Papers and Originals

Physician and Scientist*

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We meet, as is our custom, as near as possible to St. Luke's Day to pay tribute to William Harvey, and we meet for the first time in this great new college. Having been accorded by you, Mr. President, the honour and privilege of being chosen to deliver the annual oration, I am bound to remind you of the donor's injunctions. The orator was asked to commemorate all the benefactors by name and to specify what they had done for the benefit of the College. He was asked to exhort the Fellows and Members of the College to search and study out the secrets of nature by way of experiment and to continue in mutual love and affection among themselves. He was to deliver his oration in a proper form and in the Latin tongue.

The passage of three centuries has made it difficult to carry out these instructions literally. Perhaps if his orator tried he would orate to an empty hall. I shall therefore concentrate entirely on my duty to exhort you all to search and study out the secrets of nature by way of experiment.

Thirty-four years ago, when I first became a member of the College, it would not, I think, have been unfair to note that nearly three centuries of such exhortation had left singularly little mark on Fellows and Members. Very few of them had seemingly felt the urge to study nature's secrets by way of experiment. In fact, in my youth I often noted a certain hostility between physicians and scientists—particularly those whose inquiries had led them to, or near to, a study of disease in man. I have often wondered whether there is an antipathy between the roles of physician and scientist; if so, what is the nature of this antipathy; and whether it is inherent in these two occupations. I owe a great deal of my interest and information to my former friends and teachers, Thomas Lewis and Wilfred Trotter, who each combined the roles of physician and scientist, though Trotter was, as Lord Moynihan is reported to have said of himself, "a physician doomed to the practice of surgery." In a small way I have tried to combine the two, though I have been fortunate always to be under the shelter of the Medical Research Council or a university. In fact, I have been a lucky man who has been paid a salary for indulging in my two hobbies.

Let us now look into the reasons why it is so difficult to combine the roles of physician and experimental scientist.

Reasons that Do Not Withstand Critical Examination

1. That Science is an Occupation Peculiar to Laboratories

As we shall see later, the essence of science is method. Certain exercises are best carried out in laboratories, and progressively so because of the help which can be given by increasingly accurate and versatile machines; but not all. Let me remind

you that the most revolutionary hypothesis in the last century and a half, the evolution of species by natural selection, was born out of a study of animals and plants in the Galapagos Islands by Charles Darwin, and of animals and plants in the islands of the East Indies by Alfred Russel Wallace. The fact is that there are some questions that can be answered only by work in the field, which includes the clinic. Because a piece of work is done in the field does not make it less scientific. Because a piece of work is done in the laboratory, and with elaborate apparatus, does not make it good science. Perhaps now is the time to explode another fallacy—that long words are scientific. In fact, the reverse is true. As I have written elsewhere, the use of long words is one of the commonest forms of self-deception, and self-deception and good science are ill bed-fellows. The great scientists I have known usually couch their thoughts and ideas in relatively simple language, though, as Sherrington showed so clearly, new concepts often demand new words to describe them.

2. That Observation and Experiment are Fundamentally Different

It has often been held that the method the physician uses to acquire facts is that of observation, while that used by the scientist is experiment, and that there is a fundamental difference between them. This, I think, is to misunderstand the nature of experiment. Experiment is no more than planned observation. If an observer has witnessed the association between two series of events he may wonder if this association represents a causal sequence. He may therefore deliberately alter one factor at a time to see if, and in what way, this alteration affects the result. Now this, in fact, is what the practising physician is doing every day. My opinion has not materially altered since I wrote fifteen years ago (Pickering, 1949):

