The Architecture of the Right Ventricular Outflow Tract in the Normal Human Heart and in the Presence of Ventricular Septal Defects

By Robert P. Grant, M.D., Fred M. Downey, M.D., and Hugh MacMahon, M.D.

A detailed understanding of the outflow tract of the right ventricle is needed for further progress in the diagnosis and surgical treatment of cono-truncal cardiac anomalies. Previous studies of the musculature in this region overlooked or undervalued its intrinsic muscular system and considered the bulbar musculature simply a part of the over-all muscular bundles of the two ventricles. This may have been because the authors did not take into consideration evidence that the musculature of the right ventricular outflow tract has a different embryologic origin than has the remaining musculature of the ventricles.

The present studies are based upon careful dissections of the outflow tracts in normal and congenitally abnormal human hearts. The studies affirm the existence of an intrinsic bulbar musculature which appears to be only secondarily coupled to the remaining ventricular musculature and may be different from it in still other regards. In addition, the studies shed light on the morphogenesis of outflow tract anomalies and point to a different theory of the manner in which ventricular septal defects and infundibular stenosis develop than has prevailed in the past.

Nomenclature

Although the heart is a three-dimensional structure, pathology nomenclature and methods for study are essentially one-dimensional. Structures are named because they protrude, indent, or marginate rather than because of a relationship to over-all functional structure.

While this is not the place to reorient cardiac anatomic nomenclature, it is necessary for the purposes of this study that certain "place names" of cardiac morphology be accurately defined.

Crista Supraventricularis

This term has been used for widely diverse components of the outflow tract. Monckeberg, Abbott, and others had defined it as the portion of the free wall of the right ventricle that vaults the outflow tract; the musculature of the septum plays no part in this definition. More recent authors have followed Keith in fitting the term to embryologic theory. They consider the crista to consist of two muscle bundles on the septal surface of the outflow tract, the "septal" and the "parietal" bundles, which are believed to be derived from the two muscular ridges of the fetal bulbus cordis. And still other authors use the term to define a horizontal ridge low on the septal surface that separates the inflow from outflow portions of the right ventricle.

The term crista supraventricularis was introduced by the French anatomist Wolff in 1791. He used it simply to describe the mass of right ventricular tissue that lies between the tricuspid and pulmonary rings without regard to the muscular components it comprised or its embryologic origin. In this usage, it belongs to the free wall of the right ventricle, forming the medial wall of the outflow tract, and against which the aorta curls at its root. Indeed, prior to Wolff, this region had been called the "aortic wall" and the "fleshy pons" of the right ventricle. Wolff likened it to a spur ("eperon"). In translating it into Latin, spur becomes crista; and perhaps this is where the confusion developed, for the English language is readier to translate.
crista as "crest" than "spur," and the crista supraventricularis has been treated by English and American writers as a crest or ridge on the septal surface of the heart, and not as a spur. Nevertheless, Wolff recognized that the muscle mass between the two orifices of the right ventricle is unique, having no parallel in the left ventricle, and he felt it deserved separate designation. In the present study we shall use Wolff's definition.

**Moderator Band and Trabecula Septomarginalis**

As early as da Vinci, anatomists had noted a free band of muscle extending from the septal surface to the free wall of the right ventricle. The anterior papillary muscle, which supports the anterior leaflet of the tricuspid valve, usually originates from it. In 1837 King gave it the name "moderator band" as a result of his conjecture that it might control the capacity of the right ventricle as a sort of governor, permitting dilatation when too much blood might surge into it. On the septal surface the moderator band is continuous with a ridge of musculature originating at the membranaceous septum. This entire muscle structure including the moderator band was named "trabecula septomarginalis" by Tandler, and he suggested that the moderator band was simply that portion of this muscle mass that emerged from the septal surface to extend into the free wall of the right ventricle. With fine Gallic diffidence French anatomists have called Tandler's trabecula "le faisceau innominé." Certain writers have occasionally included the trabecula within their definition of a crista supraventricularis but this does not appear to enhance the usefulness of either term. As will be seen, separate identification of the trabecula septomarginalis may be useful, since this probably identifies the most caudal contribution of the bulbus cordis to the ventricular myocardium. On the other hand, the myocardial fibers of the moderator band are continuous not only with those of the trabecula septomarginalis but with other muscular components of the outflow tract, and the presence or absence of the moderator band and its size in hearts with ventricular septal defects is often a useful lead in studying the bulbar musculature.

