THE CIRCULATION IN ANAESTHESIA

Applied Physiology and Pharmacology

EDITED BY

C. PRYS-ROBERTS

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MA, DM(Oxon), PhD(Leeds), FFARCS
Professor of Anaesthetics
University of Bristol

BLACKWELL SCIENTIFIC PUBLICATIONS
OXFORD LONDON EDINBURGH MELBOURNE

Editorial offices:
Osney Mead, Oxford, OX2 0EL
8 John Street, London, WC1N 2ES
9 Forrest Road, Edinburgh, EH1 2QH
214 Berkeley Street, Carlton
Victoria 3053, Australia

First published 1980

Printed in Great Britain at
the Alden Press, Oxford
and bound at
Kemp Hall Bindery

DISTRIBUTORS

USA
Blackwell Mosby Book Distributors
11830 Westline Industrial Drive
St Louis, Missouri 63141

Canada
Blackwell Mosby Book Distributors
86 Northline Road, Toronto
Ontario, M4B 3E5

Australia
Blackwell Scientific Book
Distributors
214 Berkeley Street, Carlton
Victoria 3053

British Library
Cataloguing in Publication Data

The circulation in anaesthesia.
1. Anesthesia 2. Blood – Circulation
I. Prys-Roberts, C
612'.1'024617 RD82

ISBN 0-632-00425-8

Contributors

A. P. ADAMS, PhD MB BS FFARCS, *Clinical Lecturer, University of Oxford; Consultant Anaesthetist, Nuffield Department of Anaesthetics, Oxford, UK*

R. D. BASTRON, MD, *Professor of Anesthesiology, University of Iowa, Iowa, USA*

G. P. BIRO, MD PhD, *Associate Professor of Physiology, University of Ottawa, Ottawa, Canada*

E. I. EGER, II, MD, *Professor of Anesthesiology, University of California, San Francisco, USA*

P. FOËX, MD DPhil, *Clinical Reader, Nuffield Department of Anaesthetics, University of Oxford, Oxford, UK*

B. J. GERSH, MB ChB DPhil MRCP, *Department of Cardiology, Mayo Clinic, Rochester, Minnesota, USA*

I. D. S. GILLIES, BSc MB FFARCS, *Consultant Anaesthetist, Hammersmith Hospital; Honorary Lecturer, Royal Postgraduate Medical School, London, UK*

VALERIE A. GOAT, MB ChB FFARCS, *Consultant Anaesthetist, Nuffield Department of Anaesthetics, Oxford, UK*

C. E. W. HAHN, BSc MSc DPhil, *University Lecturer in Medical Physics, Nuffield Department of Anaesthetics, University of Oxford, Oxford, UK*

R. F. HICKEY, MD, *Associate Professor of Anesthesiology, University of California, San Francisco, USA*

D. E. LONGNECKER, MD, *Professor of Anesthesiology, University of Virginia, Charlottesville, USA*

R. G. MERIN, MD, *Professor of Anesthesiology, University of Rochester, Rochester, New York, USA*

J. D. MICHENFELDER, MD, *Department of Anesthesiology, Mayo Clinic, Rochester, Minnesota, USA*

HELEN T. PASK, BSc PhD, *Wellcome Research Fellow, Departments of Anaesthetics and Biochemistry, University of Bristol, Bristol, UK*

C. PRYS-ROBERTS, MA DM PhD FFARCS, *Professor of Anaesthetics, University of Bristol, Bristol, UK*

J. G. ROBERTS, MB BS DPhil FFARACS, *Associate Professor of Anaesthetics, Flinders University of South Australia, Adelaide, Australia*

N. TY SMITH, MD, *Professor of Anesthesiology, University of California, San Diego, California, USA*

L. STRUNIN, MD MB BS FFARCS, *Professor of Anaesthetics, King's College Hospital Medical School, University of London, London, UK*

