C A R D I A C   I R R E G U L A R I T Y - A STUDY

IN THE RELATION OF STRUCTURE TO FUNCTION

(WITH 43 ILLUSTRATIONS)

by

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"Now-a-days all scientific knowledge has increased so largely that specialisation is inevitable, and every investigator is confined more and more, not only to one department of science, but as a rule, to one small portion of that department. In the case of such cognate sciences as physiology and comparative anatomy this limiting of the scope of view is specially deleterious, for Zoology without physiology is dead, and physiology in many of its departments without comparative anatomy can advance but little. .... Nothing but good can, in my opinion, result from the incursion of the non-specialist into the realm of the specialist, provided that the former is in earnest".

(GASKELL - THE ORIGIN OF VERTEBRATE

Preface.

In presenting this thesis, I have to acknowledge various sources of indebtedness. To Professor Muir, in the first place, I owe it that I began and continued to pursue scientific research in medicine. It was at the instigation of Dr. James Mackenzie, that I undertook the study of the present subject, and I am indebted to him, not only for his personal assistance and interest when I was working under his guidance in his wards, but also for the supply of much of the material on which the present investigation is based. I have also to acknowledge my sense of obligation to Dr. Thomas Lewis, with whom I have been collaborating in the experimental investigation of the function of the specialised muscle of the heart. To both Dr. Lewis and to Dr. F.W. Price, I am obliged for some of the material on which I have based the observations detailed in this thesis. But it is to Professor Arthur Keith, more than to any one else, that I am indebted for any light than I may possibly have thrown on the study of heart disease from the standpoint of comparative anatomy and physiology.

I have to admit that the title of the thesis may not be justified by the results, which have been obtained.

No/

No pretence is made, however, that the problems, which have been stated, have been finally solved. On the contrary the difficulty of finding a solution has led to an emphasis on the necessity of correctly appreciating and stating the problem. Physiological and pathological research is often in the paradoxical position in which every new discovery adds new difficulties, and the recent research work on the heart in health and disease, bears this out. Not that the work has been futile; the intelligent collaboration of so many workers in kindred fields and on different aspects of the same subject cannot but lead to a more correct and through appreciation of the subject of study; and the spirit which has inspired modern medicine demands that if the forces of disease are to be harnessed and guided, their biological substratum must first be understood.

C O N T E N T S.

CHAPTER I.

PRELIMINARY CONSIDERATIONS.

The function of the cardio-vascular system is the maintenance of a supply of nutrition to the various parts of the body. This is accomplished by a closed system of vessels whose complexity varies with the degree of development and differentiation of the organism of which it forms an organic part. The propulsion of the contents of this closed system of vessels is maintained by a co-ordinated variation in pressure exercised by the contracting and relaxing vessel walls. In the invertebrate animals, and in the early embryonic life of the vertebrates the tubes are as yet undifferentiated and the movements are often peristaltic in character and comparable with the movements of the intestine. In the lower invertebrates there is no differentiation of any part of the vascular system into a heart and in the higher invertebrates the heart is represented by a comparatively simple dilatation of a part of one or more of the main vessels. The distribution of the contents of/

of the vascular system is secured in these animals by rhythmic waves of contraction and relaxation in which the whole system of vessels participates in a co-ordinated and regular fashion. The circulatory movements in the embryos of vertebrates are probably of a similar character. I am indebted to Dr. J.F. Gemmell for a demonstration of the movements in the hearts of very young fish. Here it was observed that peristaltic waves passed along a dilated vascular tube from the region of the gills. The contractions were slow and orderly, and it was noted that they occurred in a rhythm corresponding exactly with the movements of the gills. This observation affords not only a direct evidence of the peristaltic character of the simplest circulatory movements, but also a very clear proof of the deeply seated biological inter-dependence of the circulatory and respiratory systems. The further development and differentiation of the cardio-vascular system proceeds 'pari passu' with the appearance of new specialisation of function and structure in the animal kingdom.

The embryonic heart of vertebrates presents in the earliest/

earliest stages of development, a form which is essentially the same in all the members of this division of the animal kingdom. It originates in the Elasmobranchs and Amphibians as a single tubular cavity, and in the Teleosts Sauropsida and Mammals as a paired tubular cavity. These structures lie in the splanchnic layer of the mesoblast on the ventral aspect of the anterior portion of the primitive gut immediately behind the gill clefts. At a very early stage three layers can be recognised, an outer serous layer and an inner layer of endothelial cells and between these a layer of primitive muscle cells. In respect of its histological structure it cannot be distinguished from the larger vessels which enter it and leave it. It is essentially a larger and more strongly developed blood vessel lying in the longitudinal axis of the embryo in its ventral aspect. Its further development is characterised by a formation of outgrowths from the dorsal (auricle) and ventral (ventricle) walls of the tube, and the tube subsequently folds on itself, so that the vessel of exit at the cephalic end comes to lie in close proximity to the dorsal outgrowth on the caudal half of the tube (Fig. 1). By this /

this process of folding, it is seen, that the embryonic tubular heart becomes divided into two chambers, ah auricle and a ventricle. Before entering the auricle the blood collected by the veins flows into a common pool, the sinus venosus (S.V. Fig. 1), which becomes separated from the auricle by the development of two valves. These valves are muscular and originate as two free flaps of the invaginated walls of the sinus venosus. Two valves are also developed at the junction of auricle and ventricle; these are myxomatous outgrowths of the endothelium lining the tube at the junction of auricle and ventricle, and they do not contain muscle tissue. Valves are also developed as endothelial outgrowths at the orifice of exit from the ventricle. By the formation of chambers separated by valves a mechanism is evolved which determines the propulsion of the blood in the direction of the waves of contraction, and at the same time prevents regurgitation into the sinus venosus and collecting veins. The heart has now become differentiated into the following parts:- (1) the sinus venosus acting as a collecting basin from the veins, (2) the auricle which represents the primitive venous/

venous portion of the heart, (3) the auricular canal lying between the dorsal outgrowth of the auricle and the ventral outgrowth of the ventricle, (4) the ventricle corresponding to the primitive arterial portion of the heart, and the truncus arteriosus which represents a specialised part of the primitive arterial portion, becoming continuous with the ventral aorta.

The ventral aorta gives off on its right and left sides a series of afferent branchial arteries which run between adjacent gill clefts and after passing through the capillaries in the gills are formed into two efferent branchial arteries, one on the right side and one on the left; these right and left efferent branchial arteries unite to form the dorsal aorta which lies on the ventral aspect of the vertebral column and gives off toward the caudal aspect of the embryo the vitelline arteries to the yolk sac, and the allantoic arteries to the urinary bladder and allantois. The allantoic arteries are of course absent in the fish. The blood distributed to the yolk sac is purified and returned by the vitelline veins. These unite with the allantoic veins and the veins from the gut to form the portal vein which is distributed to the liver, the blood returning from the liver/

liver to the sinus venosus in the hepatic veins. Along with the hepatic veins there open into the sinus venosus the Ducts of Cuvier, which are formed by the junction on either side of the anterior cardinals and posterior cardinals.

In the case of the Anamnia the embryo leaves the egg for an aquatic life and makes use of the branchial system of vessels for respiration. In the case of amphibians the entire allantois developes into the bladder. In the Amniota whose respiratory demands are from the first subserved by the presence of lungs, the branchial vessels undergo considerable modification, and in the case of birds and some reptiles the allantoic system of vessels may disappear. In mammals the embryo has a long intra-uterine existence. The allantois comes into close relationship with the walls of the uterus through the chorionic villi, and the nutrition of the foetus is secured by an interchange of substances maintained by the placental circulation.

The gradual differentiation of structure and specialisation of function which characterises the embryonic growth of the mammalian heart is but a repetition in a sense of the various stages at which the vertebrate heart/

heart has arrived in its development from the undifferentiated tube in Amphioxus to the extremely complicated organ in man.

In the vascular system of the mammalian embryo structures appear and disappear, which have, as far as we can judge, no special significance except that every organism and every part of the organism must inevitably tread the path of its predecessors in the phylogenetic series, discarding in its progress the simpler instruments of function which have proved sufficient for the lower orders of life in their arrested development. The modifications which occur in the mutually interdependent circulatory and respiratory systems in their ontogenetic and phylogenetic evolution are of particular interest in the present study. In Amphioxus and in Fishes the gill clefts are the special organs of respiration. In the Amphibians the lungs proper appear for the first time, although for a certain period, during their aquatic life, the respiratory functions are performed in gills. In all Amphibians, with the exception of the Perennibranchiata, the gilled stage is but a preliminary to the lung stage. With the appearance of lungs in the Amphibians the morphology of the heart becomes changed in that the auricle becomes divided by a septum/

septum into a right and left chamber, the left chamber being reserved for the reception of the blood from the newly developed organs of respiration. This specialisation of function and structure becomes more complicated as the vertebrate series advances. The appearance of a fully developed respiratory system is associated with changes in the branchial vessels as well as in the heart. In the mammalian embryo, and in the vertebrate series generally, there is a gradual differentiation of the heart into a four chambered organ, the right side of which deals with the venous blood and the left side with the blood which has become arterialized in the lungs. The branchial vessels which play such an important part in Fishes and Amphibians never become functional as such in Sauropsida and Mammals. In these latter classes the embryonic branchial arteries which do persist give rise to important vascular trunks of the head (carotids), anterior extremities (subclavians), and lungs (pulmonary arteries) and also to the roots of the aorta, one or both of which may remain.

But it is not alone in their morphological characters that a progressive and parallel development is recognised in embryonic and phylogenetic development. The pulsations or waves of contraction which determine the flow of blood undergo a marked change corresponding with/

with the increased complexity of structure in both cases. The slow rhythmic waves of contraction synchronous with the respiratory movements of the mouth in the young fish have already been noted. In the adult fish the waves of contraction may be followed from the larger veins through the sinus venosus auricle and ventricle to the conus arteriosus. In the adult fish however the contraction waves are more frequent and pass more rapidly from the caudal to the cephalic end of the heart than in the young fish. In the exposed mammalian heart the contractions follow each other with great rapidity and the individual contraction wave is so rapid in its passage along the heart that the whole chamber, auricle or ventricle, appears to contract simultaneously. I have watched the contracting heart of a guinea-pig embryo which was so young that the structures were still transparent; here the events of the cardiac cycle followed each other in a slow deliberate manner, resembling the wave of contraction passing from one chamber to another in the heart of the fish. The cycles followed each other at about the rate of 15 to the minute. In the adult guinea-pig the rate of the heart beat is about 250 to 300 per minute, and the two main events in the cycle, the auricular and ventricular contraction, appear to be instantaneous/

instantaneous, though separated by a distinct pause. There is thus in the phyllogenetic development of the vertebrate heart as also in the development of the embryonic mammalian heart a gradual change in the functional properties of the cardiac structures, whereby the waves of contraction become more and more rapidly transmitted as differentiation of structure and function proceeds.

When the heart has assumed the complicated form, which it presents in the higher vertebrates, the course of the wave of contraction is, however, still the same as it was when the primitive organ was only a single tube. Gotch has shown by means of electrometer records that in the ventricle of the tortoise or the rabbit, which in its fully developed form has become bent and twisted on itself, the wave of contraction begins at the auricular base, passes to the apex and makes its exit at the arterial or aortic base. Lewis has demonstrated that the wave of contraction in the normally beating auricle begins at the junction of the superior vena cava with the right auricle at a joint which will be described in a later chapter (p.149). The actual course of the wave of contraction in the auricles has not been definitely ascertained, but it presumably spreads from its seat of origin/

Buchanan (F). Journ. of Physiol. Vol XXXVIII No 5. p lxii

Gotch (F) Heart Vol 1. No 3 p 235.

origin through the tinea terminalis and the pectinate muscles, thence though the fibres of the auricular ring to the system of muscle which provides a junction between the auricular and ventricular muscle. The evidence would thus appear to point definitely to the conclusion that the path of the peristaltic wave of contraction in the primitive and embryonic cardiac tube is maintained in the complicated organ of the adult mammal. But the rate of propagation of the contraction wave varies not only between more simple and more complicated hearts, but also between different hearts of the same species under different conditions of metabolism, and also between different parts of the same heart in its normal state of functional activity. Thus, if the propagation rate in the tortoise, rabbit and goldfinch, be compared, extraordinary differences will be noted. Gotch has found that in the ventricle of the tortoise the rate is 90 m.m. per second; in the ventricle of the rabbit he found it to be 3 metres per second; Dr. Florence Buchanan estimated from electrometer records that the heart of the goldfinch contracts at a rate of over 900 beats per minute; this represents an exceedingly high rate of propagation of the contraction wave. Gotch states also that the rate over the ventricle varies from 3 metres per second /

second when the heart is beating at 300 per minute to 1 metre per second, when the heart is beating at 150 to 180 per minute and that when the heart begins to fail the rate of propagation becomes still further reduced. Finally, the speed of the wave varies in different parts of the same heart, contracting under normal conditions; Gotch records that in the auricle of the tortoise the rate at 12°C. is about 120 m.m. per second, while the rate in the ventricle is about 90 m.m. per second.

In this connection reference may be made to the fact that the co-ordinated sequence of events in the cardiac cycle has been attributed to a diminution in the rate of propagation of the contraction wave in the bundle of muscle, which connects the auricle with the ventricle. The mechanical efficiency of the heart depends on an orderly sequence at a certain interval of contraction/ and relaxation in auricles and ventricles respectively. Just as proper contraction of the ~~briefs~~ biceps implies the participation of a mechanism, which secures relaxation of the triceps so the efficient contraction of the auricles implies a condition of relaxation in the ventricles; and a lapse of time between the cessation of auricular contraction and the commencement of ventricular contraction during which the auriculo-ventricular apertures become closed by the valves, is necessary to secure the propulsion/

propulsion of the blood. If, for example, in the case of the rabbit, the wave of contraction were to pass from auricles to ventricles at a rate of 3 ~~inches~~ metres per second then from the mechanical point of view the auricular and ventricular contractions would be practically simultaneous and the functional advantage of the auriculo-ventricular valves would be rendered useless. The delay which does occur between auricular and ventricular contraction is attributed to the relatively low power of conductivity, which the auriculo-ventricular muscle bundle (Bundle of His) is supposed to possess. Whether such a simple explanation is in itself sufficient to account for the phenomenon of auriculo-ventricular delay, and whether, more particularly, every variation in the length of this delay is to be attributed to an abnormal condition of the bundle referred to, will be the subject of detailed examination in a subsequent chapter (p.).

The foregoing preliminary considerations have been advanced in order to emphasise the fact that the heart in its ontogenetic and phyl~~l~~ogenetic development adapts itself to the increasingly complex demands of an ever-changing series of circumstances. This adaptability is secured by a specialisation in the structure of the heart itself/

itself as the central organ of the cardio-vascular system, but an effective maintenance of the circulation can be secured only by the active co-operation of the accessory parts of the circulatory apparatus. Not only must there be an orderly sequence of contractions of the cardiac chambers providing for a competent action of the intra-cardiac valvular apparatus, but the whole system of vessels in virtue of their intrinsic movements and aided by the mechanical accessories of direct muscular action and the pumping and aspirating effect of the respiratory apparatus, must contribute to the onward flow of the blood. If the term "cardiac mechanism" be employed to denote the central organ of the cardio-vascular apparatus that should be done without losing sight of the fact that in meeting an abnormal demand under either physiological or pathological conditions the heart has at its disposal a power and means of adaptation which no mechanical device could afford. It might be considered possible to regard the heart as a mechanism, and to calculate the work which it actually does under certain circumstances; but this could only be approximately estimated by determining the amount of blood propelled with each systole, the velocity imparted to the blood, the degree of peripheral resistance and the number of cardiac contractions in a unit/

unit of time. The elusive character of the indispensable data in such an estimation is obvious; and when it is recognised that these data are themselves the expression of a variable and unstable combination of physiological circumstances absolutely beyond the control of the observer, it will be clear that the term "mechanism" can be employed in this context only in a very arbitrary and unprofitable sense; allowance must always be made for the fact that it is a vital machine.

Even when the cardio-vascular apparatus is normal there is considerable variation in the rate of the flow of blood. The rate of flow is determined to a degree by the demand for oxygen and nutrition, and the supply of blood to certain organs may be varied and regulated without interference with the general flow of the circulation. Local demands are met by constriction of one set of vessels and compensatory dilatation of another set; but when large quantities of blood are required in several parts of the body, as in cases of violent exercise, the supply is furnished by a general increase in the rate of circulatory flow. When the demand for an increased flow of blood becomes general, this is always accompanied by an increase in the work of the heart. It might be thought that a dilatation of peripheral arterioles would secure an increased supply of blood without necessitating an/

an increase in the force of the cardiac beat. The extent to which such a compensation can occur must however, be insignificant, because of the balance of relations which exist between the amount of blood propelled, the general pressure and the rate of flow. For example, if there is a general demand for an increased supply of blood to the limbs during exercise, a diminution in the general arterial pressure in these areas would so reduce the difference between the arterial and venous pressures that the rate of flow in the capillaries would be insufficient to maintain the necessary supply of venous blood to the heart. Thus any considerable increase in the rate of flow necessitates an increase in the work of the heart; and a constantly high rate of blood flow apart from any obvious defect in the cardio-vascular apparatus may lead in the long run to a failure on part of the heart to continue to meet the abnormal demand. This is probably the condition of affairs in those cases of exophthalmic goitre which are complicated by cardiac failure.

Again, the work of the heart may be increased by a heightening of the peripheral resistance to the blood flow. Even in health there may be considerable variations in the peripheral resistance. These variations may/

may or may not be compensated by an increase in the work of the heart. Exposure to cold produces contraction of the peripheral arterioles. When this is not met by an increase in the work of the heart to maintain the nutrition and heat of the parts exposed, the tissues are devitalised and exposed to the risks of necrosis. The irritation of sensory nerves may also produce constriction of arterioles over an extended area, and this increase of peripheral resistance is usually met by an increase in the work of the heart. In chronic Bright's disease and in arteriosclerosis there is a constant increase in the peripheral resistance, due to perpetual tonic contraction of the smaller arterioles; this condition is soon reflected in the hypertrophy of the heart which is necessary to the performance of additional work. In many, if not in most of these cases, the cardiovascular apparatus breaks down from an exhaustion of the physiological reserve which enabled it to adapt itself to the enhanced demand during the earlier stages of the disease.

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Hill

Mackenzie (J.) British Medical Journal 1910 - 234.

The inter-dependence of the respiratory and circulatory system has been referred to repeatedly. Their mutual influence in morphological development and in physiological activity is apparent. The tonus of the venous blood to the heart and the propulsion of the blood through the heart and lungs is assisted to an enormous extent by the variations in intra-thoracic pressure consequent on the respiratory movements. I have on other occasions called attention to the fact that an interference with the freedom of the respiratory movements over a prolonged period, may diminish this accessory circulatory force to such a degree that the extra work on the heart may lead to a final inefficiency of the cardio-vascular apparatus. When there is extensive deformity of the chest wall due to caries of the spine, advanced rickets or other causes, the patient may die with all the evidence of cardiac failure. Fluid in the pleural sacs, adhesions of the pleurae, extensive fibrosis or collapse of the lungs may also interfere to such an extent with the flow of blood through the lungs and also with the circulatory assistance of the expanding and contracting spongy lung substance, that cardiac failure may ultimately ensue.

Another extra-cardiac mechanical embarrassment which may prove prejudicial to the circulatory flow and terminate in cardiac failure occurs in the abdominal vessels. I have observed in several cases of epidemic cerebro-spinal meningitis a sudden rise of the pulse rate from about 100 to/

to 130 per minute. Accompanying the rise in rate the pulse became small and weak. Pallor of the lips and face with general languor and weakness were also present. In 24 to 48 hours after the onset of the change in the pulse rate, death ensued. Post-mortem examination of these cases revealed a condition of extreme dilatation of the capillaries and venules of the abdominal viscera. The kidneys, liver and intestinal walls were engorged with blood. Death had occurred from circulatory failure as a result of bleeding into the splanchnic area, the phenomenon no doubt originating in an involvement of the vasomotor apparatus by the inflammatory process in the central nervous system.

Other instances of failure of compensation in the circulatory system attributable to extra-cardiac causes might be cited. Abnormalities or perversions of the functions of glands whose internal secretions exercise a tonic or regulatory influence on the circulation, may ultimately lead to circulatory failure. These conditions, though they undoubtedly exist, are ill-defined and obscure, complicated as they usually are by other disturbances in the organism. Enough has been said however to show that in estimating the factors which contribute to cardiac failure cognizance must be taken of the fact that/

that every part of circulatory apparatus participates actively in the propulsion of the blood, and that numerous accessory forces are necessary to the maintenance of an efficient circulation. Wherever the initial weakness or lesion lies, the first evidence of circulatory disease is usually reflected on the heart itself. It is only when the last barrier gives way, or threatens to give way that the patient first becomes aware of those symptoms arbitrarily known as "heart disease".

In sharp contrast with the foregoing instances of chronic circulatory failure due to extra-cardiac causes are those in which the embarassment of the circulation is due to causes operating in the heart itself. These cases are as a rule the result of endocarditis and myocarditis following acute rheumatisms or one of the infections, or they not infrequently result from defective blood supply due to atheroma of the coronary arteries or stenosis of the coronaries by syphilis of the aorta. The objective clinical signs often manifest themselves in an interference with the orderly sequence of events in the cardiac cycle. The contraction of the auricles is reflected in a pulsation in the jugular vein and the contraction of the ventricles is detected by a pulsation at the apex of the heart or in the radial artery. By means/

means of polygraph records these events and their ~~tissue~~ time relations may be correlated, so that the observer has a means of determining whether the normal sequence of events is maintained; whether for example every auricular contraction is followed by a ventricular contraction, whether the delay between auricular and ventricular contraction is normal in length, or whether there is any auricular contraction at all. These and other disturbances of co-ordinated cardiac contraction may be more accurately determined by means of the electrocardiogram. When an abnormal series of events in the cardiac cycle manifests itself in the form of a dissociation of auricular and ventricular contraction, with, as a rule, extreme slowing of the ventricular rate, the condition is known as "heart-block". When there is no evidence of auricular contraction on the polygraph or electrometer records and the radial pulse reveals the character of what is known as an irregular irregularity, the condition is termed "auricular fibrillation". These two conditions and some allied forms of irregularity constitute the subject of the present investigation. In the next two chapters the anatomical basis of co-ordinated cardiac action will be described and discussed.

CHAPTER II.

THE AURICULO-VENTRICULAR SYSTEM OF THE MAMMALIAN HEART,

Although the groundwork of modern research in the physiology of the heart was laid thirty years ago by Gaskell in his well-known investigations, it is only within the last seven or eight years that a systematic attempt has been made to correlate the results of experiment with the anatomical structure of the organ. For the great advances in this latter aspect of the subject, the examination of the morphology and minute structure and their relation to function, science is chiefly indebted to Aschoff and his pupils in Germany, and to Keith and his pupils in this country. Not that physiologists have been in the meantime inactive, for the recent researches of Leonard Hill, Einthoven, Lewis, Rothberger and Winterberg, Hering, Miss Buchanan and others have added enormously to our knowledge of the phenomena of cardiac activity. The work of these observers is all the more important in that with them for the first time pathological reaction has been regarded as a subject for physiological research and the anatomical basis of these reactions have not been left out of account. Perhaps most important from/

from the point of view of practical medicine is the fact that pharmacology and clinical observation have contributed their quota to the sum of knowledge on the subject. No one interested in this branch of science can afford to overlook the important and suggestive results of the work of Cushny and his pupils on the action of certain drugs and poisons on the organs of the circulation; and the researches of James Mackenzie and Wenckeback with their followers in this country, ~~and~~ on the continent and in America have made the results of this recent research work a matter of first rate interest and importance for the every-day practice of medicine. In fact, there is to-day no department of medical science in which such a diversity of talent and practical insight has intelligently co-operated to produce practical results as that which concerns the study of the heart in health and disease.

In describing and discussing the general morphology and minute anatomy of the specialised structures in the heart I propose to deal first with:-

I. The microscopic Anatomy of the cardiac muscle and its blood supply.

II. The general morphology and minute anatomy of the specialised auriculo-ventricular muscle system.

1. THE MICROSCOPIC ANATOMY OF THE CARDIAC MUSCLE AND ITS BLOOD SUPPLY.

The muscle substance of the heart is composed of transversely striated fibres which present striking differences from the fibres of skeletal muscle. Whereas the fasciculi of skeletal muscles are composed of single fibres, the fibres of the cardiac muscle are continuous with each other. The cardiac musculature is really a syncytium (Kölliker, M. Heidenhain) composed of fibres continuous in their long axis and intimately connected with each other by side fibres passing almost transversely between neighbouring strands. It is no longer held that mononuclear segments are divided from each other by transverse bands of cement substance for in well prepared fresh pieces of tissue properly fixed, a continuous portion of a fibre may be seen to contain several nuclei at regular intervals; segmented portions do occur, but they are isolated in their distribution, being most frequently found in the papillary muscles and in the circular fibres surrounding the orifices of the cardiac chambers. The function of these so-called "cement lines" which appear to interrupt the continuity of the fibre is still obscure. That they divide the fibre functionally is /

is highly improbable because it has been observed that the fibrils pass through them (v. Ebner, M. Heidanhain). Examined in fresh preparations it is seen in many cases that the "lines" do not traverse the whole breadth of the fibre; in some cases they extend partly across the fibre and in other cases they cross it completely but in an irregular staircase fashion. According to v. Ebner the lines represent a dying phenomenon. Eppinger regards them as pathological in origin. M. Heidanhain believes that they are the expression of a functional activity of the fibre, and that they are in some way associated with its growth. In the human subject the "lines" are from 1 μ to 1·7 μ thick and they consist of parallel perpendicular rods. They occur at irregular intervals which have no relation to the position or distribution of the nuclei in the fibre, so that their presence does not in any sense indicate a separation of the fibre into cells.

The "cement lines" are absent at birth and are most obvious in advanced years (Aschoff). The fibres possess nuclei, sarcoplasm, fibrillary substance and sarcolemma which differs from that of the skeletal muscle fibre in not being of a chitinous nature; the sarcolemma is a very delicate protoplasmic membrane and is often richly impregnated with granules. The nuclei lie inside the fibre and are elliptical in shape; they are 7-16 μ long/

long and 5-9 μ broad and possess a well marked chromatin network and a nucleolus; at each pole of the nucleus there is a mass of granular protoplasm, the sarcoplasm is more richly developed than in skeletal muscle and contains strongly refractile granules which in adult life take on a yellow or yellowish brown colour. Except that in atrophic and wasting conditions they are usually very prominent their presence is not known to possess any significance. The contractile substance of the cardiac muscle fibre is composed of bundles of fibrils, the sarcostyles. These are somewhat prismatic in shape and lie towards the periphery of the fibre, the centre of the fibre being occupied by the nuclei and its surrounding sarcoplasm. The sarcostyles exhibit longitudinal and frequently transverse striation, the former being due to the fibrils and the latter to doubly refractile substances which the fibrils contain. The transverse striation is sometimes obscured by the sarcolemma. Not only do the fibrils maintain a structural continuity through the "cement lines" referred to, but they bridge the spaces between neighbouring fibres, a number of fibrils from one fibre becoming detached and passing uninterruptedly into its neighbour, to become continuous with its fibrils. In this way there is an unbroken continuity of structure from the/

the entrance of veins to the exit of the large arteries through the whole length of the heart. This is the pathway along which the waves of contraction pass; on their route they may be subjected to nervous or other influences depending on a modification of their structure; a recognition of the fact that the heart muscle is a reticulated syncytial tissue and not composed of independant fibres like skeletal muscle or of independant cells like parenchymatous organs, is of fundamental importance for a proper understanding of the physiology and pathology of the organ.

THE BLOOD SUPPLY TO THE HEART MUSCLE.

A clear conception of the nature of the blood supply to the cardiac muscle is indispensable to an interpretation of some of the most important features of heart disease. Cohnheim regarded the coronaries as end-arteries and most pathologists have accepted his view in this respect. More recent investigations have however tended to upset the idea. Hirsch and Spalteholz have succeeded in injecting preparations with coloured gelatine which exhibited an extraordinarily rich anastomosis between the smaller arteries and arterioles of the two coronary arteries and between adjacent branches of the same coronary artery./

artery. This anastomosis has been demonstrated in every part of the heart, and it has been seen in the human heart as well as in the heart of the dog and of the calf. The vascular ramifications are very easily demonstrated in young hearts where even on microscopic examination the dense network of small vessels is a striking feature.

The abnormally rich blood supply of the heart is a characteristic of the organ in the lower members of the vertebrate kingdom. In the fish and amphibians a special coronary system is but poorly developed and the muscle is nourished by a process of absorption by which the blood is sucked into the dilating chambers from the cardiac cavities like water into a sponge; on contraction the blood is squeezed out and propelled onwards to be replaced by a fresh supply during the succeeding diastole. It is not too much to say that in the human heart an analogous process is at work. The nutritional supply of the cardiac muscle differs essentially from that to any other part of the body. During ventricular systole the blood is forced into the aorta and thence throughout the body; but while the ventricles are contracting the blood can be forced only into the larger branches of the coronary arteries, which from their situation are not exposed to the pressure of the ventricular systole. The ventricle cannot/

cannot force blood into its own substance while it is in a state of contraction. The result is that the muscle substance receives its nutritional supply during diastole in much the same manner as the fish, and the return of the venous blood occurs with the subsequent systole. ~~It~~ In the human heart the blood is sucked in through the coronaries from the aorta whereas in the lower hearts it is sucked in from the cavities of the auricle and ventricle. It is thus obvious that in the heart the conditions of nutrition are of a very unusual character. For its proper nourishment a forcible expulsion of blood from the left ventricle is not so important as a high pressure in the aorta during ventricular diastole; it is for this reason that disease and mechanical incompetence of the aortic valves gives rise to a form of cardiac weakness not usually amenable to treatment which consists in slowing of the rate of contraction. This whole question will be fully discussed later, when some cases of cardiac disease due to an inadequate coronary circulation are under consideration. (p.155).

II. THE GENERAL MORPHOLOGY AND MINUTE ANATOMY OF THE SPECIALISED MUSCLE SYSTEMS.

The main thesis developed in the preceding pages is that the wave of contraction in the vertebrate heart passes from the entrance of the veins along a continuous substratum of muscle tissue through auricles, auriculo-ventricular junction and ventricles to the region of exit of the large vessels. Till the year 1893 the existence/

muscle forces blood into its own substance while it is in a state of contraction. The result is that the muscle substance receives its nutritional supply during diastole in much the same manner as the brain, and the emptying of the venous blood occurs with the beginning of systole. It thus obvious that in the heart the conditions of nutrition are of a very unusual character. But the proper nourishment a forcible expulsion of blood from the left ventricle is not so important as a high pressure in the aorta during ventricular diastole; it is for this reason that disease and mechanical incompetence of the aortic valves gives rise to a form of cardiac weakness not usually amenable to treatment which consists in slowing of the rate of contraction. This whole question will be fully discussed later, when some cases of cardiac disease due to an inadequate coronary circulation are

Tawara – Das Reizleitungssystem des Säugetierherzens. Jena 1906.

IV. THE GENERAL MORPHOLOGY AND ANATOMY OF THE SPECIALIZED MUSCLE SYSTEMS

The main thesis developed in the preceding pages is that the wave of contraction in the vertebrate heart passes from the entrance of the veins along a continuous tube of muscle tissue through auricles, auriculo-ventricular junction and ventricles to the region of existence of a muscular connection between auricles and ventricles in the mammalian heart was generally doubted or denied. Although Gaskell had in 1883 described a muscular continuity between the various chambers of the heart in cold blooded animals, Stanley Kent was the first to record an observation of the presence of an auriculo-ventricular muscular continuity in the heart of the mammal. The publications of His, in which a more detailed description of the structures were given, appeared shortly afterwards. It is however to the researches of Tawara under Aschoff's guidance that science is indebted for an exhaustive description of the morphology and minute anatomy of the auriculo-ventricular musculature and its relations to the ordinary muscle of the auricles and ventricles respectively.

II. THE AURICULO-VENTRICULAR MUSCLE SYSTEM.

Tawara compared the auriculo-ventricular system to a tree, the roots of which are embedded in the inter-auricular septum near the coronary sinus and the main trunk of which lies on the inter-ventricular septum, piercing the fibrocartilaginous septum between the auricles and ventricles, ultimately spreading its branches and fine twigs in the subendocardial layer of the ventricles for/

for the most part at the bases of the papillary muscles. The observations of Tawara have been confirmed in the main by subsequent researches although a number of new points have been raised necessitating a modification of some of the conclusions at which he arrived.

It would serve no useful purpose in the present instance to follow the wide-spread ramifications of the literature to which this subject has given rise. The main object of the thesis will best be served by giving a macroscopic and microscopic description of the structures as I have observed them in the human heart and in the heart of the sheep. I have examined this special muscle system in a great variety of mammalian hearts including those of the monotreme, (Echidna) and the kangaroo with the result that the general morphology, while showing considerable variations in different species, and also in different members of the same species, presented on the whole similar features, (1) in its site of origin in the inter-auricular septum, (2) in the course of its main stem along and through the fibrous septum and ~~pass~~ pars membranacea septi and (3) in the distribution of its two main subdivisions in the subendocardial tissue about papillary/

Stanley Kent. — Journ. of Physiol. 1893 Vol XIV p 233.

His (Jun) — Arb. a. d. med Klinik 1893

Retzer — Arch. f. Anat. und Physiol. 1904

Braeunig — Inaug. Dissert. Leipzig 1904

papillary muscles in the right and left ventricles.

Tawara's work stands out pre-eminently from that of his predecessors in that he was the first to recognise the wide-spread arborisations of the system beneath the endocardium of the ventricles. He made it clear that the distribution of Purkinje fibres in the ungulate heart, obvious even on naked eye examination are to be regarded as the terminal processes of the auriculo-ventricular muscle system where the fibres of the latter become continuous with the ordinary muscle fibres of the ventricles.. Stanley Kent, His, Retzer and Braeunig had already published records of observations on the subject showing that a muscular continuity did exist between auricles and ventricles in the mammalian heart, but each of these observers was under the impression that while the fibres of the muscle bundle originated in the inter-auricular septum, they became continuous with the ventricular muscle immediately beneath the fibrous septum or pars membranacea septi. I have chosen for description the sheep's heart and the human heart for the following reasons:- (1) Those who desire to work out the anatomy of this muscle system should commence with the sheep's heart because it is a good representative of the ungulate heart, and it is the ungulate heart which gives the easiest key to the course of the main subdivisions/

subdivisions of the bundle and shows most readily that the bundle does not terminate in the roof of the inter-ventricular septum but is distributed widely inside the ventricles. In the ungulate heart the continuation of the Purkinje fibres with the main subdivisions of the bundle on the one hand and the ordinary muscle of the ventricle on the other, is easily demonstrated; and the ungulate hearts are the only mammalian hearts in which this is the case. Moreover we shall see that a clear conception of the course of the divisions of distribution of the bundle in the ungulate heart and of the relation of these subdivisions to the chordae tendineae, affords an insight into the phylogenetic relationship of this muscle system to the auriculo-ventricular muscle in the lower vertebrate hearts. (p.134). (2) The human heart does not contain Purkinje fibres.[x] The distribution of the main subdivisions is difficult or impossible to determine with the naked eye; in this respect the human heart resembles that of the dog, cat or rabbit, and will be described because such a description may be taken to apply in a general sense to the hearts of these laboratory animals; a description of the human heart is also necessary in view of its examination in pathological conditions.

x (The fibres in the auricles which have been described as such are not really Purkinje fibres; fibres with a large amount of protoplasm, few fibrils and little transverse striation are almost always to be found in the auricles of persons of advanced years; they are usually seen where there is a considerable amount of fibrous or elastic tissue and they are not Purkinje fibres).

THE SHEEP'S HEART.

Macroscopic Examination - If a fresh sheep's heart be opened and washed for twelve hours in running water an extensive meshwork of fine pale threads will be seen to stand out from the shining grey reddish background of the endocardial surface of the ventricles. This network will be found to be more dense in the lower two thirds of the ventricles, more especially round the papillary muscles and in the apices; towards the orifices of the chambers the threads are fewer and less distinct. More careful examination will disclose the fact that the threads of the network are slightly elevated above the general level of the endocardium. Where the ventricular walls are smooth the threads appear to rest in close apposition to the general musculature, but towards the ~~species~~ apices of the ventricles and where the inter-ventricular septum becomes continuous with ~~a~~ the parietal walls the threads become more elevated at places, and they occasionally leave the solid wall of the heart to cross in short bridges from one part of the ventricle to another; in this way the spongy appearance which is not infrequently seen at the ventricular apices consists of fine trabeculae of ordinary muscle fibres mixed up with the paler threads of the general network. Not infrequently in the left ventricle a small cord or cords may pass from the flat surface of the inter-ventricular septum/

septum to the papillary muscles. Such cords bear at first sight a close resemblance to the chordae tendineae of the mitral ~~crisp~~ cusp in the immediate neighbourhood, but these are usually found on closer examination to contain fibres belonging to the system under discussion. In the right ventricle the network may be seen to radiate from the anterior papillary muscle at a point where the moderator band is inserted into that structure. The moderator band varies in size and appearance in different sheeps' hearts. In some cases it is thin and paler than the ordinary muscle, and then it is found to consist exclusively of fibres belonging to the network; in other cases it is thick with a pale streak on one side or in its centre, and in these cases the fibres of the network are found to be accompanied by ordinary muscle fibres. The moderator band emerges from the right side of the inter-ventricular septum at the insertion of the papillary muscles to which the chordae tendineae of the septal cusp of the tricuspid are attached, and passes diagonally across the ventricle to the anterior papillary muscle.

In the hearts of older sheep the cords of the network are surrounded by a thin layer of fat cells. This tends to a slight elevation of the network from the muscle on which it lies and to a more definite delimitation from the surrounding structures. A good demonstration of the network can be obtained by fixing the heart in Formol-Müller solution/

solution and afterwards preserving it in 70% Alcohol; thus prepared the network assumes a greenish gray colour which stands out in relief from the greyish brown ventricular muscle.

In each ventricle the network is the ramification of a single branch which descends on the side of the inter-ventricular muscular septum from the region of the pars membranacea septi. Each of these branches represents the right and left subdivisions respectively, of the auriculo-ventricular bundle (Bundle of His)(Fig 3). The division of the bundle takes place as a rule below and in front of the fibro-cartilogenous septum between the regions of attachment of the right and posterior aortic valves. It is possible to follow the right and left branches to the point of division of the main bunble. The right branch may be followed from the moderator band; prepared in this way it is found to emerge from the muscular septum in which it lies at a varying depth beneath the endocardium; its course from the point of division is in a downward and forward direction in the muscle beneath the septal cusp of the tricuspid. It rarely becomes subendocardial before reaching the moderator band, and it does not appear to give off any branches before it becomes subendocardial. The dissection is rendered easy by the fact that the branch is enclosed in a fibrous tissue sheath and/

and it is not infrequently surrounded by a layer of fat. In the left ventricle the network of ramifications spreads from the flat surface of the inter-ventricular muscular septum. Examination of this surface will, as a rule, reveal the presence of two pale cords deviating from a common stem a short distance below the adjacent corners of the right and posterior aortic cusps; these two cords are the main subdivisions of the left branch of the bundle, and as can be observed extend into the subendocardial network. The left branch emerges from the muscle of the septum at a varying distance beneath the point of division of the bundle. The depth in the muscular septum at which this division takes place varies in different hearts. In the human heart it takes place on the roof of the septum, while in the heart of the horse the division may take place at a depth of half an inch beneath the roof of the muscular septum. Having followed the system to the point of division of the bundle, the bundle itself may now be traced upwards and backwards through the auriculo-ventricular fibro-cartilagenous septum to a site between the fibrous septum and the auricular endocardium. In this region the tissue of the bundle, while sharply demarcated from the ordinary cardiac musculature is in very close relationship with the central fibrous body of the heart, and this renders its isolation by dissection a matter of considerable difficulty; it is however possible in/

in many cases to follow it along the right side of the septum to its origin in the auriculo-ventricular node (Tawara's Node) which lies in the lower aspect of the inter-auricular muscular septum just behind the fibro-cartilagenous septum. Here the fibres of the node become continuous with the ordinary muscle fibres of the auricle. Although it is said that the musculature of the node is continuous with the muscular wall of the coronary sinus by means of "transitional fibres" this continuity cannot be demonstrated in macroscopic specimens.

Microscopic Examination - The muscular connections of the node with the auricle and the relationships of the node and main bundle to the surrounding structures can be satisfactorily studied only by the examination of serial sections. The block of tissue which must be excised for this purpose is prepared as follows:- the anterior border of the block is delimited by an incision in the long axis of the heart, and at right angles to the auriculo-ventricular groove, through a point about 1 c.m. in front of the adjacent corners of the right and posterior aortic cusps; this incision passes through a point in the immediate neighbourhood of the orifice of the right coronary artery. The posterior border of the block is marked by an incision parallel to the first incision and passing through the anterior edge of the coronary sinus. Both incisions pass through/

through the wall of the aorta and on the right side through the septal cusp of the tricuspid; the second incision passes on the left side through the aortic cusp of the mitral valve. The block is freed by two parallel horizontal incisions joining the first two; the first of these latter is made parallel to the auriculo-ventricular groove on the right side and about 2 cm. above it; the second is made to include a depth of 1 cm. of muscle from the roof of the inter-ventricular muscular septum. The block should be incised only after the heart has been thoroughly fixed in a fixing reagent such as formalin or Formol-Müller, and subsequently hardened in alcohol. It should not be trimmed for final embedding until the hardening and distorting action of the first absolute alcohol has given it a permanent shape. It is important for purposes of orientation to have the ultimate shape such that the bundle lies as nearly as possible in the course in which it is situated in the living heart. To secure this end it is sometimes necessary to fix the block in splints during the process of hardening in alcohol. Blocks from the hearts of ungulates where the fibro-cartilagenous septum contains bone should be decalcified before hardening. In the case of the human heart the blocks should always be placed in a decalcifying solution, as even where there is no evidence of calcification on diseased valves there may be deeply seated deposits of

lime/

lime salts in the centre of the block. The process of decalcification if properly carried out, and if followed by careful subsequent treatment does not in any way interfere with the ordinary examination of normal or pathological specimens. On the contrary it will be found that such treatment facilitates the preparation of serial sections from a block of tissue such as this, which from its compound character is extremely difficult to cut even under the most favourable conditions.

In embedding the block special care should be taken in its orientation so that when the sections come to be made the plane in which they are cut may be chosen with a view to the easy recognition of the relations of the different structures, The sections may be cut in a plane parallel to the second two incisions made in the excision of the block; in such sections the bundle will be represented more or less in its long axis in its course from the node to the point of division; this is the plan which has been followed in preparing the sections of the sheep's bundle which are about to be described. On the other hand the sections may be cut in a plane parallel to the first two incisions made in the excision of the block, and in this case the bundle will be cut in a transverse direction. This latter method has been adopted in the case of preparations from the human heart; it is also the/

the method which provides the easiest orientation in the case of all small vertebrate hearts which can be embedded as a whole and examined in serial sections throughout. In the case of normal hearts the best differentiation is obtained by staining with haemalum and Van Gieson. In the examination of pathological specimens I have in addition employed Haemalum and eosin and also Weigert's elastic tissue stain. When the observer is accustomed to Haemalum and Eosin in ordinary pathological technique, this method is probably the most satisfactory also in examination of the auriculo-ventricular system in the human heart.

MICROSCOPIC EXAMINATION OF THE SHEEP'S AURICULO-VENTRICULAR SYSTEM.

