Papers and Originals

Harvey's Third Circulation. De Circulo Sanguinis in Corde*

D. EVAN BEDFORD, C.B.E., F.R.C.P.

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Tardy Recognition

It has always seemed strange to me that while Harvey has been universally credited with elucidating the systemic and pulmonary circulations his recognition of the third and quite separate coronary circulation has never received due attention. In *De Circulatione Sanguinis* he replied to Riolan's objections to a twofold circulation as follows: "it was possible for the learned gentleman here to add a third, very short circulation; namely, from the left ventricle to the right one driving a portion of the blood round through the coronary arteries and veins, which are distributed with their small branches through the body, walls and septum of the heart," and later, "for what should the coronary arteries pulsate in the heart save to drive blood on by that impulse? And why should there be coronary veins except to acquire blood from the heart? Add further that a valve is very commonly found in the opening of the coronary vein preventing entry into it, but favouring egress from it. So a third circulation must certainly be admitted by one who admits a general circulation passing through both lungs and brain."

In his memorable oration of 1961 Sir Arthur Thomson retraced the slow and faltering footsteps of those who contributed to the consummation of Harvey's discovery in regard to the general circulation over two centuries of time. Today the third circulation has become of first importance, so that the time seems ripe to trace the gradual progress of ideas since Harvey's day so as to understand better the problems which confronted those who followed him in unravelling the secrets of the coronary circulation.

We have grown accustomed to think of Harvey as a physiologist, yet in fact he was primarily an anatomist and styled himself "Professor of Anatomy in the College of Physicians of London" on the title-page of *De Motu Cordis*. In his lectures he defined anatomy as "that faculty which through inspection and dissections reveals the uses and actions of the parts," thus indicating that the study of structure is the first step to understanding function, and therefore I shall first speak of anatomy.

Anatomy of the Coronary Circulation

By the end of the sixteenth century Vesalius had portrayed the vessels which crown the heart as in fact Leonardo da Vinci had done before him. Harvey was undoubtedly the first to appreciate the nutritive function of the coronary arteries, and next in time and importance, as Keynes puts it, came Richard Lower, a versatile genius and dexterous dissector who assisted Willis in his work on cerebral anatomy; and Sir Charles Symonds has given us a fascinating account of his association

with Willis at Oxford. Lower (1669) noted the change in colour of venous blood after passing through the lungs and even conceived the idea of a pulmonary bypass, such as is now used in cardiac surgery, as a substitute for the lungs. He dissected the coronary arteries and demonstrated intercoronary anastomoses by injecting one artery from another, recognizing the importance of this discovery in these words: "There is everywhere an equally great need of vital heat and nourishment so deficiency is very fully guarded against by such anastomoses."

Raymond de Vieussens of Montpellier, a most industrious physician, possessed of an urge to seek out the secrets of nature, gained a great reputation in anatomy by his *Neurographia Universalis*, but, unfortunately, tarnished it later by speculative dabbling in the field of chemistry so that his *Treatise on the Heart* (1715), published in the year of his death, did not receive the acclaim it merited. He made many outstanding contributions to the anatomy of the heart, describing and portraying the course of distribution of the coronary arteries and veins in detail, including the valve between the coronary vein and sinus which still bears his name. He first discovered the third coronary artery, which he named the adipose artery, arising separately from the aorta and coursing over the conus arteriosus to form the anastomotic ring of Vieussens. This accessory coronary artery is now known to occur in 40 to 50% of normal subjects and is rarely occluded, so that it may provide a useful anastomotic channel in coronary disease. It was renamed the conus artery by Schlesinger *et al.* (1949), and in spite of its small calibre it has been catheterized in living man by selective coronary angiography (Gensini *et al.*, 1967).

Vieussens's most important discovery relates to the intramural circulation of the heart. Influenced by Cartesian ideas, he postulated that there must be direct channels between the heart cavities and the myocardium admitting the ferment which caused the blood to expand, so he devised experiments to prove this hypothesis and to refute Lower's assertion that the lining membrane of the heart was impervious. With a small ivory syringe he injected the coronary arteries and veins with mercury and saffron dye and found that his injections passed directly into the heart cavities through small openings in the endocardium. He concluded that the circulation in the heart differed from that of other organs and envisaged blood being forced out of the muscle into the heart cavities during systole. This systolic squeeze was later confirmed by Porter's experiments (1898). Vieussens embellished his theories with a good deal of speculation, but undoubtedly he was the first to demonstrate the thebesian circulation.

