

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



The Junction Between the Left Atrium and the Pulmonary Veins: An Anatomic Study of Human Hearts

H. NATHAN and M. ELIAKIM

Circulation 1966;34:412-422

Circulation is published by the American Heart Association. 7272 Greenville Avenue,
Dallas, TX 75214

Copyright © 1966 American Heart Association. 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>

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

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2436. Phone: 410-528-4050. Fax: 410-528-8550. E-mail: journalpermissions@lww.com

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

The Junction Between the Left Atrium and the Pulmonary Veins

An Anatomic Study of Human Hearts

By H. NATHAN, M.D., AND M. Eliakim, M.D.

THE SPHINCTER-LIKE FORMATIONS and the myocardial sleeves which have been described around the pulmonary veins in the dog have been generally found to be better developed in the superior than in the inferior vessels.¹ The present study on human hearts was undertaken because, to the best of our knowledge, no detailed description of the structural differences in the various pulmonary veins at their junctions with the atrium have hitherto been reported. Apart from anatomic accuracy it is believed that such differences in the atrial-venous junctions may be of physiological and pathological importance. In addition, with further development of surgical techniques, knowledge of these differences may prove to be of value to the cardiac surgeon.

Methods

The study was made on 16 hearts obtained from autopsies performed in the Jacobi Hospital,* New York. These included whites and Negroes, both males and females. The patients were aged 16 to 63 years. The hearts were removed together with the pulmonary vessels and a part of the lungs. The superior caval vein was cut above the opening of the azygos vein; the inferior caval vein was cut at the level of the diaphragm. The atria were separated from the ventricles at the level of the atrioventricular sulcus. They could then be examined from both the inner and outer sides. The thickness of the posterior wall of the left atrium was measured by means of a micrometer caliper provided with a ratchet stop, which allowed measurement at a constant pressure, and a vernier, which permitted reading with an accuracy of 0.1 mm. Measurements were made between the entrance of: (1)

From the Department of Anatomy, Hebrew University-Hadassah Medical School, and the Department of Internal Medicine B, Hadassah University Hospital, Jerusalem, Israel.

*Jacobi Hospital is affiliated with the Albert Einstein College of Medicine, New York.

the right and left superior pulmonary veins; (2) the right and left inferior pulmonary veins; (3) the right superior and inferior pulmonary veins; (4) the left superior and inferior pulmonary veins.

Each specimen was cleaned of remnants of pericardium, fascia, vessels, and nerves, in order to expose the myocardial fibers as clearly as possible. Stuffing of the atria and the large vessels with cotton facilitated the dissection. The natural color of the myocardium was better retained in fresh specimens or those preserved at 4 C, while Formalin fixation was satisfactory for following the course of the fibers and fascicles. Particular attention was paid to the atrial-venous junction and the extension of the myocardial fibers in the pulmonary veins. The length of the myocardial venous sleeves at the various sites of the venous wall and the length of the extrapulmonary portion of the veins were also measured. Schematic drawings of the course of the myocardial fibers and photographs of the dissected specimens were made in all cases.

Observations and Descriptions

A common pattern in the arrangement of the superficial myocardial fibers of the atria was observed in most of the specimens and will be described first. Individual variations from the common pattern, as well as particular characteristics of the atrial venous junction of each of the pulmonary veins, will then be given in detail.

Common Basic Patterns (Fig. 1)

The common basic pattern consists of a main circular fascicle of fibers (a, a', a'', a''') running peripherally around the area of the openings of the pulmonary veins in the left atrium. The upper part of this fascicle (a), running horizontally above the right and left superior pulmonary veins, is formed by:

