Review Article

PHYSIOLOGICAL MECHANISMS INVOLVED IN THE CARDIOVASCULAR RESPONSES TO POSTURAL STRESS

MB Dikshit

The intrathoracic blood volume reduces each time a person changes posture from supine to erect, resulting in a temporary fall in blood pressure and pooling of blood in the legs. Cardiovascular reflexes involving the autonomic nervous system increase heart rate and peripheral resistance to maintain arterial blood pressure while constriction of the capacitance veins helps to continue the venous return to the heart in order to maintain cardiac output. In this brief review, current concepts of the physiological processes involved in the various cardiovascular responses to postural stress are discussed with special emphasis on the possible causes of failure of the reflex response in apparently healthy individuals. This understanding has a special bearing on vasovagal syncope in aircrew.

Keywords: blood pressure; head up tilt; heart rate; postural hypotension.

IN day to day activity, a change of posture from supine to erect is a stress that imposes a threat to the maintenance of normal blood pressure and cardiac output because of the rapid reduction in the central blood volume, and pooling of blood in the legs. Reflex cardiovascular adjustments must then be brought into play to avert the fall in blood pressure which otherwise may result in postural hypotension which can produce serious disability. It stands to reason that in certain work situations such as aviation where exaggerated postural stress occurs frequently as a routine, the integrity of the cardiovascular reflex mechanisms which help to maintain blood

pressure is of primary importance. It is therefore the aim of this paper to review the current understanding of the cardiovascular reactions which help to maintain blood pressure during postural stress and the physiological mechanisms which bring about these reactions.

A change from the supine to the erect posture transfers about 600 ml of blood into the legs (42). The hydrostatic pressure gradient set up by the gravity effect reduces the pressure at the brain level by about 25 mm Hg as compared with that at the heart level while below the heart level the pressure increases equally on the arterial as well as the venous side, and is about 80 mm Hg higher than the heart level pressure at the foot end (35). The veins are highly distensible structures because they contain viscoelastic tissue (40). This promotes the pooling of blood in the dependent regions, and with the continuation of the postural stress, the intravascular pressure will exceed that in the adjacent extravascular tissue and result in an outward filtration of the blood, further enhancing the pool formation and the loss in circulating fluid volume. Unless prompt adjustments are brought about by initiation of compensatory cardiovascular reflexes, the arterial blood pressure and the cardiac output may fall to dangerously low levels.

Reduction in central blood volume and fall in the venous return to the heart (pre-load) reduce the afferent input from the low-pressure cardiovascular and the arterial baroreceptors (3,17) to the solitary tract nucleus. This information is integrated in the medulla by the paramedian reticular nuclei (27), the hypothalamus and the cortex (5). The co-ordinated out put of the autonomic nervous system is directed to the heart and the peripheral vasculature to increase the heart rate and the vascular resistance to maintain the arterial blood pressure, and to constrict the capacitance veins to reduce the extent of pooling of the blood in the legs in order to promote venous return. The details of these physiological reactions are discussed hereafter.

Reflex heart rate changes

The reflex heart rate increase that occurs during postural stress could be attributed to a reduction in vagal tone, an increase in sympathetic activity or a combination of both the factors.

The immediate heart rate increase with standing – the commonest postural stress in day to day life is abolished by atropinisation, but is unaffected by beta-adrenoceptor blockade with propranolol, and is therefore brought about by a withdrawal of vagal tone(14). These authors also noted a rebound vagotonia which produces a relative bradycardia after about the initial 30 beats after attaining erect posture, and attributed this effect to muscular activity associated with standing because this part of the reflex was absent when the subjects were tilted head up by 70 deg during which the leg muscles are not brought in to play. Vagal tone withdrawal as a cause of the reflex tachycardia which accompanies a fall in the arterial blood pressure was also suggested by others (22, 29), but

vasodilator drugs were used in both these studies to produce the fall in blood pressure in supine subjects. The attenuation of the reflex tachycardia during head up tilt (HUT) was more marked with beta-adrenoceptor blockade than with vagal blockade (32), suggesting that sympathetic stimulation of the heart is mainly responsible for the effect.