The series of sections commences with those from the upper border of the block and gradually descends to the lower border; thus in the first sections the most prominent structure is the aortic wall and in the last the inter-ventricular muscular septum. Following the series in this order a section is met with in which the fibro-cartilaginous septum is a prominent feature. On the posterior aspect of the septum there may be seen a small mass of muscular tissue standing out in marked contrast from the surrounding muscle in virtue of the complicated network arrangement of its fibres and the pale yellow colour which these fibres assume/

assume ~~assume~~ with the Van Gieson stain. The fibres are also narrower in diameter than those of the surrounding muscle whose colour is more of a dark brown hue. The nuclei in the network are rounder and smaller and relatively more numerous. There is a considerable quantity of fat round about the network although there is no sharp line of demarcation; a few of the fibres of the surround- muscular tissue pass directly into the network; some of these fibres pass in longitudinal strands from the direction of the coronary sinus, but they present no modification of structure, and are not, so far as can be seen, to be regarded as "transitional fibres" between those of the network and the muscular wall of the sinus. On the right side the network is separated from the fibrous attachment of the septal cusp of the tricuspid by a small amount of auricular tissue, and the auricular tissue is itself separated from the network by a narrow layer of fat cells and delicate fibrous tissue through which occasional auricular fibres penetrate to become embedded in the main mass of the network. On the left side the network is separated from the fibrous insertion of the aortic cusp of the mitral by a small amount of auricular muscle and a strand of fat and fibrous tissue through which communicating muscle fibres are seen to pass. In the succeeding sections the network (the node of Tawara) increases in/

in its dimensions preserves its complicated appearance and general relations but gradually infringes on the main body of the fibro-cartilagenous septum against whose right side it is firmly embedded and into whose structure occasional isolated strands of the network are found to wander. On the ventricular side of the septum a small round mass of tissue stained a faint yellow and sharply demarcated from the ventricular muscle is now seen (Fig. 4). On closer examination it is found to be a reticulated network of fibres; but here the fibres are large and broad, they contain a large amount of protoplasm, longitudinal striation is indistinct, and where present is seen only at the sides of the fibres and transverse striation is everywhere less distinct. The fibres vary greatly in size and shape and contain one, two, or sometimes three ~~and~~ but seldom four nuclei. In the following sections the network on the auricular side diminishes in size posteriorly, but gradually eats its way into the septum anteriorly. The auricular parts of the bundle in its anterior part, where it is penetrating the septum, has now assumed a form and structure identical with that which characterises the small ventricular portion already described. Soon the auricular and ventricular portions are seen to become continuous, although there is as yet no evidence of any connection between the ventricular part of the bundle and the ordinary ventricular musculature. (Fig 5) At the present stage we have a picture of the auriculo-ventricular bundle in its course through the fibro-cartilagenous septum which separates the/

the auricles and ventricles; the bundle may be recognised as consisting of two parts which differ essentially in their histological appearance; the posterior part presents the characters of a network of fine fibres such as was described in the first sections in which it appeared; this finely reticulated mass which no longer shows muscular connection with the fibres of the inter-auricular septum passes almost suddenly into a network of large coarse fibres, rich in protoplasm and showing little or no striation; stained by appropriate methods the anterior portion is found to contain glycogen whereas the posterior portion contains ~~some~~ none. The finely reticulated part of the bundle (the node) contains an abundant supply of small vessels in addition to a moderately large vein, and there is considerably more interstitial fibrous tissue than is to be found in ordinary auricular or ventricular muscle. In the anterior part the bundle is divided into strands by coarser sheaths of fibrous tissue and the fibres within the strands are themselves interspersed in a fine fibrous tissue network. In the next sections the anterior fibres while preserving their reticulated conformation present the appearance of having been cut mostly in their long axis. The bundle gradually extends forwards and then forward and downwards on to the roof of the interventricular septum. When opposite the adjacent corners of the right and/

and posterior aortic valves the anterior part of the bundle has already become embedded in the muscular septum and quite separate from the fibro-cartilagenous septum, which once more separates it from the lower portion of the finely reticulated node (Fig 4(57)). At this point the bundle enclosed in its fibrous tissue sheath, is equidistant from the endocardial surfaces of the right and left ventricles on either side, and the fibrocartilaginous septum above. Followed a short distance downwards and forwards it is found to divide into two, each subdivision remaining enclosed in a thick capsule of fibrous tissue. When the end of the series is reached the right and left subdivisions are still deep in the interventricular musculature.

The further course of the right and left branches may be followed by the examination of a series of sections from a block of interventricular septum extending from the anterior margin of the first block, to an incision parallel to that side and passing through the septum in front of the septal attachment of the moderator band. The lower margin of the block should be made by an incision passing below the septal insertion of the moderator band where it should meet the anterior margin of the new block; the excision is completed by vertical and horizontal incisions, which will include the remainder of the two main branches as far as the edges of the first two incisions. The tissue/

tissue is still attached to the heart by the moderator band, a small portion of which should be retained.

Beginning with the sections from the upper side of this second block the right and left branches of the bundle are found still to lie deep in the inter-ventricular musculature. The left branch is somewhat larger than the right, and it very soon takes a downward and outward direction till it lies beneath the endocardium of the left ventricle. In its subendocardial position it retains its fibrous tissue sheath although the latter becomes fused with the ordinary loose fibrous tissue in that region. The structure still presents a reticulated form although the fibres appear for the most part to be cut transversely. There is a great variation in the size and shape of the fibres and by this time they exhibit a very pale homogeneous appearance characteristic of the Purkinje type. Further down, the capsule of the branch becomes thinner till it would appear to lie surrounded only by the ordinary sub-endocardiac fibrous tissue, although separated from the ventricular muscle by a general sheet of connective tissue. The individual strands of the branch are still surrounded by a delicate web of connective tissue; each strand is composed of from four to eight fibres, and the single fibres cut transversely appear large and contain from one to three nuclei lying in a clear mass of homogenous proto-plasm whereas the periphery of the fibre is granular and slightly/

slightly striated. Very occasionally a small strand is seen to leave the main mass and pass into the general musculature of the ventricles.

The right branch may now be followed from the site at which it lies in the beginning of the series from the second block. It is, like the left branch, enclosed in a fibrous sheath and may be followed downwards and forwards till it enters the moderator band. During its course it lies about 1·5 ~~m.m~~ mm. beneath the endocardium of the right ventricle. It presents histological features similar to those described for the left branch. It is to be noted that the left branch reaches the subendocardial layer long before the right branch enters the moderator band. In some cases the right branch emerges beneath the endocardium before it enters the band and in the band itself may lie beneath the endocardium; in other cases it may pass through the band surrounded by ordinary muscle and not become sub-endocardial till it reaches the anterior papillary muscle; occasionally the moderator band consists solely of the right branch of the auriculo-ventricular system.

The right and left branches have now been followed to sites where their presence is easily determined by naked eye examination. It has been pointed out already that they become continuous with the extensive ~~network~~ subendocardial network which lies on the papillary muscles of the right and/

and left ventricles respectively, and which spreads in a less distinct and less extensive manner on the other parts of the inner surfaces of the ventricles, especially in the lower two thirds of the chambers. It will be noticed that at a varying distance from its appearance beneath the endocardium (usually o.5 - 1 cm.) the left branch divides into two, a large posterior division which courses horizontally in the direction of the posterior papillary muscle and a smaller anterior division which may be followed downwards and forwards to the anterior papillary muscle, and the surrounding part of the ventricle in the region of the apex. The thin pale threads which occasionally cross the trabeculae, and the fine threads which may be seen to cross the ventricular chamber from one papillary muscle to another usually consist of Purkinje fibres: not infrequently a small cord may be seen to cross the chamber from the septal wall to one or other of the papillary muscles; these cords belong also to the auriculo-ventricular system. Only very seldom do the strands leave the ~~endocardium~~ subendocardial position on the septum to penetrate deeply into the heart wall. It is only after the ramification of the main subdivisions takes place that the Purkinje cells become continuous with the ordinary muscle cells of the ventricles. I can confirm the observation of Tawara that in isolated parts Purkinje fibres may be seen subendocardially which by the examination of serial sections cannot/

cannot be brought into continuity with the general system. Such fibres are often found near the auriculo-ventricular orifices. (p.37). This was a striking feature of a specimen of Echidna (monotreme) in which I examined serial sections of the whole heart. The right branch in this heart as in the case of the sheep did not give off any ramifications till it reached the papillary muscles. Round the papillary muscles and in the lower two thirds of the right ventricle the Purkinje fibres were in a continuous network; isolated strands of considerable size in the upper third and near the flaps of the valves could not be followed into continuity with the system in the lower two thirds. Another peculiar feature of this heart was that whereas the right branch ended in Purkinje fibres, there were no such fibres to be seen in the left ventricle.

Nerves:- An important characteristic of the auriculo-ventricular system in the sheep is the ease with which nerves can be demonstrated in the structure. Several small nerves may be seen to enter the node from the inter-auricular septum. These subdivide and reunite coursing among the fibres of the system in the form of a network. They may be followed into the moderator band on the right side, and as far at least as the point of division of the left branch on the left side. Nerve cells can also be demonstrated as far as the papillary muscles.

Lymphatics:- Some significance is also to be attached to/

to the fact that the main bundle and its branches is surrounded by a system of lymphatic vessels. This possibly accounts in part for the ease with which the structure can be dissected. The importance of the presence of the lymphatic sheath will be referred to later.

The foregoing description is based on the examination of a single heart, but may be taken as representing the characteristic features and most common relations of the system. The hearts of other two sheep showed slight variations, more particularly in the course of the main subdivisions of the branches. These variations may be confirmed by naked eye examination and comparison of a number of hearts from the same species. The description applies also in a general way to the hearts of all ungulates and in a degree to the mammalian heart generally.

THE HUMAN HEART.

Macroscopic Examination - A comparison of the inner ventricular surfaces of a number of human hearts suggests at once the great variation in the conformation and relations of the small structures, papillary muscles, muscular trabeculae and pale cords, which made up the picture. But when a human heart is compared with the heart of a sheep or other ungulate the contrast is still greater. In the left ventricle of the human heart there is no sign of a pale cord emerging/

emerging from the interventricular muscular septum below the pars membranacea septi; there are no anterior and posterior cords coursing towards the anterior and posterior papillary muscles; and the papillary muscles and lower portions of the ventricle are not covered with a pale network of fine threads shining through the translucent endocardium. A more careful examination of the human heart however reveals the fact, that although the internal surface of the left ventricle is subject to great individual variations, that portion of the inter-ventricular septum beneath the right aortic valve and the pars membranacea septi is always flat. This flat portion is usually in the form of a triangle with the apex towards the base of the heart; here the endocardium is less transparent than in any other part of the ventricle. Closer examination of some hearts in this region shows that the dull appearance is due to pale streaks which deviate from the region of the pars in the forms of a fan(59), the more posterior portion descends almost perpendicularly in the direction of the posterior papillary muscles, while the more anterior portion is directed forwards and downwards on the septum in the direction of the anterior papillary muscles. In the upper third of the septum the fan-shaped structure usually presents a more or less homogenous appearance, but as the endocardium becomes more transparent the streaked character becomes apparent, and lower down still the diverging streaks may collect into three or four bands which are prolonged/

longed towards the bases of the papillary muscles and the apex of the ventricle. The structure usually disappears from naked eye observation when the inner surface of the ventricle becomes trabeculated. Crossing the muscular trabeculae at the apex fine pale cords may be seen which resemble the extension of the Purkinje network in the same region in the sheep. Very occasionally a thin pale cord may be seen to pass from the fan-shaped structure on the septal wall through the cavity of the ventricle to the anterior or, as is more frequently the case, to the posterior papillary muscle. These cords correspond to the twigs of the left branch of the bundle described in the sheep. The appearances described do not manifest themselves in an easily recognisable form in every human heart. In older hearts and especially in hearts which are hypertrophied and dilated, the outline is often more manifest. Sometimes fresh specimens afford a more satisfactory demonstration than the same hearts when fixed and hardened; on the other hand fixation in Formol-Müller and preservation in 70% alcohol has been seen to bring out the distribution of the system in a heart which in the fresh condition showed it only in a very vague form.

In a suitable specimen where the structure is specially well-marked and probably also where the subendocardial connective tissue is not too abundant, the fine threads of which the fan-shaped structure is composed may be seen to cross/

cross each other in all directions.

The internal structure of the right ventricle is even more variable than that of the left (Fig 10.) In the ungulate heart the moderator band is always well developed and from its position is readily recognised. This is not the case in the human heart, in which it is not always easy to recognise the band from the other muscular trabeculae at the apex of the ventricle. The septal wall of the right ventricle is covered in its upper third posteriorly by the septal cusp of the tricuspid, whose cordae tendineae are inserted into small papillary muscles which are embedded in the septal muscle at the middle of the septum. In front of these papillary muscles are the large longitudinal trabeculae of the pulmonary bulbus, and below the papillary muscles the septal wall is smooth. Crossing from this smooth part of the ventricular wall to the base of the anterior papillary muscle may be seen a trabecular muscle on whose surface close examination may reveal the presence of a pale dull streak coursing in the long axis of the trabeculae. Should the specimen be a suitable one this thread may be followed on to the smooth surface of the septal through whose translucent endocardium it may be easily recognised; it may still be traced upwards and backwards to the crista supra-ventricularis, where it is lost to/

to view below and in front of the pars membranacea septi.[x] On the septal wall there is no trace of arborisation from the main branch, but in the trabeculae round the bases of the papillary muscles fine threads and delicate bands may be seen. Some of these consist solely of fibrous tissue but others contain muscle fibres and are in all probability the terminal twigs of the auriculo-ventricular system. In some instances a small pale muscular cord may be seen traversing the cavity of the ventricle from one papillary muscle to another. A point of some interest is that both in the right and left ventricle these terminal twigs may be represented by delicate membranous bands instead of round cords or threads.

Having indicated the nature of the general distribution of the right and left branches to the corresponding ventricle, as seen on naked eye examination, it remains to follow the branches into the main bundle. There are some hearts which lend themselves better than others to successful dissection; probably the presence of fat and lymphatic spaces round the bundle and its branches is an advantage in/

[x] The dissection of the right branch in its course between the septal wall and the crista supra-ventricularis is a matter of extreme difficulty. It can very rarely be accomplished. Keith has some specimens which show it.

in this respect. It seems also to be the case that when the heart is oedematous the process of preparation is easier. In any case the fresh heart should be left 24 hours in running water then packed with cotton wool and placed in Kaiserling's solution in which it should be left till properly fixed. It should then be transferred to 70% alcohol for 24-48 hours. Before dissection it should be allowed to lie for some days in glycerine and water. It is always difficult to dissect out the main branch of the bundle because of its intimate connection with the pars membranacea septi and the septum fibrosum. More especially is this the case in older hearts where the bundle is almost invariably subdivided into strands by thick septa of fibrous tissue which are continuous with the fibrous tissue of the pars. On the auricular side of the pars the main mass of the bundle or node is found lying closely applied to the septum fibrosum from which it cannot be removed except by tearing or cutting; on its upper and right sides it can be easily separated from the surrounding structures. As a separate structure, it cannot be followed any distance behind the posterior aspect of the septum fibrosum and does not so far as can be seen from naked eye examination come within a considerable distance of the coronary sinus.

Retzer/

Retzer succeeded in demonstrating the course and relations of the main bundle by exposing the heart to Macallum's process of maceration. The heart was macerated until the connective tissue could be removed easily. In Retzer's preparation the connective tissue became so soft that the auricles were readily separated from the ventricles, leaving only the muscular connection through the auriculo-ventricular bundle. In this way he found that the bundle lay on the roof of the inter-ventricular septum and underneath the pars membranacea septi; it could be followed back to the trigonum fibrosum and forward to the ventricular muscle with which he believed it to become continuous in the roof of the septum; he further describes the posterior part, that is the node, as possessing two contributory branches, one from the muscle of the interauricular septum and the other from the muscle of the septal cusp of the tricuspid valve. However, great the merit of his method of preparation, and however exact his description of the course and relations of the main part of the bundle, Retzer failed to recognise, as of course did also Kent, His and Braeunig, that the bundle does not immediately become continuous with the ventricular muscle on the roof of the ventricle, but is distributed by means of a complicated subendocardial network as Tawara first described it.

<u>MICROSCOPIC EXAMINATION</u> /

MICROSCOPIC EXAMINATION

The method employed in the excision and preparation of a block of the node and bundle has been described above (p.38). In the case of the sheep the series was cut in a plane parallel to the course of the main bundle. In the case of the block from the human heart about to be described, the series was prepared from sections cut in a plane at right angles to the course of the main bundle. This is the method which I invariably employ in the examination of pathological specimens, because it seems to provide an easier means of orientation, and also to afford a more accurate means of estimating the extent to which the bundle is invaded by fibrous tissue in the hearts from old subjects. The undulating course which the bundle sometimes follows, and the extent to which such undulation ~~and~~ is increased by hardening, is apt to lead to deceptive appearances in sections which are parallel to its long axis. The capacity to allow for these sources of deception is admittedly a matter of experience, and the fact that I have always employed the transverse method in the examination of smaller hearts, which were cut 'en bloc' may account for my preference for this method.

The/

The series to which the following description applies was prepared from the heart of a child six months old. The sections were examined from behind forwards.[x] After proceeding through a number of sections of inter-auricular septum and inter-ventricular muscular septum a specimen is noted in which a small crescentic mass of tissue closely applied to the annulus fibrosus is readily distinguished from the rest of the auricular muscle with which it seems to be in immediate contact. Under the low power of the microscope this small mass stands out from the neighbouring muscle in virtue of its paler colour with the Van Gieson stain, the comparatively large number of nuclei in its substance, and the closely packed character of its constituent elements. Its general relations to the surrounding structures are seen in Fig. 11 . Above and to the right is seen the thick dense mass of pinkly stained tissue representing the annulus fibrosus and the root of the aorta, The left half of the upper portion of the section consists of the lower part of the inter-auricular septum with its fibres streaming down in a loose fashion towards the septal cusp of the tricuspid. The lower half of the section consists of the roof of the inter-ventricular muscular septum separated/

x The block is cut from before backwards and mounted in series from behind forwards, so that the orientation is such that the observer looks at the heart from the front. The terms "right" and "left" used in the text are thus not meant to signify 'towards the right side of the heart' or 'towards the left side of the heart', but on the right or left side of the microscopic picture that is on the right or left side of the heart when looked at from the front.

separated from the structures above by the septum fibrosum. In close apposition to the left side of the annulus fibrosus and at the corner where that structure becomes continuous with the fibrous septum separating the auricular from the ventricular muscle, lies the small mass of dense pale multi-nucleated tissue which represents the first appearance of the auriculo-ventricular system. Examined more closely the fibres of this dense meshwork are seen to be in continuation with the fibres of the auricular septum above and also with the loose fibres lying on the left between the meshwork and the endocardium of the right auricle. Examination of the bundle with a higher power at this point shows that there is in some parts of the tissue no evidence of an interlacing of fibres; the picture suggests rather in such places a dense syncytium packed with nuclei in a small amount of protoplasm traversed by a number of fine fibrils. In other parts the structure presents a looser appearance; the meshwork is more open and the threads or fibres of which it is composed can be more closely examined. The individual fibres are joined up in a very irregular fashion and there is no systematic distribution of nuclei. The nuclei vary greatly in shape and some are embedded in protoplasm while others appear to lie in vacuolar spaces. A system of fine fibrils appears to permeate the structure in a continuous and irregular way; at the/

the edges of the bundle or node which are adjacent to the auricular muscle a direct continuity of auricular and nodal tissue is observed. Striation is absent in the node. There is a very rich supply of delicate blood vessels, but no nerves can be seen.

Continuing the series the node is seen to increase in size, while preserving its crescentic form, with the convexity directed towards the right auricular endocardium. It still presents the same dense multinucleated appearance and its structure now comes into a more extensive connection with the auricular muscle on its left and lower aspects. In the sections a little further forward the node is increased in size and its lower and outer aspect is immediately beneath the auricular endocardium; it is now separated entirely from the auricular muscle by a fibrous tissue sheath with the exception of a small portion at its uppermost extremity (Fig 11); on the right side it is still closely applied to the annulus fibrosus, into which it has eaten its way to a slight extent. (Fig 11) Further forward still the whole node is surrounded by a fibrous tissue capsule which demarcates it completely from the auricular muscle; it has now entered the substance of the annulus fibrosus. On its lower and outer aspect is the fibrous attachment of the septal cusp of the tricuspid, while on the right side of the annulus fibrosus the insertion of/

of aortic cusp of the initial [mitral] is seen as well as the posterior cusp of the aortic valve~~s~~. (Fig 11.)

After entering the annulus fibrosus the bundle courses downwards and to the left till it lies in the centre of the pars membranacea septi. (fig. 11.). Here it presents a rounded appearance; it has become divided into eight or ten smaller compartments by septa of fibrous tissue; it (~~tissue~~) still preserves an irregular network appearance, there are comparatively fewer nuclei and there are numerous small blood vessels. Closer examination shows also that the syncytial character of the earlier structure has become slightly modified, and that there is evidence of the presence of a few distinct muscle fibres; no striation can however be detected. Proceeding downwards and forwards it comes to lie on the roof of the inter-ventricular muscular septum from whose muscle fibres it is still separated by a connective tissue sheath. From its lower right side a few fibres are seen to deviate to the right beneath the left ventricular endocardium; these fibres are enclosed in connective tissue sheaths and are separated from the ventricular muscle by a thick lamella of connective tissue. The fibres themselves are easily distinguished from the ordinary ventricular muscle fibres by the fact that they are larger and paler, having a pale greenish yellow colour, whereas the ordinary muscle fibres are stained a yellowish brown. The nuclei are now relatively/

relatively fewer in number, rounded and irregular in shape and large in size. Here and there in the course of a fibre there is slight transverse striation. These fibres descending on the septal surface of the left ventricle represent the first appearance of the left branch of the bundle. The portion of the bundle from which these fibres of the left branch emerge becomes gradually cut off from the main mass by an invagination of the tissue of the pars so that a separate mass is now recognised towards the left representing the commencement of the right branch (Fig. 11). This right branch enclosed in a thick fibrous capsule can be followed downwards and forwards on the left side of the inter-ventricular muscular septum beneath the fibrous attachment of the septal cusp of the tricuspid; at the same time the fibres from the left branch continue to descend on the other side of the septum. The existence of the left branch as a single cord is soon lost sight of, the only indication of its presence being the thin layer of interwoven fibres lying beneath the endocardium of the septal surface of the left ventricle. The pars has by this time disappeared from the sections, and the inter-ventricular septum comes into immediate contact with the root of the aorta. In those sections which show the right branch after it has passed beneath the fibrous attachment of the septal cusp of the tricuspid, the branch is seen to take an almost perpendicular course; it is still isolated from the ventricular muscle; cut in its longitudinal axis an/

an opportunity is afforded of observing the character of its fibres; they are large and pale with peripheral fibrils, and a large amount of homogeneous central protoplasm with large irregular rounded nuclei. Free communication between neighbouring fibres cannot be made out; striation is present in isolated parts. Perhaps the most striking feature of the right branch is its great diminution in size in spite of the fact that it has parted with ~~some~~ none of its fibres to the surrounding septal musculature.

The foregoing description gives a general indication of the course and relations of the node and main stem from their origin in the inter-auricular septum till they emerge in right and left branches beneath the right and left surfaces of the inter-ventricular muscular septum. The histological appearances are those more or less characteristic for the heart of an infant, and must not be taken as applicable to older hearts. An outstanding feature of the histology of the auriculo-ventricular system is the great variation it exhibits, first of all in hearts of different species, and secondly in hearts at different ages in the same species. This point will be discussed more fully at a later stage.

In the meantime, reference must be made to the variations which may be noted in the course and relations of the main stem and of its two branches. The position of the node itself may be said to be almost invariable. Very occasionally there is a variation in the proximity of its tissues to the fibrous attachment/

attachment of the mitral valve; in its more anterior portion the node is invariably in the closest relationship with the fibrous attachment of the septal cusp of the tricuspid. The main stem may vary considerably in its course through the annulus fibrosus and pars membranacea septi. It may on leaving the auricle and entering the annulus fibrosus preserve its course nearer the right side of the heart so that when it has descended to the lower aspect of the pars it takes a sharp turn towards the left ventricle to divide into its right and left branches. In the second place it may on entering the annulus fibrosus, take a course downwards and towards the left ventricle so that in the pars it comes to occupy a central position; in such cases when it divides at the lower end of the pars it is lying on the roof of the inter-ventricular muscular septum, and the microscopic sections give the picture which represents the main stem and its divisions as 'riding on the ventricular septum'. In the third place, in its descent from auricle to ventricular septum it may deviate more than usual in the direction of the left ventricle, and in such cases the point of division is situated more on that aspect of the ventricular septum towards the left ventricle. It is important to note that when the main stem has followed the third course, the right branch does not as a rule become subendocardial immediately after its division,/

division, but sinks into an inter-muscular septum in the roof of the septum, to wend its way through the muscle of the septum and reach the endocardium of the right ventricle at a varying distance from the septal roof. The possible deception to which the latter course of the right branch may give rise can be realized only by those who have examined a number of hearts through the main stem and the commencement of its branches. The right branch shortly after its commencement undergoes a marked diminution in size and it not infrequently happens that when it dips down into the septum it is readily lost sight of. More especially is this the case when the sections are cut on a horizontal plane; and this is one of the reasons why I emphasise the advisability of examining the human heart from a series cut in a ~~frantic~~ frontal plane.

With regard to the variation in the minute structure of the node and main bundle at different ages, it may be said that while in early life the structure preserves to some extent its embryonic character, in later years it more closely approaches the appearance of ordinary cardiac muscle. In young and in adult hearts the auricular fibres are directly continuous with the tissue of the node; the continuity of structure is not secured through special 'transitional fibres'; on this point my observations confirm those of Mönckeberg in every respect. With advancing years the node loses its compact syncytial appearance; it assumes/

assumes more the character of a complicated network of fine fibres in whose interstices there is a considerable amount of fibrous and elastic tissue. The tissue itself more closely approaches the character of the ordinary auricular muscle, taking on the Van Gieson stain in an approximately similar fashion and exhibiting on closer examination the presence of transverse striation in many of its fibres. Perhaps the outstanding feature of distinction between the node and auricular muscle in older hearts is the pinkish colour of the former due to the presence of connective tissue; of course even in young hearts there is a considerable amount of connective tissue in the node, and fibrous tissue and elastic tissue may be demonstrated in its structure when they are not yet present in an appreciable amount in the ordinary cardiac muscle. The main stem changes also in its histological characters with advancing years. There is in most cases an increase in the number and size of the septa which divide it longitudinally. The structure itself appears as if it had become stretched, having lost to a great extent, its closely reticulated arrangement and now suggesting the appearance of strands of fibres coursing in the long axis of the stem. Nuclei appear to be relatively fewer than in young hearts, and the presence of/

Mönckeberg – Untersuchungen über das Atrioventrikular-bündel im menschlichen Herzen – Jena. 1908.

of fibrils and transverse striation is well marked. There are numerous blood vessels, also lymphatic spaces in and around the bundle.

The next variations requiring attention are those pertaining to the course and distribution of the main branches on the inner surface of the ventricles. Reference has already been made (p. 50) to the great dissimilarity which is presented by the trabecular and papillary arrangements in a series of human hearts, and as has been suggested in the macroscopic description, these varied arrangements determine in a degree the differences in the course and distribution of the auriculo-ventricular system with which they are supplied. I have never attempted to follow in serial sections this distribution in the human heart; to a certain extent it is described by Tawara in his original publication, but the most complete description which has appeared is that which is given by Mönckeberg in his exhaustive treatise on the subject. Fahr has also followed and reproduced in a model the course and distribution of the system in a young human heart.

<u>The Right Branch</u>:- Mönckeberg in his description regards the course of the right branch as being divisible into three parts, (1) an upper subendocardial part, (2) an intermediate intermuscular portion, and (3) a lower subendocardial/

subendocardial portion; this subdivision applies only to that part of the right branch which extends from its origin on the roof of the septum to the base of the anterior papillary muscle where it begins to ramify. Bearing in mind the fact that the point on the roof of the muscular septum at which the main bundle divides depends upon the deviation in its course through the annulus fibrosus and the pars membranacea septi, it will be seen that in those cases where there is considerable deviation towards the left ventricle and where the right branch dips immediately into a fibrous septum in the roof of the muscular septum, the first part of the course described by Mönckeberg will be wanting. In such cases the right branch will be found to consist of only two portions, an intermuscular portion reaching to the point where it emerges on the septum of the right ventricle and a subendocardial portion extending down the septum and along the moderator band to the base of the anterior papillary muscle. When , however, the main bundle descends more directly, preserving a relative proximity to the right auricular surface, or descends in the middle of the pars, its division takes place more on the summit of the ~~crista supraventricularis~~ interventricular septum and the right branch occupies in the commencement of its course a subendocardial position. The distance through which this subendocardial position/

position is preserved is very variable, scarcely ever, according to Mönckeberg, exceeding 4 mm. During this first subendocardial portion of its course the branch diminishes greatly in diameter. It is surrounded by loose connective tissue and wide lymph spaces, and its substance is interspersed with a large number of small blood vessels and capillaries. In older hearts the surrounding connective tissue may contain a considerable amount of fat. The fibres of the branch in this part appear to run parallel, they are rather smaller than the fibres of the main bundle, do not contain many nuclei, take on the Van Gieson stain well and show a considerable amount of transverse striation; they bear a strong resemblance to the ordinary ventricular fibres.

The second or intramuscular portion of the right branch lies behind the small papillary muscles on the septal wall to which the chordae tendineae of the septal cusp are attached. It lies at a varying but usually very little depth beneath the endocardium. The length of the portion in one of Mönckeberg's cases was 13 mm. The course of the branch is almost vertical and in transverse section is seen to become reduced in diameter as it is followed downwards. The fibres are still small though slightly thicker than in the first part; the reduction in the diameter is due to an accumulation of the fibrils of/

of several fibres into a single fibre; the branch is enclosed in a connective tissue capsule and does not part with any of its fibres to the neighbouring ventricular muscle.

The point of emergence of the third portion to a subendocardial position varies in different hearts. It is very often distinguishable on naked eye examination immediately below the base of insertion of the septal papillary muscles although in many cases it cannot be detected until the region of the moderator band is approached. In the moderator band itself the branch may again become intramuscular to emerge beneath the endocardium on the anterior papillary muscle. While, as has been noted already, the branch undergoes a very great reduction in calibre during its intra-muscular course in the septum, its diameter is increased again in the third portion. This increase in diameter is to be referred not only to an increase in the size of the individual fibres, but also to an increase in their number. According to Mönckeberg, in this part a transition between the fibres of the branch and the so-called Purkinje fibres takes place. This conclusion is based on the finding that immediately after leaving its intramuscular position the fibres are seen to contain glycogen, whereas previously they contained none. I have already suggested the inadvisability of applying the term 'Purkinje fibres' to these structures in/

in the human heart, (p. 33), and shall revert to the subject when discussing the appearance of the terminal ramifications of the left branch (p. 78). The distribution of the right branch after it leaves the moderator band and reaches the anterior papillary muscle is by no means constant, although Mönckeberg found that the commencement of the ramification in his cases consisted in a subdivision of the branch into three main strands. One strand coursed forwards towards the trabeculae at the apex and the anterior parietal wall of the ventricle, a second took a circuitous path round the base of the papillary muscle to be distributed behind, and the third encircled also the papillary muscle to become distributed on the trabeculae and parietal wall on the outer side of the cavity. A further description is rendered impossible on account of the extremely complex and varied conformation of the muscular substance on the trabecular surface of the cavity. No strands of ramification could be detected on the septal surface. A point of importance to be noted is that, while many of the pale strands and cords which bridge over the inter-trabecular spaces, represent the terminal arborisations of the auriculo-ventricular system, many of these structures consist of ordinary muscle fibres and others are composed of connective tissue only. Considerable difficulty is presented in the attempt to trace the continuity/

continuity of the special fibres with the ventricular musculature because of the close similarity of the two structures in most hearts.

The Left Branch:- The site of emergence of the left branch from the main stem beneath the pars membranacea septi has been described above. Its course in a diverging fan-shaped form beneath the endocardium on the septal wall towards the papillary muscles and apical trabeculae has also been referred to in the macroscopic description of the heart. Whereas the fibres of the right branch are enclosed in a single sheath for a considerable part of its course, namely, from its origin till it reaches the anterior papillary muscle, the fibres of the left branch remain together only for a very short distance; in fact in those cases in which the main stem deviates to the left through the pars on its path from the annulus fibrosus and the division takes place on the left side of the pars there may be no well defined single branch at all on the left side. In such cases the fibres often emerge gradually from the main stem at the point of division in the form of a sheet or thin layer. When the division of the main stem takes place on the right side of the pars or in the centre there is usually a ~~small~~ short left branch; in the former/

former case it is rather longer than in the latter. The main feature of the left branch then is that immediately or very shortly after it leaves the main stem its constituent fibres spread out in a fan-shaped form and continue to lie enclosed in connective tissue beneath the septal endocardium. There is during this part of their course no association with the ventricular musculature, or if there is it must only be very exceptional. It was seen that in the case of the right branch the fibres underwent a sudden change in size and appearance immediately they emerged from the muscular septum to take up a subendocardial position. On the left side the fibres on the whole possess a greater and more constant similarity to the ordinary cardiac fibres than do those on the right; but ~~while~~ when the fibres on the left also show variations in their size and structure such variations occur at irregular intervals and apparently in different parts of the same fibre. Throughout the whole extent of the fan-shaped prolongation large fibres rich in protoplasm and poor in fibrils with rounded or oval vesicular nuclei may be seen side by side or in continuity with fibres which from their microscopic characters can scarcely be distinguished from ordinary cardiac muscle fibre. Such appearances are not present in every heart, and the determining factor in their occurrence which is certainly not age, is not understood./

stood. These are the fibres which have been referred to by Mönckeberg and others as Purkinje fibres. The real Purkinje fibres are present normally and invariably in the ungulate heart; to these structures in the human heart they admittedly bear a resemblance but from them they are easily distinguishable. If in the ungulate heart they are occasionally found in the subendocardial layer of the ventricle, apparently dissociated from the ramifications of the auriculo-ventricular system still there is every reason to believe that developmentally they are always in relation to that system (p.134). In the human heart on the other hand they are only occasionally and without any known reason found in connection with the auriculo-ventricular system and what is more important, fibres bearing a resemblance to the Purkinje fibres and indistinguishable from the so-called Purkinje fibres in the human ventricles are seen in pathological conditions of the human auricles. In degenerative fibrosis of the human auricles fibres are met with which are larger than normal, contain a larger amount of protoplasm, show little striation, and possess rounded or oval vesicular nuclei. It is because there has been a tendency to attach an undue importance and significance to the presence of such fibres in the auricles, that it would be well to reserve the special term for the characteristic type which occurs in the ungulate heart. This suggestion contains in no sense a reflection on the accuracy/

accuracy of Mönckeberg's description or on the validity of his conclusions; they are the most thorough that have so far appeared on the subject.

I have been able to confirm Mönckeberg's observations on the more minute structure of these large fibres in the human auriculo-ventricular ramifications. Small thin blocks were cut in a plane parallel to the endocardial surface of the left ventricle; these were prepared so as to include a few ordinary ventricular fibres for comparison; the thin block was placed in a slit made in a thin block of liver tissue and the whole mass was impregnated with silver. The advantage of a thin outer coating of liver tissue is that the coarse impregnation is taken up by the liver substance and a more delicate and regular impregnation occurs in the underlying muscular structure which is the object of examination. The microscopic sections were cut in a plane parallel to the general course of the fibres and at right angles to the endocardial surface so as to include both ordinary and special muscle. The most outstanding feature on superficial examination was the difference in the extent to which the two types of muscle fibre had become impregnated. The ordinary muscle was dark and the fibrils and transverse striation stood out very clearly; the bundle fibres were large and pale, the striation more faint and less frequent and the fibrils less abundant (Fig). Specially prominent in the bundle fibres/

fibres in some places were deeply impregnated cement lines occurring at more or less regular intervals and usually transverse to or slightly bent across the fibre; they did not present the stair-step picture of the cement lines seen in ordinary cardiac muscle. In some parts those cement lines appeared to give rise to a slight constriction of the fibre and to divide it into protoplasmic compartments although there was no interruption of the fibrils in their course. The peculiar appearance determined by these constrictions suggests a similarity to the nodes of Ranvier in medullated nerve fibres. This has a particular interest in view of similarity between nerve structure and nodal structure (specialised muscle of the heart) suggested by Keith and myself in a description of the heart of Echidna (monotreme). The constrictions cannot be regarded as dividing the fibres into cellular elements; two or three nuclei may occur in one protoplasmic compartment and two or three compartments may be seen in series without a nucleus. While these structural variations may be found in hearts of any age, they are most marked in those from older subjects. The nuclei in these fibres vary considerably in size and shape; they lie in the protoplasm which is comparatively large in amount and they are relatively fewer in number than the nuclei in the main stem. Occasionally they appear to lie in/

Nagayo – Zieglers Beiträge z. p. Anat. 45 – 1909.

in vacuolar spaces in the protoplasm.

In some cases there is a large number of vacuolar spaces without nuclei, and a considerable portion of a fibre may appear to be quite devoid of contents of any description. It is not improbable that in such cases the contents have become dissolved out in the process for microscopic examination. In other cases the fibres contain homogenous or granular matter whose chemical properties and significance require further notice. The large transparent appearance of the Purkinje fibres suggested to Aschoff the possibility that they might contain glycogen and at his instigation the ungulate heart was examined by Nagayo with the result that this substance was demonstrated in the bundle and its ventricular extensions. Nagayo found the glycogen distributed in the Purkinje fibres in two forms; in a diffuse finely granular form between the fibrils, and in large coarse granules in the protoplasm round the nuclei. Of some interest and probably possessing a significance to be discussed later (p.182) is the fact that whereas the main stem and its ventricular extensions contain glycogen the node contains little or none. Nagayo's examination of the human heart showed that in thirty cases three contained a considerable amount of glycogen in the ventricular ramifications, nine contained a small amount and in the remainder there was practically/

practically none. Mönckeberg carried out an independent and almost simultaneous investigation of the subject in the human heart. He realised that the demonstration of glycogen depended on the freshness of the material, the method of its fixation, and the process of embedding. But allowing for these sources of variation the presence or absence of glycogen was associated with other predisposing causes, and he came to the general conclusion that this substance was present as a rule in the hearts of strong and well nourished subjects, whereas it was usually absent in the hearts of those who were weak, poorly nourished and cachectic. In those hearts in which glycogen is present there is no regularity or consistency in its distribution in the fibres of the ramifications. In the same strand some fibres may be free from glycogen while others contain it in abundance; in other cases glycogen may be present in only limited parts of the same fibre. The inconstant character of its occurrence in any heart has proved disappointing to those who had hoped by its means to be able to follow to their termination the branches of distribution of the bundle.

The problem of following out the terminals of the system on the left side has not been any more successfully solved than on the right side. This difficulty is of course referable to the fact that the end portions of the system/

system are scarcely distinguishable from the ordinary cardiac muscle fibres. It was noted in the macroscopic description of the fan-shaped portion of the left branch on the septal wall that in suitable cases a crossing of the strands could be observed. Microscopic examination shows that although the individual strands cross each other there is comparatively little communication between the individual fibres of the same strand. While it is ~~time~~ true on the whole that the fibres preserve an independent course there are here and there short communicating fibres, and in some places these communications may be of a complicated character suggesting small "nodal centres" where there is an intricate communication and exchange of fibrils from several fibres. What the actual significance of these "nodal centres" may be it is difficult to say. Speaking generally the fibres of the branch increase in number in their descent on the septum; with the increase in the number of the fibres there is most probably an increase in the total number of fibrils; whether the nodal centres are associated with a division and re-distribution in some places and a combination and centralisation in others is a matter worthy of further investigation. Following the fibres from the septal wall on to the trabecular and papillary muscles the observer encounters two great difficulties, when the criterion/

Keith and Flack - Lancet 1906 No ii.

Fahr - Verhand. d. deutsch path Gess. XII. 1908.

criterion as to the identity of the fibres is the amount of protoplasm and the number of the fibrils; because on the one hand the terminals of the system may be indistinguishable from ordinary muscle fibres and on the other hand large fibres may occur in the heart, (~~e.g.~~ as in the auricle), which have nothing to do with the auriculo-ventricular system. It is the case that Tawara, Mönckeberg, Keith and Flack and Fahr, regard the so-called Purkinje fibres in the human heart as being invariably associated with the system and as being, when present, a reliable guide to its distribution, but while I am not prepared to dispute the authority of these observers, I am inclined with Arnold to accept with reserve the finality of a solution based on such a criterion.

Although there is no satisfactory means of following in microscopic preparations the strands of the bundle till they become continuous with the ordinary muscle, thus providing a feature of its general distribution, still it is possible to demonstrate a continuity of structure in the case of individual fibres. This can readily be done by examining a small cord which may on macroscopic examination be found to cross from the lower aspect of the septum to the base of one of the papillary muscles. If the cord and a piece of the papillary muscle be/

be cut in serial sections and if the fibres of the cord be large and easily distinguished, then it will be found that they spread in the subendocardial layer of the papillary muscle and that some of them dip into the ordinary muscle to become continuous with its fibres. The continuity of structure may also be demonstrated in the muscular trabeculae in suitable cases.

It may be taken then on the combined macroscopic and microscopic evidence that the auriculo-ventricular system in the human heart bears a general resemblance in its morphology and relationships in its structure and distribution to that which is so easily examined in the sheep. In the human heart the examination is rendered much more difficult on account of the similarity between the special and the ordinary muscle fibres. The outstanding facts are that the system is distributed by a right and left branch to the right and left ventricles respectively; that the distribution takes place to the papillary muscles and the trabeculae in the ventricular apices, and that it is almost exclusively confined to the lower portions of the ventricles, and lastly that although the main branches course on the septal walls that few or none of their fibres are distributed to the upper portions of these walls.

THE NERVE SUPPLY OF THE AURICULO-VENTRICULAR SYSTEM.

Reference has already been made to the fact that the/

the presence of nerves in the node, main stem and primary branches of the system in the sheep's hearts can be demonstrated by the ordinary histological methods. When special technique for the demonstration of nerve elements is employed the relation of nerve to muscle is seen to be very intimate.(Fig 12) Wilson employed the vital methylene blue method in the hearts of the calf, sheep and pig, and found a very rich supply of fine nerve elements and ganglion cells in the closest relationship with the muscular elements of the node, the bundle and the commencement of its subdivisions. The ganglion cells may occur in groups of considerable size, and the nerve fibres thread their way through the tissue in small bundles and in the form of a plexus. The majority of the fibres possess varicosities and appear to be non-medullated, although medullated fibres may also be seen. The plexuses which surround the muscle fibres are composed of very fine varicose fibrils which are easily distinguished from elastic fibres. Although in his first publication, Wilson was unable to describe the nerve elements in the human heart, he suggested that in all probability appropriate methods would establish their existence in that organ as well. It was left to Aschoff to be the first to show that also in the system in the human heart nerve structures could be demonstrated. By the/

the methylene blue method he found medullated and non-medullated fibres in the main stem and in the left branch. Mönckeberg shortly afterwards demonstrated nerve elements in the bundle of a foetal heart.

THE AURICULO-VENTRICULAR SYSTEM AS A SPECIAL ORGAN.

The foregoing descriptions of the sheep's heart and the human heart should suffice in themselves to make it obvious that in the auriculo-ventricular system we have a highly specialised organ performing a highly specialised function in the economy of the heart. The extremely complicated arrangement of its peculiar fibres, its rich blood supply, and its special nerve supply, are features which distinguish it from the general cardiac muscle. Enclosed in a firm fibrous sheath and surrounded with lymph spaces it has no communication with the heart muscle between the inter-auricular septum on the one side and the papillary muscles and trabeculae at the apices of the ventricles on the other. To say that it constitutes the muscular connection between auricles and ventricles is to state a fact; but to leave the matter there with the suggestion that its functions are those or even a modification of those of ordinary cardiac muscle, is to render inevitable a total misconception of the special functions of this important organ. Its physiology will be dealt with after we have considered the morphology and structure of/

of the sino-auricular system (the node of Keith and Flack), and its relation to the auriculo-ventricular system in the vertebrate heart generally. This will be done in the next chapter.

CHAPTER III.

THE SINO-AURICULAR NODE: ITS STRUCTURE AND ITS RELATIONS TO THE AURICULO-VENTRICULAR SYSTEM IN THE VERTEBRATE HEART.

