The need of research in medicine : the Harveian oration delivered before the Royal College of Physicians of London on St. Luke's Day, 1907 / by Frederick Taylor.

The Harveian Oration
1907

Frederick Taylor, M.D.

THE NEED OF RESEARCH IN MEDICINE

THE HARVEIAN ORATION

DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS OF LONDON ON ST. LUKE'S DAY, 1907

BY

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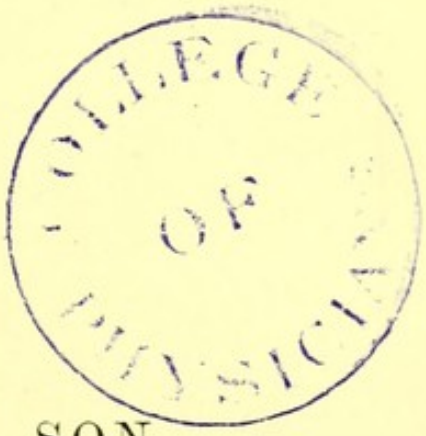

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TO

SIR R. DOUGLAS POWELL, BART., K.C.V.O.,

M.D.LOND., HON. M.D.DUB., LL.D.ABERD., D.SC.OXON.

PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS

PHYSICIAN-IN-ORDINARY TO HIS MAJESTY THE KING

THIS ORATION IS DEDICATED

WITH HIGH ESTEEM AND KIND REGARD

THE HARVEIAN ORATION

ON

THE NEED OF RESEARCH IN MEDICINE.

Mr. President,—In accepting at your hands the office of Harveian Orator, and in entering upon my task this day, I have tried to think that I need not excuse myself for undertaking it nor apologise for any want of that fitness which you have the right to demand. It would be disloyal of me to throw any doubt upon the wisdom of your election, and my plain duty was to fulfil your wishes to the best of my ability. But the more I have considered the subject which lies before us to-day, and the more I have read of the orations which have been given

in recent years, the more I feel the honour that has been conferred upon me in the present appointment, the more oppressive and arduous at the same time seems the duty with which that honour is associated. I enter upon the task with no less, but more, apprehension than can have troubled my predecessors lest I should fail in doing justice to the subject : with much greater certainty than anyone can have entertained, that my presentation of it will fall short of excellence.

We are met here to-day in honour and memory of William Harvey, and for the purpose of carrying out the wish expressed by him that an oration should be delivered annually in the College, with certain definite objects. It is conceivable that a bequest similar to Harvey's, and accompanied by like conditions, might have been made by a Fellow of moderate attainments, of ordinary abilities, and distinguished by no great achievements in medical or physiological research. The fact that the present oration has been imposed upon us by one of the

greatest of medical scientists, who first discovered the true relations of the heart and its movements to the blood which passes through its cavities, gives an importance to the oration which it might not otherwise have had, and justifies the practice which has been almost universal of making an eulogium of Harvey a necessary part of the orator's duty.

It is scarcely necessary for me to recall the facts of Harvey's life. Born at Folkestone in 1578, he was educated at Canterbury and went to Cambridge at the age of 16 years, where he took the degree of Bachelor of Arts three years later. For his medical education he proceeded to Padua, where he studied under Fabricius of Aquapendente, and becoming a Doctor of Physic there at the age of 24 years, received in the same year at Cambridge the degree of Doctor of Medicine. Soon afterwards he married and commenced practice, and being entered on the roll of candidates for the Fellowship of this College in 1604 he became a Fellow three years later, at the age of

29 years. In 1610, at the age of 32 years, he was appointed physician to St. Bartholomew's Hospital, and some years later he received the Court appointment of Physician Extraordinary to James I, and some ten years later again he was made Physician-in-Ordinary to Charles I, whom he accompanied on two or three occasions to Scotland, and with whom he was present at the Battle of Edge Hill in 1642. He retired from his Court appointment in 1646 at the age of 68 years, and soon afterwards withdrew from practice and died full of honours in his eightieth year. The point of interest to us all here is when and how he carried on the observations and experiments which have made his name famous, and which have rightly earned for him the title of discoverer of the circulation of the blood. And it is quite clear that it was comparatively early in his career that he was in a position to roll away the clouds of doubt, misconception, and obscurity which enveloped the question of the heart's action, and to come to the correct conclusions as we know them in the

present day. The treatise, indeed, 'Exercitatio de Motu Cordis et Sanguinis,' was published in 1628, when Harvey was 50 years of age, but he states in his preface that the substance of the book had been given in his lectures before this College for nine years or more, and in his notebook dated 1616—that is, twelve years previously—the essential facts are referred to.

I shall not attempt here to open up again the discussion upon this subject, to state the position of the question at the time he dealt with it, or to give in any detail the arguments based upon innumerable observations and experiments upon animals, living and dead, which convinced him of the truth. Suffice it to say that his chief points are the position and direction of the valves in the veins; the effects of ligatures upon the vessels; and more than all perhaps, his ingenious calculation that the amount of blood passing through the heart in the day, as estimated by the size of its cavities and the number of beats per minute, was vastly more than was introduced into the body from

outside in the same time. Thence came the conclusion that the blood must not only *move* in the vessels, which was already known, but that it must move from the heart and come back to the heart repeatedly—that is to say, must move in a circle. "*Cœpi egomet mecum cogitare, an motionem quandam quasi in circulo haberet.*" What, therefore, Harvey discovered was not the movement of the blood, but its circulation from the heart into the various parts of the body and thence back again to the heart, from the heart again into the lungs, and thence back again to the central pulsating organ. In his own day the events which he asserted were doubted; in more recent times, when the fact of the circulation can no longer be denied, Harvey's claim to have discovered it has been disputed, and even comparatively lately the subject of the Harveian oration by Dr. George Johnson was a disproof of the statement by Italian physicians that this great physiological discovery was made by one of their countrymen, Cesalpino. But Harvey's work was not confined to the subject of the circulation of the

blood, involving though it did an enormous amount of experimentation and much correspondence subsequently in defence of it. For besides some medical observations which have been lost, there is his large work on 'Animal Generation,' with shorter treatises on parturition, on the uterine membranes and humours, and on conception. And a perusal of these can only increase our admiration for his wonderful diligence in research, showing, as they do, the thorough and untiring way in which he subjected any question that he considered to the test of actual observation and experiment.