M. K. SYKES, MA MB BChir FFARCS, *Professor of Clinical Anaesthesia, Royal Postgraduate Medical School, London, UK*

Preface

Anaesthesia is a unique specialty. Unlike most other medical specialists, the anaesthesiologist's stock-in-trade is the administration of potent poisons whose primary effect is the abolition of the conscious state. Ever since the tragic death of Hannah Greener under chloroform anaesthesia in 1848 anaesthesiologists have been aware of the very fine dividing line between the desirable primary effects of anaesthesia, analgesia and muscle relaxation, and the often undesirable side-effects of the drugs on the cardiovascular and other systems. For the first eighty years of clinical anaesthesia only the healthiest and fittest of patients were considered to be acceptable risks. Patients with known cardiovascular disease—hypertension, ischaemic heart disease, valvular disease or anaemia—were accepted for anaesthesia with great reluctance because anaesthesia and surgery in these patients carried a high morbidity and mortality. With experience gained during the rapid developments of cardiac surgery, anaesthesiologists became less worried about the management of patients with severe cardiac dysfunction. Now, the anaesthesiologist is expected to provide safe anaesthesia for any patient under almost any conditions, elective or emergency. To achieve this the anaesthesiologist relies on technical skills backed by a thorough knowledge of the basic sciences relevant to anaesthesia: biochemistry, physiology, pharmacology, physics. This book is an attempt to bring together those aspects of these basic sciences as they apply to the cardiovascular system and its regulation, and the effects of anaesthetics on the components of the system, and on the whole system in man and animals.

The contributors to this book are all anaesthesiologists, or basic scientists who work or have worked in departments of anaesthesiology. Their contributions are a mixture of basic science, applied science and clinical medicine, and are designed to provide the medical student, postgraduate anaesthesiologist and the seasoned veteran with an up-to-date account of the circulation in anaesthesia. It is not an immutable statement but a declaration of the present state of the art as interpreted by an international group of serious students with a common interest.

Some aspects of the circulation in anaesthesia are not included in this book and the gaps are noteworthy, for instance in relation to haemorrhagic and other forms of shock, and the effects of regional anaesthesia on the circulation. That chapters on these aspects of the circulation are not included is the result of failure on the part of a few authors to submit the chapters which they had agreed to write. This is becoming an

almost inevitable consequence of multiple authorship of books, but one which is regrettable. A companion to the present volume, originally planned to cover the clinical aspects of the circulation in anaesthesia, also foundered for the same reason. Some of the chapters on clinical measurement which would have appeared in that volume have therefore been included in the present volume, adding somewhat to the length, but I hope also to the value.

Some of the concepts presented in this book may be new and perhaps controversial to the anaesthesiologist who learnt his cardiovascular physiology some years ago. These changing interpretations of physiology and biochemistry in particular have stood the test of ten to fifteen years' questioning, and represent the influence of improved technology in allowing us to observe more carefully the workings of what William Harvey in his treatise on the circulation of blood described as 'wondrous motions'. No doubt some of these interpretations will change in future years, and future generations of anaesthesiologists may look back with a wry smile at our current efforts.

Cedric Prys-Roberts
Bristol.

Contents

SECTION 1
PHYSIOLOGY

CHAPTER I
The Myocardial Cell and its Metabolism

ROBERT G. MERIN &
HELEN T. PASK

The primary function of the myocardial muscle cell is the development of tension and decrease in its length in order to eject blood from the cavities it encloses (together with millions of its fellows, of course). Although this function must be performed repetitively at a rate commensurate with the demands of the body for the nutritive arterial blood and the need for disposal of the by-products of this nutrition, we will not discuss the mechanisms and control of heart rate. Rather, we shall focus on the contractile behaviour of the myocardial cell.

ANATOMY

The major components of the myocardial cell can be divided into: the *membranes* including the plasma membrane or sarcolemma, the sarcoplasmic reticular membrane and the mitochondrial membranes. While the sarcolemma obviously defines the cell, the other membranes enclose the *subcellular organelles*, the sarcoplasmic reticulum (SR) and the mitochondria.

The nucleus can also be considered one of these organelles, but its main function is to direct the growth and repair of the cell through the DNA–RNA mechanisms which are beyond the scope of this discussion. The third major subcellular component is that of the *contractile proteins* which are organized into *fibrils* and are responsible for the contractile function of the cell. Finally, the cytoplasm (sarcoplasm), enclosed by the sarcolemma and bathing the other two components, completes the gross anatomy of the cell [21, 40].

