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This Week's Citation Classic®

Borst H G, McGregor M, Whittenberger J L & Berglund E. Influence of pulmonary arterial and left atrial pressures on pulmonary vascular resistance. *Circ. Res.* 4:393-9, 1956. [Dept. Physiology, Harvard School of Public Health, Boston, MA]

Pulmonary vascular resistance was determined over a wide range in the dog. Pulmonary artery and left atrial pressures showed a marked effect on resistance by modifying vascular distension, this effect being most notable at low levels of pressure and flow. [The *SCI*® indicates that this paper has been cited in more than 215 publications.]

The First of 300

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The Hagen-Poiseuille equation describes the resistance encountered by fluid passing through tubes. Blood vessels, in contrast to rigid conduits, react to a rising perfusion pressure by an increase of diameter which towers the resistance to flow. Although the relationship of pressure to flow in the pulmonary circulation was previously described,[1,2] we were able to prove that any rise of outflow pressure in the extremely distensible pulmonary vasculature would per se lower resistance. This finding was important for the understanding of the effects of changes of left ventricular filling pressure on pulmonary hemodynamics and thereby on the workload of the right heart, especially in the presence of left ventricular failure. The experimental design chosen for this study allowed for fully controlled investigations of the pulmonary vasculature and its response to pharmacological agents as well as to hypoxia and hypercarbia.

Recognition of one's work as a *Citation Classic,* I suppose, usually comes to experienced researchers who sooner or later hit a gold vein. This was not so in my case: after some fourth year student's work on lung burns at the Department of Physiology, Harvard School of Public Health, and a surgical internship at Stanford University, I returned to the former institution, which was headed by James L. Whittenberger. The years spent in this department (1954-1956) witnessed an unusually lucky scientific marriage between pulmonary physiology, represented by Whittenberger, J. Mead, and T. Radford, and cardiovascular physiology which was carried by S.J. Sarnoff, E. Berglund, and R.B. Case. While the former group was solving fundamental problems of airway mechanics, the latter performed advanced studies of left ventricular function and, subsequently, its interdependence with pulmonary hemodynamics.

When, as a young (cardiovascular) surgeon I returned to Boston, I was more than a little surprised, and even somewhat dismayed, to find myself an operating assistant to Sarnoff, a man in whom the physiologist's wisdom was combined with a keen surgical mind. At that time, he introduced apico-aortic bypass for the alleviation of aortic valve stenosis, which many years later became a clinical reality. Sarnoff had me design an in vivo right heart bypass pump circuit for controlled differential perfusion of both lungs which allowed for study of the effect of pharmacological agents and of hypoxia and hypercarbia on the pulmonary vasculature whereby one lung served as a control of the manipulated one. For this purpose, the normal passive response of the pulmonary vessels to changes in inflow and outflow pressures as well as in airway pressure had to be known. We subsequently published several papers, including this *Classic* paper, on these subjects.[3-5] The paper on left atrial pressure was in fact my first publication in a series now approaching 300! As modest as my surgical abilities at the time was my understanding of physiology. This makes me all the more grateful to my prestigious coauthors who let me write and publish a paper which subsequently attained apparent significance.

I presume our work has been quoted so frequently because of its practical importance. Early on this was true, e.g., for the understanding of pulmonary hypertension and its modification by drug in congenital shunt anomalies.[6,7] Recently, it has had implications for heart, heart-lung, and lung transplantation[8] where knowledge of the mechanical factors entering pulmonary vascular resistance and its therapeutic maneuverability by pharmacological agents and inspiratory gas concentrations are of crucial importance both for surgical indications and ultimate results.

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