"If we take a patient afflicted with a malady, and we alter his conditions of life, either by dieting him, or by putting him to bed, or by administering to him a drug, or by performing on him an operation, we are performing an experiment. And if we are scientifically minded we should record the results. Before concluding that the change for better or for worse in the patient is due to the specific treatment employed, we must ascertain whether the result can be repeated a significant number of times in similar patients, whether the result was merely due to the natural history of the disease (or in other words to the lapse of time) or whether it was due to some other factor which was necessarily associated with the therapeutic measure in question. And if, as a result of these procedures, we learn that the therapeutic measure employed produces a significant though not very pronounced improvement, we would experiment with the method, altering dosage and other detail to see if it can be improved. This would seem the procedure to be expected of men with six years of scientific training behind them. But it has not been followed. Had it been done we should have gained a fairly precise knowledge of the place of individual methods of therapy in disease, and our efficiency as doctors would have been

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enormously enhanced. Moreover, we might have learned a great deal about the nature of the diseases concerned. And it is to be noted that in this instance the use of the experimental method carried no penalties for the patient that are not inherent in therapeutics anyway. In fact, by demonstrating that certain measures are actually harmful the experimental method in the long run protects the patient."

It is a very interesting and sad commentary on Harvey's exhortation that his successors have, in fact, been performing experiments ever since without knowing it, without being interested in the answers, and without being able to design their experiments in a way which would yield answers. Such design we owe to R. A. Fisher and Bradford Hill. Fisher was interested in the comparative efficacy of chemical manures and designed experiments to test them, taking into account the variety of soil patterns and the range of variation in the plants being tested. These, of course, are the same kind of problems as are presented to therapeutics. The controlled therapeutic trial so beautifully, and to my mind ethically, designed by Bradford Hill is the outcome. It represents the best method yet devised to show how far therapies are effective with the least human suffering and loss of time. While the older random therapy represents unorganized and unplanned experiment, the controlled trial is planned experiment. Neither Fisher nor Hill, incidentally, is a physician, showing the great importance of outside influences and the weakness of closed intellectual societies.

3. That Medicine is an Applied Science

I have often heard it said that the scientific basis of medicine is applied physiology, and of therapeutics applied pharmacology. The idea, as I understand it, is that fundamental truths are revealed in laboratory experiments on lower animals and are then applied to the problems of the sick patient. Having been myself trained as a physiologist, I feel in a way competent to assess such a claim. It is plain nonsense. To apply data gained from experiments on an anaesthetized carnivore or rodent to an unanaesthetized primate is, in the first place, unwarrantable. In the second place, assumptions are made about the nature of the disease process that are quite without foundation. As August Krogh (1929) once remarked: "The problems of physiology are so complicated that, to put it tersely, one cannot expect to be able to reason correctly from the facts for more than five minutes at a stretch."

Medicine and the Origin of Science

Medicine and astronomy are the two parents of modern science. In the University of Oxford the senior Chairs in Chemistry and Physics arose from Dr. Lee's benefaction to improve the teaching of medicine; the Sherardian Chair of Botany began in the Faculty of Medicine, and the Linacre Chair of Zoology is the outcome of a benefaction left by the founder of this College. Perhaps the contribution of medicine to the parentage of science is exaggerated by the example of Oxford. Nevertheless, it is fair to ask whether, had there not been a faculty of medicine in the mediaeval university, we should have had science in all its splendour and productivity as we know it to-day. And it is right to note at this point that the new method of science, the method of experiment and measurement, has never been more elegantly displayed than in Harvey's *De Motu Cordis*.

But in many ways the child has outstripped the parent. Medicine still retains more than a trace of the habit of mind of the mediaeval schoolman in its make-up which science has shed. Before, however, attempting to analyse the difference in the way physicians and scientists usually approach their

problems, it will be well to glance at science and the scientific method.

Science and the Method of Science

Natural science is an ever-changing body of knowledge won by the scientific method. The scientific method is without question the most powerful intellectual tool forged by the mind of man. William Harvey was one of its most distinguished users. The scientific method is designed to ask and answer questions, and can be used to investigate any set of phenomena; for example, as operational research it was most successfully used in the prosecution of the war against Adolf Hitler.