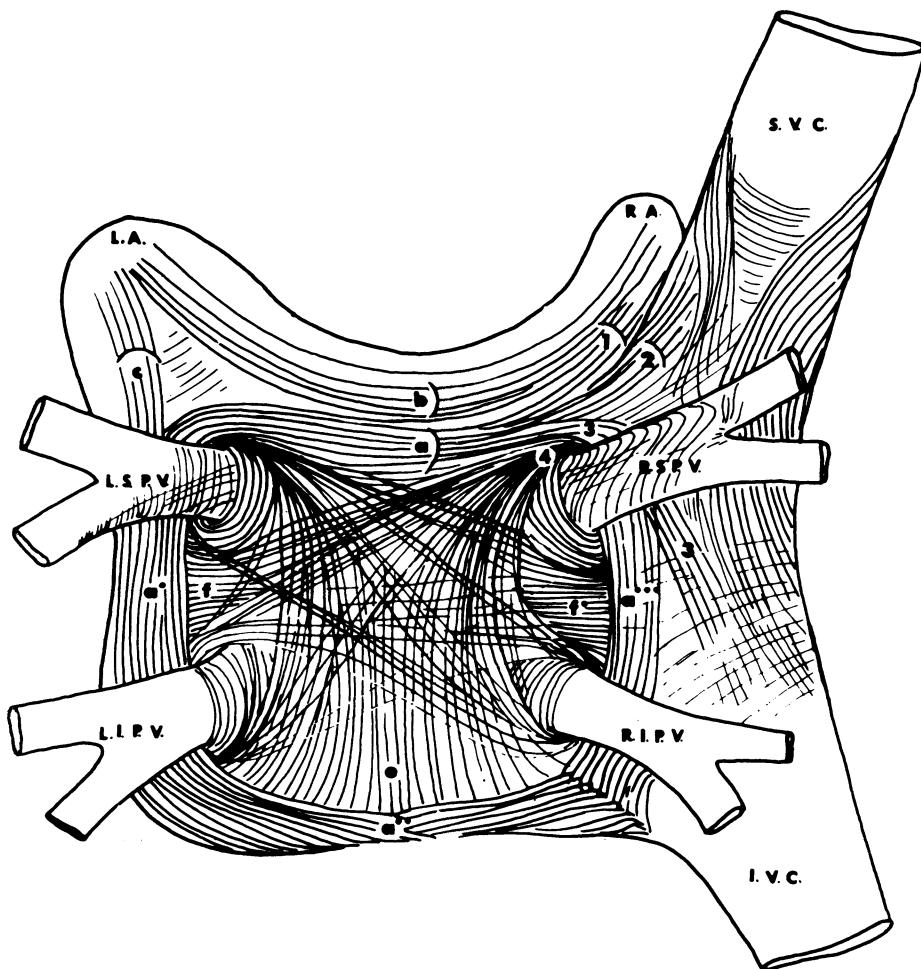


Figure 1

The common pattern of the superficial myocardial fibers of the left atrium (posterior aspect). A main circular fascicle (a , a' , a'' , and a''') runs peripherally around the area of the openings of the pulmonary veins. An interatrial fascicle (b) runs between the right (RA) and the left (LA) atrium. Some fibers (c) descend from the left atrium into the left part (a') of the main circular fascicle. Circular fibers leaving the main fascicle turn around the openings of the pulmonary veins, forming sphincter-like structures; other fibers extend over the veins as myocardial sleeves. Loops of fibers coming from the atrium are seen over the right superior pulmonary vein (R.S.P.V.) and returning to the atrium. Oblique, vertical (e), and transverse (f , f') fascicles of fibers are also seen on the posterior atrial surface. L.A. = left atrium; R.A. = right atrium; S.V.C. = superior vena cava; I.V.C. = inferior vena cava; R.S.P.V. = right superior pulmonary vein; L.S.P.V. = left superior pulmonary vein; R.I.P.V. = right inferior pulmonary vein; L.I.P.V. = left inferior pulmonary vein.

- (1) fibers descending from the right atrial appendage;
- (2) fibers descending from the wall of the superior caval vein;
- (3) fibers ascending from the right atrium; and
- (4) fibers of the right side of the same main circular fascicle (a'''), which ascend and turn to the left, around the right superior pul-

monary vein. A bunch of fibers descending from the right atrial appendage forms a broad "interauricular fascicle" (b) which ends in the left atrial appendage. Most of the fibers of this interatrial fascicle run parallel and intermingle partially with the upper part (a) of the main circular fascicle. Other fibers (c)

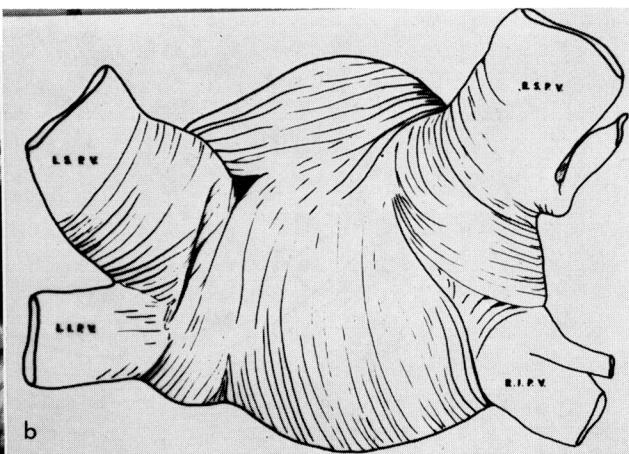
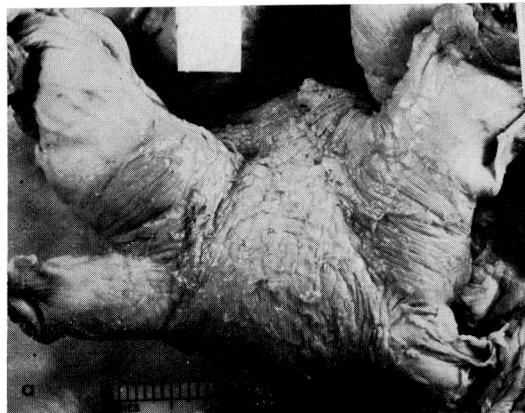


Figure 2

Predominant vertical pattern: (a) posterior aspect of left atrial specimen; (b) schematic representation. Note that the myocardial sleeves are better developed around the superior pulmonary veins than around the inferior veins.

descend from the left atrium into the left part (a') of the main circular fascicle. Many fibers of the main circular fascicle end in the atrioventricular fibrotic rings, while new fibers arise from these rings. In the immediate vicinity of each of the pulmonary veins, muscle fibers leave the main fascicle and turn around the opening of these veins, forming a sphincter-like structure; some of these circular fibers may extend to a greater or lesser degree over the vein, contributing to the formation of the myocardial sleeves which cover the venous walls to a variable distance. Other

fibers leaving the main fascicle run obliquely on the posterior surface of the left atrium toward the openings of other pulmonary veins, forming more or less conspicuous oblique fascicles. Another layer of fibers is seen appearing from beneath the main circular fascicle (e, f, and f') on the posterior surface of the left atrium. The fibers of this layer, which are situated between the right and left inferior pulmonary veins, run a vertical course (e), while those between the superior and inferior right or left pulmonary veins run a transverse horizontal course.