If we look in more detail at the organization of the heart muscle cell, we see that the fibrils are connected in a syncytium, both transversely and longitudinally (Fig. 1.1). At the ends of each cell, the sarcolemma is differentiated in the intercalated discs which serve to separate the cells. In each cell, the same sarcolemma invaginates into the sarcoplasm to form the transverse (T)-tubular system which serves to bring the surface plasma membrane in closer approximation to the myofibrils. The SR, although not continuous with the sarcolemma, is closely applied to it in these invaginations at the sub-sarcolemmal cisternae. The remainder of the SR is distributed throughout the cell in close approximation to the myofibrils, thus providing a secondary avenue of com-

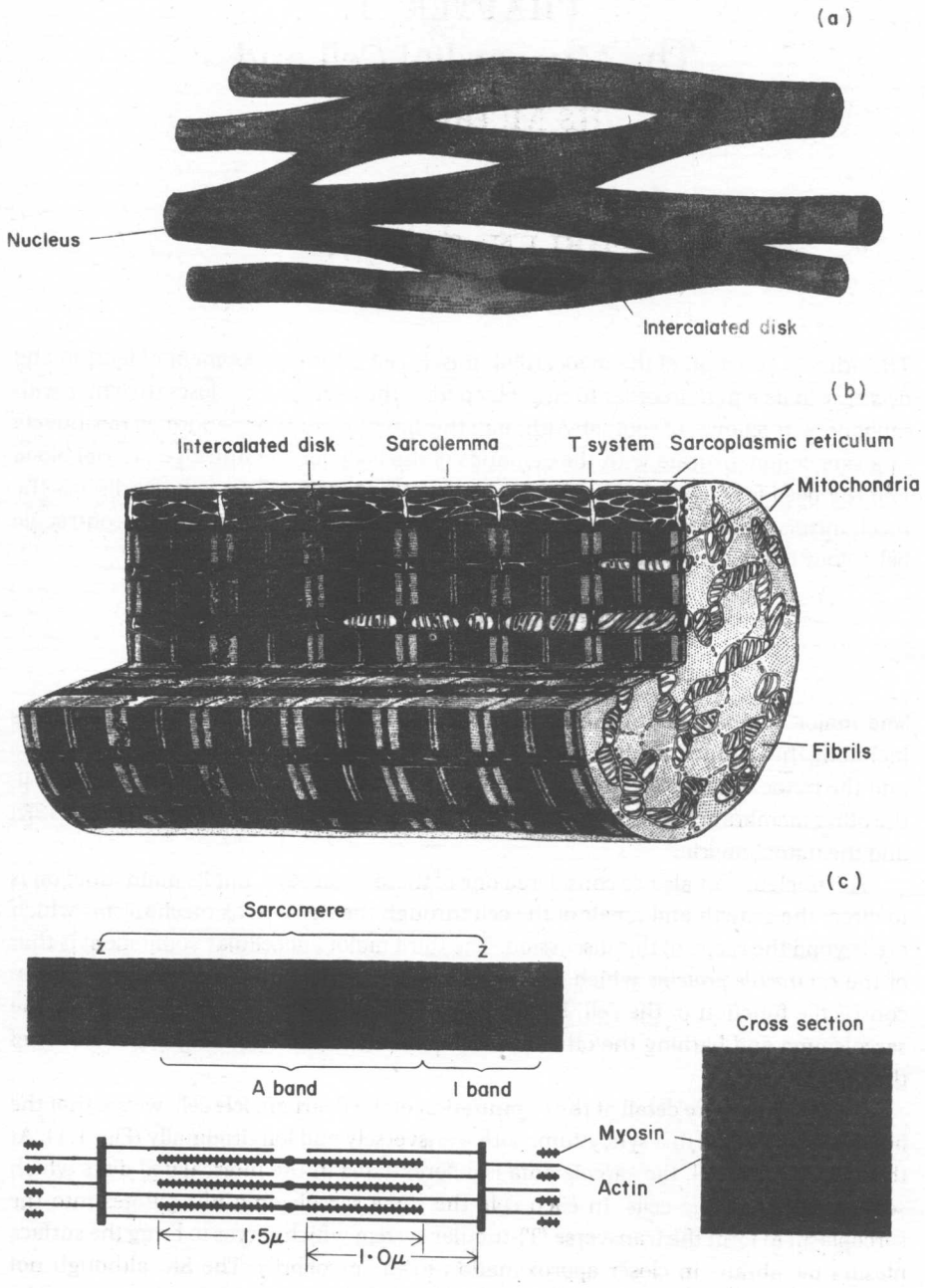

Fig. 1.1. Morphology of cardiac muscle. (a) Syncytial formation of cardiac muscle. (b) Morphology of individual muscle fibre. (c) Morphology of myofibril, showing relation of actin and myosin fibres. (From Sonnenblick [40], by courtesy of the author and publishers.)

munication between the sarcolemma and the contractile proteins. The mitochondria are also widely distributed in heart muscle, as befits an aerobic organ, since oxidative metabolism occurs exclusively in these organelles. They may also serve in transport functions.