Thebesius (1708) repeated these experimental injections and concluded that the foramina which bear his name communicated with the coronary veins rather than the arteries as Vieussens had supposed. Abernethy (1798) distended the thebesian foramina by waxen injections, and much later Grant and Viko (1929), using a dissecting microscope, succeeded in

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injecting the foramina directly and found that they communicated freely with the coronary veins but not directly with the arteries. Grant and Regnier (1926) concluded that the thebesian vessels represent the primitive embryonic circulation of the spongy myocardium before the coronary arteries appear, and in fishes they remain more important than the coronary vessels proper in nourishing the heart. Finally Wearn and his co-workers (1933), using a celloidin injection too thick to penetrate the capillaries, identified direct channels between the coronary arteries and the heart cavities which they named arterio-luminal and arterio-sinusoidal vessels. So Vieussens's speculations on the coronary circulation, belittled at the time, have proved to be nearer the mark than his critics supposed.

Coronary Anastomoses

More than two centuries were to elapse before Lower's demonstration of intercoronary arterial anastomoses was finally confirmed. During the eighteenth century Thebesius, Haller, Morgagni, and Senac supported Lower, but in the nineteenth century controversy arose. Hyrtl (1873), then a leading anatomist in Europe, using an injection and corrosion technique, denied the existence of coronary arterial anastomoses except at capillary level, a view shared by Henle.

Ligation of the coronary arteries in dogs, first performed by Chirac in 1698 and by Erichsen in 1842, had always caused fatal cardiac arrest, and, following the experiments of Cohnheim and Schulthess-Rechberg (1881), the idea that the coronary arteries were "end-arteries" gained general acceptance. Herrick (1912, 1918) has indicated how Cohnheim's opinion kept alive the notion that acute coronary occlusion in man was essentially a finding of the deadhouse and how this delayed the clinical recognition of coronary thrombosis. However, the validity of Cohnheim's experiments and conclusions was questioned by later physiologists, who showed that, with better techniques, coronary ligation need not cause immediate death, and gradually physicians and pathologists began to realize that long-standing coronary occlusion with fibrous infarction was often found at necropsy in patients dying from other causes.

Pratt (1898) introduced the idea of "functional end-arteries," when the resistance in the anastomotic channel exceeds the filling pressure, and to a large extent this is true of the coronary vessels. Coronary occlusion usually leads to infarction, but the area infarcted is always smaller than that normally supplied by the occluded artery, especially if occlusion is gradual and the collateral channels are well developed.

During the present century the question of coronary anastomoses has been widely investigated, using more sophisticated injection techniques combined with radiography, stereoradiography and corrosion methods, by Gross (1921), Spalteholz (1924), James (1961), and Fulton (1965) with many others, and all have shown that anastomoses between the coronary arteries at precapillary level are numerous and abundant. Haller's finding of extracoronary anastomoses with adjacent arteries in the thorax has also been confirmed (Hudson *et al.*, 1932).

Today a working knowledge of the distribution of the coronary arteries and of the blood supply to the neuromuscular tissues is needed by physicians, surgeons, and radiologists; for, as James (1968) has shown, the site of occlusion may be correlated with the events and complications of cardiac infarction, and a precise knowledge of the radiological anatomy of the coronary vessels is essential for the interpretation of selective coronary angiography.

Coronary Physiology

Harvey's third circulation is far more intricate than the other two, and the first to turn his mind to its physiological problems

was Johannes Baptista Scaramucci, who practised at Urbino and Macerata in central Italy and belonged to a learned society—the Imperial Academy of Searchers into Nature. His works were all printed locally and must be of great rarity, for, though his theories have often been quoted, sometimes incorrectly, all references to them in the literature are citations from Haller. His novel concepts of the mechanism of coronary flow were published in 1689 in a tract entitled *De Motu Cordis Mechanicum Theorema*, and later incorporated in a larger treatise published in Urbino in 1695, a copy of which Mr. Payne has kindly traced in Padua.

Scaramucci started from the hypothesis that the movement of the blood through the substance of the heart was not continuous but halted during systole by muscular compression of the intramyocardial vessels. He next postulated that the superficial coronary arteries were filled during systole but were unable to empty through the veins owing to obstruction in the rigid myocardium, so that no blood flowed from the coronary vein. During diastole blood was impelled by the peristaltic force of the arteries through the relaxed myocardium into the veins and right heart. He also believed that the intramural vessels were squeezed empty during systole.