The discovery of a muscular connection between auricles and ventricles satisfied the demands of those whose conception of co-ordinated cardiac action presupposed the existence of such a muscular continuity. With the discovery, however, there appeared also the possibility of the solution of a problem which had long excited the interest of physiologists, namely, the site of origin of the contraction or stimulus to contraction in the heart. Tawara, recognising the peculiar character of the structure with which he had to deal, suggested that the auriculo-ventricular node was the "predominant cardio-motor centre". From the node he imagined that the contraction wave spread first through the auricular fibres giving rise to the auricular contraction, and that the impulse from the same centre travelled through the main stem and its branches to give rise to the subsequent ventricular contraction. Aschoff was also disposed to regard the auriculo-ventricular node as the "centre of automatic cardiac movement". On a priori grounds it had always seemed more likely that the cardiac contraction should begin in the neighbourhood/

Wenckebach – Arch. f. Anat. u. Phys. (Phys. Abt.) 1906.

Koch. – Zieglers Beiträge. 42. 1907.

neighbourhood of the superior vena cava and Wenckebach had described a muscle bundle at the junction of the superior cava and auricle which he regarded as constituting the exclusive muscular connection between sinus venosus and auricle in the same way as the auriculo-ventricular system preserves the muscular continuity between auricles and ventricles; he regarded this muscle also as the site of origin of the auricular contraction. Koch, however, after a careful examination of serial sections failed to find any structure resembling that of the auriculo-ventricular system in the region of the bundle described by Wenckebach. He found that the superior cava was to some extent separated from the auricle, though not by a sharp line of fibrous structure, such as that which separates auricles from ventricles, and he left the question open as to whether or not the ganglion cells in the sino-auricular sulcus might not in some way be associated with the impulse to contraction. Wenckebach's bundle in any case consisted, as far as could be made out, of ordinary cardiac muscle fibres. Koch prosecuted his enquiry by an examination of the areas of pulsation in the dying heart. It is well known that in the dying heart the ventricular chambers are the first to cease beating. Koch found that while the auricles continued to show evidence of pulsation after the ventricles had ceased, that that part of the auricles which continued longest to pulsate and which there-fore/

Keith and Flack - Journal of Anat. and Physiol. 41. 1907 fore, possessed "the strongest power of rhythmic contraction" was situated in the inter-auricular septum at the mouth of the coronary sinus and corresponded with the position in which the node of the auriculo-ventricular system is to be found. He came to the conclusion that "the stimulus to automatic cardiac action originates in the node of Tawara, which lies in the wall of the coronary sinus."

It was at this stage in the investigation of the subject that Keith and Flack made the important discovery in the heart of the mole, where they found at the sino-auricular junction of the superior vena cava a structure which in its essential details, resembled the node of the auriculo-ventricular system. These authors had directed their attention to the remnants of embryonic structure at the entrance of the great veins recognising that in the lower vertebrate hearts the experimental physiologists, (Gaskell, Macwilliam, Engelmann, Hering and others) had proved that the first hypersensitive part of the cardiac tube lay at the junction of the sinus venosus with the auricle. The remains of the venous valves are the only guide to the junction of sinus and auricles in the mammalian heart, and a part of the right venous valve is to be found not infrequently beneath the endocardium on the upper aspect of the tenia terminalis just opposite that portion of the salcus/

salcus terminalis, which lies between the superior vena cava and the right auricular appendix. Round about a small artery which constantly encircles the superior cava in this region Keith and Flack found in the human heart the structure for which they were searching. "The artery", they note, "is surrounded by fibrous tissue in which are numerous peculiar muscle fibres some nerve cells, and nerve fibres. The nerve cells and fibres, we find from dissection, to connect with the vagal and sympathetic nerve trunks which form so rich a plexus and exert as powerful an effect at this junction. The musculature of the superior cava becomes continuous with that of the auricle and of the auricular canal, both on the outer and inner side of the artery. Our search for a well differentiated system of fibres within the sinus which might serve as a basin for the inception of the cardiac rhythm has led us to attach importance to this peculiar musculature surrounding the artery at the sino-auricular junction. In the human heart the fibres are striated,fusiform, with well marked elongated nuclei, plexiform in arrangement and embedded in dense-packed connective tissue - in fact, of closely similar structure to the Knoten (Tawara's node). The amount of this musculature varies, depending upon how much of the sinus has remained of the primitive type; but in the neighbourhood/

neighbourhood of the tinea terminalis there is always some of this primitive tissue found. Macroscopically, the fibres resemble those of the auriculo-ventricular bundle in being paler than the surrounding muscle. (This pallor may be due to the excessive amount of connective tissue - Mackenzie). They can be dissected out on the superior vena cava in the region corresponding to the right venous valve. Another remarkable point in connection with these fibres is the special arterial supply with which they are provided. These arterial branches embrace the sino-auricular junction. It will be seen that they come from both right and left coronary arteries, and from what may be termed "the sino-auricular arterial circle". For some time there seemed to be some confusion on the part of subsequent observers as to the site and structure of the node. This is accounted for by the earlier description given by Wenckebach of a muscular connection and the attempts made to confirm his conclusions. Further difficulty arose from the use of the term, "Purkinje fibres". Keith and Flack never used the term in their descriptions, and Koch quite rightly emphasises the fact that there are no such fibres associated with the sino-auricular node in the human heart. The observations of Keith and Flack have, however, been fully confirmed by Koch, Mönckeberg, and others. As in the case of the auriculo-ventricular system the ungulate heart affords the most suitable/

suitable material for those who desire to gain an idea of the position of the node and its finer structure. For this reason, I have chosen the pig's heart for a detailed description of the technique of examination and the findings.

THE SINO-AURICULAR NODE IN THE PIG'S HEART.

Macroscopic examination:- If the right auricle is examined on the endocardial surface of its posterior wall the remains of the right venous valve may be seen extending from the region of the coronary sinus round the right margin of the inferior vena cava and upwards towards the tenia terminalis as it passes below and in front of the entrance of the superior vena cava. In some cases the valve may be followed on to the endocardial surface of the lower aspect of the posterior wall of the superior cava. If now the heart be held up to the light to examine the line of junction of the superior cava with the auricle, a narrow crescentic translucent area will be noticed in the lower part of the superior cava posteriorly. This translucent area is immediately above the sulcus terminalis and represents the caval extension of the sino-auricular node. If the epicardium and sub~~endo~~epicardial fat be carefully removed from the outer surface of this area the translucent tissue may be found to be continuous with a fine strip of pale yellow tissue distinguishable from the reddish brown auricular muscle and composed of fibres/

fibres apparently running in a direction parallel to the sulcus terminalis (Fig 13) This strand of tissue extends from the angle of junction of the right auricular appendix with the superior cava about 3 c.m. along the region of the sulcus terminalis. A search in its structure will usually reveal the presence of at least one moderately large artery. In exceptional cases the pale strand may appear on the roof of the tinea terminalis beneath the endocardium, but as a rule it is confined to the sub-epicardial layer. The ease with which the structure is demonstrated macroscopically varies in different hearts, but the translucent tissue which has been described is invariably present in the pig and may be taken as a safe guide.

Microscopic examination:- The block for microscopic examination is prepared by two incisions parallel to the sulcus terminalis and at right angles to the lumen of the superior cava. One incision is made 0·5 c.m. below the sulcus and the other 1 c.m. above the sulcus. The upper incision will be through the wall of the vein only; the second incision will pass longitudinally through the tinea terminalis, and will be carried outwards so as to include a small portion of the right auricular appendix. Towards the inside the block is removed by freeing it from the muscular connections of the base of the superior cava with the posterior part of the inter-auricular septum, and the infundibulum/

infundibulum of the left auricle. The sections are cut in a plane at right angles to the lumen of the vein, and it is advisable to begin with the tissue on the lower side of the block. In this way orientation is rendered easy because the first sections will not include the whole circumference of the opening of the vein, but will be free from tissue on the inner margin while the outer margin of the block may be easily recognised by the presence of the muscle of the auricular appendix. By the early recognition of the relative position of these structures it will be easy to recognise the position of any structures which appear in the later sections when only the circular lumen of the vein will be in evidence. Van Gieson's solution should be used for staining. Tracing the series which commences from below, the most prominent structure to be first encountered is the tinea terminalis with its fibres cut longitudinally. On the outer side of the sections lies the complexly arranged muscular strands of the auricular appendix. A section is soon met with in which beneath the epicardium a small narrow longitudinal strand of tissue stands out in sharp contrast with the fibres of the tinea. This strand is situated on the posterior aspect of the block about 0·5 c.m. from the tissue of the appendix. Its most striking feature is its pallor which distinguishes it from the darkly brown stained muscle./

muscle. It presents also a slightly pinkish colour and at first sight under the low power may be very suggestive of nerve tissue. It gives the impression of having contained some substance in its meshes which had become dissolved out in the process of fixation or embedding. Compared with the strands of ordinary muscle against which it lies it exhibits a complicated network appearance although on closer examination it is found to be composed of fibres which have been cut longitudinally. In some instances individual fibres may be seen, which show no evidence of fibrils and no suggestion of transverse striation; such fibres appear to be divided into a very large number of small compartments by delicate membranes coursing irregularly and diagonally across their substance; these dividing membranes appear to be stained faintly pink and to be continuous with the limiting membrane round the fibre. Nuclei are very plentiful and are small and irregular in shape, though for the most part somewhat round (Fig 14.) There may be every stage of transition in the character of the fibrils from that which has just been described to those which are in direct continuity with the ordinary muscle fibres and indistinguishable from them (Fig) This continuity of structure between the node and the adjacent musculature may be observed at each end of the spindle and in/

in some cases a gradual transition takes place between the tissue of the node and the adjacent muscle fibres of the tinea terminalis on its inner aspect. In other cases, however, the nodal structure is sharply demarcated from the fibres which lie to its inner side by large lymph spaces (Fig. 14). Following the series it is noted that the length of the spindle increases until it measures about 3 c.m. and extends as far as the outer edge of the posterior wall of the caval entrance, where the auricular appendix comes into close proximity with the outer wall of the vein. The sections now traverse the translucent area in the lower part of the posterior wall of the vein. In some cases, small islets of muscle may be seen beneath the endocardium in this area; these probably represent the vestiges of the venous valves. There may be a moderately sized artery in the bundle and it is interesting to note that the nodal tissue in some places is arranged so as to form part of the outer arterial wall; in the same way the smaller vessels are closely surrounded and supported by nodal tissue.
As the sections advance into the translucent portion of the wall the whole breath of the later from epicardium to endocardium is seen to be composed of nodal tissue. The tissue is very dense consisting of a closely packed meshwork of fibres whose individual character it is difficult to/

to determine except at those parts on its outer aspect where it is in continuity with the ordinary muscle of the vein. It contains a large number of nuclei in comparison with the caval or cardiac muscle fibres. With the Van Gieson solution it is stained pale with a distinctly pinkish hue and stands out in sharp contrast against the dark brown colour of the striated fibres; it contains no transverse striations except in the intermediate fibres preserving the continuity with the caval muscle.(Fig. 15).

As the sections are followed in the series those containing the translucent tissue become gradually exhausted and there now begins to appear towards the outer and anterior aspect of the caval wall (and 1 - 1·5 m.m. above and in front of the point of junction of the upper angle of the auricular appendix with the wall of the vein), a collection of narrow interlacing fibres which are stained a faint brown and which contain a relatively large number of nuclei though not so many as the tissue which has just been described. If these fibres be traced still further in the wall of the vein they will be found to uddergo a process of condensation and to give the appearance as if they had penetrated into or originated from this dense irregular meshwork in the caval wall (Fig. 15). This meshwork is stained faintly brown, it contains a large number of nuclei, and although in parts there is evidence that it is composed of closely interwoven fibres/

fibres in other parts it suggests rather a multi-nucleated syncytium of cardiac protoplasm. Examined under a high power it looks as if in it a number of fibres had broken up allowing a free exchange and communication between their different elements. Throughout the tissue there is a large number of small vacuolar spaces in some of which nuclei are lying. Although the structure is in communication with the more loosely arranged lacework of narrow fibres already described, and through those in communication with the translucent structure and the nodal tissue lying in the sulcus terminalis it seems at one part to be fairly sharply demarcated from the muscle of the vein. This is at its upper end where it is dovetailed between an inner and outer strand of ordinary muscle from which it is separated by some loose fibrous tissue through which nevertheless a few fibres maintain a continuity. In this loose fibrous tissue there is a fairly large artery surrounded by small bundles of nerves in which are some ganglion cells. The foregoing description of the node in the pig's heart is taken from the examination of a single heart. It applies, however, with slight modification to the morphology and structure of the organ in the pig's heart generally, and also more or less to the appearances presented in the hearts of other ungulates. Attention is specially called to the upper/

upper extension of the structure on to the outer and anterior aspect of the caval wall. This appearance of part of the node on the anterior aspect of the vein has ~~now~~ never been described, previously, and its relation to the structure found in the turtle will be referred to later. (p.110).

In some cases the lower part of the node may be more on the subendocardial than on the subepicardial side of the tinea terminalis. There may also be considerable variation in the microscopic character of the translucent portion; in some cases it looks more like modified cardiac muscle and in other cases it resembles nerve structure, although when nerves are present they can be distinguished. The important point is this, that within the limits of the widest variation there is no example of this structure in the ungulate heart, which does not at once suggest that we are dealing with a highly specialised structure related in its function to nerves on the one side and to muscle on the other. Its peculiar structure, its special nerve supply (Fig 16), and blood supply, its situation at the entrance of the heart and its close similarity to a part of the auriculo-ventricular system mark it out as in all probability playing an important part in the functional activity of the circulatory apparatus.

It does not come within the purpose of the present review to make more than a passing reference to the sino-auricular nodes in other mammals except in the case of the human/

human heart. Mention may, however, be made of the fact that in the case of the common laboratory animals, the dog and the cat, the node although it is distinguishable from the surrounding structures does not, as a rule, exhibit the definite characteristics, which would enable the observer to define its limits and extent so easily as in the case of the pig. In these animals the fibres of the node approach in their structure more closely those of the ordinary cardiac muscle, although in well fixed specimens the characteristic structure and disposition of the fibres is distinct.

THE SINO-AURICULAR NODE IN THE HUMAN HEART.

Macroscopic Examination:- The macroscopic examination of the node in the human heart is attended with great difficulty. It is only exceptionally that it can be made out as distinct from the ordinary muscle. In some cases, however, and especially where there is great hypertrophy of the right auricle it may be seen in the subepicardial tissue in the sulcus terminalis between the auricular appendix and the vena cava. When it contains a large amount of connective tissue as it not infrequently does, this may aid in its dissection. Keith had demonstrated the node in a case of acromegaly which is in the College of Surgeons Museum, and which presents the interesting feature that the node is hypertrophied in proportion to the hypertrophy of the/

the rest of the heart.

Microscopic Examination:- The block for microscopic examination is prepared in the same way as that already described for the pig's heart. Considering the relatively large size of the human right auricle, more especially since the hearts which come under routine examination are usually dilated or hypertrophied in this part, it is expedient to retain only such a portion of the block as is necessary for examination. The limits of the upper and lower incisions made in the pig's heart are retained. The block is completed by two vertical incisions, one about 3·5 c.m. from the appendicular angle through the salcus terminalis, and the other out 1 c.m. in front of the appendicular angle. Within the limits of these incisions it will be seen that the structures which have been described in the pig's node will be found, if they occupy as they almost invariably do a similar morphological position. The sections are cut parallel to the tinea terminalis and at right angles to the lumen of the superior cava. The muscle of the auricular appendix will be found to the outer side of the sections. The node lies underneath the epicardium on the outer aspect of the tinea terminalis. Its presence may usually be detected more readily by the relatively large amount of connective tissue between its fibres; this is a more striking characteristic than any peculiarity in the size, shape or staining/

staining of its fibres. A ready clue to its situation is the presence of a moderately large artery around whose outer coat the fibrous musculature of the node is closely packed. It is spindle shaped, and its greatest length is about 3 c.m., and its breath about 2 m.m. Numerous nerve bundles may be seen in its vicinity although it is only in exceptional cases that they are to be found inside the structure. The fibres are narrow, often slightly paler than those of the ordinary muscle, and they are usually surrounded by fibrous tissue. In the human subject the character of the muscle approaches more closely that of the normal cardiac muscle than in any other mammalian heart which I have examined.

THE COMPARATIVE ANATOMY AND DEVELOPMENT OF THE SPECIAL MUSCULATURE OF THE HEART.

Gaskell in summing up his views on the meaning of the cardiac beat says that "the beat of the heart of cold-blooded vertebrates depends upon the rhythmical power of the muscular tissue of the large veins and sinus being greater than the rhythmical power of the other parts of the heart, and that in all cases the greater or less rhythmicity of any part of the heart depends upon the nature of the muscular fibre of which that part is composed". In Chapter I. attention was called to the developmental process whereby/

whereby the heart was evolved ontogenetically and phyllo-genetically from a simple tube whose contractions were peristaltic in character to a highly differentiated organ, whose chambers heat in rhythmic sequence at definite and regular intervals. It was pointed out that the contraction wave passed along a tissue whose continuity was preserved unbroken from the point of entrance of the great veins to the point of exit of the large arteries. The apparent simultaneity of contraction of the auricular muscle fibres or ventricular muscle was attributed to the rapidity with which the wave of contraction passed over them. The auricular and ventricular outgrowths from the primitive cardiac tube are composed of differentiated muscle fibres with transverse striations and containing a large number of longitudinal fibrils relative to their sarcoplasmic content. Gaskell interpreted the sequence of events in the cardiac cycle of the lower vertebrate heart in the light of ~~his~~ the main properties in relation to contraction, which he attributed to cardiac muscle in general, the property of rhythmicity and the property of conductivity. On the basis of a mutual relation between these properties he offered an explanation of the sequence of events in the contraction of the heart; and for the variation in these properties he found an anatomical basis. "Starting with a tube of equal character throughout, we see how by modifications of portions of the tissue in the two regions/

Gaskell - Schafers Physiology. Vol II. p. 169.

regions of the auricle and the ventricle into a more rapidly contracting, more rapidly conducting, less rhythmical tissue we obtain an efficient heart, which shall not merely pass the blood on, but by the forcible and nearly simultaneous contraction of all parts of its auricular and ventricular walls respectively, keep up in a most efficient manner a high blood pressure in the arterial system, while at the same time owing to the absence of modification of the tissue between the auricles and ventricles, i.e. the canalis auricularis, whereby it still retains its original more rhythmical, but slower conducting power, the useful purposeful pause between the auricular and ventricular contractions is brought about". According to Gaskell, in the development of the adult heart from the primitive cardiac tube the anatomical and physiological characters of the embryonic organ are retained in three situations, in the sinus venosus, in the canalis auricularis, and in the bulbus arteriosus. The anatomical characteristics consist in a maintenance of the circular arrangement of the muscle and the preservation of the non-striated condition of its fibres. At the same time the embryonic physiological properties are retained in as much as the muscle possesses the power of rhythmical contraction in a high degree and its power of conduction is very low. The sinus venosus contracts first because of its greater rhythmicity, and there is an interval between auricular/

auricular and ventricular contraction, because of the low power of conductivity of the connecting muscle, (canalis auricularis). We shall now enquire whether the structures in the mammalian heart, which we have described as sino-auricular node and auriculo-ventricular system are related to those so-called embryonic remnants, the sinus venosus and the canalis auricularis, which were found by Gaskell to possess such significance in his physiological experiments on the hearts of cold-blood vertebrates. Although the bulbus arteriosus is related in structure and in certain of its physiological properties to these other "remnants of the primitive tube", it does not command the same interest in the present study, because so far as we know it has no physiological homologue in the mammalian heart; anatomically it is represented in the infundibulum of the right ventricle (Keith), but it would appear to have ceased to exercise an independant influence in the circulatory movements.

THE PRIMARY DIVISIONS OF THE VERTEBRATE HEART.

Before describing in detail the special musculature at the junctions of the cardiac chambers, it would be well to define exactly the limits of these chambers in the hearts of the lower vertebrates, and the indications which these limits afford in determining the remains of the primary divisions and junctional lines in the mammalian heart.

The/

The accompanying diagram (Fig. 2) is a composite representation of the lower vertebrate heart, it is constructed after the diagram used by Keith and Flack in their first communication on the subject.

It is seen that the lower vertebrate heart consists of five primary divisions:-

1. Sinus Venosus.
2. Canalis Auricularis.
3. Auricle.
4. Ventricle.
5. Bulbus arteriosus.

These five chambers are connected by junctional tissue, which is muscular. The point is not raised here as to how far the nerve supply to the heart exercises an influence on this connecting musculature; the fact of fundamental importance is that muscular continuity is preserved from the entrance of the great veins to the bulbus. A very brief reference has been made already to the process of folding and twisting, which the primitive tube undergoes in the process of its development into the more complicated organ. Of equal importance for an understanding of the relations of the structures in the more complicated organ to their representatives in the more primitive type is a recognition of the fact that in its evolution the five chambered organ becomes telescoped so that the sinus venosus, canalis

auricularis/

auricularis, and bulbus arteriosus are absent as such from the higher organ. In this process of invagination then, the "embryonic remains" or undifferentiated parts in the lower vertebrate heart to which Gaskell attributed so much importance, must undergo a profound change, for it is exactly these portions, which are lost to view. Consulting the diagram representing the five primary divisions of the vertebrate heart, (Fig. 2), the parts marked in red are those in which the muscle is of the embryonic type - non striated, strongly rhythmical and possessing slow conducting power. These are the portions of the lower vertebrate heart, which are most sensitive to stimuli of various kinds, and which, when stimulated, continue for some time to act as a centre from which waves of contraction are propagated in a rhythmic fashion through the cardiac muscle.

It would take us far beyond the scope of this investigation to give a full account of the phylogenetic and ontogenetic disappearance of the sinus venosus and canalis auricularis. But in order to appreciate fully the peculiarity of structure, and possible functions of the special muscular systems in the mammalian heart, it is necessary to have a clear idea of the histological characters and morphological position of the special musculature in a few/

few representative hearts from the lower vertebrates. For this purpose the hearts of the bream, the turtle, and echidna (monotreme) will be described very shortly.

<u>THE HEART OF THE BREAM (FISH):-</u> The five primary chambers are present in this heart, (Fig. 2). The sinus venosus is formed by the junction of the right and left Ducts of Cuvier from the cephalic end and the hepatic vein from the caudal end. The sinus venosus is not really a cardiac chamber; it is merely the main stream into which the tributary veins flow before the blood enters the heart, On naked eye examination its walls are found to consist of a pale tough tissue whereas the auricular wall from which it is sharply demarcated by a constriction is composed of more friable yellow material. It is separated from the auricle by two large valves which lie, one ventrally and the other dorsally, their adjacent ends meeting at the outer aspects of the line of junction between the sinus and the auricle (Fig 17, 18.). A section cut through the sinus wall and auricular wall transversely to the venous valves, shows at the basal attachment of the valves a thick ring of tissue corresponding to the constriction between sinus and auricle. This ring is spongy in consistence, and somewhat paler than the auricular muscle. (Fig. 11). The ring of tissue is the special sino-auricular muscle of the bream's heart; it is the representative in this particular heart of/

of the nodal tissue which has been described in the region of the sulcus terminalis in the pig and in man.

Microscopic examination of this region of the heart was carried out by means of a series of sections cut from right to left at right angles to the valves. The sections included the proximal part of the sinus wall, the sino-auricular ring, the venous valves and a small part of the adjacent auricular wall. This sinus wall is composed for the most part of elastic tissue and fibrous tissue. There are a few non-striated muscle fibres, but no suggestion of any tissue which could be compared to nodal tissue. There is no muscular connection in the form of a bundle or of bundles between the sinus wall and the auricular muscle. Lying between the sinus wall and the auricular wall is the ring of tissue already referred to. This ring is composed of a very complicated meshwork of fine muscle fibres, which are stained a pale yellow and which contain a large number of small round nuclei. It is very vascular, being intersected in all directions by a close network of fine capillaries. The diameter of the ring is constant all round. Its fibres communicate freely with those of the venous valves; the fibres of the venous valves are stained more darkly and exhibit transverse striation. There are distinct strands of muscle running down from the contiguous ends of the venous valves into the/

the auricular muscle. These are the only parts at which there is a direct communication between the reticulated muscle of the ring and the ordinary auricular muscle. On the two outer edges of the sinus wall large nerve trunks course down beneath the epicardium to the angles of junction between the sinus and the auricles. At these angles there are large groups of ganglion cells. Some of the nerve fibres and ganglion cells lie in the ring. Other nerve fibres descend beneath the epicardium which they penetrate to occupy an intramuscular position in the auricular wall; many of these deviate dorsally till they come of lie in the basal wall in which they may be seen in very close relationship with muscle fibres. These nerve trunks are from the right and left sympathetic and vagal trunks, the right being associated with the right duct of Cuvier and the left being associated with the left duct of Cuvier. The mass of ganglion cells on the right side correspond to Remak's ganglion in the frog and to the ganglion cells in the sulcus terminalis and "interauricular space" in the mammal. The importance of recognising this relation of the main nerve trunks to these two important venous channels will be referred to later. (p.157).

There is a direct muscular continuity between auricle and/

and ventricle at the auriculo-ventricular junction. The fibres are arranged round the whole orifice and course down from one chamber to the other in a longitudinal direction, parallel to the blood stream. On the auricular side of the orifice the muscular arrangement appears more complex than lower down beneath the valves where the fibres lie in parallel strands. There is on the auricular side a thickened ring of nodal tissue comparable with that which is situated at the sino-auricular orifice. The fibres are here arranged more in a circular fashion. They are thinner and more delicate than the fibres of the auricle with which they are in direct continuity. The connecting fibres at the auriculo-ventricular orifice are distinguished from those of the auricle and ventricle proper by the pallor of their staining with Van Gieson, by the more rounded shape of their nuclei, and by the relative infrequence of striation and poverty in fibrils. The connecting fibres gradually become continuous with the spongy network of muscle in the interior of the ventricle. It is to be noted that in their course from the more circularly arranged network on the auricular side of the orifice the fibres lie for a considerable distance between the auriculo-ventricular valves and the ventricular muscle and separated from the latter by a thick layer of connective tissue. There is no evidence of muscular tissue in the auriculo-ventricular valves, although as was pointed out the/

the venous valves at the sino-auricular orifice are composed of muscle fibres. The muscular network of the auriculo-ventricular ring is freely intersected with fine blood capillaries, and bundles of nerves are present in the neighbourhood. The sino-auricular and auriculo-ventricular orifices lie at a considerable distance from each other in this heart. The sino-auricular valves lie at right angles to the long axis of the body. The basal wall runs directly in the form of a flat band from the base of the ventral valve to the auriculo-ventricular orifice, and the auricle represents a bulging of the dorsal wall on the opposite side. (See Fig.17(2)).

THE TURTLE'S HEART:- The heart of the turtle is more complicated than that of the bream. Lungs have developed and the central organ of the circulation has become modified to suit the exigencies of the new respiratory apparatus. The auricle has become divided into a right and left chamber by a muscular septum, the left auricle receiving the blood from the lungs by a pulmonary vein and the right auricle receiving the blood from the rest of the body through the sino-auricular orifice, which is still guarded by two large valves. In the turtle the large veins entering the sinus come into closer proximity with the posterior wall of the auricles than in the case of the bream; that is to say, the existence of the sinus venosus as/

as a separate chamber has already begun to disappear and the right superior vena cava (right duct of Cuvier) and left superior vena cava (left duct of Cuvier in the fish, and left superior vena cava and coronary vein in the mammal) enter the right auricle almost independently and without first of all meeting in a common sinus. Their orifices are, however, guarded by well developed venous valves, which are contiguous on the right side at the upper and right corner of the right auricle at the upper angle of the right auricular appendix, and which meet at their other extremity at the lower left side of the auricle in the basal wall near the auriculo-ventricular groove. (Fig 18(2)). The inferior vena cava also pours its contents into the orifice guarded by the valves. The pulmonary vein is developed in close association with the tissue of the left wall of the sinus venosus and is closely related to the base of the left venous valve.

To examine the sino-auricular nodal tissue in the turtle's heart a block is excised in a manner similar to that described for the pig's heart, (p.91). It will be seen that in general conformation the external surface of the turtle's right auricle bears a close resemblance to that of the pig (Fig 13(2)) Posteriorly there is a well-defined sulcus separating the superior caval portion of the sinus from the appendicular portion of the right auricle; this sulcus runs from/

from the sino-appendicular angle downwards and inwards towards the inferior vena cava. The lower incision is made parallel to this sulcus and sufficiently below it to leave the venous valves in the block; the upper incision parallel also to the sulcus should be about ·5 c.m. above the sulcus in the case of the heart of a large turtle. The sections are cut in a series at right angles to the venous valves beginning with the side to which the auricular appendix is attached; throughout the main part of the series the venous valves should appear in transverse section. (Fig. 23).

It is at once obvious that with respect to the presence of nodal tissue the condition in this heart differs greatly from that in the heart of the bream. There is nothing in the nature of a specialised ring situated at the sino-auricular junction. In the earlier part of the series a continuity of muscle fibre can be traced from the sinus wall into the auricular wall through the venous valves which are composed of ordinary cardiac muscle fibres arranged circularly; the muscle fibres of the sinus wall as well as those which preserve the continuity of structure cannot be distinguished from those of the auricle. When, however, a certain stage in the series has been reached, usually about half way between the outer and inner margins of the superior cava, the fibres of continuity on the posterior wall through/

through the sulcus between sinus and auricle present an appearance which distinguishes them readily from those of ordinary muscle(Fig 13) The fibres here course directly from the sinus into the auricle without any intervention of the valvular muscle, although the muscle of the posterior valve is in direct continuity with that of the auricle (Fig.23). This band of muscular continuity which, be it remembered, is not the only source of muscular connection between sinus and auricle is distinguished most readily from the ordinary cardiac muscle by the relatively large number of nuclei which it contains. More closely examined it is seen to be more pale in its staining, the fibres are thinner and more delicate and contain few fibrils, and no transverse striations, and there is an interlacing network arrangement of the fibres in bundles lying in a framework of connective tissue. (Fig.23). Nerves and nerve cells and a rich supply of small blood vessels are also present. The extension of the connecting bundle into the auricular wall is very short, the fibres becoming continuous almost immediately below the base of insertion of the right venous valve. If now the extension of the bundle be followed backwards or upwards into the sinus wall, it will be found to come from a point at a considerable distance above the sino-auricular junction(Fig 13a) To follow this extension, the series must be examined backwards towards the auricular appendix. The sinus continuation of the structure may be found in this way to start from a point on the anterior surface/

surface of the sinus or superior cava almost opposite to part at which the nodal continuity between sinus and auricle already described on the posterior surface, is situated. It lies in front at a distance of 0·3 - 0·5 c.m. above the sino-auricular junction in a large heart and is surrounded by the sinus musculature from which it is easily distinguished in virtue of the relative pallor of its staining, the compactness of its structure and its relatively large nuclear content (Fig 24) Closer examination of its structure shows its resemblance to the caval extension of the sino-auricular muscle in the pig. The dense meshwork suggests a closely interlaced syncytium of fibres passing in all directions with fibrils freely inter-communicating. The nuclei which are small and rounded lie sometimes in the substance of the syncytium and in other parts in small vacuolar spaces scattered irregularly throughout the structure. This structure may be followed from the front of the sinus outwards to its outer border in a direction parallel to the sino-auricular groove; it may then be followed from the outer border inwards and downwards on the posterior surface of the sinus till it becomes continuous with the sino-auricular connecting bundle already described. (Fig. 23). Special attention is directed to the close similarity, which this structure has in respect of its position and minute appearance to the sino-auricular node in the pig. In each case part of the specialised muscle/

muscle lies some distance above the sino-auricular groove and may be followed to the front of the superior cava, although it extends posteriorly below the sulcus into the auricular muscle. It is not "sinus muscle" or "remains of sinus venosus" or "embryonic remnant of primitive tube"; it is a well defined structure in each case just as distinct from sinus muscle as it is from auricular muscle. Nor is this surprising because the ring at the sino-auricular groove in the bream's heart was also found to be equally distinct from sinus and auricle.

The auriculo-ventricular junction in the turtle is composed of connecting muscle fibres, which surround the auriculo-ventricular orifice in its whole extent. These fibres run in longitudinal strands from the more circularly arranged muscular constriction of the canalis auricularis (Fig 19(2)). This circular disposition of the fibres immediately above the auriculo-ventricular orifice is associated with an interlacing arrangement, with an increase in the amount of intermuscular fibrous tissue, and with a distinct absence of transverse striation as compared with the ordinary cardiac muscle. The flattened portion of the auricles known as the basal wall, extends from the lower part of the sinus, which lies in closest proximity to the ventricle, to the canalis auricularis, (Fig. 2). Thus in one part of the heart there is direct muscular continuity over a very short/

short distance between sinus venosus auricles (basal wall) canalis auricularis, auriculo-ventricular connection and ventricle. On the dorsal side of the canalis auricularis there is an immediate continuity of structure between the muscle fibres of that part of the heart and the muscle of the bulbus arteriosus; that is to say, there is a direct path of muscular continuity between the auricles and bulbus without the intervention of ventricular muscle. The significance of these anatomical facts in relation of the sequence of events in the cardiac contraction will be discussed in a later chapter, (p.221). Meanwhile it is sufficient to recognise that muscularly, the sinus is connected with ventricle (along the basal wall) without the intervention of auricle, and that auricle is connected with bulbus (along the canalis auricularis) without the intervention of ventricle; there is thus a muscular continuity almost in a straight line and though specialised fibres between sinus venosus and bulbus arteriosus. The exact relations of the auriculo-ventricular muscle to the venous valves and the existence of a possible mass of specialised muscular tissue at the opening of the pulmonary vein, which developes in the wall of the sinus, has not been worked out fully. In the heart of the lizard there is a large mass of spedialised muscle surrounding the orifice of the pulmonary vein and containing/

containing a specially rich blood and nerve supply. This structure is very closely related to the inner and lower attachment of the venous valves to the basal wall in front of the opening of the left superior vena cava. The suggestion is made here, although the question obviously demands further research, that the auriculo-ventricular system is anatomically and functionally linked up with special muscle lying behind the venous valves and possibly associated phylogenetically with a portion of the sino-auricular ring in the fish (bream), (Fig.18 and p.130). The full significance of this suggestion can be realised only when the development of the auriculo-ventricular system in the mammalian heart is understood. (p.121).

THE HEART OF ECHIDNA.

The heart of Echidna (monotreme) is specially interesting, affording as it does an example of the organ in the most primitive mammals. The situation and finer structure of the sino-auricular node does not differ materially from that which has been described in the case of the pig. The main mass of its tissue lies in close opposition to the tinea terminalis with whose fibres the fibres of the node are in direct continuity. Its extension into or from the wall of the superior cava is also well seen. In the nodal tissue of the specimen examined and described by Keith and myself attention was mainly directed to the fact that/

that this structure in this animal presented all the features of a neuro-muscular end-plate. Sharply demarcated at its sides from the auricular muscle by wide lymph spaces the structure of its fibres suggested the idea of nerve structure rather than that of muscle. In fact it was with the greatest difficulty that in parts a definite opinion could be given as to whether the nerve and muscle fibres were not in direct continuity While I have come to the conclusion that the nerve and muscle fibres are not continuous there is no gainsaying the fact that in the node the nerve bundles break up into a plexus whose fibres are intimately interspersed with the complicated reticulum of nodal muscle. Nerve cells in small nerve bundles, whose fibres break up and course among the muscle fibres, may be seen throughout the structure, (Fig. 16).

Examination of the auriculo-ventricular muscle provided the most interesting results. The auriculo-ventricular node and bundle did not differ in its situation or main structural characteristics from that which has been described for mammals generally. The left branch going to the left ventricle spreads out from the main bundle in the region of the pars in much the same way as it does in the human heart. Purkinje fibres could not be seen in the left ventricle whereas they were present in abundance in the right ventricle. If the right auriculo-ventricular orifice be now examined it will be/

be seen that the annular ring of fibres on the auricular side of the orifice present an appearance similar to that seen in the auriculo-ventricular node. They are pale in colour, with rounded nuclei, and striation is rarely present. The fibres further appear to contain vacuolar spaces as if in the process of fixation and embedding some of their contents had dissolved out. The most important feature, however, is that in some places strands of these peculiar pale fibres with rounded nuclei may be followed into the flaps of the auriculo-ventricular valves, and at two different points this extension of the annular fibres could be followed into the muscle of the right ventricle (Fig 11) There is thus in this particular heart not only the special mammalian connection afforded by the supraventricular bundle and its branches to right and left ventricles, but there is in addition a few strands of fibres running diredtly from the annular ring of the right auricle into the muscle of the right ventricle. These strands are, as we shall see, most readily explained on the assumption that they are phylogenetic remains which have survived the process of invagination of the canalis auricularis into the ventricle. On the left side the auricle is separated completely from the ventricle by fibrous tissue, except in so far as continuity is preserved through the ordinary bundle and its branches. In the case of the rabbit and rat, I have observed the fibres described by Curran which run directly into the ventricle from/

from the main bundle before it enters the septum fibrosum (p.164). But in the case of Echidna the strands which descend in the flap are situated at a distance from the main bundle. They descend from the ordinary remains of the annular ring.

In the preceding account of the comparative anatomy of the special musculature in the vertebrate heart, it is to be noted that the descriptions given of the various hearts apply only to the animals mentioned and not to the classes to which they belong. Very considerable variations are found for example among fishes. In the skate for instance, the venous valves do not lie in a direction at right angles to the long axis of the body; they course diagonally across the posterior wall of the auricle and where they are contiguous on the left side, are inserted into the basal wall in the immediate neighbourhood of the auriculo-ventricular orifice; the sinus muscle thus lies very close to the connecting muscle between the auricle and the ventricle, (p 131). In amphibians and reptiles very considerable differences in the distribution and extent of the special musculature is found to exist, but sufficient has been explained in the short account given of these three hearts to render intelligible the interpretation which will be given of the nodal structures in the human heart./

heart.

THE PHYLLOGENETIC RELATIONS OF THE HUMAN HEART

The primitive structures whose remnants in the human heart are the subject of interest here are (1) the sinus venosus, (2) the venous valves, and (3), and canalis auricularis.

The sinus venosus in the human heart:- This structure or its remnants are recognised by comparison with the position and relations of the structure as it is sometimes found in a mal-formed foetus. Keith and Flack have represented in diagramatic form, the variations which the sinus may show in such malformed human hearts, and the appearances they exhibit when compared with a normal human heart, the heart of the wallaby and the frog's heart, (Fig.20). The view in this diagram shows the venous or auricular end of the heart looked at from the dorsal side. The sinus, as we have noted in the case of the bream, is seen in the frog (E) to be formed by the union of three great vessels - the right Duct of Cuvier (right superior vena cava), the left Duct of Cuvier (left superior vena cava), and the inferior vena cana (the hepatic vein in the fish). In the human heart, as in that of mammals generally, the sinus venosus has become invaginated into the auricular expansion of the auricular canal, so that its remains must be looked for/

for, submerged in the posterior wall of the auricles. On the outer surface of the heart the guide to its presence is the muscle of the walls of the superior vena cava and the coronary sinus (the representative of the left superior cava, (Fig. A, B, C.). Keith points out that besides the musculature of these two vessels the sinus is represented by a deep stratum of muscle, which runs between the two venous valves beneath the auricular endocardium; this stratum extends from the sulcus terminalis on the right to the interauricular septum on the left, and extends downwards to the inferior vena cava (Fig 21(c)). In the internal surface of the auricle a somewhat general idea of the limits of the sinus remains may be obtained from such portions of the venous valves as can be made out. The extent to which the venous valves are represented in the mammalian heart, and also in the human subject, varies very considerably. The Thebesian and Eustachian valves are almost invariably present and occupy an almost constant position. The Eustachian valve may in some instances be followed upwards on the outside of the inferior cava to the line of junction of the superior cava with the auricle; it represents the remains of the right venous valve and the structures immediately on its left side belong to the original sinus. At its lower margin the Eustachian valve courses upwards towards the inter-auricular septum between the inferior cava and the coronary sinus; /

sinus; this latter extension does not represent a portion of the right valve as it exists in the fish, but is a new formation joining the right and left venous valves, and it may be seen in its full development in the bird's heart. The Thebesian valve on the other hand is a direct extension of the right venous valve; it (Fig. 18). maintains a position to the outer and lower aspect of the coronary sinus, and may be followed to the auriculo-ventricular groove to a point in very close proximity to the node (Tawara's) which constitutes the commencement of the specialised auriculo-ventricular system. The structures immediately to the left of and above the Thebesian valve, belong to the original sinus. It is only in very rare cases that a trace of the left venous valve can be distinguished. In the heart of a kangaroo I have been able to follow it from the lower border of the superior cava along the inter-auricular septum on the left side of the inferior cava, and above the coronary sinus till it disappeared in the auriculo-ventricular groove in front of the coronary sinus in conjunction with the Thebesian valve (Fig. 18). The structures on the right side of this remnant of the left venous valve are to be regarded as belonging to the original sinus. The general conclusion indicated by these findings is that all the structures falling within the/

the limits of the vestiges of the right and left venous valves are to be regarded as belonging to the sinus venosus; as in the case of the turtle the sino-auricular node lies in close relationship with the right venous valve so in the case of the pig and in the human heart the same node is found in a corresponding position. The important point arises as to whether Tawara's node does not also lie within the limits of the venous valves. We have followed the right venous valve as the valve of Thebesius to the auriculo-ventricular groove at a point in immediate proximity to this node; and in the kangaroo's heart the left valve joined the inner extremity of the right valve in the same place. It is admittedly a matter which demands further investigation, but as we shall see later there is considerable evidence for the view that the node of the auriculo-ventricular system is developed from part of the original sino-auricular node, (p.130), while the extension of the system through the septum fibrosum into the ventricles is to be regarded as the condensed representative of the specialised ring and tube of auriculo-ventricular muscle, which in the primitive heart preserves the continuity between auricle and ventricle. Another opportunity is taken of discussing this problem more fully. (p. 130).

Keith and Flack have suggested that possibly there may be/

be remnants of the sinus in the left auricle of the human heart. This possibility is no doubt enhanced by the fact that the pulmonary vein makes its first appearance in the wall of the sinus venosus. In. Fig.20 F. it is seen that in the frog's heart the musculature of the sinus at the sino-auricular junction (s.a.j.) includes within it the orifice of the pulmonary vein. It was noted above that in the heart of the lizard a considerable mass of muscle and nerves continuous with, and in immediate contact with, the sinus wall, lay at the entrance of the pulmonary vein to the left auricle. The close relationship of the pulmonary vein to the sinus is also seen in the malformed heart of the human foetus in Fig.20.D. "It is, therefore, possible that as part of the auricular canal, which is to become the vestibule of the left auricle expands (v.), a part of the sinus musculature is also involved in the process and may persist in the left auricle of the human heart around the orifices of the pulmonary veins." As against this view, however, is the fact that no trace of the venous valves is to be found in the left auricle, and the only trustworthy guide to remains of the original sinus in the presence of such vestiges. In any case, it is scarcely credible that even if there were such persistant portions of the sinus walls that a functional importance could be attached to them. Emphasis has been laid/

laid on the fact that in the bream it is not the sinus wall, but the sino-auricular ring, and in the heart of the turtle, pig and human subject, it is not the "remains of the sinus venosus", but a well defined and obviously specialised structure, which is to be regarded as the "nodal tissue" at the entrance to the heart. "Embryonic remains of the primitive cardiac tube" these may be all over the auricles, but it is extremely unlikely that they possess any physiological importance in the sense that to them under any circumstance, there can be delegated the functional activities of the sino-auricular node; in any case I should not be disposed to attach any importance to their presence except on the evidence of conclusive physiological experiment.