It is one of the definite objects for which Harvey caused this oration to be founded that the Fellows of the College should be exhorted to search and to study the secrets of Nature by way of experiment; and in fulfilling this part of my duty I may call attention to some passages in the introduction to his work on Generation as illustrating his own convictions at that time as to the necessity of looking to Nature herself for all knowledge and truth:

"For although it is a new and difficult road in studying Nature, rather to question things themselves, than by turning over books to discover the opinions of philosophers regarding them, still it must be acknowledged that it is the more open path to secrets of natural philosophy, and that which is less likely to lead into error.

"Nor is there any just cause wherefore the labour should deter anyone, if he will but think that he himself only lives through the ceaseless working of his heart. Neither, indeed, would the way I propose be felt as so barren and lonely, but the custom, or vice rather, of the age we live in, when men inclined to idleness prefer going wrong with the many to becoming wise with the few through dint of toil and outlay of money. The ancient philosophers, whose industry even we admire, went a different way to work, and by their unwearied labour and variety of experiments, searching into the nature of things, have left no doubtful light to guide us in our studies."

But he continues, we must not allow that all truth was engrossed by the ancients and that nothing remains to be known; remarkable discoveries have been made and toil is sweet "when the pains of discovering are

amply compensated by the pleasures of discovery."

"It were disgraceful, therefore, with this most spacious and admirable realm of nature before us, and where the reward ever exceeds the promise, did we take the reports of others upon trust and go on coining crude problems out of these, and on them hanging knotty and captious and petty disputations. Nature is herself to be addressed; the paths she shows us are to be boldly trodden, for thus, and whilst we consult our proper senses, from inferior advancing to superior levels, shall we penetrate at length into the heart of her mystery."

And further he says:

"Diligent observation is therefore requisite in any science and the senses are frequently to be appealed to. We are, I say, to strive after personal experience, not to rely on the experience of others.

"I would, therefore, have you, gentle reader, to take nothing on trust from me concerning the generation of animals; I appeal to your own eyes as my witnesses and judge."

It has often been remarked that Harvey's work is one of the best examples of the inductive method, and that the time at which he

worked precludes the possibility that he could have been influenced by a study of Bacon's 'Novum Organum.' But it is interesting to remark that Harvey was not conscious that he was working on any new method, but only that he was returning to a system which had, indeed, been long neglected, which had been, nevertheless, as he believed, in past ages employed by those whom he speaks of as the ancient philosophers. It may be difficult to form an accurate idea from what writings have come down to us of the extent to which men's minds in the middle of the seventeenth century were set upon the desire for a more intimate acquaintance with natural phenomena, but that desire cannot possibly have been as intense or as widespread as it is now. Amongst fellows and members of a college of physicians or of surgeons, amongst the members of the profession of medicine in general, amongst the scientific men throughout the kingdom, whether they be chemists or physicists—not now confined, as long ago they were, almost entirely within the ranks

of the physicians—amongst all these, I say, there is really little need to press home the necessity of research and experiments.

Harvey's injunction to search and study out the secrets of Nature by way of experiment wants to be addressed to the lay public, not, indeed, that they may experiment themselves, but that they may promote and forward such experimentation, or at least not hinder and obstruct it. No less than Harvey, in his day, we realise, and would impress upon those outside the profession, that Nature is something more than dry bones and dead anatomy; that not so much what they are as how they work is what must be known with regard to the structures of the body before we can satisfy our needs as physicians, striving to ward off disease, to keep the human machine in proper working order and to prevent it stopping altogether. Can one imagine anyone attempting to teach a student or boy the use of a steam engine or even a more simple piece of mechanism by merely showing him the machine at rest? Until they move, the piston and cylinders,

fly-wheel and cog-wheels have no meaning; when in action the influence they have one upon another, the prime movers and the secondary pieces, can be seen in their proper relations. Complicated as a steam engine may be, it is simplicity itself compared with the human or animal machine, which involves not only principles of pure physics, but of a chemistry of the highest degree of complexity, of physics which seem to differ materially from those of the inorganic world, and of a vital force—that life, which as yet nobody understands and of which no one has even been able to give a satisfactory definition. Is it surprising that in these circumstances the necessity is felt of testing the vital operations in action and not resting content with the mere observation of the changes which have taken place in the structures as the result of internal or external influences?

Opposed to this necessity from the point of view of a desire for knowledge is the humane sentiment so largely entertained and operating for restricting the interference of science with the comfort and existence of the lower

animals. In whatever degree justified from the point of view of sentiment there is no doubt that these restrictions enforced by Parliament must limit the number of members of the profession, must limit the number of Fellows of this College, who can enter upon any experimental researches, and must prevent to a large extent our full compliance with the precept of our great predecessor in this College. It is perfectly true that research is still possible and experiments may yet be undertaken without interfering with the comfort of any other animal than the highest of all, man himself; but the progress that can be made, with such limitations, is exceedingly slow; and the opportunities are so infrequent that few of us can hope to gain any truth thereby. Experiments of any value, research of any depth, almost necessarily fall into the hands of a few persons, those usually who have obtained permission, almost reluctantly given and jealously criticised, to perform experiments upon living animals. In Great Britain there are 34,258 persons on the Medical Register, and the

persons licensed under the Vivisection Act in 1906 numbered 402. Of these, 123 performed no experiments. While allowing that not everyone wishes to experiment or is competent to experiment with any advantage, we cannot help regarding this as a very small proportion of a body of scientific men, to be allowed by the community or State to make any consistent and proper effort to improve their knowledge and their power over disease. The results of such a policy are only prevented from being disastrous by the intimate relations of scientific men all over the world; and by the fact that the defects of research in one country may be compensated by the enthusiasm for more accurate knowledge in another. Harvey, at least, felt the absolute importance of going direct to Nature, and living Nature, in order to solve the problems of the circulation; he exposed the heart of deer and other animals in order to study the rhythm and mode of contraction of the cavities; and it is obvious that by such a method only can a correct conclusion on this point be arrived at.

