A Defence of the Thesis that “The opportunities of the general practitioner are essential for the investigation of disease and the progress of medicine”¹

Sir James Mackenzie, M.D., F.R.C.P., LL. D., F.R.S

Consulting Physician to the King in Scotland, Director of the St. Andrews Institute of Clinical Research, Consulting Physician to the London Hospital

Introduction

My object is to demonstrate that the conception of medical research which is dominant to-day is so immature and imperfect that it renders fruitless much of the research work. Indeed, so imperfect is the conception that fields essential to medical progress are not recognized. It is well, therefore, that men engaged in medical research should at intervals pause and consider what they are doing, so that they clearly realize the object of their endeavour and be certain that their methods are suited to their purpose. Never in the history of medicine has there been such activity as now, and there never was a time when it was more necessary to have a clear perception of aims and methods, especially as great schemes are being launched in legislature, in research, and in education. If these schemes be based upon immature experience and imperfect knowledge, the progress of medicine may be hampered for generations.

We are all the creatures of circumstance, and our ideas are moulded by our experiences. Those employed in the study of medicine look at the subject in the light of their own experiences. As the subject is so large, one individual can have an experience of but a small part, so that there is no one capable of seeing it as a whole. The result is that medicine has to be studied in sections, and this leads to specialism. The authorities who guide and direct the progress of medicine are therefore men with but a limited experience, and this leads to a limited outlook. In an attempt to bring together a body of men whose united experience, it might be thought, would cover the whole field, there is a danger that some section may be wanting, and thus a distorted view or a view lacking in perspective may be obtained.

A review of medical progress reveals the fact that medicine is emerging, slowly and hesitatingly, from a past burdened by tradition and even superstition. The conception of what constitutes medical science is still so imperfect that no clear understanding exists on what lines it should be pursued. While the aim of medicine may be recognized, the methods by which this aim may be achieved are not yet understood, and this lack of understanding is leading medicine astray.

In dealing with the clinical aspects of research, and particularly with the opportunities of the general practitioner, I must dwell upon the limitations of laboratory methods, and I may seem to belittle their importance. That is far from my intention. No one recognizes the importance of laboratory methods more than I do, and probably no clinical observer has received greater help from them. Indeed, I consider that I have a better appreciation of their methods than many who indiscriminately belaud them. My experience not only enables me to appreciate their value, but also to recognize their limitations.

Successful Methods in Research

Let us briefly look at one aspect of the subject by considering where medical research has been successful. The highest aim of all research is the prevention of disease. If we take the instances where this aim has been achieved we find a uniform method of procedure. In every case the clinical observer, by the exercise of his peculiar methods, took the first step. He recognized in the sick man the signs of disease, he differentiated these signs in such a manner that he was able to recognize separate forms of disease. He recognized these signs at such an early period that he detected the circumstances that favoured or induced the disease. He was then able to take steps to

¹ Being a lecture delivered at St. Mary’s Hospital, in the Institute of Pathology and Research during the course on Pathological Research in its Relation to Medicine. First Published British Medical Journal 1921;1:797-804
prevent the disease. Such is the history of the prevention of such diseases as typhoid fever, syphilis, rabies. At other times he has not been able to carry the investigation so far, and recognizing his limitations he handed the subject over to the laboratory worker, as in malaria and allied diseases.

Such in brief is the method which common sense tells us should be followed in the case of every disease, but where is the clinical observer to be found to-day?

A foolish idea has arisen that the methods by which he made his contributions to research are so easily understood that they need little consideration, and so easily recognized that they need no special investigation, and that their possibilities are exhausted. There never was a greater fallacy. We know that it takes many years before a man becomes trained in bacteriological technique. It requires a much longer time to train a man to recognize the early symptoms of disease. It takes many years of experience to put intelligent questions to the patient, and more years of experience to enable the replies to be interpreted.

The part which the clinical observer should play in medical research is to-day not recognized, and there follows as a consequence an insurmountable obstacle to attaining the chief aim in medicine – the prevention of disease. If you do not recognize the early symptoms of disease you can never recognize the circumstances that favour or cause its onset. This to me is such plain common sense, that it is one continual source of wonder that our authorities fail to see it.