The auricular canal of the Human Heart:- In the simplest form of the heart (See Fig. 2) the auricular canal which joins the sinus venosus to the ventricle is differentiated according to Keith into three parts, a basal portion opposite the auricle, (1-3), an annular part between the auricle and the ventricle, (3-3), and an invaginated or intra-ventricular part, (4-4). The basal part of the auricular canal can be understood only by reference to the form which it presents in lower vertebrates. The auricle or auricles are outgrowths of striated muscle from the dorsal wall of the primitive tube, and the ventral wall remains/

remains unspecialised as the basal part. It preserves a straight muscular path of continuity between the sinus venosus and the annular or auricular ring at the auriculo-ventricular orifice; it was along this direct path that Macwilliam believed the wave of contraction to pass in a sino-ventricular rhythm, which occurred without the intervention of an auricular contraction. In the human, as in the mammalian heart generally, the basal wall as such no longer exists. It has become modified or displaced by the transformations which have occurred in the evolution of the heart. These transformations are associated with the growth of an inter-auricular septum, and the formation of a vestibule to the left auricle; no less important than these factors in the modification of the basal wall, is the gradual invagination of the auricular canal into the ventricle with the formation of papillary muscles which in their contraction exercise a considerable traction on the auriculo-ventricular junction leading to an atrophy of the auriculo-ventricular muscle except at that part where it is protected by the growth of the interventricular septum (p.134); it is highly probable that a part of the auricular canal thus protected by the interventricular septum belongs to the basal portion, and ultimately forms part of the specialised auriculo-ventricular system in the mammal.

The annular part of the auricular canal is that ring of/

of circularly disposed fibres, which lies on the auricular side of the auriculo-ventricular orifice, and which has been described in the heart of the bream and of the turtle as constituting the commencement of the specialised auriculo-ventricular system in these hearts. In the mammalian heart they have almost disappeared as a ring, although in the heart of Echidna, we have pointed that they are still represented on the auricular side of the tricuspid orifice by groups of pale non-striated fibres, which here and there send extensions into the tricuspid valves. Their disappearance in the mammalian heart may be attributed to the new mechanical conditions involved by the development of the strong papillary muscles in the ventricles, to which the valvular flaps are attached; this supposition is rendered more likely by the fact that in Echidna the annular fibres have disappeared altogether on the left side where the papillary muscles are more strongly developed. The developmental conditions under which we suppose it possible that part of the basal wall might have been preserved in the evolution of the mammalian heart, make it almost certain that part of the annular ring has survived. These conditions, as we have seen, depend upon the fact that in the process of invagination of the auricle into the ventricle the auriculo-ventricular muscle is protected posteriorly/

posteriorly by the development of the inter-ventricular muscular septum, and those fibres which survive as a result of this protection, come to lie on the surface of the septum and constitute part of the auriculo-ventricular connecting tissue in the mammalian heart, the remainder of the annular fibres as has been point out, undergoing atrophy from mechanical causes.

The invaginated portion of the auricular canal is composed of the fibres, which extend more or less longitudinally from the annular ring into the ventricles. In the bream and turtle they were seen to be present all round the auriculo-ventricular junction. In Echidna a few strands were present on the right side, but no trace of them was found on the left. In the higher mammalian hearts they are absent from the orifices having disappeared for reasons already indicated. They are, however, represented in the septal extensions (right and left) of the auriculo-ventricular system of mammals.

In the foregoing short account of the comparative anatomy of the vertebrate heart with special reference to the subject under discussion, an attempt has been made to give an explanation of the phyllogenetic appearance of the two specialised neuro-muscular end-plates in the human heart. The so-called sino-auricular node presents little or no difficulty. It is the homologue of the sino-auricular/

auricular ring in the fish. In its neuro-muscular tissue one would expect that there was the commencement of a new series of events in the cardiac cycle. The explanation of the origin of the auriculo-ventricular system is not quite so simple. I have suggested the possibility of a composite origin for this structure. The parts of the primitive heart, which may be represented are, (1) a portion of the sino-auricular ring, (2) a portion of the basal wall and annular ring, and (3) part of the invaginated portion of the auricular canal. The evidence which may be adduced in favour of the view that the sino-auricular ring is represented in the auriculo-ventricular system may be stated as follows:-

(a) Tawara's node lies in very close proximity to the points at which the right and left venous valves are lost in the auriculo-ventricular groove, so that in some hearts at least the node may be said to lie within those limits which contain the remains of the sinus. It is admitted that in the human heart for example, the node lies a considerable distance in front of the coronary sinus, and I have never observed a case in which the fibres of the node were even near the muscle fibres of the wall of the coronary sinus; still on the other hand, I have observed cases in which the remains of the right venous valve extended on to the auricular surface of the pars membranacea septi, and in these case the node certainly lay within the recognised limits/

limits of the sinus remains. Again, in the heart of the mouse I have observed an extension of the nodal tissue of the auriculo-ventricular system into the wall of the coronary vein (or left superior vena cava - left Duct of Cuvier) in exactly the same way as the tissue of the sino-auricular node in the same series extended into the wall of the superior vena cava (right Duct of Cuvier).

(b) I have pointed out that although in the bream the two ends of the sino-auricular orifice at which the right and left Ducts of Cuvier, with the right and left branches of the sympathetic and vagus nerves, enter the heart, lie equidistant from the auriculo-ventricular orifice, still in the skate the sino-auricular orifice and valves occupy a diagonal position, so that the end at which the left Duct of Cuvier enters comes to lie in close proximity to the auriculo-ventricular orifice (Fig. 17). In this case a portion of the nodal tissue of the sino-auricular ring is separated from the auriculo-ventricular muscle connection by a very much shortened basal wall. In the mammalian heart the line of junction between the orifice of the superior cava (right Duct of Cuvier), and the coronary sinus (left Duct of Cuvier), occupies a diagonal position, so that the opening of the coronary sinus comes to lie in close proximity to the auriculo-ventricular groove. With the process of invagination of the sinus into the/

the posterior wall of the auricle the right and left Ducts of Cuvier enter the auricle at different parts and the suggestion is that the left Duct of Cuvier has carried with it a portion of the sino-auricular ring just as another portion has been retained at the junction of the auricle with the right Duct of Cuvier.

(c) If it be the case that the sino-auricular ring is represented in the auriculo-ventricular system, then in all probability a small portion of the basal wall is retained in preserving the continuity between the sinus portion and the surviving part of the annular ring, because there can be little doubt that whatever structures are concerned in the development of the system the fibres of the annular ring form one part.

(d) A further point in favour of the view that the primitive sino-auricular nodal tissue is represented in the system is the important fact demonstrated by Rotberger and Winterberg that while the right sympathetic influences the so-called sino-auricular node, the left sympathetic acts more particularly on the auriculo-ventricular system.

While these considerations no doubt support very strongly the view which I have advanced as to the composite character of the system, it is admitted that on embryological evidence based on the examination of the human heart, much may be said in favour of the hypothesis put forward by Keith and Flack, that the auriculo-ventricular connection/

connection consists purely and simply of a condensation of the annular and invaginated fibres of the auricular canal protected by the mechanical conditions under which the heart assumes its complicated form.

Retzer's theory as to the origin of the auriculo-ventricular system is based on embryological investigation of the pig. He found that the right and left venous valves in the embryo arise from invaginations of the walls of the sinus venosus. He attempted to trace the fate of the sinus by following the structural differences which characterised the valves. The right valve divided forming the valves of Eustachius and Thebesius, which surrounded the coronary sinus, while the left valve pierced the fibrous septum to preserve a muscular continuity between auricles and ventricles. In an embryo of 20 m.m. the left venous valve, he says, lies in the form of a small strand on the roof of the interventricular septum on which it bifurcates into the right and left septal branches. While I can confirm Retzer's observation as to the mode of formation of the venous valves, and also as to their extension as far as the fibrous septum, it is impossible to accept his interpretation that the left venous valve is continued into the ventricular cavities, and ultimately becomes the auriculo-ventricular system. There is no evidence in the phylogenetic development of the/

the heart to warrant any such conclusion, and in this particular instance the histological appearances in the embryo are too equivocal for the support of a theory which is not in accord with the obvious facts of comparative anatomy.

THE ORIGIN OF THE FINER BRANCHES OF DISTRIBUTION IN THE VENTRICLES.

There still remains for consideration the mode of origin of the terminal arborisations of the right and left branches of the auriculo-ventricular system in the ventricles. If a large heart from one of the lower vertebrates be examined macroscopically, there may be seen in the cavity of the ventricle very fine delicate pale threads coursing from one bundle of muscle tissue to another in the spongy substance of the chamber. These thread-like strands appear to be continuous with the invaginated fibres of the auricular canal, which constitute part of the auriculo-ventricular muscle connection. They are present all round the chamber, but are often more numerous towards the posterior wall of the ventricle or ventricles (Fig 15) The suggestion which I put forward is that this network of fine threads is the homologue of the terminal extension of Purkinje fibres scattered throughout the subendocardial layer of the ventricles in the ungulate sheep's heart. In the lower heart they are in continuity with/

with a cylindrical disposition of the auriculo-ventricular muscle; in the sheep's heart they are in continuity with the single cord, which takes the place of the cylindrical arrangement, (Fig.25.). The network itself does not atrophy in the evolutionary process, because it is not exposed to the mechanical disabilities affecting the cylinder, and its strands being arranged in the form of a network their anatomical and functional continuity is preserved in direct association with the surviving bundle, which lies on the roof of the inter-ventricular septum, between the auricles and ventricles.

A very strong support of this interpretation of the origin of the subendocardial network is to be found in an examination and comparison in different ungulate hearts of the distribution of the Purkinje system. Attention has been drawn to the fact, (p.34) that strands of Purkinje fibres not infrequently cross the cavity of the ventricles from the septal wall to the papillary muscles, from one papillary muscle to another, and among the trabeculae in the form of pale cords or threads. Mönckeberg has subjected these extensions of the auriculo-ventricular system to a very thorough examination. He has found that some of the cords are associated with the Purkinje system, and that others consist of fibrous tissue only, while still others are composed of ordinary cardiac muscle; the two latter types he regards/

regards as being quite independent of the ramifications of the bundle. While Mönckeberg's description of the varieties of these cords is accurate, it is quite possible that he has missed the full significance of their varied constituents, when he states that some of them have nothing to do with the branching of the auriculo-ventricular system. Although anatomically and physiologically, they no longer form part of that system, still developmentally it is more than likely they stand in close relation to it. These cords are, as a rule, best seen in the left ventricle. Occasionally they course from the septum to a papillary muscle; they may become attached towards the base of the muscle, or in its middle or very occasionally near the apex. The nearer the apex the attachment takes places the more likely is the cord found to be composed of fibrous tissue. Also if the cord is attached to the septum behind the fan-shaped extension of the left branch, it is almost certain to be fibrous. Specimens are sometimes seen in which a cord attached to a papillary muscle near the apex gives the impression that it is a chorda tendinea, and it is highly probable that all these cords are really "aberrant chordae tendineae". I am inclined to regard the chordae tendineae of the valves, these "aberrant cordae tendineae" and the bundle itself with its branches, as modifications of the same primitive structures, namely, the ventricular extensions of the invaginated auricular/

auricular canal. According to this view the Purkinje ramifications on the papillary muscles were at one time in direct continuity with the annular fibres of the auricular ring through the fibrous cords, and valvular flaps, whose originally muscular substratum has disappeared as the result of the mechanical influences mentioned above. (p. 128). The network retains its connection with the sole surviving strand of the original auriculo-ventricular musculature. This view explains why it is that the ramifications of the bundle are almost exclusively confined to the original parietal wall of the ventricle and the papillary muscles, while they are almost never to be found on the muscular septum, which is of later development. Such strands of the bundle as are present on the septum.are on its lower part and give the impression as if they had been carried upwards with the development of the septum from the apical region of the original chamber. It would also account for the fact that occasionally short strands of Purkinje fibres may be encountered, more especially near the venous base of the ventricle, whose continuity with the general network cannot be determined, (p. 49,).

THE RELATION OF THE SINO-AURICULAR NODE TO THE AURICULO-VENTRICULAR SYSTEM.

The relation of the sino-auricular node to the auriculo-ventricular system has been the subject of considerable controversy/

Retzer – Anat. Record 1908.

Thorel – Münch. med. Wochenschr. 1909. No. 42.

Koch – Münch. med. Woch. 1909 No. 46.

Keith and Flack – Journal of Anat and Physiol. 1907 No. 41

Fahr – Verhand. d. d. path. Gess. XII 1908

Schwartz – Inaug. Dissert. Giessen 1910.

Mönckeberg – Lubarsch-Ostertag Ergebnisse XIV. p. 594.

troversy. Retzer in the embryological study of the question already referred to, pointed out that the left venous valve constituted, in the embryo at least, a bridge of continuity between the two systems. He explains, however, that whereas he could recognise in the ventricles the "forerunners of the ultimately Purkinje fibres" they were not to be seen in the auricle. Thorel has stated that "a specific muscular connection whose fibres exhibit a structure of the Purkinje type, exists between the sinus node of Keith and Flack on the one side, and the node of Aschoff and Tawara on the other". Thorel's investigations were carried out on the human heart. The determination of the presence of specialised muscle in the human auricle is, as has been pointed out already, a matter of great difficulty, in as much as the appearance which is presented by ordinary muscle fibres where fibrous tissue is present is readily productive of a fallacious interpretation. Confirmation of Thorel's suggestion has not been forthcoming from those who have further investigated the subject. Koch, Keith and Flack, Fahr, Schwartz and Mönckeberg, have failed to find any such connection of specialised fibres. The examination of a number of smaller hearts from rabbits, cats, rats and mice, was made by Keith and myself. The hearts were cut serially from one end to the other, but we failed to find any connection between one node and the other, except that which was formed by the ordinary/

ordinary muscle of the auricle. We examined also the posterior auricular wall of the pig and the sheep, in which the nodal tissue is specially distinct, but found no evidence of any special internodal connection. The nodal tissue of the sino-auricular node could be followed in every instance into ordinary auricular muscle in the immediate neighbourhood of the orifice of the superior vena cava.

But while there is no evidence of a specialised muscle connection between the two nodes in the mammalian heart, I would again refer to the suggestion already made that phyllogenetically both nodes are possibly derived from a common source, namely, the sino-auricular ring in the fish; the left node with the left nerves must in this case have been carried downwards with the left superior cava (coronary vein) into a position of close proximity to the auricular canal, while the right node with the right nerves remained at the line of junction of the superior cava with the auricle. The two nodes are still in the mammalian heart connected by the ordinary auricular muscle, but as we shall see in the next chapter, it is highly probable that their physiological inter-dependence is determined also through the nervous system, (p.215).

CHAPTER IV.

THE FUNCTIONS OF THE SPECIALISED MUSCLE OF THE VERTEBRATE HEART.

The observations which have been made on the functions of these structures, and the interpretations which have been suggested, have been influenced largely by the researches which Gaskell conducted thirty years ago. As stated by him, the main problems in the physiology of cardiac movement centred round two leading questions; the first dealt with the origin of the cardiac beat, and the second with the sequence of events in the cardiac cycle. Around these problems there has raged a controversy which, though it may have been productive of invaluable results, possesses now little more than historic interest. This controversy was concerned with what is known as the "myogenic" and "neurogenic" theories of the heart movements. According to the "myogenic" theory the cardiac beat originates in the muscle, and the wave of contraction is conducted along the muscle fibres from auricles to ventricles, ~~and~~ the commencement and sequence of events depending solely on the properties of the muscle fibres, and being in no way influenced by nerves. According to the "neurogenic" theory the cardiac beat originates as the result of a nervous impulse; the wave of contraction is conducted along the chambers of/

of the heart through nervous paths, and the sequence of events is determined by the control of the nervous system. If this method of stating the position of the protagonists of the two schools is simple and crude, it is neither more simple nor more crude than most of the arguments which have been advanced in support of the respective theories. If a small piece of tissue excised from the apex of a pig's ventricle be placed in saline solution under pressure, it is found to contract rhythmically; this is claimed as evidence in support of the myogenic theory; on the other hand, it is pointed out that every fibre of cardiac muscle is surrounded by a plexus of nerves, although it is only one or two observers who have ever been able to see this, and the experiment with the apex of the frog's ventricle is claimed in support of the neurogenic theory. Again, it is possible to fix up an excised mammalian heart on am apparatus, and to perfuse it with nutritive or non-nutritive fluid so that it may continue to beat for hours in rhythmic sequence. From such a experiment conclusions are drawn on the assumption that the heart is acting as if it were still performing its function as an organic part of the living body. A pursuit of this controversy, through its irrelevant and contradictory paths would do nothing to serve the purpose of the present investigation. It is sufficient to/

Langendorff – Arch. f. d. Ges. Physiol 1906 p112.

to state that the most permanent contributions to our knowledge of the physiology of the heart from the myogenic side were made by Gaskell himself; and these no one who is working on the subject can afford to overlook.

Before leaving this aspect of the question, reference must be made to the fact that in the progress of this controversy terms have been employed, which, if continued, in use, cannot but lead to confusion and fallacy. Chief among these is the term "automaticity". The definition of automaticity in this context which is most frequently quoted by physiologists, clinicians, and pathologists, is that given by Langendorff, who regards it as "the capacity in a motor apparatus in itself and without external impulse to develope the continuous stimuli which produce movement". Wenckebach who has applied the theory clinically with admittedly fruitful results, says, "Thus with the help of the new theory, we have found the heart to be a primarily self-acting organ, which by virtue of its inherent properties, is able to preserve its rhythmical action, even in the presence of many disturbing influences, and to meet many different claims on it." It is contended that this automaticity in the case of the heart resides in the specialised tissue at the sino-auricular junction. Unless the definition is capable of an interpretation which is not apparent on the surface, in its terms there is attributed to the heart a functional capacity, which is quite/

quite inconsistent with its existence as part of an organised body. In view of the considerations which were put forward in Chapter I. an automaticity of the heart is unthinkable. It arises primarily as an organic part of the embryo; its embryonic and phylogenetic development occurs in the closest relationship with the growth of the organism. It responds to every new demand made in the course of that complicated growth, and its own shape and evolution is determined by the needs of an ever varying series of circumstances. In disease as in health it is capable of responding to extraneous stimuli from various sources. Intra-cranial abnormalities, abdominal irritation and pulmonary disease may each be reflected in the character of cardiac action. It may be that the term automaticity has been misunderstood; if it has, a more explicit definition should be given; if not, it should be discarded altogether, in as much as it corresponds to nothing in nature so far as the heart is concerned. Modern research on the heart is no longer concerned with the claims of the myogenic or neurogenic theories; the question is not whether the nerves or muscle control the sequence of events in the cardiac cycle, but in what way muscle and nerve co-operate to secure co-ordinated cardiac action.

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Keith and Mackenzie – Lancet 1910 Vol.

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THE CHARACTER AND SITE OF THE SPECIALISED MUSCLE WITH RESPECT TO ITS POSSIBLE FUNCTIONS.

Before proceeding to relate the experimental evidence on which a rational conception of these structures might be founded, it would be well to recapitulate very shortly the main facts relative to the character and position of the specialised muscle bundle. In a communication by Keith and myself three years ago we said that "the result of our investigations has been to believe that all those areas of specialised musculature, such as have been described as nodes, are really areas where the musculature of the heart comes into an extremely intimate contact with the nervous system, that the structures which we designated "nodal tissue" are really neuro-muscular contacts. We found that those areas of the heart of the tortoise, which Gaskell found to have the greatest power of originating the heart's impulse, and those areas which Macwilliam found to possess the highest degree of inherent rhythmicity were made up of a mixture of nerve and muscle fibres". We stated further that "much might be said in favour of the hypothesis advanced by Retzer that the 'nodal tissue' may have something in common with the spindles described by Sherrington in voluntary muscle". We pointed out in favour of this view that, whereas the spindles of voluntary muscle did not degenerate after section of the nerves supplying the muscle, it was also the case that after section/

section of the auriculo-ventricular bundle, its extensions into the ventricle did not undergo atrophic change. Further, it had been found that the specialised muscle systems do not participate in an atrophy or hypertrophy of the heart as a whole. We believed this to indicate the possession on part of the bundle of properties other than those which belong to a structure like a nerve whose only function is to convey impulses or stimuli in one direction. We attributed to the bundle in its capacity as a connecting link between auricles and ventricles the capacity of co-ordinating in some way the auriculo-ventricular sequence. In so doing, we had no intention of questioning the supreme control, which the node of Aschoff and Tawara exercises over the ventricular contraction, but we suggested that in addition to this efferent control, the subendocardial ventricular extensions of the bundle might on further investigation, be found to possess in addition sensory properties. The discovery of a mixed nerve supply by Aschoff and his pupil Fraülein Engel to the auriculo-ventricular node and its branches might be cited as tentative evidence in favour of this contention. Nor does the fact that the nodal structures possess the anatomical characteristics of neuro-muscular spindles imply the conclusion that a spinal reflex arc is part of the mechanism of co-ordination. In a later communication dealing with this same point, I suggest-ed/

ed the comparison of the cardiac movements with those of the intestine rather than with those of the locomotor apparatus. In support of this, I cited the work of Bayliss and Starling on the nervous co-ordination of intestinal peristalsis. The peculiar fitness of such a comparison is obvious when it is remembered that in its embryonic and early phyllogenetic state the cardiac structure and movements are not unlike those of the gut. Even in the case of locomotion in primitive organisms, such as the earthworm, the peristaltic contraction of opposing strands of circular and longitudinal muscle fibres may be compared to the movements of the intestine or of the primitive heart. The exact manner in which the nodal tissue plays its part in the regulation of the sequence of events in the cardiac cycle, is still a matter for further investigation, but of this there can be no doubt, the neuro-muscular tissue, which has been described constitutes the "end-plates", which represent the anatomical basis of this co-ordinated action.

With regard to the position of the end-plates it has all along been recognised that the sino-auricular organ must have something to do with the conditions which determine the commencement of the events in the cardiac cycle. Keith and Flack in their original communication, stated that they supposed "that the sino-auricular node might prove"

prove to be the starting point of the heart's contraction". The position of the auriculo-ventricular organ marked it out at once as the structure which provided a basis of functional continuity between auricular and ventricular contraction.

The opportunity may be taken here of suggesting another respect in which the location of these end-plates may indicate the possible nature of their function. In the bream it was seen that the two nodes were in the form of two rings at points of constriction of the cardiac tube. At these constrictions the valves are attached to the inner wall of the tube. The nodal rings may be regarded as sensitive sphincters situated at points where the blood stream passes from one chamber to the other, and where regurgitation is prevented by a valvular apparatus. The sino-auricular ring lies in the sino-auricular constriction at the basal attachment of the venous valves and the auriculo-ventricular ring lies at the auriculo-ventricular constriction at the point of attachment of the auriculo-ventricular valves. The location of the nodal structures is such that they, as highly sensitive organs, are subjected to the varying pressure exercised by the blood in the contracting and relaxing tube. Here again, the analogy of the intestine might be useful; for the pyloric and ileo-coecal valves might be compared with the nodal sphincters, which guard the/

Hering - Arch. f. d. ges. Physiol. 1907 - CXVI - p 143.

Gaskell - Journal of Physiol. 1883 - IV - p 43.

MacWilliam - Journal of Physiol. 1888 - IX - p 167 the entrance to the chambers of the heart. When in later development the rings have become modified into end-plates, their position at the sino-auricular and auriculo-ventricular orifices has not changed, and as has been suggested the extensions of the latter into the cavities of ventricles leaves it in a position where it is exposed to the variations of intra-cardiac. pressure.

EXPERIMENTAL EVIDENCE OF THE FUNCTION OF THE SINO-AURICULAR END-PLATE.

It is impossible within the scope of the present review to refer to all the work which has been done on this aspect of the subject. Before the discovery of Keith and Flack observations on the dying heart led to the conclusion that the highest degree of rhythmicity was possessed by tissue at the orifices of the great veins; Hering thought that this applied in particular to the orifice of the superior cava. Gaskell found that a variation in the rate of cardiac contraction could be produced by the application of varying degrees of heat to the sinus venosus; and in the mammalian heart Macwilliam states that the rate is influenced when the tissues in the neighbourhood of the superior cava are heated. Excision or ligature methods have also been employed in cold blood animals with the result that it has been found that any injury/

Lewis and Oppenheimer. Heart. 1910 - ii - p 147

Wybauw - Arch. internat d Physiolog. 1910 Vol X.

Koch - Medizin Klinik 1911 No 12.

injury which breaks the muscular continuity between sinus and auricle leads to a temporary cessation of the auricular contraction, while the sinus continues to beat. The application of this method to the mammalian heart has led to conflicting results. These experiments are subject to the serious objection that they have not been performed on the heart in situ.

The first conclusive proof that the sino-auricular node is concerned with the commencement of the series of events known as the cardiac cycle came from Lewis and Oppenheimer. Lewis found by means of the string galvanometer that the auricular contraction began invariably at a point which he located between the superior cava and the auricular appendix. The dogs' hearts on which the experiments were performed were afterwards examined by A. Oppenheimer and B.S. Oppenheimer, who found that this point corresponded exactly with the thickened upper end of the sino-auricular end-plate.

Wybauw using also the string galvanometer arrived at the conclusion that the auricular systole began "at a point described by Keith as the site of the sino-auricular node and by Koch as the site of the sinus node". The hearts were subsequently examined by Koch who was able to confirm that the site referred to corresponded exactly to the position of the nodal tissue.

Flack has carried out a series of important investigations/

Flack – Journ. of Physiol. 1910 Vol 41.

Arch. internat. d physiol. 1911, Vol XI. Fasc 1.

vestigations into the functions of the node. The experiments were performed on rabbits, dogs, and cats.

(1) First of all he studied the effect of cold on the node. This was done by the application of a thin cooled silver rod in some cases, and in others by the perfusion of ice cold water through a small silver canula held upon the node, and in still other cases by freezing the node with ethyl chloride, carefully protecting the surrounding parts of the heart with cotton wool. The effect in all cases was the same, namely, an immediate slowing of both auricles and ventricles. It was only when the cold was applied in the region of the node that the rhythm of all four cardiac chambers was affected; applied at other parts of the auricle surrounding the superior cava its effect was practically nil.

(2) In the second place, the effects of electrical stimulation were observed. For this purpose platinum electrodes were employed every part of which, except the points, was isolated by rubber. In the first five experiments the Kronecker coil was used with the ordinary zinc-carbon immersion battery. In the later experiments the Guelcher's thermo-electric battery was used together with Kronecker's interrupter with the mercury "spülkontact". This interrupter has two mercury contacts, one leading to the electro-magnet of the vibrating rod, the other to the/

the induction coil. The advantage of the arrangement is that the current to the electro-magnet is separate from that to the coil, the current of the latter is therefore, not in any way interfered with by the former, and is thus always constant. The effects of electrical stimulation are summarised by Flack as follows:- "(a) with weak stimulation of the node, usually about 40 units Kronecher coil, there occurs a marked inhibition of both auricles and ventricles; (b) With slightly higher stimulation, usually 50 - 60 units, a mixed effect of inhibition and acceleration of both auricles and ventricles is obtained, the acceleration usually predominating; (c) with slightly increased stimulation, 60 - 80 units, a very marked acceleration of the rhythm in both auricles and ventricles, is brought about; This acceleration is so marked that the recording tambours cannot record it; (d) With strengths above this either a very marked acceleration of rhythm occurs, or an altered rhythm of auricles and ventricles during stimulation followed by a marked quickening of the rhythm after cessation of the stimulus. The latter may possibly be a ~~spiced~~ spread effect owing to the strength of the current used. It is to be noted that in cases (a), (b), and (c), the same degree of stimulation applied to other parts of the superior cava, and its line of junction with the auricle gives no such results. When applied/

applied to the auricles the slighter degrees of stimulation give no effect or a slight quickening of the auricular beat. Stronger stimulation induces peculiar wave-like contractions of both auricles, but not of the ventricles. The peculiar wave-like contractions have been called 'wogen'. Upon the kymograph these are recorded mostly as irregular lines, but to the naked eye they are altogether different from the quickened beat induced by stimulation of the node. The latter are quick forcible little beats, the former (wogen) have but little force, the contractile power of the auricles being apparently depressed. The higher strengths (60 - 80 units) when applied to the different parts of the ventricles give no effect. A strength such as 400 units which, when applied to the apex, will induce only a slight quickening, applied to Kronecker's vaso-motor centre in the inter-ventricular septum will induce fibrillary contractions. These effects of electrical stimulation of the node would appear to be of great interest clinically, inasmuch as stimulation of the node either through its blood supply or through its nerves may conceivably give rise to these conditions of slow heart beat, irregularly accelerated and slowed beat, greatly quickened beat and possible altered rhythm of auricles and ventricles".

(3) In the third place, <u>the effects of clamping and ligaturing</u>/

ligaturing the node were observed. The effects of clamping the node were found to depend on the pressure exerted in the experiment. For this purpose either ordinary forceps or Spencer-Wells forceps were used. The effects with moderate pressure were varied, depending evidently on the amount of stimulation produced. There occurred (a) mostly a marked quickening of the whole heart rhythm, (b) occasionally an altered rhythm of auricles to ventricles, and (c) sometimes a slowing of the whole cardiac rhythm. Similar treatment applied to other parts of the superior cava auricles and ventricles produced no effect. The most astonishing feature of the clamping experiments was, however, produced by pressure firm enough to destroy or obliterate the node. In this case, as well as by ligaturing, Flack found little or no change in the cardiac rhythm. He suggests that owing to the slight variation in the position of the node that some parts of it might not have been included in the clamp or ligature. This would seem to be not improbable; although with total destruction of the node the auricular contraction might possibly, as he suggests, have originated in Tawara's node at the coronary sinus. In this case a shortening of the interval between auricular and ventricular contraction would have occurred, but he made no observations on this point (See Hering's experiments, - p.158).

Experiments/

Experiments were next made to determine whether electrical stimulation of the node produced effects similar to those obtained by stimulation of the vagus and sympathetic nerves. It was found that both the node and the nerves were more responsive to quick rates of stimulation (20 - 100 per sec.) than to slow (3 - 5 per sec.) An attempt was ~~next~~ made to ascertain the relationship of the vagus and sympathetic nerves to the node. The chief points investigated were, the effect of the application of atropine and muscarine to the node, the effect of stimulation of the nerves during the application of cold to the node, and the effect of stimulation after tight clamping. The atropine was applied carefully to the nodal area for 1 - 2 minutes, the surrounding parts of the heart being protected by cotton wool. It was found that in all cases the effect of stimulation of the vagus on auricles and ventricles was abolished. The effect was quite transitory, lasting only 2 - 3 minutes. This corresponds with the duration of the effect when the drug is injected into the blood. With regard to muscarine applied in the same manner, its effect was to slow markedly the rate of the heart beat. At the same time, the effect of the vagus nerve was greatly increased. It was found that whereas without muscarine it took 50 units Kronecker coil to slow in a marked degree the rate of beat, a much greater/

greater effect was produced by 25 units after the application of muscarine. With a longer application of the drug to the node the effect of the vagus upon the heart seems to be abolished, the organ continuing to beat with a slow depressed contraction. The effect of muscarine, whether applied locally or injected into the blood stream is abolished by the local application of atropine to the node.

Experiments were also carried out to test the effect of the accelerator and vagus nerves after the application of cold to the node. Ethyl chloride was sprayed directly upon the site of the node, the surrounding parts of the heart being guarded by cotton wool. Three experiments were performed; in one case the effect of the left accelerator was abolished, in another the effect of both accelerators and in the third that of the right only disappeared. The influence on the vagus of cooling the node was observed in two cases; in one case the vagal influence of the right was abolished while that of the left was retained, and in the other case the influence of the right vagus on rate of beat was inhibited while it retained its effect on the character of the contraction; in the second case an influence of the left nerve on the cardiac movements could not be elicited before the application of cold to the node. Flack himself, regarded the freezing method as being open to objections, hence he applied it only/

only in a few cases, and continued his investigation of the same aspect of the subject by observing the effect of the vagus and accelerator nerves after clamping the node. After carefully ascertaining the strengths which produced an undoubted response on part of the nerves, the area of the end-plate was tightly clamped with Spencer-Wells. forceps, the forceps being left on. The results obtained agree with those produced by atropine, only they are more conclusive. In six cases out of seven, it was found that by clamping, the inhibitory effect of stimulation of the vagus on the contraction of auricles and ventricles was abolished. In the single case in which a negative result was obtained Flack suggests that the clamped area in the heart of the dog employed, may not have included the whole of the nodal tissue; in this case, although the effect of vagal stimulation was retained, the influence of stimulation of the right sympathetic was abolished. In other experiments, it was found that the effect of left vagal stimulation was variable; in most cases where the nerve was acting at first, clamping resulted in a disappearance of the effect of stimulation, in two cases, however, the effect upon the auricles only was abolished, and in one of these the effect subsequently returned.
Of special interest is the fact, that in one case an ill-fitting pair of forceps admitted of the effect of vagus stimulation,/

stimulation, which, however, disappeared when the node was properly compressed. In these experiments it was found that with one exception the right vagus exerted a more powerful influence on the rate of the cardiac beat than the left; in some cases the effect of stimulation of the left branch was not appreciable. The variations, which occur after stimulation of the left branch when the sino-auricular end-plate is clamped suggest a variability and irregularity in the distribution of the vagal branches.

The results of Flack's investigations have been given in some detail, because they constitute an almost conclusive proof of the conception, which we have formed on anatomical grounds that the sino-auricular node is a neuro-muscular end-plate through which the regulating influences of the vagus and sympathetic nerves are communicated to the cardiac muscle. That the right vagus and sympathetic play the primary part in this influence is also a matter of great importance in view of the suggestion based also on anatomical evidence that the sino-auricular node is more closely associated with the structures lying in association with the right Duct of Cuvier, whereas the so-called auriculo-ventricular node is more closely associated with the structures connected with the left Duct of Cuvier, and therefore with the left vagus and sympathetic fibres. (p.130).

In/

Hering – Arch. f. d. ges. Physiol. Bd. 136.

Koch. – Mediz. Klinik 1911 No 12

Rothberger and Winterberg – Arch. f. d. ges. Physiolog. 1910 Bd. 135.

In this connection a recognition of the results of Hering's experiments is important. He touched the region of the node in dogs and in cats with a glowing platinum needle. The result of this, according to Hering, was that the auricular contraction was no longer dominated by the sino-auricular node, but that heterotopic stimuli were developed in the auriculo-ventricular node. This conclusion was based on the fact that subsequent to the interference with the sino-auricular node a change in the interval between auricular and ventricular occurred, so that the contractions of auricle and ventricle were simultaneous or almost simultaneous. Hering emphasises the fact that the most markedly simultaneous auriculo-ventricular rhythm occurred in those animals in which the destruction of the tissue was most extensive. The hearts were subsequently examined by Koch, who was able to report the presence of a circumscribed lesion in the node, and in one case an almost complete destruction of the whole of the nodal tissue. In other cases only the superficial fibres were destroyed; but in all a lesion of some degree had been produced.

Of great importance in the problem of the relation of the nerves to the end-plates of the heart are the investigations of Rothberger and Winterberg. Their experiments carried out almost at the same time as those of Flack and quite/

quite independently, point to a confirmation of the latter's suggestion that the right sympathetic is closely associated with the function of the sino-auricular end-plate while the left sympathetic exercises a dominating influence on the function of the auriculo-ventricular end-plate. Their observations, however, indicate more far-reaching conclusions, for they found that while stimulation of the left sympathetic could give rise to an auriculo-ventricular rhythm, that is to an almost or completely simultaneous contraction of auricles and ventricles in which the contraction was believed to originate in the auriculo-ventricular node, this rhythm could be abolished and replaced by a normal rhythm by stimulation of the right sympathetic. It sometimes happened as in the case of Flack's experiments, that unequivocal results could not be obtained. Stimulation of the left sympathetic might fail to produce a simultaneous rhythm. In such cases a cooling of the sympathetic supply to the sinus node not infrequently admitted of the production of an auriculo-ventricular rhythm when the left sympathetic was stimulated. These varying results in some of their experiments the authors attribute to a mixing of the fibres of the right and left sympathetic branches. They were unable to obtain conclusive results from similar experiments with the vagal branches, a fact which may also be due to the mixed character/

Gaskell – Journal of Physiol. 1884. p457.

Wooldridge and MacWilliam – Arch. f. anat. und Physiol
1888 – ix – p167.

character of the nerves.

Further discussion of the function of the sino-auricular end-plate will be deferred until the experimental evidence as to the possible functions of the auriculo-ventricular system has been described.

EXPERIMENTAL EVIDENCE OF THE FUNCTION OF THE AURICULO-VENTRICULAR END-PLATE.

The interest which surrounds this question is historically bound up with observations which have been made on the heart since the classical researches of Harvey. Harvey observed that between auricular and ventricular contraction there was a pause, and noticed that occasionally several auricular contractions might be followed by only one ventricular contraction. The transmission of waves of contraction along tissue was studied by Romanes in the embrella of the jelly-fish, and his observations formed the starting point of Gaskell's well-known work on the heart of the lower vertebrates. Gaskell showed that the propagation of a wave of contraction from the great veins through the heart to the arteries depended upon the integrity of the muscle tissue, along which it passed, and in the mammalian heart Wooldridge and Macwilliam came to the conclusion that the ventricular beat was conditioned by the influence of the preceding auricular beat. The more/

His (jun) Arb. a. d. med. Klinik Leipzig 1893

Wiener med. Blätter 1894.

Humblet – Arch. internat. d. physiol 1904 I p278.

Arch internat d. physiol 1905 III p 330.

Hering – Arch. f. d. ges. Physiolog. 108 1905.

more recent work on the relation of ventricular to auricular systole naturally began with the discovery of Stanley Kent and of His, that the mammalian auricles and ventricles were connected by a strand of muscular tissue. Although he had not as yet submitted his anatomical discovery to experimental investigation, His suggests the question "whether this bundle really conducts the stimulus from auricle to ventricle". In the following year, however, he was able to state from further examination that "the bundle provided not only an anatomical connection but also a physiological connection between auricles and ventricles. Through the left auricle of a rabbit he passed a small knife and made an incision, which divided the septum in the region of the bundle, producing auriculo-ventricular dissociation. In 1904 Humbelt destroyed the bundle in the perfused heart of a dog and produced a dissociation of the cardiac rhythm. In a subsequent series of experiments he ligatured the bundle in seven perfused hearts, and in each case obtained dissociation. In an eighth case, dissociation resulted before the application of the ligature.

It cannot be said, however, that conclusive proof of the necessity of an integrity of the bundle for co-ordinated cardiac movement had been given before the publication of Hering's observations. Hering killed his dogs with ether and/

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Tawara – Arch. f. d. ges. Physiolog. 1906. CXI. p 300.

septum in the region of the bundle, producing auriculo-ventricular dissociation. In 1904 Humblet destroyed the bundle in the perfused heart of a dog and produced a dissociation of the cardiac rhythm. In a subsequent series of experiments he fractured the bundle in seven perfused hearts, and in each case obtained dissociation. In an eighth case, dissociation resulted before the application

Erlanger – Zentralblatt f. Physiolog. XIX. 1905.

of the ligature.

It cannot be said, however, that conclusive proof of the necessity of an integrity of the bundle for co-ordinated cardiac movement had been given before the publication of Erlanger's observations. Erlanger united his work with other and then having removed the blood from the heart he made an incision through the bundle and subsequently perfusing the organ through the aorta he found that the auricles and ventricles contracted each regularly, but in complete dissociation. From his curves he was able to demonstrate as a result of his incisions that:-

1. The auricles contracted more frequently than the ventricles, but both contracted regularly.
2. Spontaneous or artificial contractions do not pass from auricles to ventricles or vice versa.
3. The ventricles now contract automatically, as do the auricles.

The hearts were examined by Tawara, who was able to state that the incisions had produced a discontinuity of the bundle fibres. Through these experiments then, proof was afforded that the bundle in the dog's heart preserved a functional connection between auricles and ventricles, and it was natural to suppose that since its presence had been demonstrated in the heart of other mammals and in man, that in these cases also it fulfilled a similar purpose.

Almost at the same time Erlanger published the results of his experiments, which were performed also on the heart of the dog. In his first experiments he attempted to ligature the heart _in situ_, but only in one case out of seven was dissociation observed. In the subsequent experiments he employed a clamp, but only in two cases out of

seven/

Erlanger and Hirschfelder – American Journal of Physiology XV p 153

Erlanger and Blackman – Heart 1909-10 I p177.

Tawara – Zeitsch. f. experim. Path u. Therap. III 1906.

seven was he successful in producing dissociation. He then had a clamp made specially, the lower blade of which was fashioned in the form of a long-shafted fish hook bent at right angles. He introduced the hook between the pulmonary artery and the aorta into the left ventricle, and then passed the point of the hook into the septum below the bundle posterior to the region of the pars. The blades of the clamp could be tightened as desired, and the bundle in this way exposed to varying degrees of pressure. In seventeen experiments he succeeded in producing dissociation in sixteen instances. The hearts were examined by Retzer'who found that in every case in which the rhythm had been disturbed the bundle had been damaged. These experiments were confirmed and extended in later publications by Erlanger and Hirschfelder.and by Erlanger and Blackman.

Tabora working in Hering's laboratory, followed Erlanger's methods and confirmed his results. He believed, however, that the incision method was preferable to that of clamping in that the technique was more exact, and the general damage to the heart was not so extensive. At the same time the clamping method had the advantage of allowing a graduated interference with the function of the bundle, whereby it was possible to produce first of all a partial elimination of ventricular systoles, and later with firmer pressure a complete dissociation. Tabora in addition/

Cohn and Trendelenburg — Zentralblatt f. Physiolog. XXIII 1909.

Kronecker and Busch. — Rep. Brit. Assoc. f adv. of S. 1899 p 895.

addition administered digitalin and found that it increases the disturbance of the rhythm which had already been induced by slight pressure.

More recently Cohn and Trendelenburg have carried a very extensive series of investigations on the perfused heart. They used the incision method to interrupt the course of the bundle. Experiments were performed successfully on 29 cats, 4 rabbits, 17 dogs, 2 apes, and 4 goats. When the results were communicated to the Physiological Congress complete serial sections had been examined in 14 cases. With the cat and the rabbit it had been found that there was no well-defined line of incision, which in every case could be relied on to give rise to dissociation. This conclusion was based on the microscopic examination of serial sections from 6 cats and 3 rabbits. The failure to produce dissociation in these cases is attributed to the fact that strands of fibres were found to descend from the node or main bundle into the right ventricle before the bundle entered the septum fibrosum. On this account it would, they say, be impossible to produce by a single incision, a complete interruption of the auriculo-ventricular fibres.

It might be well at this point to refer to the fact that other observers have contended that section of the bundle in the rabbit may not be followed by dissociation. Kronecker and Busch ligatured the bundle without producing dissociation,/

dissociation, but they do not give anatomical details. Pankal ligatured the bundle in 24 rabbits, and came to the conclusion that when the bundle alone is caught no dissociation follows, but when a considerable amount of the surrounding tissue is included the rhythm is disturbed. Pankal's communication is accompanied by several drawings and curves in support of his contention.

With regard to these equivocal results in the case of rabbits and cats, it must be borne in mind that the hearts of these animals are comparatively small, and it must be a matter of extreme difficulty to include the bundle in a ligature or incision on every occasion. In proof of this, may be cited the early failures of Erlanger who worked first of all with ligatures and failed to obtain successful results, and then with a clamp, which he had to discard in favour of a specially devised instrument. I can confirm the presence of the early descending fibres from the node into the right ventricle in the hearts of rabbits and of rats, but I should not be disposed to believe that such fibres could assume the function of the whole auriculo-ventricular extensions in almost every rabbit, without there being some dislocation of the cardiac rhythm. If partial destruction of the bundle produces a partial dissociation of auriculo-ventricular contraction it is difficult to see why complete section of the bundle does not at least produce a certain degree of disturbance in/

Eppinger and Rothberger. – Zeitsch. f. Klin. Med. 70.1.2.

in the rhythm. Without more definite evidence I am disposed to believe that where dissociation has not occurred the bundle has not been completely severed. The problem however, requires further study, and could be readily solved so far as the early descending fibres are concerned by means of the electrocardiogram. For Eppinger and Rotberger have shown that when the right branch of the bundle is cut the ventricular contraction begins in the left ventricle, and the form of the electrocardiogram is that of a left ventricular extrasystole, whereas when the left branch is cut the ventricular contraction begins on the right side and the form of the electrocardiogram is that of a right ventricular extra-systole. If it be the case in those rabbits that the bundle has been severed, and that the continuity is preserved by the fibres, which descend directly into the right ventricle, then the ventricular contractions would be found by the electro-cardiogram to be exclusively right ventricular extra-systoles.

The experiments of Cohn and Trendelenburg on the hearts of dogs, apes and goats, fully confirmed the earlier results obtained by Hering and others. They are all the more convincing in that the evidence as shown by curves and microscopic examination is practically complete.

