ALVEOLAR DUCT CONSTRUCTION

and the

HUMORAL REGULATION OF THE LUNG

by

HAL JOHN HESTER COLEBATCH (M.B., B.S.)
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University of Adelaide,
South Australia.

How this work advances medical knowledge

1. Alveolar duct constriction or constriction of the lung

Prior to my own studies (presented at a meeting of the American Physiological Society, 1962, 1,2) alveolar duct constriction as a response separate from bronchoconstriction was either not known, or not believed to have been established to occur. Widdicombe, after reviewing experiments claiming to show constriction of the lung states, "All these experiments indicate clearly that provided alveolar collapse does not occur, smooth muscle contraction does not constrict the lung." But he added the proviso that, "Stronger or different stimuli or the use of other species are desirable before this conclusion can be general."

Referring to our studies of microembolism of the pulmonary arterial circulation, with barium sulphate (2), Radford suggested that reduced distensibility of the lung - reduced pulmonary compliance - might have been caused by contraction of the smooth muscle of the interlobar septa (4). He suggested that such a change was unlikely to be quantitatively significant except with acute and maximum stimulation. The findings reported in my own studies in both gas and liquid filled lungs, do not support the interpretation that alveolar ducts are closed off, but indicate that the distensibility of the ducts and alveoli change together.

The findings in the isolated living liquid-filled lung establish that constriction of the lung by histamine, or "spontaneous constriction," are quantitatively significant in both cat and dog lungs and related to the relative abundance of smooth muscle in alveolar ducts. No similar studies are available. The object of Radford and Lefcoe's studies in the liquid-filled lung was to determine whether contraction of bronchial smooth muscle reduced distensibility of the lung, by increasing resistance to longitudinal lengthening (5).

Arising out of my studies of the liquid-filled lung is a quantitative analysis showing how smooth muscle confined to a part only of the fibre network can control the size of the alveoli as well as of the alveolar ducts. In this way the distensibility of the airspaces, or gas exchange units, may be controlled locally. It is worth noting here that the distribution of gas flow to different regions of the lungs at ordinary breathing frequencies depends on the elastic distensibility of airspaces and hardly at all on the distribution of gas flow resistance offered by the airways (6). Therefore a local change in the distensibility of a group of airspaces appears to provide both a sensitive and an appropriate mechanism for regulating the distribution of ventilation.

2. Humoral regulation of the lung

Although it is well known that adrenaline relaxes airway smooth muscle (3) and that histamine excites the release of adrenaline from the adrenal glands by a direct action on the medullary cells (7), the concept of the humoral regulation of the distensibility of the lung through the actions of histamine and adrenaline has not been developed previously. Similarly the humoral regulation of the pulmonary circulation and the overall concept that pulmonary blood vessels and the respiratory portion of the lung have a common humoral regulation could not be developed on the basis of previously reported data. Aviado (8) in his review suggested that histamine dilated pulmonary blood vessels in intact animals, although he did propose that bronchoconstriction might be associated with pulmonary venous constriction. Both Aviado (9) and Daly (10) favour pulmonary vasoconstriction as the main effect of adrenaline.

Prior to these studies there was no satisfactory concept as to the physiological role of histamine normally present in lung tissue. It has

been suggested that only for non-mast cell histamine has a physiological role been demonstrated and that there is no evidence that the physiological role of mast cells is related to their content of histamine (11). My own findings show that the significance of the role of histamine is related to its action locally in the lungs and to the fact that its main direct effect is on the airways perfused by the pulmonary circulation. On this basis it is possible to propose that histamine provides a homeostatic mechanism, tending to preserve gas exchange, by influencing the distribution of both blood and gas flows away from damaged and towards normal respiratory tissue, and that the antagonism of histamine, by adrenaline released by histamine from the adrenal glands, provides a negative feedback system tending to confine constriction of airways and of pulmonary blood vessels to the site of local histamine release.