Once this is seen, the next question is, Who is the man that has the opportunity for seeing the early stages of disease, and the circumstances that favour its onset? There is only one person, and that is the general practitioner.

The Diseases Common among the People

When we started our enterprise at St. Andrews, we reflected that if success were to attend our efforts we must clearly perceive what we were aiming at. Our chief aim was the prevention of diseases which are common among the people of the country.

The question arose “What are those diseases?” Seeing that we have now a Ministry of Health one would naturally expect that this knowledge would be in its possession. Seeing also that doctors are being educated to combat these disease, it might have been expected that educational authorities would know. But a brief inquiry revealed the fact that this knowledge does not exist.

The reason for the absence of a knowledge so essential to intelligent law-making, education, and research, is that it can only be obtained by the general practitioner, and no one ever thinks of asking him to undertake any inquiry.

We therefore started an inquiry into this matter, and met unexpected difficulties. However, we got an insight into the matter that revealed defects in medical knowledge so great that they more than justified our undertaking.

One fact that came out clearly was that the impression that great progress had been made in recent years was scarcely justified, so far as the recognition and prevention of disease was concerned. We found that discoveries of the origins of common diseases were so few during the past fifty years that we had difficulty in recognizing any advance. A little consideration revealed the reason.

The Progress of Medicine during the Past Century

A hundred years ago we can trace medicine following two distinct paths: There was the clinical school, mainly British, in which the chief instrument was the clinical observer with his trained senses and his mind stored with the fruits of his past experience. There was the growing laboratory school, mainly continental in its origin, which received a great impetus when Virchow introduced the theory of cellular pathology. Up to fifty years ago the trained observer was slowly unravelling the early symptoms of disease, discovering the beginnings of disease and their cause. With the increase of knowledge of the structure of the body and of the modifications produced by disease, and by improved laboratory technique, pathology gradually came into prominence. The dead-house became the centre of great activity. The accurate observation of diseased organs revealed on the post-mortem table led the physicians to seek in the living the evidences of these diseased organs, and thus was laid the foundations of pathology which we know to-day. The seeming sufficiency of this method of study led to a classification of disease based upon the morbid appearances of the organs, a classification which survives and influences teaching to-day.

There is a delusive precision in this classification which has had a pernicious effect on medicine as a whole. It may be true of disease as seen from the dead-house point of view; it may be partly true of disease as seen from the point of view of the medical and surgical wards, but it is so little true as to be misleading when looked at from the point of view of the general practitioner. It is misleading because it deals only with end-results, a totally different matter from the early stages of disease. These end-results may be the diseases imposed upon a constitution already enfeebled, or the outcome of a process whose symptoms in the early stages have never been recognized. One outcome of this classification has been to rivet the search on those signs which occur only in advanced states of disease – when, that is to say, damaged tissues produce a physical sign. So powerful has this influence been that attention is now concentrated on the search for improved
methods by which these physical signs can be revealed. So many methods have been discovered that men have to devote themselves to special branches, and we see the result in the specialism of to-day. It seems not to have been grasped that the specialist can only recognize disease after it has gone so far as to damage the organs, and no specialist ever sees the early stages of the disease in which he specializes.

Following upon the introduction of more accurate pathological investigation came the microscopic theory of disease, with its startling revelations and successes. The imagination of the medical world was fired, and the most exaggerated expectations were formed of what it could do, and thus it practically superseded all other methods of investigation, and speedily attained that dominant position which it holds to-day. Following in its track came the introduction of the methods of other sciences, and there arose that conception of medicine which looks to the laboratory as the only sphere of progress. As a result the methods of the clinical observer by which so much had been achieved fell to the background, and as an investigator he gradually disappeared. This was a calamity, and the more so that neither the part he should play or his opportunities which he possesses are understood.

**Movements in Circles**

Between the town of Burnley and the village of Haworth, where Charlotte Brontë lived, there stretches a wide moor. Some of my friends started one day to walk from Burnley to Haworth. About an hour after they started a heavy mist fell and they lost their way. They happened on a shepherd’s cottage and the shepherd gave them their directions. In three hours they were back again at the cottage, having wandered in a circle. This well-known tendency to walk in a circle is a human peculiarity that affects not only bodily movements but mental. History shows civilizations that arise, make a little progress, then make no further progress, but move round and round and gradually relapse. Religions, too, can show the same process. This kind of arrested development affects individuals, for we all know how many young men start out in life with every prospect of going far, and after middle age are found muttering the shibboleths of their youth.