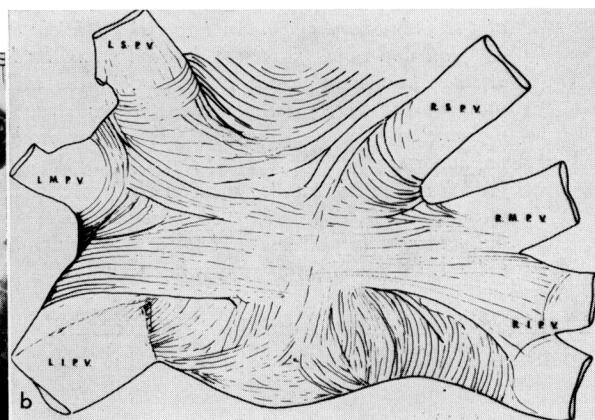
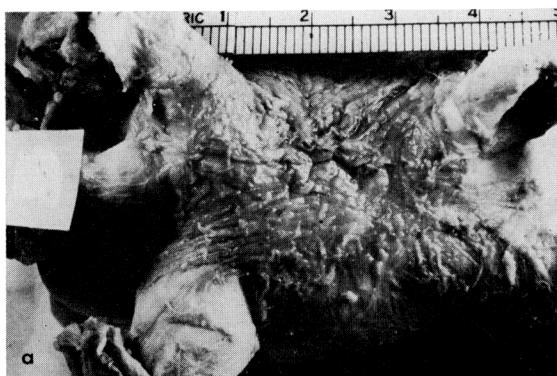


Figure 3

Predominant horizontal pattern: (a) posterior aspect of left atrial specimen; (b) schematic representation. Three veins are present on each side.

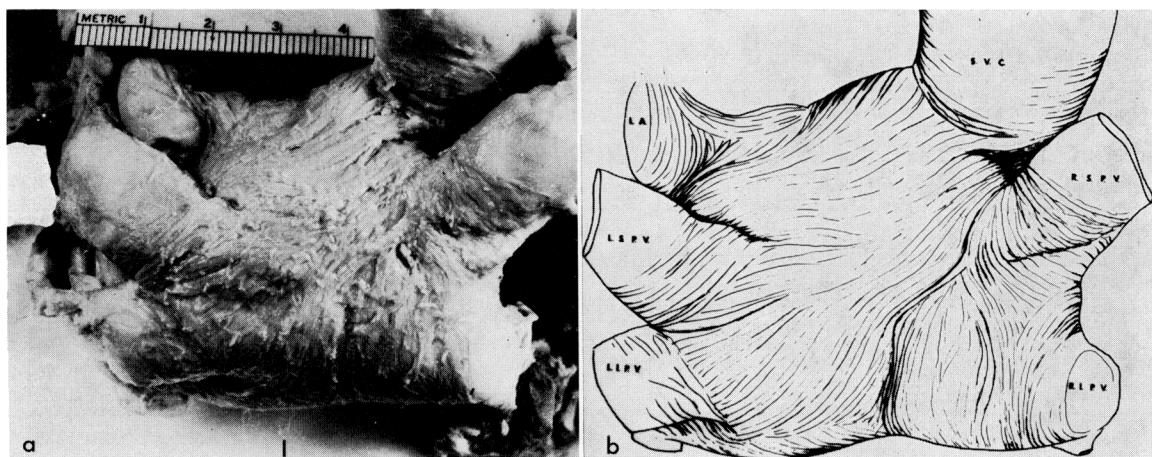


Figure 4

Predominant oblique pattern: (a) posterior aspect of left atrial specimen; (b) schematic representation. The sphincters are better developed around the superior than around the inferior pulmonary veins. The right inferior pulmonary vein was cut close to the atrium.

Therefore, the area of the left atrium, circumscribed by the openings of the pulmonary veins, is crossed by myocardial fibers running in all directions, obliquely, transversely, and vertically, intermingling and decussating each other. The predominance of certain groups of fibers running in the same direction but more superficially than the others gives the individual characteristics to each specimen (figs. 2 to 5).

Individual Variations in Arrangement of Myocardial Fibers in the Left Atrium, Atrial-Venous Junctions, and Myocardial Venous Sleeves

The predominant direction of the fibers in the posterior surface of the left atrium, between the various pulmonary veins, is variable, and different patterns were found. The most frequent patterns, according to the direction of the fibers, were the following: (1) vertical, where the main predominant fascicles are

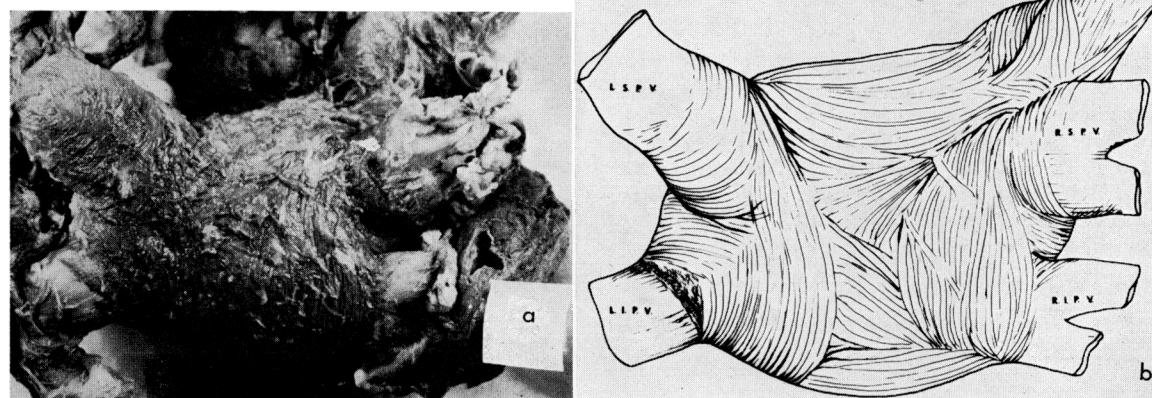


Figure 5

"Mixed" pattern: (a) posterior aspect of left atrial specimen; (b) schematic representation. Fascicles of vertical fibers are seen close to the pulmonary veins on both sides. Oblique fibers are seen between the vertical fibers. The myocardial sleeve and the sphincter of the left inferior pulmonary vein is less conspicuous than those of the other veins.

formed by the vertical fibers (fig. 2); (2) horizontal, where the superficial fascicles are formed predominantly by the transverse fibers (fig. 3); and (3) oblique, where the predominant superficial fascicles ascend obliquely, most frequently from left to right (fig. 4).

