[54]. Generally, peripheral resetting of arterial baroreflex occurs under conditions of sustained change in arterial pressure, e.g. chronic hypertension[55,56], but there may be acute resetting of the reflex also. There are three types of peripheral resetting: (i) *Instantaneous resetting*. Fall in receptor activity during diastolic phase of the cardiac cycle at the same pressure is known as instantaneous resetting[57–59]. (ii) *Acute resetting*. Acute resetting of baroreceptors occurs within a few cardiac cycles after change in pressure and stabilizes at changed pressure level in minutes[53,58,60]. (iii) *Chronic resetting*. Decreased vascular compliance could cause a fall in arterial baroreceptor activity during chronic hypertension and could produce less strain on arterial baroreceptor endings[55,56,61]. Chronic hypertension produces a sustained increase in strain on arterial baroreceptor endings. This changes the diameter of the aorta and carotid sinus regions which then remain stable. The baroreflex sensitivity is decreased and the resetting of arterial baroreceptors at the new threshold stimulus is complete.

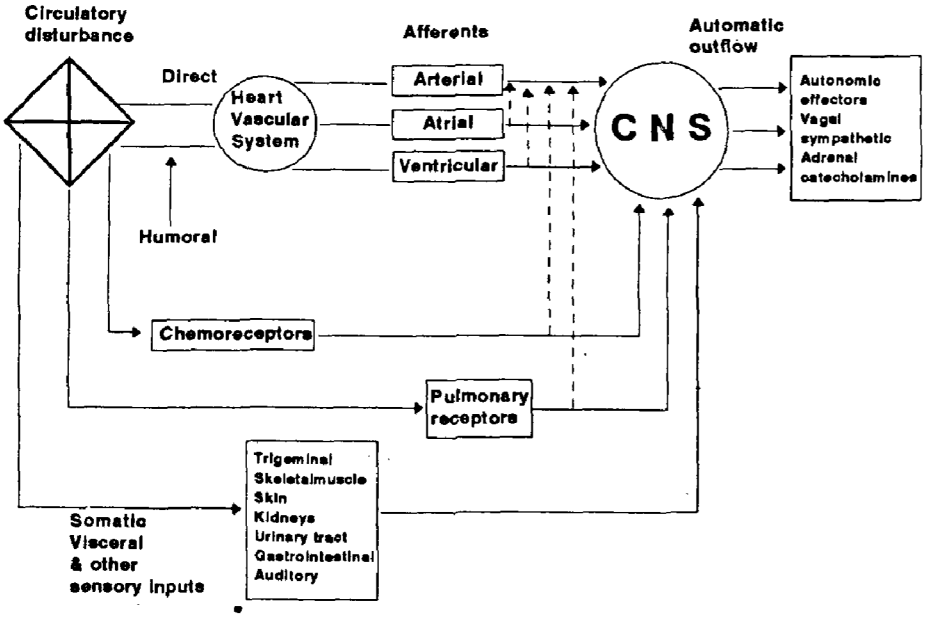

Figure 1. Illustration of various possible sites of the integrated baroreflex regulatory control. Any circulatory disorder directly affects the heart and the vascular beds, changes vascular pressure and changes input from various cardiovascular receptors to the central nervous system (CNS). Autonomic effectors include vagal and sympathetic efferents and release of adrenal catecholamines. Arterial baroreflex activity is modulated by other cardiovascular receptors, chemoreceptors, pulmonary receptors and other somatic, visceral and sensory inputs.

Central resetting

When the efferent sympathetic activity is significantly different for the same level of baroreceptor input it is called central resetting of the baroreflex. Central resetting is also influenced by other neural reflexes and/or humoral agents[48,62] in certain conditions, e.g. during exercise and hypoxia. It is suggested that neurons involved in central inhibition of sympathetic efferent activity may be less sensitive to increase in the arterial baroreceptor input[47].

The resetting of baroreceptors and the baroreflex plays an important role in the cardiovascular regulation in physiological and pathophysiological conditions. Central resetting of baroreflex under certain conditions, e.g. severe hypoxia, may involve baroreflex-dependent changes as well as baroreflex-independent changes[48]. Central resetting of the baroreflex is mediated through both suprapontine and bulbo-spinal pathways involved in autonomic integration of cardiovascular regulation[48].

Acute baroreflex resetting during hypotension

Ajmaloon (Hamdard, India), a preparation from *Rauwolfia serpentine* and certain herbs, reduces blood pressure in humans and animals in a dose-dependent manner[63]. Intravenous administration of 100 mg/kg Ajmaloon in anaesthetized rabbits and monkeys produced significant fall in arterial blood pressure, with no significant change in heart rate. The systolic arterial pressure–heart rate curve shifted to the left following the intravenous injection of Ajmaloon and at the same pressure, heart rate was lower and thus showed an acute resetting of the baroreflex. Loss of tachycardia response to fall in arterial pressure in Ajmaloon-treated animals suggests a drug-induced suppression of normally existing sympathetic excitatory influence in response to hypotension. It also suggests a significant fall in baroreflex sensitivity at the lower arterial pressure caused by the drug.