As evidence of the extreme importance of comparative anatomy and physiology in the study of this as of other branches of/

of medical science, is the fact that Gaskell's original observations on the heart of the tortoise have been confirmed in another respect in the mammalian heart. In fact, it is possible to detect Gaskell's inspiration in all the recent work on this subject. In the incision experiments of Hering, and Cohn, and Trendelenburg, and also in the clamp experiments of Erlanger it was found that where the section of the bundle was incomplete or where the pressure was not extreme the dissociation was partial. As already stated the device adopted by Erlanger rendered it easy to expose the bundle to varying degrees of pressure, and he found as did Gaskell that there might be:-

(1) an increase in the interval which normally occurs between auricular and ventricular contraction,

(2) an occasional elimination of a ventricular systole after an auricular systole.

(3) a regular recurrence of eliminated ventricular systoles, that is the absence of every tenth, ninth, eighth, seventh, sixth, fourth, or third ventricular systole, although the auricular series of contractions was complete.

(4) a failure of the ventricle in its response to alternate auricular beats, that is the establishment of a 2 : 1 rhythm, when the auricle beats twice as rapidly/

rapidly as the ventricle.

(5) a response of the ventricle to every third beat of the auricle, that is a 3 : 1 rhythm in which the auricle beats three times as rapidly as the ventricle.

(6) a complete dissociation between auricular and ventricular contraction, that is when both auricles and ventricles beat regularly, but each pursues an independent rhythm.

Although the evidence of experiment is convincing in respect of the contention that a disturbance of co-ordination in the auriculo-ventricular rhythm is usually associated in experimental cases with partial or complete destruction of the bundle, this must not be taken to mean that any and every interference with the bundle will produce dissociation slight or complete. Destruction of a small part of the bundle may be produced experimentally without any interference with the rhythm and either of the main branches may be severed without affecting, so far as curves can show, the co-ordinated contractions of auricles and ventricles[x]. There is in the bundle, as in every other organ in the body, a certain amount of physiological reserve whereby it is enabled to perform its/

[x] It is possible to demonstrate the section of one branch by the electrocardiogram

its functions, in ordinary circumstance, to all appearances normally, even although there be a slight variation from its normal structure. It is important to bear this in mind in view of the fact that unwarranted significance is occasionally attributed to "fibrosis" and "small collections of lymphocytes" in hearts which are the subject of pathological examination.

But more important than this is the converse, namely, that auriculo-ventricular dissociation may occur in the absence of any demonstrable lesion in the bundle or its main branches. It may be brought about, (1) by the injection of poisons, for example by digitalis, adrenalin, aconitine, muscarine, or physostygmine; it occurs (2) as a physiological condition in hibernating animals; (3) it has been found to supervene in experimental asphyxia; and (4) it may follow stimulation of the vagus.

AURICULO-VENTRICULAR DISSOCIATION PRODUCED BY POISONS. x

The most important work on this subject is that which has been done by Cushny, and his pupils. He has found that by the administration of aconitine the normal sequence of events /

x I have avoided the use of the term 'heart-block' throughout the whole discussion, because it presupposes a definite and improved relation of ventricular to auricular contraction. It means, as it is employed in the literature, that dissociation cannot occur so long as there is anatomical and functional integrity of the junctional tissues.

events in the cardiac cycle can be so upset that almost every form of clinical irregularity can occur. The conditions which predispose to the occurrence of one form of irregularity in preference to another under the influence of aconitine are unknown, and are probably to be referred to the accidental affinities for the poison possessed by the important tissues at the time of administration. In any case Cushny found that the intravenous injection of 0·2 mg. of aconitine into a dog in 0·05 mg. does produce irregularity of the heart as a rule, and that in some cases the irregularity had the form of auriculo-ventricular dissociation. An increase in the interval between auricular and ventricular contraction was very often seen, in some cases the interval which is normally 0·1 sec. in the dog might be increased to 0·3 sec. The interval might be so long as to give the appearance of a reversed rhythm, the ventricular systole beginning just immediately before the next auricular one. A common form of irregularity was the 2 : 1 rhythm in which the auricular rate was twice that of the ventricular; on the other hand a reversed 2 : 1 rhythm might occur in which the ventricular rate was twice that of the auricular. In some cases the auriculo-ventricular interval would increase with each beat until the ventricular contraction would drop out altogether; the interval following the elimination of a ventricular systole/

Cushing – Journ. of Exp. Medic. 1897. II. p.233

Tabora – Zeitsch. f. exp. Path u. Therap. 1906 III p 454.

James Mackenzie – Diseases of the Heart. 1908.

Buchanan – Journal of Physiol. XLII. 1911. p XIX.

systole would be very short, the next one longer and so on until the series terminated again by the elimination of another ventricular beat; this is a well-known clinical phenomenon, and it is important to recognise its occurrence in acute poisoning. In two experiments there was complete dissociation, the auricles and ventricles beating in independent rhythms. A point of particular interest, and which will be referred to later, in discussing a case of dissociation in diphtheria (p. 231) is that under aconitine the independent ventricular rhythm was much quicker than it is in cases where the bundle is incised or clamped; in Cushny's cases the ventricular rate was almost as great as the auricular rate.

Cushny and Tabora have each published evidence of the influence of digitalis on the auriculo-ventricular rhythm, and James Mackenzie has long ago established the fact that similar phenomena occur in connection with its clinical administration.

AURICULO-VENTRICULAR DISSOCIATION IN HIBERNATING ANIMALS.

This interesting phenomenon has been described by Dr. Florence Buchanan. The observations were made on dormice by means of the capillary electrometer. It was found that when the animal was very torpid, showing no signs of respiratory movements for several consecutive minutes, and having a pulse frequency of from 12 to 30 a minute,/

minute, the records showed only ventricular effects; the ventricular systoles occurred at irregular intervals and the slower the pulse the greater appeared to be the irregularity. Dr. Buchanan believes that the auricles were either at a standstill or that the movements were very slight because the distance between the ventricular beats on the record was so great that had there been any ordinary auricular contractions they would have been shown. This conclusion was further supported by the fact that when the ventricular rate increased to about 40 per minute well marked auricular effects appear# but at longer intervals than the ventricular effects. With a further increase in the ventricular rate there was a corresponding increase in the auricular rate until when the ventricles were beating at 100 per minute the auricles showed practically the same rate. On more than one occasion, however, and with different dormice the auricles did not overtake the ventricles until the rate was about 300 per minute. When once the auricular rate overtook the ventricular rate, and passed it, it never fell behind again except for a few beats at a time. The auricular rhythm was less regular than the ventricular rhythm until the latter was overtaken, but while being overtaken the ventricular rhythm was apt to become very irregular, one or more ventricular systoles being dropped here and there, while/

while the auricular systoles continued, giving the records the appearance which is familiar in cases of complete dissociation produced by vagus stimulation in other mammals. Even when the two series were nearly at the same rate they were, as a rule, absolutely independent of each other, now the one and now the other being accelerated or retarded for a few seconds. Occasionally the auricular rate would be brought into co-ordination with that of the ventricle; then there would occur a series of beats in co-ordinate rhythm, but with a gradually increasing interval between auricular and ventricular systole until an auricular beat would occur without a corresponding ventricular beat: this is the phenomenon described by Cushny and referred to above in the description of the effect of aconitine.

In Chapter I, reference was made to the evidence from comparative anatomy and embryology of the deeply seated relation between the heart and the lungs; and this was cited later when objection was taken to the use of the term 'automatism' in connection with the cardiac contractions. There could be no more conclusive and illuminating evidence on this point than that which is afforded by Dr. Buchanan's observations of the relation of the respiratory to the circulatory movements in hibernating dormice. The respiratory rate was found to increase as the cardiac contractions became more frequent. Until the heart rate reached/

reached 200 per minute, the respiratory rate was more or less the same as the auricular or ventricular rate. When the breathing was of the Cheyne-Stokes type the auricular contractions were absent during each period of apnoea, apparently disappearing just before the apnoea began and reappearing just before the breathing commenced. Simultaneous respiratory and circulatory records were not taken, but Dr. Buchanan points out that if the observations as to the precise time of onset of apnoea and its exact relation to the disappearance of the auricular contractions be correct, it would suggest that it is those changes in the blood which are known to affect the respiratory centre which are first directly or indirectly responsible for the presence or absence of the auricular contractions in the deeper stages of hibernation. The fact that the auricular beats disappeared before the dyspnoea ceased and reappeared before the stage of apnoea was at an end, renders it improbable that the mechanical effect of the respiratory movements had influenced the appearance of the auricular contraction by increasing the intra-auricular pressure. Whatever be the explanation of the phenomenon the fact remains that it demonstrates the close relationship if not the identity of some of the influences, which control the respiratory and circulatory movements.

AURICULO-VENTRICULAR DISSOCIATION AS A RESULT OF EXPERIMENTAL ASPHYXIA.

The/

Lewis and Mathison — Heart 1910 II p47.

The occurrence of auriculo-ventricular dissociation in experimental asphyxis has been studied by Lewis and Mathison They found that if a cat be asphyxiated for periods varying from 1 - 7 minutes, a successive series of changes takes place in the character of the cardiac rhythm. Within one, two or three minutes of the onset of asphyxia the interval between auricular and ventricular contradtion is increased; ultimately this increase leads to the elimination of a ventricular systole; in some instances, the records showed that the interval might increase, so that a certain auricular contraction occurred simultaneously with the ventricular contraction of the previous cycle. Subsequent to the elimination of a ventricular beat, and the resultant long pause, the interval abruptly becomes very short, and then goes on increasing to repeat the whole process. With the deepening of asphyxiation the stage of prolonged intervals between auricular and ventricular systoles is succeeded by a rhythm in which every alternate auricular systole is followed by a ventricular systole; finally the rhythm passes into one of complete dissociation, in which both auricles and ventricles beat regularly, but at independent rates, which bear no simple numerical relation to each other. As a rule, when artificial respiration has been established, a rapid and complete recovery of the normal rhythm ensues even from the most complete degree of dissociation. The disturbances of the rhythm produced by/

by asphyxiation are thus seen not to differ materially from those described in aconitine poisoning and in hibernation.

DISTURBANCE OF AURICULO-VENTRICULAR CO-ORDINATION BY VAGAL STIMULATION

The influence of stimulation of the vagus on the movements of the heart in the lower vertebrates was the subject of very extensive researches by Gaskell. That aspect of the subject which concerns us here, has reference only to the "depression of conductivity", through the junctional areas between the cardiac chambers. Gaskell found that as a result of vagal stimulation such depression took place "at the two natural blocking points", namely, the sino-auricular and auriculo-ventricular junctions. In his experiments with the suspended heart he frequently obtained, on stimulation of the vagus, especially in the case of the crocodile tortoise and snake, an absolute standstill of both auricles and ventricles, although the sinus continued to beat regularly. "In these cases it was perfectly clear upon inspection that the contractions of the sinus stopped absolutely at the sino-auricular junction and did not pass into the auricle." Before referring to the influence of vagal stimulation on the sequence of events in the mammalian cardiac cycle, reference must be made to a very important feature of Gaskell's preliminary observations/

Gaskell. – The Transact. Intern. Congress of Med. Copenhagen 1884. Physiology p29.

observations on this subject. He recognised the necessity of separating the inhibitory from the accelerating fibres in the frog's vago-accelerator nerve, in order to obtain the pure effects of inhibitory action. He demonstrated the striking contrast between the effect of stimulation in the frog as ordinarily given, and that of its two components, the intra-cranial vagus on the one hand, and the sympathetic on the other, and also the great variability of the results obtained by simultaneous stimulation of vagal and sympathetic fibres in the same nerve. This is confirmatory of the view put forward with regard to the variable results obtained by Flack and by Rothberger and Winterberger, which have been described in the discussion on the function of the sino-auricular end-plate (p.159). It was there suggested that the mixed character of the nerves and the irregularity of their branching and inter-communications afforded an explanation of those results, which were apparently contradictory. There were three outstanding phenomena in connection with his stimulation of the intra-cranial vagus, which struck Gaskell as being of special importance. Describing the effects of stimulation of the intra-cranial vagus, he says:- "In the first place I have been able to obtain absolute standstill with a strength of current immensely weaker than what is required to obtain the slightest effect when the vago-augmentor nerve (that is, the mixed nerve) /

nerve), is stimulated. In one case the strength of current was as weak as is just necessary to cause contraction of a striated muscle upon stimulation of its motor nerve, the secondary coil being at 35 c.ms. from the primary with one Daniell cell; at the distance of 12 cms. from the primary it was just perceptible to the tongue. In the second place, it is astonishing how long the standstill sometimes lasts after the stimulation is over. Thus one of my tracings shows that a stimulation of the intra-cranial vagus, lasting thirty-eight seconds, caused the suspended heart to remain absolutely still for 290 seconds, that is, for 252 seconds after the stimulation had ceased. In the third place, it is possible to keep the heart absolutely still by means of continued stimulation for a very much longer time than is possible when the vagus is stimulated in the ordinary manner. Thus, I have kept the heart absolutely quiescent for as long a time as 28 minutes by continued stimulation of the intra-cranial vagus with a weak stimulus (second coil between 12 and 11 cms. from primary)".

These observations of Gaskell are given in some detail because they make it obvious that stimulation of the vagus as it is usually carried out in experiments on the mammalian heart, give little or no indication of the manner in which the heart is affected by vagal influences of pathological origin. A disturbance of the cardiac action due to nervous irritation/

James Mackenzie - British Med. Journ. II 1107. p.111. (1906)

irritation must take place as the result of stimulation of isolated nerve cells, connected with a few fibres; these isolated cells form part of a reflex arc, the afferent fibres to which run from the region in which the irritating cause is situated. A pathological reflex stimulation may be purely vagal in character. From the complex character of the vagus in the mammal there is no experiment, which so far can be said to give an indication of the reflex irritation, which in this way arises from the selective stimulation of the intra-cranial vagal fibres. A very striking example illustrative of this point is described by James Mackenzie. He observed that swallowing, which even in normal conditions is recognised to have an inhibitory effect on the heart's action, produced an elimination of ventricular systoles in a patient, who had previously shown from the records, an increase in the interval between auricular and ventricular contraction. In this case the efferent fibres in the 7 reflex arc of deglutition had also stimulated some of the cells of the vagal centre. In the same way irritation from the stomach gall-bladder, urinary bladder, urethra, etc. may occasion an interference with cardiac action such as could not be reproduced experimentally by stimulation of the vagus nerve which as a single nerve possesses mutually antagonitistic properties in virtue of the mixed/

Lewis – Mechanism of the Heart Beat – 1911 – p 109 fig 81.

and p 275 fig 136.

mixed character of its fibres.

It has been shown, however, that experimentally the stimulation of the vagus in a dog may produce a rhythm in which the auricle beats twice as rapidly as the ventricle, and in which this rhythm began with the onset of vagal stimulation and continued while the stimulation lasted. In other cases there may be a sudden standstill of the whole heart. On the removal of the stimulus the auricle commences to beat first, and after an interval greater than the normal auriculo-ventricular interval the ventricle beats; following the next auricular beat there may be no response from the ventricle, but the auriculo-ventricular interval gradually diminishes until the heart resumes its normal rhythm.

While the experimental production of complete dissociation by vagal stimulation in the otherwise uninjured mammalian heart is difficult or impossible there is sufficient evidence to show that, where the auriculo-ventricular end-plate has been partially destroyed or rendered inefficient by incision or clamping with a consequent slight interference with the normal rhythm, a complete dissociation may be induced by vagal stimulation. This is of great clinical importance as indicating the complex character of the circumstances, which have to be taken into account in the analysis of dissociation as a manifestation of disease. It is practically certain that vagal irritation is never capable/

Volhard — Deutsch. Arch. f. klin. Med.
1909 XCVII p 346

Rihl — Zeitsch. f. exp. Path. u. Therap.
1905 II p 83

capable by itself of producing complete and prolonged dissociation. In this connection it is interesting to note that digitalis, according to the investigations of Gaskell, Tabora, and James Mackenzie may increase a condition of disturbed rhythm already present, and that atropine, a drug which is supposed to have a paralysing effect on the vagal endings, may antagonise the effect of the digitalis. Atropine however, has never been known to affect a dissociation which has been prolonged and complete. On the other hand, cases are on record in which atropine has antagonised the effect of digitalis; in Volhard's case atropine abolished an increase of disturbed rhythm which had been produced by digitalis; and Rihl records a similar effect.

The various conditions which conduce to auriculo-ventricular dissociation have been fully discussed in order to emphasise the fact that this phenomenon is not in every clinical case to be attributed to a lesion of the auriculo-ventricular end-plate. In some cases it may be the result of what might be termed "an experimental pathological lesion". Cases in which the bundle is traversed in its whole diameter by a completely destructive lesion are beyond question; and it is practically certain that no such lesion can occur without absolute dissociation. On the other hand in acute toxic disease such as diphtheria, the presence of 'small round celled infiltration' in scattered foci in the node or bundle is a lesion, the significance of which it is impossible to determine/

Mackenzie and Robertson – B.M.J. Oct: 15th 1960 determine, especially since in such cases the remainder of the cardiac muscle is invariably affected to a greater or lesser extent. This will be referred to later (p 236).

THE CARDIOMOTOR FUNCTION OF THE AURICULO-VENTRICULAR END-PLATE.

It is obvious from the foregoing considerations that there is a sense in which the end-plate acts as a conducting mechanism. Its interruption is followed by an interference with the auriculo-ventricular sequence. Whether it conducts an impulse or impulses from auricles to ventricles or from the node (which from its morphological characters and staining properties and absence of glycogen in obviously a special and distinct part of the end-plate) to the ventricles it is impossible so far to say. The influences in the node or main bundle, which determine ventricular contraction pass down in the two main branches which go to the right and left ventricle respectively. When the left branch is cut the right ventricle contracts first and the left ventricle follows; when the right branch is cut the left ventricle contracts first and the right ventricle follows (Eppinger and Rothberger). A very interesting confirmation of this particular function of the connecting muscle is seen in the case of the bird. It was pointed out by Dr. Jane Robertson and myself that in case of the bird's heart there was no bundle of His, and no subendocardial network round the/

Mackenzie I. — Verhand. d. deutsch. g. Ges. 1910.

the papillary muscles in the left ventricle corresponding to that found in all other animals with four complete cardiac chambers. Nor was there any cylindrical extension of the auricular canal into the ventricle, such as is present in all cold-blooded vertebrates. On the left side the auriculo-ventricular muscular extension had become completely atrophied, and the left auricle was separated completely from the left ventricle by a ring of fibrous tissue. On the right side the auricular canal had not become invaginated to the same extent as on the left side, and the auricular extension into the right ventricle remained in the form of a large muscular valve on the parietal side of the orifice. There are no papillary muscles, (~~p~~). In the heart of the pigeon a small leash of the original auriculo-ventricular fibres ~~are~~ is preserved at the posterior end of the valve, where it is attached to the auriculo-ventricular groove near the interventricular muscular septum, and just below the opening of the left superior vena cava (coronary sinus), which in the bird also lies near the venous base of the right ventricle. This is the only muscular connection, which we found to exist between auricles and ventricles, and it is peculiar in this respect that the bird would appear to be the only vertebrate in which the auriculo-ventricular connection is confined to one side, (viz: the right side)

pf/

Flack — Arch. inter. d. Physiol. Vol XI fasc. 1 1911 p120.

Buchanan — Journal of Physiol Vol XLII. 4. p xix.

of the heart. We expressed ourselves with reserve as regards the possible function of this small connecting bundle in as much as it appeared to us at the time not to differ in structure from the ordinary cardiac muscle, and its fibres appeared to become continuous immediately with the ventricular muscle at the right venous ostium.

Any doubt as to the importance of its presence was soon dissipated by the experimental investigations of Flack who found that the inclusion of this bundle in a ligature passed a little below the summit of the base of the ventricle led to complete auriculo-ventricular dissociation. The experiments were carried out in such a way as to make it clear that this was the only part in which the connection between auricles and ventricles ~~preversed~~ preserved the physiological continuity. In the first place, isolated ligatures were passed round the whole auriculo-ventricular connection, and it was only when this last portion was ligatured that allorythmia was produced; and in a second series it was found that a single ligature in this region resulted in dissociation.

A further confirmation of this interpretation of the peculiar anatomy of the bird's heart came from Dr. Florence Buchanan, who had carried out a series of investigations with the capillary electrometer. She found that the effect produced by the bird's heart differed from that obtained from all other vertebrates examined (reptiles and mammals). This difference she correlated with the absence of papillary muscles on the right side. But if we consider the results of Eppinger and Rothberger in this context a further light may be thrown on the subject. They found, as we have seen, that section of either of the main septal branches of the auriculo-ventricular end-plate did not result in dissociation but that a difference in the electrocardiogram effect was produced, which indicated that on section of the left branch the ventricular contraction began on the right side and vice versa. Dr. Buchanan's electrometer records suggest that in the bird's heart, as in no other vertebrate heart, the ventricular contraction commences normally in the right ventricle. How far this short leash of fibres in the bird's heart may ultimately be found to differ from ordinary cardiac muscle is a subject requiring further investigation. I have, since our first examination of the anatomical side of the problem observed the presence of nerve cells and nerve fibres accompanying the small bundle, but more than this it is impossible to say at present, except that the relative shortness of the connecting bundle in the bird is in marked contrast with that observed in other vertebrates, and is of particular importance as we shall see in regard to the question of the cause of the interval, which exists between auricular and ventricular contraction in all normal hearts, (p. 121).

While then there is a sense in which the functional tissues between auricles and ventricles possess the properties of a conducting mechanism, there has been attributed to them another/

another function of perhaps even greater importance, that of originating the stimulus which produces ventricular contraction. It has already been pointed out that before the discovery of the sino-auricular end-plate both Aschoff and Tawara looked upon the node which they described as the centre of automatic cardiac movement. They did not mean, as has so often been believed and misunderstood before and since that time, that at this point the heart began to contract automatically and without any directing impulse from an extra-cardial source; but they regarded the node as a centre from which a wave of contraction was first propagated through the auricles, and then through the bundle and its branches to the ventricles. When the presence of the sino-auricular end-plate was established beyond doubt, the idea that the "lower structure" was a organ which generated stimuli to contraction receded into the background, and it was looked upon, by clinicians especially, more as an organ which carried into the ventricles the impulse, which, generated in the sino-auricular node, had been conveyed to it during contraction through the walls of the right auricle. It has as a matter of fact, been demonstrated as we have seen that the right auricular muscle which contracts first lies in the region of the sino-auricular end-plate, so that there is no question in normal circumstances of a stimulus affecting auricular contraction arising in the/

the auriculo-ventricular node. As usually conceived, the sequence of events in the cardiac cycle begins with some impression on the auricular tissue round the sino-auricular end-plate determining the commencement of auricular contraction; the stimulus to contraction is propagated along the auricular muscle and passes along the node and bundle and through its branches to the papillary muscles of the ventricles, which in their turn are stimulated to contract. There is thus a continuous passage of the stimulus along a substratum of muscular tissue from the entrance of the superior cava to the basal attachments of the aorta and pulmonary artery. The interval which normally occurs between auricular and ventricular systole is attributed to a depression in the rate of conductivity through the auriculo-ventricular functional tissues; and this depression in the rate of conductivity finds its explanation in the structural character of the connecting muscle, which is said to have retained not only the histological features, but also the physiological properties of embryonic cardiac muscle.

The outstanding difficulty in the acceptance of this view is that these functional tissues do not, as we have seen, present the characters of embryonic muscle; and even if they did, it would be difficult to believe that tissue which only in virtue of its microscopic appearances resembles embryonic/

embryonic tissue would in the adult possess the functional properties of that tissue. Admittedly the fibres of the bundle in some animals possess few fibrils relative to the amount of their sarcoplasm, transverse striation may be practically absent, and the nuclei may be round as contrasted with the elongated nuclei of ordinary cardiac muscle. But in the human subject the tissue of the bundle does not resemble embryonic tissue even in these respects. In addition to this, there is the fact that the auriculo-ventricular end-plate has a rich and independent nerve supply, which can be traced into its extensions into the ventricles. Where there is a resemblance to embryonic tissue the structure of the bundle presents histological features akin to those of nerve and of muscle but differing from either. It may be said to be more closely related on the whole in its appearance to the structure of Sherrington's muscle spindles.

If the end-plate be considered in its whole extent, it does not present on its auricular side the appearance as if it were so related to the auricular muscle as to be the direct means of transport of a stimulus coming from the fibres of the contracting auricle. That there are auricular fibres which preserve a structural and muscular continuity between the auricle and the node, there can be no doubt; but these fibres course through a loose space surrounding the/

the node, a space which is occupied with varying amounts of fat and a large number of lymph channels. The whole conformation and structure of the node relative to its surroundings gives one the impression that here as in the case of the sino-auricular end-plate a new series of phenomena begins, and that this end-plate bears the same relation to the ventricles that the other has to the auricles.

The significance of this suggestion will be realized when it is remembered that in discussing the origin and relations of these structures, it was pointed out (p.130), that the one end-plate occupied a site relative to the right superior vena cava (right Duct of Cuvier), which the other occupied relative to the coronary sinus (left superior vena cava or left Duct of Cuvier). It was further suggested that in each end-plate part of the structure described as the sino-auricular nodal ring in the bream was represented. In support of this contention it is necessary here again to revert to the important experiments of Rothberger and Winterberg. We have seen (p.158), that they found that the right sympathetic is closely associated with the function of the sino-auricular end-plate while the left sympathetic is associated with the function of the auriculo-ventricular end-plate. It was found that stimulation of the left sympathetic could in some cases give rise to a rhythm in which the auricular and ventricular contractions were practically simultaneous; whether by this means the stimulation of/

of the node had effected an elimination of the sino-auricular effect or whether it had counterbalanced the inhibitory effect of the vagus on the nodal tissue of the auriculo-ventricular system, it is difficult to say; in any case it was found that a simultaneous stimulation of the right sympathetic abolished the effect of the stimulation of the left sympathetic, so that a normal rhythm was again established. It happened that in some cases in which stimulation of the left sympathetic failed to produce a simultaneous rhythm, if in addition to the stimulation of the left sympathetic the right sympathetic were cooled, that rhythm could be induced. As has been repeatedly pointed out, it is extremely difficult to obtain uniform results in experiments with the nerves going to the heart, on account of the varying complexity of their content and arrangements, but these investigations make it clear that the end-plates are structures through which the nervous control of the heart is exercised in part at least. The manner in which that control is exercised, and the nature of the control has not been determined. In a broad way the sympathetic fibres have an accelerating and augmenting influence on the cardiac beats, while the vagal fibres have a slowing and depressing effect. The cardiac movements are not controlled by nerves in the same manner as the movements of the skeletal muscles. The heart can be isolated/

Hering. – Zentralbl. f. Herzkrank. März 1912 No 3 p 77.

isolated from its extracardial nervous relations and continue to beat rhythmically. But an isolated heart beats less frequently than the same heart in its organic relations. Severed from its inhibitory centres it beats more rapidly; if in addition the accelerators are eliminated it beats more slowly. If first of all the accelerators are excluded, the rate diminishes, and if then the vagal fibres are cut the rate may increase slightly. But in addition to the effect on rate, the elimination of nervous influence affects the strength or tone of the individual contractions. Section of the vagal nerves is followed by a shortening of the period of contraction of both auricles and ventricles, and also by a shortening of the interval between the contractions, so that generally speaking, the rate of conductivity is increased; at the same time the strength of the contractions is apparently increased; if now the rate be increased by artificial stimulation there is a corresponding diminution in the strength of the contractions, whereas, according to Hering, if the rate be increased by section of the vagi, there is no such diminution in the strength of the contractions. These conclusions are in accord with the results of Gaskell's researches by which it was demonstrated that in the tortoise the primary action of the vagus on the cardiac muscle resulted in a depression of all the properties which he

arbitrarily/

arbitrarily attributed to cardiac muscle in general; it produced a depression of rhythmicity, excitability, conductivity, contraction, force and tonicity. The primary action of the sympathetic was antagonistic and opposite to the action of the vagi.

But even when it is suggested that these nervous influences are communicated to the cardiac muscle through the intermediary of the end-plates, the difficulty still remains of explaining the manner in which co-ordinated rhythm is maintained. It would appear that the mutually antagonistic influences of vagus and sympathetic play upon the two end-platês in harmony, and that there is normally a balance in the influences exerted by the one node on the auricles, and by the other on the ventricles. There are thus two primary considerations to be kept in view in analysing the functions of the end-plates; first, the balance between the two end-plates, themselves, and secondly, the balance between the accelerator and depressor fibres in each end-plate. Stimulate the left sympathetic, (Rothberger and Winterberg), and either the balance between the two nodes in destroyed, or the balance between the sympathetic and vagal supply to the auriculo-ventricular end-plate is destroyed and the result is a dislocation of the co-ordinate sequence of auricular and ventricular contraction. This would indicate that the correlated sequence of events in the cardiac cycle/

Mönckeberg. – Verhand. d. Deutsch. path. Ges. 1910 p 64 cycle depended not so much on the auricular muscle between the two end-plates and on the propagation of a stimulus through that muscle, as on the balance of the nervous influences, which affect the two nodes independently. In support of this contention might be cited a case reported by Mönckeberg in which tumor masses occupied the interauricular septum between the coronary sinus, and the auricular ventricular node, (but not invading the latter) thus intercepting the wave of contraction on its route from the superior cava to the auriculo-ventricular end-plate; in this case there was no interference with the sequence of events in the cardiac cycle. It would, however, not have been too much to expect that if the node depended in its function for the reception of such stimuli from the auricular muscle, in this case, some disturbance would have resulted; more especially as the hypothesis on which this conception of cardiac rhythm is founded demands an integrity of the muscle tissue in these parts where the amount of muscle is attenuated as it is in the interauricular septum behind the node.

VENTRICULAR EXTRA-SYSTOLES:

Further evidence in support of the view that the auriculo-ventricular end-plate acts independently of the auricle is to be found in the relation of the vagus to the clinical phenomenon known as ventricular extra-systoles.

I/

Hering – Arch. f. d. ges. Physiol. 1900. LXXXII. p. 1.

Lewis – Mechanism of the Heart Beat 1911 p126.

Rihl – Deutsch. Cong. f. inn. Med. XXIX. 1912.

Bauer – Deutsch Cong. f. inn. Med. XXIX 1912.

I am aware that Hering and Lewis have laid great emphasis on the fact that these ventricular premature contractions occur under suitable conditions "when all nervous connections between heart and central nervous system have been severed", and that they have regarded it as of primary importance to search the heart and not the nervous system in the patient, who is subject to these disturbances. The actual condition of the heart is not a matter which affects the present argument; it is readily granted that a pathological condition of the organ may be in most, if not in all cases, a necessary predisposing element in the production of the phenomenon; but what is of importance is the fact, demonstrated in a recent communication by Rihl, one of Hering's collaborators, that extra-systoles may be excited by pressure on the vagus. The extra-systoles are evoked some time after pressure is applied, and may not appear until pressure is removed; the phenomenon may occur quite independently of the inhibitory effect of the nerve on the heart rate. It may give rise to ventricular or auriculo-ventricular (that is, simultaneous auricular and ventricular) extra-systoles, and occasionally when the systoles occur in series their elimination may be effected by pressure on the vagus. Baker states that pressure on the closed eyes may very occasionally give rise to extra-systoles, and also to slowing of the pulse. The inference from these observations is that the ventricle is influenced/

Lewis - Quart. Journ. of Med. Vol 5 No. 19. p.333.

influenced by the extracardial nerves through the auriculo-ventricular end-plate, and without the intervention of the auricle. When that influence manifests itself in the form of a rhythmic anomaly, such as an extra-systole, it is due to a disturbance in the balance of the mutually antagonistic nerve forces acting on what are perhaps pathologically hypersensitive tissues in the heart.

TRIPLE RHYTHM: That type of cardiac arrythmia known as regular irregularity, in which the radial beats occur in regularly recurring groups of three, may be interpreted on the assumption that the auriculo-ventricular end-plate is concerned in its production; and that the ventricular contractions are in part at least determined by the influence of that end-plate without the intervention of the sino-auricular node and auricular contractions. The characteristic feature of the majority of these cases of so-called "triple rhythm" is that an extra-systole with a compensatory pause follows on two normal ventricular beats, which occupy a normal relation to the preceding auricular contractions; the auricular rhythm is normal and every third auricular contraction occurs at a period when the ventricle is already under the influence of the extra-systole. Lewis has come to the conclusion, which is in perfect accord with my interpretation of the anatomical relations of the end-plate to the ventricles, that these "premature /

"premature ventricular contractions arise as a rule in the special tissues which unite the auricular and ventricular musculature". It would seem, therefore, that in these cases of triple rhythm with normally beating auricles and abnormally beating ventricles, we have to deal with a phenomenon which suggests an influence of the auriculo-ventricular end-plate acting independently of the sino-auricular end-plate. The cases occur not infrequently in the convalescent stages of the acute infections and the arrhythmia is of a transient nature and possesses no serious prognostic significance. In what particular part of the tissues, which co-operate to produce a normal rhythm, the pathological interference takes place, it is so far impossible to say. It may be in the vagus fibres, but the effect of administration of atropine or vagal pressure on the condition has not so far as I know, been described. It may be that the end-plate itself is the seat of the abnormal condition, or on the other hand, the ventricular muscle may be in a condition of metabolic instability, or the cavities may be in a state of hyper-distension from laxity of their walls.

SINUS BRADYCARDIA: Another instance of a type of cardiac irregularity which may be interpreted on the supposition that the two nodes act in co-ordination independently in some degree, of the auricular tissue, and are correlated in their/

Laslett. – Quart Journ of Med. N.S. No 18 p 263.

their function through the nervous system is that of a case of paroxysmal bradycardia, recently described by Laslett. In this case there was a complete irregularity of the radial pulse associated with perfect co-ordination of the auriculo-ventricular rhythm, except for occasionally interpolated extra-systoles of the ventricle. The feature of the case was a paroxysmal slowing of the heart rate during which the patient suffered from giddiness, weakness, and a feeling of lassitude. The length of the cardiac cycle was at times two seconds, and where there were extra-systoles it might extend to three seconds; after a prolonged intermission of this character the length of the cycles gradually diminished. A series of cycles from a tracing during a paroxysm shows their duration to be 2, 1·6, 1·6, 1·3, 1·26, and 1·8 seconds; this represents an average pulse rate of 37·6 per minute. An interesting and important point is that, although there was such a marked depression of the beat rate, there was no prolongation of the interval between auricular and ventricular contractions; the interval as shown by the records was invariably ·2 sec. It is generally accepted that a slow rate of heart beat is accompanied by a slowing of the rate of conduction of the wave of contraction or stimulus to contraction from one end of the heart to the other; this is an outstanding instance of the fallacious conclusions which might be drawn/

drawn by regarding 'conductivity' as a property of cardiac muscle on which an analysis of arrhymias can be based. If in Laslett's case the conductivity in the auricles was depressed, as on general grounds there is every reason to believe that it was, it is perfectly clear that that depression of conductivity in no way interfered with the normal interval between auricular and ventricular contraction; in other words the time that elapses between auricular and ventricular contraction is dependent upon the integrity of the auriculo-ventricular end-plate, a normal condition of its regulating nerves and the influences which affect them, and a normal response from the ventricular muscle with which the terminals of the end-plate are continuous; whether muscle is depressed or increased is a matter of no importance. It is, of course, recognised that in this particular case the conductivity of the auricles might be depressed by the influences which produced the arrhythmia without at the same time affecting the ventricular muscle; for Gaskell found that in the reptilian heart generally, the effects of vagal stimulation were, as a rule, confined to the auricles. But this would be further proof in favour of my contention that the auricular end-plate acted independently of the wave of contraction, which passed along the auricular fibres.

The irregularity in this case was certainly determined by some unusual influences affecting the sino-auricular end-plate only. Simultaneous respiratory curves showed that it differed from the sinus irregularity in youth described by Mackenzie in that its onset showed no relation to the movements of respiration. That it was vagal in origin, although predisposed to by exertion, there can be little doubt, in as much as the administration of atropine at a time when the pulse was slow and irregular, produced an increase in the rate to 78 per minute with a total disappearance of the arrhythmia. Finally the question arises as to the manner in which this case demonstrates an extra-muscular co-ordination of the two end-plates through their nerves, while it is probable that the auricular tissue had little or no co-ordinating influence. I take it that the presence of a normal auriculo-ventricular interval indicated the integrity of the auriculo-ventricular end-plate, and that this end-plate at least was not being subjected to the impression of abnormal vagal stimuli. The appearance of ventricular extra-systoles during the long pauses are to be regarded as an attempt on part of the normal vagal influence on the ventricles to compensate for the abnormal vagal influence on the auricles. A normal rhythm is secured, as I have pointed out by a balance of the influences which control the end-plates. Up to a certain point the auriculo-ventricular end-plate was able to adjust itself to the abnormal sinus effects, but when complete adjustment failed, that failure expressed itself in the form of ventricular/

ventricular extra-systoles originating in the end-plate. The actual point at which the stimulus producing the extra-systoles originated is difficult to determine While the diminution in the blood supply to the ventricles as a consequence of the extreme slowing of the heart's contraction may have produced a certain degree of irritability in the ventricular muscle, it is likely that the determining stimuli were of supreventricular origin. In order to estimate the value of this suggestion regarding the increased irritability of the muscle it would have been necessary to know whether the extra-systoles occurred towards the end of the paroxysms when the lack of sufficient nutrition made itself felt, or whether there was a greater disposition to their appearance after a series of paroxysms closely following one another. The stimuli may have been of extracardial vagal origin and occasioned by the influences which affected the sino-auricular end-plate; on the other hand, they may have occurred apart from extracardial influences as such extra-systoles are a frequent occurrence in the perfused heart. Laslett's case was the subject of a vesical calculus; it was the attacks of colic due to this condition of the urinary system of which she complained, and although she had suffered from giddiness and weakness, she had never had any symptoms referable to the heart. Laslett was/

was at first inclined to attribute the bradycardia to vesical irritation, but as the paroxysms continued after removal of the calculus, he gave up this view. It is scarcely justifiable to express a contradictory opinion on the condition of a patient whom I have not examined, but I would suggest that in the absence of the evidence of a source of vagal irritation in any other part of the body, one is still driven to the conclusion that after all the original irritation of the urinary tract may have continued to be the determining factor for some time after the source of that irritation had been removed. The presence of the calculus and its concomitant inflammation might not only have been the immediate cause of vagal irritation, but it may also have been responsible for the production of a condition of irritability of the vagal centres associated with the urinary tract, and that irritability may have afterwards responded to stimuli which without the original condition, would not have produced any abnormal effect. Nervous irritability is not infrequently a constitutional condition which remains in abeyance in the absence of extraneous sources of excitement, but when once it has been called into activity the instability is increased and stimuli of a more delicate character or from a different source, may suffice to give it a symptomatic expression. Under any circumstances this case is important in as much as it emphasises/

emphasises the necessity of looking for and treating extracardial sources of cardiac irregularity, even although a diseased heart may be the necessary pathological substratum on which these extracardial influences play in the production of the symptoms. It is a well known fact that in operative procedure, dilatation of the urethra or anal sphincters, or excision of the knee joint, may, even when the heart appears to be normal, be productive of a dangerous depression of the circulatory system, which manifests itself in extreme slowing or quickening of the cardiac beat with occasionally an almost imperceptible pulse at the wrist. It is much more likely that if the heart be already diseased the incidence of irritation from these and other similar sources may give rise to profound disturbances of the cardiac action.

THE CARDIO-MOTOR INFLUENCE OF THE VENTRICULAR PORTION OF THE AURICULO-VENTRICULAR END-PLATE.

The preceding considerations make it manifest that the auriculo-ventricular end-plate provides not only an anatomical and physiological basis of the auricular and ventricular connection, but that it possesses in itself cardio-motor functions in the same sense in which these functions have been seen to belong to the sino-auricular end-plate. There is no question of an 'upper' (sino-auricular), and 'lower' (auriculo-ventricular) node; there is no precedence of the one/

one over the other except in the matter of time, and there is no subjection of the 'lower' node to the 'upper' node except in the sense that the influence of the former is normally exerted later in the cycle in the interests of co-ordinate action.

There remains for consideration the question as to the influence of the ventricular extensions of the auriculo-ventricular end-plate after they have been severed from their connection with the node on the auricular side of the fibrous septum. When complete dissociation has been produced by incision or by clamping of the bundle, the ventricle after a pause proceeds to beat slowly and regularly. The ventricular rate in the human subject when the bundle has been intercepted by disease is on an average about 30 per minute, although it may be under 20 and over 40. It has been concluded from electrocardiogram effects that the course of the wave of contraction in the isolated ventricle (that is where the bundle is severed) is the same as that in which the normal cardiac rhythm is preserved. It has also been found that when the ventricular portion of the end-plate has been isolated it does not undergo atrophy. Hence the idea that isolated portions of the nodal tissue continue to exercise an effect on the rhythmic contraction of the muscle, and that so long as the complete ventricular extensions remain intact/

intact in a case of complete auriculo-ventricular dissociation, the rhythmic contraction of the ventricle will remain normal so far as the course of the contraction wave is concerned, only the rate of contraction will be reduced.

THE ORIGIN OF PREMATURE CONTRACTIONS: The problem of locating the site of stimulus formation in cases of premature contractions (extra-systoles) is a very difficult one. At one time it was believed (Hering) that anomalous contractions both of the auricles and ventricles might originate in a focus of irritation in almost any part of the cardiac musculature, (ectopic beat formation). It was, however, considered highly probable that in many instances the stimulus originated, in the nodal tissue or part of the nodal tissue belonging to the two end-plates. A third possibility which was entertained was that 'embryonic rests of the sinus venosus lying in the posterior walls of the auricles might be the site of origin of these contractions, when they occurred in these chambers. With regard to this latter possibility it has already been pointed out that the sino-auricular node or end-plate is not an 'embryonic rest' of the sinus walls, and that so far no masses of tissue which could be described as such have been observed in the auricular walls, and that in any case, even if there were, it is highly improbable that they would possess physiological properties enabling them to initiate/

Lewis and Silberberg. — Quart. Journ. of Med. Vol 5. No. 18.

initiate cardiac contractions. The idea that any part of the heart wall can become a centre of ectopic impulse formation is based on the physiological property of cardiac muscle, which enables it even in small strips, free so far as one knows from nerves, to contract rhythmically under suitable conditions, for example, when exposed to a certain degree of pressure. The problem cannot as yet be regarded as finally settled, but practically all the evidence points to the conclusion that premature contractions originate only in the central fibres or in the fibres of distribution of the end-plates. A very important contribution to the solution of this problem has been made quite recently by Lewis and Silberberg. Premature contractions may be auricular or ventricular, and their incidence and type may be recognised on polygraph tracings. It has been found as a matter of experience that the majority of patients who persistently suffer from this form of irregularity show either the auricular type only or the ventricular type; a mixed form is very seldom seen in the same case. Electrocardiographic examination, however, presents a much more accurate and precise means of ascertaining the nature of the contraction. "It may be taken as a general rule" according to Lewis and Silberberg, "that the outline of the electrocardiographic curve, whether it is associated with an auricular or with a ventricular beat, is an index of the direction/

direction taken by the contraction wave in the corresponding musculature. It is consequently an index of the points of origin of such contraction waves. Now premature contractions give rise to electric curves which when compared with those of the rhythmic beats, are usually of anomalous form, and the variation in the types found in conjunction with premature contractions arising in auricle or ventricle respectively is considerable. The association of the particular anomalous complex with the point of origin of the beat to which it is due is not fully understood; that is to say, the points of origin cannot be accurately located at the present time; but this minute localisation does not concern us. We are content to start from the conclusion that in the single patient a given type of electric complex represents a definite course of the contraction wave, and that such a complex indicates the origin of the contraction at a definite point or in a definite area known or unknown". These authors examined three cases showing premature auricular contractions, and six cases showing premature ventricular contractions. The results obtained were very definite, and constant, pointing to the general conclusion, that in the same patient the site of action of the abnormal stimulus and the resulting form and course of the contraction remained the same in the same patient "from day to day, from week to week, from month to month, and even from year to year". The importance of the invariable character/

character of the results in the same patient is enhanced by the fact that there was good reason to believe that in some cases there was a widespread disease of the cardiac musculature; and it is highly probable that although the site of irritation and the consequent course of the contraction wave may have varied in different cases, the actual seat of the commencement of contraction was in immediate association with some part of the end-plates. Taking the six cases in which ventricular extra-systoles were present, it was found that the electro-cardiographic effects fall into three classes, and that these three classes were representative with very few exceptions of a very large number of ventricular extra-systole effects from an extensive series of other cases, which the authors had examined. The three groups referred to are regarded as exhibiting:- (1) Cases in which the extra-systole began in the right ventricle and probably in association with the right branch of the end-plate; this group included the largest proportion of cases. (2) Cases in which the extra-systole began in the left ventricle and probably in association with the left branch of the end-plate; this group comprised a slightly smaller proportion than the first group; and (3) Cases in which the extra-systole would appear to have originated in the main mass of the end-plate; this constituted the smallest group. The extra-systoles which/

James Mackenzie – Quart. J. of Med. 1907-8. I. p. 1.

which find expression in auricular contractions probably arise in association with the nodal tissue of either the sino-auricular end-plate, in which case the contraction may or may not resemble a normal auricular contraction (see p.214); or they may originate in association with the nodal tissue of the auriculo-ventricular end-plate in the part designated the node, in which cases there may be expected a simultaneous or almost simultaneous contraction of auricles and ventricles. This classification of extra-systoles is not new; it was fore-shadowed some years ago by James Mackenzie, who recognised the likelihood of premature contractions finding their origin in some irritation of the auriculo-ventricular node.