The oblique and vertical patterns are the most common, while the horizontal is less frequent. In some cases the fibers cross each other and intermingle in such a manner that no predominance of direction is observed (fig. 6). In other cases (fig. 5), a predominant fascicle running in a certain direction is split, and fibers running in other directions appear between the cleaved fibers.



Figure 6

"Mixed" pattern: The muscular fibers in this specimen intermingle with each other with no predominant direction. The left part of the atrial wall, adjacent to the left superior and inferior pulmonary veins (arrow), is devoid of myocardium. In contrast to the right pulmonary veins, the left pulmonary veins have no myocardial sleeves and sphincters.

The results of the measurements show that the atrial wall is not uniformly thick (table 1). The upper part of the left atrial wall, particularly the area between the right and left superior pulmonary veins, was consistently found to be thicker (average 1.8 mm) than the inferior part, between the right and left inferior pulmonary veins (average 1.0 mm). The former area appears as a decussation center of the main fascicles of the posterior atrial wall. No significant differences were found between the thickness of the right and left sides of the posterior atrial wall (average 1.0 and 0.8 mm, respectively). In some specimens, the atrial wall adjacent to the openings, generally of the inferior pulmonary veins, appeared totally devoid of muscle fibers (fig. 6). The atrial wall at these sites was very thin and consisted only of endocardium covered with some connective tissue and the pericardium.

Atrial-Venous Junctions and Myocardial Sleeves Extending over the Pulmonary Veins

The atrial-venous junctions, as mentioned previously, were formed mostly by the sphincter-like fibers which, leaving the mean circular atrial fascicle, turn around and embrace the openings of the pulmonary veins (fig. 1). Longitudinal fibers from the main circular and the oblique fascicles may also continue over the veins. Marked variations, however, may be found between the pulmonary veins of the same specimen as well as between different specimens. The sphincters around the superior pulmonary veins were in general somewhat thicker and more conspicuous than those around the inferior veins (figs. 2, 4, and 7). In most of the specimens, myocardial sleeves extended over the pulmonary veins

Table 1

Thickness of Posterior Surface of Left Atrial Wall at Four Different Sites (Between the Pulmonary Veins)

| | Thickness of left atrial wall (mm) between | | | |
|---------|--|-----------|-----------|-----------|
| | RSPV-LSPV | RIPV-LIPV | RSPV-RIPV | LSPV-LIPV |
| Range | 1.0 — 4.2 | 0.6 — 1.8 | 0.6 — 1.7 | 0.4 — 1.4 |
| Average | 1.8 | 1.0 | 1.0 | 0.8 |

RSPV and LSPV = right and left superior pulmonary veins; RIPV and LIPV = right and left inferior pulmonary veins.

Circulation, Volume XXXIV, September 1966

for a variable distance (table 2). In some veins the sleeves extended as far as the hilus of the lung, or even beyond it. On the other hand, some veins, more often the inferior than the superior ones, had no myocardial extensions (figs. 2, 4, and 7). Furthermore, as previously mentioned, the atrial wall adjacent to these veins sometimes appeared devoid of myocardium (fig. 6).

The myocardial sleeves were formed by one or more layers of fibers running in circular, longitudinal, oblique, and spiral directions. Loops of fibers leaving the atrium and returning to it after covering the venous wall to a variable distance were seen very often (fig. 1). The free border of the muscular sleeves generally ran an oblique course, that is, its distance from the atrium was different on the various sides of the venous wall. Here, again, the superior pulmonary veins were found to have longer and better developed myocardial sleeves than the inferior veins (table 2) (average values R.S.P.V., 13 mm; R.I.P.V., 8 mm; L.S.P.V., 18 mm; L.I.P.V., 10 mm) (figs. 1, 2, 4, 5, and 7). When a pulmonary vein branched off, the myocardial sleeve, if present, was sometimes seen to accompany both branches (fig. 7); in other cases, however, it continued in only one of the branches. Measurements of the length of extrapulmonary portions of the pulmonary veins, as well as the length of the veins from the heart to the first division, are also presented in table 2.

Variations in the number of pulmonary vein openings into the atrium are well known and were also observed in our specimens. The general pattern of arrangement of the myo-

cardial fibers varied accordingly in each of these cases.

A very conspicuous myocardial sleeve consistently extended from the right atrium over the superior caval vein, at an average distance of 24 mm (table 2), while over the inferior caval vein such extensions were either absent or very small (fig. 1).

Embryological Considerations

The variations in the pattern of arrangement of the atrial myocardium at the atrial-venous junctions and the myocardial extensions over the veins should be analyzed in the light of the embryological development of the atrium and the veins.²⁻⁸ It is well

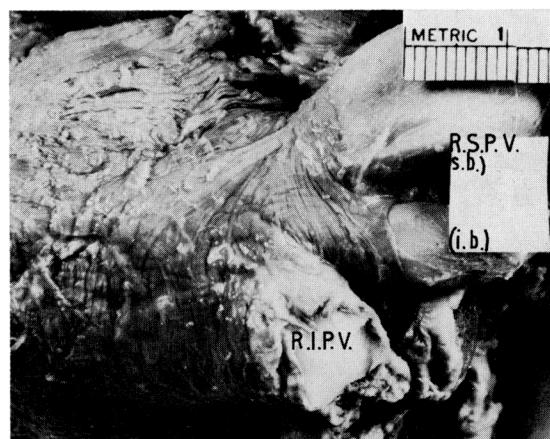


Figure 7

The right superior pulmonary vein (R.S.P.V.), which divides into two branches close to the atrium, has a very well developed muscular sphincter and a myocardial sleeve which extends beyond its division over both branches. On the other hand, the right inferior pulmonary vein (R.I.P.V.), cut close to the atrium, shows no muscular extension.