The advent of the present Parliament has seen another attempt made by certain associations to bring about the total abolition by Act of Parliament of the practice of experiments upon animals, and I think I should take this opportunity to make some reference to it; and in consequence a Royal Commission, of whom our late President, Sir William S. Church, is a member, has been appointed by the Government to investigate the subject afresh and to report upon it. The Commission held its first meeting to hear evidence upon October 31st, 1906; it held sittings in Lent and Easter terms of this year; and it has published the evidence in three separate volumes. This College, among others, was invited to send a representative to give evidence before the Commission, and I had the honour of being asked to join you for this purpose. We drew up a short memorandum on the evidence we were prepared to submit, and we appeared before the Commission on March 5th, 1907. A copy of our evidence and examination has been published in the Minutes of Evidence which

form the appendix to the second report issued in the spring, and it is unnecessary for me to attempt to recapitulate in any detail what we brought under the notice of the Commissioners. For the most part they were the facts and arguments with which the Fellows of this College are familiar, with which they have defended the practice of vivisection for years from the assault of those who would abolish it. But there are a few points to which reference may perhaps be permitted on the present occasion. The arguments of our opponents are concisely two : (1) that vivisection is useless and (2) that it is immoral. With regard to the first it is surely a matter on which we have the greatest right to our opinion. The failure to get immediate results is not an argument against any methods of procedure, unless immediate results are the only things demanded. A knowledge of the fact that the blood circulates is of the greatest importance at the present day : the acquirement of this knowledge was greatly advanced by Harvey's experiments upon

living animals. But it is in the last thirty years since the passing of the last Act that the most remarkable amount of evidence has been provided of the value of experiments upon living animals. The whole science of bacteriology to which we owe antiseptic surgery, antitoxin prophylaxis and treatment in the diseases both of man and of animals, is impossible without operations and experiments upon living animals.

The second objection to the practice of vivisection—namely, that it is immoral—must be judged of by other criteria. Nobody can seriously believe that the medical profession advocates the practice for any other reason but that it supposes it to be of value to humanity and even to the higher divisions of the animal kingdom, or that any individual member of the profession employs it for mere amusement, or from the gratification of any feeling or passion. The profession advocates it ostensibly and actually because it believes that the apparent harm or apparent wrong which it carries with it is enormously overshadowed by the benefit

which accrues to the human race in general. The physician's duty is to do all in his power to save life and alleviate suffering among his fellow creatures, and he reasonably thinks that the sacrifice of life and comfort to a relatively small number of the lower animals is not too high a price to pay for such a consummation. For centuries animals have been killed for food, slaughtered in battle, maimed for sport, or kept in captivity for the mere pleasure or convenience of man. Our contention is that the justification for the pain or suffering we cause—often infinitesimally slight—is quite as complete as that of those who eat meat, amuse themselves by fishing and shooting, or take up arms to defend their country. But without arguing this further I should like again to refer to a point which is, I think, often overlooked by those who imagine that the medical man who can assist at experiments on living animals must have a heart of stone, and must be little better, or even worse, than the members of the brute creation on which he operates. The medical man has before him

as part of his daily life numbers of human beings, it may be his dear friends or relatives, suffering the incapacity, pain, or weariness of illnesses, often prolonged over weeks and months. Is it surprising if he feels something more for them than he does for the lower animals which are submitted to vivisectional experiments? Count all the animals that are the subjects of experiments, perhaps mere punctures in the skin, or feeding with distasteful morsels. What are they compared with the hundreds of thousands of human creatures who suffer death and linger in painful illnesses, which nothing but very continued patient observation and research of Nature by way of experiment is ever likely to prevent or to alleviate? There is no fear to my mind of the profession being brutalised even by witnessing vivisectional experiments, much less by the mere knowledge that such experiments have been performed, or by acquaintance with the results that have been obtained from them. It will be many, many years before the physical infirmities of the human race will

be diminished to such a point that no room is left for the exercise of sympathy and humane sentiment on the part of the medical profession. Had some of our opponents more knowledge of the enormously difficult problems presented by disease, could they picture to themselves the thousands, nay millions, of sufferers upon the face of the earth, one cannot help thinking that they also would be converted to the view that the alleviation of all this suffering and the prolongation of life did indeed justify the sacrifice of animal life which the profession thinks necessary.

The consideration of the question of the value of experiment and research leads one to think on the one hand of the enormous progress which has been made in medicine in the last few years; on the other, of the large measure of our ignorance of natural phenomena in relation to diseases and its treatment or control. The great triumph of the last thirty years is the discovery of the dependence of so much of human disease upon the growth of parasitic organisms. In the

Harveian oration in 1881, Dr. A. W. Barclay, discussing the germ theory of surgical suppuration as put forward by Joseph Lister and the early experiments on splenic fever in animals, asked these questions:

"Can it be that the specific fevers of the human race have each their own bacillus? May the exhaustion of the menstruum serve as an explanation of their termination in individual cases; and the loss of reproductive powers be the cause of the termination of an epidemic? May we hope in each of them some day to inoculate a mild form of the disease which will preserve the individual from a more severe attack?"

In the following year was announced the discovery of the tubercle bacillus by Koch, and this was followed at no long intervals by other discoveries which very nearly supplied the affirmative answer to Dr. Barclay's first question. And although there remain many infectious diseases of which no specific organism can as yet be shown certainly to be the cause, still the resemblance between them and those in which an organism is recognised is so close, that the discovery of an organism

may be reasonably expected. This expectation is justified by the fact that there is progress, although it is slow. Only some five years ago the remarkable disease, sleeping sickness, after a comparatively short period of scientific and skilled research, has been discovered to be the result of infection by a protozoon, the trypanosoma, and not only that, but the exact method by which infection is conveyed—namely, by the bite of a dipterous insect, *Glossina palpalis*—has been clearly shown. The association of the new organisms, discovered by Colonel Leishman, known commonly as Leishman-Donovan bodies, with a tropical disease, kala-azar, in which splenic enlargement is associated with anæmia, is another remarkable achievement of the last few years; and finally, within still more recent times this branch of pathology claims another triumph in the discovery by Schaudinn of an organism in the blood and secretions of patients suffering from that terrible scourge of humanity, syphilis. Even if our results were no faster than this—three new specific organisms in five years—it

would be progress of a most satisfactory kind.