Leopkky (24) also observed that the heart rate during HUT in subjects who had taken 40 mg propranolol orally two hours before the test was about 20 beats/min less than the heart rate during HUT without the drug. He did not study the effect of vagal blockade. During exposure to positive (radial) acceleration stress (which produces large and rapid transfer of circulating blood to the peripheries) the tachycardia response was attenuated by both, vagal blockade and beta-adrenoceptor blockade, and was almost abolished when combined blockade was used to denervate the heart pharmacologically (6).

The above evidence suggests that the reflex tachycardia seen with postural stress can be attributed to a combination of vagal withdrawal and sympathetic excitation. A deactivation of the arterial baroreceptors, and not of the low pressure cardiopulmonary receptors, is responsible for the reflex tachycardia (3). This conclusion can be drawn because when low pressure cardiopulmonary receptors are selectively deactivated by using low levels of lower body negative pressure in normal subjects, a sympathetically mediated vasoconstriction in the forearm occurs without a tachycardia (3,18).

Changes in the peripheral vascular resistance during postural stress

Sympathetic excitation which occurs as a result of postural stress brings about a selective increase in the tone of the resistance vessels in the muscular, splanchnic and renal vascular beds (3). Studies in normal subjects who faint after prolonged standing in the erect posture have revealed that on fainting there is a sudden vasodilatation in the forearm vascular bed implicating the resistance vessels in the muscles in the maintenance of arterial blood pressure during postural stress (8). However, in subjects who fainted during postural stress given after heat exposure, vasoconstriction in forearm vessels was not reduced, and a sudden dilatation in the splanchnic vessels was thought to be the precipitating cause of the syncope (23). Further, postural faint has been observed in patients with bilateral leg amputation (16) therefore suggesting that other vascular beds, notably in the splachnic region, are also involved. Splanchnic blood flow reduces by about 30% during exposure of normal subjects to lower-body negative pressure and this contributes to about 33% of the total increase in peripheral vascular resistance (34). Autopsy findings in patients with diabetic autonomic neuropathy who had suffered from postural hypotension revealed that the greater splanchnic nerve was found to have undergone degenerative changes while this nerve was intact in patients who did not suffer from autonomic neuropathy (25). This suggests that the increase in the splanchnic arteriolar resistance plays a role of paramount importance in the adjustment of the cardiovascular system

to this stress. Arterial baroreceptor deactivation which occurs during postural stress forms the afferent limb of the sympathetic reflex which produces the vasoconstriction in the splanchnic bed (4).The increase in the renal vascular resistance activates the renin-angiotensin system which in turn produces angiotensin II to enhance the arteriolar resistance (3).

It has been an "anatomical guess" that about 70% of the circulating blood is found in the veins which are sympathetically innervated, and because of their viscoelastic composition, small reduction in their calibre can produce large shifts of the blood contained in them (40). However, there was only a transient increase in the pressure in leg veins during head up tilt and lower body suction in normal subjects in whom the peripheral vascular resistance increased (36). These workers concluded that the transient constriction of the capacitance vessels only supported the resistance vessels in the immediate readjustment to postural stress. Cardiac output and blood pressure during positive acceleration, which is a form of exaggerated postural stress, was maintained in subjects with total autonomic blockade, and this was attributed to the enhanced venomotor tone in the capacitance vessels (6). In subjects who were about to faint as a result of postural stress, increasing the venous return by contracting leg muscles delayed the onset of the faint (47). Also, during syncope, sympathetically mediated venomotor tone was not reduced (13). The above suggests that constriction of the capacitance vessels is necessary for the maintenance of the preload, and therefore that of the cardiac output, during postural stress.

