CHAPTER II

HISTORICAL REVIEW.
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Although the investigations on the cardiovascular structures in the vertebrates have been made since the later part of the 15th century till date, yet very little study has been made on the innervation of these structures. A short historical review of all the previous investigators who have some sort of bearing on the present work is being given here.

Scarpa (1794) located ganglia at the base of the heart in man, calf and horse whereas Remak (1838) traced ganglia and nerves in the coronary sulcus of man. By 1875 many Russian and French observers had traced ganglia in the heart of vertebrates in support of the neurogenic theory. Ludwig, 1848; Bidder, 1852, '66, '88; Schweigger-Seidel, 1871; Langerhans, 1873; Gerlach, 1876; Fischer, 1877; Klug, 1881; Dogiel, 1882, '90; Retzius, 1892; Remon y Cajal, 1892; Berkley, 1894; Jacques, 1894; etc. observed the terminal nerve plexus in the myocardium of amphobians and other lower vertebrates.

Tawara (1906), in his monograph, 'Das Reizleitungssystem des Saugetierherzens', described numerous nerve fibres accompanying the atrioventricular bundle and its branches. Imchanitzky (1908) described the nervous co-ordination of the auricles and ventricle of the heart of the lizard. Wilson, 1909; Engel, 1910; Meiklejohn, 1913;
and Scaglia, 1927, all found nerves within the bundle but considerable species differences were reported. Woolard (1926) claimed that very fine fibres of the intracardiac network actually penetrated the substance of individual heart-muscle fibres and ran therein for considerable distances giving off at intervals small terminal loops and swellings. Similar observations were also made by Boeke (1932).

Glomset and his co-workers (1941, 48, '45, '52) observed the nervous tissue in abundance in the atria, atrioventricular groove and the ventricles of equine, porcine, bovine, ovine, canine, and human hearts. Numerous nerve fibres and ganglion cells were also observed by them in the periphery of the atrioventricular node, and on the top of the bifurcation of the bundle. They further observed that nerve fibres follow the Purkinje strands wherever they go. Nerve fibres and ganglion cells form approximately one-half of the Purkinje bundle. They observed large nerve trunks in the sulcus terminalis, and among the muscle fasciculæ in the ventricles.

Walls (1942) observed the cardiac ganglia in relation to the atria but the sinuatrial node was seen to have a poor nerve supply and the atrioventricular bundle totally devoid of nervous tissue. Nonidez (1943)
studied the structure and innervation of the conducting system of the heart of dog and rhesus monkey and suggested that the rich parasympathetic nerve supply to the atrio-ventricular node as compared with the innervation of the sinu-atrial node may account for such phenomenon as the production of atrioventricular block through electrical stimulation of vagus and questioned the parasympathetic innervation of the ventricles.

Truex and Copenhaver (1947) in their studies on the histology of moderator band in man and other mammals observed several large nerves in fascicles crossing the band, and delicate pale staining nerve fibres in intimate contact with the surfaces of the Purkinje fibres. Akkeranga (1949) also studied the nervous system of the Purkinje Fibres in the vertebrate heart. In the translations of Wilhelm His J r. (1863-1934) publications, Bast and Gardner (1949) have stated that in the vertebrates of all classes the heart beat in an adult manner before it contained cerebro-spinal nerves or ganglia. Unipolar cells were observed in fishes and amphibians whereas multipolar cells were observed in the birds and mammals. They have further mentioned that because of the positional relationship of the heart to the mouth cleft and the head ganglia, it follows that in fishes and amphibians the
entrance occurs only along the trunk of the superior venacava; thus the largest and earliest ganglionic masses are found at the sinus venosus whence the nerve trunks, and cell groups proceed toward the atria and ventricle. In the chicken, as well as in man and the cat, the entrance occurs along the arteries. In the space between the aorta and the pulmonalis, there arises the bulbar plexus which sends out the coronary nerves. Later, along the veins, other nerves and ganglia masses appear in the region of the sinus venosus and the posterior wall of the atria.

