INTRODUCTION

THE PRESIDENT'S command to deliver the 272nd Harveian Oration in the tercentenary year of the publication of the *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus* is an honour to be prized with humble gratitude, but with a due sense of its heavy responsibility, by any man, especially by one whose father obeyed the call to this high duty fifty-five years ago.

Harvey, the acknowledged Father of modern physiology, returned to the Greek method of experiment which had been in almost complete abeyance since the time of Claudius Galen (A.D. 130–200), "the first Father of experimental physiology", whose authority and teaching had remained sacrosanct for more than thirteen hundred years. The tercentenary of the publication of Harvey's immortal discovery in the work described by Albrecht von Haller as "Opusculum aureum" was appropriately and splendidly commemorated by the celebrations organized by this College. In no way could its significance have been more suitably and graphically shown than by the remarkable cinematograph films of Harvey's original physiological experiments as repeated by Sir Thomas Lewis and Dr H. H. Dale, Fellows of the College, who have been eminent in

obedience to Harvey's exhortation "to search and study out the secrets of nature by way of experiment". Further, the historical aspect of the tercentenary has been permanently marked by the College in the production of a facsimile of the first edition of the *De Motu Cordis*, and by the appearance of two other Harveian books, a reproduction of the first English translation in 1653 of the *De Motu Cordis* (Nonesuch Press), and *A Bibliography of the Writings of William Harvey, M.D.* (Cambridge University Press), both due to the pious devotion of a licentiate of the College, Mr Geoffrey Keynes.

John Freind (1675–1728), the elegant scholar and eminent physician, when commenting on the history of the circulation, wrote in 1725: "From this discovery of our great countryman (Harvey) many improvements, even in the cure of distempers, might be made: he had thoughts of composing such a work himself, to show the advantages of this doctrine, in relation to practice, but was prevented by sickness and death: the design of the Architect was very noble, and I with some of his successors might finish it. At present I shall hint only at two or three particulars, which will convince us, of what use a perfect knowledge of the circulation may be to us, if rightly applied, in the practical part of our profession". He then points out that bleeding vessels in an amputation or other wound should be

ligatured and not painfully cauterized, that in cases of aneurysm the vessel should be tied in preference to compression, and that the discussion which had lasted almost two centuries, whether in pleurisy a vein should be pricked on the same or on the opposite side, was futile. If more than two centuries ago the learned author of *The History of Physick from the Time of Galen to the beginning of the xvi Century* apparently thought the task difficult and accordingly acted with wise discretion, it is now obviously, from limitations of both time and capacity, impossible to attempt more than the barest outline of the accumulated knowledge of the diseases of the circulatory system since Harvey's time. A course which recalls the self-administered reproach of Thomas Tenison (1636–1715) when giving "a true and plain account" of Francis Bacon's works: "Sometimes mean men get a stock of reputation by gathering up the *Fragments of the Learned*; as Beggars (they say) have gotten estates by saving together *The Alms of the Rich*". An attempt to piece together the history of the various forms of cardiac disease is attended by no small difficulties: it often happens that the same ideas occur to several minds at the same time but that simultaneous and identical solutions are not published synchronously, thus making it far from easy to decide who really deserves the rather barren crown of priority. Another obvious objection to

such a subject is that it entails lists of men and dates; but as many of these names are those of Fellows of this College it will surely be in obedience to Harvey's injunction to commemorate these benefactors of the College, for can any benefaction be more welcome than new and true knowledge?

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History of Cardio-vascular Diseases since Harvey's Discovery

It is impossible to estimate how much information about the diseases of the heart and vessels was lost with those works of Harvey which were either destroyed when his lodgings in Whitehall were plundered by the Roundheads in 1642 or, though designed, were never completed, such as "The Practice of Medicine conformable to the Thesis of the Circulation of the Blood", and that mentioned at the end of his second Disquisition to John Riolan in the following words: "I shall have much to put forth in my Medical Observations and Pathology which, so far as I know, has yet been observed by no one, about the innumerable diseases concerned with disturbances of the circulation and their cure".

The knowledge of cardio-vascular disease which was very slight at the time of the discovery of the circulation has since come through several channels: (1) the accumulation of data provided by anatomical observation, normal and morbid, (2) unaided clinical observation, (3) as the result of the application of instruments of precision to the examination of patients, and (4), probably most important, the in-

formation derived from physiological and pathological experiments. Though these four headings are attractive as a means of sketching the birth and advance of modern knowledge, it is in practice difficult, and indeed somewhat inconvenient, to follow them out rigidly or attempt to make them absolutely watertight; there will therefore be much overlapping, as will at once be only too obvious.