**Muscle Bundles of the Ventricle**

Since the efforts of Richard Lower in the seventeenth century to unroll the musculature of the heart there have been countless studies of the directional arrays of the fibers of the myocardium. In certain species of animals it appears to be possible to develop what appear to be cleavage planes between these arrays. Such seemingly independent directional arrays are called "bundles." The bundles of the left ventricle have been studied in many different species. The extent to which these bundles are morphologically distinct from one another has been the subject of controversy for many years. The embryogenesis of myocardium is such that it is extremely unlikely that in any mammalian species the bundles are completely separate; all bundles have fibers in continuity with fibers of adjacent bundles and species vary mainly in how numerous these bridges are. In our experience and that of others in recent years, it is quite apparent that in man the ventricular myocardium consists of the same directional arrays as in other mammals, but fibers of continuity and fibers with transitional directions are so frequent that no true cleavage planes exist. Nevertheless it is possible to separate individual directional arrays by sundering these points of continuity. In short, grossly the human ventricular myocardium appears to be genuinely a muscular syncytium, and the term "bundle" identifies a directional component of myocardial fibers rather than a discrete and independent group of fibers. For this reason the term "muscle component" is used instead of "muscle bundle" in the present study.

**Methods of Study**

In order to study the directions of myocardial fibers, the fibers must be rendered separable but with enough tensile strength that they will not tear easily. No ideal method for doing this has yet been devised. After experimenting with a number of tanning and other methods, none appeared to be superior to the general method originally used by Lower and later by MacCallum and by Mall. The heart is immersed in water acidified with acetic acid.
RIGHT VENTRICULAR OUTFLOW TRACT

dead and simmered just below the boiling point for 3 to 4 hours. This removes much of the fat and softens connective tissue. At this stage, further fat and other connective-tissue structures including valvular and endocardial tissues are easily removed mechanically. Then, to restore the tensile strength of the fibers, the heart is carried through increasing concentrations of ethyl alcohol, with final dehydration for 3 to 4 days in absolute alcohol. Dissection is best done under a dissecting microscope. One must be cautious, however, not to dry the specimen under hot illumination, for the fibers will become tough and brittle.

Detailed dissections of the outflow tract of the right ventricle were performed on 15 dog hearts and seven normal human hearts. The hearts in six cases of ventricular septal defect were dissected completely, and partially in four others, including two cases of truncus arteriosus. Twenty-two additional human hearts with cono-truncal abnormalities from various sources were studied without dissection of the musculature, but with landmarks developed from the dissection as guides. In the present study the musculature of the septal region of the right ventricle and of the crista supraventricularis alone was studied, and no effort was made to study the architecture of the free wall. It is recognized that the number of heart studies is small and makes it impossible to develop a complete and secure picture of the architectural abnormalities of the cono-truncal anomalies, so that this must be viewed as a preliminary study.

A word about the embryogenesis of the interventricular septum may be appropriate for understanding these studies. It has been known for more than a century that two different muscular tissues join to form the septum. One, growing from below, arises as an invaginating septum at the apex of the ventricular loop. It is often referred to as the muscular part of the interventricular septum. The other, growing from above, is an extension into the outflow tract (the bulbus cordis) of a septum that spirals down the truncus arteriosus to divide it into a pulmonary artery and an aorta. In the truncus, this septation is fibrous. Its extension into the bulbus, following the two bulbar ridges, is muscular and is called the bulbar part of the interventricular septum. Thus, the closing of the interventricular septum depends upon these two muscular septa, each derived from relatively opposite ends of the ventricular loop, meeting, overlapping, and fusing.

In studying the final stages of septal closure, embryologists have been most interested in the formation of the membranaceous septum. But this is only one place where the two tissues meet, and in the adult heart it is a relatively small region of the zone of fusion. The pathway of fusion extends from the membranaceous septum laterally to the general region of the moderator band. Then, since bulbar musculature is found only on the right ventricular surface of the interventricular septum, there is a large area of fusion of the two tissues where the invaginating septum grows over the posterior surface of the bulbar musculature to form the outflow tract of the left ventricle. While the sequence of events leading up to fusion of the membranaceous septum have been extensively and repeatedly studied, there appears to have been no study of the events leading to the fusion elsewhere of the two tissues.