Increase in ventilation during HUT and lower body negative pressure application increases venomotor tone (36). During inspiration there is a siphoning of blood from the abdominal areas into the thorax because of pressure gradient created between the two regions by the decrease in the intra-thoracic pressure during inspiration and the associated increase in intra-abdominal pressure due to the descent of Diaphragm. During this phase the pressure gradient between the femoral veins and the inferior vena cava in the abdomen is relatively reduced but remains positive to ensure some amount of upward flow of blood from the legs into the abdomen (35). However, Willeput et al (49) found more than 50% fall in the venous return measured using an ultrasonic flow recorder in 7 out of 10 recumbent subjects during inspiration. The upward flow was reduced even further if the subjects resorted to pure diaphragmatic breathing while during rib cage breathing the situation improved. The situation is likely to be exaggerated during postural stress. On the basis of these observations it may be concluded that during inspiration the venous return from the abdomen to the thorax is maintained while the upward flow from the legs into the abdomen is restricted. During expiration, the abdomen to thorax flow continues because of the positive pressure gradient which is maintained between these regions(35) while the upward flow from the legs into the abdomen is reestablished. In certain situations like prolonged standing in the hyperlordotic posture during which the inferior vena cava may get compressed by Diaphragm at the thoraco-abdominal junction, the venous return from the legs may be impaired severely enough to precipitate a faint (8).

Hormones involved in the mediation of vasoconstrictor response

Noradrenaline released at the sympathetic nerve terminals is a potent vasoconstrictor of the resistance and the capacitance vessels (2). In experimental animals, selective destruction of noradrenergic fibres by injection of 6-hydroxydopamine causes a significant fall in blood pressure (31). Depletion of noradrenaline at the nerve terminals in humans brought about by the administration of drugs or because of disease produces postural hypotension (38). The level of the circulating hormone increases with increasing head up tilt (33), and with lower body negative pressure (17).

Angiotensin and vasopressin are also potent vasoconstricting agents during postural stress (3). The former produced by the renal renin-angiotensin system, may act directly on the vascular smooth muscle of the resistance vessels, may enter the cerebral spinal fluid at the area postrema (44) to influence sympathetic out flow in an unknown manner (31), or may potentiate the constrictor effect of noradrenaline (3). More recently it has been postulated that isorenin-angiotensin system present in the medullary regions may be more important in controlling peripheral vasoconstrictor tone (31). The role of vasopressin in modulating the tone of the resistance vessels is more controversial.In dogs this hormone was shown to have powerful constrictor influence on the muscle resistance vessels (1), and was released with a decrease in the tone of the low pressure cardiovascular receptors as well as the arterial baroreceptors (3). More recently, however, it has been shown in human subjects that eventhough moderate deactivation of the baroreceptors in the low and the high pressure vessels by graded lower body suction produces a high degree of sympathetic activation and an increase in circulating noradrenaline, only overt hypotension induces a significant increase in circulating vasopressin (17).

Changes in cardiac output

The cardiac output falls by about 19-20% on standing up from the recumbent posture (35,46). This is attributed to the reduction in the venous return to the heart which can only be partially compensated by constriction of the capacitance vessels (30). The stroke volume decreases by about 38% (46), but the reflex tachycardia limits the fall in the cardiac output. The application of graded postural stress by increasing the degree of head up tilt produces a progressive fall in the cardiac output until 20 deg HUT is reached, and thereafter there is no further fall in this variable because of the incremental increase in the heart rate, and also possibly because of an increase in the myocardial contractility produced by sympathetic excitation (4). Contrary to this, Matalon and Farhi (26) found that the fall in cardiac output and stroke volume in their subjects who were given incremental head up tilt stabilised at a tilt angle of 60 deg while the heart rate rise had stopped at 45 deg HUT. This suggests that between 60 deg - 90 deg HUT,the compensatory mechanisms limit any further reduction in the preload or that the hydrostatic pressure gradient which depends on the sine of the angle of the head up tilt (15,26)

is not severe enough after 60 deg tilt to produce any further peripheral pooling. More recently we have seen that the cardiac output computed from the left ventricular ejection time by the method of Harley et al (20) fell by about 17.5% in normal subjects tilted 70 deg head up, while the stroke volume fell by about 36% with a compensatory increase in the heart rate (11). The evidence therefore points out that eventhough compensatory mechanisms come into play, the fall in cardiac output during postural stress can be only partly compensated by the sympathetic reflex venoconstriction and the tachycardia.