I

Anatomical Observation

Anatomy is an indispensable step to the more complex science of physiology which explains the vital forces of the body and this, though it may be helped by anatomy, demands observation of or experiment on the living organism. Fabricius' description of the valves in the veins stimulated Harvey to find out their use by the experimental method. Gaskell's physiological demonstration of the muscular continuity between the auricle and the ventricle was made on reptiles and was supposed to be confined to them until 1893, when the auriculo-ventricular bundle was described in mammals by Stanley Kent and by W. His, junior; in 1906 Tawara gave a full account of the junctional system, including the auriculo-ventricular node and the bundle previously described by Kent and His, the fibres of the bundle being continued into the Purkinje fibres which line

the interior of the ventricles and communicate with their muscular fibres; this was followed in 1907 by Keith and Flack's discovery of the sino-auricular node, the normal pace-maker of the mammalian heart; the later anatomical observations were subsequent to and directly stimulated by the needs of the new cardiology, for Mackenzie's epoch-making book on the pulse was published in 1902. Thus it may be noted that, just as medicine is deeply indebted to the experimental method, so also science owes a debt to medicine, and that they two "according well may make one music as before".

The capillaries. It must have been an almost insuperable obstacle to the conception of the circulation that the arteries and veins gradually diminishing in size ended in the tissues without any visible communications. The probability of some continuity had been rather vaguely foreshadowed by Aristotle and Erasistratus, and it was assumed that there were direct communications between the arteries and veins, resembling in miniature what is now known as an arterio-venous aneurysm, and indeed the direct communication between the coronary arteries and the Thebesian vessels recently shown by Wearn. This was the view held in the seventeenth century by Riolan, Cornelius ab Hogeland, and Descartes.

Henry Power (1623–68), the author of *Experimental Philosophy, in three Books, containing new Ex-*

periments, Microscopical, Mercurial and Magnetical, 1664, was a correspondent of Sir Thomas Browne and, as his subsequent letters show, took heed of the advice, probably given him in 1647 when at Cambridge, to make himself "master of Dr Harvey's piece *De Circul. Sang.*" In an unpublished manuscript (1663, Sloane MS. 1343) in the British Museum, for a transcript of which I am much indebted to Dr Charles Singer, Power describes how, although using Leeuwenhoek's lens, he could never detect any opening between the arteries and veins, though in a letter to Sir Thomas Browne in 1649 he speaks of "the minute and capillary chanells". Richard Lower in his *Tractatus de Corde*, 1669, inferred that there were hair-like tubes too small to be seen uniting the arteries and veins. The tercentenary of the birth of Marcello Malpighi, the father of histology, on 10 March 1628 and that of the *De Motu* appropriately coincide, for in 1661 he provided the final proof of Harvey's discovery by recognizing the capillaries in the frog's lung. He also saw the red blood corpuscles in the mesenteric vessels of a hedgehog, but as he regarded them as fat cells, Antony van Leeuwenhoek, "the immortal Bedell" as B. Ward Richardson christened him, who described them fully in his *True Circulation of the Blood* in 1686, has the credit of their recognition. Johannes Swammerdam, however, had actually noted the

presence of red blood cells as early as 1658, but his observation was not made public until 1738 when Boerhaave brought out Swammerdam's *Biblia Naturae*. Luciani gives the credit of first seeing with a microscope the red corpuscles in the capillaries of a living animal (an embryo chick) to Lazzaro Spallanzani in 1771.

After the discovery of the capillaries there was a long interval before this most essential part of the circulatory system received due attention. Thomas Young in 1808 had the foresight to assume as probable variation in the size of the capillaries. Poiseuille in 1834 noticed the central core of red cells and the peripheral layer of plasma with the more slowly moving leucocytes. The view that the capillary circulation was a mere passive communication between the arterioles and the venules was definitely modified by Stricker's observation in 1865 that the capillaries became constricted from swelling of the endothelial cells. In 1873 Rouget observed on the surface of capillaries the cells which bear his name, and described their contraction; this was confirmed by Vimtrup and by Krogh; but Aschoff and Ohno disputed this and regarded them as adventitial cells, a view endorsed by Clark and Clark, who observed contraction of the capillary endothelium both before the Rouget cells appear and in areas devoid of Rouget cells when these have developed. In 1879 Roy and

Graham Brown showed that the calibre of the capillaries is constantly changing without corresponding alterations in the arteriolar pressure. The study of the capillary circulation then languished; but the invention of capillary microscopy by Lombard in 1912 again stimulated investigation, and it has now been proved that the walls of the capillaries have independent powers of changing their calibre. The mechanism of variations in the size of the capillaries—their dilatation and constriction—has been much discussed; there are obviously several possibilities: what share is played respectively by the direct action on the capillaries of the vasomotor nerves discovered by Claude Bernard in 1851, by chemical influence, and mechanically by the conditions of the circulation in the arterioles and venules? In a review of the subject in 1921 Hooker concludes that while the capillary bed responds to both chemical and nervous influences, the chemical are concerned with dilatation and the nervous with constriction.

The capillary circulation, thanks to the experimental labours of Dale, Laidlaw, Richards, Krogh, and Lewis, has been placed in a new light. It appears that the capillary area as a whole is in a constant state of flux; while the great portion is relatively empty, various parts of it open for a time, so that with a constantly changing condition of the con-