

This Week's Citation Classic

Heath D & Edwards I E. The pathology of hypertensive pulmonary vascular disease. A description of six grades of structural changes in the pulmonary arteries with special reference to congenital cardiac septal defects. *Circulation* 18:533-47, 1958. [Mayo Clinic; and Mayo Foundation, Univ. Minnesota, Rochester, MN]

Progressive histological changes occur in the small pulmonary blood vessels as an association of the chronic pulmonary hypertension complicating many congenital cardiac septal defects. This progression is so stereotyped as to allow the recognition of six grades of change. [The SC® indicates that this paper has been cited over 300 times since 1961.]

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"The advent of cardiac surgery in the early 1950s brought with it an urgent and unexpected demand for a comprehensive understanding of the pathology of an area virtually previously ignored by morbid anatomists, namely, the pulmonary circulation. It became vital to know the pathology of the pulmonary hypertension which complicated many of the congenital cardiac anomalies coming to surgery and in particular to know if the altered pulmonary haemodynamics and vascular lesions were reversible or not. The only information available at that time was the data gathered in the US in the thirties by a British cardiologist, Oscar Brenner,¹ who had published five papers on the histology of the pulmonary vasculature. He told me in later years that he had had the greatest difficulty in publishing these articles which subsequently became classics, the reason given being that the subject was of no interest to doctors.

"In the 1950s I held a junior training post in cardiology in Sheffield in the north of England working in the field of congenital heart disease under James W. Brown and William Whitaker.

It became increasingly apparent to us that pulmonary hypertension was exerting great influence on the clinical picture of our patients, but we were totally ignorant of the underlying pathology of the pulmonary circulation. I forsook cardiology for pathology, I thought then temporarily, to work for a year at the Mayo Clinic as a Rockefeller Fellow to study the pathology of pulmonary hypertension with Jesse E Edwards, a world authority on cardiac pathology.

"Here it proved possible to show that the pathological changes in the pulmonary arteries in congenital cardiac shunts followed a stereotyped pattern in which distinct grades could be recognised. The significance of this paper was that it was followed by two others^{2,3} showing that each of these succeeding histological grades had close physiological relationships so it became possible for the first time to look at sections of lung and interpret the appearances in haemodynamic terms. This later was shown to have great relevance to the reversibility of pulmonary hypertension following surgical correction of defects. This work was possible at the Mayo Clinic because of the wonderful spirit of friendliness and cooperation there that allowed me to wander at will through the files of the departments of pathology and physiology and so put the whole story together. This was an exhilarating experience for a young man trained in the more traditional approach of British morbid anatomy. Indeed this very functional approach to histopathology learned at the Clinic has remained with me ever since and has not met favour in some quarters.

"In 1953 I said to Bill Whitaker, 'Do you think there is enough in the pathology of pulmonary hypertension to make an MD thesis?' Some 30 years later I can look back over five books and 200 papers on the subject and smile at the question. I never found my way back to cardiology. This paper proved to be a gateway to a professorship in pathology, a doctorate of science, and a lifetime spent in asking and answering questions about the pathology of the pulmonary circulation."

1. **Brenner O.** Pathology of the vessels of the pulmonary circulation. *Arch. Intern. Med* 56:211-37, 1935.
2. **Heath D, Helmholtz H F, Jr., Burchell H B, DuShane J W & Edwards I E.** Graded pulmonary vascular changes and hemodynamic findings in cases of atrial and ventricular septal defect and patent ductus arteriosus. *Circulation* 18:1155-66, 1958.
3. **Heath D, Helmholtz H F, Jr., Burchell H B, DuShane J W, Kirklint J W & Edwards I E.** Relation between structural changes in the small pulmonary arteries and the immediate reversibility of pulmonary hypertension following closure of ventricular and atrial septal defects. *Circulation* 18:1167-74, 1958.