The points which have just been considered afford a remarkable instance of the way in which clinical research has availed itself of the results of anatomical and physiological investigations. The conclusions must be regarded, as Lewis suggests, as tentative so far; nevertheless it must be admitted that the rational basis on which these types of cardiac irregularity can now be interpreted is a tribute to the efforts of those who in late years have busied themselves with the problems of the relation of structure to function in the domain of cardiac pathology.

It must be understood that this analysis of extra-systoles, made solely from the point of view of their

Hering – Arch. f. d. ges. Phys. 1900 LXXXII p1.

Slassen – Arch. internat. d. Physiol 1901 III p338.

Lewis – Heart – 1909-10 I. p 83

Cushny – Heart – 1909-10 I p1.

relation to the end-plates, does not take cognizance of the multiple factors which may determine their occurrence. For example, increased interventricular pressure may be an exciting cause; when the aorta is clamped extra-systoles occur (Hering). Retardation of the inflow of blood to the heart by obstructing the large veins may also give rise to extra-systoles (Stassen). Ligation of the branch of a coronary artery is followed as a rule by their occurrence (Lewis). They may also be induced by the injection of certain poisons, more particularly (Cushny) digitalin, aconitine, adrenalin, muscarine, and physostigmine. As we have pointed out above, their incidence may in some cases be subject to affected by vagal influences. But although this great variety of contributing causes may participate in the production of the phenomenon, the particular point which it is sought to emphasise here, is the probability that when premature contractions do occur they occur in connection with some part of the cardiac end-plates.

THE PROPERTIES OF THE CARDIAC MUSCLE.

The property of the cardiac muscle which concerns us at the present juncture is that in virtue of which it manifests periodic variations of excitability. This is the outstanding physiological characteristic which distinguishes cardiac muscle from skeletal muscle. Any part of the/

the heart tends to respond rhythmically to a stimulus which acts continuously. An instance of this is seen in the snail's heart, which if quiescent can be made to beat rhythmically by distending it. A small strip of muscle from the wall of the ventricle of the frog or tortoise may be quite motionless, and on being subjected to a continuous electric stimulus, such as that of a succession of alternating induction currents following one another with very great frequency, it begins to beat rhythmically. No satisfactory explanation has ever been offered of this peculiar property. To say that it is because it cannot be tetanised is merely to describe it in other words; the same thing may be said of the application of the term 'refractory' to the period between successive contractions. It may be that the rhythmicity of the movements is in some way associated with the conditions of metabolism in the structure. The cardiac muscle is in a state of almost incessant activity; day and night, year in and year out, there is a constant demand on its functions, and the only rest which it gets is that which occurs between successive contractions in the rhythmic sequence. An indirect proof of this may be seen in the hibernating animals observed by Dr. Florence Buchanan in which the depression of physiological activity was accompanied by profound changes in the rhythm of the heart. The anabolic and katabolic activities of the muscle are probably related to relaxation and contraction/

contraction respectively. The question now arises how it is that the contractions of the organ are related to this fundamental property of its substance. It is well-known that in the hearts of cold-blooded animals the response to stimuli depends on the part of the organ to which the stimuli are applied. If the external surface of the auricular or ventricular wall of the heart of the tortoise be touched with the point of a needle, a single contraction will result. If the auriculo-ventricular ring be touched with the slightest stimulus there occurs immediately a rhythmic series of contractions. If now the auricular and ventricular muscle on either side of the ring be explored it will be found that there is a very sharp line of demarcation between those parts which respond by a single contraction, and those which respond by a rhythmic series. This phenomenon can be elicited equally well when the sinus and large veins and extra-cardial nerves and most of the caudal parts of the auricles have been removed. It will be recognised that this sensitive ring is the auriculo-ventricular nodal ring in the tortoise and the homologue of the auriculo-ventricular end-plate in the mammal. In the mammal its extensions are spread all over the inner surface of the ventricles, but it is not known in what degree its physiological properties in the mammal resemble those of the corresponding tissue in amphibians and reptilians. It is known that the endocardial/

Koch. – Mediz Klinik – Jahrgang 12.3. (1912).

endocardial surface of the mammalian ventricles is very sensitive to mechanical stimuli, but whether this is to be attributed to the network ramifications of the end-plate it is difficult to say. If a strip of ventricle or auricle with a small attached portion of the ring be removed from the heart of the tortoise, it will be found to beat rhythmically on the slightest irritation of the nodal portion, whereas only a single contraction arises from a single stimulation of the auricular or ventricular part of the strip. It would be a matter of extreme importance to know whether in the human heart the presence of end-plate extensions in excised portions of cardiac muscle exhibited any difference in their rhythmicity to portions in which the end-plates were not represented. Recent observations on the hearts of a human subject, and of a dog, by Hering, and anatomical examination of the same hearts by Koch would tend to show that such a difference did really exist. In these two hearts Hering had cut up the right auricle by incisions extending in some parts from the superior cava to the auriculo-ventricular sulcus. The various pieces were, however, retained in connection with each other, and with the whole heart. It was found in each case that a particular portion of the muscle preserved its rhythmic activity after movements in the rest of the heart had ceased. Hering suggested the possibility that these movements/

Lewis - Mechanism of the Heart Beat - 1911.

ments might have been due to remains of the fibres of the original auricular canal round the right auriculo-ventricular ostium. But Koch was able to point out that in each case the strip referred to contained very considerable portions of the sino-auricular end-plate. If it could be shown that the presence of nodal tissue even in isolation from the end-plates endowed the ordinary muscle with which it was connected with special rhythmic properties which distinguished it from the muscle, which contained no nodal tissue, such a conclusion might be of invaluable service in elucidating the problem of various forms of cardiac irregularity. We have suggested the probability, based on experimental clinical, and anatomical evidence, that the ectopic impulse formation in premature ventricular contractions is associated with the extensions of the sino-auricular end-plate. Premature auricular contractions may be referred to similar anatomical conditions. Now, if this hypothesis be found to be applicable in the analysis of premature contractions, a very important light might be thrown on the paroxysmal tachycardias; because the general conclusions to which the important work of Lewis on this subject points is that the paroxysmal tachycardias are in reality a rhythmic series of premature contractions, originating in ectopic impulse formation. Some of the auricular tachycardias would certainly appear to arise from abnormal/

abnormal influences operating on the node of Tawara, and a case of this kind clinically diagnosed by Lewis and confirmed by anatomical examination is described in Chapter V. (p.137). Some auricular tachycardias do not apparently arise from ectopic beat formation in Tawara's node, and the electric effect would suggest that they do not arise in the sino-auricular. There obviously is a difficulty in the acceptance of the anatomical hypothesis that premature contractions arise in connection with nodal tissue, because so far as is known the only nodal tissue in the right auricle is that associated with the sino-auricular end-plate and that which is represented by the auricular portion of the auriculo-ventricular end-plate (Tawara's node). It may be, however, that the auricular contraction depends upon the manner of escape of the impulse from the sino-auricular node. The invariability of the auricular electric effect in the normal rhythm makes it practically certain that the same portion of auricular muscle is the first to contract in every normal auricular beat. This would suggest that the node and direction of escape of the impulse never varies in normal conditions. We have pointed out, however, that the sino-auricular end-plate is in direct continuity with ordinary cardiac and caval musculature in a variety of places, and it is not impossible that the direction of escape may be a determining factor in the production of premature auricular contractions/

contractions or extrasystoles, and therefore also in the incidence of auricular tachycardias of certain types. The course of the contraction wave through the auricular muscle has not yet been definitely ascertained. But there is no doubt from Lewis' observations that if the contraction were to begin on the posterior wall of the auricle instead of anterior wall or auricular appendix, a different electric effect would be produced.

As in every department of research work conclusions of this kind must be regarded as tentative, but it would seem not improbable that the presence of nodal tissue is an indispensable factor in the origin of premature beats in any given area of the heart.

No mention has been made of nerve supply in the discussion of this particular point; but from what was said in the anatomical description of the nodal tissue, it is taken for granted that the nerves in the normal condition exercise a predominating influence on the functions of the end-plates. I would suggest, therefore, as a working hypothesis, that the functions of the cardiac muscle may be regarded from the following points of view:-

1. The cardiac muscle, apart from nerves and nodal tissue, may contract rhythmically in response to continuous stimulation; although it is not suggested that such properties/

properties may not be due to the accumulated and stored effects of its connection with nerves and nodal tissue through the syncytial ramifications of the ordinary cardiac muscle.

2. The rhythmicity of the cardiac muscle is enhanced by its association with nodal tissue. This would appear to be the case even when such nodal tissue is isolated from the main mass of the end-plate as in idio-ventricular rhythm when the auriculo-ventricular bundle is severed by experiment or disease. Separated from the main mass portions of the end-plate do not undergo degeneration; they are separate from the ordinary heart muscle except at their terminals, but they have a separate blood supply, and have also a nerve supply including nerve cells, which in some ungulates may be demonstrated as far down as the papillary muscles. Whether their anatomical integrity and partial functional activity is associated with the independent action of these nerve cells is not known.

3. The inherent rhymicity of the cardiac muscle is controlled by its connection with the end-plates and their nerves of supply. The strength of the contractions and their frequency is determined by the influence which spreads from these through the muscular syncytium on the heart walls. It is possible that nerve influence

may/

may act on the ordinary muscle directly, but there is no conclusive anatomical or physiological evidence of this. It is more likely that every response to nerve influence so far as it affects co-ordination comes through the end-plates.

On the basis of these conclusions it is possible to formulate shortly an hypothesis of the co-ordinating functions of the end-plates.

1. Normally the two end-plates through their continuity with auricular and ventricular muscle respectively exercise a dominating influence on the potential rhythmicity of the walls of these chambers. Their respective influences are co-ordinated through the continuous efferent impressions conveyed to them through their nerves of supply. An interference with the normal character of these efferent impressions, with the structure of the end-plates or with the metabolic stability of the ordinary cardiac muscle may lead to an interference with the normal rhythm of the heart. The balance of co-ordinated cardiac action is maintained by a balance in the respective influences of the two end-plates.

2. Normally each end-plate through its double nerve supply from vagal and sympathetic sources exercises a determining influence on the rate and strength of the cardiac chambers/

chambers with which they are associated. In a normal rhythm a balance is maintained between the inhibitory action of vagal stimuli and the augmentory action of sympathetic stimuli; or stated from the point of view of nutrition by the anabolic influence of the vagus, which induces relaxation or rest and the katabolic influence of the sympathetic, which induces activity. Any disturbance in this balance between the antagonistic nerve influences, arising in the nerves themselves, or in their respective end-plates or in the cardiac muscle with which they are associated, may lead to an interference with the normal rhythm of the heart. The normal activity of auricles or ventricles is maintained by a balance of the nerve influences which act on the two nodes respectively.

3. There are thus in the analysis of cases of cardiac irregularity from this point of view, four factors to be considered; the influences of the two end-plates, and the two antagonistic influences of each end-plate. The pathological activity of one end-plate may manifest itself in abnormal action of the other end-plate. Thus when the sino-auricular end-plate is affected either locally or through its nerve supply the activity of the ventricles as determined by the auriculo-ventricular end-plate/

end-plate may be abnormal. (Experiments of Flack, Rothberger and Winterberg and Laslett's case of sinus bradycardia, pp.196). The response of the auriculo-ventricular end-plate is to be regarded in such cases as evidence of an attempt to adapt or accommodate the ventricle to the abnormal influences acting on the auricle.

4. It is possible that the ventricular extensions of the auriculo-ventricular end-plate may under normal conditions influence the contractions of the auricles. This was put forward as a hypothesis by Keith and myself some years ago. It is supported by the fact that the ventricular branches do not undergo degeneration when the main bundle is severed. Experimentally it is supported by the observations of Gaskell on the heart of the tortoise. When the auricles are cut away from the ventricle so that the coronary nerve is the only structural connection between the ventricle and the sinus, the auricles continue to beat, while the ventricle remains quiescent. Stimulation of the coronary nerve near the ventricle or of the ventricle itself in the neighbourhood of the attachment of the nerve produces a slowing of the rate of beat, and of the strength of the auricular contractions. The strength/

strength of stimulus to the ventricular muscle in such cases is not necessarily enough to cause contraction of the quiescent ventricle. The importance of this observation is enhanced by the fact that the structural relations of the coronary nerve and its accompanying specialised muscle render it possible as we saw in a previous chapter, that this structure may be associated with the phyllogenetic development of the auriculo-ventricular end-plate. It need scarcely be repeated that the demonstration of such efferent impulses does not involve the idea of a spinal reflex arc in the co-ordinating mechanism of the cardiac rhythm.

It must be recognised that the functions of the end-plates themselves are concerned only with one aspect of the mechanism of accommodation in the heart. There are undoubtedly other nervous mechanisms of an afferent character, comparable with the depressor nerve in the rabbit. But these considerations demand more definite analysis than they have yet received, and do not come within the scope of the present review. It must, however, be once more emphasised, that no examination of the heart, clinical or pathological is complete unless it involves a recognition of the nervous system.

There are numerous other points which are naturally suggested/

suggested by the interpretation of the end-plates which has been given. Are the functions of the end-plates related to the refractory period of the cardiac muscle? Is the refractory period determined with a view to the anabolic recovery of the muscle after contraction and in what way is this related to the inhibitory action of the end-plates through the vagus? These and other associated problems of a very suggestive character must be left for future consideration. There is only one point in this connection to which I would refer. We saw that the cardiac wave of contraction passes along the whole heart from the veins to the aorta. It is supposed according to the myogenic theory that in the tortoise, for example, this wave is regulated by differentiated properties of the cardiac muscle. But if we examine closely the hearts of those lower vertebrates in which a bulbus arteriosus still remains as a definite structure, it will be found as illustrated in Fig. 1 , that the muscle of the auricular canal is continuous with that of the bulbus, without any intervention of ventricular muscle. From the point of view of muscle conduction, the bulbus lies quite as close to and in the same immediate connection with the auricular canal as does the ventricle. The question arises why/

why it is that the ventricle normally contracts before the bulbus. There is no reason if the theory of muscle conduction represents the facts, why bulbus and ventricle should not contract simultaneously. It has been explained that bulbus follows ventricle in virtue of the refractory state of the muscle occurring at definite periods. But what is the refractory period, and what influences control it?

CHAPTER V.

THE POST-MORTEM APPEARANCES IN 16 CASES OF CARDIAC IRREGULARITY.

While there is no denying the great advantage which has come to the study of medicine from the cellular theory of pathology, it is a question whether through it much has been done to throw any light on the relation of the symptoms of heart disease to the abnormal conditions in the structure of the organ. The cellular pathology has been concerned more with the changes in individual cells, than with the changes in the organs composed of these cells. Cells are no doubt the units, but their function individually bears only a remote relation to the function of the organ, as a whole. The literature of pathology abounds in histological data, which have practically no significance in the interpretation of the causes which produce the symptoms of heart disease; cloudy swelling, fatty degeneration, fatty infiltration, and fibrosis, have been described in various cardiac conditions, but the extent to which these changes are responsible for disease is a matter on which no definite conclusion can be reached. For example, the most advanced cases of fatty degeneration of the heart occur in/

in acute states of phosphorus poisoning, in anaemia and in chronic toxaemias generally, but in none of these cases is failure of the heart a marked symptom of the disease. On the other hand, where valvular lesions are present, and where there is great hypertrophy of the heart, the amount of fat in the muscle is, in the majority of cases, practically negligible.

I have examined a number of hearts from cases of acute disease, and the result of this has been to fail to find in the great majority of these cases, any clue to cardiac failure in the condition of the heart muscle, and these were all cases in which it was believed clinically that death was due, in the first instance, to failure of the heart. In eight cases, which died from acute pneumonia, there was no heart which showed evidence of structural change, such as might account for failure of the organ to perform its work. In ~~one out of~~ six cases of typhoid fever, there was one case in which the acute myocarditis was present. In this case, however, an attack of diphtheria had preceded the onset of typhoid fever by about three months. Four cases of typhus fever were examined, and in none of these did the heart show any evidence of structural change, beyond a slight cloudy swelling, and some fatty degeneration.

Out/

Out of four cases of acute rheumatism, there was one in which there was an advanced myocarditis, and out of four cases of diphtheria, there was three in which myocarditis was present. In each of these cases, six to ten pieces of muscle from various attacks of the organ were examined. No significance can be attached to the presence of cloudy swelling or fatty degeneration, in as much as it is impossible to define the extent to which this degeneration must be present, in order to interfere with the normal activity of the organ. There can be no doubt, that in practically every case of toxaemia or continued fever, the heart muscle undergoes changes of this character in a greater or lesser degree, but it is remarkable that these changes are usually of a transient character, and with very few exceptions, leave permanent results.

With regard to the anatomical changes in chronic heart disease, the results of examination have been equally unsatisfactory. It is only in a very small proportion of cases of heart disease that genuine inflammatory conditions of the cardiac muscle can be regarded as a possible source of the cardiac weakness. The fibrosis which is not infrequently present in cases of chronic heart disease has two sources. In the first place, it may be the result of previous inflammatory/

inflammatory lesions, and, in the second place, it may be the result of a degeneration of the cardiac muscle due to defective nutrition. Speaking generally, the number of cases in which fibrosis is due to defective nutrition, is out of all proportion to the number in which inflammation is the primary cause. With the exception of diphtheria, and a very few cases of acute rheumatism, there is no infection which as a rule attacks the heart in such a manner as to leave its functions impaired, by the production of a general myocarditis. ~~in a slight degree.~~ Acute rheumatism and some forms of septicaemia may give rise to diffuse degeneration of the cardiac muscle, but in the great majority of rheumatic hearts, there is no evidence from the inflammatory changes in the muscle fibres to account for the cardiac weakness. Where fibrosis is present in rheumatic hearts, it is situated for the most part, in the papillary muscles, and in the posterior walls of the ventricles. Fibroid hearts which occur in advanced years, and especially in cases of atheroma and syphilis of the aorta, are to be attributed to defective nutrition, due to narrowing of the coronary arteries.

While the work of Krehl and Romberg, and the pupils of the Leipzig School, has done much to stimulate an interest in/

in the anatomical basis of heart disease, it cannot be accepted without further investigation that general myocarditis is a prominent factor in the pathology of heart disease. Albrecht's researches have done little or nothing to throw new light on the subject. This is probably due to the fact that he carried on his work under a total misconception of the normal anatomical character of the muscle tissue of the heart. He regarded the cardiac tissue as being composed of parenchymatous cells and not of a syncytium of muscle fibres, and he compared hypertrophy of the heart to the cloudy swelling which occurs in parenchymatous organs, such as the kidney or liver.

With the appearance of the more recent advances in our knowledge of the anatomy and physiology of the heart, new possibilities have been opened up with regard to the interpretation of the structural and functional basis of cardiac disease. The outstanding feature of heart disease, as it is known clinically, is the irregularity of the cardiac action. Where weakness is present, it is not simply a weakness of an irregular heart due to degenerate muscle, but the weakness is in most instances secondary to a disturbance of the normal sequence of evidence in the cardiac cycle, and this disturbance produces an interference with the proper nutrition of the heart (p.27). We have seen that the end-plates which we have described, perform an important function/

function in the co-ordination of cardiac action, and possibly also in the adaptation of the heart to the demands of the organism as a whole.

It is, therefore, in examination of cases of heart disease, a matter of first rate importance to see whether or not these end-plates are intact. We have seen, however, that the end-plates constitute only one part of the regulating mechanism, and although our knowledge of the nerve supply to the heart is still in a very unsatisfactory condition, it is imperative that the main masses of nerves should also be examined. It is, of course, also important that the general condition of the cardiac muscle should be taken into account, because even although the nerves and end-plates are healthy, regular and normal cardiac action will depend also on a healthy cardiac muscle.

Before proceeding to describe the cases which have been examined, I should like to emphasize a preliminary consideration which should not be lost sight of in any attempt to analyse the anatomical bases of a case of cardiac irregularity. The work of Cushny on the effect of poisons, such as aconitine, on the action of the heart, makes it evident that where the patient has been suffering from acute poisoning such as diphtheria, it should be borne in mind that any form of cardiac irregularity may occur without/

Cowan Fleming and Kennedy — Lancet. Jany 1912.

without structural degeneration of the cardiac muscle.

Every form of cardiac irregularity which has been described clinically, may be produced by poisons without the concomitant production of diffuse structural changes; but even where acute myocarditis is present, no conclusion can be drawn as to the relation of such structural changes to the form of irregularity which the heart may have presented. For instance, it is not a matter of any consequence in the interpretation of a particular form of irregularity if the sino-auricular and auriculo-ventricular end-plates be degenerate so long as the rest of the cardiac muscle is degenerate also. In other words, the importance of a particular lesion in the interpretation of an irregularity must depend on the localised character of the lesion, and on the fact that it is not accompanied by diffuse degeneration in other parts of the heart. For this reason one is bound to regard many of the recently published cases of irregularity of the heart in acute disease as being due to poisons, and as possessing little or no importance from the point of view of the problem of the relation of structure to function, (e.g. Heart-block and nodal rhythm - Cowan, Fleming and Kennedy.).

CASES /

CASES EXAMINED.

I do not propose to give an exhaustive clinical account of the cases about to be described. I shall content myself with stating the nature of the clinical condition which in every case was diagnosed by means of the polygraph or electro-cardiogram or both, and I am indebted to Dr. James Mackenzie, Dr. Lewis, and Dr. F.W. Price for all these hearts, together with the notes on their clinical condition.

1. Three cases of auriculo-ventricular dissociation were examined.
2. Two cases were examined in which there was an interference with the length of the interval between auricular and ventricular contractions.
3. One case of paroxysmal tachycardia was examined.
4. Ten cases of auricular fibrillation were examined.

1. AURICULO-VENTRICULAR DISSOCIATION.

(a) Three cases of this condition were examined, and they comprised one case of diphtheria, and two cases in advanced years, with extremely slow ventricular pulse and epileptiform attacks typical of the Stokes-Adams syndrome. The interesting point about the case of diphtheria consisted in this, that although the patient showed definite dissociation/

dissociation with a regular and slow ventricular rhythm, there was on anatomical examination hot the slightest evidence of lesions of the end-plates. The ventricles were in a very advanced state of degeneration, (Fig 27) more particularly in the region of the papillary muscles. The nerves, although not examined exhaustively showed no signs of disease, although in the cardiac muscle the lesions were most marked round the small vessels where the nerves lie (Fig 26) The importance of this case lies in the fact that we have here a condition of complete dissociation without any involvement of the node or bundle. Whether the determining factor in the condition lay in an undiscovered lesion of some part of the nervous system, or in the advanced myocarditis in the ventricles, it is impossible to say. In any case as we have suggested it is not only necessary that the end-plate should be intact, but the nervous system and the cardiac muscle, between which the end-plate acts as an intermediary, must also be healthy to secure normal cardiac action.

(b) The second case of dissociation occurred in an old lady of 72 years, who for eighteen months had suffered from epileptiform attacks accompanied by a pulse rate varying from 18 to 34. The heart was small and slightly atrophied. Beyond some culcareous deposits on the bases of the cusps of the aortic valves and a diffuse thickening of/

of the pars membranaces septi, there was no evidence to the naked eye of anatomical changes in the heart. The muscle on microscopic examination showed a slight degree of brown atrophy. The arteries appeared to be normal. Examination of the auriculo-ventricular bundle showed that it had been destroyed in its whole diameter in its passage through the pars membranacea septi. There can be no doubt that this lesion extending from a general involvement of the root of the aorta produced the condition which was responsible for the dissociation. The sino-auricular end-plate in this case showed no evidence of disease.

(c) This case was a man of 55, who suddenly and without any previous warning of heart disease took an epileptiform attack. He was found on examination to have a pulse rate of 26 per minute. For a year he suffered from transient attacks of this nature with extreme slowing of the pulse which was never known to rise above 40 per minute, and which on occasions was as low as 20. On post mortem examination, there was no evidence of brain disease, and his heart was of normal size, and the muscle presented a normal appearance to the naked eye. There was no evidence of abnormality in the valves or coronary arteries. Microscopic examination showed the heart muscle to be normal. Examination of the auriculo-ventricular bundle showed/

showed that the node and main bundle were normal in their whole extent. The left branch of the main bundle immediately to the left of the pars membranaces septi had undergone complete degeneration, and only a few fibres of the right branch remained. No cause could be found for this condition of the main branches immediately after the point of division, but there can be no question that their degeneration represented an anatomical basis of the cardiac symptoms from which the patient suffered.

2. CHANGE IN LENGTH OF THE AURICULO-VENTRICULAR INTERVAL.

Two cases were examined in which the length of the auriculo-ventricular interval was abnormal. In one case it was lengthened, reaching at times ·3 sec. and in the second case it was ·05 to ·1 sec. It has been assumed that any variation in the normal length of this interval which is represented on polygraph tracings as the space between 'a' and 'c' is to be attributed to some abnormality of the auriculo-ventricular junctional tissues, that is, the node and main bundle of the auriculo-ventricular end-plate. When the interval is over ·2 sec. it is supposed that the bundle has been partially destroyed; when the interval is under ·1 sec. it is supposed that the impulse to both auricular and ventricular contraction arises in the region of/

of the auriculo-ventricular node or bundle; it has also been assumed that when the interval is between ·1 sec. and ·2 sec. the focal origin of the stimulus to contraction lies between the two end-plates in the auricular muscle. These explanations are obviously based on the results of experiments on animals. It is known that partial destruction of the auriculo-ventricular bundle produces a prolongation of the interval and that this prolongation is often a premonitory sign of complete or partial dissociation, and it has been tacitly assumed that when this prolongation or incomplete dissociation occurs it must be due to a lesion in the bundle. In the second place simultaneous contraction of auricles and ventricle may be produced in cold-blooded animals by irritating the auriculo-ventricular ring and the conclusion drawn from this has been that where such simultaneous contractions exist the auriculo-ventricular junctional tissues must be subjected to some form of irritation. In the third place, where the interval is neither long enough to suggest disease of the bundle nor short enough to suggest simultaneous contraction it is supposed that a focus of irritation is acting on the heart and determining its rhythm somewhere between the sino-auricular node and the auriculo-ventricular node. The fallacy of this latter deduction is obvious in view of/

of the fact that the wave of contraction passes along the auricular muscle at a rate at least of 3 metres per second, and such a rate is too great to admit of any obvious difference in the auriculo-ventricular interval even if the stimulus did arise in the auricular tissue. We have also pointed out the great probability that impulses to contraction arise both pathologically and physiologically in the specialised tissue, and not in the ordinary muscle healthy or diseased.

(d) The first case was that of a woman of 45 years who suffered from rheumatism and mitral disease. She suffered from attacks of cardiac irregularity. The pulse rate varied from 70 to 110 per minute and on the polygraph tracings the a-c interval was sometimes ·3 sec. Administration of digitalis was followed by a dropping of ventricular beats, and on one occasion by a temporary dissociation. Post-mortem examination showed the heart to be enlarged and every chamber hypertrophied. There was shortening of the chordae tendineae, and narrowing of the mitral orifice. The other valves were healthy. The end-plates showed no sign of disease. The auricular muscle was not diseased. In this case the prolongation of the a-c interval could not be accounted for by disease of the functional tissues.

(e) This was the case of a young man of 31 years with symptoms/

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of acute rheumatism and continuous fever. The pulse ranged between 115 and 125 per minute, and was regular in rhythm. The a-c interval ranged between 0·5 and ·1 sec. The heart muscle was the seat of a diffuse myocarditis, affecting the ventricle more particularly. The aortic and mitral valves were covered with recent vegetations. The sino-auricular end-plate was normal. The nodal part and a portion of the main bundle was in isolated places the seat of small round-celled infiltration of a lymphocytic type, but there was no extensive destruction of the muscle tissue of the end-plate. I would not attach any significance to the affection of the end-plate in view of the extensive lesions in the myocardium. The possibility, even the probability that the interference with the a-c interval in this case was toxic in origin must be placed in the foreground. The case must be interpreted in the light of Cushny's experiments with aconitine, and in the absence of electro-cardiographic tracings it is not possible to say that the auricular contractions did not originate in the sino-auricular end-plate. In the same catagory I would place the series of cases recently described by Cowan, Fleming and Kennedy, in which these authors attributed an interference with the length of the a-c interval in acute infections to lesions in the auriculo-ventricular node and/

and bundle, although they themselves refer to generalised affection of the myocardium to which they appear to attach no significance. To be of any value in the interpretation of function a lesion in the heart must be localised and must occur in a subject not suffering from the effects of acute toxaemia. Prolongation of the a-c interval may be ~~provuded~~ produced by stimulation of the vagus (Lewis), and simultaneous auriculo-ventricular contraction may be produced by stimulation of the sympathetic (Rothberger and Winterberg).

3. PAROXYSMAL TACHYCARDIA.

This is a condition of extremely rapid action of the heart, which comes on in paroxysms. The rapid action commences suddenly and ceases suddenly, and in this respect it is to be distinguished from ordinarily extreme rapidity of the pulse.

(f) The case about to be described was that of a man of 61 years, who for six months had been suffering from weakness and shortness of breath, which disappeared when he lay down, and was but slight when he was in the recumbent position. When standing he often felt very giddy and shaky on his legs. He had had rheumatic fever five years previously. On physical examination, the heart was found to be enlarged, and the pulse was of the Corrigan type. There was a systolic murmur at the apex and a diastolic/

diastolic murmur at the aortic cartilage.

The irregularity of the heart consisted in frequent extra-systoles and short paroxysms of tachycardia. The irregularity was most marked when he was standing and tended to disappear when he lay down. He sometimes lay for hours without appreciating the presence of irregularity but when he stood up the paroxysms and extra-systoles returned. It was found that there was a critical angle during the change from the horizontal to the vertical position at which the tachycardia commenced. Firm abdominal pressure with the hands or with a binder prevented the irregularity in the upright position. The pulse between the paroxysms was slow and regular. At times it was as low as 37 per minute, and then a sinus bradycardia was present. When extra-systoles were present during the period of slow pulse they were of the auricular type and some of them were supposed to originate in the node of the auriculo-ventricular end-plate. During the normal rhythm the a-c interval was 0·2 sec. and during the paroxysms the interval was 0·06 sec. The case was examined clinically by Lewis with the polygraph and the electro-cardiogram and he came to the conclusion that during the paroxysms the impulse to contraction originated in the node of the auriculo-ventricular end-plate, the auricular and ventricular contractions being practically simultaneous/.

simultaneous. The curves from the electro-cardiogram also suggested that the impulse to auricular contraction originated away from the sino-auricular node, and was probably situated in the auriculo-ventricular node. The case is fully described by Lewis in Heart No. 1, p. 360, and his diagnosis was that this was a case of paroxysmal tachycardia due to abnormal impulse formation in the auriculo-ventricular node. The post-mortem examination showed a heart much enlarged and dilated in all its chambers. It weighed 22 oz. There were recent vegetations on the aortic and mitral cusps. The aortic cusp of the mitral valve was perforated, the perforation being about 0·5 cm. in diameter. There was considerable thickening and distortion of the cusps of the aortic valves. The arteries were normal. The cardiac muscle was normal except that there was hypertrophy of some of the fibres in the right auricle, left ventricle and right ventricle. The sino-auricular end-plate was normal. The main branch and subdivisions of the auriculo-ventricular end-plate was normal so far as could be made out, but there was slight infiltration and some destruction of the fibres of the node of the auriculo-ventricular end-plate. The infiltration was not very extensive, and was for the most part situated round the small vessels; Fig.29 shows the degree of infiltration in a part where it was most marked;/

marked; Fig. 28 shows the part of the heart from which the section was taken. Above the node, and in the inter-auricular septum beneath the attachment of mitral valve there was a considerable amount of inflammatory infiltration with destruction of the auricular muscle. (Fig. 30). This inflammatory exudate was probably the result of a spread of the process from the mitral valve whose cusp was perforated. The question arises here as to the interpretation to be put on these findings. As Lewis anticipated, there was undoubtedly a lesion of Tawara's node, although it is not very extensive, and that lesion is to be explained on the assumption that it spread from the valvular lesion. The case was a chronic one, and there is scarcely any question of a toxaemia here, although a perforated valve suggests a septicaemia which, however, may have been in a chronic form. The problem to be solved is whether this irritation in the node and its neighbourhood was sufficient of itself to convert a normal rhythm into a paroxysmal tachycardia in which the sino-auricular impulses were neutralised, and the whole cardiac action was dominated by the irritated auriculo-ventricular node. A very important factor in the onset of the paroxysms was, as we saw, the state of the blood pressure in the venous cistern. A low pressure in this cistern undoubtedly contributed/

contributed to the onset of the attacks. This, however, was not the only cause in as much as during the slow period extra systoles were present, and as we saw a sinus bradycardia was occasionally in evidence. This, of course, at once suggests that the sino-auricular end-plate as well as the auriculo-ventricular end-plate was involved in the irregularity. But there was nothing in the histological appearances of the sino-auricular end-plate to signify disease. So far as could be made out the nervous structures in the heart were not affected. Considering, however, that there was a sinus bradycardia during the slow periods, and an auriculo-ventricular tachycardia during the rapid periods, and that the change from the one to the other was effected through a variation in intracardial pressure, the idea at once suggests itself that there was some dislocation of the balance between the two end-plates. An auricular tachycardia may be observed in animals bled to death and this tachycardia may be replaced by a normal rhythm if fluid be injected into one of the caval veins, so as to increase the intra-~~annular~~ auricular pressure. Again Rothberger and Winterberg, as we have repeatedly pointed out, were able to produce simultaneous auricular and ventricular contractions by stimulating the left sympathetic. It is not improbable that the irritation of the inflammation in/

in the neighbourhood of the auriculo-ventricular node produced an effect comparable with the stimulation of the left sympathetic and that the lowering of intracardiac pressure was the additional factor necessary to the onset of the paroxysms.

4. AURICULAR FIBRILLATION.

This condition is closely allied to tachycardia. The auricles instead of contracting very rapidly do not contract at all; they are in a state of tremor or present evidence of undulatory movements. The ventricular beats are very irregular in their incidence; it is characterised by the type of the radial pulse known as irregular irregularity of the heart. The diagnosis of fibrillation of the auricles in these forms of irregularity is confirmed by polygraph tracings; in these tracings the "A" waves in the venous pulse are absent, and James Mackenzie advanced the suggestion some years ago, that the auricles were paralysed. Lewis discovered that the auricles were really in a state of fibrillation, and his discovery was confirmed independently by Rothberger and Winterberg. The discovery was made by these three workers by means of the electro-cardiogram, and has now been generally accepted. In the electro-cardiographic tracing the normal auricular effect is absent, and is represented by small movements, such as are obtained when the/

the auricles are experimentally exposed to the influence of a faradic current and enter into a state of fibrillation.

Four types of cases have been examined in which auricular fibrillation was proved to be present clinically.

1. Two cases in which the disease was acute and there was evidence of venous stasis due to pulmonary disease.
2. Two cases in which there was evidence of more chronic circulatory stasis.
3. Four cases of long standing mitral disease in which the fibrillation had been present for a considerable period.
4. Two cases in which there was no clinical evidence of valvular disease.

1. (g) This was the case of a child of eight years with broncho-pneumonia. Eight hours before death the pulse was irregular, and the venous tracings showed no signs of an 'a' wave. Post-mortem examination showed great distension of the right auricle. Microscopic examination of the heart showed slight cloudy swelling of the muscle fibre. The end-plates appeared to be normal.

(h) This was a child of 6 years also suffering from broncho-pneumonia/

broncho-pneumonia. The polygraph tracings indicated 12 hours before death a state of fibrillation of the auricles. Post-mortem examination showed the right auricle and large veins to be greatly distended. Microscopic examination failed to reveal an abnormality either in the cardiac muscle or in the end-plates.

2. (i) This was a case of bronchitis and emphysema in a woman of 50 years. The pulse 8 hours before death was rapid and irregular and the polygraph tracings indicated auricular fibrillation. Post-mortem examination showed bronchitis and emphysema of the lungs with oedema in the dependant portions. The right side of the heart was dilated and hypertrophied. There was considerable fatty infiltration of the right ventricle. The muscle fibres showed fatty degeneration. The end-plates appeared to be normal.

(k) This patient was the subject of mitral stenosis of rheumatic origin. Up till the day before death it had been possible to obtain 'a' waves on the jugular curve. These waves, however, disappeared and the pulse became very irregular. Post-mortem examination showed a very advanced degree of mitral stenosis. The cardiac muscle did not show evidence of degeneration. The left auricular wall was very much hypertrophied/

trophied, and the right auricular wall was hypertrophied in a lesser degree. The sino-auricular and auriculo-ventricular end-plates showed an excess of fibrous tissue but were otherwise normal.

3. (m) This patient was a rheumatic subject, suffered from mitral stenosis, and had shown signs of auricular fibrillation for at least 6 months. Post-mortem examination showed the heart to be enlarged in all its cavities. The chordae tendineae of the mitral valve were shortened and there was fibrous degeneration of the papillary muscles. The left auricle was the seat of advanced myocardial degeneration, although the walls appeared to the naked eye to be greatly hypertrophied. (Fig 31.) The muscle fibres which remained were very large for the most part, the nuclei were large and irregular, and the fibrils appeared at places to have become broken up, and loosened from the sheath of the fibre. Some of the fibres were in a state of hyaline degeneration (Fig 32) The number of normal fibres was proportionately very small. The end-plates appeared to be normal.

(n) This patient was also a rheumatic subject and suffering from mitral stenosis and aortic disease. Signs of auricular fibrillation had been present for a year at least. Post-mortem examination revealed the presence/

presence of a large heart with an adhesive pericarditis; the left ventricle in its posterior aspect and in the papillary muscles showed evidence of extensive starvation fibrosis. The left auricle showed evidence of myocardial degeneration similar to that described in the last case. (Fig.33). The end-plates appeared to be normal.

(o) This patient, also the subject of rheumatism with mitral aortic disease had shown signs of auricular fibrillation for two years. Post-mortem examination showed here also a pericarditis and an enlarged heart. The microscopic evidence of disease corresponded exactly with that described for the last case. There was extensive nutritional changes in the ventricles and the left auricle and in a slight degree the right auricle showed myocardial degeneration (Fig. 34). In some parts there were considerable masses of small round cells and the muscle fibres appear to have been completely destroyed.(Fig 35) (Fig 38)
In the nerve cells in the posterior inter-auricular sulcus there was evidence of extensive infiltration The ganglion masses presented what is described in anterior polyomyelitis the condition of 'neuronophagia'(Fig 39)
The end-plate appeared to be normal.

(p)/

(p) This patient was the subject of mitral and aortic disease following rheumatism, and had shown signs which might presumable be regarded as pointing to auricular fibrillation over a period of 5 years. Post-mortem examination showed an hypertrophied heart more especially involving the right ventricle and the left auricle. The papillary muscles and to a lesser degree other parts of both ventricles showed signs of a starvation fibrosis. The left auricle was hypertrophied and showed the signs of myocardial degeneration, which have been described above (Fig 37). The end-plates contained a considerable amount of fibrous tissue, and the fibrous septa of the auriculo-ventricular end-plate were abnormally thick and the muscle bundles correspondingly small; they were otherwise normal.

(q) This patient had been the subject of cardiac weakness for 15 years. There was no evidence of valvular disease. The pulse had been continuously irregular for 3 years. The patient died with all the signs of chronic circulatory failure. Post-mortem examination showed the heart to be considerably dilated. The ~~ventricular~~ auricular walls were extremely thin in some places almost transparent. There was very advanced atrophy of the papillary muscles and extensive evidence of fibrosis in the ventricular walls./

walls. The aorta showed typical evidence of syphilitic disease, and there was marked stenosis of the apertures of the coronary arteries. Microscopic examination showed that thes fibrotic areas in the ventricles were due to starvation. In the auricular walls the muscle fibres had undergone a peculiar "foamy" degeneration (Figs 40, 41, 42, 43). The chemical nature of the change has not been thoroughly examined, but it is not any ordinary fatty change. The transition of the fibres into the "foamy" substance is easily made out, and in addition there are the pigment granules which reveal the original muscular character of the tissue. The end-plates showed no sign of disease. The disease in this case is primarily due to defective nutrition owing to stenosis of the coronary arteries. It is obvious that if an insufficient amount of blood gains entrance to the coronary system ~~that~~, the tissue supplied by the terminals of the longest arteries will be the first to suffer. This is actually what has happened in this case; but all over the cardiac muscle there is evidence that the heart generally has suffered from malnutrition. This is seen from the presence of small areas of fibrosis in which brown pigmentary granules are lying, representing the remains of degenerate muscle fibres (Fig. 36). The heart/

heart in other words, has died from slow starvation, and the auricular fibrillation is the evidence of this prolonged dying phenomenon.

(s) This patient was 60 years of age, and had been the subject of 'cardiac weakness' for four years. There was no evidence of valvular disease, but his heart had been continuously irregular and for 18 months at least there would appear to have been fibrillation of the auricles. The post-mortem examination in this case showed enlargement and dilatation of the heart. The valves appeared to be healthy. There was a general diffuse fibrosis of the ventricular muscle. The auricular walls were very thin. There was extensive atheromatous narrowing of the coronary arteries. The fibrosis in the ventricles was obviously due to lack of nutrition. There was an extensive degree of hyaline degeneration of the muscle fibres of the auricular walls. The end-plates appeared to be normal On the whole the appearances in this case correspond closely with those described in the last.

A feature of all these cases of chronic auricular fibrillation, is the evidence of starvation of the heart muscle. Particular/

Particular importance is attached to the character of the pigmentary deposits in the fibrosis. This is definite evidence that the so-called fibrosis is not newly formed connective tissue, or the healed remains of inflammatory areas, but the skeletal remains of muscle fibres. These areas do not, as a rule, take on the pink stain with Van Gieson's solution, a fact which shows that they do not consist of normal fibrous tissue.

When we review these ten cases of auricular fibrillation the most striking feature is the variety of anatomical conditions which may be associated with its presence. It is no doubt a clinical entity in as much as its presence is associated with, (1) an irregular irregularity of the ventricular beat, (2) an absence in the jugular pulse of the 'a' wave, which corresponds to auricular contraction, and (3) an absence in the electro-cardiographic tracing of the 'effect' associated with contraction of the auricles. When the auricles are fibrillating _in situ_ in the exposed heart of an animal the cavities are in a distended condition; the walls are either in a state of tremor or they present undulatory movements, which would appear to be due to different portions of the muscle contracting at the same time with intervening portions in a condition of temporary rest. There is a gradation from a fine tremor which resembles extreme tachycardia of the auricles to that condition of fibrillary/

fibrillary undulation known as auricular fibrillation. Now speaking generally all clinical tests, even in this case, those of the electro-cardiogram, are extremely coarse compared with the subtle and unstable phenomena of vital activity. It is readily understood that identical responses may be obtained by instruments in the examination of phenomena which vary widely in their biological character and in their determining causes. It is not to be supposed that even although the auricles are in a more or less inactive state physiologically in all these cases, that that inactivity is in each case due to one and the same cause. A very cursory glance at the results of the anatomical examination of the cases we have reviewed, shows what a variety of conditions may be associated with auricular fibrillation. It may occur, (1) as a dying phenomenon in the heart, (2) as the result of the administration of some poisons in extreme doses, (Cushny), (3), in cases of high pressure in the auricles from obstruction to the blood flow, as in broncho-pneumonia and emphysema, (4) in cases of narrowing of coronary arteries, and (5) in cases of mitral stenosis with myocardial degeneration of the left auricle.