Intimately connected with this branch of inquiry, as to the ultimate cause of the specific fevers, is the question as to how they are contracted, and recent observations have shown that some diseases, believed to be contained in the air, or to be conveyed by the air, or by fomites, or through adherence to various solid bodies, are really transmitted by the bites of insects. These are malaria by various forms of anopheles, yellow fever by the *Stegomyia fasciata*, sleeping sickness and trypanosomiasis by the *Glossina palpalis*, plague by rats or rat fleas, typhoid fever by flies, and it has been suggested, relapsing fever by bugs. In two of these instances at least the discovery has been followed by enormous benefit to various communities, not through the cure of the disease, but through its prevention. Under skilled advice in various parts of the world the campaign against the malarial or yellow fever mosquito has been successfully pushed by the screening of sleeping apartments to prevent the entrance

of the insect, by drainage of the water-logged areas of the soil, by protection of small collections of water from the entrance of the insect to lay eggs, and by destruction of the larvæ when accessible. It is remarkable what a change this new discovery necessitates in our conceptions of the ætiology of some of these diseases and even in the names. Marsh miasms are no longer the agents in the production of the disease; marsh fevers and paludism may still remain as names for the complaint, but *malaria*, derived from the Italian *mala aria* and perpetuated in the names of the *Plasmodium malariæ* and *Hæmamœba malariæ*, is obviously now a misnomer.

Another fact of recent date is that whereas the organisms of infectious diseases were thought to be quite the lowest forms of vegetable life, and chiefly the schizomycetes or fission-fungi, an increasing number of diseases are shown to be due to the entrance into, and proliferation within, the body of definitely animal forms or protozoa, which in some cases go through definite stages of growth,

with sexually differentiated forms and a definite sexual method of reproduction. These protozoa are the malarial organism, the trypanosoma of sleeping sickness, the Leishman-Donovan bodies of kala-azar, the amœba of dysentery, and, finally, there are good grounds for believing that the *Spirochæta pallida* of syphilis and the *Spirochæta Obermeieri* of relapsing fever are only forms of trypanosoma. While so much interest centres about the specific diseases we must not lose sight of the fact that myriads of small ailments, and not a few fatal forms of disease, are due to the pyogenic organisms. The uncomfortable lesions known as boils, small abscesses, catarrhs, and the hundred and one forms of petty inflammation, which take off so much from the enjoyment of life, are due to the omnipresence of these pyogenic organisms; while deeper abscesses, erysipelas, pyæmia, and septicæmia represent the results of a high degree of virulence in the organisms insufficiently combated by the resistive systems of the body.

In any address concerned with the memory

of Harvey the problems concerning the circulation of the blood must, of course, hold a foremost place; and there are some subjects which have recently engaged the attention of clinical physicians to which reference may properly be made. One is the nature of the heart's beat; another is the structure of the blood; a third is the condition of the arterial tension or pressure. All who have read Harvey's works will remember the passage in which he states his sensations on exposing the mammalian heart.

"When I first gave my mind to vivisections as a means of discovering the motions and uses of the heart and sought to discover these from actual inspection, and not from the writings of others, I found the task so truly arduous, so full of difficulties, that I was almost tempted to think with Frascatorius that the motion of the heart was only to be comprehended by God. For I could neither rightly perceive at first when the systole and when the diastole took place, nor when and where dilatation and contraction occurred, by reason of the rapidity of the motion, which in many animals is accomplished in the twinkling of an eye, coming and going like a flash of lightning, so that the systole

presented itself to me now from this point, now from that: the diastole the same; and then everything was reversed, the motions occurring, as it seemed, variously and confusedly together. My mind was therefore greatly unsettled, nor did I know what I should myself conclude, nor what believe from others."

But "at length by using greater and daily diligence, having frequent recourse to vivisections," he was enabled to recognise certain fundamental facts in the cycle of the heart's contractions. He observed that the movement which corresponded to the impulse was one of systole and not of diastole, and there was an alternate contraction of the two auricles and of the two ventricles,

"the motion of the auricles preceding, that of the heart itself following; the motion appearing to begin from the auricles and to extend to the ventricles."

Further, he noted that in the dying organ the ventricles failed before the auricles.

"The heart, therefore, ceased to pulsate sooner than the auricles, so that the auricles have been said to outlive it, the left ventricle ceasing to

pulsate first of all; then its auricle; next the right ventricle; and finally all the other parts being at rest and dead as Galen long since observed, the right auricle still continues to beat, life, therefore, appears to linger longest in the right auricle."

His further observations upon the development of the chick and upon the human embryo showed the precedence of the auricle—that the auricle, indeed, as he puts it—"Both lives before the heart and dies after it."

The dependence of the ventricle upon the auricle under normal conditions and the occasional entire independence of the ventricular beat have acquired recently considerable clinical importance in connection with the phenomena or phenomenon known under the rather undesirable term "heart-block." The movements of the auricle during life have always been difficult to investigate directly; and even in the cardiographic tracing the elevation which is attributed to the auricular beat is obviously obtained only by a transmission of movement through the mass of the heart or ventricle; the contraction of the auricle, however, may produce a wave in the

jugular vein, and a tracing taken from the skin over that vessel may thus give a safe indication both in respect of time and of force of the contraction which is taking place in that part of the heart. Numerous observations of synchronous tracings from the jugular vein, the apex of the heart, and the radial pulse, with which the names of Wenckebach and of Dr. Mackenzie, of Burnley, are associated, have shown that while in health the auricle and ventricle contract in succession, in certain circumstances the ventricle may beat one half as many times as the auricle, or only one third as often; or even that the two contractions may hold no constant relation to one another at all. Gaskell showed experimentally by dividing the auriculo-ventricular ring so as to leave only a small portion of muscle connecting the ventricle to the auricle, that the transmission of the auricular beat to the ventricle might be prevented, and cases of disease have occurred in which the ventricular beats have been less than those of the auricle, in which, therefore, presumably

only every other auricular contraction had been transmitted to the ventricle. In some such cases post mortem there have been found gummata or fibroid lesions involving the auriculo-ventricular ring, so as to act virtually in the same way as Gaskell's incisions, leaving only a narrow bridge by which the wave of contractions could pass from the walls of one cavity to those of the other.