Table 2

Measurements of Myocardial Sleeves Covering the Pulmonary and Caval Veins and the Total Extrapulmonary Portion of the Pulmonary Veins (Fifteen Specimens)

| | Length of the myocardial sleeves extending over the veins (mm) | | | | | | Length of extrapulmonary portions of pulmonary veins (mm) | | | | |
|---------|--|------|------------|------|-------|-------|---|-------|-------|-------|----|
| | Pulmonary veins | | Vena cavae | | | | RS | | RI | LS | LT |
| | RS | RI | LS | LT | S | I | RS | RI | LS | LT | |
| Range | 5-25 | 1-17 | 8-24* | 1-19 | 15-33 | 8-10† | 20-42 | 10-30 | 12-38 | 13-31 | |
| Average | 13 | 8 | 18 | 10 | 24 | 9 | 30 | 21 | 29 | 20 | |

*In one specimen there was no myocardial sleeve.

†Sleeves were found in only three specimens.

known that the atria arise developmentally from two different parts: (1) the original atrial part of the cardiac tube, and (2) the venous sinus and the originally single pulmonary vein, which are absorbed and incorporated in the right and left atrial walls, respectively. Like the myocardium of the ventricles, the myocardium of the original atrium develops early from the epicardial mantle. On the other hand, the atrial wall of venous origin is totally devoid of myocardium at the beginning,³ and the muscle develops only in the later stages. We were unable to find specific descriptions of the embryological process of myocardial formation in the venous part of the atrial wall and the muscular sleeves extending over the pulmonary veins. As far as we are aware, it is not known whether this myocardial formation results from a differentiation of the mesodermal tissue around the venous wall or from invasion of muscle fibers of epicardial mantle origin. Whatever the process may be, it seems that the formation of the atrial wall by absorption of the embryonal pulmonary vein and its main branches and by its later muscularization is a main factor in determining the anatomic variations in this area, that is, the different number and length of the main pulmonary veins, variations in the arrangement of the myocardial fascicles in the posterior wall, the venous junctions, and the myocardial venous sleeves.

Discussion

Most anatomic treatises confine themselves to very general descriptions of the superficial cardiac musculature of the atria, mentioning in particular the horizontal interatrial fascicle, the vertical fascicle, and the circular fibers around the venous openings. Although detailed descriptions of the atrial musculature may be found in the literature,⁹⁻¹² to the best of our knowledge no descriptions of the *variations* of the superficial fascicles on the posterior atrial wall and the atrial-venous junctions are available. The myocardial-venous sleeves, although mentioned by Wale¹³ as early as 1641, have usually been neglected both by anatomists and physiologists.

In his early description, Wale¹³ reported the presence of the "fleshy fibers" covering the vena cava in the proximity of the heart of man, ox, and dog. He also observed that every heart movement starts in the vena cava. Striated muscle in the walls of the pulmonary veins was described by Rauschel,¹⁴ in 1836, and later by Elischer,¹⁵ Arnstein,¹⁶ and Stieda.¹⁷ The last two authors^{16, 17} used the term "atrial sheath" and described its presence in several species including man. Since then the presence of striated cardiac muscle around the pulmonary veins in different species, including man, has been confirmed both macroscopically and histologically by numerous investigators.¹⁸⁻³¹ The distance to which striated muscle stretches into the pulmonary veins has been found to vary from one species to another, and in many cases it reaches the small vein divisions in the lungs.¹⁸ According to Favaro¹⁹ the smaller the animal the deeper the cardiac muscle penetrates in the veins within the lung. In the albino rat striated muscle occupies the entire medial layer of the pulmonary veins which, significantly enough, are devoid of smooth muscle.²⁸ Benninghoff²⁰ and Bargmann and Doerr²⁷ described the myocardial sleeves in man as extending to the pericardial reflexion line, while Amano²¹ observed them as far as 15.8 mm beyond that line, and in fetuses even in the intrapulmonary portion of the veins. Our own observations in the present and previous studies¹ have confirmed that, in man and dog, atrial striated muscle may extend as far as the lung border and beyond it.

The function of the cardiac muscle in the pulmonary venous wall has not been investigated thoroughly. Three possible functions have been considered:

1. Throttle Valve Action

It is generally believed that the venous sphincters and sleeves exert a valve action that prevents reflux of blood from the atrium into the veins during systole.²²⁻²⁶ This concept has been supported by the roentgenological observations of contraction of the atrial-venous junction during systole in man.³² Closure of the atrial-venous junctions has also been

described in dogs³³ in experimental conditions, when the pulmonary venous pressure falls below 6 to 7 mm Hg.

