THE INNERVATION OF THE HEART

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Clinical and research workers are occasionally confronted by problems concerning cardiac innervation that may not be answered by the scanty details given in textbooks, and special articles usually deal with only one facet of the subject. A résumé of available information may therefore prove helpful.

The heart is innervated by both sympathetic and parasympathetic nerves, and afferents from the parietal pericardium are also conveyed through the intercostal and phrenic nerves. The autonomic nerves, like the somatic, are under the control of higher centres.

HIGHER CENTRES CONTROLLING VISCERAL ACTIVITIES

The idea that visceral functions are controlled by higher centres was expressed by Willis (1664), but despite many intervening suggestive observations Hughlings Jackson (1873–74) was the first to state clearly, as a result of his clinical and pathological observations, that visceral activities must be represented at various levels in the central nervous system. Until comparatively recently the cerebral cortex was regarded as of subsidiary or negligible importance in relation to the autonomic nervous system, but it is now recognized that there is both motor and sensory autonomic representation in the cortex, with overlapping and close integration of somatic, autonomic, and other cortical areas, a fact explaining the common association of somatic and visceral effects and the correlation between somatic, autonomic, and mental states. Evidence on these matters has been obtained mainly by comparative researches, and the observations reported by many workers on the autonomic effects produced by stimulation, section, or ablation of various parts of the brain and cord have been reviewed or evaluated by Spiegel (1932), Hoff (1940), Miller (1942), Gellhorn (1943), Bucy (1949), Walsh (1951), Cloake (1952), and others. They reveal how gradually the importance of the frontal cortex, hypothalamus, and brain stem in controlling visceral activities was established. Recently, information about autonomic representation in the human brain has begun to accumulate as a result of clinical, operative, and pathological observations (Penfield and Rasmussen, 1950; Meyer et al., 1947; Freeman and Watts, 1947, 1948; and Beck, 1950). These observations on the human brain tend to confirm in several respects the findings in animals, although the localization of centres, the pathways of the tracts involved, and the degree of response to stimulation are not always similar in man and animals. It can be stated, however, with reasonable certainty that the frontal lobes influence autonomic activities. This cortical participation in the control of visceral innervation is shared by subcortical centres in the hypothalamus, and perhaps in the corpus striatum and the anterior lobe of the cerebellum. These activities are correlated and integrated by two-way cortico-hypothalamic interconnections (Le Gros Clark, 1948; Le Gros Clark and Meyer 1950), directly or via relays in the thalamus. The hypothalamus in turn is linked to lower centres in the brain stem and spinal cord, such as the vagal nuclei and the cells in the lateral horns of grey matter in the cord, by tracts the exact course of which has not yet been determined precisely even in animals. Despite this, the existence of afferent and efferent pathways linking
the hypothalamus with lower centres in the brain stem and cord concerned with cardiovascular, respiratory, and other autonomic activities is undoubted.

Having stressed, albeit briefly, the importance of these higher centres in controlling autonomic activities, let us now consider the sources of the sympathetic and parasympathetic cardiac fibres.

**The Sympathetic Contribution**

The sympathetic fibres innervating the heart are the axons of cells located in the lateral (intermedio-lateral) grey columns of the upper 4–5 thoracic segments of the spinal cord. They are myelinated preganglionic fibres and they leave the cord in the ventral roots of the corresponding spinal nerves. They soon enter white rami communicantes passing to adjacent ganglia in the paravertebral sympathetic trunks. Some relay in these ganglia, but others run upwards in the trunks to the cervical ganglia before forming synapses with efferent or postganglionic neurons (Fig. 1). The postganglionic axons are unmyelinated or thinly myelinated, and those for the heart run in the various cardiac branches of the sympathetic trunks. Thus in the sympathetic component of the autonomic nervous system the synapses between pre- and post-ganglionic neurons are often at considerable distances from the structure innervated, e.g. some of the cardiac postganglionic fibres arise in the superior cervical ganglia and are lengthy. By contrast parasympathetic postganglionic fibres are short.