It is believed that normally the transmission of this wave is by means of the bundle of fibres, which, passing from the muscular fibres of the right auricle, dividing and running down each side of the septum of the ventricles, and ending partly in the musculi papillares, is known as the auriculo-ventricular bundle of His; and in some cases of the kind this bundle appears to have been involved. For some time has been recognised a group of cases in which a very slow pulse of 35 or 40 in the minute has been associated with attacks of faintness, giddiness, or actual convulsions; and these cases have been described as Stokes-Adams' disease. Probably all, or most of them, are cases where

the infrequent radial pulse is due to a ventricle contracting only half as often as the auricle, and where the consequent inadequate supply of blood to the brain gives rise to the striking cerebral symptoms. But this does not exhaust the interest and importance of the subject of cardiac contractions studied from this point of view, *i. e.* the comparison of the time relations of the auricular and ventricular beats, as shown by radial and jugular tracings. For it appears that, whereas in health the stimulus to contraction starts in the muscular fibre at the mouth of the large veins and spreads through the auricle and ventricle, in certain circumstances the ventricle may contract independently of the auricle and may continue this improper performance for long periods of time, though not without as a rule inconvenience, irregularity, or feebleness of the beat. Dr. Mackenzie has also made interesting observations on the action of digitalis upon the heart; and it is obvious that there is a large field for research into the action of other drugs upon the contraction of its different chambers.

We may hope that useful results will accrue from these studies by which our treatment of this group of diseases may be materially improved.

The last few years have witnessed a remarkable increase in our knowledge of the corpuscular elements of the blood. The recognition of the circulation in Harvey's time must have been greatly impeded by the fact that the arteries and veins contained blood of different colour, and the great discoverer himself did not succeed in clearing up this difficulty. Indeed, neither in his time nor for many years afterwards does the cause of the colour of the blood seem to have been known, though Lower in 1669 recognised that the change of colour was due to air in the lungs. On the 200th anniversary of Harvey's birthday Dr. Andrew Duncan delivered in Edinburgh an oration, "De laudibus Gulielmi Harvei," and speaking of the blood he says:

"About this fluid, from which indeed the immortal Harvey has deserved and derived the highest honour, many things still remain to be searched

out: among others, the cause of the red colour is still unrevealed."

And again he says: "Hanc igitur questionem proponere liceat: unde color sanguinis?" The solid elements of the blood are now known to us and the chemical constitution and physiological value of the hæmoglobin, which is their important constituent. But while a generation ago we knew little more than that the blood contains red cells or corpuscles, blood discs or erythrocytes, and white cells, colourless cells or leucocytes; we are now able to recognise, as the result of improved methods of staining, which are every year added to, that the leucocytes are of several varieties; and that these varieties hold a definite numerical relation to each other in the normal blood, but that in disease the numerical proportions vary in more or less definite ways, dependent in many cases no doubt upon the varying conditions of the bone-marrow, but in other cases at present entirely unexplained. The coarser methods of estimating the relative number of corpuscles have given place to more accurate

measures; and the enumeration of corpuscles, both red and white, has proved to be of much value, even when the deviations from the normal are but slight, in various cases of infective disorder, whether local or general. In addition, much useful information has been derived from investigation into the specific gravity of the blood and its rate of coagulation, its viscosity, the degree of its alkalinity, and other facts as to the chemical constitution, both of the plasma and of the corpuscles, of which last the curious and interesting cases of methæmoglobinæmia and sulphæmoglobinæmia are examples.

The subject of blood-pressure is also one upon which much valuable work has been done, since instruments have been devised both for demonstrating and recording the movements of the artery which constitute the pulse. Wilkinson King had employed levers to show the movement of pulsations in veins; and Carl Vierordt applied the same principle to the arteries and constructed a sphygmograph in which, by a complicated system of leverage, a tracing was made upon the cylinder

of a kymographion. But the weight and friction were too great to allow a true record of the pulsations.

The sphygmograph of Marey is free from these defects, and is portable, and has given us tracings with which we are all familiar; but in spite of much good work done with it, it has never won a position of confidence with the profession in general. Its own defect, that in its first form it only indicated but did not measure arterial pressure, received attention at the hands of two distinguished Fellows of this College, Sir John Burdon Sanderson and Dr. Mahomed, and the additions made by the latter to Marey's instrument did certainly very nearly meet the difficulty; and the estimate of the pressure combined with the outline of the tracing gave information which was often of great importance. I know it is heresy to say anything which would cast a doubt upon our forefathers' knowledge of the variations in the pulse, but I cannot help thinking that there are conditions of the pulse which could not then be appreciated as they are desired to be in the present day. And I

am convinced that there is no method by which the student can so quickly acquire a *tactus eruditus* as by a constant comparison of his sensations with the readings of a properly constructed sphygmograph. In the present day it will always be desirable when a record has to be made to go somewhat further than touch can go. The final appeal must be to instruments : for the undulations and character of the collapse to the sphygmograph, for the actual tension to one of the numerous instruments recently invented or modified by Oliver, Hill and Barnard, and Gibson in Great Britain, Erlanger, Riva-Rocci, and others abroad, by which either directly by contact with the radial pulse or indirectly by pressure of a band upon the brachial artery, the pressure is measured by a mercurial manometer. Even till quite recently improvements have been made in these instruments, especially with the object of differentiating between the variations of blood-pressure which take place within the compass of a single beat, namely, the blood-pressure at the time of the ventricular contraction (or systolic pres-

sure) and that at the time of the ventricular relaxation (or diastolic pressure), the latter of which is the more difficult to estimate.