2. Active Expulsion of Blood into Left Atrium

The finding of striated muscle in the entire media of the pulmonary vein of the rat has led to the assumption that its contraction in association with the cardiac activity facilitates the filling of the left atrium during diastole. Systolic contractions of the extrapulmonary portion of the pulmonary veins have actually been observed in the rat and mouse.^{13, 30, 34-36} In hypothermic newborn mice the sequence of contractions was found to be: veins, atria, and ventricles.³⁰ Interestingly, Hooker and associates³⁰ observed that the veins may sometimes transmit their contractions to the ventricles without a visible atrial contraction. Carrow and Calhoun³¹ suggested that a peristaltic or "milking" action toward the heart was produced by the contractions of the myocardial fibers which run from the atrium over the veins and back to the atria again.³¹

3. Regulation of Pulmonary Venous Pressure and Blood Flow

The basic tonus of the striated muscle and its possible changes due to various physiological and pharmacological stimuli may be of importance in the regulation of the pulmonary venous pressure and blood flow. The pressure-flow relationship of the extrapulmonary portion of the pulmonary vein in dogs has been recently investigated; increasing flow rates were found to raise the pulmonary venous pressure and decrease the venous resistance.³⁷ A similar decrease in pulmonary venular resistance with increased flow rates was later reported by Kuramoto and Rodbard.³⁸

The pulmonary veins are also capable of reacting to many different pharmacological and physiological stimuli. Spasm of the large pulmonary veins *in vitro* has been produced by anoxia, acetylcholine, epinephrine, and histamine.^{39, 40} A venoconstrictive effect of carbon dioxide in the isolated perfused lung of the cat⁴¹ and dog⁴² has also been demonstrated. Other stimuli causing pulmonary ve-

nous constriction in intact animals or man are: hypoxia,⁴³⁻⁴⁵ steam inhalation,⁴⁶ starch embolization,⁴⁷ endotoxin,⁴⁸ alloxan,⁴⁹ serotonin,^{37, 50-53} histamine,^{37, 50, 51} epinephrine and norepinephrine,^{37, 50} acetylcholine,³⁷ and hypertonic solutions.^{1, 54} Stimulation of the stellate ganglion³⁷ as well as of the aortic body chemoreceptors⁵² also lead to pulmonary vasoconstriction. In all of these cases, however, no effort has been made to differentiate between smooth and striated muscle contraction as the factor responsible for the spasm. Furthermore, the nerve supply of the extra-cardiac striated muscle as related to the myocardium of the heart should be investigated more thoroughly.

Differences in structure between the atrial junction of the superior and inferior pulmonary veins was first described in dogs by Eliakim and associates.¹ The present study on human hearts confirms that, in general, like in the dog, the atrial wall is thicker between the superior pulmonary veins than between the inferior pulmonary veins. Likewise, the sphincter-like formation and the myocardial venous sleeves are more developed around the superior pulmonary veins than around the inferior ones, although the differences do not seem to be as marked as in dogs. The significance of these differences in structure is entirely unknown. It is well established that, in healthy individuals, the blood flow through the lower lobes is slightly larger than the flow through the upper lobes, while the reverse is true in patients with advanced mitral stenosis.⁵⁵⁻⁵⁸ Pulmonary venous hypertension following the administration of hypertonic solutions into dogs is more pronounced or may be confined to the superior pulmonary veins;¹ these findings are in keeping with the more developed sphincters described around these veins.¹ A sphincter mechanism, more pronounced in the superior pulmonary veins, was also demonstrated following occlusion of the opposite pulmonary artery, hypoxia, or administration of epinephrine or serotonin to dogs.⁵⁹

Whether the anatomic variations in this region play any role in the regulation of the

blood flow through the various lobes of the lung in man, both in health and in pathologic-al conditions, remains to be proved.

A detailed knowledge of the anatomy of the left atrial-pulmonary venous junction may perhaps be of help to the cardiac surgeon because of the occurrence of isolated lesions involving the pulmonary veins. Congenital stenosis of the pulmonary venous-left atrial junction has been described in man.⁶⁰⁻⁶² In the case of Reyke⁶⁰ there was atresia of the right upper lobe vein and stenosis of all others. Another patient described by Ferenz and Damman⁶¹ had atresia of the left lower pulmonary vein and stenosis of the upper lobe vein. Still another case was described by Bernstein and associates.⁶² These lesions, if unrecognized and untreated, invariably lead to severe pulmonary hypertension, early heart failure, and death.

Summary

Some anatomic features of the posterior wall of the left atrium, the atrial-pulmonary venous junctions, and the myocardial sleeves extending over the pulmonary veins, as observed in 16 human hearts, are described.

Different patterns of direction of the myocardial fibers of the atrial wall were found in the different specimens. The atrial wall between the upper pulmonary veins was consistently thicker than that between the lower ones. Similarly, the sphincter-like structures of the atrial-pulmonary venous junctions were generally more conspicuous, and the myocardial venous sleeves better developed in the superior than in the inferior pulmonary veins. The physiological and pathological implications of these findings are discussed.

Acknowledgment

Part of this work was performed in the Department of Anatomy of the Albert Einstein College of Medicine in New York. We are indebted to the late Prof. E. Scharrer, then Head of the Department of Anatomy, for his constant help and support during the execution of the work. Our thanks are also extended to Mr. S. Edberg for his help in collecting the specimens, to Prof. B. Fruhman for his kind help in photographing the specimens, to Mrs. E. Salomon for the careful execution of the drawings, and to

Mr. E. Khazzan, working under a summer research fellowship from the Albert Einstein College of Medicine, for his help in the dissection of the specimens.