The afferent cardiac fibres in the sympathetic nerves are the peripheral processes of cells lying in the dorsal root ganglia of the upper 4–5 thoracic spinal nerves and the central processes enter the cord through the corresponding dorsal nerve roots. There they form synapses with cells in

![Fig. 1.—Diagram showing connections of sympathetic cardiac nerves. From higher centres in cortex, hypothalamus, and brain stem to neurons in lateral grey column of upper 4–5 thoracic cord segments—heavy continuous lines. Preganglionic fibres from lateral columnar cells to cervical and upper thoracic sympathetic trunk ganglia—dotted lines. Postganglionic fibres from trunk ganglia to cardiac plexus—less heavy, continuous lines. The afferent pathways are not indicated.](http://heart.bmj.com/)

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the posterior and lateral columns of grey matter and, like their somatic counterparts, they take part in the formation of reflex arcs and also transmit impulses to second relays of afferent neurons which convey information about visceral activities upwards to higher centres. In addition they give off collaterals which act as association fibres and assist in integrating activities in adjacent segments.

The Sympathetic Cardiac Branches. Three pairs of cardiac sympathetic nerves are derived from the cervical ganglia of the sympathetic trunks, and others come from the upper 4–5 thoracic ganglia (Fig. 2 and 3).

The superior cervical sympathetic cardiac nerve originates on each side from the lower part of the superior cervical ganglion or from the sympathetic trunk below it, and runs downwards near the trunk behind the carotid sheath. It usually unites with the corresponding vagal cardiac branches, and as the conjoined nerve descends it communicates through slender rami with the pharyngeal, laryngeal, carotid, thyroid, and recurrent laryngeal nerves. At the root of the neck it lies behind the subclavian artery. On the right side the nerve passes posterolateral to the innominate artery and aortic arch to the cardiac plexus: on the left side it lies in contact with the left common carotid artery and curves downwards across the left side of the aortic arch to the cardiac plexus. It always communicates with cardiac branches from the middle and inferior cervical sympathetic ganglia and occasionally unites with them or the corresponding vagal groups of cardiac nerves.

The middle cervical sympathetic cardiac nerve(s) is derived from the middle cervical ganglion or the adjacent part of the sympathetic trunk, and other filaments may be contributed to it by the vertebral ganglion (ganglion intermédiaire). It may proceed independently to the cardiac plexus, lying near and communicating with the superior sympathetic cardiac nerve, or it may coalesce with a vagal cardiac branch on one or both sides en route to the cardiac plexus. It is connected with the tracheal, cesophageal, and thyroid branches of the sympathetic trunks and is often the largest of the sympathetic cardiac nerves.

The inferior cervical sympathetic cardiac nerves consist of a variable number of filaments arising from the stellate ganglia and ansa subclavia, a single nerve being uncommon. They often combine with each other or with other cardiac nerves before entering the cardiac plexus, and inconstant twigs from them are sometimes attached to the delicate bundle of fibres connecting the phrenic nerve to the homolateral ansa subclavia.

The thoracic cardiac nerves (Fig. 3) consist of a variable number of filaments derived from the second to the fourth or occasionally fifth thoracic ganglia inclusive. When the first thoracic ganglion is not fused to the inferior cervical ganglion it also gives off a cardiac filament, but when a stellate ganglion is present (it exists in 75–80 per cent of human subjects) its inferior cardiac branches contain fibres from both ganglia.

The thoracic cardiac nerves run forwards and medially and some may enter the cardiac plexus directly, or they unite with neighbouring filaments destined for the trachea, cesophagus, aorta, or pulmonary structures and then separate again into their component elements as they approach the structures to be innervated; this can be shown by microdissection. The lowest thoracic cardiac filaments are interconnected with the upper rootlets of the para-aortic nerve (Mitchell, 1938, 1947).