Baroreflex responses during acute hypoxia

It is well known that in animals respiratory status affects the autonomic vaso-constrictor response[64]. In mild hypoxia there is a slight and gradual rise in total peripheral resistance, and during severe hypoxia where arterial Po2 falls below 35 mm Hg, rise in autonomic effect on total peripheral resistance is abrupt. Abrupt rise in peripheral resistance at Po2 below 35 mm Hg is attributed to stimulation of chemoreceptors. Due to increase in ventilation during exposure to hypoxic breathing, the pulmonary stretch receptors are also stimulated. This also modulates the peripheral resistance. The ratio between the activity of pulmonary stretch receptors and chemoreceptors reflects the magnitude of the rise in total peripheral resistance through the ANS due to hypoxia. The pulmonary stretch receptor mediated inhibitory effects on peripheral resistance are known to be cortically-mediated[65]. Heart rate response mediated through the ANS is also altered during hypoxic breathing. Mild hypoxia causes increase in heart rate, but severe hypoxia produces increased bradycardia.

Sustained bradycardia occurred in animals with intact CNS. In pontine (infracollicular decerebration) animals there was an increase in heart rate at all levels of hypoxia. In suprapontine preparations of thalamic animals only, bradycardia occurred even at a mild level of hypoxia. It has been suggested that the tachycardia response to hypoxia is mediated through bulbo-spinal regions. Thus bradycardia response to hypoxia is due to stimulation of the chemoreceptors and suppression of cardiac slowing during mild hypoxia is caused by stimulation of the pulmonary stretch receptors due to hyperventilation. Magnitude of inputs from two sets of receptors (chemoreceptors and pulmonary stretch receptors) to the autonomic centres determines the autonomic effector response during respiratory disturbance (hypoxia). This in turn triggers the CNS to modulate the respiration in order to meet the demands of oxygenation of arterial blood during any kind of respiratory stress. In humans hypoxia with hypocapnia, produced tachycardia without any significant change in pressure or in baroreflex sensitivity. During exercise the changes were similar except that baroreflex sensitivity was depressed more than what was expected by exercise alone.

Baroreflex response during acute experimental anaemia

While in hypoxia Po2 falls, in haemodilution the Po2 may be normal but the oxygen-carrying capacity is reduced in proportion to the reduction in hematocrit[66]. Acute haemodilution in dogs produces increase in cardiac output and fall in total peripheral resistance. The magnitude of these effects depends on the degree of haemodilution. It was observed that in dogs with a low control heart rate (60–80 beats/min) with intact autonomic innervation and following beta blockade, the increase in cardiac output was almost entirely owing to an increase in heart rate[37]. Whereas in dogs with high basal heart rate following (i) cholinergic blockade, (ii) or bilateral vagotomy, and (iii) or bilateral vagotomy plus beta-blockade, the increase in cardiac output was entirely owing to an increase in the stroke volume (Figures 2 and 3). Thus the tachycardia response to haemodilution was primarily mediated through the efferent vagus nerves, and the efferent sympathetic nerves did not make any significant contribution in the reflex regulation of acute fall in the oxygen-carrying capacity of the circulating blood[37]. In another study on anaesthetized cats we

observed that the increase in cardiac output on acute haemodilution was largely due to an increase in stroke volume with small increase in heart rate[67]. This could be due to low vagal tone in our anaesthetized cats. Haemodilution attenuated the excitatory effects of phenylephrine. The reduced sensitivity of the drug under such conditions could be due to reduced myocardial oxygen supply, suppression of the excitatory effects by local vasodilating agents and certain other factors which control vascular responsiveness to drugs. Baroreflex systolic pressure–heart rate relationship was not altered by haemodilution. However, at the same level of systolic pressure, heart rate showed an increase corresponding to the degree of haemodilution and reset itself at that level. The sensitivity of baroreflex tachycardia response to hypotension was attenuated only during severe (HCT-14%) haemodilution (Figure 4).