Left ventricular function during postural stress

Postural stress was expected to result in an increase in myocardial contractility because of the sympathetic excitation produced (45). On the contrary, we have recently reported that myocardial contractility computed from the systolic time intervals as recommended by Weissler et al (48) was reduced during postural stress given by 70 deg head up tilt in normal young male subjects, and was seen as a significant prolongation of the pre-ejection period (PEP) and the PEP:left ventricular ejection time ratio (12). Both the findings are indicative of compromised left ventricular function (48). Application of increasing lower body suction at the level of the iliac crests produced an incremental fall in the cardiac output and the stroke volume (28), and reduction in myocardial contractility evaluated from systolic time intervals (19). The latter workers attributed the reduction of myocardial contractility to a combination of a decrease in preload and an increase in the after-load produced by the peripheral vasoconstriction.

From the above discussion the complexity of the reflex cardiovascular response to postural stress becomes evident. The reflex arc can be theoretically interrupted anywhere in the chain, and its failure to produce the so called normal reaction to the stress viz., the reflex tachycardia and the increase in peripheral vascular tone (in the resistance and the capacitance vessels) may result in an incapacitating postural hypotension. If it occurs in aircrew during flight, the end result could be disastrous. It is because of this that a detailed clinicophysiological assessment of the cardiovascular system is carried out in individuals who have been selected for special missions (9) or in patients who have had an episode of syncope (10).

Intolerance to postural stress in normal young subjects has been reported regularly in western literature (21, 41). However, in a large series of 166 head up tilt table tests in normal military men, we failed to see syncopal reactions (10). It often becomes extremely difficult to determine whether a subject who has had a fainting attack is normal in the true physiological sense or not.

Abnormal response to postural stress is usually classified as asympathicotonic or sympathicotonic (15, 27). The former is the more serious variety, occurring in patients with neurological disorders such as diabetic autonomic neuropathy, tabes dorsalis and the Shy-Drager's syndrome (5). In this type of

reaction there is no reflex tachycardia on assuming postural stress, while the blood pressure falls without any obvious peripheral vasoconstriction. Detection of such response is therefore relatively simple,and detailed clinical examination and investigations will more often than not bring out the pathology involved. However, when postural hypotension occurs in an otherwise normal individual, it often becomes extremely difficult to establish the reason for the episode. In such individuals, the sympathicotonic type of reaction is commonly seen in which the initial normal response to the stress is interrupted by a sudden tachycardia followed by hypotension with various signs and symptoms of pre-syncope and/or frank syncope.

Why should the normal compensatory mechanisms prove to be inadequate in such persons? It is possible that the postural stress lasts for too long a period, and the pooling of blood in the periphery continues to flourish in spite of the compensatory mechanisms. If associated with heat exposure, the peripheral pool formation may be enhanced because of the dilatation of the skin blood vessels. Emotional distress, fear, anxiety, pain and discomfort may precipitate a reflex dilatation of the resistance vessels (7, 39). Standing in the hyperlordotic posture(as on parade) can interrupt venous return by compressing the inferior vena cava at the thoraco-abdominal junction (8). A pre-existing reduction in circulating fluid volume because of dehydration (as in heat exposure, vomiting, fluid deprivation) or haemorrhage can further aggravate the situation. The possible sequence of events can be as follows. A hyperexcitation of sympathetic nervous system occurs because of sudden fall in central blood volume. This produces a marked tachycardia, and an increase in myocardial wall tension. During this phase the ventricles tend to beat on near empty chambers to stimulate the ventricular pressure receptors and activate a vaso-depressor reflex which produces a precipitous fall in the arterial blood pressure and the heart rate (43). The subject recovers rapidly on cessation of the postural stress when the temporarily sequestered circulating blood volume is rapidly restored to normal. A careful search for the precipitating factors must therefore be carried out in such apparently normal individuals who have undergone an episode of the common vaso-vagal faint in order to arrive at a conclusion as to the cause. Even after this, it is difficult to predict in such individuals as to whether the episode will recur or not. Repeated postural stress tests at regular intervals may be done in order to establish this. Their interpretation however must be based on a sound appreciation of the physiological response of the cardiovascular system to the stress.

