Pulmonary Circulation

***From basic mechanisms
to clinical practice***

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Imperial College, UK

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DEDICATION

To my family, Shirley, Penelope and Caroline
J.M.B.H.

To my family, Clare, Imogen and Edmund
N.W.M.

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FOREWORD

It is a great pleasure to contribute a brief introduction to this new book on the pulmonary circulation. As the authors point out in their Preface, Hammersmith Hospital has always had a strong link with the pulmonary circulation. Indeed, the introduction of cardiac catheterization into the UK by Sir John McMichael, Professor of Medicine, in the early 1940s played a large part in developing the 'Hammersmith tradition'. The story is worth briefly recounting here.

Cardiac catheterization was introduced by Werner Forssmann in Germany in 1929. Although he thought this technique might have important applications, the powers that be decided otherwise. Indeed, Professor Sauerbruch, a leading surgeon in Berlin, said that he was not interested because he "ran a clinic not a circus!". Subsequently, André Cournand and Dickinson Richards in Bellevue Hospital, New York, put the procedure on a sound clinical basis. The first publication appeared in 1941.

McMichael had been interested in the measurement of cardiac output by a rebreathing acetylene method. Apparently, his colleague, E.P. Sharpey-Schafer first saw the paper from Cournand's group, and together they decided to try the new technique to obtain right atrial blood samples to measure cardiac output by the direct Fick method. The first patient catheterization at Hammersmith took place in November 1942. McMichael then asked the Medical Research Council (MRC) for approval to study normal volunteers, but was told no committee would assent to such an unorthodox procedure. However, Sir Edward Mellanby, secretary of the MRC, said McMichael could make a personal approach to the Friends Ambulance Unit, formed during the War from Quaker conscientious objectors. As a result, 135 cardiac catheterizations were performed in a little over a year, and in February 1944 McMichael read a paper to the Physiological Society which the session chairman, Sir Thomas Lewis, referred to as "startling". The first publication appeared later that year, but the reaction of London consultants was strongly hostile. Nevertheless, McMichael and his team persevered, and the importance of cardiac catheterisation in the management of patients with heart disease no doubt played a role in his election to the Royal Society, a rare honour for a clinician. The boldness of taking the study to normal volunteers gave Hammersmith a reputation for cutting edge, investigative research which extended to other invasive procedures such as liver biopsy.

Turning to the present book, many reviews have been written about the pulmonary circulation, and I wondered whether the authors could come up with

a new approach. Happily they have done so, producing a splendid, pithy, highly-readable book with superb illustrations. I am certain that many people who think that they are well abreast of research in the field will gain a lot from the book. It will be a great boon to research students and other people embarking on a career. I wish it well.

John B West

PREFACE

Hammersmith Hospital ['the Hammersmith'], and the former Royal Postgraduate Medical School, have a tradition of research in the field of the Pulmonary Circulation, stemming from the clinical research of Sir John McMichael and Paul Wood in the 1940s, and John Goodwin, Jack Shillingford, Celia Oakley and Robert Steiner in the 1950s and 1960s. John West's pioneering studies on pulmonary haemodynamics and the distribution of pulmonary blood flow in the same period (1958–1969) used radioisotopic methods; expertise in angiographic (Chapters 9 and 13.1) and radionuclide studies (Chapter 5.2) continues. More recent research has focused on pulmonary vascular remodeling and the genetics of pulmonary vascular disease.

The pulmonary circulation is, in mammals, the largest of all the circulations and the vehicle of gas exchange for the whole body. It is exposed to alveolar hypoxia, on the one hand, and to the venous return from all other tissues, on the other. Thus, the pulmonary circulation 'sees' the metabolic, inflammatory and immunological products of all tissues, whether they are healthy or diseased. The microcirculation serves as a vascular filter for particulate matter, such as platelet aggregates and microemboli; in addition, the capillary endothelium and blood act as a metabolic filter, converting hormones and other signalling molecules (e.g. angiotensin I and nitric oxide, NO) into active or inactive states. The filtering function of the pulmonary circulation may lead to disease as in pulmonary embolic disease following the break-up of systemic venous thrombi.

As with other organ systems, there has been an explosion of knowledge in the last 20 years, particularly in the basic sciences. In section I of this book, we pull together the physiological knowledge and principles gained in the era 1950–1980 (Chapters 2 and 4, in the main) with the advances in the basic sciences from 1980 to the present day (Chapters 3 and 5–8). Section II (Clinical Practice) covers the investigation, pathogenesis and management of pulmonary hypertension, oedema and intrapulmonary shunting, with an emphasis on "disease mechanisms".

Our aim is to provide a concise and illustrated "road-map" of each topic. For further reading, we have referred mainly to recent Review articles, but particularly relevant original publications are listed. The pulmonary circulation can be viewed in many different guises — genetic, developmental, anatomical, physiological, haemodynamic, cellular, signalling, remodelling, as well as a medium for gas and fluid exchange — in health and disease. This "Introductory Guide" aims to emphasize the many facets of pulmonary vascular biology and medicine.

J.M.B. Hughes and N.W. Morrell

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