THE CARDIOVASCULAR REFLEXES

H. B. KEENLEYSIDE, M D *

THIS REVIEW is an attempt to discuss briefly some of the extremely diverse autonomic reflexes that affect the cardiovascular system. A large number of widely varied reflex phenomena are active in normal physiology, pathological physiology, and during surgical procedures.

The carotid sinus and aortic depressor reflexes constitute a mechanism of the utmost importance in the regulation of blood pressure (1). Pressoreceptors situated in the carotid sinus and aortic arch are tonically activated at any blood pressure above approximately 70 mm. Hg. (2, 3). The higher the arterial pressure the more rapidly do individual receptors discharge impulses, and the larger the number of receptors excited. Below about 70 mm Hg, all pressoreceptor impulses cease. Thus when arterial pressure rises from normal to higher levels, pressoreceptors inhibit central vasomotor and cardio-accelerator tone. This results in vasodilatation, bradycardia, and reduction of blood pressure. As arterial pressure falls from normal to lower levels, pressoreceptor impulses decrease, and central vasomotor and cardio-accelerator tone rises. Thus vasoconstriction, tachycardia, and rise in blood pressure follow (1, 3, 4).

Early in haemorrhagic shock, the pressoreceptor reflexes maintain blood pressure by vasoconstriction, but when pressure levels fall to approximately 70 mm. Hg, the pressoreceptors are inactive, and unable to meet the emergency. However, the chemoreceptors of the carotid and aortic bodies become more active as blood pressure falls, and serve to forestall further reduction in pressure. The carotid and aortic body chemoreflexes, unlike the pressure reflexes, are an emergency mechanism for blood pressure maintenance. The chemoreceptors are maximally active under severe conditions, and require anoxia and hypercapnia as stimuli to activity. Although the pressoreceptor reflexes are easily depressed by anaesthetics, the chemoreceptors are not (3). Kenney and Neil (5) have recently shown that chemoreceptors discharge vigorously in haemorrhagic shock. Haemorrhage leads to reduced excitation of pressoreceptors and reflex vasoconstriction, and intense constriction of arterioles supplying the chemoreceptors also occurs. Blood flow through the chemoreceptors is thereby reduced, tissue oxygen tension falls and carbon dioxide accumulates. The chemoreceptors then become active even though the oxygen tension of blood leaving the lungs may be normal. The result is an increase in vasoconstriction and tachycardia, and a tendency to sustain the blood pressure.

The sino-aortic mechanism has been known for many years to be vitally important in the regulation of the circulation. Recently it has been discovered that there are reflex mechanisms of great complexity in the heart and lungs; these reflexes may ultimately be shown to play an important part in control of the circulation (6, 7, 8). Daly and Verney (9) described the left heart reflex. They observed a reflex slowing of heart rate when left ventricular pressure is

*Department of Anaesthesia, McGill University, Montreal

raised. This reflex could supplement the aortic depressor reflex, and in fact there is histological evidence that stretch receptors in the aortic arch and left ventricle are part of the same system (6). The coronary chemoreflex (Bezold reflex) has aroused great interest (6, 8). A reflex fall of blood pressure and heart rate follows the injection of certain chemical substances into the coronary circulation. Substances which elicit the reflex are veratridine, serotonin, and adenosinetriphosphate, among others. Receptors for the reflex have not been found, but they must lie in the course of the coronary circulation. Serotonin is a substance released from disintegrating platelets, and adenosinetriphosphate may be liberated from damaged myocardium. Thus the possibility exists that circulatory collapse following coronary artery occlusion is partly reflex in origin.

A reflex fall of blood pressure and heart rate has been observed when the pressure in the pulmonary circulation is raised. This is the pulmonary depressor reflex (6). Its receptors lie in the pulmonary vascular bed. The purpose of this reflex may be to cause reflex systemic vasodilatation as a means of moving blood from the pulmonary to systemic circulation, when pressure rises to a dangerous height in the pulmonary vessels (8). Another depressor reflex is elicited by the injection of certain substances into the pulmonary circulation, or by inhalation of certain gases into the lower respiratory tract. This is the pulmonary depressor chemoreflex. It arises from receptors deep in the lung. Serotonin by injection and bromine by inhalation are two substances capable of evoking the response. The pulmonary chemoreflex may possibly become activated in pulmonary embolism. Experimentally, distension of the right or left pulmonary artery by a cuffed catheter produces no change in systemic blood pressure. Yet a profound fall of blood pressure and heart rate often accompanies multiple small pulmonary embolism. It has been suggested that serotonin, liberated from small pulmonary emboli, might activate the pulmonary chemoreflex and lead to circulatory collapse (6, 8).