Baroreflex response during coronary artery occlusion

Acute coronary artery occlusion causes myocardial ischaemia. This induces autonomic adjustment in the cardiovascular system. Excitation of cardiac afferent nerves produces reflex which is cardioinhibitory and vasodepressor responses with a fall in sympathetic tone[68,69]. This vasodepressor response is abolished in acute myocardial infarction due to the interruption of vagal afferent fibres[70]. Inactivation of the ventricular sensory nerve endings, due to chronic myocardial

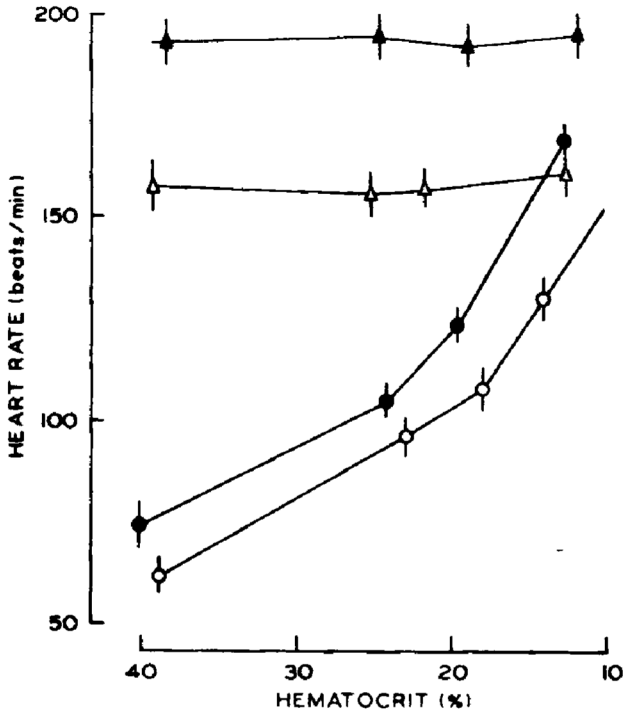

Figure 3. Heart rate changes with fall in hematocrit following graded normovolemic hemodilution in control (•), beta blocked (o), vagotomized (Δ), and vagotomized plus beta blocked (▲) dogs.

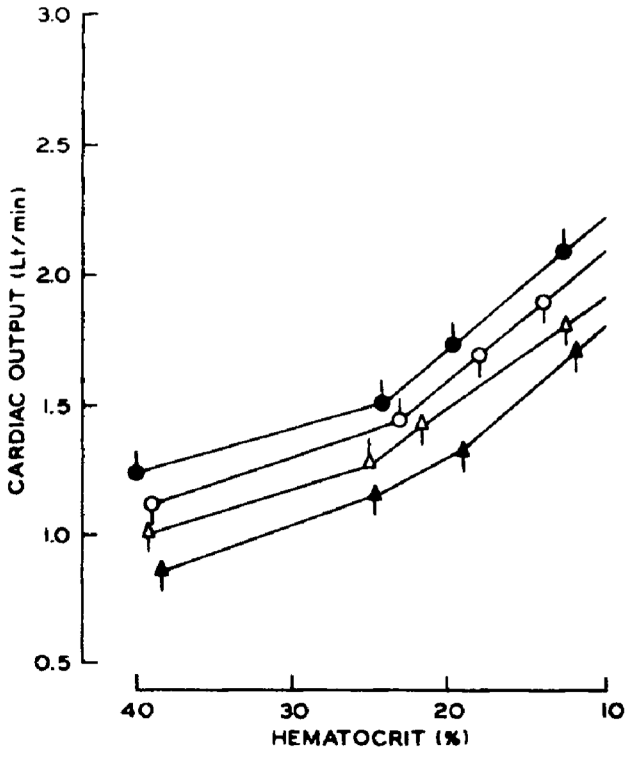

Figure 2. Increase in cardiac output with fall in hematocrit due to graded normovolemic hemodilution in control (•), beta blocked (o), vagotomized (▲), and vagotomized plus beta blocked (Δ) dogs.

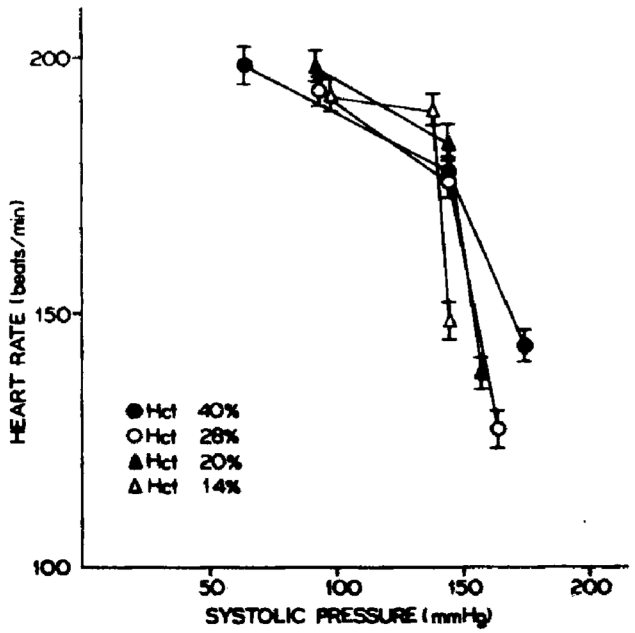

Figure 4. Baroreflex arterial pressure–heart rate relationship before and after graded acute hemodilution in cats.

infarction as well as by impairment of cardiac reflexes in response to changes in cardiac filling is known to occur[71]. In clinical studies the status of autonomic reflex control has been used for assessment of degree of risk for sudden death, because baroreflex-mediated changes in heart rate can provide a useful criterion to assess autonomic neural control of the heart[18]. Acute coronary artery occlusion attenuates baroreflex control of heart rate in response to an increase in arterial pressure[30,72].

