period that result eventually in structural alterations such as arterial medial and right ventricular hypertrophy. This concept is reinforced by the finding of a similar delay in time before elevations occur in the rate of synthesis of protein in the right ventricle, and of RNA in the pulmonary trunk. Right ventricular and pulmonary arterial systolic blood pressures are also not increased during the first two weeks of monocrotaline treatment. Other changes in the arterial wall might includeearly myogenic, neural or hormonal influences predisposing to heightened muscular tone. The effect of DL-propranolol on the response to monocrotaline was examined in view of the b-adrenergic antagonism shown by the L-sterisomer. In addition, both stereoisomers have local anesthetic properties, and inhibit calcium uptake by isolated sarcoplasmic reticulum with an ED50 of 10-4M. Therefore, propranolol decreases adrenergic activity and decreases calcium movement into the cell by both a direct and indirect action. Concurrent administration of propranolol prevented cardiac hypertrophy over the period of the experiment. It is unclear, however, whether the protective effect of propranolol in preventing cardiac hypertrophy is exerted on the heart or lungs. Initial examination of slides prepared from the lungs of propranolol-treated rats suggested that medial hypertrophy is not so marked; quantitative determination of medial thickness has not yet been done. Treatment with propranolol also lessened the increase in pulmonary arterial blood pressure caused by monocrotaline.

This observation offers the opportunity to explore at which level propranolol is acting: capillary bed, muscular arteries, or heart—and by which of its several pharmacologic actions. This may provide a degree of insight into the mechanism of monocrotaline toxicity.

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Chemoreceptor Effects on Perfusion of Hypoxic and Atelectatic Lung


Controversy persists concerning the reduction in pulmonary blood flow following acute lobar atelectasis. Most investigators observed decreased blood flow to atelectatic or unilaterally hypoxic lungs.1 However, some investigators found unaltered blood flow to acutely atelectatic lobes.2 These unchanged levels of blood flow were associated with moderate systemic hypoxemia, due to a high pulmonary shunt. Evidence that a similar phenomenon may occur during unilateral hypoxia is provided by Himmelstein and colleagues.3 One of their 5 subjects, who developed marked systemic hypoxemia (SaO2 = 70%) when 8 percent oxygen was administered to 1 lung, also failed to shift pulmonary blood flow away from that unilaterally hypoxic lung.

The present studies were conducted to see if the level of arterial Po2 itself might influence the perfusion of an acutely collapsed or hypoxic lobe.

METHODS

Male albino dogs were anesthetized with sodium pentobarbital and respirated with a dual piston respirator and a Carlen tracheal divider. Cardiac output and left pulmonary arterial blood flow were obtained by electromagnetic flow probes implanted via median sternotomy. Pressure data and blood samples were obtained from a Swan-Ganz pulmonary artery catheter, and from a femoral arterial cannula. Blood gas levels were determined by standard electrodes. Data were taken at 10-20 minute intervals according to several experimental designs:

Hypoxic ventilation (left)-6 dogs
1) Both lungs ventilated with room air; 2) both lungs ventilated with oxygen; right lung continues to receive oxygen while, 3) left lung ventilated with 6 percent O2 in N2; 4) left lung ventilated with N2; 5) left lung returned to 6 percent O2 in N2. Then, while the left lung continues to receive 6 percent O2 in N2, 6) right lung ventilated with room air; 7) right lung returned to 100 percent O2; 8) both lungs return to room air.

Hypoxic ventilation (right)-5 dogs
The above maneuvers were duplicated except that the left and right lungs were reversed, left for right and right for left. However, the test sequence remained the same.

Hypoxic ventilation (left, sino-aortic denervated)-6 dogs
The maneuvers in the first experiment were duplicated in dogs which had undergone sino-aortic denervation of carotid and aortic chemoreceptors and baroreceptors two to three weeks previously.4

Atelectasis (left)-6 dogs
Steps 1,2,3,6 and 7 of the first experiment were repeated in the same sequence except that instead of ventilating the left lung with 6 percent O2 in N2 (steps 3,6 and 7), the left lung was made acutely atelectatic by denervation (step 2) and then occluding its airway.

Atelectasis (left, sino-aortic denervated)-6 dogs
Fourth experiment was conducted on dogs denervated as in third experiment.

RESULTS

Left lung blood flow decreased significantly from control during hypoxic ventilation (Fig 1) or acute atelectasis (Fig 2) of the left lung in both intact and denervated dogs as long as arterial hypoxemia was prevented (P < 01). When mild arterial hypoxemia was induced by room air ventilation of the right lung while the left lung remained collapsed or hypoxic, blood flow to the left lung increased to near control levels in intact animals, but was unaffected in chemodenerverated animals. Signifi-

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Relative perfusion of the left lung is significantly reduced when the left lung is collapsed while the right lung inspires oxygen, but returns to control levels in intact animals during systemic hypoxemia (top line) when the right lung is ventilated with room air.

**Discussion**

In this study, mild systemic arterial hypoxemia appears to attenuate the reduction in blood flow to acutely atelectatic or hypoxic lung regions. This attenuation may result from pulmonary blood volume changes initiated by central mechanisms in response to chemoreceptor stimulation. Alternatively, active vasomotor changes in all of the large pulmonary arteries may stiffen these arteries.