The attack on the problem is carried out as four successive steps:

1. The relevant facts are collected and recorded.
2. The facts are classified into series or sequences.
3. A short formula, or hypothesis, is sought which will enable the sequences to be described in a simpler, more comprehensive and convenient manner.
4. Experiments are designed to test the hypothesis. To a scientist there is no absolute truth; truth is a relative term. A hypothesis becomes more probably true the more often it stands up to experiment, and the more rigorous these experiments are.

Science begins by being descriptive—that is to say, phenomena tend to be classified by kind. It proceeds by becoming quantitative—that is to say, by classifying phenomena in such a way that numerical values can be assigned to them. For it becomes daily more evident that the fundamental laws of nature are quantitative and statistical, and that the greatest strides are made when numerical relationships are uncovered.

The scientific method thus represents disciplined curiosity. An observation arouses a doubt or question. Either it does not fit with an accepted hypothesis or else there is no hypothesis. And so the research worker goes on collecting and classifying and formulating and testing hypotheses. He is obsessed by his ignorance and by his desire to know. Once he knows, or thinks he knows, then he ceases to contribute to that branch of knowledge and it is time to seek a new field or leave the stage.

The Antithesis Between Medicine and Science

1. Knowledge and Ignorance

As has been noted, ignorance, and the awareness of being ignorant, is the *sine qua non* of a productive scientist. Unless he does not understand something and keenly wants to do so, he is unlikely to begin a piece of work and certainly will never finish it. So long as he remains in this mind he will be productive. Once he knows, or thinks he knows, his usefulness is ended.

It is quite different for the physician. His patient expects him to know; indeed, if the patient finds out that his physician does not know he is quite likely to leave him for one who does, or rather for one who says he does. From the time of Galen to our own, therefore, medicine has always presented a façade of systematized knowledge, or alleged knowledge, for, like religion, medicine could not tolerate ignorance. To parody Voltaire, if a cause did not exist it was necessary to invent one. Mediaeval medicine and mediaeval theology thus both bore heavily the imprint of the schoolmen. Elaborate and all-embracing theories of the nature of a disease and its causation have had an irresistible appeal. These persisted,

and indeed blossomed, long after Harvey. To quote Wilfred Trotter (1935):

"The characteristic feature of the period was the exuberance with which doctrine flourished. Almost every eminent medical personage—who might well at the same time be making solid contributions of fact to medicine—was the exponent of a theoretical system of disease. This system, devised by the inventor according to some inspirational method of his own, was often as detached from reality as it was precise and dogmatic. It is impossible to review the innumerable systems that sprang into life and often so surprisingly survived; I can only mention a few names taken almost at random from Garrison's well-known work, and trust to be able to convey some of the quality of their doctrines.

"Early in our period there is Georg Ernst Stahl, whose life almost exactly corresponds with the interval between the death of Harvey and the birth of Hunter. He taught an animism which regarded the body as a mechanical puppet, whose functions were maintained by the direct action of the soul. Misbehaviour of the soul was therefore the cause of bodily disease. It seemed to be a necessary consequence of this theory that drugs could have no action on the body and like a good rationalist Stahl denied that they had. His responsibility for the many animists and vitalists who followed him is perhaps less heavy than for the phlogiston theory with which he burdened chemists, for this theory is perhaps the most perfect example in the world of ideas of the mysterious viability of the false. Then there is John Brown, whose life coincides roughly in time with that of Hunter, and who was the author of the famous Brunonian system. This product of reason is said to have been remarkably complete and consistent; it divided disease into sthenic and asthenic, and treated them respectively with opium and alcohol, drugs to which Brown himself, less tough than his system, early succumbed.