These four depressor reflexes arising from the heart and lungs all have their afferent fibres in the vagi (6).

In the walls of the great veins and right atrium are vagal nerve endings which respond to changes in venous pressure. Much conflicting evidence concerning the physiological purpose of these nerve endings has accumulated (6, 7). Bainbridge (10) discovered that rapid infusions of large quantities of saline caused a reflex increase of heart rate. The stimulus for the reflex is presumed to be increased pressure in the great veins. Aviado and his colleagues (11) arrived at a completely opposite conclusion. These workers found that increasing the pressure in the isolated perfused right heart caused a reflex fall of blood pressure and heart rate. But it is not known what physiological purpose might be served by a depressor reflex caused by increased pressure in the right heart; the typical response in muscular exercise is cardiac acceleration and not slowing (8). Another reflex possibly arising from the right atrium was suggested by McDowall (12). He believed that reflex vasoconstriction following haemorrhage was due to a reduction of venous pressure in the great veins and right heart. He had insufficient evidence to support his view that the reflex arose from the venous side of the circulation. But Kenney and Neil (5) have shown that vasoconstriction

after haemorrhage occurs due to strong excitation of chemoreceptors. Thus the reflex originally described by McDowall as coming from the right heart may instead arise from the chemoreceptors (6, 13).

Reflexes causing changes in the circulation may be initiated by non-physiological stimuli during the course of surgical procedures. These reflexes exert deleterious effects on circulatory homeostasis. Such reactions usually arise when the plane of anaesthesia is light, since in this situation autonomic nerve pathways are active, at times even hyperactive. When reflexes of non-physiological origin occur during surgery, the homeostatic sino-aortic mechanism then functions in such a way as to oppose the untoward circulatory changes.

Stimulation of the carotid sinus during surgery of the neck may cause dangerous circulatory reactions (14). Pressure stimulation of a sensitive carotid sinus results in arterial hypotension and cardiac slowing or asystole. Hypersensitivity of the sinus reflex is most often found in elderly patients with arteriosclerosis or hypertension (15, 16). The reflex is also more active in hyperthyroid patients, and in those with infections of the neck (17). Lahey and Eversole (18) emphasize the necessity of differentiating the hypersensitive carotid sinus reflex from true cardiac arrest at operation. Asystole due to the sinus reflex is hardly ever fatal, and rarely persists longer than one minute after the initiating stimulus is removed. The sinus may be affected by external or internal pressure stimuli. External stimuli occur notably during thyroidectomy and incision of the cervical abscess in Ludwig's angina. The reflex may also follow pressure on the sinus by the anaesthetist's hand, or by shoulder braces used for support in the Trendelenburg position (19). Stephen, Nowill, and Martin (20) have noted the reflex after internal pressure stimuli. During the surgical repair of arteriovenous fistulae, hypotension and bradycardia may occur owing to increased pressure in the sino-aortic area. The injection of dye into the carotid artery for arteriograms may also initiate the reflex.

Burstein *et al.* (21) have studied the cardiocirculatory disturbances which may occur in intrathoracic surgery. Intercostal nerve stimulation due to rib periosteal scraping and rapid rib spreading may lead to auriculoventricular conduction defect, nodal rhythm, and arterial hypotension. Intrathoracic manipulations may cause direct vagus nerve stimulation and evoke sudden bradycardia and hypotension. The reactions following pleural incision are usually not severe. Arterial hypotension and bradycardia may result from manipulation of the pulmonary hilus, from direct mechanical pressure on the vagus nerve, or from traction on the oesophagus (21). Cardiac arrest has occurred following persistent traction on the hilus (22). Vagotomies should be performed low in the chest since the vagus nerve in this area is less sensitive to stimulation. The vagus at the level of the heart or higher in the chest is the most sensitive portion of the nerve (21). Manipulation of the pericardium, especially inflamed pericardium, results in severe reactions. They are more severe than those due to myocardial or intracardiac stimulation, and can be detected clinically as acute arrhythmias (23). Occasionally, severe reflex disturbances are observed at the time of ligation of the pulmonary artery and veins and clamping of the bronchus (24).