In dogs the tachycardia response was related to the duration of coronary artery occlusion with intact ANS as well as after beta blockade, indicating inhibition of vagal efferent nerve activity. Heart rate response in dogs to coronary artery occlusion was abolished following atropine injection (i.v.) or bilateral section of vagus nerves. In normal dogs, the sensitivity of baroreflex tachycardia response to fall in arterial pressure and the bradycardia response to rise in pressure, four hours after acute occlusion of left anterior descending coronary artery (LAD) was attenuated. In beta-blocked animals, tachycardia response after the occlusion of LAD was almost abolished. Atropinization or vagotomy attenuated the peak sensitivity of baroreflex-mediated bradycardia response, whereas the peak sensitivity of baroreflex tachycardia response was increased after bilateral vagotomy. The bradycardia response was enhanced after beta-blockade. Thus acute myocardial ischaemia attenuates arterial baroreflex control of heart rate. The fall in baroreflex sensitivity following LAD occlusion involves parasympathetic efferent nerves[30]. In another study we observed that the cardiovascular reflex effects of intravenously administered phenylephrine and nitroprusside were attenuated after occlusion of LAD[73]. Acute LAD coronary artery occlusion produced a fall in arterial pressure and stroke volume. It also produced a rise in cardiac output due to increase in heart rate (Figures 5 and 6). Arterial baroreflex and cardio-pulmonary reflexes are known to be depressed in chronic congestive heart failure. The baroreflex dysfunction is suggested to be abnormal in the afferent limb rather than the central or efferent limbs of the reflex arc[36].

Influence of other cardiac sensory receptors on the arterial baroreceptor-mediated reflex responses

Left ventricular receptor stimulation by intracoronary infusion of veratrine attenuates arterial baroreflex control of heart rate. The fall in sensitivity of the reflex and the heart rate is mediated by parasympathetic motoneurons common to both reflex arcs[3]. Further, the resetting of the reflex to a lower operational set point is suggested to be mediated by cardiac sympathetic motoneurons common to both the reflex arcs[3].

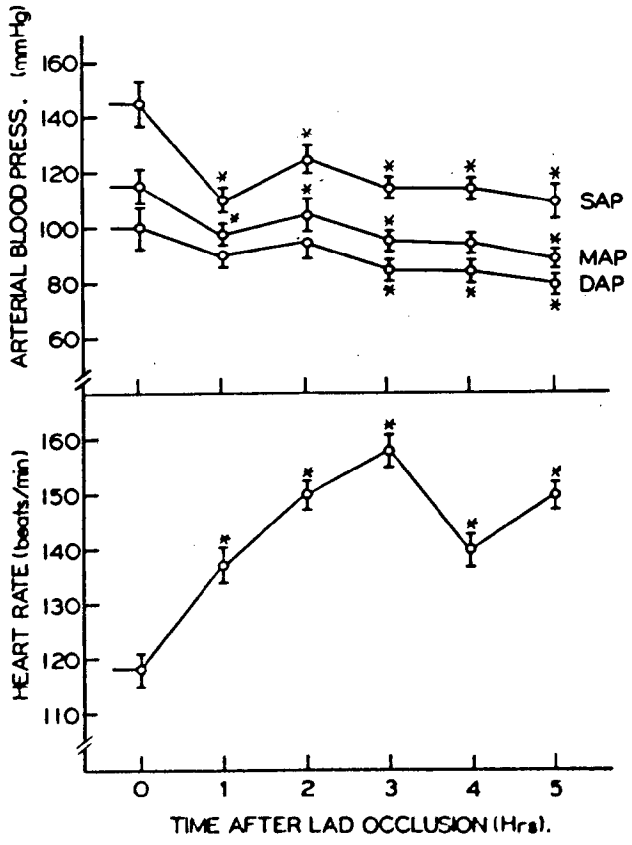

Figure 5. Effect of acute occlusion of left anterior descending coronary artery (LAD) on arterial blood pressure (systolic arterial pressure, SAP; diastolic arterial pressure, DAP; mean arterial pressure, MAP) and heart rate in dogs.