How nearly he predicted current views is illustrated by a quotation from Paul Wood's textbook (1968)—"During systole ventricular contraction prevents blood flowing through the coronary vessels which penetrate the left ventricular muscle and large arteries on the surface dilate to form an elastic reservoir which in recoil during diastole acts as an accessory pump forcing blood onwards"—surely almost a paraphrase of Scaramucci's theorems.

His remarkable conception of coronary haemodynamics attracted little attention at the time and was soon overshadowed by the long controversy over Stroem's hypothesis (1707) that the coronary vessels were filled in diastole because their mouths were closed in systole by the aortic semilunar cusps, so that the coronary arterial pulse was diastolic in time, an error repeated as late as 1866 in Ozanam's treatise on the pulse.

Stroem's hypothesis was much debated during the eighteenth century; by the nineteenth century most anatomists had rejected it, and many competent observers had shown that the coronary pulse was systolic in time. However, the controversy was renewed in 1855 when Brücke, professor of physiology in Vienna, revived Stroem's theory and engaged in a stormy dispute with Hyrtl, his anatomical colleague. Brücke conceived an autoregulation of the heart, each ventricular contraction being terminated by cessation of coronary flow and the next contraction initiated by restoration of flow in diastole. He was apparently quite unaware that this idea had been developed in detail by Scaramucci two centuries before him.

The controversy over Stroem's hypothesis was finally settled in Chauveau's laboratory in the Veterinary School at Lyons, where, with Marey, he was the first to perform cardiac catheterization in unanaesthetized horses. Under his direction Rebatel (1872) investigated the coronary circulation in horses, recording simultaneously the velocity of coronary flow and aortic and coronary arterial pressure. He showed that the coronary pulse was systolic and that as the pressure rose in systole the velocity diminished owing to resistance in the compressed myocardial vessels, increasing again in diastole. Porter (1898) confirmed the systolic coronary pulse and also the "systolic squeeze" of Scaramucci. Though the validity of Rebatel's tracings is questionable, nevertheless his was the first attempt to replace speculation by experimental demonstration of coronary flow.

During the present century physiological investigation of the coronary circulation in animals has been intensified by use of vastly improved and complex apparatus, and the whole subject was admirably reviewed in Anrep's classical paper (1926). Since that time cardiac catheterization has come into clinical

use and physiological investigation of the coronary circulation has been switched from animals to man. I cannot review the vast field of modern physiological research, but I venture to summarize present opinion in these simple terms—Coronary flow through the left ventricle is intermittent and predominantly diastolic, whereas in the right ventricle, in which systolic muscular compression of the intramural vessels is relatively feeble, coronary flow is continuous and predominantly systolic. While the left ventricle throttles its own blood supply in systole, its systolic squeeze drives blood onwards towards the veins. During diastole there is a sudden increase in coronary flow into the empty myocardial vascular reservoir, which thus functions as a sort of third ventricle.

Coronary Heart Disease

Harvey was familiar with ossified arteries and concluded that blood "does not pass with the same rapidity through occluded or impeded paths as it does meandering through open free patent ones" (*De Circulatione Sanguinis*). Ossification of the coronary arteries was recognized at the start of the eighteenth century by Thebesius and Senac, and Morgagni described chest pain which was doubtless often anginal in such cases. Yet the history of coronary heart disease really starts with Heberden's account of angina pectoris given at the College in 1768, which quickly led to its widespread recognition by contemporary physicians all over Europe. He had no idea that anginal pain arose from the heart and went no further into its cause than to postulate a spasmodic rather than an inflammatory disorder, but none the less his precise account of the symptomatology ranks as a masterpiece among original descriptions of a new disease and as one of the great milestones in the history of cardiology after Harvey.

Jenner was the first to relate Heberden's angina to ossified coronary arteries, and he communicated his opinion to the Fleece Medical Society, where later Parry read a paper on the same subject; but they delayed wider publication for fear of alarming John Hunter, in whom Jenner had diagnosed angina pectoris, and by the time Parry had published his *Inquiry into Syncope Anginosa* (1799) Jenner was preoccupied with vaccination against smallpox. It seems remarkable today that a busy country practitioner should have made two such major discoveries in medicine, and regrettable that this College should have refused to admit him to Membership except by examination, though later the President, Sir Lucas Pepys, requested Jenner to vaccinate his grandson, and happily we have made amends and given his portrait a place of honour in the Censors' room.