Results

The Normal Right Ventricular Outflow Tract

The septal surface of the right ventricular outflow tract normally has the dimensions of an isosceles triangle. The three apices of this triangle are the midpoint of the base of the posterior cusp of the pulmonic valve, the point where the moderator band emerges from the septal surface, and the point where the tricuspid ring crosses the membranaceous septum. Normally the three points are relatively equidistant from one another. This triangle in turn is congruent with a larger triangle representing the entire right ventricular septal surface. The relationship between the two triangles is useful in studying distributions of hypertrophy and dilatation in the right ventricle. Normally the distance from the posterior pulmonic valve to the membranaceous septum is relatively equal to the distance from the membranaceous septum to the posterior sulcus of the heart, and these two dimensions span the flow path in the right ventricle.

In figures 1A, B, and C are shown schematically the major directional components of the normal human bulbar musculature and their relationships to tricuspid, pulmonic, and aortic orifices and to left ventricular musculature. There are no discrete, isolatable fiber masses as the figures would suggest, but many gradations of fiber direction and abundant fiber continuities among these components. The schemata are to be viewed as graphs, demonstrating the major but by no means the only directional components of right ventricular outflow musculature.

There have been no previous detailed studies of this musculature. Mall had concluded
that "the muscle bundles of the conus form relatively simple rings which attach themselves to the root of the aorta," and Tandler,\(^1\) the most thorough student of cardiac musculature, considered there was too much individual variation to permit detailed description. Neither of these views is correct. All components shown in the diagrams have been identified in every normal human and dog heart studied, and there is remarkably little variation in their directions and relationships from heart to heart.

In general, there are two layers of muscular components that form the intrinsic musculature of the right ventricular outflow tract. The superficial components are more complex and tend to have superior-inferior directions with their major mechanical effect apparently to shorten the outflow tract. The deeper layer, on the other hand, is simpler and has a horizontal direction, which, on shortening, would narrow the outflow tract.

The superficial layer consists essentially of three components (fig. 1A). They are best studied by first identifying the posterior cusp of the pulmonic valve for, at the midpoint of its base, can be seen a crease that separates two important components in this layer. (The crease is often best seen by first peeling off the fibrous sheet of endocardium overlying it; Keith\(^8\) called this crease the infundibular raphe.) Lev\(^9\) has named the two components the septal bundle (inserting on the left side of the cusp) and the parietal bundle (inserting on the right side of the cusp). From the embryologic data of Kramer,\(^4\) Kjellberg\(^10\) and Lev\(^9\) have suggested that these two components are developed from two bulbar ridges, extensions of the ridges in the fetal truncus arteriosus which fuse to divide the truncus into the aorta and pulmonary artery. In hearts with truncus arteriosus, however, we have been able to identify a component in the ventricular wall having the location of the normal septal component and leading to a small moderator band, indicating that the septal component may develop normally even when the muscle ridges of the truncus are absent. Furthermore, in cases of transposition where the lie of the ridge is presumably markedly abnormal and perhaps reversed, the septal component with its moderator band contribution can often be seen to be in normal position. While the muscular ridges undoubtedly make important contributions to bulbar musculature, there are so many components in this region that it is probably unwise to ascribe particular ones to specific fetal structures until more is known about cardiac morphogenesis.

A third component of the superficial layer of bulbar musculature is one that inserts on the right side of the pulmonic ring, descends within the crista supraventricularis to course obliquely across the septum, and contributes a major part of the fibers of the moderator band. It can be called the oblique component (component 3 in fig. 1.1). It has not been previously described, perhaps because it is somewhat hidden by the parietal component, which often passes under, or interweaves through, or, less commonly, passes over in its course.