This appeal to instruments is no real reflection upon the skill of our forefathers. Science and the acquisition of knowledge necessitate an increase in the capacity of our senses. The sense of sight, already apparently the best trained, and commanding the greatest amount of detail, was improved by the use of lenses many years ago, and Malpighi saw the blood moving in the capillaries in 1661, thus confirming Harvey's deductions as to the circulation. What the microscope has done for vision should be possible in the case of the other senses. And yet how little has been accomplished. The stethoscope is no magnifier, but only a means of conveniently stretching our ears into places they cannot easily reach, and the microphone has not been found to be of great value in medicine. The senses of taste and smell may be supplemented by an entirely different procedure—that of chemistry, and thus happily it is no longer the duty of the physician to taste the urine

in cases of suspected diabetes. But failing this help he who is defective in either of these faculties—and there are many such—may have to rely upon the assistance of some more gifted colleague. We should welcome every addition to our resources for increasing or supplementing our receptive faculties, such as the sphygmographs and sphygmomanometers are intended to do. The subject of blood-pressure, to which these instruments are auxiliary, opens up a large field of clinical and pathological research; much is known, but still much has to be learned on these various points, viz. the rise of arterial tension in later life, its relation to renal affections, its relation to the internal secretions of the ductless glands, such as the thyroid and the supra-renal, the influence of the arterial tension itself in the production of symptoms and of disease, and many others.

Amongst the experimental work which has been done recently under the auspices of this College none perhaps has been more interesting, of greater value, or more in accordance with the spirit of the man whom we com-

memorate to-day than those researches which were laid before us in the Croonian lectures of 1906 by Professor Ernest H. Starling. His subject was the chemical relations of the functions of the body; and among the striking facts that he brought forward was this—namely, that the secretion of the pancreas is caused not so much by nervous influence as formerly believed, as by the chemical action induced by the entry of the chyme into the first part of the duodenum. Thus the acid chyme entering into the duodenum causes the production from the mucous membrane of a chemical substance—secretin; this secretin is absorbed and carried by the blood-vessels to the pancreas, which it stimulates to produce the pancreatic juice. Similar chemical reactions take place in other parts of the alimentary canal, and as Professor Starling remarks:

"We see that, from the entry of the food into the stomach until its passage through the ileo-cæcal valve there is a continuous chain of chemical reflexes, and that the process in any section of the alimentary canal calls forth the activity of the

digestive apparatus in the immediately following section."

All these results have been arrived at only after a long series of experiments; not, of course, only by Professor Starling, but by others, of whom Professor Pawlow, to whom the Baly medal was awarded by this College in 1905, has been perhaps the most prolific and most original. It is, I am sure, a subject for sincere congratulation that the College has felt itself justified in awarding in the present year the same medal "in memoriam Gulielmi Baly, M.D.," to one of its own Fellows, Professor Starling, as having been "deemed to have most distinguished himself in the science of physiology, especially in the two years immediately preceding the award."

I cannot turn from this subject without referring to the fourth of Professor Starling's Croonian lectures—that one in which he showed, as demonstrated by ingeniously conducted experiments, that the growth and development of the mammary glands was dependent, not on nervous influences, but upon the absorption of chemical substances emana-

ting from the fœtus. The reference to these facts will no doubt suggest to many of those present that the Royal College of Physicians itself, not only in the perpetuation of this Harveian oration but also in its annual lectureships and in its award every one, two, or three years of certain prizes, directly stimulates research, much of which must be by way of experiment, so as to carry out fully the wishes expressed by Harvey, the founder of this address. It is true that the subjects of recent Lumleian lectures have been largely based on clinical results and do not often suggest the employment of much experiment, but the Goulstonian lectureship has been more fruitful in work of this kind. The Croonian lectures "on one or more subjects in anatomy, physiology, and pathology, with a view to the prevention, control, and cure of diseases," have constantly been illustrated by important experiments, of which the lectures already mentioned by Professor Starling and those by Dr. W. H. R. Rivers "On the Action of Drugs on Fatigue," are good illustrations. In both of these were

brought before us most laborious, painstaking, and cleverly devised experiments from which valuable conclusions could be derived. The Oliver-Sharpey lecture was endowed in memory of the late Dr. Sharpey with the intention to promote physiological research by observation and experiment on man himself, and to encourage the application of physical knowledge to the prevention and cure of disease and the prolongation of life; the Horace Dobell lecture is given with a view to encourage research into the ultimate origin, evolution, and the life-history of bacilli or other pathogenic micro-organisms; the Baly medal is awarded to "the person who shall be deemed to have most distinguished himself in the science of physiology," and it is quite certain that few at the present time will be held to have taken a leading place in this science who have not engaged in experimental research; the Moxon medal is awarded to the person who should be deemed to have most distinguished himself by observation and research in clinical medicine; and the Parkes-Weber prize is

awarded for the best essay on the subject of tuberculosis, in both of which subjects experiment is possible. Lastly, the Bisset Hawkins memorial medal is a stimulus to experiment, though in a department of which Harvey and his contemporaries probably had but a faint conception—namely, that of sanitary science.

I cannot pretend that I have exhausted, scarcely indeed have I commenced, the enumeration of the advances in medicine and medical physiology of recent times. To two more at least I must refer, and they stand both in that group of results which are more welcome to the lay mind—namely, the immediately practical results of treatment. The earliest outcome of bacteriology, before bacteriology as a science was formulated, when only it became certainly known that micro-organisms were a cause of disease, was the improvement in surgical practice which, initiated by our great countryman Lord Lister, has led up to the present theory and practice of asepsis in surgery. To the possibility thus attained of operating with a

minimum of risk of infection is due the advance which the last few years have seen in this branch of the Ars Medicinæ.