References

1. Abboud FM:Vascular responses to norepinephrine, angiotensin, vasopressin and serotonin. Fed Proc 27:1391, 1968.

2. Abboud FM,Schmid PG and Eckstein JW: Vascular responses after alpha adrenergic receptor blockade - I.Responses of capacitance and resistance vessels to norepinephrine in man. J Clin Invest 47:1, 1968.

3. Abboud FM, Heistad DD, Mark AL and Schmid PG: Reflex control of the peripheral circulation. Prog Cardiovasc Dis 18:371, 1976.

4. Abboud FM, Eckberg DL, Johannesen UJ and Mark AL:Carotid and cardiopulmonary baroreceptor control of splanchnic and forearm vascular resistance during venous pooling in man. J Physiol (Lond) 286:173, 1979.

5. Bannister R: Testing autonomic reflexes. IN Autonomic Failure, edited by R Bannister, Oxford, Oxford Medical Publications, 1983, p 52.

6. Bjursted S,Rosenhamer G and Tyden G: Acceleration stress and effects of propranolol on cardiovascular responses. Acta Physiol Scand 90:491, 1969.

7. Blair DA, Glover WE and Greenfield ADM: Excitation of cholinergic vasodilator nerves to human skeletal muscles during emotional sress. J Physiol(Lond) 148:633, 1959.

8. Bridgen W, Horvath S and Sharpey-Schaefer EP: Postural blood flow of normal subjects with observations on vasovagal fainting reactions as a result of tilting,lordotic posture, pregnancy and spinal anaesthesia. Clin Sci 9:79, 1950.

9. Dikshit MB,Banerjee PK, Kulkarni JS, Iyer EM and Singh MM: Medical evaluation of cosmonauts - Physiological stress testing. Aviation Medicine 28: 107,1984.

10. Dikshit MB,Banerjee PK and Rao PLN: Orthostatic tolerance of normal Indians and those with suspected abnormal cardiovascular reflex status. Aviat Space Environ Med 57:168, 1986.

11. Dikshit MB,Banerjee PK, Rao PLN and Iyer EM: Left ventricular ejection time based cardiac output changes in pilots and non-pilots during orthostatic stress. Ind J Med Res 83:301, 1986.

12. Dikshit MB,Banerjee PK, Rao PLN and Iyer EM: Systolic time intervals in pilots and non-pilots during 70 deg head up tilt. Aviat Space Environ Med 57:332, 1986.

13. Epstein SE, Stampfer M and Beiser GD: Role of capacitance and resistance vessels in vasovagal syncope. Circulation 37:524, 1969.

14. Ewing D J, Hume L, Campbell I W, Murray A, Nielson J M M and Clarke BF: Autonomic mechanisms in the control of initial heart rate response to standing. J Appl Physiol 49:809, 1980.

15. Gauer OH and Thron HL: Postural changes in circulation. Handbook of Physiology. Section 2, Circulation III. Washington, DC, Amer Physiol Soc, 1966, p 2409.

16. Glick G and Yu PN: Haemodynamic changes during vasovagal reactions. Am J Med 34:42, 1963.

17. Goldsmith SR, Francis GS, Cowley AW and Cohn JN: Response of vasopressin and norepinephrine to lower body negative pressure in humans. Am J Physiol (Heart and Circ Physiol 12) 243:1970, 1982.

18. Grassi G, Gavazi C, Cessura A, Picotti G B and Mancia G: Changes in plasma catecholamines in responses to reflex modulation of sympathetic

vasoconstrictor tone by cardiopulmonary receptors. Clin Sci 68:503, 1985.

19. Grayboys TB,Forlini JF and Michaelson ED: Systolic time intervals during lower body negative pressure. J Appl Physiol 37:329, 1974.

20. Harley A, Starmer CF and Greenfield JC: Pressure flow studies in man. An evaluation of the duration of the phases of systole. J Clin Invest 48:895, 1969.

21. Hickler RB, Hoskins RG and Hanilin JT: The clinical evaluation of faulty orthostatic mechanisms. Med Clin N Am 44:1237, 1960.

22. Leon DF, Shaver JA and Leonard JJ: Reflex heart rate control in man. Am Heart J 80:729, 1970.

23. Lind AR,Leithead CS and McNicol GW: Cardiovascular changes during syncope induced by tilting men in the heat. J Appl Physiol 25:268, 1968.