The moderator band is an exceedingly useful structure in interpreting the bulbar musculature. Even with the most painstaking dissection it has been impossible to identify the proportion of its fibers that are derived from each bulbar component. The oblique component appears to make the largest contribution, and contributions from the deeper component may be only secondary syncytial fusing. In the present series of cases, hearts with ventricular septal defects due to absence of the oblique component had no moderator band, or at most a very slender structure derived entirely from the septal component. Absence of the moderator band, whether or not associated with a ventricular septal defect, should be viewed as a congenital anomaly of cardiac musculature for it represents a disturbance in the joining of bulbar and ventricular components of the right ventricle.

Beneath the superficial muscular components of the bulbus is a deeper layer of musculature much less varied in direction (fig. 1B). It originates on the membranous septum and aortic-pulmonary tendon, sweeps laterally at right angles to the direction of

Circulation, Volume XXIV, August 1961
flow in the right ventricle, and curls anteriorly at the lateral margin of the right ventricle to merge in the right ventricular free wall, some portions also becoming continuous with the outermost layers of left ventricular musculature. The most inferior part of this layer originates from the membranaceous septum and contributes fibers to the moderator band. Cephalad is a thicker part originating from the aortic-pulmonary tendon. This tendon is a fibrous ring at the root of the aorta and a major site of insertion of left ventricular muscle. The tendon originates from the membranaceous septum and the right (anterior) trigone of the left ventricle; it meets a similar fibrous ring at the root of the pulmonary artery, and it inserts in the left (posterior) trigone (fig. 1C). Farther cephalad the deep bulbar musculature encircles the right ventricle immediately below the pulmonic ring, passing over the aortic-pulmonary tendon, where the latter extends posteriorly.
Beneath this deep bulbar layer is the superficial sino-spiral muscle bundle of the left ventricle (fig. 1C), but there is no cleavage plane between the two layers, and myocardial continuity is as evident here as elsewhere in the heart. Nevertheless, it is interesting that the septal branch of the left coronary artery, which arises from its parent artery immediately behind the pulmonary artery, tends to run most of its course in or near a plane separating the deep bulbar and the ventricular musculature, emphasizing the developmental independence of the two.

The structures that develop from the path of junction between the bulbar and ventricular musculature are of especial importance, for here will be encountered developmental anomalies whenever there is a disturbance in differentiation of bulbar or ventricular parts of the heart. The moderator band and the membranaceous septum are such junctional structures and have already been mentioned. The septal leaflet of the tricuspid valve also depends developmentally upon both bulbar and ventricular musculature and is often deformed in anomalies of this region. The horizontal ridge of musculature extending from the membranaceous septum to the moderator band, called the crista septomarginalis, is also a junctional structure; it is formed in the main from bulbar musculature, especially deep components and parts of the oblique component. This ridge is an especially useful landmark because it is usually easily identified and it serves to demarcate inflow from outflow tracts, and bulbar from ventricular musculature. Another junctional structure is the septal papillary muscle, also called Lancisi's papillary muscle, which subtends chordae tendineae of the anterior leaflet of the tricuspid valve. This is the only papillary muscle of the tricuspid valve that is derived entirely from bulbar musculature. Anatomically, it emerges from the septal surface of the right ventricle low in the outflow tract about midway between medial and lateral walls, but its muscle fibers are derived from the septal component of bulbar musculature, with some fibers coming from the oblique component. Here then is a structure that, from the origin of its muscle fibers to the insertion of its chordae, spans the diameter of the outflow tract, and for half of this distance lies free in the outflow stream of the right ventricular chamber. As a result, the size of the papillary muscle and the degree of its displacement from the septal component, where its fibers originate, may be gauges of the type and amount of hemodynamic stress in the outflow tract during development. Structures such as this offer ready, simple elements for approaching the architecture of the heart from a semi-quantitative point of view. Needless to add, abnormalities of this papillary muscle and its chordae are related to defects in fusion of ventricular and bulbar musculature and are often associated with malformation of the septal leaflet of the tricuspid valve.

Muscular Architecture of Ventricular Septal Defects

Congenital defects of the ventricular septum are of three general types according to location. 1. Defects at the A-V ring such as are seen in association with persistence of the ostium primum of the atrial septum and with A-V cushion defects. Almost certainly these defects are partly at least due to a fusion failure between bulbar and muscular septa, for they lie adjacent to the A-V ring beneath the junction of the septal and posterior leaflets of the tricuspid valve, for this is where the two septa meet. 2. Defects in the main body of the inflow tract of the right ventricle, the "muscular" septal defects. These are often circuitous, sinus-like tracts through the septum, margined by well-formed trabeculae carneae, and they usually are unassociated with other cardiac malformations. 3. Defects in the outflow tract of the right ventricle, the "bulbar" septal defects. These may lie anywhere in the triangle formed by the outflow tract and are frequently associated with other anomalies of the bulbar and truncal regions of the heart. They tend to be circular, smooth-edged, gaping holes communicating between the two ventricular chambers.