Mechanical irritation of the respiratory tract may cause bradycardia and hypotension by a vagal reflex (17, 25). The reflex may be set up by tracheal intubation, by inflation of an intratracheal cuff (26), or by mucus or gastric content inhaled into the larynx and trachea (27, 28). Reid and Brace (26) first described reflex bradycardia and cardiac arrhythmias following tracheal intubation. Since then there have been numerous reports of cardiac inhibition to the point of complete arrest due to intubation, and most ascribe the disturbances to a vagovagal reflex initiated in the respiratory tract (29, 30, 31). However, Burstein *et al.* (21) observed sinus tachycardia most frequently during intubation. Since then, King, Elder, Dripps *et al.* (32, 33), and Stephen, Martin, and Nowill (34) have also observed increase in heart rate and blood pressure following intubation.

Chemical irritation of the respiratory tract may also exert reflex effects on the heart (25). Johnstone (35) found that inhalation of cyclopropane or ether can produce bradycardia and serious cardiac arrhythmias, including cardiac arrest. This inhibition of the heart is probably caused by a vagal pulmocardiatic reflex initiated by stimulation of vagal nerve endings in the air passages by the anaesthetic agent. Atropine will prevent serious reflex inhibition of the heart resulting from the inhalation of irritant anaesthetic agents. Johnstone (36, 37) has also shown that ether will abolish ventricular arrhythmias associated with cyclopropane anaesthesia, probably by stimulation of the vagal pulmocardiatic reflex.

The exact nature of the celiac plexus reflex is controversial. Burstein and Rovenstine (38) described the reflex as due to increased tone of the splanchnic sympathetic nerves resulting from atropine administration, ether anaesthesia, and stimulation in the region of the celiac ganglion. They noticed that, during upper abdominal operations, the systolic blood pressure suddenly fell to a level almost as low as the diastolic pressure, though the diastolic pressure and pulse rate remained relatively normal. Burstein and Rovenstine believe that this marked narrowing of pulse pressure is probably due to diminished cardiac output. But the underlying mechanism for the reduction in cardiac output they did not explain. Reduced output of the heart could result from either reduced venous return or diminished force of cardiac contraction. Stimulation of the celiac plexus might lead to loss of tone of the great veins (39), and thus a reduction in venous return. Smith (40), however, believes that the reduced cardiac output is more likely due to decreased force of cardiac contraction. Experimentally, Burstein and Rovenstine (38) found that the celiac plexus reflex is intensified by atropine administration or vagal section, but alleviated by physostigmine. On the other hand, Smith (40) has recently observed that atropine will abolish a marked celiac plexus reflex. Smith therefore believes that the reduction in cardiac output is due to diminished force of cardiac contraction resulting from vagal inhibition of the heart.

Reflex circulatory changes during neurosurgery have been observed by Howland and Papper (41). The oculo-cardiac reflex is well known. The afferent limb of this reflex, the trigeminal nerve, is stimulated when a head rest presses on the eyes with the patient in the prone position. Bradycardia and hypotension result. An interesting series of disorders was observed during stimulation in various

parts of the cranium and its contents. The sites of stimulation were the galea pericranium, dura, cortical veins, and temporal and frontal lobes. Stimulation was either mechanical or by means of the electrocautery. The changes consisted mostly of cardiac slowing and arrhythmias, and were likely due to vagal inhibition of the heart. On two occasions manipulation of the dura provoked cardiac arrest. They also noted bradycardia and apnoea following stimulation of the uncus gyrus of the temporal lobe with the electrocautery. Bergner (42) reports a case of reflex cardiac arrest following the application of pressure to the floor of the fourth ventricle.