Efferent accelerator and some afferent fibres from the heart and great vessels pass through these nerves, and because of their importance in the treatment of angina pectoris (White and White, 1928; Govaerts, 1936; White, 1940; Lindgren and Olivierona, 1947; and White and Bland, 1948) they have aroused considerable interest. They were rediscovered comparatively recently (Braeucke, 1927; Ionesco and Enachescho, 1927), but as Mitchell (1949) showed, thoracic cardiac branches had been demonstrated at least one hundred years earlier by E. H. Weber (1815) in a calf and by Swan (1830) in man.
Fig. 2.—The left side of the neck and upper thorax showing the main branches of the left sympathetic trunk and vagus nerve in these regions. To avoid overloading the picture many of the finer filaments, which cannot be seen clearly without the aid of a dissecting microscope, are not shown.
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The Parasympathetic Contribution

The cardiac parasympathetic fibres are carried in the vagi and in the cranial parts of the accessory nerves that join them. The cardiac preganglionic fibres are myelinated and originate in the dorsal vagal nucleus and from a group of cells partially commingled with the nucleus ambiguus. Both these nuclei are elongated columns of cells lying in the medulla oblongata. The cardiac fibres are conveyed to their terminations in the vagus nerves and their branches, and they end by forming synapses with postganglionic neurons in ganglia in the cardiac plexus or in the wall of the heart. Synaptic relays close to or within the viscous supplied are characteristic of parasympathetic innervation and in consequence parasympathetic postganglionic fibres are relatively short compared with their sympathetic counterparts, and more circumscribed in their distribution. This is one reason why parasympathetic effects are more localized than sympathetic effects.

The dorsal vagal nuclei are of mixed type and represent fused efferent and afferent columns of neurons. The visceral afferents ending in these nuclei are the central processes of cells located in the inferior vagal (nodose) ganglia, situated on the vagus nerves just below the jugular foramina and the peripheral processes of these cells are distributed through the vagi and their branches to receptor endings in the heart, great vessels, and the many other structures supplied by these nerves.

After emerging from the skull through the jugular foramina each vagus nerve descends through the neck in the carotid sheath, lying behind and between the internal jugular vein and the internal and common carotid arteries.
The right vagus nerve enters the thorax by crossing the first part of the subclavian artery, behind the right internal jugular vein, and gives off its recurrent laryngeal branch. Descending posterior to the right innominate vein, it then inclines posteromedially behind the superior vena cava and medial to the vena azygos to reach the right side of the trachea and the root of the right lung. The left vagus nerve enters the thorax between the left common carotid and subclavian arteries, behind the corresponding innominate vein, descends across the left side of the aortic arch where it gives off its recurrent laryngeal branch, and then reaches the root of the left lung. The further course, connections, and distribution of these nerves need not be described here.

The Parasympathetic Cardiac Branches. These are variable in their size, number, and distribution, and arise from the vagi both in the neck and thorax (Fig. 2 and 3). The variability is apparent if one compares the descriptions and illustrations of these branches in the works of Walter (1783), Scarpa (1794), Swan (1830), Valentin (1843), Bourgery (1844), Hirschfeld and Leveille (1853), Schwalbe (1881), Sobotta and McMurrich (1907), Mollard (1908), Müller (1924), Braeucker (1927), Hovelacque (1927), Arnulf (1939, 1950), Hantz (1951), and many others, and one has confirmed it by personal observations. However, a general pattern is evident, and the cardiac branches may be divided into three groups—superior, middle, and inferior; all are interconnected at various levels with sympathetic branches, and sometimes with other nerves.

The superior vagal cardiac branches are two or three filaments which leave the vagus nerve in the upper part of the neck and after a short course they almost invariably join the homolateral superior cervical sympathetic cardiac nerve (p. 161). They often communicate with the vagal pharyngeal and laryngeal branches and occasionally with the carotid sinus and descendens cervicalis nerves.

The middle group consists of one to three branchlets arising in the lower third of the neck. They communicate with the sympathetic cardiac nerves and may unite with them, most commonly with those arising from the middle, vertebral, or inferior cervical ganglia. If they remain separate they pass directly to the cardiac plexus, lying posterolateral to the innominate artery and aortic arch on the right side, and lateral to the left common carotid artery and/or subclavian artery and aortic arch on the left side. Branches curve around the roots of the subclavian arteries, or on the right side around the innominate artery, to reach the anterior surface of the ascending aorta where they assist in the formation of the pre-aortic plexus.