The coronary theory was strongly supported by Allan Burns in his textbook on heart disease (1809), in which he explained effort pain in terms of relative cardiac ischaemia and performed the decisive experiment of provoking muscular ischaemia by exercising a limb girt with a ligature. Such an experiment was repeated by Sir Thomas Lewis 120 years later in his investigation of ischaemic pain.

Delays in Recognition

The stage now seemed set for the clinical recognition of coronary heart disease; but it was not to be, and instead the curtain went up on a long and fruitless controversy over the cause of anginal pain, which became a battleground of rival hypotheses for over a century, and as late as 1925 Louis Gallavardin wrote: "alongside the suffering of the anginous patient is the suffering of the physician who attempts to study the cause of the disease."

There were other reasons for the delay in recognizing coronary heart disease. The first half of the nineteenth century

was above all an era of physical diagnosis, and physicians flocked to Paris, where the stethoscope had become the symbol of a renaissance in clinical medicine. Coronary disease, concealed from auscultation and percussion, was almost completely ignored by Corvisart, Laennec, and Bouillaud, the leading Parisian teachers, and fared no better in Vienna at the hands of Skoda and Rokitsky, or in Dublin, where Stokes and Bellingham were obsessed with fatty heart.

The idea of neuralgic or functional angina spread from the Continent to this country, and before long the symptoms described by Heberden became confused with those of neurotic and vasomotor disorders, and terms such as false or pseudo-angina and even *angina sine dolore* became current. In the early part of this century Sir Clifford Allbutt's strong opposition to the coronary theory of anginal pain almost succeeded in ousting it in favour of his aortic theory, and undoubtedly this delayed the recognition of coronary heart disease.

Pathologists were no less blind than physicians to the significance of coronary disease. Ruptured heart and cardiac aneurysm were attributed to fibrous myocarditis, which was regarded as inflammatory on the authority of Virchow and Rokitsky. Acute infarction was mistaken for fatty degeneration, and "fatty heart" became a fashionable diagnosis. It was not until the end of the last century that German pathologists, notably Ziegler and Weigert, established the ischaemic basis of acute infarction and fibrosis and related them to coronary occlusion.

A Great Landmark

The next great landmark in the history of coronary heart disease was the general recognition of the clinical features of acute cardiac infarction. Though this condition was a well-described clinical entity by the end of the last century and had been fully reviewed by von Leyden (1884) and in René Marie's Paris thesis (1896), physicians were still preoccupied with physical signs, and probably regarded these papers as no more than a further contribution to the seemingly endless dispute over the cause of anginal pain.

It remained for American physicians to establish once and for all that coronary thrombosis, far from being a pathological curiosity, was a common clinical condition which could often be diagnosed with assurance, and that it was compatible with life and even with health in those who recovered well. The pioneer in this "new deal" for coronary heart disease was James Bryan Herrick of Chicago, the first to describe sickle-cell anaemia, and, like Allbutt, a man of literary tastes, well versed in the history of angina pectoris. His first paper, in 1912, met with no better fate than von Leyden's; but his second paper, in 1918, at last struck home and set in motion a widespread investigation of all aspects of coronary heart disease. He knew the importance of putting this disease on the clinical map and foresaw that an episode of acute infarction might become a keystone in diagnosis. He was the first to record the electrocardiogram in cardiac infarction, and encouraged Dr. Fred Smith to investigate the serial cardiographic changes produced by coronary artery ligation in dogs.

In 1920 Pardee reported the cardiogram of acute myocardial necrosis in man, and by 1928 Parkinson and I had recorded successive changes portraying the process of necrosis and healing. The use of chest leads increased the scope and accuracy of diagnosis, and soon it became evident that many patients complaining of angina of effort already had healed infarction, and that even when the cardiogram at rest was normal an exercise test could often provoke diagnostic ischaemic changes. Thus the electrocardiogram provided for the first time an objective clinical sign of coronary heart disease, the lack of which had for so long hindered diagnosis; and today selective

coronary cineangiography, introduced by Mason Sones, has given us an additional means of demonstrating cardiac ischaemia.

Incidence of Coronary Heart Disease

The recognition of coronary thrombosis and of ischaemic changes in the electrocardiogram opened up a new era in the diagnosis of chest pain and resulted in a rapid increase in the number of cases of angina pectoris and cardiac infarction seen in hospital and private practice, so that the idea of a modern epidemic of coronary disease naturally arose.