"The air of caricature never fails to show itself in the products of reason applied relentlessly and without correction. The observation of clinical facts would seem to be a pursuit of the physician as harmless as it is indispensable. Reason, however, could scarcely stop at so elementary a phase as this, and it seemed irresistibly rational to certain minds that disease should be as fully classifiable as are beetles and butterflies. This doctrine found its eminent cultivator in the great Sydenham, but bore perhaps its richest fruit in the hands of Boissier de Sauvages. In his *Nosologia Methodica*, published in 1768, the year of Hunter's appointment to St. George's, this Linnaeus of the bedside grouped diseases into 10 classes, 295 genera, and 2,400 species. Towards the end of our period these particular developments met an opponent in Broussais, who lived till Lister was 11 and Pasteur 16. For Broussais disease in the sense of the nosologist had no existence. Diseases were for him consequences of local irritation and resulted in gastroenteritis, which was the essential pathological lesion of all maladies. Broussais' quality is shown by his aphorism *La nature n'a aucun pouvoir de guérison naturelle*: believing this, he knew that recovery depended solely on the exertions of the physician. Since the condition he had to contend with was always an irritation and could be met by reducing the patient, he set himself to starve and bleed with a dreadful rigour. The lapse of a hundred years has made this doctrine seem no more than gruesome balderdash, but it was not without plausibility for the contemporary world. In fact, no less a surgeon than the great Dupuytren was a believer, and was accustomed to add to his mere surgical powers of reducing his patients the sterner measures of his colleague.

"If these instances give a fair sample of what the intellect was doing for medicine for 200 years, it is not perhaps surprising to find Hunter about the middle of that period exclaiming impatiently, 'Why think?'"

This passion for general theories to explain all unexplained disease persists. When I was a student and house-physician, it was focal sepsis, and my patients were asked to sacrifice teeth, tonsils, appendices, and other of their less necessary organs on its altar. Later came the psychosomatic era, then diseases of adaptation, now autoimmunity; the list of diseases is the same, only the cause changes and of course the treatment, though not its efficacy.

It is easy enough for people like myself, who are not, and never have been, engaged in the hurly-burly of private practice, to regard these hypotheses with a certain distant irony.

But if one daily has to give such patients advice, patients who keep themselves *au courant* with the *Reader's Digest*, it is a little more difficult to preserve a wholly open mind. Intellectual nihilism is the very stuff of which scientists are made, but it is scarcely convenient for a practising physician. There is no doubt that William Kempner saved lives with his rice-fruit diet, even though this was based on argument of gossamer proportions derived from the *in vitro* behaviour of kidney slices. I, for one, suspecting the diet was effective but lacking the fire of conviction lent by revealed truth, was less successful in persuading my patients to bear its deadly monotony.

2. The Need to Act

The function of a university has been defined as the pursuit of knowledge for its own sake. So is the aim of science. The scientist is not concerned with whether any discovery he makes will be useful, useless, or harmful. He cannot, by the very nature of knowledge; for the unknown is the unknown. The scientist is not called on to make a judgment or even a provisional conclusion until, in his opinion, the evidence warrants it. As Lewis (1925), in one of his more dramatic moments, put it:

"The purity of a science is to be judged by the paucity of its recorded hypothesis. Hypothesis has its right place, it forms a working basis; but it is an acknowledged makeshift, and, as a final expression of opinion, it is an open confession either of failure or at the best of purpose unaccomplished. Hypothesis is the heart which no man with right purpose wears willingly upon his sleeve. He who vaunts his lady love ere yet she is won, is apt to display himself as frivolous or the lady a wanton. For this reason often times I have been particular to set forth evidence upon evidence for a given conclusion in the book, feeling that no doctrine is sufficiently supported if yet another serious argument may be urged in its favour."

The physician is less fortunate. When he is consulted by a severely ill patient he gathers all the relevant data he can, forms the best judgment he can, and acts, in the sense that he begins a series of investigations to establish the diagnosis and begins a course of treatment with the intention of modifying it in the light of new evidence. His task is made much easier by being mapped out for him by what have become, virtually, a set of rules. Thus, diseases are classified and named; the criteria for distinguishing them are set out, a course of treatment for each is prescribed, sometimes based on experience, often on a hypothesis concerning the nature of the disease.

