Configuration of Elastic Tissue of Pulmonary Trunk in Idiopathic Pulmonary Hypertension

By Donald Heath, M.D., and Jesse E. Edwards, M.D.

A study was made of the configuration of the elastic tissue of the pulmonary trunk in 6 cases of idiopathic pulmonary hypertension. The ages of the patients ranged from 12 to 54 years. The pattern was that of the adult pulmonary type in the 5 female patients, whereas it more closely resembled the fetal, aorta-like type in the single male patient. These data are interpreted as indicating that idiopathic pulmonary hypertension is acquired in most cases but that it may be present from birth in a minority of instances.

The characteristic clinical history of patients who have idiopathic pulmonary hypertension suggests that it is acquired in childhood or early adult life. Most patients with this disease live normal lives before the development of intractable pulmonary hypertension and congestive cardiac failure, which usually lead to death within 3 years or so. Berthrong and Cochran, however, found that 2 of their patients with this disease who also had a small patent foramen ovale were cyanotic from birth, suggesting that the pulmonary vascular resistance had been abnormally increased from birth. Study of the histologic structure of the pulmonary trunk in such cases may shed some light on this problem, for recent work suggests that the configuration of the elastic tissue of this artery depends on whether pulmonary hypertension is present from birth or develops later in life. This communication describes the microscopic structure of the elastic tissue of the pulmonary trunk in 6 proved cases of idiopathic pulmonary hypertension and discusses the significance of the results.

Material and Methods

Six patients who had idiopathic pulmonary hypertension were included in the study. All of these patients showed the clinical, roentgenologic, and electrocardiographic features characteristic of severe pulmonary hypertension, and it was subsequently demonstrated at necropsy in each instance that congenital cardiac anomalies were not present. The cases fulfill the criteria generally accepted as necessary for the diagnosis of "primary pulmonary hypertension." Five patients (cases 1 to 5) were female, their ages being 12, 21, 30, 36, and 54 years, respectively; the other patient (case 6) was a 23-year-old man. Cardiac catheterization had been performed in cases 3 and 6, and the results of this investigation are shown in table 1. In each case, the diagnosis was confirmed at necropsy. All patients had dilatation and hypertrophy of the right ventricle, dilatation of the right atrium, pulmonary-valve ring, and pulmonary trunk, and atherosclerosis of the pulmonary arteries.

Transverse blocks of the pulmonary trunk and the aorta were removed from sites 2 em. above the respective valves and were embedded in paraffin. Histologic sections were prepared and stained by Verhoeff's method to demonstrate the elastic tissue; van Gieson's counterstain was employed. A histologic study of the configuration of the elastic tissue in both vessels was made; in each instance, the tissue of the pulmonary trunk was designated as "aortie" or "adult pulmonary" in type. This classification is based on the following data. In the fetus, the configuration of the elastic tissue in the media of the pulmonary trunk (fig. 1a) is similar to that of the aorta (fig. 1b), although minor differences are present. Both vessels contain many elastic fibrils among the smooth muscle and collagen. These fibrils are long, uniform, crenated, and tightly packed, and are parallel with one another. Although this configuration of elastic tissue remains in the adult aorta (fig. 1c), changes occur in the normal pulmonary artery, so that the adult appearance is one of a loosely arranged network of branching, irregularly arranged elastic fibrils (fig. 1d). A transitional pattern is found in infancy. In severe pulmonary hypertension, the media of the elastic pulmonary artery thickens in all cases, but the configuration of the
Table 1
Cardiac-Catheterization Data in Two Cases of Pulmonary Hypertension

<table>
<thead>
<tr>
<th>Arterial blood pressure, mm. Hg</th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>Radial</td>
<td>Pulmonary</td>
<td>Radial</td>
</tr>
<tr>
<td>Case</td>
<td>Mean</td>
<td>Pulse</td>
<td>Mean</td>
</tr>
<tr>
<td>3</td>
<td>66</td>
<td>42</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>70</td>
<td>44</td>
<td>65</td>
</tr>
</tbody>
</table>

*We are indebted to Dr. E. H. Wood, Section of Physiology, Mayo Clinic, for these data.*

elastic tissue is related to the type of underlying disease. In cases of large ventricular septal defect or widely patent ductus arteriosus, wherein pulmonary hypertension is present from birth, the media of the pulmonary artery retains the fetal relationship to the aorta and has an elastic configuration similar to that of the aorta. In atrial septal defect of the foramen-ovale type or mitral stenosis of rheumatic origin, wherein pulmonary hypertension is acquired, the configuration of elastic tissue in the media of the pulmonary artery is like that of the adult pulmonary vessel.

A previous study\(^3\) of the histologic structure of the pulmonary trunk at different ages in 71 control cases, in 44 cases of congenital heart disease with pulmonary hypertension, and in 31 cases of congenital heart disease with pulmonary stenosis should be consulted for a detailed description and a discussion of the significance of the various configurations of elastic tissue that may be found in the pulmonary trunk of such patients.

**Results**

In cases 1 to 5, the configuration of elastic tissue in the pulmonary trunk was of the adult pattern (fig. 2a-e). It was indeterminate in case 6 but resembled the fetal, aorta-like pattern more than it did the adult pulmonary configuration (fig. 2f). In all instances, the configuration of the aorta was normal.

**Comment**

It has been shown previously\(^3\) that a difference exists between the configuration of the elastic tissue of the pulmonary trunk in the group of patients with a free communication between the systemic and pulmonary circulations from birth, such as a large ventricular septal defect or a widely patent ductus arteriosus, and that found in those patients in whom pulmonary hypertension is acquired later in life, as with an atrial septal defect or mitral stenosis on a rheumatic basis.