The inferior vagal cardiac branches arise from the main nerve at the cervicothoracic inlet or within the upper thorax. Cardiac twigs from the right recurrent laryngeal nerve join one derived from the vagus nerve in the superior mediastinum, and this conjoint nerve may also unite with one or more thoracic cardiac sympathetic nerves before passing on the right side of the aortic arch to the cardiac plexus. On the left side one fairly large vagal branch usually detaches itself above the level of origin of the left subclavian artery and runs across the left side of the aortic arch to the cardiac plexus. In addition, the left recurrent laryngeal nerve and the parts of the vagus nearby invariably give off a number of filaments which end in the adjacent part of the cardiac plexus.

A few ganglion cells may be detected microscopically along the course of both sympathetic and parasympathetic cardiac nerves, becoming more numerous as the heart is approached.

The Cardiac Plexus

The various vagal and sympathetic cardiac nerves end in this plexus (Fig. 3) and in it they lose their individual identities, if they have not done so already through fusion with other nerves, although in some lower animals the right and left groups of nerves remain separate and are distributed mainly to the corresponding sides of the heart.

It is customary to describe the cardiac plexus as consisting of superficial (anterior) and deep (posterior) parts, and some have subdivided it still further. The superficial part, lying in the concavity of the aortic arch, usually receives the superior cervical sympathetic and inferior vagal cardiac nerves of the left side. The deep part, which lies behind the aortic arch and anterior to
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the tracheal bifurcation, receives all the other vagal and sympathetic cardiac branches. Actually, subdivisions of this nature are artificial, as there is comparatively little difference between the depth of the so-called superficial and deep parts; besides, both are interconnected so freely that they may be regarded as a single unit, although some tendency to division into right and left halves is sometimes apparent, and from these the right and left coronary nerves mainly arise.

However, there is a more superficial part of the plexus lying anterior to the ascending aorta and termed the pre-aortic plexus (Arnulf, 1939, 1950). It is tenuous in nature and is formed mainly by filaments from the left vagal and sympathetic cardiac nerves, which incline forwards to reach the anterior surface of the ascending aorta (Fig. 2). It is always reinforced by a few twigs from the corresponding nerves of the right side, which curve around the innominate artery to join the plexus.

Several ganglia, in which a proportion of the vagal preganglionic fibres relay, are present in the plexus. The largest, the ganglion of Wrisberg (1800), usually lies below the aortic arch, between

![Fig. 4.—Branching bundles of nerve fibres in subepicardium of left atrium (x90). The following details apply to all the photomicrographs reproduced, and will not be repeated in subsequent legends. Sections are from the rabbit and are stained with combined intravital and supravital methylene blue. The relative lack of background detail is explained by the fact that, owing to the thickness of the sections used, partial preliminary clearing in glycerine ammonium picrate was necessary before microscopy was possible.](image)

the tracheal bifurcation and the division of the pulmonary trunk. Other minute parasympathetic ganglia are located in the wall of the heart, mainly in the atria and interatrial septum and in areas near the roots of the great vessels. These lie in the subepicardial tissue and are termed intrinsic
cardiac ganglia. In man and most mammals they are scarce or absent in the ventricles (Davies et al., 1952).

Filaments from the right and left halves of the cardiac plexus converge towards the coronary arteries, forming subsidiary plexuses around them and sending offshoots along their various branches. Other slender twigs from the cardiac plexus pass directly to adjacent parts of the heart, pericardium, aorta, superior vena cava, and pulmonary vessels. The nerves lie initially in the subepicardial tissue and branch within it (Fig. 4 and 5), communicating with adjacent filaments through delicate strands. Some fibres innervate the vessels and epicardium, others penetrate and supply the myocardium (Fig. 6), and a number reach the subendocardial tissue where they unite with other similar fibres to form a fine network (Fig. 7). The fibrous pericardium (Fig. 8) is probably supplied chiefly by the phrenic and intercostal nerves and its sensitivity is of somatic rather than autonomic type.

**CARDIAC AFFERENT AND EFFERENT NERVES**

All the cardiac nerves contain both afferent and efferent fibres, with the exception of the branches derived from the superior cervical sympathetic ganglia which are believed to transmit only efferent fibres.