The difference in morphology between muscular and bulbar septal defects suggests that there may be a difference in their manner of development. At early fetal stages, the myocardium is a spongy sinusoidal mass, and it
RIGHT VENTRICULAR OUTFLOW TRACT

is not difficult to visualize the "muscular" septal defect as representing persistence of a type of sinus tract, where sinusoidal elements failed to be obliterated during later condensation of the myocardium. On the other hand, the round gaping character of the bulbar septal defect suggests that it is the result of failure of certain muscular components of the bulbus ever to develop, that a discrete part of bulbar musculature is absent.

This proves to be the case. When the hearts with bulbar defects were dissected with the schemata of figure 1 as a guide to normal musculature, in all hearts one or more directional components was found to be absent. The location of the defect in the outflow tract proved to be a function of the particular muscular component or components that had failed to develop, and the remaining musculature of the bulbus consisted of directional components that could be related to those present in the normal heart. This was especially easy to demonstrate in hearts with single, small defects. When the defect was large and associated with other complex outflow derangements, it was more difficult to be confident that the remaining bulbar musculature represented components present in the normal heart. On the other hand, it was in these hearts with extensive defects that the absence of specific components was most obvious. For example, in cases of persisting truncus arteriosus or so-called single ventricle, often there was only a single muscular component ridging the region where bulbar musculature would have been present. Usually it resembled the septal component in its origin and distribution, and no other bulbar musculature could be identified.

Kjellberg and his associates have suggested that in hearts with extensive defects the derangement may be due to displacement of one or both of the two bulbar ridges mentioned earlier that lie at opposite points on a diameter across the bulbus and are extensions of the spiraling truncal ridges that form the truncal septum. This hypothesis is derived in part from the once widely held notion that unequal size of pulmonary artery and aorta in congenital heart disease is due to eccentric growth of the truncal septum. Shaner, however, has offered convincing evidence that in most instances such inequality is a consequence of a hemodynamic abnormality resulting from the congenital lesion and not to eccentric septation. Among cases in the present study in which eccentric septation might have been expected, as in pulmonary atresia, structures known to be derived from the bulbar ridges, such as the membranous septum, were normally located. While the hypothesis of Kjellberg and his associates is plausible, in none of the hearts studied in this series was it needed to explain the bulbar musculature derangement.

A muscular defect communicating between right and left ventricles involves three layers of septal musculature, two bulbar and one ventricular, and the architectural defect at all three levels must be examined. As far as the superficial bulbar layer is concerned, after familiarity with the musculature by dissecting normal and abnormal hearts was acquired, it became possible to identify the absent component readily from the surface topography alone, without dissection. The deep bulbar layer was more difficult to evaluate because, unlike the superficial components, only part of a deep component might be absent in a given case. While the missing component in the superficial layer governed where the defect would lie in the outflow tract, the missing deeper component seemed to determine how big the defect would be and whether or not the foundation of the aortic root would be disturbed (i.e., whether or not "over-riding" or dextro-position of the aorta would be present).

On the other hand, at the third level (the left ventricular part of the septum), no specific bundle or component defect could be identified to indicate a basic architectural defect of this layer. The left ventricular fibers ramified and otherwise increased their numbers on each side of the defect, so that the general density, directions, and distribution of fibers in the left ventricular layers of the septum appeared to be unaltered by the defect.