As a student I had never heard of coronary thrombosis and did not make my first clinical diagnosis until 1924 in a case admitted to the surgical wards at the Middlesex as an acute abdomen, as often happened in those days. Working at the London Hospital with Parkinson in 1926, I watched the epidemic spreading around the neighbourhood as local practitioners began to recognize coronary thrombosis, and by 1930 it had become a common and familiar illness. Nature does not change her habits overnight, and it was obvious to me at the time that new knowledge and improved diagnosis were responsible for this rapid increase in the clinical prevalence of coronary disease. A similar sequence of events occurred later in the field of congenital heart disease, of which I saw only occasional cases before the advent of cardiac catheterization, angiocardiology, and cardiac surgery, after which the number of patients seen in hospital and practice increased by geometrical progression.

History suggests that angina pectoris was common in the past, though the popular idea of a mortal disease ending in sudden death discouraged the recognition of milder cases. Heberden, a general physician not specially concerned with heart disease, saw 100 cases of the more severe type, Allan Burns found it frequent in Glasgow, and Huchard and Allbutt obviously had a vast experience of it. As long as the cause of anginal pain was in dispute its diagnosis was always doubtful and even necropsy was not decisive. As Allbutt rather cynically remarked—"call no man anginous till he be dead and not even then unless he has played the game." I am not competent to assess mortality statistics, but Maurice Campbell (1963) in his masterly study of the death rate from heart disease over the last 80 years has shown the importance of the changing age structure of the population and of changing methods of certification and diagnostic habits in explaining the increased mortality from heart disease after 1924. In the case of coronary disease the death rate increased by geometrical progression like an infectious disease in a non-immune population, and he explains the epidemic as a spread of new knowledge in ever-widening circles via physicians, pathologists, and practitioners to the lay public.

Robb-Smith (1967) has studied the age-specific death rates in those aged over 45 in England and Wales from the standpoint of a pathologist, and concludes as follows—"there is no known evidence for an increased age-specific incidence of coronary thrombosis or myocardial infarction from English or American post-mortem studies."

I am well aware that others have reached different conclusions—for example, Ryle and Russell (1949) and Sir Maurice Cassidy in his Oration of 1946. After watching the course of events over the last 40 years, particularly the increasing use of electrocardiography in the diagnosis of chest pain, I have formed the opinion that, prior to the clinical recognition of coronary thrombosis, mortality statistics are completely unreliable as an index of the true age-specific incidence of coronary heart disease. It is not to be doubted that we encounter this disease far more often today than in the past, but I believe that this is adequately explained by a big increase in the middle-aged and elderly population, together with our far greater ability to recognize it, thanks to new knowledge and vastly improved means of diagnosis.

Treatment

Heberden advised alcohol and opium for severe anginal pain, and since then a multitude of remedies have been advocated, but only a few of them are worthy of mention.

A century ago Lauder Brunton (1867) introduced amyl nitrite with the idea that it lowered the blood pressure, and in 1879 Murrell found that nitroglycerin had a similar action. Nitroglycerin remains unsurpassed as a remedy for the relief of anginal pain, though its precise mode of action is still uncertain; for long it was assumed to dilate the coronary arteries, but recent haemodynamic investigations suggest that its most important effect is to reduce myocardial work rather than to increase coronary flow.

The next important advance was the introduction of therapeutic myxoedema by Blumgart and his colleagues in Boston (1933) for the relief of persistent coronary insufficiency. They first advocated total thyroidectomy, and later radioactive iodine and antithyroid drugs were used to the same end. There is no doubt that this form of treatment often brings a considerable measure of relief to patients with intractable anginal pain and I still use it occasionally, but myxoedema is not a very tolerable state. Today we aim to reduce myocardial rather than general metabolic activity by propranolol, which is proving a valuable new method of treatment in selected cases.

Anticoagulant therapy for myocardial infarction, pioneered by Dr. Irving Wright of New York, promised to be an important advance in treatment, and it is a sad comment on the difficulty of establishing the value of a remedy that there should still be such a clash of views about it; but, whatever our final conclusions may be, there is no doubt that it can reduce the incidence of pulmonary embolism and that, judiciously used, it can save lives. On the other hand, I believe that little is to be gained by the routine use of anticoagulants in all cases, which has resulted in patients being moved from their homes to hospital in the most dangerous stage of the illness, some of them dying before reaching the wards.