This framework is, in general, an oversimplification of the phenomena of disease. Here was the young Mackenzie's reaction (quoted by Gibson, 1963):

"For some years I thought that my inability to diagnose my patients' complaints was due to personal defects; but gradually, through consultations and in other ways, I came to recognize that the kind of information I wanted did not exist." He continued: "About 1883 or 1884 I resolved to begin a series of careful observations entirely for my improvement, never dreaming of research, for I was under the prevalent belief that medical research could only be undertaken in a laboratory or, at least, in a hospital with all the appurtenances. I merely sought to find out something about the nature of my patients' complaints. I had recognized that when the patient had some physical sign, and when disease had made considerable ravages in the body, a moderately accurate diagnosis could be made; but in the vast majority of my patients there was no physical sign, or if there was a physical sign, I was not sure of its relationship to the patient's ill-health. . . . I had thus placed before me two definite objects, at which to aim: (1) understanding of the mechanism of symptoms, and (2) understanding of their prognostic significance."

Nevertheless, it is difficult for a physician to depart far from the system of rules into which he was initiated as a student

and examined before qualification. Lewis, revolutionary as he was in his own small sphere, was quite orthodox outside it. Bright's remarks on the disease named after him are so pertinent that they seem as fresh and relevant to-day as when they were written; but the treatment he gave his patients invokes in us a wry smile of pity tinged with contempt that he should have believed in his poultices, blisters, and purges. As A. E. Boycott once remarked to me: "If you are going to be a revolutionary in one field, you must be a conservative in the rest."

3. The Qualitative and Quantitative Approach

Science begins by being descriptive—that is to say, phenomena are classified by kind. It develops by becoming quantitative—that is to say, size or number becomes decisive. It was in fact the quantitative aspect that Harvey regarded as the final proof for the circulation of the blood:

"Let us suppose how much blood the left ventricle contains in its dilatation when it's full, either by our thought or experiment, either two ounces or three ounces or one-and-a-half ounces. I have found in a dead man above two ounces.

"Let us suppose likewise, how much less in the contraction, or when it does contract itself, the heart may contain, and how much less capacious the ventricle is, and from thence how much blood is thrust out of the *arteria magna*; for in the Systole there is alwaies some thrust forth, which was demonstrated in the third Chapter, and all men acknowledge, being induced to beleieve it from the fabrick of the vessels, by a very probable conjecture we may aver that there is sent in of this into the arterie a fourth, or a fifth, or sixth at least an eighth, part. So let us imagine, that in Man there is sent forth in every pulse of the heart, an ounce and a half, or three drams or one dram of blood, which by reason of the hindrance of the portals cannot return to the heart.

"The heart in one half hour makes above a thousand pulses, yea in some, and at some times, two, three or four thousand; now multiply the drams, either a thousand times three drams, or two drams, or five hundred ounces, or such a proportionate quantity of blood, transfused through the heart into the arteries, which is a greater quantity than is found in the whole body. So likewise in a Sheep or a Dog if there pass (I grant ye) but one scruple, in one half hour there passes a thousand scruples, or about three pounds and a half of blood; in whose body for the most part is not contained above four pounds of blood, for I have tried it in a Sheep."

The classification of diseases, on which the practical art of medicine depends, is purely qualitative. Education, at least in the clinical years, is dominated by the problem of kind, that of degree is scarcely considered at all. The medical man in being, and in making, is obsessed with the division between health and disease, physiological and pathological, normal and abnormal. All the phenomena he meets have to be classified in such terms. As has been already mentioned, most natural phenomena are related to one another quantitatively. The phenomena that the physician classifies as normal and abnormal are no exception. Phenomena whose relationship to one another is essentially quantitative are divided qualitatively by an artificial and arbitrary division into normal and abnormal. And so the physician is blinded by his upbringing to the true relationship.