The idea of autonomic afferents may conflict with some preconceived notions, but many visceral fibres in sympathetic and parasympathetic nerves are afferents, and the conception of the autonomic nervous system as purely efferent is a misconception. There are no fundamental differences between the somatic and autonomic components of the nervous system in this or other respects. They originate from the same primordial cells, they develop together, they are built up from the same basic units or neurons associated in similar reflex arcs, they comprise central and peripheral parts, and structurally they are always related and often closely connected. Any separation, therefore, is artificial rather than fundamental, and is based chiefly on functional grounds.

*Afferents.* The afferent fibres are the processes of cells in the inferior vagal ganglia and in the dorsal root ganglia of the upper 4–5 thoracic spinal nerves. The central processes of the vagal
fibres end mainly in the homolateral dorsal vagal nucleus, but others, or axon collaterals, end in the heterolateral nucleus, in the cardiac nucleus adjacent to the nucleus ambiguus, or in the grey matter of the formatio reticularis. The central processes of the spinal fibres end by forming synapses around cells in the posterior and lateral grey columns of the cord. One has mentioned already that both vagal and spinal fibres take part in the formation of reflex arcs, and that impulses are also carried upwards to higher levels in the brain stem, hypothalamus, thalamus, and cortex.

The peripheral processes of the cells in the vagal and dorsal root ganglia reach the heart and related structures through the cardiac branches of the vagi and sympathetic trunks and, thereafter, through the cardiac plexus and its offshoots. They do not relay in any of the extrinsic or intrinsic cardiac ganglia, but terminate in free endings, spirals, networks, and in other structures of a reputedly sensory nature, which are receptive to pain, stretch, pressure, chemical, and other stimuli. These are present in the subepicardium, between the cardiac muscle fibres, in the subendocardium, in the aortic arch bodies, and in the coronary arteries, aorta, and other great vessels passing to and from the heart. Many of the terminal nerve fibrils are beaded or varicose. The impulses originating in these structures are transmitted to the central nervous system via sympathetic and parasympathetic afferent fibres and are involved in cardiac and vasomotor regulatory mechanisms.

Many of the afferent vagal fibres from the heart and great vessels (Fig. 9) are concerned in reflexes that depress cardiac activity and in some animals they are aggregated in a separate vagal component, the depressor nerve (Cyon and Ludwig, 1866–67); in man these fibres may run in cardiac filaments of the vagal laryngeal nerves (Mollard, 1908).

Afferent pain fibres from the heart and aorta are conveyed mainly or entirely through the middle and inferior cervical and the thoracic sympathetic cardiac nerves, but those carried in the cervical nerves descend in the sympathetic trunks to the upper thoracic region, and all the fibres pass through rami communicantes to the upper 4–5 thoracic spinal nerves. Their cell stations are in the corresponding dorsal root ganglia, and the central processes of the cells enter the cord...
through these dorsal nerve roots. This explains why in the treatment of angina pectoris attention is concentrated on the upper thoracic sympathetic trunk ganglia and rami, or on the corresponding dorsal spinal nerve roots. Interruption of these pathways by injection or operative techniques suppresses pain of cardiac origin, although in a minority of patients referred pains may still be experienced in the region of the ear and lower jaw; this is abolished by injection of the mandibular nerve (Lindgren and Olivecrona, 1947), but persists after destruction of the superior cervical sympathetic ganglion (White and Bland, 1948). Presumably the afferents involved in such cases travel in the vagi; incidentally thick myelinated vagal fibres of afferent type end in the adventitia of the coronary arteries. The dull sense of oppression felt during anginal attacks in the suprasternal and supraclavicular regions is not abolished by complete sympathetic denervation of the heart, and this suggests that some cardiac or vascular afferents are conveyed through the phrenic nerves. These nerves supply fibres that enter the pericardium, and the left phrenic nerve contributes a filament or filaments to the left anterior pulmonary plexus, which is closely interconnected with the cardiac plexus. Thus some phrenic fibres could easily reach the heart and great vessels, either directly or through the cardiac plexus. The phrenic nerves could also receive cardiac afferent fibres through other interconnections, such as those between them and the stellate ganglia and their ansae, which also supply a group of cardiac nerves. There are other possible explanations of the persistent sense of oppression; a small proportion of the afferent fibres in the middle cervical sympathetic nerves may not descend to the thoracic region before entering the cord, but may enter it through the fifth, sixth, or seventh cervical nerves; or some afferents may travel upwards for a certain distance in the vagi and then pass through the constant communications that exist between them and adjacent branches of the cervical sympathetic ganglia.