Myofibrils

The myofibrils are organized into sarcomeres composed of the structural contractile proteins, actin and myosin (Fig. 1.1). The thick myosin filaments are interposed between the thin actin filaments which are attached at one end to the fibrous Z line. The characteristic 'bands' seen under the light microscope are thus seen to be the overlapping actin and myosin filaments (A band) and the free standing actin filaments extending from either side of the fibrous Z line (I band). The degree of overlap is important in the well-known relationship between resting muscle fibril length and force development, Starling's Law of the Heart (Fig. 1.2) [40]. If the overlap between the filaments at rest is too great (Fig. 1.3(a)), then little force can be developed before the two filaments collide. If the separation is too large (Fig. 1.3(b)) then the surface area available between the two proteins is insufficient for adequate interaction (the nature of which will be discussed below). Consequently, there appears to be an optimal rest length (Fig. 1.3(c)), the L_{max}, at which the most efficient interaction between the thick and thin filaments can occur.

A major subcellular difference between skeletal muscle and cardiac muscle is the

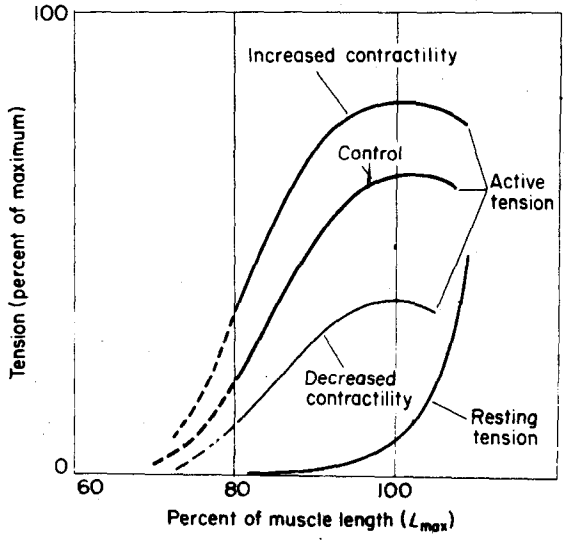

Fig. 1.2. Relation between tension development and resting muscle length (Frank–Starling relation) in isolated papillary muscle. (From Sonnenblick [40], by courtesy of the author and publishers.)

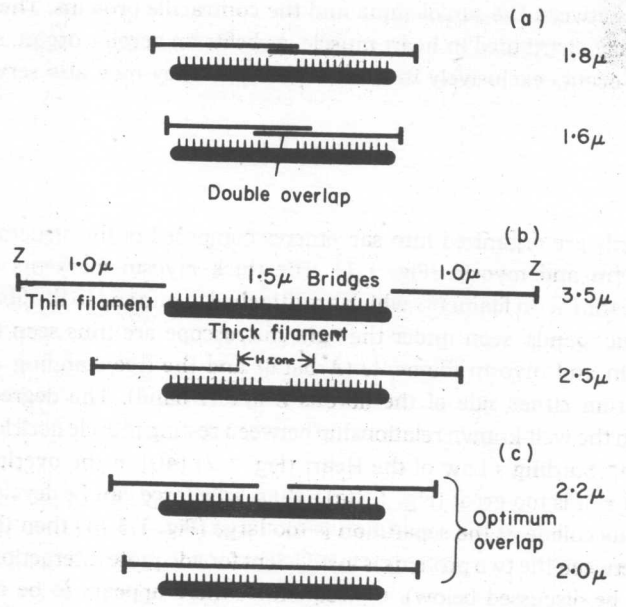

Fig. 1.3. Relation between sarcomere length, filament overlap and the optimum development of contractile force. (a) Double overlap—inadequate tension development. (b) Overseparation—inadequate tension development. (c) Optimum overlap—maximum tension development. See also Fig. 3.1. (From Sonnenblick [40], by courtesy of the author and publishers.)

distribution of the organelles. In cardiac muscle, the T-tubules and the mitochondria are more numerous and occupy a larger proportion of the cell, while the sarcoplasmic reticular network is more abundant in skeletal muscle (Fig. 1.4). Recent work has indicated that the SR may be even less widely distributed in cardiac muscle than indicated in Fig. 1.4 [19, 20]. The physiologic import of these differences will be discussed below.