During the last ten years evidence has multiplied suggesting that the disease essential hypertension represents a kind of disease hitherto unrecognized, or recognized dimly, in which the deviation from the norm is quantitative not qualitative; it is a disorder not of kind but of degree. It is perhaps not unexpected that this hypothesis should have been very differently received—by non-clinical scientists as a glimpse into the obvious; by physicians as dangerous nonsense.

4. Individual or Group

The physician is necessarily concerned with individual patients, the scientist with grouped phenomena—that is to say,

phenomena that recur sufficiently often to suggest that the features which they share have a meaning. Too much can be made of this difference because most of the practice of medicine is based upon the same recurrent phenomena, such, for example, as those associated with lobar pneumonia, myocardial infarction, and acute appendicitis. However, the really difficult cases, and those which reveal the great physician, are those in which familiarity with these recurrent phenomena does not suffice. The additional factor is the doctor-patient relationship—that is to say, that sympathetic personal relationship which enables the doctor to understand an individual human being's problems, including his reaction to his disease, and which gives the patient faith in his physician and thus freedom from fear. The ability to form and to use this relationship is slowly built up by personal experience, by trial and error, and by increasing familiarity with the problems that contemporary life poses and the ways in which individuals react to them. In this respect the physician approaches more closely to the novelist than he does to the scientist. Both physician and novelist are concerned with the desires, ambitions, and frustrations of human beings, singly and in constantly changing groups, and with their reactions on one another; but while the novelist merely observes, understands, and tells, the physician is called upon to act.

5. Competition for Time and Energy

One of the lessons learned by anyone who has seriously attempted scientific work is its immense demands on time and energy. One gets possessed by the problem. It drives all else out of mind and frequently wakes one from sleep. Indeed, many of the best ideas have awakened the fortunate originators. This monopoly of time and attention which scientific work exercises, and indeed demands, is difficult to combine with the practice of medicine. Lewis told me that he finally decided to give up private practice when he found himself in his laboratory working on a dog and confronted by an angry practitioner with whose patient Lewis ought then to have been in consultation and whom he had forgotten. When in later life Lewis was hot on the trail, he did his ward rounds from 10 to 12 on Monday and 2 to 4 on Thursday and his out-patients on Thursday mornings, but at other times nothing could shift him from his laboratory bench.

Many great physicians and surgeons did important scientific work before they entered practice, or in their early years, but had to give up as they became busier. Unless one is in a university post with a competent junior to whom one can delegate, it becomes increasingly difficult to spare the time and continuity of effort that scientific work demands. That the physician places himself first and foremost at the service of the sick—and may it ever be so—is the chief reason why scientific work is so difficult for him.

Are the Attitudes of Mind of the Physician and the Scientist Irreconcilable or may there be a Synthesis?

I have now set out, as I understand them, some of the difficulties that face those engaged in the practice of the physician's art in becoming experimental scientists. I would doubt whether I have set them out fully or fairly in the sense of putting the proper emphasis on each one of them.

I now come to the end of my task, and to its most important questions. What of the future? Are the roles of physician and scientist likely to drift further apart or will they come nearer together?

In predicting the future it is difficult to avoid wishful thinking. My life, such as it has been, has been an attempt to reconcile the two, to try to live both lives and to enjoy both. So I begin as a biased advocate. Nevertheless, there are grounds for optimism.