The other advance on the therapeutical side is intimately connected with the subject of prevention and immunity. One might say that the history of it goes back to the time of the inoculation of smallpox two centuries ago—that crude method, yet scientific up to a certain point, of preventing a great evil by substituting a smaller one for it. Then came the far-reaching discovery of Edward Jenner, that the pustular disease of the udders of cattle, the *cowpox*, when communicated, as it often was, accidentally to men or women in the course of milking, protected these men or women from subsequent infection with smallpox. Hence came vaccination as a preventive of one of the most loathsome diseases suffered by man; transmissible, as shown by Jenner himself, from man to man, so that an active virus was continually produced and reproduced sufficient to cause in successive cases an immunity to the graver disease without itself running riot or exceed-

ing, unless from accidental circumstances, its proper functions.

So for almost a century the matter stood. Vaccination for the prevention of smallpox remained an isolated method, the saviour probably of thousands of lives, the preserver of millions of comely faces, undergoing no material alteration, except in detail as to the preservation of the lymph and as to the source of the supply, which is now the calf's abdomen instead of the child's arm, unchallenged so far as smallpox is concerned by any other method of immunising or fortifying the body against this infection. So one may suppose it will remain until the organism of smallpox is discovered. For it is again on the discovery of, and researches on, micro-organisms that the development of methods of prevention and treatment has had to depend. The virus of smallpox and of cowpox—and they are probably identical—lent itself, as it were, almost unasked for the purpose of immunisation without any question of organisms. Progress only became possible in other diseases when the virus or toxin

could be obtained almost as desired from the associated and causative bacteria. Koch announced the discovery of the tubercle bacillus in 1882. In 1891 the attempt was being made in all parts of the world to cure pulmonary tuberculosis by the use of toxins derived from these bacilli. That the hopes entertained of this treatment were not realised is no reflection upon the experimental method itself. Work on similar lines has led up to the enormously practical results, taken altogether, of diphtheria antitoxin, of tetanus antitoxin, of inoculations of serum for the prevention of plague and of typhoid fever, and of the later opsonic methods. Disappointments there have been, and there will be more. The subject is full of difficulties, and very much, of course, remains to be learned. There are diseases of which the organisms have not been discovered; there are organisms from which vaccines cannot be prepared; there are vaccines and serums which have not cured the disease for which they were made. No better illustration perhaps could be given of the modern use of

experimentation to search out the secrets of Nature and to apply them to the well-being of the community than the history just briefly outlined, and still in the making, of treatment and prevention by antitoxic serum and vaccines.

I have spent thus much time in considering some of the modern results of experimental research in medicine, as a small part only of the immense progress which has been thereby accomplished. I had in my mind to call attention to the reverse of the medal, and to suggest how much remains to be done. It is perhaps a thankless task, perhaps an unwarrantable expenditure of time; and yet one cannot help thinking what a labour of Hercules—I had almost said a labour of Sisyphus—it must prove to be to stamp out the infectious diseases from off the face of the earth, as we are hopefully trying to do. Of the diseases of which we know the micro-organisms, few can we cure, few can we prevent or exterminate. Influenza, a scourge fifty or sixty years ago, yielded up the secrets of its existence almost directly it reappeared

in a bacteriological age, but in the fifteen years that have passed since then we have made no advance. Influenza goes its own way, breaks out in scattered epidemics from time to time, without obvious reason or obvious cause, attacks some individuals over and over again, spares others entirely, invades the different organs in the most erratic manner, and defies all our efforts to control it. Consider also two other infective diseases, of which in recent years the organisms have been clearly isolated—plague and sleeping sickness, the latter extending over tracts of Africa formerly free from it, the former killing its thousands in the week in India and holding its own year after year. We may, of course, admit that science has not a free hand here; that ignorance, indifference, prejudice, as well as religious, political, racial, and financial difficulties have to be overcome in order to make any material progress in such an enormous task as it must in either case prove.

The more one thinks of these problems the more one sees that the solution lies in pre-

vention rather than cure; prevention on a large scale, and therefore prevention by the State, with the assistance of, or in spite of, the public. Smallpox has been stamped out of the Germany army by efficient compulsory vaccination; hydrophobia has been stamped out of the British Isles by the efficient measures of the Local Government Board; malaria and yellow fever are being controlled by public measures of sanitation and prevention. In the last three cases it must be observed that the agent of transmission is an animal—dog or insect—and that no moral considerations have yet been advanced as an objection to its ruthless destruction when it is known to be a *particeps criminis*.

Of many of these diseases, while much remains to be discovered, there is enough known to be of value in the preservation of human life. Our greatest daily paper recently pointed out that so much is now known with regard to the general behaviour of disease in communities, if not in individuals, that the results of these diseases can be predicted with absolute certainty, and that consequently

public officials, if unhampered with petty local and private considerations, could undoubtedly control the course of events and save both life and public money. The exanthemata, however, remain mysteries. Very familiar with their clinical characteristics, we are wholly ignorant of their micro-organisms. Possibly the stain that will colour them has not been invented. Bacteriology has been largely indebted to aniline dyes, or as our last Harveian orator, Professor Osler, racily put it, "Sir William Perkin and the chemists made Koch possible," and it may be that another chemist has yet to be born before the secrets of all the infective diseases are revealed. To speculate as to what would be our position if we could eradicate all the known pathogenic micro-organisms is perhaps to enter upon a wild-goose chase. Even if we regard the human pathogenic organisms of disease as being comparatively limited, it is almost inconceivable that we can stamp them out, while with great probability in proportion as these organisms are got rid of they will be replaced by others

derived either from animals or from other sources of which we now have little cognisance. But we are too far off from the extirpation of existing infective agents to make the question of their successors a matter of practical politics. The good results of the last sixty years since sanitary medicine first became the subject of State care justify, and demand indeed, continued action on the same principles.

But the cure and prevention of infective diseases are only a part of the task which lies before the profession. Pathology is not all inflammation, even if inflammation is mostly micro-organism. There remain degenerations and new growths, and mechanical troubles, and congenital deformities. The field for research is enormous, the necessity for research is patent, and even if the number of workers who can conduct research on the highest lines is limited, whether on social, financial, or moral considerations, there can be no doubt that the profession as a body will continue to support actively the maxim contained in Harvey's exhortation to search

and study out the secrets of Nature by way of experiment.