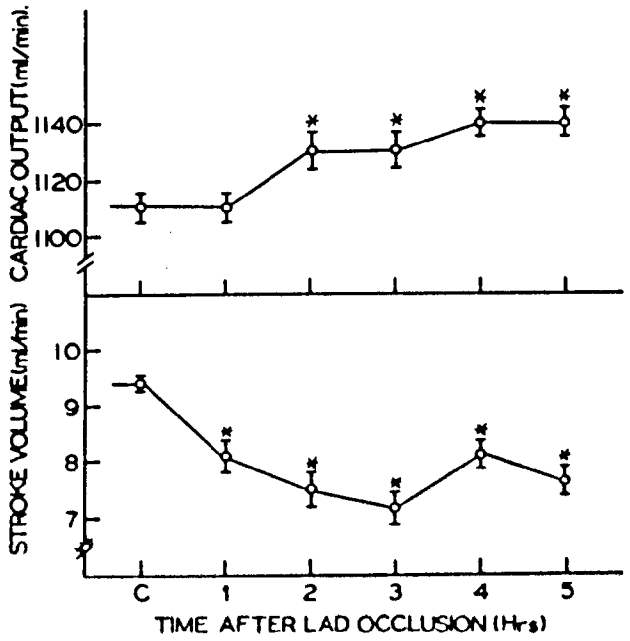

Figure 6. Increase in cardiac output and fall in stroke volume following acute occlusion of left anterior descending coronary artery (LAD) in dogs.

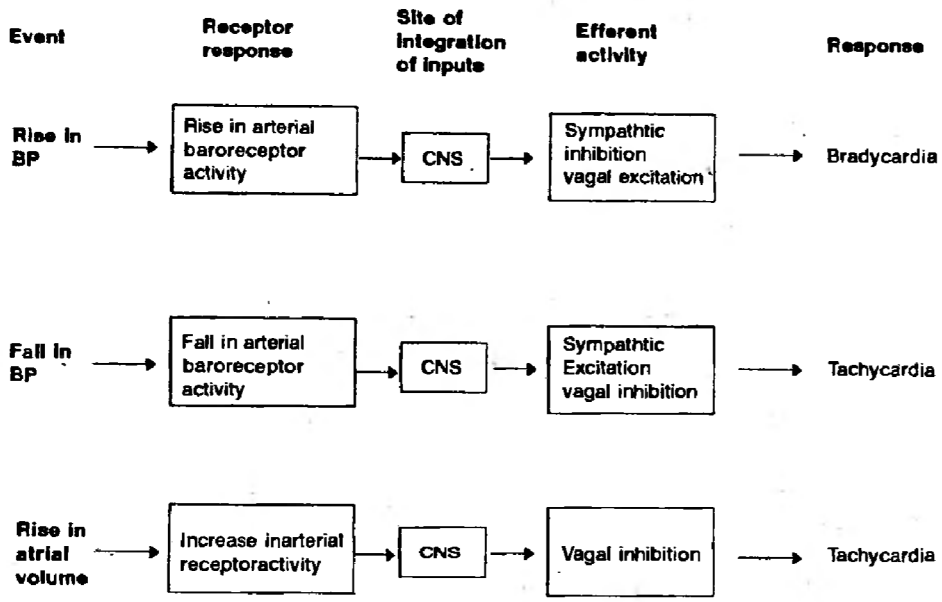

Figure 7. Scheme of chronotropic response to stimulation of arterial baroreceptors/atrial receptors.

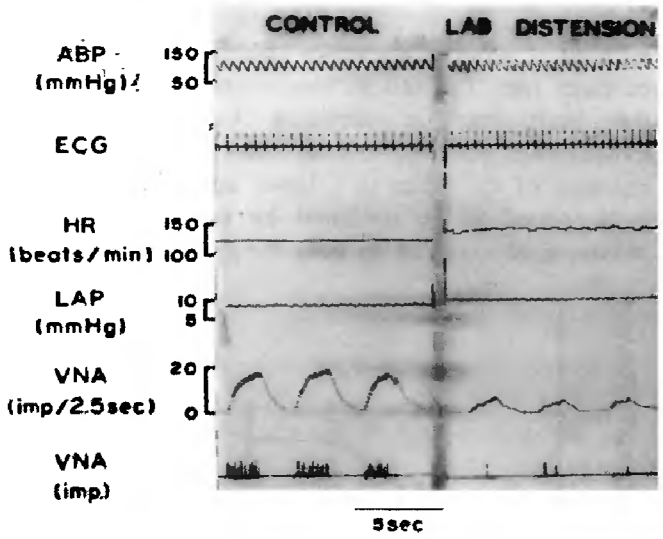

Figure 8. Arterial blood pressure (ABP), electrocardiogram (ECG), heart rate (HR), left atrial pressure (LAP), cardioinhibitory vagal efferent fibre activity (VNA) and integrated activity (VNA) over 2.5 sec before (control) and during inflation of left atrial balloon (LAB distension) in dogs.