References

- ELIAKIM, M., STERN, S., AND NATHAN, H.: Site of action of hypertonic saline in the pulmonary circulation. *Circulation Research* 9: 327, 1961.
- FEDOROW, V.: Ueber die Entwicklung der Lungenvene. *Anat Hefte* 40: 529, 1910.
- TANDLER, J.: Development of the heart. In *Manual of Human Embriology*, vol. 2, edited by F. Keibel and F. P. Mall. Philadelphia, J. B. Lippincott Co., 1910, p. 534.
- BROWN, A. J.: Development of the pulmonary vein in the domestic cat. *Anat Rec* 7: 299, 1913.
- AUER, J.: Development of the human pulmonary veins and its major variations. *Anat Rec* 101: 581, 1948.
- NEILL, C. A.: Development of the pulmonary veins. *Pediatrics* 18: 880, 1956.
- LOSS, J. A., AND DANKMEIJER, J.: Development of pulmonary veins in the human embryo. *Compt Rend Ass Anat* 42: 961, 1955.
- LOSS, J. A.: Development of the pulmonary veins and the coronary sinus in the human embryo. Doctoral Thesis, University of Leyden, 1958.
- KEITH, A.: Anatomy of the valvular mechanisms around the venous orifices of the right and left auricles, with some observations on the morphology of the heart. *J Anat Physiol* 37: 221, 1903.
- KEITH, A., AND FLACK, M.: Form and nature of the muscular connections between primary divisions of the vertebrate heart. *J Anat Physiol* 41: 172, 1907.
- PAPEZ, J. W.: Heart musculature of the atria. *Amer J Anat* 27: 255, 1920.
- THOMAS, C. E.: Muscular architecture of the atria of hog and dog hearts. *Amer J Anat* 104: 207, 1959.
- WALE, J. DE: Epistola ad Casp: Bartholin de motu chyli et sanguinis, 1641. Quoted in ref. 39, p. 83.
- RAUSCHEL, F.: *De Arteriarum et Venarum Structura*, Breslau, 1836. Quoted in ref. 26.
- ELISCHER, J.: Ueber quergestreifte Muskeln der ins Herz mündenden Venen des Menschen, 1869. Quoted in ref. 20, p. 154.
- ARNSTEIN, C.: Zur Kenntniss der quergestreiften Muskulatur in den Lungenvenen. *Centr Med Wissensch (Berlin)* 15: 692, 1877.
- STIEDA, L.: Ueber quergestreifte Muskelfasern in der Wand der Lungenvenen. *Arch Mikrobiol Anat* 14: 243, 1877.
- AKAZA, S.: Ueber das Vorkommen von quergestreiften Muskelfasern in der Wandung der

- Lungenvenen. Mitt Med Ges Tokio 13: 1899. Quoted in ref. 20, p. 158.
19. FAVARO, G.: Il miocardio pulmonare: Contributi all'istologia umana e comparate dei vasi polmonari. Int Mschr Anat Physiol 27: 315, 1910.
 20. BENNINGHOFF, A.: Blutgefäße und Herz. In Handbuch der mikroskopischen Anatomie des Menschen, vol. 6, part 1, edited by Wilhelm v. Möllendorff. Berlin, J. Springer, 1930, pp. 154 and 158.
 21. AMANO, S.: Beitrag zur funktionellen Struktur der Lungenvenen. Trans Soc Path Jap 23: 842, 1933.
 22. TAKINO, M.: Vergleichende Studien über die histologische Struktur der Arteriae und Venae pulmonales, die Blutgefäßnerven der Lunge und die Nerven der Bronchien bei verschiedenen Tierarten, besonders über die Beziehung der Blutgefäßnerven zu den glatten Muskeln der Blutgefäße. Acta Scholae Med Univ Imp, Kioto 15: 321, 1933. Quoted in ref. 26.
 23. TAKINO, M., AND EZAKI, Y.: Ueber die Besonderheiten der Arteriae und Venae pulmonales bei verschiedenen Tieren, besonders beim Menschen. Acta Scholae Med Univ Imp Kioto 17: 1, 1940. Quoted in ref. 26.
 24. OTTERBACH, K.: Beiträge zur Kenntnis des Lungenkreislaufes: die Genese des Myokardüberzuges des Mundungsteiles der Vena pulmonalis. Morphol Jahrb 81: 547, 1938.
 25. BUCCIANTE, L.: Architettura e struttura della guaina miocardica delle vene cave polmonari e del seno coronario dell'uomo. Med Sper Arch Ital 6: 273, 1940. Quoted in ref. 26.
 26. BURCH, G. E., AND ROMNEY, R. B.: Functional anatomy and "throttle valve" action of the pulmonary veins. Amer Heart J 47: 58, 1954.
 27. BARGMANN, W., AND DOERR, W. (editors): Das Herz des Menschen, vol. 1. Stuttgart, Georg Thieme Verlag, 1963, pp. 124 and 127.
 28. KLAVINS, J. V.: Demonstration of striated muscle in the pulmonary veins of the rat. J Anat 97: 239, 1963.
 29. KOSIR, A.: Presence of myocardial tissue in the pulmonary veins of the mouse. Abstract 358. Excerpta Med (I) 18: 80, 1964.
 30. HOOKER, C. W., McALISTER, H. A., JR., AND ELLIS, F. W.: Active contractions of the large thoracic veins in certain mammals. Anat Rec 148: 292, 1964.
 31. CARRON, R., AND CALHOUN, M. L.: Extent of cardiac muscle in the great veins of the dog. Anat Rec 150: 249, 1964.
 32. KJELLBERG, S. R., AND OLSON, S. E.: Roentgenological studies of the sphincter mechanism of the caval and pulmonary veins. Acta Radiol (Stockholm) 41: 481, 1950.
 33. LITTLE, R. C.: Volume pressure relationships of the pulmonary-left heart vascular segment: Evidence of a valve-like closure of the pulmonary vein. Circulation Research 8: 594, 1960.
 34. LOUVEL, J., AND LAUBRY, J. J.: Les veines. In Les Petits Précis. Paris, Librairie Maloine, 1950.
 35. CHAVOIS, L.: Place aux veines, ou rôle initial du secteur veineux dans la circuit sanguin, 1952. Quoted in ref. 39, p. 84.
 36. CHAMPY, C., AND LOUVEL, J.: Le contraction de la veine cave supérieure. Bull Acad Med 119: 718, 1938. Quoted in ref. 39, p. 84.
 37. ELIAKIM, M., AND AVIADO, D. M.: Effects of nerve stimulation and drugs on the extra-pulmonary portion of the pulmonary vein. J Pharmacol Exp Ther 133: 304, 1961.
 38. KURAMOTO, K., AND RODBARD, S.: Effect of blood flow and left atrial pressure on pulmonary venous resistance. Circulation Research 11: 240, 1962.
 39. FRANKLIN, K. J.: A Monograph on Veins. Springfield, Illinois, Charles C Thomas, 1937.
 40. SMITH, D. J., AND COXE, J. W.: Reactions of isolated pulmonary blood vessels to anoxia, epinephrine, acetylcholine and histamine. Amer J Physiol 167: 732, 1951.
 41. NISELL, O.: Reactions of the pulmonary venules of the cat with special reference to the effect of the pulmonary elastance. Acta Physiol Scand 23: 361, 1951.
 42. BEAN, J. W., MAYO, W. P., O'DONNELL, F., AND GRAY, G. W.: Vascular response in dog lung induced by alterations in pulmonary arterial CO_2 tension and by acetylcholine. Amer J Physiol 166: 723, 1951.
 43. HALL, P. W.: Effects of hypoxia on post-arteriolar pulmonary vascular resistance. Circulation Research 1: 238, 1953.
 44. RIVERA-ESTRADA, C., SALTMAN, P. W., SINGER, D., AND KATZ, L. N.: Action of hypoxia on the pulmonary vasculature. Circulation Research 6: 10, 1958.
 45. RUDOLPH, A.: Pulmonary venomotor activity. Med Thorac 19: 184, 1962.
 46. AVIADO, D. M., JR., AND SCHMIDT, C. F.: Respiratory burns with special reference to pulmonary edema and congestion. Circulation 6: 666, 1952.
 47. SINGER, D., SALTMAN, P. W., RIVERA-ESTRADA, C., PICK, R., AND KATZ, L. N.: Hemodynamic alterations following miliary pulmonary embolization in relation to the pathogenesis of the consequent diffuse edema. Amer J Physiol 191: 437, 1957.
 48. KUIDA, H., HINSHAW, L. B., GILBERT, R. P., AND VISSCHER, M. B.: Effect of gram-nega-