One of the duties which remain to me as Harveian orator is the "commemoration of all the benefactors of the said College." As years flow on—and it is now two centuries and a half since this injunction was conveyed to the Fellows of the College—the literal fulfilment of this requirement presents increasing difficulties. Benefactors, small and great, of one kind and another have been many. From an enumeration in detail of all the benefactors, with the good they conferred upon the College, I may perhaps be excused, and a somewhat abridged list will, I hope, be accepted in discharge of this duty. Harvey himself has been one of the greatest of them. In his lifetime he made an addition to the building of the College at his own expense, consisting of a great parlour, a meeting room, and a library above, and he furnished the library with books and the museum with objects of curiosity and a variety of surgical instruments. Shortly before his death he conveyed to the College his estate at Bur-

marsh. But Harvey was not the first benefactor. Linacre, who was the real founder of the College, inaugurated as it was in 1518, held the first meeting in his own private house, which he subsequently made over to the College. Caius, who was President of the College from 1555 to 1561 and from 1562 to 1571, first instituted the College Annals and revised its statutes. The names of numerous benefactors are perpetuated in the various lectureships, medals and prizes associated with this College, to some of which I have already, in another connection, referred. An account of these is given in the list of Fellows, Members, Extra-licentiates, and Licentiates of the Royal College of Physicians published annually, and I need do little more than enumerate them. The Lumleian lecture in Surgery, or the chirurgical lecture, was founded by Dr. Caldwell and Lord Lumley in 1581. The conditions have been altered and three lectures are delivered annually in the subjects, of which surgery is, as a rule, but little represented. A special interest attaches to this lectureship in that

Harvey himself was the fourth holder of the office, gave his first lecture in 1616, and continued to lecture to within a few years of his death. If, as is believed, he employed this lecture for the propagation of his views on the circulation, the surgical characteristics must have been early lost.

Dr. Goulston, in 1632, left money for the payment of a lecturer who was to be one of the four youngest Doctors in Physic of the said College and the lecture was to be delivered over a dead body if it could be procured. This provision no longer holds, but the lecturer is still one of the four youngest Fellows. Dr. William Croone was a Fellow of the College whose desire that a lecture should be founded at this College was only twenty-two years after his death—namely, in 1706—actually provided for by the will of his widow. The property which she left for this purpose was largely increased in value in 1886. Nearly a century and a half passed before any similar benefactions were received; but during the last sixty years the College has benefited on nearly a dozen occasions by

the receipt of bequests of sums of money either to found lectureships or prizes or medals. The bequests are from the widow of Dr. W. Wood Bradshaw, from Dr. Gavin Milroy, from the widow of Dr. Thomas Fitz-Patrick to found lectureships, from Dr. Swiney to found a prize, and from Miss Johnstone, of Bath, to found a scholarship in memory of Dr. Samuel George Jenks. Lectures, prizes, and medals have been founded by Dr. George Oliver in memory of Professor William Sharpey, by Dr. Dyster in memory of Dr. William Baly, by Captain Williams in memory of Dr. Bisset Hawkins, and by Dr. Horace Dobell. The Murchison scholarship and the Moxon medal are the outcome of subscriptions for the purpose of perpetuating the memory of those two distinguished Fellows of this College.

But there are many others who have at different times bequeathed sums of money or presented objects of professional or antiquarian interest to the College, one of the last of whom is the late Mrs. Begley, who left as a legacy the sum of £500 free of duty

"to show her admiration of the faculty and gratitude to some of its members during her widowhood." Many of our presidents have been mindful of their affection for the College during their term of office, and among these the Fellows can gratefully count, Mr. President, yourself. And in one sense all the presidents of this College have been its benefactors, in the time and thought and care they have successively devoted, often in the midst of an exacting professional career, to the interests of the College.

To this commemoration of benefactors it is my duty to add the exhortation to others to imitate them. Harvey does not specify to whom his exhortation is to be addressed: it is "others" who are invited to contribute their endeavours for the advancement of the Society according to the example of these benefactors. Before now a Harveian orator has read the word "benefactors" in a less material spirit than runs through what I have been recording, and has taken them to be those Fellows who have most contributed to the store of knowledge and industry in medical

science and labour in the welfare of humanity, or have by their lives given examples to be followed by their successors. Whichever view be taken, Harvey cries out from the remote past to us to imitate their good deeds.

It remains only to exhort the Fellows and the members of this College to continue in mutual love and affection among themselves, without which neither the dignity of the College can be preserved nor yet particular men receive that benefit by their admission into the College which else they might expect, even remembering that "Concordiâ res parvæ crescunt, discordiâ magnæ dilabuntur." As others have said, this should be an easy task. We are drawn together not only by our association in the welfare of this College, but by the necessity of a greater knowledge of Nature in all its intimate workings, by our unanimous desire to prevent and cure disease, to alleviate pain and prolong life, by the sympathy we all have for suffering humanity. Rival views may indeed be held, and all physicians do not practise in the same way; but these are the

differences which must exist while human minds are as they are, and they do not prevent that mutual respect and affection for one another which Harvey was so desirous to see perpetuated. We can at the present time faithfully say that the feeling is not confined to the Fellows or members of this College but is extended to other members of our great profession, to the sister College with whom we have had during more than twenty years the most friendly and intimate scientific and educational relations.

The motto of this College should never be forgotten:

ὁ βίος βραχύς ἡ δε τέχνη μακρή.

Wagner in 'Faust' says:

"The search of knowledge is a weary one, and life
how short!
How often have the heart and brain, o'ertasked,
Shrunk back despairing from enquiries vain!
Oh! with what difficulty are the means
Acquired, that lead us to the springs of knowledge!
And when the path is found, ere we have trod
Half the long way—poor wretches! we must die!"

Life is too short for disagreements, and by united action alone can we effect what it is our life's work to accomplish.

"Quam felix, et quanta foret respublica, cives
Si cunctos unus conciliasset amor!"

ADLARD AND SON, IMPR., LONDON AND DORKING.