CAST CHANGES IN CARDIAC OUTPUT, SYSTEMIC ARTERIAL BLOOD PRESSURE OR HEART RATE DID NOT OCCUR. WHEN THE TEST CONDITIONS FOR THE LEFT AND RIGHT LUNGS WERE REVERSED (EXPERIMENT 2), THE BLOOD FLOW CHANGES WERE ALSO REVERSED, AS ANTICIPATED. WITH THE ONSET OF ACUTE ATELECTASIS OR HYPOXIC VENTILATION OF THE LEFT LUNG, THE ELECTROMAGNETIC FLOW PROBE REVEALED A PROMINENT RETROGRADE COMPONENT OF FLOW FROM THE LEFT PULMONARY ARTERY IN DIASTOLE. THIS SUGGESTS THAT BLOOD ENTERS THE PULMONARY ARTERIES OF BOTH LUNGS DURING SYSTOLE, BUT FLOWS RETROGRADE OUT THE PULMONARY ARTERY OF THECollapsed OR HYPOXIC LUNG AND INTO THE PULMONARY ARTERY OF THE NORMAL LUNG DURING DIASTOLE.
vessels during systemic hypoxemia causing an increased pulse pressure to be transmitted downstream to the resistance vessels.

If local atelectasis or hypoxia causes the resistance vessels of the affected lung to operate as a vascular waterfall, then the increased systolic pressure may raise mean flow significantly. The increased flow through resistance vessels in a lobe thereby would reduce the blood volume available for retrograde flow during diastole. This effect may exaggerate or prolong the effect of a moderate or transient hypoxic episode in subjects with acute atelectasis, since increased flow through the atelectatic region may increase pulmonary shunt, further lowering arterial P,O,. Thus, there appears to be a chemoreceptor-mediated interaction between local and systemic effects of hypoxia on the pulmonary circulation, which has aspects of a positive feedback system.

Summary of the 19th Aspen Conference

Thomas C. Lloyd, Jr., M.D.*

To be invited to summarize an Aspen conference is a well-recognized honor, and before proceeding, I want to thank the organizers of the meeting, and my unknown sponsor, for giving me this distinction. Beyond the importance of the honor, I was pleased to have been provided this opportunity, for I wanted to attend on any terms, and to come as summarizer seemed easier, at the time, than to prepare an abstract. But it turns out that this is a very difficult job, and late at night while preparing for the final session it occurred to me that the "honor" may, in this case, have been bestowed as a retribution for some past offense. This panacea has only partially dissipated upon exposure to sunlight.

My interests in the pulmonary circulation have been in the response to alveolar hypoxia, in neurogenic regulation of pulmonary vessels, and more recently, in regulation of systemic vessels secondary to reflexes initiated by pulmonary vascular constriction. Regulatory systems have been important to me, and I will freely incorporate that bias in this summary, in the belief that the summary should not be a synopsi, per se, but should be an opinionated, but (I hope) provocative overview. In doing so, I regretfully will fail to give adequate recognition to many of the presentations, and will probably misinterpret others.

We all know that the pulmonary circulation has at least three roles to play: 1) it provides blood for gas exchange and has the apparent ability to optimize that function by setting its tone in accord with gas tensions; 2) it interposes an active metabolic system between systemic veins and arteries which alters blood composition by scavenging some materials and producing others; and 3) it provides a sensory system for cardiorespiratory control by way of several lung reflexes influenced by the vascular status. This conference has particularly stressed the first two, but even so has revealed such a diversity of topics that it was difficult to organize discrete sessions under a single title. This diversity is a sign that we are more aware of the complexities of the lungs. Furthermore, it is an indication that we are welcoming the inquiries of different groups, such as cell biologists and biochemists, to what long has been a plumber's trade. Indeed, the absence of hemodynamic review at this meeting would have been complete had it not been for a somewhat nostalgic argument that arose concerning the best way to represent vascular resistance. Diversity, however, makes my job harder, and I confess to feeling at times more like a spectator than a participant.

The effects of hypoxia have been summarized separately by Dr. Coumand, but because of personal interests, I will include some of the effects of hypoxia in my view. I will try, however, to convince you that much of the material reported under that topic is not germane to hypoxic vasoconstriction in whole lung, but is more a study of general properties of smooth muscle. In that regard we have heard from Drs. Bohr, Clyman and Sourbrada how the pulmonary artery may behave if it is deprived of oxygen, and of its dependence upon oxygen or glucose for energy. Dr. Bohr reviewed the sequence of events leading to constriction, including the role of calcium, and Dr. Sourbrada showed bath calcium to be a determinant of the response of isolated vessel to severe oxygen depletion. Both groups showed that aerobic as well as anaerobic pathways can generate ATP, and Bohr showed that anaerobic capacity can be enhanced by storing vessels under hypoxic conditions. Such "adapted" vessels were able to constrict in response to epinephrine where they otherwise would not. I infer that Dr. Bohr believes the pulmonary artery to be relatively hypoxic in cire and to have developed anaerobic...

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REFERENCES