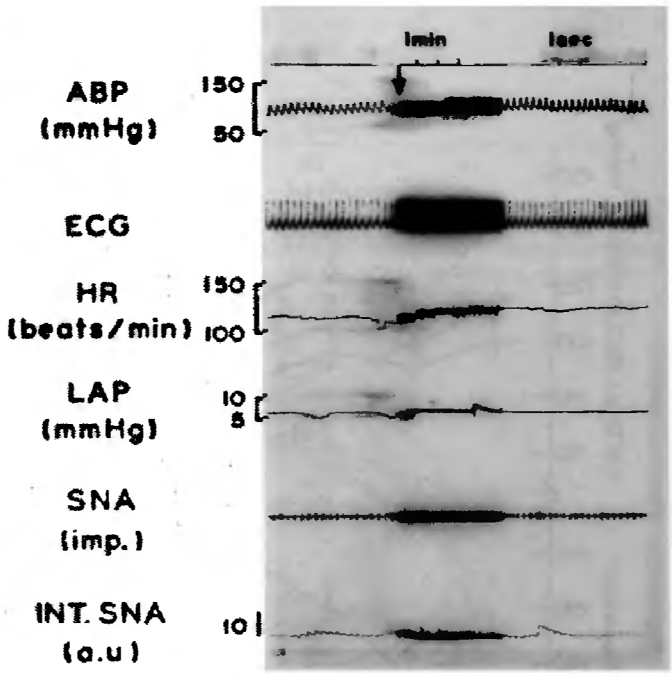

Figure 9. Original record showing arterial blood pressure (ABP), electrocardiogram (ECG), heart rate (HR), left atrial pressure (LAP), cardiac sympathetic efferent activity (SNA) and integrated SNA activity (INT SNA) before and during inflation of left atrial balloon. Balloon was inflated at arrow (↓) shown at the top.

The cardio-pulmonary low-pressure receptors are known to participate primarily in reflex regulation of blood volume[6,13–16]. In dogs, localized stimulation of atrial receptors produces a reflex tachycardia response[2,15,17]. Since arterial baroreceptors are also known to regulate arterial pressure by reflex changes in the heart rate and by vasoconstriction, it suggests that these two sets of sensory receptors reflexly influence both the cardio-vascular system and the autonomic efferent output[2,18–26]. Roddie *et al.*[16] suggested that excitation of cardio-pulmonary receptors inhibits the arterial baroreflex through a central mechanism. Interaction between two groups of cardiovascular sensory receptors has also been observed by other investigators[19,23,27–29]. The cardiovascular reflex effects produced by arterial baroreceptors and atrial receptors involve both vagal and sympathetic efferents and afferents[1,2,74–77]. In one of our studies on

studies on anaesthetized cats and dogs we recorded the sympathetic cardiac efferent nerve activity and cardioinhibitory vagal efferent nerve fibre activity on stimulation of the arterial baroreceptors, atrial receptors or both types of receptors simultaneously[2]. Arterial baroreceptor-mediated chronotropic effect involved both sympathetic and parasympathetic limbs of the autonomic nervous system (Figure 7). However, cardio-acceleration produced by localized stimulation of the left atrial receptors was mainly due to withdrawal of parasympathetic tone[1,2] (Figure 8) and not excitation of sympathetic efferents (Figure 9). On stimulation of both types of cardiovascular receptors simultaneously, net result was a slight inhibition of the baroreflex tachycardia response to hypotension and an augmentation of baroreceptor-mediated bradycardia response to the increase in arterial pressure[2]. Thus atrial receptors modulate the arterial baroreceptor-mediated chronotropic response to change in arterial pressure. The role arterial baroreceptors and atrial receptors play during change in their natural stimulus and in resetting the reflex chronotropic responses is summarized in Figure 7.