Efferents. The parasympathetic cardiac preganglionic fibres arise on each side from a group of cells lying adjacent to the nucleus ambiguus and from the dorsal vagal nucleus. They are carried
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in the vagus nerve and its cardiac branches to the cardiac plexus where a proportion of the fibres form synapses in its ganglia. Others proceed through the plexus and relay in the intrinsic cardiac ganglia. The postganglionic or efferent fibres reach the cardiac muscle and the unstriated fibres in the vessel walls through the various branches of the cardiac and coronary plexuses described above.

The sympathetic cardiac preganglionic fibres originate from cells in the lateral (intermedio-lateral) grey columns of the upper 4-5 thoracic spinal cord segments, and the representation is inverted, the ventricular fibres arising above those for the atria. They reach the sympathetic trunks through the white rami communicantes between the upper thoracic spinal nerves and corresponding ganglia of the sympathetic trunks. Some form synapses in these ganglia and others ascend to the cervical ganglia before relaying, and the postganglionic or efferent fibres are conveyed to the cardiac plexus in the various cervical and thoracic sympathetic cardiac nerves already described. They do not relay in the cardiac ganglia, but pass in the various branches of the cardiac and coronary plexuses to the structures they supply.

The atria, the sinu-atrial node, and the atroventricular bundle are supplied by both vagal and sympathetic efferent fibres, and some of the fibres innervating the ventricles accompany this bundle. The available evidence suggests that the ventricular supply is predominantly although not entirely sympathetic, but the problem of whether conduction from the atria to the ventricles is myogenic, neurogenic, or a combination of both remains sub-judice, with the balance tilted in favour of the myogenic theory (Davies and Francis, 1952).

There is much argument about the exact mode of termination of autonomic efferent fibres in the heart and other visceral structures. A discussion of this problem is outside the scope of this communication. Suffice it to say that several observers have described small bulb and loop endings within the muscle fibres (Woollard, 1926), but others believe that the nerve fibres end by joining together in an extremely delicate terminal reticulum or syncitium (Fig. 10), while some go further and claim there is also a syncitial relationship between the terminal nerve fibres and the cells they innervate. This hypothesis has aroused much controversy, but if a terminal syncitium does exist in the autonomic nervous system, the neuron theory with its insistence on the anatomical discontinuity of all neurons and theories based on chemical mediation across hypothetical gaps will require revision. Eminent neurohistologists (Schabadash, 1930; Stöhr, 1932, 1950; Reiser, 1933; Boeke, 1940, 1949; Jabonero et al., 1951; and Jabonero, 1952) have propounded the idea of a terminal reticulum in the autonomic nervous system, and in the case of the heart it has received

FIG. 10.—Terminal nerve network around arteriole (× 700).
support from the studies of Vitali (1937), Meyling (1948), Akkeringa (1949), and Field (1951). The syncitial conception has been criticized, amongst others, by Nonidez (1936, 1937, 1939 and 1943), Maximow and Bloom (1948), and Weddell and Zander (1951).

In general the vagal efferent impulses produce slowing or inhibition of the heart and constriction of the coronary arteries. The sympathetic efferents produce cardiac acceleration and coronary dilatation. The effects on the coronary vessels are the reverse of those produced by sympathetic and parasympathetic nerves on most other vessels, and functionally this is understandable because increased and decreased cardiac activity necessitate a greater and lesser blood flow respectively.

**SUMMARY**

Visceral control by higher nervous centres is stressed.

The origins, pathways, and connections of the sympathetic and parasympathetic cardiac fibres are described.

Details are given of the sympathetic and vagal cardiac branches and of their communications with other nerves.

Information about the cardiac plexus, its ganglia and the mode of termination of its fibres is briefly reviewed.

The chief features of the cardiac afferents and efferents are epitomized.

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