Hemingway (1950) has pointed out that unilateral removal of the second and fifth thoracic sympathetic ganglia leads to some slowing of the heart and diminishes the response to exercise. He quotes Chapman et al (1948) to emphasize that in spite of considerable individual variation section of the right side seems to have greater affect on the heart rate than the section of the left side. Conti (1950) studied the different segments of the conductive system on human hearts and observed in each segment some ganglionic cells either isolated or grouped as small ganglia. Baird and Robb (1950) observed nerve cells and ganglia in the interatrial septum and just anterior to the atrioventricular groove in dorsal and ventral portions of the septum, but not in the A-V node,
the bundle or its branches in the heart of a puppy. Small bundles were also observed in the interatrial septum in the region of the atrioventricular node. No cell bodies were located in the node, bundle or its main branches. Nerve cells were observed in the interatrial septum and according to them they were presumably parasympathetic in nature. Nerves accompany the septal blood vessel.

Tcheng (1951) completed the observations of Nonidez (1939, '43) by the method of impregnation of silver of Weber, and observed that the nervous threads are less numerous in the wall of the right ventricle than in that of the left ventricle. Field (1951), in ascertaining the nervous components of the heart of sheep, rabbit, rat, guineapig, dog, macaque, chimpanzee, gorilla and man pointed out that the vagus nerve was responsible for depressing the activity of the conducting system. According to him the nerve fibres present within the atrioventricular bundle are responsible for regulating the conduction of the cardiac stimulation of the contraction. Glomset and Cross (1952) have reconfirmed the findings of Smirnoff (1900) who thought that every muscle fibre within the heart is supplied with motor nerve endings.

Davies, Francis and King (1952) located unipolar, bipolar and multipolar nerve cells in the heart of a
few mammals studied by them. They inferred that the multipolar cells are efferent and the unipolar and bipolar cells are afferent in function. According to these authors the nerves related to the A-V bundle are involved in the conduction of the impulse of cardiac contraction from atria to ventricles. Nomura (1952) did also study the structure, distribution and innervation of the special heart system of the mouse.

Licata (1954) studied the cardiac innervation in the human embryonic heart in the ninth week. Cardiac branches of the vagus nerve were seen to be fully developed and more easily distinguishable than those of the sympathetic trunks. It was seen that both divisions of the autonomic supply are represented in the ninth week heart, but the parasympathetic branches from the vagus are more highly developed than the sympathetic branches. Local aggregations of neuroblasts were found in many areas in relation to the heart and the great vessels. Truex et al (1955) studied the electrical stimulation of both vagus nerves to determine the effect of stimulation upon the electrocardiographic heart rate and undertook histologic study of the intrinsic atrial neural elements. These studies indicated that the post-ganglionic sympathetic fibres reached these cardiac
structures before the post-ganglionic parasympathetic
neural elements were fully developed.

Muir (1955) has stated that nervous structures
were found to be closely associated with the sinusatrial
node from the 18th day of prenatal life onwards in the
rodents. Rossi (1955) studied the anatomy, histology,
histochemistry, embryology and phylogensis of the
muscular atrioventricular system and of the nervous
system of the region of the septa and the fibrous centre
of the human heart. He also examined the gross and
microscopic pattern associated with abnormalities of
the conduction by studying both the specialized muscular
system and the intrinsic nervous structures of the
regions referred to above. He observed nervous elements
in abundance within, and in close proximity to the
system of His-Tawara.

Abraham and his co-workers (1937, '38, '57,
'58, and '59) have studied in detail the innervation
of the heart of different vertebrates. They observed
various species differences. The intrinsic innervation
in the heart of different vertebrates was not uniform.
The heart wall received the nerve elements from the
sympathetic as well as from the central nervous systems.
Mya-Tu (1957) published an excellent review entitled, "The spread of excitation in the mammalian heart". On the basis of the investigations of the previous workers it has been inferred that the spread of excitation in the mammalian heart is extremely complicated and that depends to a large extent on the architecture of the muscular walls and the distribution of the conducting system.