1. Fahim, M. and Arndt, J. O., *J. Appl. Cardiol.*, 1989, **4**, 103–115.
2. Fahim, M. and Arndt, J. O., *Jap. J. Physiol.*, 1990, **40**, 35–55.
3. Holmberg, M. J., Gorman, A. J., Cornish, K. G. and Zucker, I. H., *Circ. Res.*, 1983, **53**, 597–607.
4. Kirchheim, H. R., *Physiol. Rev.*, 1976, **56**, 100–176.
5. Korner, P. I., in *Progress in Cardiology* (eds Yu, P. N. and Goodwin, J. F.), Lea and Febiger, Philadelphia, 1978, pp. 55–101.
6. Paintal, A. S., *Physiol. Rev.*, 1973, **53**, 159–227.
7. Abboud, F. M. and Mark, A. L., in *Cardiac Receptors* (eds Hainsworth, R., Kidd, C. and Linden, R. J.), Cambridge University Press, Cambridge, UK, 1979, pp. 437–462.
8. Downing, S. E., in *Handbook of Physiology, Sec. 2, The Cardiovascular Systems* (ed. Berne, R. M.), American Physiological Society, Bethesda, 1979, vol. I, pp. 621–652.
9. Brown, A. M., in *Handbook of Physiology, Sec. 2, The Cardiovascular System* (ed. Berne, R. M.), American Physiological Society, Bethesda, 1979, vol. I, pp. 677–689.
10. Shepherd, J. T., *Cardiovasc. Res.*, 1982, **16**, 347–370.
11. Sleight, P., in *Modern Trends in Cardiology* (ed. Oliver, H. F.), Butterworth, London, 1974, pp. 1–43.
12. Undesser, K. P., Jing-Yun, P., Lynn, M. P. and Bishop, V. S., *Am. J. Physiol.*, 1985, **348**, H827–H834.
13. Gauer, O. H. and Henry, J. P., *Int. Rev. Physiol.*, 1976, **9**, 145–190.
14. Goetz, K. L., Bond, G. C. and Bloxham, D. D., *Physiol. Rev.*, 1975, **55**, 157–205.
15. Kappagoda, C. T., Linden, R. J. and Snow, H. M., *J. Physiol. (London)*, 1973, **235**, 493–502.
16. Roddie, I. G., Shepherd, J. T. and Whelan, R. F., *J. Physiol. (London)*, 1957, **139**, 369–376.
17. Linden, R. J., in *Cardiac Receptors* (eds Hainsworth, R., Kidd, C. and Linden, R. J.), Cambridge University Press, Cambridge, UK, 1979, pp. 165–191.
18. Billman, G. E. Dickey, D. T. Teoh, K. K. and Stone, H. L., *Am. J. Physiol.*, 1981, **241**, H571–H575.
19. Chen, H. I., Chai, C. Y., Tung, C. S. and Chen, H. C., *Am. J Physiol.*, 1979, **237**, H153–H158.
20. Faris, I. B., Jamieson, G. G. and Ludbriin, J., *J. Physiol. (London)*, 1983, **337**, 563–573.
21. Felder, R. B. and Thames, M. D., *Circ. Res.*, 1979, **45**, 728–736.
22. Guo, G. B., Thames, M. D. and Abboud, F. M., *Circ. Res.*, 1982, **50**, 554–565.
23. Koike, H., Mark, A. L., Heistad, D. D. and Schmid, P. G., *Circ. Res.*, 1975, **37**, 422–429.
24. Ludbrook, J. and Graham, W. F., *Circ. Res.*, 1984, **54**, 424–435.
25. Mancia, G., Shepherd, J. T. and Donald, D. E., *Am. J. Physiol.*, 1976, **230**, 19–24.
26. Walgenbach, S. C. and Shepherd, J. T., *Mayo Clin. Proc.*, 1984, **59**, 467–475.
27. Donald, D. E. and Shepherd, J. T., *Cardiovasc. Res.*, 1978, **12**, 449–469.
28. Takeshita, A., Mark, A. L., Eckberg, D. L. and Abboud, F. M., *Am. J. Physiol.*, 1985, **236**, H42–H47.
29. Vatner, S. F., Boettcher, D. H., Heyndrickx, G. R. and Mcritchie, R. J., *Circ. Res.*, 1975, **37**, 236–242.
30. Hussain, M. E., Krishna, B., Singh, M. and Fahim M., *Jap. J. Physiol.*, 1992, **42**, 741–753.
31. Korner, P. I., *Physiol. Rev.*, 1971, **51**, 312–367.
32. Korner, P. I., West, M. J., Shaw, J. and Uther, J. B., *Clin. Exp. Pharmacol. Physiol. Suppl.*, 1974, **1**, 65–76.
33. Rowell, L. B., *Physiol. Rev.*, 1974, **54**, 75–159.
34. Smith, O. A., *Annu. Rev. Physiol.*, 1974, **36**, 93–123.
35. Chalmers, J. P., Korner, P. I. and White, S. W., *J. Physiol. (London)*, 1967, **192**, 537–548.
36. Chen, J. S., Wang, W., Kornish, K. J. and Zucker, I. H., *Am. J. Physiol.*, 1992, **263**, H1084–H1089.
37. Fahim, M. and Singh, M., *Jap. J. Physiol.*, 1992, **42**, 753–763.
38. Chalmers, J. P. and Korner, P. I., *J. Physiol. (London)*, 1966, **184**, 685–697.
39. Folkow, B., Johansson, B. and Lofving, B., *Med. Exp.*, 1961, **4**, 321–328.
40. Miller, N. E., *Science*, 1969, **163**, 434–445.
41. Schonung, W., Wagner, H., Jessen, C. and Simon, E., *Pflugers Arch. Physiol.*, 1971, **328**, 145–154.
42. Folkow, B. and Neil, E., in *Circulation*, Oxford Univ. Press, London, 1971, pp. 340–363.
43. Hilton, S. M., *Lect. Sci. Basis Med.*, 1965, 217–238.
44. Rushmer, R. F. and Smith, O. A., *Physiol. Rev.*, 1959, **39**, 41–68.
45. Linden, R. J., *Circulation*, 1973, **48**, 463–480.
46. Paintal, A. S., in *Handbook of Sensory Physiology* (ed. Neil, E.), Springer, Berlin, 1971, vol. III/I, pp. 1–45.
47. Chapleau, M. E., Hajduczok, G. and Abboud, F. M., *Clin. Exp. Pharmacol. Physiol.*, (Suppl.), 1989, **15**, 31–43.
48. Korner, P. I., *Clin. Exp. Pharmacol. Physiol. Suppl.*, 1975, **2**, 171–178.
49. Krieger, E. M., *Am. J. Physiol.*, 1970, **218**, 486–490.
50. Krieger, E. M., *Hypertension*, (Suppl. I), 1986, **8**, 7–14.
51. Brown, A. M., *Circ. Res.*, 1980, **46**, 1–10.
52. Kunze, D. L., *J. Physiol. (London)*, 1972, **222**, 1–15.
53. Chapleau, M. W., Hajduczok, G. and Abboud, F. M., *Am. J. Med. Sci.*, 1988, **295**, 327–334.
54. Salgado, H. C. and Krieger, E. M., *Clin. Sci. Mol. Med.*, 1973, **45**, 123s–126s.
55. Angell-James, J. E., *Circ. Res.*, 1973, **32**, 149–161.
56. Andresen, M. C., *Circ. Res.*, 1984, **54**, 750–759.
57. Abboud, F. M. and Chapleau, M. W., *Fed Proc.*, 1986, **45**, 296.
58. Coleridge, H. M., Coleridge, J. C. G., Poore, E. R., Roberts, A. M. and Schultz, H. D., *J. Physiol.*, 1984, **350**, 309–326.
59. Chapleau, M. W., Heesch, C. M. and Abboud, F. M., *Hypertension*, (Suppl. III), 1987, **9**, 131–141.
60. Coleridge, H. M., Coleridge, J. C. G., Poore, E. R., Roberts, A. M. and Dangel, A., *Circ. Res.*, 1982, **48**, 676–684.
61. Angell-James, J. E., *Circ. Res.*, 1974, **34**, 27–39.