The configuration of the elastic tissue does not appear to be determined by the magnitude of the pulmonary blood flow or by the absolute levels of either the systolic or pulse pressure in the pulmonary artery. We\(^3\) found previously, for example, that the configuration of elastic tissue was of the fetal, aorta-like type in a 11\(\frac{1}{2}\)-year-old child who had a ventricular septal defect and a pulmonary blood flow of 7.4 L./min./M.\(^2\), but that it was of the adult

*Figure 1*

Photomicrographs of transverse sections of control pulmonary trunk and aorta (elastic-tissue stain; \(\times 100\)). a. Pulmonary trunk from a 46-hour-old boy, showing the normal aorta-like fetal configuration of the media. b. Ascending aorta from a 46-hour-old boy, showing the normal aortic configuration of the media. c. Ascending aorta in a 53-year-old man, showing the normal aortic configuration of the media. d. Pulmonary trunk in a 53-year-old man, showing the normal adult pulmonary configuration of the media.
pulmonary type in a 27-year-old woman with atrial septal defect and a similar pulmonary blood flow of 6.7 L/min./M²; both these patients had pulmonary hypertension. In the present series also, one patient (case 3) had an adult pulmonary configuration of elastic tissue with a pulmonary blood flow of 1.9 L/min./M², whereas in another patient (case 6) who had a virtually identical flow of 2.1 L/min./M², the pattern was much more like that found in the normal fetus. Similarly, the absolute level of pulse pressure in the pulmonary trunk apparently does not determine the configuration of the elastic tissue in the wall; thus, in case 3, a pulse pressure of 42 mm. Hg in this artery was associated with an adult pulmonary configuration, whereas in the aorta in the same case, a virtually identical pulse pressure of 36 mm. Hg was associated with a typical aortic pattern of elastic tissue.

On the basis of data of this type, we think it likely that the configuration of elastic tissue in the pulmonary trunk is an expression of the time of onset of the pulmonary hypertension. When the hypertension is present from birth, as in large ventricular septal defects, the fetal configuration, closely resembling that of the adult aorta, is retained; however, when the increase of pressure occurs after the normal transition of the elastic tissue into the adult form, as in mitral stenosis caused by rheumatic fever, the pulmonary trunk thicken but the aorta-like configuration is not regained.

With the acceptance of this histologic criterion as an indicator of the time of onset of pulmonary hypertension, the presence of the adult configuration in our 5 female patients ranging in age from 12 to 54 years (fig. 2a-e) may be interpreted as indicating that the pulmonary hypertension was acquired in these cases. The finding of a configuration of elastic tissue more closely resembling that of the fetus in case 6 (fig. 2f) suggests that pulmonary hypertension was present from birth in this instance, thereby supporting the view

Figure 2

Photomicrographs of pulmonary trunk in cases 1-6 (elastic-tissue stain; × 150). a-e, Appearance in cases 1-5, respectively, showing adult pulmonary configuration of the media in each. f. (Case 6). Note the aortic type of medial configuration in this case. (The authors acknowledge with thanks the receipt of material in case 2 from Dr. Morgan Berthrong, Glockner-Penrose Hospital, Colorado Springs, Colorado.)
of Wade and Ball\textsuperscript{4} that "primary pulmonary hypertension" may be a heterogeneous group of diseases.

**Summario in Interlingua**

Esseva studiate le configuration del histos elasitic del trunco pulmonar in 6 casos de idiopathic hypertension pulmonar. Le etates del patientes variava inter 12 e 54 annos. Le configuration esseva illo del typo pulmonar adulte in le 5 patientes feminin sed resimulava plus intime le typo fetal aortoide in le unico patiente mascul. Iste datos es interprete como indication que idiopathic hypertension pulmonar es acquirite in le majoritate del casos sed que illo pote esser presente a partir del nascentia in un minoritate de casos.

**Amedeo Avogadro**

Two thousand years ago Lucretius in Rome expounded the doctrine of atoms. He expressed in immortal language the speculations of the Greek philosophers, and he described with the vividness of a great poet the movements, the unions and separations of the tiny corpuscles of which he conceived all things to be composed. The atoms had many qualities which modern science assumes even today. Vigorous motion under the appearance of rest, penetration of heat and cold depending on this movement, hooks for attachment to others, and even an unpredictable "clinamen" or swerve, which is a sort of fantastic anticipation of the uncertainty principle of quantum mechanics.

This was magnificent and represented a wonderful intuitive insight into the working of nature, but it was not science. There was no link with quantitative experimentation, the construction of which connection was lacking until modern times. Then, one might say suddenly, the science of chemistry was created by the vision of a few great men, among whom was Amedeo Avogadro (1776-1856).

The recognition by Avogadro of the distinction between atoms and molecules was the key which opened the treasury of structural chemistry; a treasury whose riches are not yet exhausted. The establishment of the true doctrine about the nature of the particles of the elementary gases rendered possible the development of the kinetic theory and the understanding of the energy relationships of these particles.

On this basis was founded the study not only of the structure of substances but of the functional relationships that govern chemical change: chemical kinetics. A true doctrine of molecules was the necessary precursor of what may truly be called both the anatomy and the physiology of chemical compounds.

There is irony in the fact that the importance of Avogadro's work was not understood for 40 years. This has a course happened to other men of science, and it should perhaps remind us that the advance of knowledge is in some measure an impersonal thing. However this may be, there is no doubt that one of the best ways of honoring the memory of the great scientists of the past is by considering the progress that has been made on the basis of their original labors.—Cyril N. Hinshelwood, *Science* 124: 708, 1956.
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