This observation indicates that bulbar sep-
Two hearts with ventricular septal defects, with diagrams. Left, the defect is subvalvular and the moderator band is prominent. Right, only the parietal component is present bridging a large defect; there is no moderator band.

tal defects are primarily disturbances in growth and differentiating of bulbar musculature and only secondarily of ventricular musculature. Evidently, in the formation of the interventricular septum, the part invaginating from the apex of the ventricular loop grows upward until it meets the bulbar musculature, and it can only grow beyond this point when there is intact bulbar musculature over which to grow. When there is a defect in the bulbar musculature this invaginating tissue cannot grow across the defect but will grow around it. No heart has yet been seen by us or described in the literature in which bulbar musculature was absent and the septum was closed by ventricular tissue alone. This suggests that the bulbar musculature plays the role of an "organizer" tissue for ventricular muscle, in the embryologist's meaning of the term. Furthermore, it raises the possibility of other fundamental anatomic and biochemical differences between the two types of cardiac musculature, each derived from opposite ends of the primitive cardiac tube. In other studies, for example, preliminary findings suggest that the two musculatures may undergo hypertrophy differently.16

If the bulbar abnormality is confined to the superficial layers alone, and deeper bulbar layers are intact, there will be a bulbar derangement but no through-and-through septal defect. In a heart with absence of the moderator band, this proved to be the case, for there was no musculature having the direction of the oblique component. Absence of the moderator band or of the septal papillary muscle should be viewed as congenital cardiac defects even though no hemodynamic abnormality is produced.

It was mentioned that the particular location of a bulbar septal defect depends upon the location of the missing superficial bulbar...
RIGHT VENTRICULAR OUTFLOW TRACT

muscular component. To illustrate this, if the septal component and the high deep component are missing, the defect will be subvalvular in location. The case in figure 2 (left) is an example of this. The moderator band is present, indicating that the septal component is not a major contributor to this structure. If, on the other hand, the oblique and low deep components are absent, the defect will be adjacent to (and might include) the membranaceous septum. If both the septal and oblique components are missing, the heart illustrated in figure 2 (right) will result. Here, the only remaining bulbar muscle is the parietal bundle and its horizontal division extending from the crista supraventricularis to the lateral wall of the outflow tract. No moderator band is present. The entire width of the low deep component is absent. Although there seem to be two bulbar septal defects in this heart, actually it is only the bridging by the parietal component, the sole remaining major septal component, which divides the defect into two holes.

Earlier it was mentioned that the presence or absence of the deep bulbar component governs the relationship of the aortic root to the septal defect. As shown in figure 1, the deep component inserts on the aortico-pulmonary tendon at the root of the aorta immediately proximal to the aortic cusps. If this muscular layer is absent (combined with the fact that left ventricular tissue cannot grow where there is no bulbar musculature) the anterior lip of the aorta will no longer have an attachment to the left ventricle, and will be supported solely by musculature of the free wall of the right ventricle (components 5, 6, and 7 of figure 1B). As a result, the right ventricular chamber will open directly into the root of the aorta. This appears to be the anatomic explanation for over-riding or dextro-position of the aorta in hearts with ventricular septal defects.

In the past, over-riding has been considered to be due to an abnormal position of the aortic root in the skeleton of the heart. Edwards20 and Schoenmakers21 pointed out that this was probably not the case, and suggested that it was due to the fact that the aorta at its root curls sharply anteriorly against the crista supraventricularis. A defect high in this region would indeed "look" into the root of the aorta. More direct proof that there is no abnormality of the skeleton of the heart in this disorder was obtained in the course of other studies that will be reported in greater detail elsewhere.22 Fine silver wire was threaded along the rings of all four ventricular orifices (mitral, tricuspid, aortic, and pulmonic) and along certain other ventricular landmarks in a series of normal hearts and hearts with various cono-truncal abnormalities including over-riding aorta. Roentgenograms in two planes at right angles to each other were obtained for each specimen. By use of methods of descriptive geometry, three-dimensional measurements were made of the location of the orifices in relation to each other and to other ventricular structures. In all cases of over-riding aorta the aortic orifice was in completely normal position with respect to the skeleton of the heart.