These varieties are, however, not to be taken as representing distinct classes in which the predisposing causes are similar or identical. In a general way, it may be contended that in each case auricular fibrillation is evidence/

evidence of a dying heart. This applies to cases of poisoning in which the organism dies in a few hours or minutes, and it may apply in a sense to cases in which the heart shows the signs of gradual dying extending over a period of years. It is in each case the evidence of exhaustion of physiological force in the auricles; it cannot, of course, occur in the ventricles, because fibrillation of the ventricles means immediate death.

There are, however, two points of view from the which(?) an arbitrary division of the cases may be made. These are, (1) those cases in which the phenomena is evidence of an acute phase on the development of heart failure, and (2) those cases in which it is a chronic accompaniment of cardiac weakness.

(1) The cases in which it is to be regarded as evidence of an acute or terminal phase in cardiac failure are such as occur with poisoning or toxaemia or obstruction of the blood flow due perhaps to pulmonary disease. It is, as a matter of fact, highly probable that a great many hearts present this phenomenon before death; it may be days or hours or only minutes before the cardiac action has ceased. I have noticed fibrillary movements of the auricles in guinea-pigs, which have been bled to death; and I have seen the same phenomenon in turtles and tortoises after the body has been turned/

turned about in various ways, so as to disturb the balance of the circulation. In the case of the turtles and tortoises, the normal movements of the auricles returned when the body was allowed to rest, and the circulating equilibrium was restored. When a guinea-pig has been bled to death and the auricles beat with a rapidity out of all proportion to the ventricular rate, or present fibrillary movements, these tremulous or fibrillary contractions may be removed by injecting fluid into the right auricle through one of the caval veins; in this way, the heart may be made to resume an absolutely normal rhythm. This is important as showing that intracardiac pressure is another factor in the maintenance of an orderly sequence of events in the cardiac cycle.

(2) Contrasted with these cases in which auricular fibrillation is one of the common terminal phases of the dying heart, are those in which this manifestation of disease is present over prolonged periods. We have described the anatomical basis of six such cases. Four of these were the subjects of mitral disease and two were the subjects of impediments to the proper supply of blood to the cardiac muscle.

In reviewing the cases of mitral stenosis; what are the factors which may be considered as having contributed/

tributed to the clinical manifestations of the disease? There can be no doubt that the degeneration of the walls of the auricles and of the left auricle in particular constitutes the fundamental lesion in these cases. No one who has examined the cases and appreciated the extent to which the normal muscle fibres have disappeared could doubt this. The musculature, as the figures bear evidence, showed signs of degeneration corresponding exactly with the condition which is found in degenerative lesions of the skeletal muscles; lesions which, for example, are characteristic of scapulo-humeral paralysis or paralysis due to degenerations or section of the nerve of supply. The question arises now as to the cause of the lesions in the auricular musculature. (i) An important factor in this respect is undoubtedly the mitral stenosis producing as it does a constant high pressure in the left auricle. Relative to its capacity for work the left auricle has more to do than any other part of the heart. This strain on its physiological resources expose it to the action of any toxic agencies which may be in the blood. It is a well-recognised fact that when metabolism or oxygenation is extremely active in a part of the body, the tissue in that part is more liable to become the seat of toxic degeneration; this relation of exhaustion to degeneration has/

has been proved by Edinger in certain affections of the nervous system, and it is highly probable that in mitral disease there is a special tendency to muscular degeneration of the left auricle on account of the excessive work it has to perform. It should be noted that although these four cases of mitral disease were of rheumatic origin there was no evidence that the degeneration of the auricular muscle was also due to the rheumatic toxine; at any rate, there were no rheumatic nodules such as have been described by Aschoff and Geipfel. (ii) In addition to the effect of strain and excessive work, the nutritional factor may have played an important part in the auricular degeneration. Attention has already been called to the peculiar circumstances under which the cardiac muscle receives its blood supply. It has been pointed out that during systole the blood reached no further than the larger branches of the coronary arteries; and that it was during diastole that the blood was sucked out of the aorta into the capillary network in the cardiac muscle. It is obvious then that two conditions at least must exist to ensure a thorough distribution of blood in the heart walls. There must be a high pressure in the aorta during diastole, and the diastolic period must be sufficiently long to allow the blood to percolate through the capillaries. In three

out/

out of the four cases aortic incompetence was present, so that one of these conditions of efficient nutrition was absent in three cases. In every case the heart beat was rapid; small systoles occupied the diastolic periods so that at times proper relaxation of the ventricles was prevented by the rapidity of the heart beat. In addition to this the chordae tendinae were shortened in every case, so that complete relaxation of the ventricles was mechanically impossible. For these reasons it is obvious that the circulation of the blood through the heart itself was impeded, and the defective nutrition in the left auricula combined with excess of work cannot but have had a deleterious effect on the muscle. (iii) It is impossible to say whether nervous affection contributed to the degeneration of the auricular muscle. In one case, as we have seen, there was unequivocal evidence of extensive degeneration of the ganglion cells in the posterior auricular walls. In this case there was an adhesive pericarditis, and it is almost certain that when there is an extensive pericarditis the nerve cells beneath the pericardium in the posterior auricular walls must, in some instances, be involved in the process. It would be an important matter to ascertain generally to what extent these cases of mitral stenosis with prolonged auricular fibrillation/

fibrillation, are also the subjects of pericarditis. The histological difficulties attending the examination of nervous structure in the heart are great, and to these difficulties are added the choatic condition of such knowledge as we possess on the source and function of these structures. (iv) While it must be recognised, as has been pointed out, that there is little or no evidence of inflammatory myocarditis in the general musculature of these hearts to account for the weakness and irregularity; there is in the ventricular muscle, and more especially in the papillary muscles and ventricular walls at the bases of the papillary muscles in almost every case some degree of fibrosis. This fibrosis is not of inflammatory origin, but it is to be referred to the inefficient character of the coronary circulation which has just been explained. If, for example, the blood supply to the posterior papillary muscles and the ventricular wall to which they are attached be considered, it will be seen that the course of the artery of supply is a very circuitous one. The main supply to the muscles may come from either the right or the left coronary. In either case the artery wends its way round the auriculo-ventricular sulcus, then down towards the apex to the base of the papillary muscles, it must then turn again upwards in the papillary muscles towards the base of the heart to the attachments of the chordae tendinae to these/

these muscles. It will be readily seen that any interference with a moderately slow and orderly contraction and relaxation of the heart wall, will tend to leave the muscle supplied by the terminals of the arteries in a state of deficient nutrition, and it is this which accounts for the fibrosis in these parts. The so-called fibrosis does not always consist of fibrous tissue; in almost every case the skeletal remains of muscle fibres can be made out, and it is perfectly obvious that the pigmentation in these areas is for the most part, the pigmentary remains of the substance at the poles of the nuclei of degenerate muscle, and not the result of blood destruction as is generally supposed. (Fig.36). What then is the significance of this fibrosis for the interpretation of cardiac weakness? Its extent in itself is not in most cases sufficient to account for muscular inefficiency in these cases. It is rather to be regarded as the evidence of a malnutrition which must affect the whole heart, but it is only manifested as an anatomical degeneration in those parts which, from their situation, suffer most. (v.) Another factor which contributes to the fibrillation is the venous stasis in the right auricle and in the auricular muscle. The high pressure in both auricles must exercise an exhausting influence on the muscle, but what is more particularly referred to here, is the probability that the venous blood plays/

plays a part. in the incidence of the fibrillation. Leonard Hill has pointed out that ligation of the coronary veins in the dog may produce auricular fibrillation. Although in chronic heart disease due to mitral stenosis, the stasis in the veins is never complete, still it must be the case that the venous return is impeded largely by two factors; firstly, by the high pressure in the right auricle, and secondly, by the fact that the auricles themselves, once they have commenced to fibrillate, cease to contribute to the onward flow of the blood by their periodic contraction, and relaxation.

These considerations then, bear out the contention that a multiplicity of factors is concerned in the predisposition to auricular fibrillation. In some cases one kind of influence may predominate and, in other cases another kind. It is unlikely that in clinical cases the phenomenon is ever due to a single intervening agency, if we exclude the cases of acute poisoning; even here the determining agency of poison cannot be regarded as an isolated factor, except in a very arbitrary sense, because in the last resort a combination of factors must contribute to any phenomenon pathological or physiological in the living organism.

A final question arises as to whether or how the end-plates may participate in the production of this form of irregularity/

irregularity. It may be taken as settled that the condition occurs without any demonstrable anatomical lesion of the end-plates. But if we were correct in our interpretation of the functions of these organs, if they constitute the mechanisms which regulate the sequence of events, what are the influences which play upon them to disturb their control over the cardiac movements?

The movements of the heart in these cases consist (1) in a complete cessation of auricular systoles and (2) in an absolute irregularity of ventricular systoles. The factors which were found to affect the auricles, render the influence of the sino-auricular end-plate impotent, even although the anatomical and functional characters of these structures be perfectly normal. Its impressions on distended and diseased auricles are ineffectual. With regard to the ventricles, it has been pointed out by Lewis that the ventricular effects on the electro-cardiogram in these cases suggest that the irregular contractions are supra-ventricular in origin, or that they arise from the node of the auriculo-ventricular end-plate. They must in that case, be influenced by stimuli, which originate above the main buhdle of the end-plate, because if they originated in the main bundle and were not affected by influences above the main bundle the ventricular contractions would be slow and regular as/

as they are in cases of complete dissociation due to experimental or pathological severance of the main bundle. It has been suggested that the rapidity and irregularity of the ventricular beat is due to the fact that the fibrillating auricles are incessantly sending small irregular stimuli into the auriculo-ventricular node, that a process of 'continual tapping on the node' is going on (Cushny, Lewis), and that, as a result of this, the ventricles respond in a rapid and irregular fashion. While not denying the possibility of this explanation being correct, - I regard it as highly improbable. This explanation presupposes that all the impulses to ventricular contraction originate either in the sino-auricular end-plate or rather in ectopic impulses in the auricular muscle. But in our analysis of the functions of the two end-plates we saw that there was good reason to believe that the co-ordination of auricular and ventricular contraction depended on a balance of the activities of the two end-plates through their nervous supply. We saw, for example, in Laslett's case of sinus bradycardia (p.196), that interference with the sino-auricular nerve supply produced an irregularity in the ventricular contractions due to premature contractions. The suggestion that is here advanced is that the irregular irregularity of the ventricular contractions in auricular fibrillation is possibly due to a/

a combination of contractions of normal origin with interpolated premature contractions arising high up in the node or main bundle of the auriculo-ventricular end-plate. The influence of the fibrillation is indirect and not direct. In other words, the balance between the two end-plates has been disturbed by the fact that the sino-auricular organ fails to exert its influence on the auricles, and the ventricular tissue is the victim of this disturbance of balance. If the auricles fail to contract an ataxy of the ventricles is produced, just as the efficiency of flexor contraction is prejudiced by abnormal action or paralysis of the corresponding extensor muscles; it is not meant that the auricles and ventricles stand to each other in the relation of extensors to flexors; but their co-ordinate contraction is controlled by mutually dependant end-plates, and inefficiency on part of the one will be reflected in abnormal action on part of the other. Of great significance in support of this contention is the fact that fibrillation may be temporarily arrested, and a normal rhythm restored by stimulation of the extra-cardial nerves. No attempt has been made to give an exhaustive account of the clinical history or post-mortem findings in these cases. Only such facts as pertain to the question at issue, have been mentioned. A very detailed examination was/

was made of all the pathological hearts examined. As a matter of routine, the following parts were examined in every case:- (1) The two end-plates in serial sections; the whole of the sino-auricular end-plate, and the node, main stem, and commencement of the two subdivisions of the auriculo-ventricular end-plate being examined. (2) Two blocks from papillary muscles, and four blocks from ventricular walls. (3) Six blocks from the left auricle, and two blocks from the right auricle. (4) Blocks from the posterior inter-auricular sulcus and septum were cut serially to examine the ganglion masses, and large nerve trunks. (5) Blocks from the wall of the superior cava, and from the auriculo-ventricular sulcus at the lower posterior border of the left auricle were also examined for their content in nervous structures.

The object of this thesis, has been, not so much the attempt to explain the anatomical basis of cardiac irregularity, as to indicate a point of view and a method by which such cases should be examined.

Fig 1.

(A), (B), and (C) show diagrammatic representations of the development of the primitive cardiac tube to a four chambered organ

S.V = Sinus Venosus

A = auricle

V = Ventricle

B = Bulbus arteriosus

Fig 1.

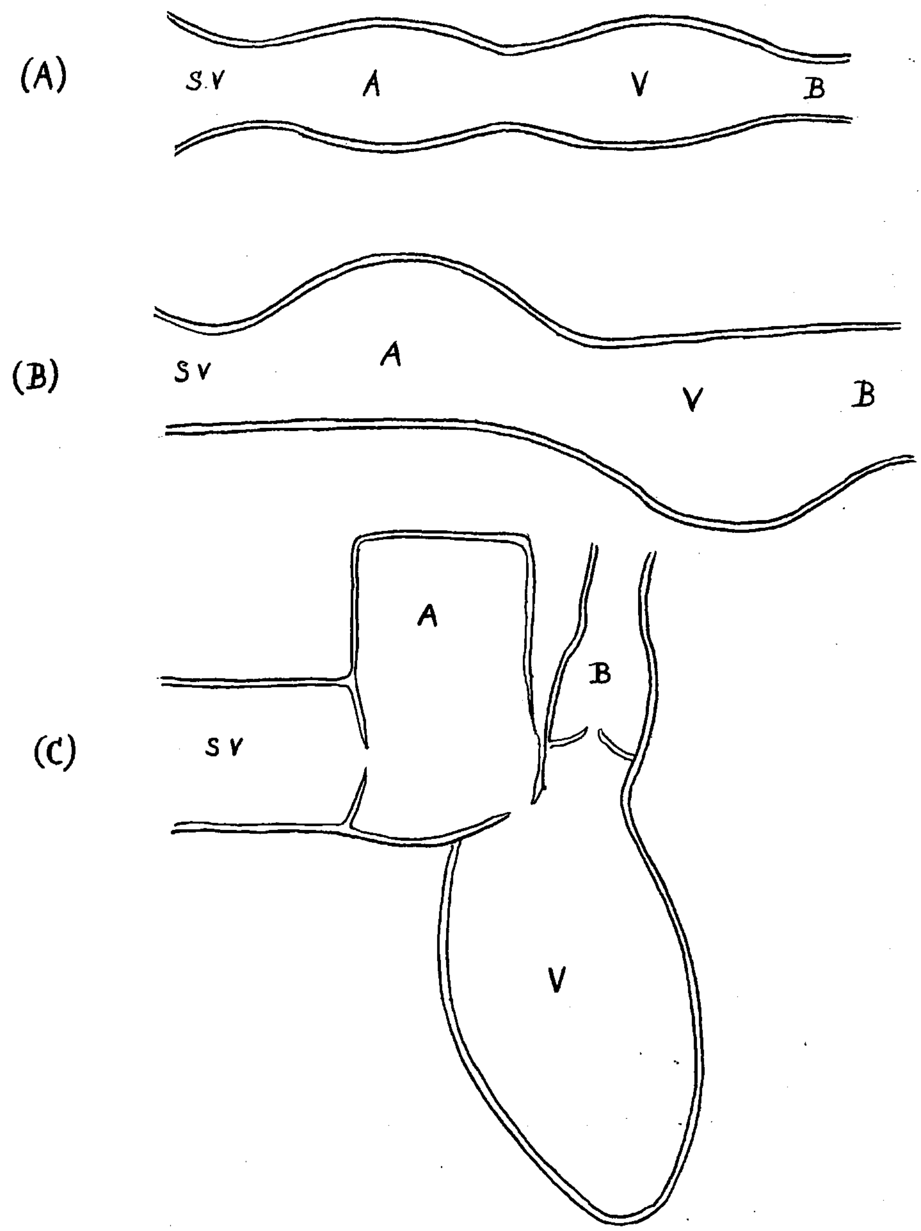


Fig 2.

Diagrammatic representation of the primitive vertebrate heart, constructed so as to show the primitive chambers and also the primitive junctional tissues.

A = Sinus venosus with the two Ducts of Cuvier opening into it.

B = The auricular canal

C = The auricle proper.

D = the ventricle

E = Bulbus arteriosus

F = The Aorta.

The red lines indicate the position of the specialised muscle in the primitive heart.

1 - 1 = Sino - auricular ring.

3 - 3 = auricular ring. (canalis auricularis)

4 - 4 = imaginary portion of auricular canal

Note the direct continuity of the muscle of the auricular canal on the dorsal side on to the bulbus arteriosus.

Fig. 2

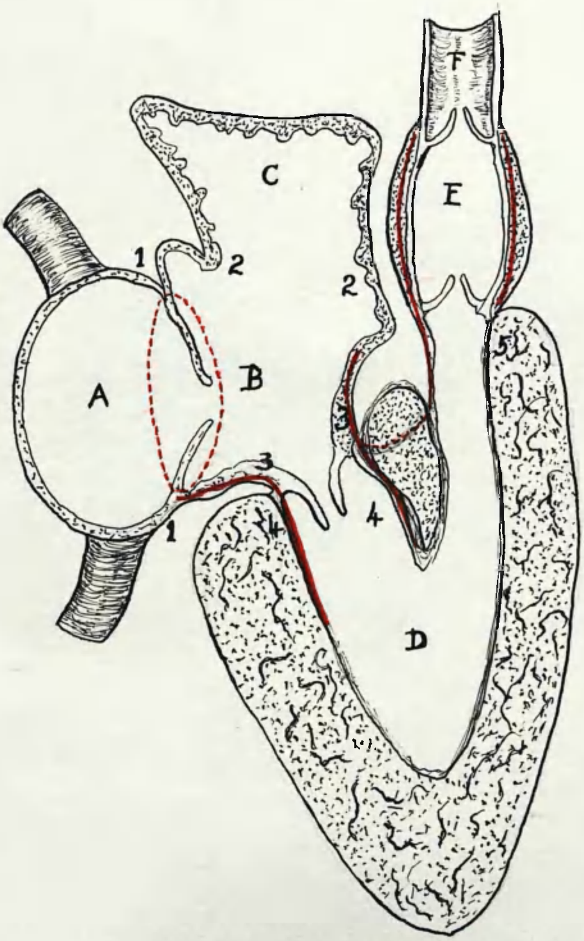


Fig 3

Frontal section through a sheep's heart to show the distribution (in red) of the auriculo-ventricular system. It is represented here with the two main branches riding on the interventricular septum. The section passes also through the fibro cartilaginous septum at whose base the main stem divides

Fig 3

Fig 4.

The series of sections from the main stem and branches of the ~~of~~ sheep's heart cut as described in the text (p 38...).

A = interauricular septal wall

V = interventricular muscular septum.

N = auriculo-ventricular node

B = main bundle

R.D. (7 & 8) = right subdivision of bundle
L.D. (7 & 8) = left " " "

3 shows the bundle piercing the septum fibrosum.

Fig 4

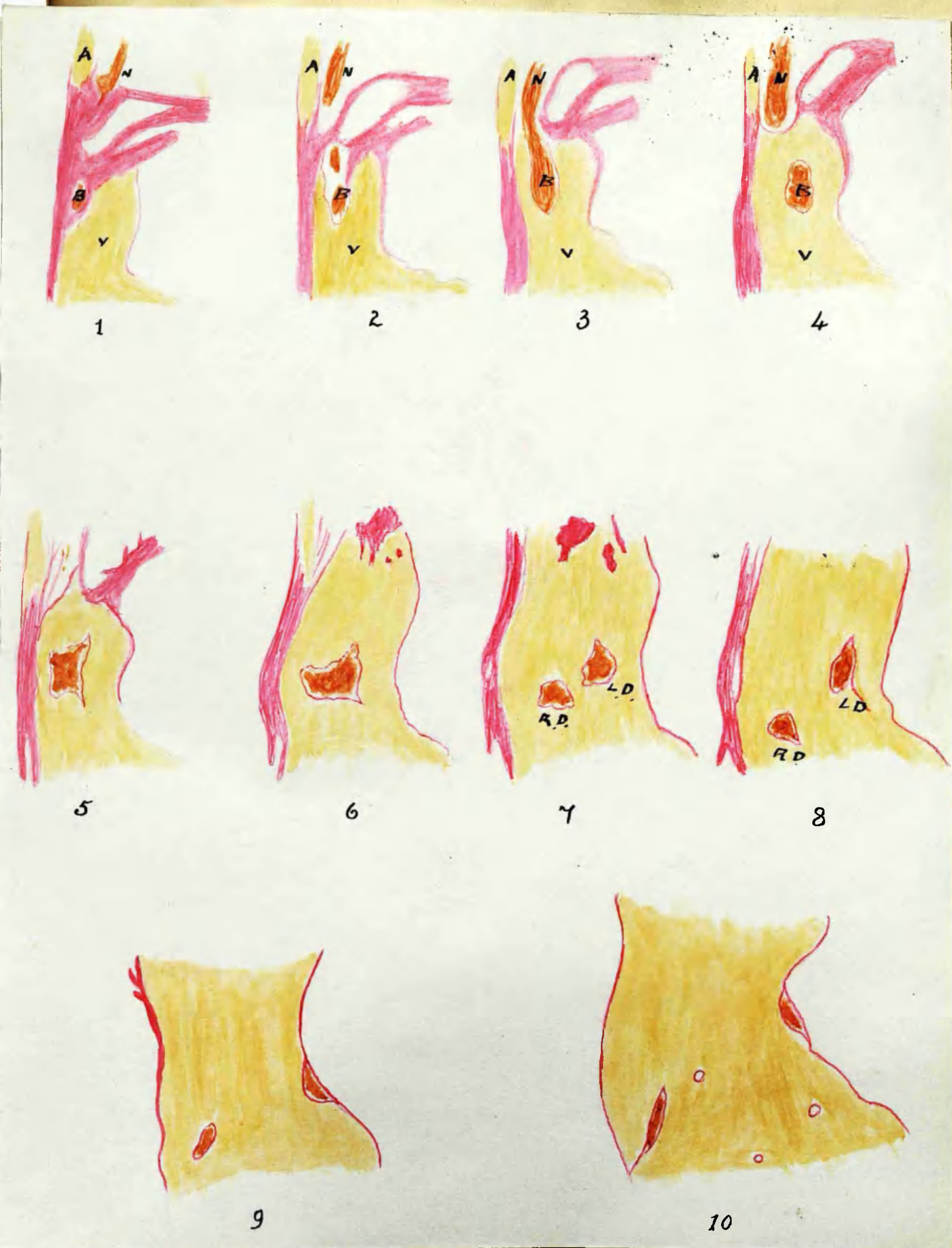


Fig.

Transverse section of strands of Purkinje fibres from the left ventricle of the sheep's heart.

Fig. 5.

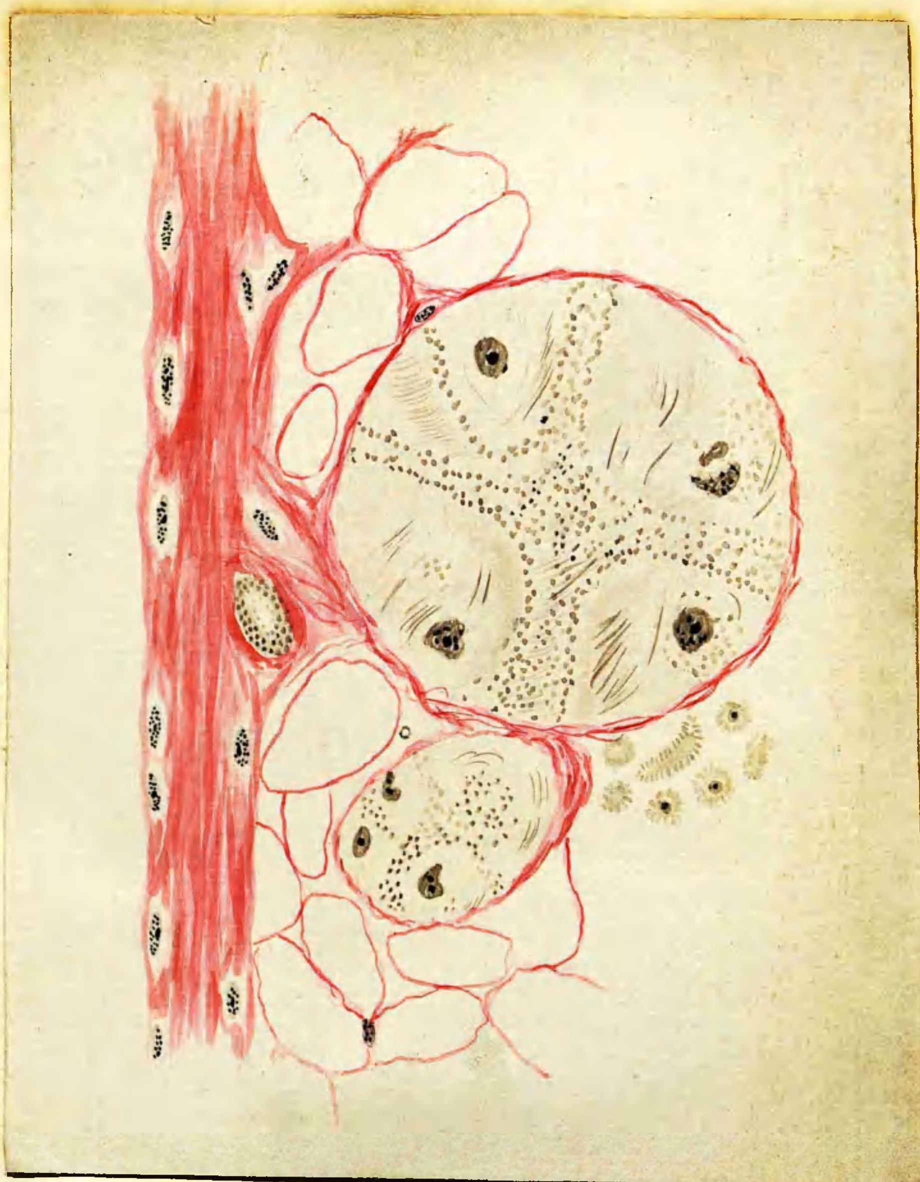


Fig 6.

section showing the continuity of Purkinje fibres with ordinary cardiac muscle fibres in the sheep's heart.

Fig 6.

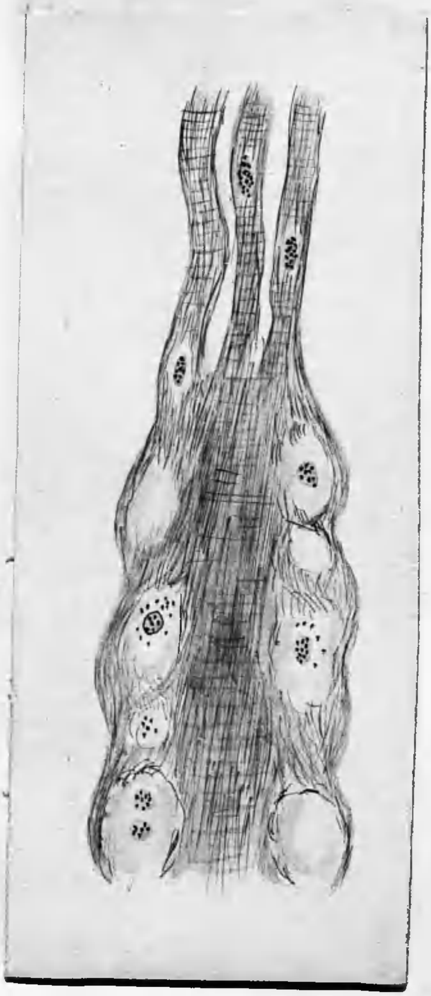


Fig 7.

Section showing continuity of ordinary muscle fibres with Purkinje fibres in a papillary muscle in the sheep's heart

Fig 7.

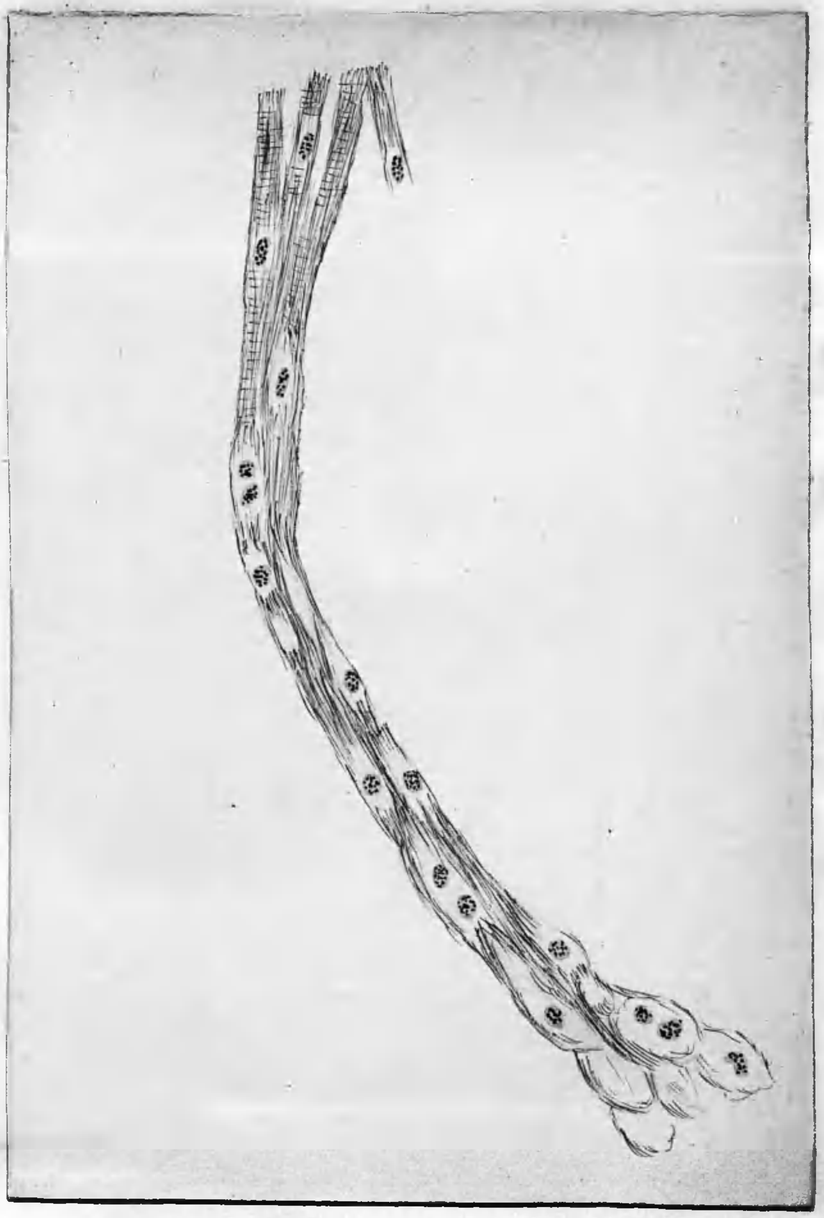


Fig 8.

Section showing continuity of nodal fibres (from the auriculo-ventricular node of the sheep) with the ordinary auricular muscle.

The nodal fibres are above and on ~~and~~ the ~~left, the~~ right, the ordinary auricular fibres below and on the left.

Fig 8.

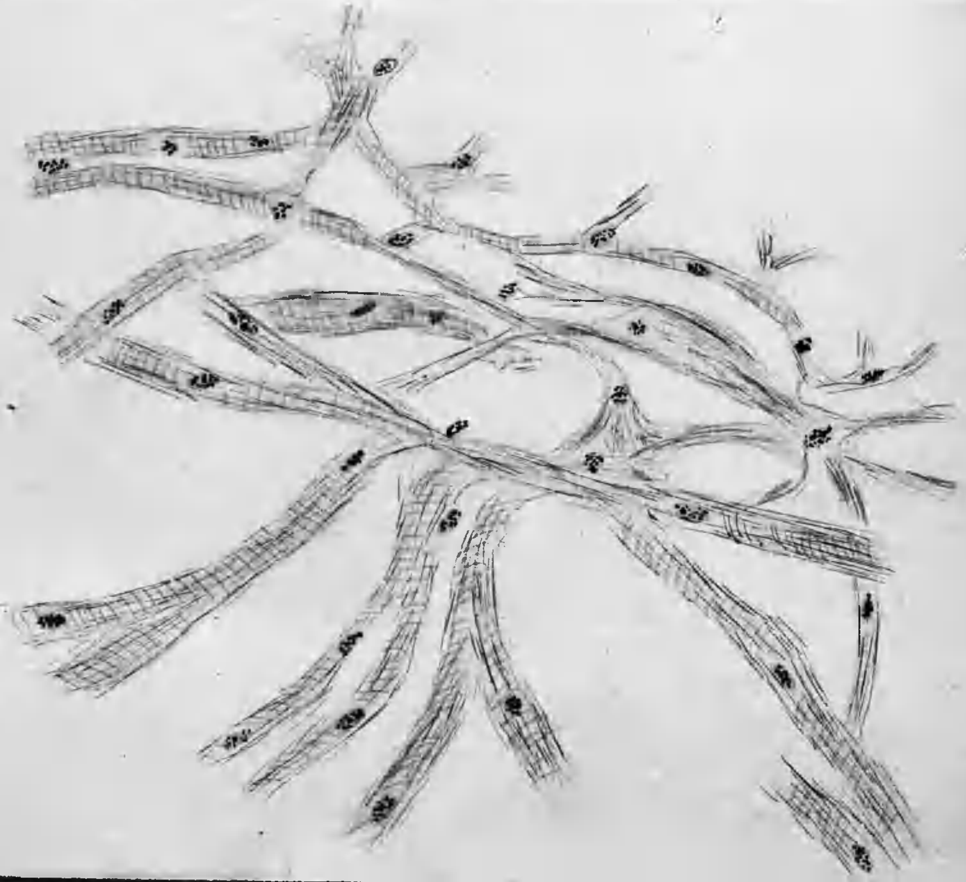


Fig. 9.

Course and distribution of the left branch of the a.v. bundle in the human heart.

Fig 9.

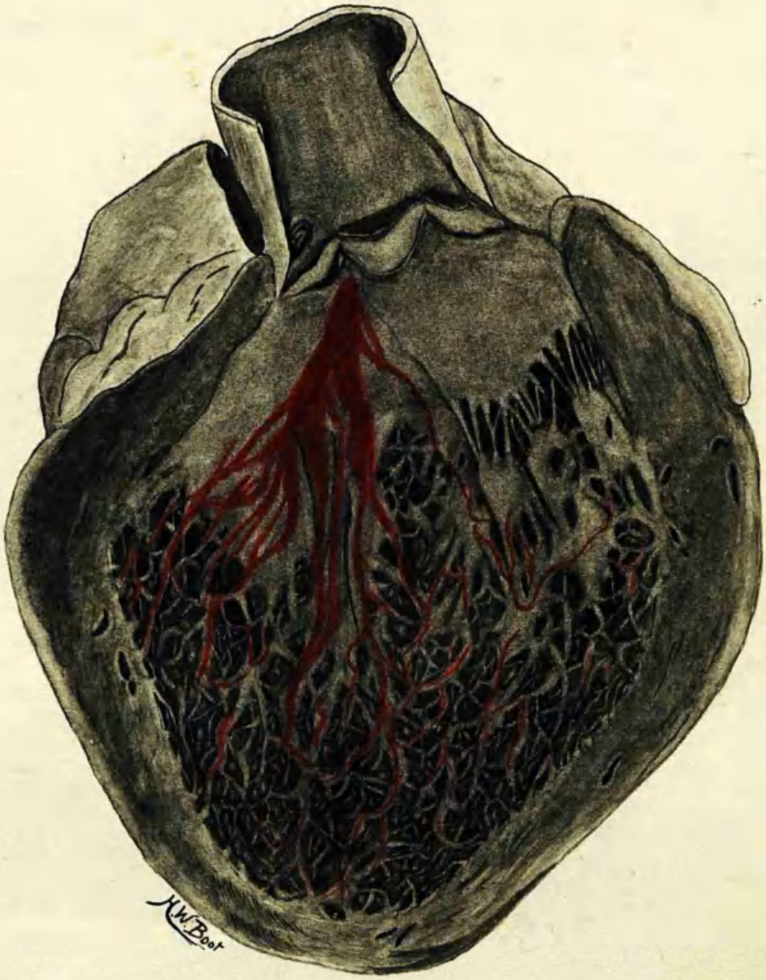


Fig 10

Course and distribution of the right branch of the bundle in the human heart.

The red spindle above the tinea terminalis indicates the position of the sino-auricular node in the human heart.

Fig 10.

Fig 11.

Diagrammatic representation of a series of sections from the a-v. node and bundle in the human subject. These are cut in a frontal plane and begin from the node and work forwards to the descent of the two main branches. The diagrams are to be looked at as if the heart were being viewed from the front (p. 57)

A = interauricular septum
V = interventricular septum.
N = node
B = bundle
L. D. = left sub-division
R. D. = right subdivision

2 shows the bundle entering the septum fibrosum.

5 shows the bundle in the centre of the pars membranacea septi with isolated strands of the left subdivision ~~one~~ beneath the endocardium of the ~~left~~ ventricle.

Fig 11.

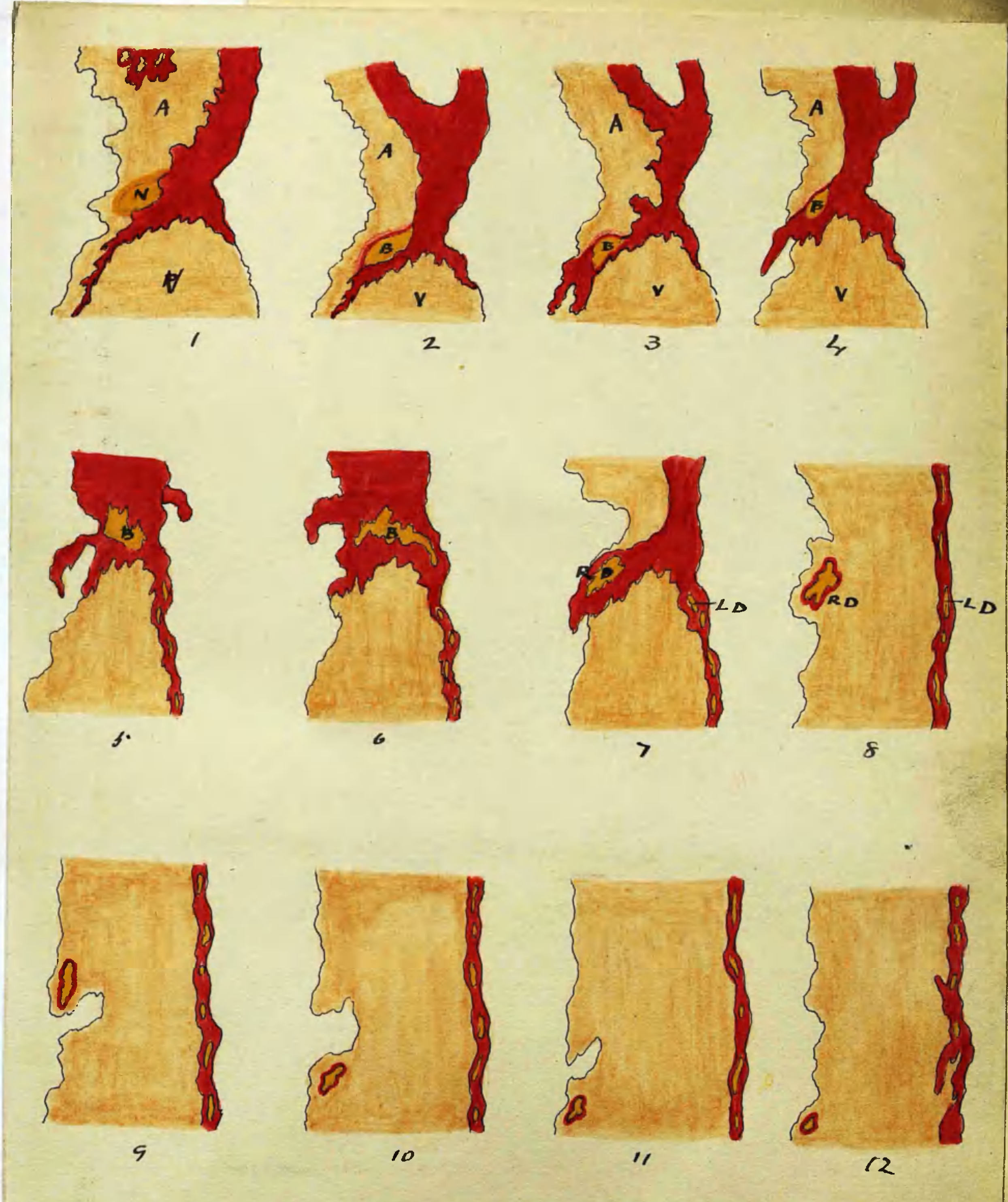


Fig 12.

Small branches of nerves stained by the vital methylene blue method in the main bundle of a heart of a human foetus of 8 months.

Fig 12.

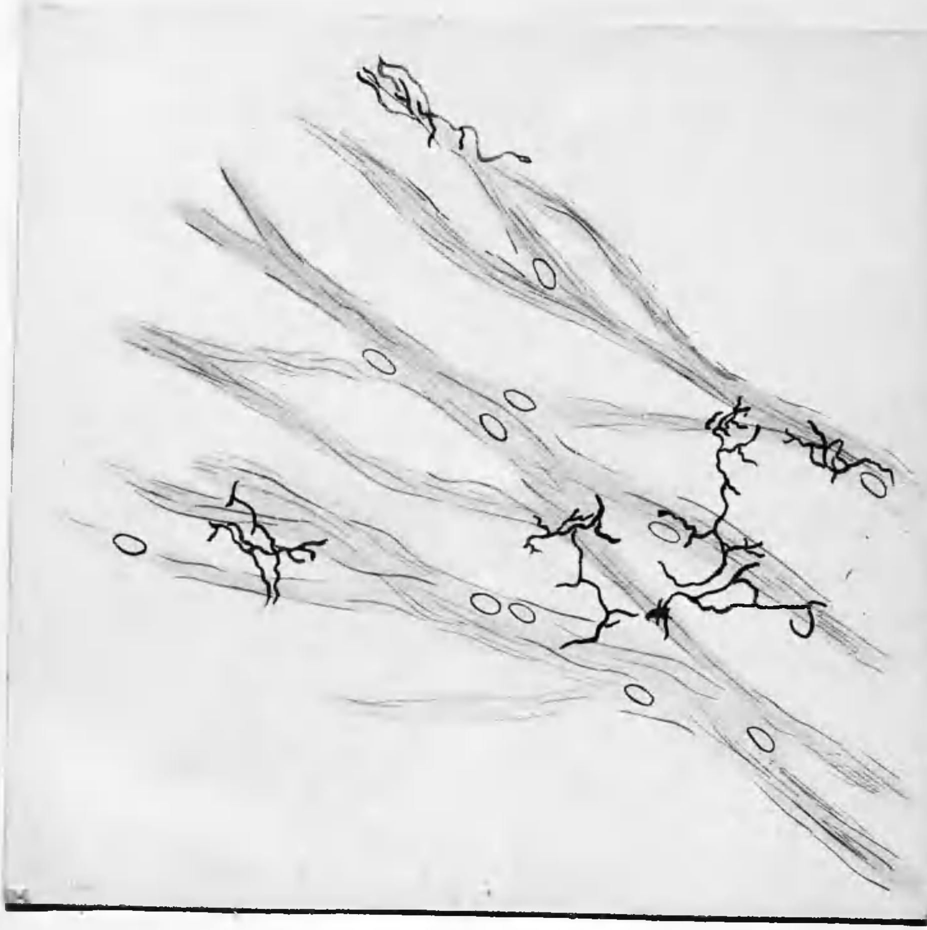


Fig. 13

A = Posterior view of the auricles of the pig's heart.