24. Leopkky J: Cardiorespiratory responses to orthostasis and the effects of propranolol. Aviat Space Environ Med 46:1164, 1975.

25. Low PA, Walsh JC, Huang CY and Macleod JG: The sympathetic nervous system in diabetic neuropathy. Brain 98:341, 1975.

26. Matalon SV and Farhi LE: Cardiopulmonary readjustments in passive tilt. J Appl Physiol (Respirat Environ and Exercise Physiol) 47:503, 1979.

27. Muira M and Reis DJ: The role of the solitary and the paramedian reticular nuclei in mediating cardiovascular reflex responses from carotid baro and chemoreceptors. J Physiol(Lond) 223: 525, 1972.

28. Murray RH,Thomson LJ, Bowers JA and Albright CD: Haemodynamic effects of graded hypovolemia and vasodepressor syncope induced by lower body negative pressure on the cardiovascular system. Am Heart J 76:799, 1968.

29. Pickering TG, Gribbin B and Sleight P: Comparison of the reflex heart rate response to rising and falling arterial pressure in man. Cardiovasc Res 6:277, 1972.

30. Rapport E, Wong M, Escobar EE and Martinez G: The effect of upright posture on right ventricular volumes in patients with and without heart failure. Am Heart J 71:146, 1966.

31. Reid JL: Central and peripheral autonomic control mechanisms. IN Autonomic Failure, edited by R Bannister, Oxford Med Publications, 1983, p 17.

32. Robinson BF, Epstein SE, Beiser GD and Braunwald E: Control of heart rate by the autonomic nervous system. Circ Res 19:400, 1966.

33. Rosenthal T, Birch M, Osikowska B and Sever PS: Changes in plasma noradrenaline concentration following sympathetic stimulation by gradual tilting. Cardiovasc Res 12:144, 1978.

34. Rowell LB, Detry JMR, Blackman JR and Wyss C: Importance of the splanchnic vascular bed in human blood pressure regulation. J Appl Physiol 32:213, 1972.

35. Rushmer RF: Cardiovascular Dynamics

4th Ed, Toranto, WB Saunders Co, 1976.

36. Samaucloff SL, Browse NL & Shepherd JT: Response of capacity vessels in human limbs to head up tilt and suction on lower body.J Appl Physiol 21:47,1966

37. Schneider PB: Orthostatic hypotension. Arch Int Med 110:240, 1962.

38. Sever PS: Plasma noradrenaline in autonomic Failure.IN Autonomic Failure, edited by R Bannister, Oxford, Oxford Med Publications, 1983, p 155.

39. Sharpey-Schaefer EP, Hayter CJ and Barlow ED: Mechanisms of acute hypotension from fear or nausea. Brit Med J 11:878, 1958.

40. Shepherd JT: Role of the veins in the circulation. Circulation 33:484, 1966.

41. Shvartz E. and Meyerstein D: Tilt tolerance of young men and young women. Aerospace Med 41:253, 1970.

42. Sjostrand T:The regulation of blood distribution in man. Acta Physiol Scand 26:312, 1952.

43. Sleight P: Cardiac vomiting. Brit Heart J 46:5, 1980.

44. Spokes EGS: Neurochemistry of autonomic failure. IN Autonomic Failure, edited by R Bannister, Oxford, Oxford Medical Publications, 1983, p 155.

45. Tuckman J and Shillingford: Effect of different angles of tilt on cardiac output, heart rate and blood pressure. Brit Heart J 28:32, 1965.

46. Wang J,Marshall R.J and Shepherd JT: The effect of changes in posture and of graded exercise on stroke volume in man. J Clin Invest 39:1051, 1960.

47. Weissler AM,Warren JV, Estes Jr EH, McIntosh HD and Leonard JJ: Vasodepressor syncope. Circulation 15:875, 1957.

48. Weissler AM,Harris WS and Schonfeld CD: Systolic time intervals in heart failure in man. Circulation 37:149, 1968.

49. Willeput R, Rondeux C and De Troyer A: Breathing affects the venous return from the legs in man. Bull Physiopath Resp 20:5A, 1984.