What is the architectural basis for the muscular stenosis so frequently seen in the infundibulum in hearts with bulbar septal defects? This is a much more difficult problem to study and will require extensive detailed fiber counts and measurements among the bulbar muscular components in normal and abnormal hearts before the answer can be given confidently. From the gross method of dissections used in the present study, in these hearts at least, the stenosis was due to selective hyperplasia of individual bulbar muscular components, and the particular location of the hypertrophied component or components determined where in the outflow tract the stenosis would occur. For example hypertrophy of the septal component alone cannot obstruct outflow. When the septal component is hypertrophied along with the parietal component, the stenosis will be immediately subvalvular. If there is no accompanying hypertrophy of the septal component, a small infundibular chamber between the site of obstruction and the pulmonic valve will result. On the other hand if the oblique component is hypertrophied, the obstruction will lie much lower in the outflow tract, adjacent to the...
GRANT, DOWNEY, MacMAHON

Figure 3

Infundibular stenosis low in the outflow tract due to hyperplasia of the oblique component. Upper left, the reconstructed heart viewed frontally as it lay in the chest. Upper right, the right ventricular chamber viewed from above through the infundibulum. The marked narrowing of the chamber at mid-position is seen. Below, the free wall of the right ventricle is reflected for a frontal view of the right ventricular septal surface, which is shown in the diagram at right; the cut surface of right ventricular free wall is shaded.

moderator band. The heart in figure 3 illustrates this, an example of a "three-ventricle" heart.

These findings suggest that infundibular stenosis is a basic part of the growth abnormality in ventricular septal defects rather than a secondary adaptation of the heart to the hemodynamic abnormality produced by the septal defect. It has been pointed out that injury to pre-differentiated tissue can result in either overgrowth or arrest of growth of the tissue. From the present studies it is suggested that in these bulbar syndromes injury to pre-differentiated bulbar primordia results in overgrowth of the bulbar muscular component in some hearts (infundibular stenosis without a septal defect); in other hearts certain components are arrested while other components overgrow (ventricular septal defect with infundibular stenosis); and in still other hearts arrest of growth alone takes place (simple ventricular septal defect if both layers of bulbar musculature are involved; topographic disturbances, such as absence of the moderator band without a transseptal defect, if only the superficial layer is involved). Thus it seems a likely hypothesis that the ventricular septal defect and the stenosis are both due to the same primordial injury in a given case, and whether hypertrophy, or defect, or both will occur is, perhaps, a function of the severity or timing of the damage to primordia of specific muscular components.

Discussion

While this study has been mostly concerned with the nature of outflow-tract architecture in normal and abnormal hearts, one of its re-
Figure 4

Schema of the valvular abnormality in Ebstein's anomaly. The heart is viewed frontally as it lies in the chest, and the right ventricular free wall is made transparent. Arrows indicate pathways of blood flow. Above, the normal tricuspid valve; below, two degrees of malposition of tricuspid valvular tissue. The valve inserts on the septum along the path of fusion of bulbar and ventricular myocardium. The difference in degree of deformity is due to differences in the extent to which lower parts of the tricuspid valve leaflets are displaced.

Results has been to direct attention to a region of the heart where congenital malformations occur that has not been greatly appreciated in the past. This is the zone of junction between bulbar and ventricular musculature. This is the zone dividing inflow from outflow tracts and extends from the membranaceous septum and septal leaflet of the tricuspid valve on the medial side of the right ventricle to the region of emergence of the moderator band laterally. For example, the ventricular abnormalities that may be associated with per-
sistence of an ostium primum lie in this zone: the ventricular septal defect lies beneath the septal cusp of the tricuspid valve, the cleft in the anterior leaflet of the mitral valve runs up to the A-V ring at this same point, frequently there is a malformed septal leaflet of the tricuspid valve, aneurysm or multiple perforations of the membranaceous septum, etc., all lesions in this junctional zone. Almost certainly the left axis deviation seen electrocardiographically in this syndrome is another result of the faulty fusion of bulbar and ventricular septum. Evidently there is a disturbance in the development of the anterior division of the left bundle branch, for this division normally is distributed on the portion of left ventricular muscle that grows over the bulbar musculature to complete the interventricular septum.

Another syndrome that appears to be due in part at least to an abnormality at the junction of ventricular and bulbar musculature is Ebstein's anomaly. Here the line of attachment of the displaced septal and posterior rim of the tricuspid valve is near or within, but never beyond, this zone of junction from membranaceous septum to moderator band (fig. 4). The portion of the tricuspid valve which affixes to the membranaceous septum is often the only part normally attached. The only hearts with obliteration of the membranaceous septum by musculature that we have seen are two cases of Ebstein's anomaly. Goerttler, on the basis of embryologic studies, first suggested that Ebstein's anomaly might be due to a defect of growth during the stage of invagination of the ventricular loop to form the septum, and our observations give circumstantial evidence that tends to confirm this hypothesis. With greater appreciation of the anatomy of this region, no doubt other developmental anomalies will be identified that are related to the manner in which bulbar and ventricular musculatures fuse to form the septum.