R.S.V.C = right sup. vena cava
L.S.V.C = left " " "
C.V = coronary vein
C.S = " Sinus
P.V = pulmonary vein.
I.V.C = inferior vena cava

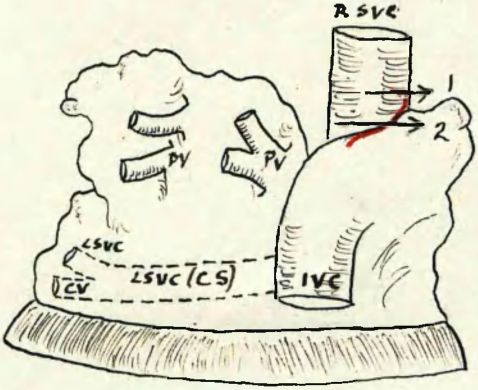
arrow 2 represents position of Fig. 14.
arrow 1 " " " Fig. 15.

B. Posterior view of the auricles of the Turtles heart.

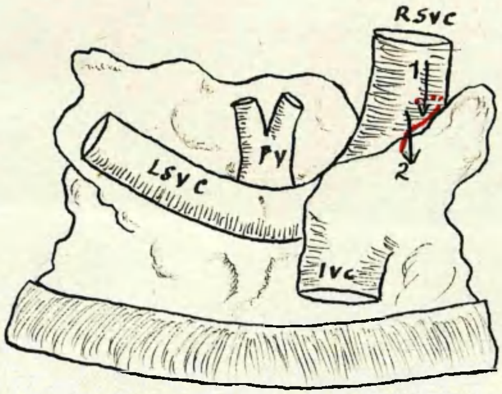
arrow 2. represents position of Fig. 23.
arrow 1. " " " Fig. 24.

The red lines in each case represent the position of the sino-auricular node.

Fig 13.



A.



B.

Fig 14.

The sino-auricular node in the pig's heart. (Fig 13)
(see Fig 13 arrow No 2.)

The nodal tissue is on the left side.
Note the multinucleated character of the tissue and the nerves & ganglion cells.

Fig 14

Fig. 15.

Upper portion of the sino-auricular node in the pig's heart. (see Fig 13 arrow No. 1.) At the upper end the nodal tissue is continuous with the muscle of the superior vena cava. In the middle the tissue is in the form of a network. Below it is in the form of a syncytium where the individual fibres cannot be distinguished.

Fig 15

Fig 16.

Detailed view of a portion of Fig 14. Showing the distribution of nerve fibres from their cells among the tissues of the node.

Similar appearance were seen in the node of Echidna (p 118)

Fig 16

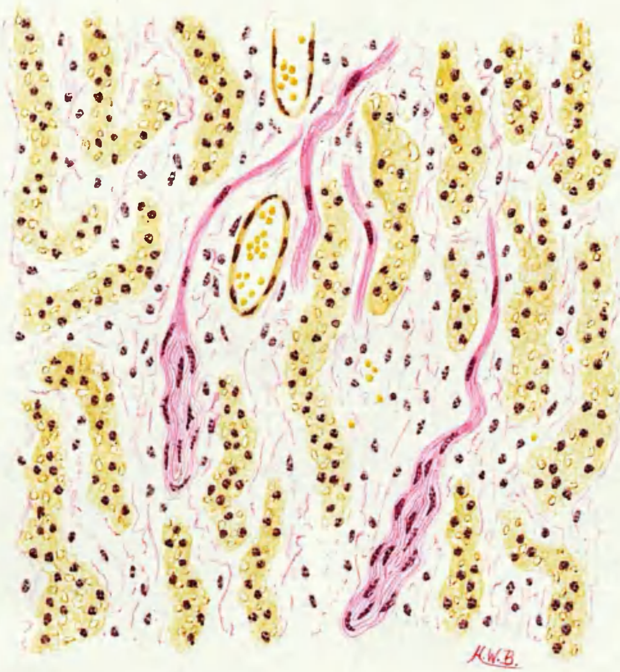


Fig. 17.

Diagrammatic representation of the hearts of the skate and the bream, showing the diagonal position of the venous valves (blue) in the former and their transverse position in the latter. The red lines represent the nodal rings, sino-auricular and auriculo-ventricular.

The figures are meant to represent the hearts when viewed from the front.

R. D. C. = right Duct of Cuvier
L. D. C = left " "
S. V. = sinus venosus
A = auricle
V = ventricle.

The dotted line (x – x) to the right (it is on the left of the Fig) cuts off the tissues which form the sino-auricular end-plate in the mammal.
The dotted line (Y – Y) to the left (it is on the right of the Figure) cuts off the nodal tissue which forms the auriculo-ventricular end-plate in the mammal.
The right and left main nerve trunks are marked yellow.

Fig 17

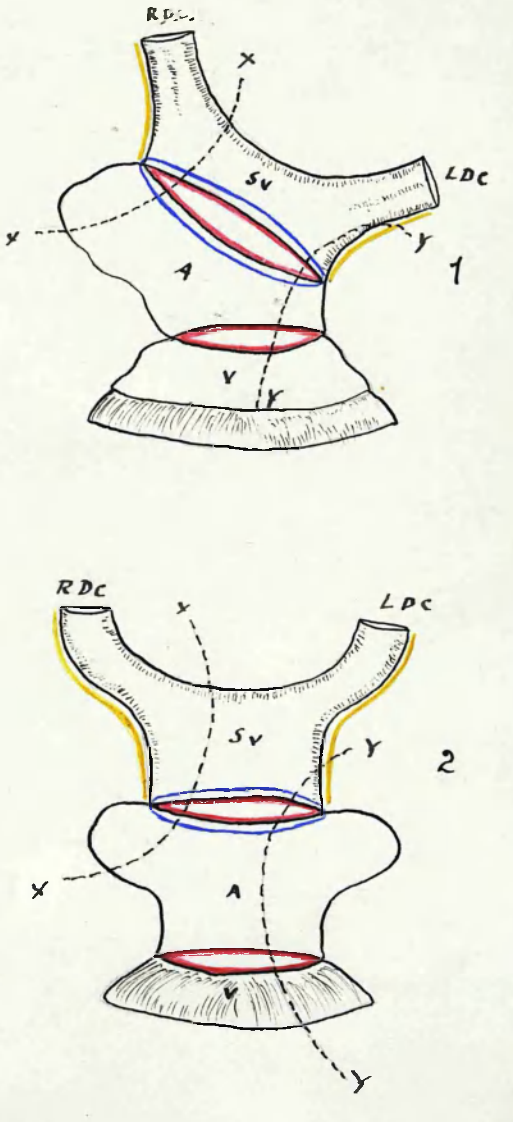


Fig. 18

Diagrammatic representations from the front of the hearts of

1. The Bream
2. The Turtle
3. The Kangaroo
4. The Pig.

A = right Duct of Cuvier or right sup. vena cava.

B = left Duct of Cuvier or left sup. vena cava (coronary sinus)

C = inferior vena cava.

D = auriculo ventricular orifice.

F = the limits of the sinus venosus. They are within the limits of the venous valves which are marked in blue.

The nodal tissues are marked in red.

G - H = the sino auricular node or ring in the bream.

K = the auriculo-ventricular ring or the canalis auricularis.

(H) = the portion of the sino-auricular ring which forms part of the auriculo-ventricular end-plate.

G represents the sino-auricular end-plate in the turtle kangaroo & pig.

R represents the right venous valve.

L " " left " "

Fig 18

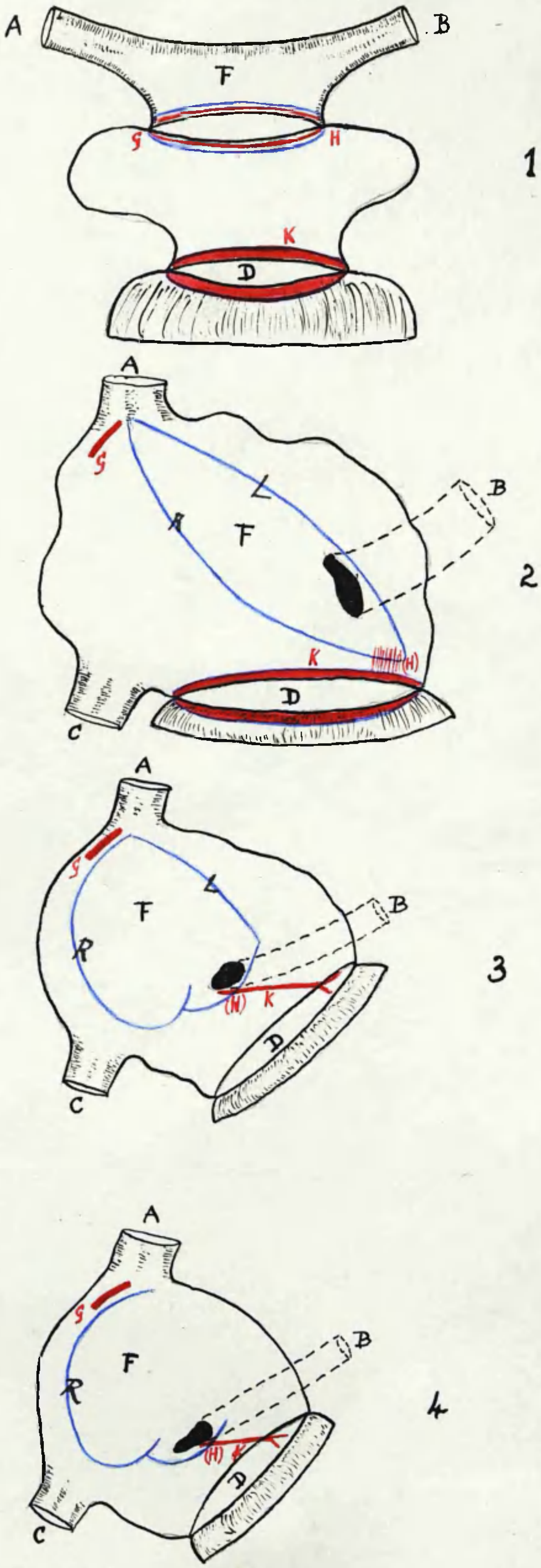


Fig. 15.

The right side of the heart of Echidna (monotreme).
This figure shows the muscle branches which descend into the right ventricle from the ~~circular~~ annular fibres of the auricular canal. into the flaps of the tricuspid valve.

Fig 19

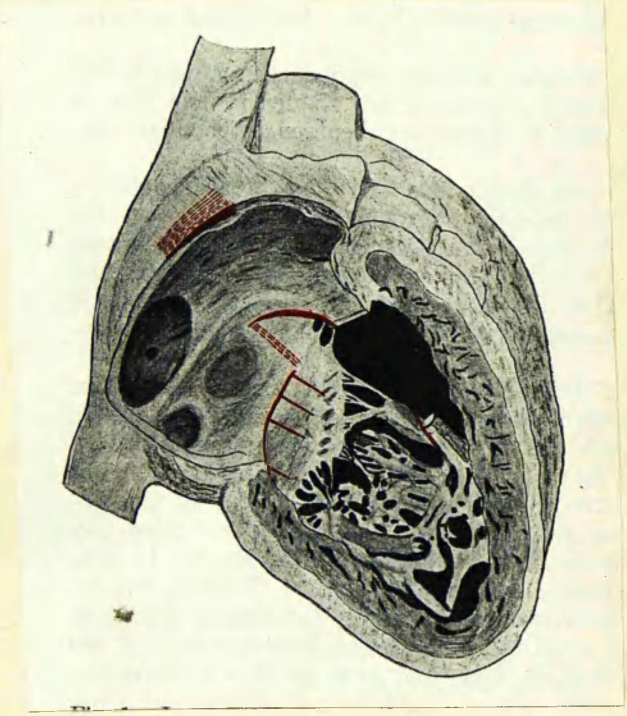


Fig 20

Series of diagrams to illustrate the parts in the human heart corresponding to the Sinus venosus of the primitive heart.

A dorsal view of the auricles of the human heart.

B. corresponding view of the wallaby's heart.

C. " " " " heart of a child in which the lungs were fused and the vestibule of the left auricle consequently unexpanded.

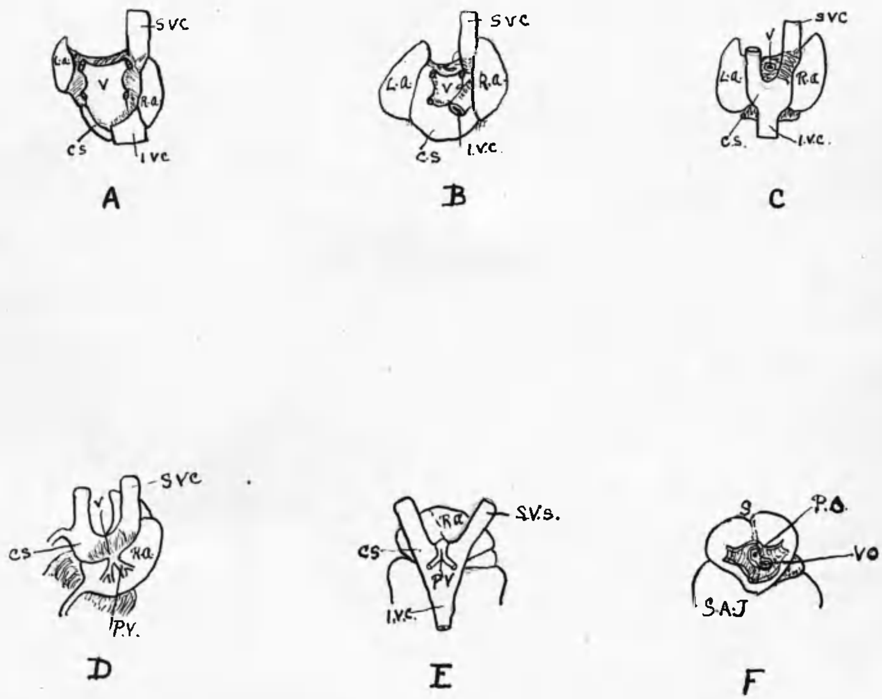
D. corresponding view of the heart of a malformed foetus in which the inferior vena cava was absent.

E. corresponding view of the heart of the frog. (Gaupp)

F. corresponding view of the heart of the frog the interior of the sinus venosus being exposed to show the pulmonary veins opening into the walls of the sinus.

p.o. = orifice of pulmonary veins.
v.o. = " " sinus venosus.
s = attachment of interauricular septum.
s.a.j = sino-auricular junction.
v = vestibule
ra = right auricle
la = left "
S.V.C. = superior vena cava.
cs = coronary sinus.
I.V.C. = inferior vena cava.

Fig 20



SVC
L.a.
V
R.a.
CS
IVC
A
SVC
L.a.
V
R.a.
CS
I.V.C.
B
SVC
V
L.a.
R.a.
C.S.
I.V.C.
C
SVC
V
CS
R.a.
P.V.
D
S.V.S.
R.a.
CS
PV
I.V.C.
E
S
P.O.
VO
S.A.J
F

Fig 21.

The auricular part of the human heart from behind, showing the musculature of the termination of the great veins

a. sup. vena cava surrounded by muscle derived from the sinus venosus.

b. inferior vena cava

c. to the right of the sulcus terminalis above c, sinus fibres cross the sulcus to form the right auricle proper

d-c part of the sulcus where the sino-auricular node lies; the arrow ↔ crosses the node transversely.

E annular fibres of the auricle

D.F. right auricular appendix.

G. fibres passing from the inter-auricular septum to the vestibule of the left auricle.

h. vestibule.

I. position of coronary sinus or left superior vena cava, showing continuity of its fibres with the right & left auricle.

L. = pulmonary veins.

N. position of muscle band which passes from the sinus venosus to the left auricle.

O. muscle of auricular canal embracing remains of sinus venosus (Keith).

Fig 21

Fig 22.

Transverse section of the heart of the heam in the region of the venous valves.

above is the sinus venosus with its two walls stained red and below is the upper part of the auricle.

The venous valves are seen at the junction at the base of the venous valves are the transverse sections of the nodal tissue of the sino-auricular ring.

V.V. venous valves.

N. nodal ring.

Fig 22

Fig 23.

Section through the sino-auricular node in the turtle heart. See Fig 13. B. arrow 2.

Above the node is continuous with the sinus wall

On the left is the right venous valve

and on the right is the attachment of the visceral pericardium.

Note the peculiar structure of the nodal tissue separated into compartments by fibrous tissue (Van Gieson's stain).

Fig 23

Fig 24

Upper part of the sino-auricular node in the turtle's heart; on each side it is (above and below) continuous with the ordinary sinus muscle of the superior vena cava.

The section is from the part indicated in Fig 13. B. arrow 1.

Fig 24

Fig. 25

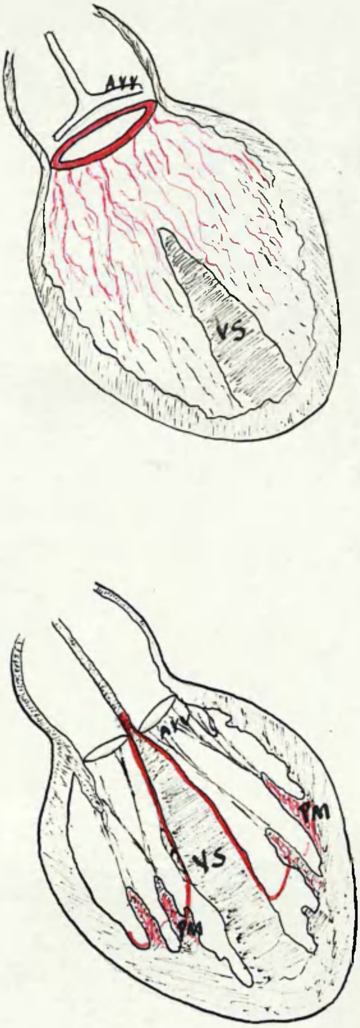
Diagrammatic representation of the mode of origin of the auriculo-ventricular valves and fibres from the ~~auricular~~ ventricular extension of the canalis auricularis.

1. This figure shows the portion of the nodal tissue extending in fine threads (marked red) from the auricular ring into the ventricle. Here the auriculo-ventricular valves are suspended from the inter-auricular septum (reptile) A.V.V.

2. When the inter-ventricular septum (V.S.) grows up to meet the inter-auricular septum and the ventricles become the seat of the invaginated auricle with the formation of the fibrous valves the a.v. fibres are congregated into a single strand which lies on the roof of the septum but the ramifications to the inner surface of the ventricle remain in association with this single remaining strand.

A.V.V. auriculo-ventricular valves
V.S. Interventricular septum
P.M. papillary muscles.

Fig 25.



1

2

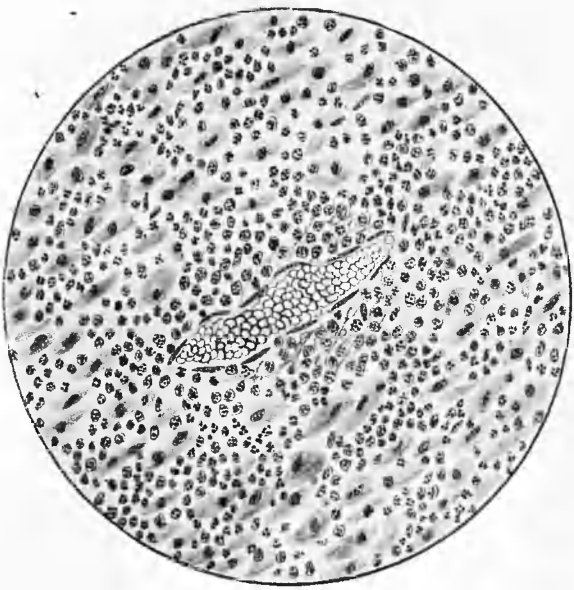
Fig 26.

Section of ventricle from case of complete auriculo-ventricular dissociation in diphtheria (Case (a) p 230).

Acute myocarditis.

In this case the node or main bundle was not affected.

Fig 26



~~FIG. 3.~~

Fig 27.

Section from another part of the ventricle of the same case

Case (a) Diphtheria p. 230

Fig 27

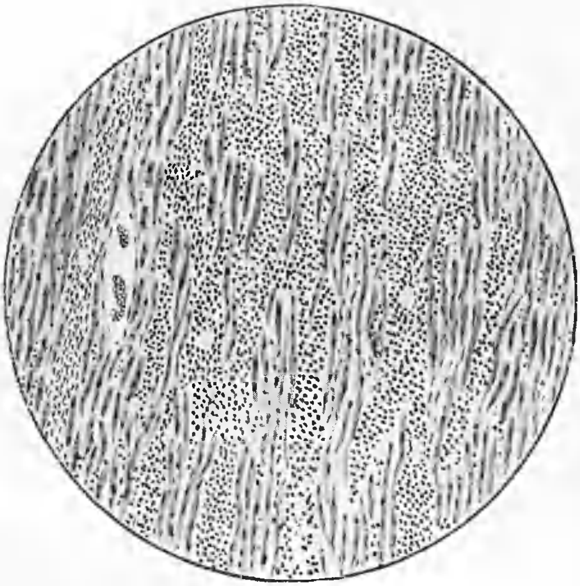


Fig. 2.

Fig 28.

This figure gives an indication of the site of the lesion in the case of paroxysmal tachycardia described on page 237 (case f).

The figure represents the base of the ventricles with the auricles removed

M = mitral valve

T = tricuspid valve

⟷ = arrow showing ~~position~~ situation from which the section from which Fig 29 was cut. This is seen to pass through the node (N)

X indicates the position in the interauricular wall from which Fig 30 was taken.

Fig 28

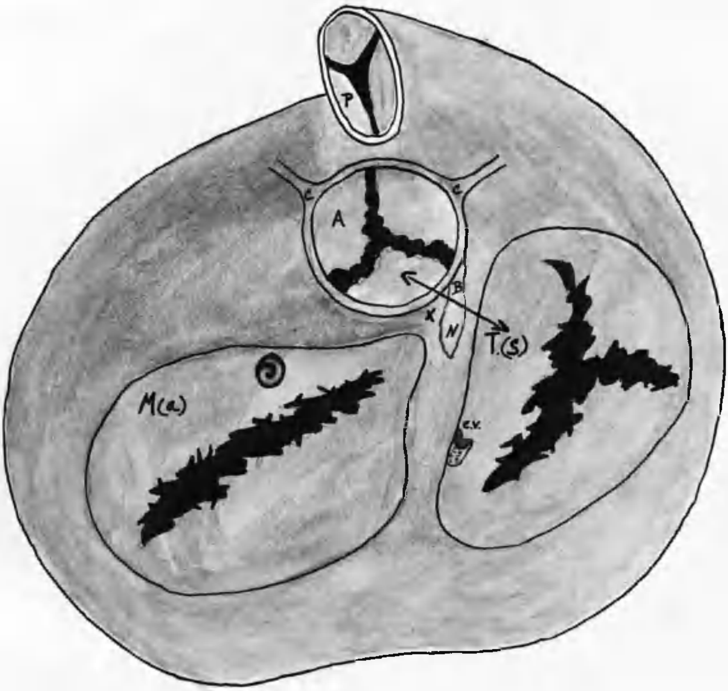


Fig 29.

Section from the auriculo-ventricular node in the region of the arrow in Fig 28.
The picture represents the affected portion of the node in its left half while the right half of the figure shows normal node.
It will be seen that there is considerable infiltration and that the muscular structure is thin and probably the seat of oedema.

Fig 29

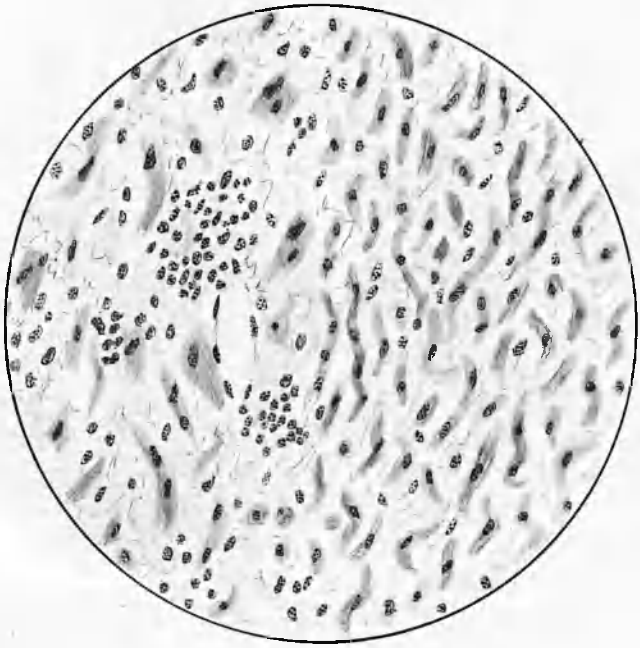


Fig 30.

This represents the tissue section at X in Fig 28. It is in the inter-auricular wall and the pale fibrous tissue represents the septum fibrosum to which the cusp of the mitral valve is attached.

Fig 30

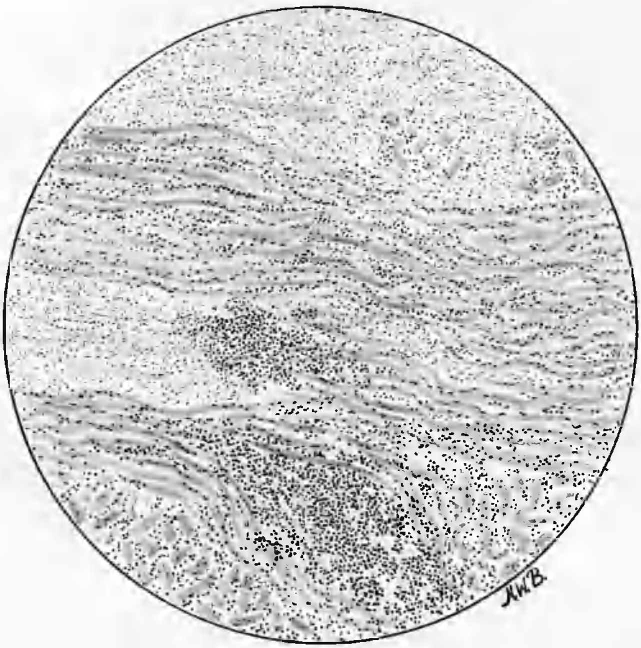


Fig 31.

Represents here is a general view of the fibrous degeneration of the left auricular wall in the cases of auricular fibrillation in mitral Stenosis Cases (m) (n) (o) (p). It is only at points that this extreme degree of muscle degeneration is seen. It is not a case of replacement of fibrous tissue as the following figures show, but a case of muscle degeneration of a primary character.

Fig 31

Fig 32.

More detailed view of the general pattern presented in Fig 31 and characteristic for some parts of the muscular tissue in cases (m) p 245 (n) p 245, (o) p. 246 (p) 247.

It is here seen how the fibrils become freed from the fibres and the tissue becomes broken up into a stringy ~~fib~~ mass of degenerate tissue, which does not stain pink with van Gieson's stain.

Fig 32

Fig 33

Another section of the same type of muscle degeneration as is shown in Fig 32. This is not fibrous tissue but a degenerate product of muscle fibres arranged in the form of a network somewhat hyaline in character. It does not stain pink with Van Gieson's stain, and does not contain an excess of elastic tissue fibres.

Fig 33

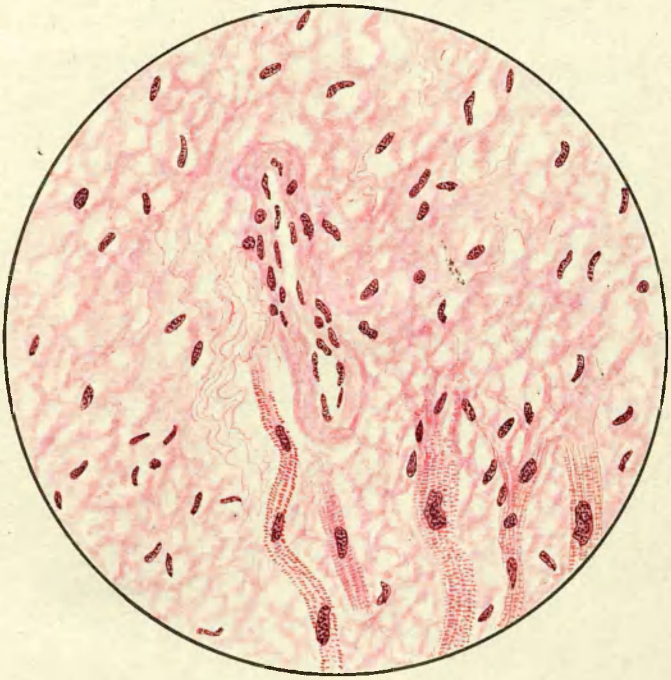


Fig 34

Acute degeneration of the muscle of the left auricular wall from case (m) p 245.

Fig 34

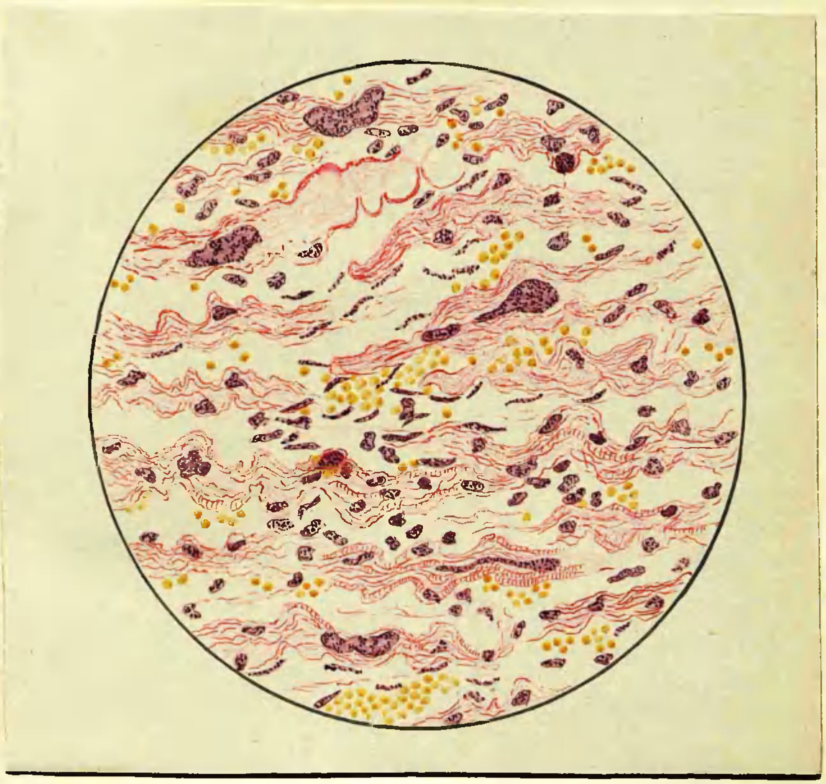


Fig 35.

Acute inflammatory infiltration & degeneration of the left auricular wall in case (n) p 248.

Fig 35

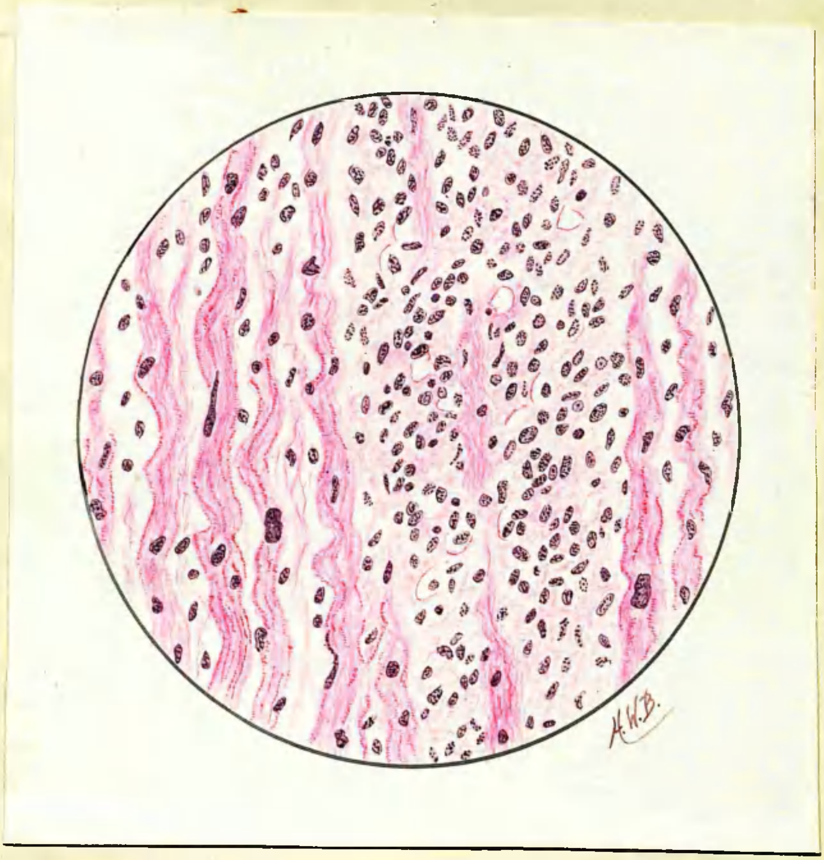


Fig 36.

Degeneration of the muscle in the left ventricle of case on p 247. This is a characteristic area of starvation fibrosis. Note the presence of pigment in the atrophic area; these pigmenting granules represent the remains of the atrophied muscle fibres.

Fig 36

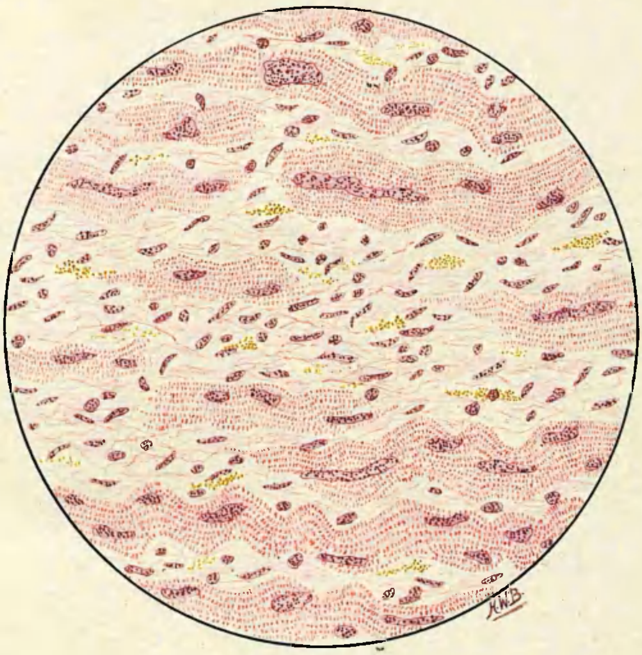


Fig 37.

Infiltration hyaline degeneration of the wall of the left auricle in case (p) p 247

The fibres are thin, ~~hyaline~~ hyaline in appearance, show no transverse striation. The nuclei are irregular in size some of them being very large.

Fig 37

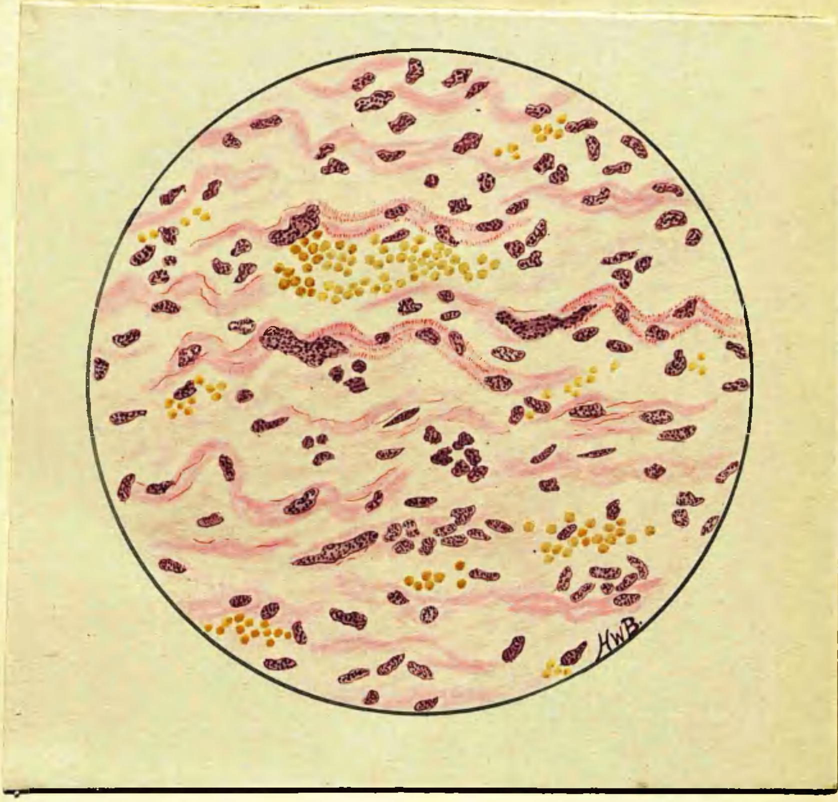


Fig 38

Section from the interauricular

Septum of case (p) p 247.

Extensive inflammatory destruction

which occurs in isolated places

Fig 38.

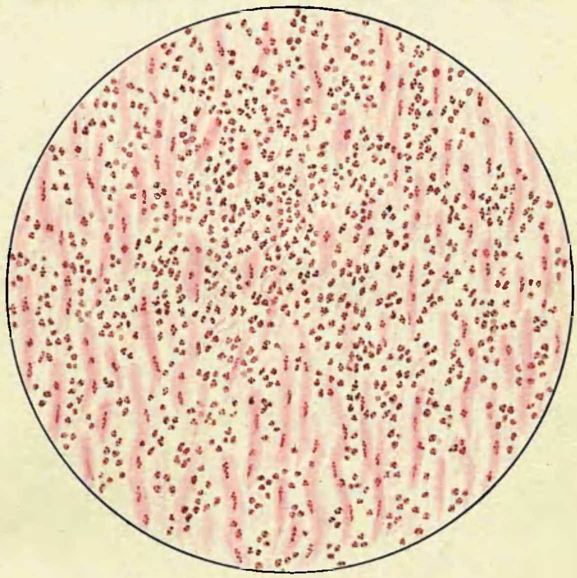


Fig 39.

Section from a ganglionic mass in the posterior wall of the auricles at the inter-auricular sulcus from case (O) p 246. The condition shows extensive leucocytic infiltration of the ganglion cells and general fibrosis of the ganglionic mass.

Fig 39

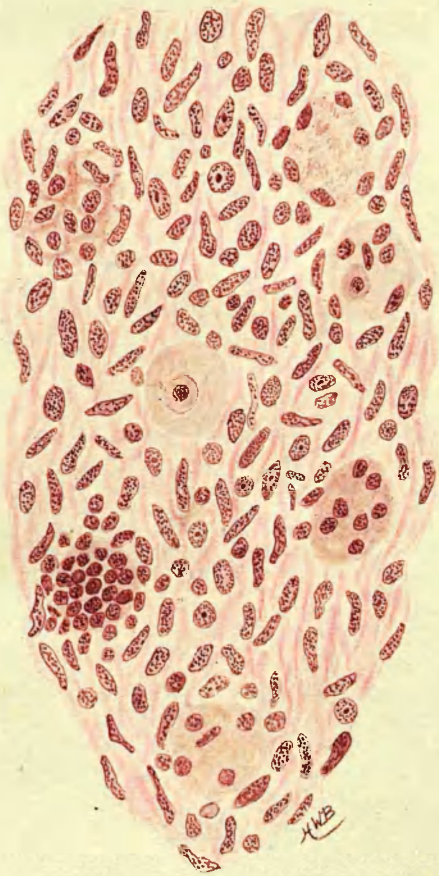


Fig 40.

General view of the auricular wall in case (R) p 247. It gives the appearance of fatty infiltration but closer examination as shown in Figs 41, 42 and 43 reveals the presence of a foamy degeneration of the muscle fibres.

Fig 40

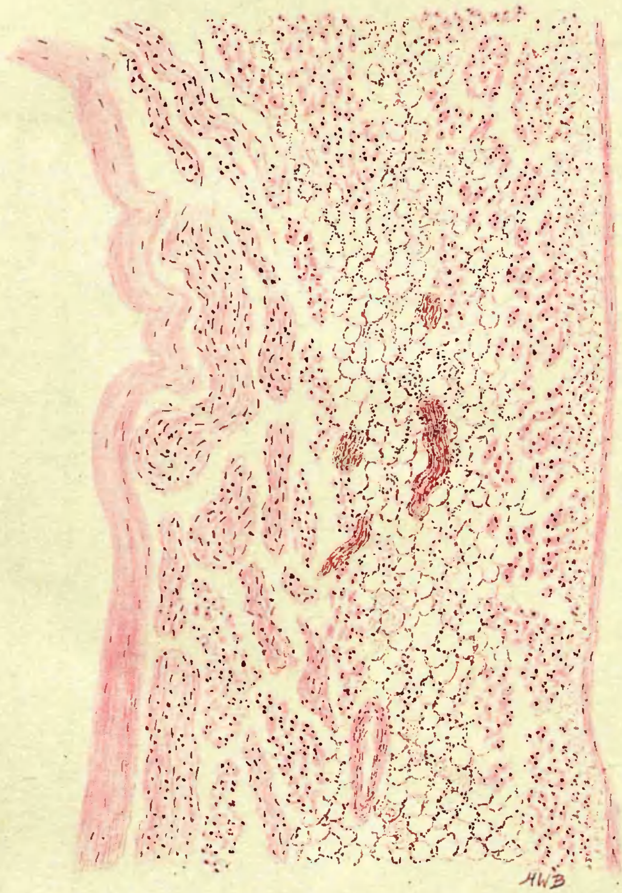


Fig 41.

The 'foamy degeneration' is seen here to surround the muscle bundles which are cut transversely. It is from case (r) p 246. The pigmentary deposit shows that the loose degenerate network represents the remains of muscle fibres.

Fig 41

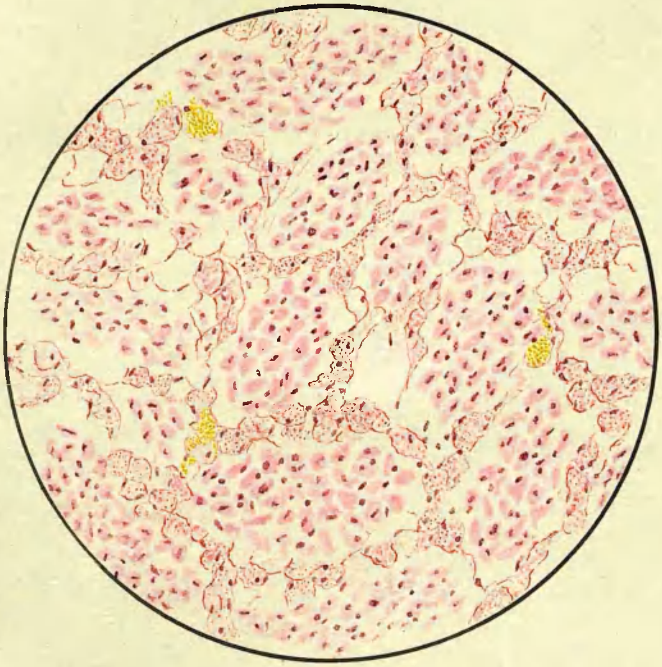


Fig. 42

More detailed view of the foamy cell degeneration. The presence of pigmentary deposits is seen here also.

Fig 42

Fig 43.

This section shows the gradual transition from the normal striated muscle fibre to the 'foamy cell' degeneration. The multinucleated character of the tissue and the pigmentary deposits are characteristic for this form of degeneration.

Fig 43.

Fig 43