Contractile proteins

There is general agreement that the development of tension and shortening in muscle is a result of the interaction between the contractile proteins, actin and myosin [7, 11, 12]. From X-ray diffraction and electron microscopic studies, it appears that the interaction is mediated through the association of the projecting 'heads' of the thick myosin filaments with a binding site on the thin actin filament (Fig. 1.5). The myosin molecules are composed of an elongated tail which is the structural support, and a globular head which is the site of the attachment to the actin thin filament and the ATPase activity. The molecules are arranged with half the 'heads' facing in one direction and the other half in the other, with the 'tails' wound around each other in

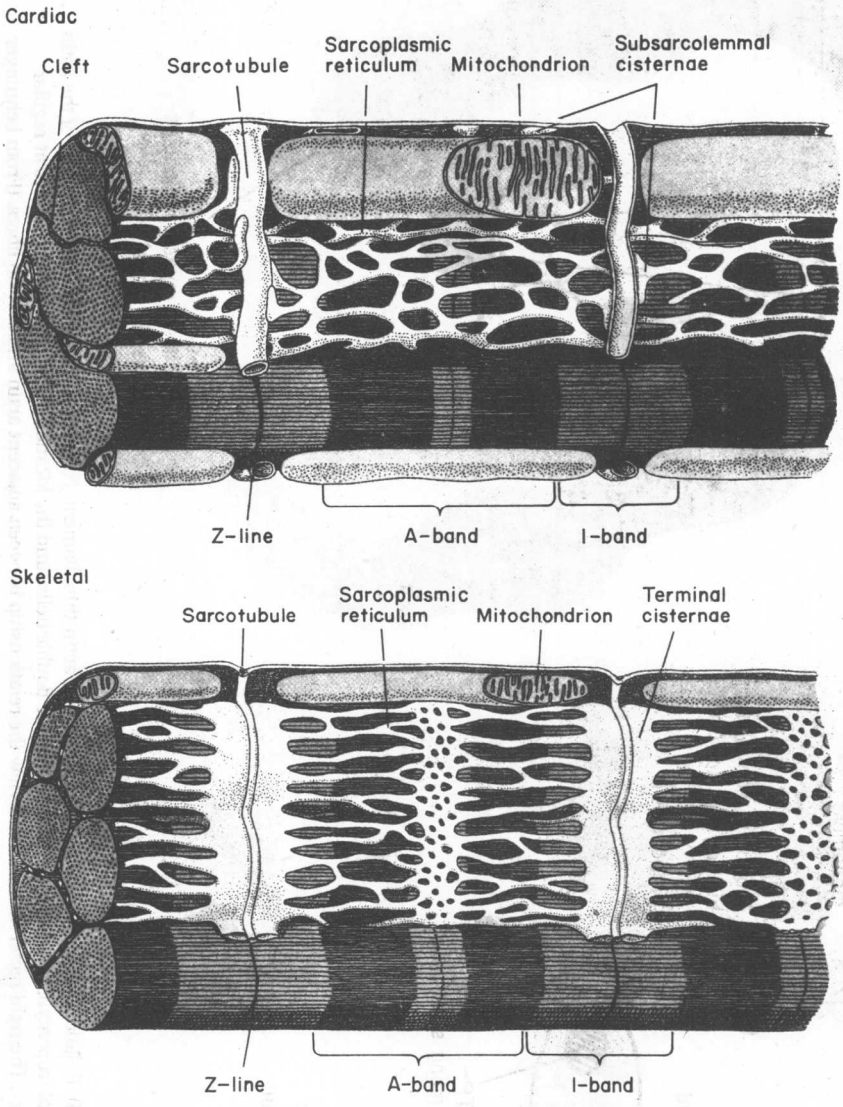

Fig. 1.4. Differences in the morphology of cardiac (upper section) and skeletal muscle (lower section) showing the different arrangement of the sarcotubules and sarcoplasmic reticulum. (From Chidsey [4a], by courtesy of the author and publishers.)

a double helical structure. The thin filament is composed of twin chains of actin monomers also arranged in a double helix. The two other 'contractile' proteins for which a function has been assigned are attached to the actin helix. Tropomyosin consists of two polypeptide chains aligned in the grooves of the actin double helix.