Another major purpose of this study has been to bring quantitative methods into the study of cardiac morphology. Understanding of cardiac function can never be complete until its morphology as a pump is also understood. Progress in cardiac physiology has depended almost entirely upon developing methods for quantifying physiologic processes. To discover the quantifiable elements of the morphology of the heart is the challenge for cardiac pathologists. Since morphology is a problem in surfaces and spaces, the quantifiable elements and mathematical tools will be different from those used by the physiologist or the biochemist. In the outflow tract of the right ventricle, for example, the quantifiable elements prove not to be discrete muscle bundles, but directional properties of a densely syncytial musculature. The particular array shown in figure 1 is, then, more a graph than a picture of a muscular system. Furthermore, as in all graphs, it is a generalization and simplification in order to have a manageable schema upon which to begin to erect an understanding of the architecture of this region of the heart.

Conclusions

Detailed dissections of the musculature of the right ventricular outflow tract were performed in a number of normal and congenitally abnormal human hearts. In cases of bulbar ventricular septal defects the dissections disclosed absence of one or more components of bulbar musculature, with the remaining musculature made up of directional components that could be related to those seen in normal hearts. It is concluded that the bulbar ventricular septal defect is not due to failure of bulbar components to fuse, but to failure of certain muscular components ever to develop; and the particular location of the septal defect in the outflow tract is a function of the lie of component or components that failed to develop.

Over-riding or dextro-position of the aorta is shown to be not due to an abnormality of the location of the aorta with respect to the skeleton of the heart, but due to failure of certain deeper bulbar muscular components to develop. As a result, the septal edge of the aortic ring no longer attaches to left ventricular musculature, and therefore the aorta faces directly into the right ventricular chamber.

The muscular hypertrophy accounting for
RIGHT VENTRICULAR OUTFLOW TRACT

infundibular stenosis also appeared to be confined to certain directional components of bulbar musculature, with actual hyperplasia of that component. The location of the stenosis in the outflow tract depended upon which component had undergone hyperplasia. It is suggested that in outflow tract anomalies, septal defects and the infundibular stenoses are both direct consequences of a primordial injury, and whether a given component fails to develop or undergoes hypertrophy may depend upon the severity or timing of the damage to that component.

Congenital anomalies of the right ventricular outflow musculature are of two types. 1. Defective development of intrinsic bulbar muscular components; ventricular septal defects and infundibular stenosis, whether or not associated with other anomalies, are examples of this. 2. Defects in the manner by which normally elaborated bulbar musculature joins and fuses with the invaginating ventricular septum to form a closed ventricular septum. Examples of this include the ventricular anomalies associated with persistent ostium primum and with A-V communis; other examples are Ebstein’s anomaly, defects and aneurysms of the membranous septum, and absence of the moderator band. With greater awareness of this zone where ventricular and bulbar musculature meet, no doubt other examples of coupling anomalies will be discovered.

Acknowledgment

The authors wish to acknowledge the generous assistance of persons who gave or loaned specimens for this study. In particular, we wish to thank Drs. Harold Stewart and Louis Thomas, of the Department of Pathology, Clinical Center, National Institutes of Health, Bethesda, Maryland, for their cooperation and assistance. Specimens were also made available by Dr. William Manion, of the Armed Forces Institute of Pathology, and Dr. Madison Spock, of the Department of Pediatrics, Duke University Medical School.

References

12. Wolff: 1791, cited by Tandler.1
22. Downey, F. M., and Grant, R. P.: To be published.
The Architecture of the Right Ventricular Outflow Tract in the Normal Human Heart and in the Presence of Ventricular Septal Defects
ROBERT P. GRANT, FRED M. DOWNEY and HUGH MACMAHON

Circulation. 1961;24:223-235
doi: 10.1161/01.CIR.24.2.223
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1961 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/24/2/223.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/