In the first place, the vulnerability of the physician has been the lack of exact knowledge concerning the nature and natural history of disease, and the extent to which the application of therapeutic measures can alter it in the patient's interests. This knowledge is being won. It is being won by advances in chemistry, physics, and biology; by our understanding of the interaction of chemical substances in living and non-living systems; by our understanding of the transmission of information to cells; by the way in which this can be modified as these cells differentiate; by the way in which this transmission of information can be altered; by the way in which changes in environment, chemical, physical, and microbial, can affect these processes; by our identifying and defining the various chemical processes that constitute the activity of the cells in the body; and by our understanding of the way in which the activity of the tissues and organs of the body are correlated and co-ordinated in the life of the whole organism. In all these processes the phenomena that can best be seen in the sick contribute to understanding. Moreover, our understanding of disease and our ability to prevent and cure it become daily more extensive.

As we look at this whole field, the most challenging, and the least conquered and understood, is that set of phenomena which we associate with the mind. Here is the great challenge to the physician and to the scientist. To the physician because it is particularly in this respect that one individual differs from another, and because the meeting and mutual understanding of minds constitute the essence of the doctor-patient relationship; to the scientist because here is presented an elementary problem of scientific method—namely, that of classifying the facts in such a way that allows numerical values to be assigned to them, and formulation of these in terms of a simple hypothesis. This challenge has been offered before to the scientific method, and

I cannot believe that it will, this time, go unanswered. I also believe that the physician, by his calling and experience, is particularly aware of this challenge, and by being, as William Harvey was, daily faced with it and becoming, as William Harvey did, more and more familiar with his material may ultimately see that simplification which represents a revolutionary new understanding.

Finally, may I say this: You may think that in my comparison of the roles of physician and scientist I have been critical of the one and not of the other. This has been the approach of a cold intellect. It is also the approach of one member of a family to another. Harvey also instructed his orator to exhort his colleagues to continue in mutual love and understanding among themselves. The role of the physician is, and always has been, an honourable one in society. He puts himself at the service of his less fortunate fellow creatures. He has to do the best he can with the knowledge that he has and can have. The role of the scientist is to increase that knowledge and give it precision. For the future of humanity the objectives of the two roles, however difficult they may be to combine in an individual and at a point of time, are ultimately one and the same.

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Some Effects of Transection of the Pituitary Stalk

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In recent years destruction of the pituitary gland, either by surgical ablation or by ionizing radiation, has been used in treating a wide range of conditions. The commonest of these are malignant tumours (particularly carcinoma of the breast), rarer indications being progressive diabetic retinopathy, malignant exophthalmos, hypertension, and Cushing's disease. Since it is now clear that function of the anterior as well as the posterior lobe of the pituitary is largely regulated by the hypothalamus through the pituitary stalk, the operation of section of the pituitary stalk is also sometimes used as treatment for these conditions. How does this operation compare with actual removal of the gland? What happens to the anterior pituitary after its isolation from the hypothalamus, and to what extent is its functional activity impaired? The account given here, which brings together the results of an extensive study on experimental animals, and includes a few observations on man, may help to answer these questions.

Blood Supply of the Pituitary Gland

An interest in the strange condition of post-partum necrosis of the anterior pituitary in women (Sheehan, 1937), which is clearly caused by a vascular disturbance, led us to make a detailed study of the blood supply of the pituitary gland, first in man (Xuereb *et al.*, 1954a, 1954b) and later in the rat, sheep, and goat (Daniel and Prichard, 1956, 1957a, 1958). We found that the basic pattern of the vascular arrangements of the gland was essentially the same in all these species.

The posterior or neural lobe (infundibular process) has a conventional arterial blood supply, but the anterior lobe (pars distalis) receives only portal venous blood—that is to say, blood which has already passed through a first capillary bed.¹ The hypophyseal portal vessels which supply blood to the anterior

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¹ McConnell (1953) and Stanfield (1960) maintain that in man the parenchyma of the anterior lobe is supplied by some small arteries as well as by portal vessels, but in our view such an arterial supply, when it exists at all, is so small as to be insignificant. This is not the case in the rabbit, however, in which the anterior lobe has a substantial arterial as well as a portal venous supply, and this is one reason why we have carried out only a few experiments with stalk section on this species.