King and Coakley (1958) made a detailed study on the intrinsic nerve cells of the cardiac atria of mammals and man. The ganglia were observed round the opening of the superior venacava, in the dorsal part of the inter-atrial groove, in the upper part of the left atrium and along the whole length of the conducting system. Ganglia were also seen associated with the coronary sinus. Nerve cells were not observed within the specialized tissue of either the S-A-node or A-V node. The majority of nerve cells were multipolar.

Gomez (1958) studied the development of innervation of the heart in 56 prenatal rats ranging from 11 to 20 days of development and 8 new born rats. He observed that at 12 days the vagal and the sympathetic fibres are intermingled near the base of the heart. The simple nerve endings is the most common type observed in the various stages of the developing rats. Bulbs
and arborizations were also seen. He has suggested that the unmyelinated bundles which follow the small sub-epicardial vessels are sympathetic in nature.

Bellairs (1959) studied the development of the nervous system in chick embryos ranging from the primitive streak stage to 13 days of incubation. He examined the neural tissue under electron microscope. Abraham and Erdelyi (1959) noticed the presence of acetylcholinesterase in the cardiac conduction system of ungulates. The atrioventricular system included more cholinergic nerves than the sinuatrial system. This led the authors to infer that sympathetic effects are dominant in the sinuatrial and the parasympathetic ones in the atrioventricular system.

Hirsch and Borghezio (1961, '62) and Hirsch (1962, '63) recorded an abundant and extensive distribution of the large and small nerves, their branches and terminal filaments in the adventitia of the coronary arteries and their divisions, as well as in all portions investigated of the much more abundant myocardium including the specialized tissue of the conductive system. The cardiac nerves and their branches in the human heart were observed to contain fibres and fibrils. Hirsch (1963a) observed many large nerves, their branches, and further divisions to filamentous terminals in the human heart.
They were specially abundant in the interventricular muscular tissue. In view of the abundant innervation of the myocardial tissues in the papillary muscles of the specialized myocardium in the conductive system and of the regional myocardium and of cardiac tissue in the dog, the rabbit, the guineapig, the rat, and the frog, he has supported the universal presumption that the amount and dispersion of nerves in all cardiac tissues suffice to provide fibril connections in abundance to every muscle band. According to him the intrinsic innervation of the human heart stands from both the sympathetic and the parasympathetic nervous system; the sympathetic by fibres only which reach directly, the parasympathetic with the possible interposition of ganglia.

Hirsch (1963 b) studied the innervation of the human heart and made a special reference to the intrinsic innervation of the heart in all the vertebrates. In the heart of the gold fish sinuous fascicles of nerve fibres are seen to extend between the muscle bands, and tortuous fibrils pass from the fibres onto or encircle the myocardial syncitium. The small alligator showed a similar arrangement in structure of the muscle tissues in the atria and the ventricles of its heart. The structure of myocardium of the atria and ventricle as well as the nerve supply in the
heart of salamander was also seen to resemble that described in fish and the alligator. Large nerves with ganglion cells were observed in the muscle tissues of the ventricle of the heart of the turtle. In the frog's heart large nerves with many ganglion cells approach the base of the heart and penetrate to the endocardium at the atrioventricular level. An additional innervation has been provided by the small nerves and the bundle of nerve fibres which emerge from the epicardial plexus. Nerves are distributed along the divisions of the coronary arteries into the heart of the chick. The myocardium of the heart of rat and guineapig was also seen to be richly innervated. A common pattern was observed in the structure and distribution of the intrinsic innervation in the myocardium of all these vertebrates. Much emphasis has been given by the author to show that each and every muscle cell of the heart is innervated.

William (1964) has given an account of the problems that are experienced in tracing a cardiac nerve pathway. Bhargava (1964) has worked on the anatomy and histology of the human heart, with special reference to the 'neurility' of cardiac nodes and the atrioventricular bundle.