Finally, it is of interest and importance to mention the "mass autonomic reflex" exhibited by subjects with high spinal cord injuries. Guttman and Whitteridge (43) observed that subjects with transection of the spinal cord at or above the fifth thoracic segment suffered mass autonomic reflex activity when distension of the bladder occurred. Manifestations of the diffuse reflex response are vasoconstriction, severe hypertension, bradycardia, excessive sweating, flushing of the face, headache, and blockage of the nasal air passages. Although such sympathetic overactivity most frequently results from distension of the bladder, it may also follow stimulation of almost any portion of the paralysed trunk, extremities, or viscera (44). Ciliberti, Goldfein, and Rovenstine (44) report numerous instances of severe hypertension during general anaesthesia in paraplegics.

SUMMARY AND CONCLUSION

The carotid sinus and aortic arch pressure reflexes are of supreme importance in the regulation of the circulation. They are tonically activated by normal physiological stimuli.

The physiological rôle of the carotid and aortic body chemoreflexes in hemorrhagic shock has been described.

Certain recently discovered reflexes, which may be important in normal physiology, have been briefly mentioned.

The physiological purpose of the venous pressure receptors is not yet established.

Deeper planes of anaesthesia depress the sino-aortic pressure reflex mechanism, and on this account fall of blood pressure due to surgical trauma is liable to occur. Light planes of anaesthesia do not depress this protective compensatory mechanism. However, during light planes of anaesthesia certain detrimental reflexes may be evoked by non-physiological stimuli associated with surgical procedure. The nature of a number of these untoward reflexes—carotid sinus, intrathoracic, and celiac plexus—has been reviewed. Reflex disturbances occurring during neurosurgery and in individuals with spinal cord injuries have also been mentioned.

REFERENCES

1. BEST, C. H. & TAYLOR, N. B. *Physiological Basis of Medical Practice*, pp. 282-287 6th ed., Baltimore: Williams and Wilkins (1955)
2. KOCH, E., cited by (5)
3. MACINTOSH, F. C. *Lectures in Physiology*, McGill University (1954).