62. Abboud, F. M. and Thames, M. D., in *Handbook of Physiology. Section 2. The Cardiovascular System. Peripheral Circulation and Organ Blood Flow* (eds Shepherd, J. T. and Abboud, F. M.), American Physiological Society, Bethesda, Maryland, Ch. 19, 1983, vol. III.
63. Fahim, M., Khan, M. S. Y. and Hameed, H. A., *Indian J. Physiol. Pharmacol.*, 1995, **39**, 101–105.
64. Korner, P. I., *Circ. Res.*, (Suppl. II), 1970, **26 and 27**, 159–168.
65. Korner, P. I., Shaw, J., West, M. J., Oliver, J. R. and Hilder, R. G., *Circ. Res.*, 1973, **33**, 63–67.
66. Bartlett, D. Jr. and Tenny, S. M., *J. Appl. Physiol.*, 1963, **18**, 734–738.
67. Talwar, A., Hussain, M. E., Gupta, C. K. and Fahim, M., *Indian J. Physiol. Pharmacol.*, 1995, **39**, 106–110.
68. Thames, M. D. and Abboud, F. M., *J. Clin. Invest.*, 1979, **63**, 395–402.
69. Reimann, K. A. and Weaver, L. C., *Am. J. Physiol.*, 1980, **239**, H316–H325.
70. Barber, M. J., Muller, T. M., Davies, B. G., Gill, R. M. and Zips, D. P., *Circulation*, 1985, **72**, 623–631.
71. Minisi, A. J. and Thames, M. D., *Circ. Res.*, 1989, **65**, 396–405.
72. Takeshita, A., Matsuguchi, H. and Nakamura, M., *Cardiovasc. Res.*, 1980, **14**, 303–306.
73. Hussain, M. E. and Fahim, M., *Indian J. Physiol. Pharmacol.*, 1994, **38**, 252–258.
74. Angell-James, J. E. and Daly, M. De. B., *J. Physiol. (London)*, 1970, **209**, 257–293.
75. Hakumaki, M. O. K., *Acta Physiol. Scand.*, 1972, **85**, 414–417.
76. Malliani, A., *Rev. Physiol. Biochem. Pharmacol.*, 1982, **94**, 11–74.
77. Oberg, B., *Annu. Rev. Physiol.*, 1976, **38**, 537–570.

MEETINGS/SYMPOSIA/SEMINARS

International Workshop on the History of Science: Implications for Science Education

Date: 22–26 February 1999
Place: Mumbai, India

The workshop will be focusing on following themes: Critical episodes in the history of science and mathematics; Historical approaches to science and mathematics curriculum; Conceptual change in science and science learning; Philosophy of science and science education.

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National Conference on Lasers and Spectroscopy

Date: 25–28 February 1999
Place: Meerut

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