- tive endotoxin on the pulmonary circulation. Amer J Physiol **192**: 335, 1958.
49. AVIADO, D. M., JR., AND SCHMIDT, C. F.: Pathogenesis of pulmonary edema by alloxan. Circulation Research **5**: 180, 1957.
 50. GILBERT, R. P., HINSHAW, L. B., KUIDA, H., AND VISSCHER, M. B.: Effects of histamine, 5-hydroxy-tryptamine and epinephrine on pulmonary hemodynamics with particular reference to arterial and venous resistances. Amer J Physiol **194**: 165, 1958.
 51. AVIADO, D. M., JR.: Pulmonary venular responses to anoxia, 5-hydroxytryptamine and histamine. Amer J Physiol **198**: 1032, 1960.
 52. BRAUN, K., AND STERN, S.: Pulmonary and systemic blood pressure response to serotonin: Role of chemoreceptors. Amer J Physiol **201**: 369, 1961.
 53. PARKER, B. M., STEIGER, B. W., AND FRIEDENBERG, M. J.: Serotonin-induced pulmonary venous spasm demonstrated by selective phlebography. Amer Heart J **69**: 521, 1965.
 54. ELIAKIM, M., ROSENBERG, S. Z., AND BRAUN, K.: Effect of hypertonic saline on the pulmonary and systemic pressures. Circulation Research **6**: 357, 1958.
 55. DOLLERY, C. T., AND WEST, J. B.: Regional uptake of radioactive oxygen, carbon monoxide and carbon dioxide in the lungs of patients with mitral stenosis. Circulation Research **8**: 765, 1960.
 56. DOYLE, A. E., GOODWIN, J. F., HARRISON, C. V., AND STEINER, R. E.: Pulmonary vascular patterns in pulmonary hypertension. Brit Heart J **19**: 353, 1957.
 57. HARRISON, C. V.: Pathology of pulmonary vessels in pulmonary hypertension. Brit J Radiol **31**: 217, 1958.
 58. STEINER, R. E.: Radiological appearances of the pulmonary vessels in pulmonary hypertension. Brit J Radiol **31**: 188, 1958.
 59. RUDOLPH, A. M., GOODMAN, N. L., GOLINKO, R. J., AND SCARPELLI, E. M.: Observations on a sphincter mechanism at the pulmonary venous-left atrial junction. Circulation **24**: 1027, 1961.
 60. REYKE, R. D. K.: Congenital stenosis of the pulmonary veins in their extrapulmonary course. Med J Aust **1**: 801, 1951.
 61. FERENZ, C., AND DAMMAN, F. J., JR.: Significance of the pulmonary vascular bed in congenital heart disease in lesions of the left side of the heart causing obstruction of the pulmonary venous return. Circulation **16**: 1046, 1957.
 62. BERNSTEIN, J., NOLKE, A. C., AND REED, J. O.: Extrapulmonary stenosis of the pulmonary veins. Circulation **20**: 891, 1959.



Otto Loewi (Nobel Prize in Medicine, 1936)

In the night of Easter Saturday, 1921, I awoke, and jotted down a few notes on a tiny slip of paper. Then I fell asleep again. It occurred to me at six o'clock in the morning, that during the night I had written down something most important, but I was unable to decipher the scrawl. That Sunday was the most desperate day in my whole scientific life. During the night, however, I awoke again, and I remembered what it was. This time I did not take any risk; I got up immediately, went to the laboratory, made the experiment on the frog's heart . . . and at five o'clock the chemical transmission of nerve impulses was conclusively proved.—A. C. CORCORAN: *A Mirror up to Medicine*. Philadelphia, J. B. Lippincott Co., 1961, p. 261.