- 4 FULTON, J F. Textbook of Physiology, pp 764-767. 17th ed, Philadelphia and London Saunders (1955).
- 5 KENNEY, R A & NEIL, E The Contribution of Aortic Chemoceptor Mechanisms to the Maintenance of Arterial Blood Pressure of Cats and Dogs after Hemorrhage *J Physiol*, 112 223 (1951).
- 6 DAWES, G S Reflex Factors in the Regulation of the Circulation. Third Conference on Shock and Circulatory Homeostasis, pp 43-131 New York Josiah Macy, Jr. Foundation (1953)
- 7 ——— Reflexes from the Heart and Lungs. *Brit Med Bull* 8 324 (1952)
- 8 DAWES, G S & COMROE, J. H., Jr Chemoreflexes from the Heart and Lungs. *Physiol Rev*, 34 167 (1954).
- 9 DEBURGH DALY, I. & VERNEY, E B cited by (6)
- 10 BAINBRIDGE, F A, cited by (6)
- 11 AVIADO, D M., Jr, *et al*, cited by (6)
- 12 McDOWALL, R J S, cited by (6)
- 13 FULTON, J F (4), p 770
- 14 RUZICKA, E. R & EVERSOLE, U. H The Carotid Sinus in Anesthesiology. *Lahey Clin Bull* 3 47 (1942)
- 15 WEISS, S. & BAKER, J. P The Carotid Sinus Reflex in Health and Disease: Its Role in the Causation of Fainting and Convulsions *Medicine* 12 297 (1933).
- 16 JUDSON, W E Hypotension Physiologic Mechanisms and Treatment *Med Clin North America*, 37 1313 (Sept 1953)
- 17 COLLINS, V. J Principles and Practice of Anesthesiology, pp 300, 434 Philadelphia Lea and Febiger (1952)
- 18 LAHEY, F H & EVERSOLE, U H Differentiation of Hypersensitive Carotid Sinus Reflex and Cardiac Arrest on the Operating Table *Lahey Clin Bull*, 6 226 (1950)
- 19 BURSTEIN, C L Fundamental Considerations in Anesthesia, pp 77, 78 New York Macmillan (1949)
- 20 STEPHEN, C R, NOWILL, W K & MARTIN, R Diagnosis and Treatment of Hypotension during Anesthesia *Anesthesiology*, 14 180 (1953)
- 21 BURSTEIN, C L, PIAZZA, T L, KAPP, L A & ROVENSTINE, E A Cardiocirculatory Disturbances during Intrathoracic Surgery *Surgery*, 25 36 (1949)
- 22 CAMPBELL, S M Anaesthesia in Thoracic Surgery *Surg Clin North America*, 34 1007 (Aug 1954)
- 23 BURSTEIN, C L & ALEXANDER, F A D Anesthesia for Thoracic Surgery *Anesthesiology*, 8. 36 (1947)
- 24 CRANDELL, D L & ARTUSIO, J F, Jr Cardiovascular Reflexes during Intrathoracic Surgery *Anesth & Analg*, 32 227 (1953)
- 25 SCHERF, D Cardiac Reflexes Originating in the Respiratory Tract *New York State J Med*, 45 1647 (1945)
- 26 REID, L C & BRACE, D E Irritation of the Respiratory Tract and its Reflex Effect upon the Heart *Surg, Gynec & Obst*, 70 157 (1940)
- 27 LEE, J A A Synopsis of Anaesthesia, p 149. 3rd ed, London Wright (1953)
- 28 BAGGOT, M G, Common and Inter-related Complications of Anesthesia, Operations and Obstetrics *Anesth & Analg*, 33 1 (1954)
- 29 DRIPPS, R. D *et al* Cardiac Resuscitation *Ann Surg*, 127 592 (1948)
- 30 AMENT, R, PAPPER, E M & ROVENSTINE, E A Cardiac Arrest during Anesthesia *Ann Surg*, 134 220 (1951).
- 31 DWYER, C S, THOMAS, P B & STROUT, W G. Cardiac Arrest on Intubation *Anesth & Analg*, 32 123 (1953).
- 32 KING, B D *et al* Reflex Circulatory Responses to Direct Laryngoscopy and Tracheal Intubation Performed during General Anesthesia *Anesthesiology*, 12 556 (1951)
- 33 KING, B D *et al* Reflex Circulatory Responses to Tracheal Intubation Performed under Topical Anesthesia *Anesthesiology*, 15 231 (1954)

- 34 STEPHEN, C R, MARTIN, R & NOWILL, W K Cardiovascular Reactions of Sunital, Pentothal or Evipal Combined with Muscle Relaxants for Rapid Anesthesia Induction *Anesth & Analg*, 32 361 (1953).
- 35 JOHNSTONE, M W General Anaesthesia and Cardiac Inhibition *Brit Heart J*, 13 47 (1951)
- 36 ——— Cyclopropane Anaesthesia and Ventricular Arrhythmias *Brit Heart J*, 12 239 (1950)
- 37 ——— Adrenaline and Noradrenaline during Anaesthesia. *Anaesthesia*, 8: 32 (1953).
- 38 BURSTEIN, C. L. & ROVENSTINE, E. A A Reflex Complicating Anesthesia during Abdominal Surgery. *Anesth. & Analg.*, 17: 134 (1938).
- 39 GORDH, T Postural Circulatory and Respiratory Changes during Ether and Intravenous Anesthesia *Acta Chir Scand* 92, suppl 102 (1945)
- 40 SMITH, B H The Nature and Treatment of the Coeliac-Plexus Reflex in Man. *Lancet*, 265 223 (1953)
- 41 HOWLAND, W S & PAPPER, E M Circulatory Changes during Anesthesia for Neurosurgical Operations. *Anesthesiology*, 13 343 (1952)
42. BERGNER, R P Cardiac Arrest Some Etiological Considerations, with Reports of Seventeen Cases *Anesthesiology*, 16 177 (1955)
- 43 GUTTMAN, L & WHITTERIDGE, D Effects of Bladder Distension on Autonomic Mechanisms after Spinal Cord Injuries *Brain*, 70 361 (1947)
- 44 CILIBERTI, B J, GOLDFEIN, J & ROVENSTINE, E A Hypertension during Anesthesia in Patients with Spinal Cord Injuries. *Anesthesiology*, 15 273 (1954)