Looking back to 40 years ago when patients were given morphine and absolute rest at home at the start, I doubt if the overall early mortality has been appreciably lowered, since hospital mortality has remained around 30% for many years. Björck (1968), reviewing 25 years' experience in Sweden, reached the same conclusion; indeed, he believes that the immediate prognosis may even have worsened in recent years as a result of moving gravely ill patients to hospital.

Intensive care units have already proved valuable as a research tool and promise to reduce the mortality in those reaching hospital safely, while intensive care ambulances, now on trial in Belfast, have reduced the hazards of the journey. It is yet too early to assess the scope of intensive coronary care in the hospital service as a whole, but the new knowledge gained should lead to improving the immediate prognosis of acute infarction.

Surgical Treatment

Surgical interruption of the nervous connexion of the heart as a means of preventing anginal pain, suggested by François Frank in 1899, was first carried out by Jonnesco of Bucarest in 1916, and since then many different neurosurgical procedures have been used, the most effective of which has been resection of the upper dorsal sympathetic chain.

Revascularization of the myocardium by muscular or omental grafts was first tried over 30 years ago, and later implantation of an internal mammary artery into the myocardium was introduced by Vineberg (1946). Postoperative angiography has shown that the implanted artery often remains patent, so that this type of operation is winning more favour. Direct surgical attack on the obstructed artery is restricted to cases showing

proximal segmental occlusion of a main vessel, and Effler (1967) regards obstruction of a dominant right coronary artery as specially amenable to direct surgery.

The indications for surgical relief of cardiac ischaemia are difficult to decide as good results have been claimed, as might be expected, for almost all surgical procedures. In 1966, Friedberg concluded that "no procedure appears satisfactory at the present time, and I don't recommend any," but cardiac surgery is advancing rapidly and we should keep an open mind on its possibilities.

Conclusion

To conclude, in tracing the desultory progression towards understanding the coronary circulation since Harvey's time, my purpose has been to indicate the main problems which had to be solved before coronary heart disease could be recognized. History shows that, as in Galen's day, long stretches of time had to be spent in argument over erroneous hypotheses, but, as Lord Cohen has shown in his Nuffield Lecture (1967), errors may be fruitful on account of the investigations required to refute them.

Today coronary heart disease is probably the most important single determinant of the limits of human life (Björck, 1968) and world-wide researches are in progress to discover its cause and prevention. When ageing proceeds more rapidly in the arteries of the heart than elsewhere we should certainly seek an explanation, and if we can find one, and so separate occlusive coronary disease from senescence, then we shall have made a start towards discovering its basic cause.

We are now so encumbered with knowledge that imaginative thinking has become more difficult than in Scaramucci's day, and it may be that we shall come to rely on the faultless mechanical mind of the computer to sort out our data. Existing hypotheses are no more than old ideas in a modern setting. The metabolic theory of angina started in Heberden's day as the gouty diathesis, then it moved to abnormal cholesterol metabolism, and more recently glucose intolerance or larval diabetes has been postulated.

Jenner in his letter to Parry mentioned concretions on the inner wall of the artery due to coagulable lymph, and Rokitsky related atherosclerosis to mural thrombosis, but his theory failed to survive Virchow's opposition. Later Duguid (1946) revised and elaborated the thrombogenic hypothesis and provided what to my mind is convincing evidence in its favour as an important basis of occlusive coronary disease.

Epidemiological investigations suggest a multifactorial aetiology which amounts to little more than the evils of civilization added to diseases common in middle age. We shall continue to seek out a primary cause for occlusive coronary disease, but meantime we must accept predisposing causes such as hypertension, diabetes, hypercholesterolaemia, cigarette smoking, and physical inactivity as a working basis for preventive measures such as are already being tested on a large scale. Ideally, prevention should be directed in the first place to those specially at risk in early adult life and before clinical evidence of coronary disease appears; but, so far, an "identikit" for the coronary-prone individual has not been convincingly established.

As this Royal College was the birthplace of our knowledge of angina pectoris two centuries ago, it will now be concerned with coronary disease, recognized today as a leading cause of disability and death from early middle-age onwards. The time will surely come to plan and put into operation measures to prevent or control the development of premature coronary disease, and I feel confident that when it does the College will be ready to advise the Ministry of Health, the medical profession, and the public on how best to proceed with such a major public health problem.

I wish to thank Mr. L. M. Payne, our librarian, for much kind help in tracing early literature, and Dr. Giuseppe Ongaro for discovering a copy of Scaramucci's work in Padua, and for a xerox copy of the text. I gratefully acknowledge Sir John Parkinson's constant guidance and my sister's help in translating Latin texts.

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