



Studies in Respiratory Physiology

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Preface

The research described in these 67 publications submitted for the degree of Doctor of Science at the University of Adelaide was performed over a period of some 20 years from 1955 to 1975. The work was carried out in three settings. From 1955 to 1960, and from 1962 to 1968 I was a member of the Respiratory Research Group at the Royal Postgraduate Medical School, London. During 1960 and 1961, I was a physiologist on the Himalayan Scientific and Mountaineering Expedition led by Sir Edmund Hillary. Since 1969, I have been Professor of Medicine and Bioengineering, and Head of the Section of Physiology at the University of California, San Diego, La Jolla, California, U.S.A.

The 67 papers have been divided into ten groups corresponding to the various areas of research in which I have worked. The following table shows the numbers of the publication in each research area (see next page).

Research Areas of Publications

<u>Group</u>	<u>Papers numbered as</u>	
1	1 - 3	Analysis of pulmonary gas exchange by measurements of expired gas using a respiratory mass spectrometer.
2	4 - 15	Distribution of bloodflow and ventilation in the normal and diseased lung as measured using short-lived cyclotron-produced radioactive gases.
3	16 - 21	Regional function of the lungs as measured by sampling within the bronchial tree using a respiratory mass spectrometer.
4	22 - 25	Pulmonary function at high altitude measured on the Himalayan Scientific and Mountaineer Expedition, 1960-61.
5	26 - 41	Study of the physiological factors determining the topographical inequality of bloodflow and ventilation in the lung.
6	42 - 43	Demonstration of regional differences of alveolar size in the lung.
7	44 - 46	Analysis of the distribution of mechanical stresses in the lung.
8	47	Comparative physiology of lung mechanics.
9	48 - 61	Study of gas exchange including numerical analysis with a digital computer, and its implications.
10	62 - 67	Determination of continuous distributions of ventilation-perfusion ratios in the lung using a multiple inert gas infusion technique.

Note 1. Main sources from which the information is derived.

The information contained in this thesis was derived from experimental work carried out at the Royal Postgraduate Medical School, London, during a scientific expedition to the Himalayas, and at the University of California, San Diego as indicated above. I was actively involved in the design and execution of all the experiments. The way in which the data were collected is clearly described in each publication.

Note 2. Extent to which I have availed myself of the work of others. Much of the work described in the thesis was carried out by a team of investigators because of the complexity of the methods. For example, the studies involving very short-lived radioactive gases (publications 4-15) required the dedicated full-time use of a cyclotron during the periods of the experiments. To clarify the role of my collaborators and myself in the various projects, I can summarize the circumstances of each group of publications.

Groups 1, 2 and 3 include papers written prior to 1961 when I was a member of a research team at the Royal Postgraduate Medical School, London. The leader of the team was Dr. Phillip Hugh-Jones. For Group 1, I was responsible for the design of the experiments, their execution, and analysis of results. For Group 2, the work was the result of a team because we were using very sophisticated techniques including a medical cyclotron to produce very short-lived radioactive gases. I was responsible for the design and execution of the experiments reported in the papers of which I am first author. Other collaborators, especially Dr. C. T. Dollery, were responsible for some

of the experiments in which I participated. The work described in Group 3 was jointly done with Dr. Phillip Hugh-Jones. I was responsible for the design and execution of all the experiments with the exception of those of paper #19, which was primarily Dr. Hugh-Jones' responsibility.

The papers in Group 4 resulted from work done on the Himalayan Scientific and Mountaineering Expedition, 1960-61, which included a team of about six physiologists. I was primarily responsible for the work described in papers 23 and 24, but took an active part in the design and interpretation of the experiments reported in the other two papers.

Groups 5, 6 and 7 contain reports of work done at the Royal Postgraduate Medical School between 1961 and 1969 when I was in charge of the Respiratory Research Group there. The work involved a number of collaborators, most of whom were postdoctoral trainees who had applied to work in my research group. In all instances, I had a key role in the design and interpretation of the experiments, and the research followed the general directions which I had planned for the research unit. The actual execution of the experiments was a team effort in all cases.

Groups 8, 9 and 10 report work carried out after I moved to the University of California, San Diego as Professor of Medicine and Bioengineering in charge of a research division. Again, I was responsible for most of the design and interpretation of the experiments. This is particularly true of Group 9. Some of the

later papers in Group 10 have had substantial input from my collaborators here, especially Dr. Peter Wagner.

Note 3. Portions of the work claimed to be original.

Briefly, Group 1 of the publications describes a new method for determining the degree of ventilation-perfusion inequality in lungs from the analysis of expired gas. Group 2 contains the first direct demonstration of the topographical inequality of bloodflow in the human lung, and the changes in the distribution which follow physiological and pathological interventions. Group 3 reports the results of a new method for determining regional pulmonary function by sampling within the bronchial tree using a respiratory mass spectrometer.

Group 4 of the publications describes experiments conducted at extreme altitudes from 5,800 m to 7,830 m in the Himalayas. The results include the highest measurements of maximum oxygen consumption made to date (Publication 25).

Group 5 contains the first analysis of the factors responsible for the topographical inequality of bloodflow in the lung. In addition, the resulting effects on gas exchange are worked out for the first time.

Groups 6 and 7 report the first direct demonstration of the regional differences of alveolar size in the lung together with an analysis of lung distortion caused by gravity. Group 8 contains the first histological demonstration of the curious behavior of sea-lion lung during compression.

Groups 9 and 10 describe a new method for determining the distribution of ventilation-perfusion ratios in the human lung together with the theoretical basis.

Note 4. Statement of which parts of this thesis have been submitted for a degree at the University of Adelaide or other university.

Publications 1 and 2 report work of which part was contained in a thesis submitted to the University of Adelaide in 1957 for the degree of Doctor of Medicine. Publications 8 and 12 report work of which part was contained in a thesis submitted to the University of London in 1960 for the degree of Doctor of Philosophy.

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