There are signs that this tendency hampers medical progress, and much of what we assume to be progress is but moving in a circle, and results which are taken as signs of progress often but add to the fog which obscures the way.

**Prognosis**

I do not develop this theme to-day, but my purpose is to direct your attention to a subject which illustrates this point of view. I choose one with which you all are familiar – indeed, many may think it so well known that it needs no consideration. It is, moreover, a subject which acts as a guide to progress, a beacon in the fog, and at the same time provides the means by which progress or the reverse can be judged. Moreover, it is a subject of the very first importance to the intelligent practice of medicine; but I do not know how to present it in a manner that will convey to you its significance so as to carry conviction.

When a true insight is obtained into what medical science means it will be found that the great obstacle to progress is a lack of understanding of prognosis. Up to thirty or forty years ago the subject was making progress slowly and crudely but definitely. During the last quarter of a century it has got such a set-back that to-day its importance is not understood, the principle which should guide to its knowledge is not appreciated, and the individual whose opportunities afford the means of acquiring this knowledge is not recognized. I have repeatedly discussed this matter with various authorities in different departments of medicine, and nowhere can I get anyone to appreciate its real nature. The newly qualified doctor is as oblivious to its importance as the mature physician who has for twenty or thirty years been engaged in life insurance examinations, in which it is currently assumed that a prognosis is necessary.

If one wanted evidence of the complete misconception of this subject, it is the practice of appointing laboratory trained men to teach clinical medicine, and the assumption that as soon as a man is qualified he is capable to examine recruits for the army and navy and candidates for life insurance. If I can get you to understand the meaning of prognosis, the futility of these procedures will be apparent to you.

**The Importance of Prognosis**

In medical practice one question arises incessantly and persistently, implied or expressly demanded of the doctor, and that question is, “What is to be the outcome of my complaint?” The patient or his friends want to know if the illness is temporary or is it to result in ill health or in death. Then other questions arise, Are there remedies for this complaint, and what are they?

To answer these questions requires a knowledge of prognosis, and one of the cherished beliefs of the public is that doctors possess that knowledge. Moreover, common sense tells us that the public is perfectly justified in expecting from the doctor a knowledge so manifestly essential to the intelligent practice of medicine.

**The Peasant and Prognosis**

I was presenting these views once to a very capable general practitioner who had had a distinguished university career. He cordially agreed, and described an...
incident which forced on him the importance of prognosis, when he entered upon practice. A few days after starting as an assistant to a general practitioner he was called to see a sick ploughman. He examined him and diagnosed a pleurisy. Pleased with his diagnosis, he, in learned fashion, informed the man’s wife. She replied, “Aye, but when is my man to be fit for his work?” My friend was taken aback – during the whole of his education he had never been taught to realize that such a question should be asked, and he could not himself answer what he recognized to be a most natural question. I have little hesitation in saying that this poor peasant woman had instinctively a better realization of the requirements of medical practice than the authorities to-day who direct medical education and research.

Let me give some instances illustrating this peculiar defect in medical knowledge.

Recruiting and Prognosis
Of the vast importance of prognosis and of the disastrous effects of a lack of knowledge of this subject we have had during the war striking evidence. When at a time of great national stress a call was made for men to join the army, it was assumed by the nation, as well as by the military medical authorities, that there existed sufficient knowledge to separate the fit from the unfit. This was really a test on the greatest scale of the adequacy of medical knowledge. At the outset the knowledge was found wanting, for large numbers of perfectly healthy men were rejected, because they presented signs whose value the medical examiners were unable to assess. Later, when the national strain became greater, and it was necessary that even those with impaired health should enter military service, the military authorities again thought they possessed the knowledge necessary to say what amount of physical effort a man was fitted for. It is unnecessary to dwell upon the complete failure that resulted. So glaring were the mistakes, so unjust were the decisions, that the whole nation was aroused and Parliament was forced to intervene. If there was ever a need for inquiry, here was one; yet the whole matter is brushed aside as if it had never occurred, and medicine has fallen back into its old ways. This illustration shows how backward is the state of medicine when the authorities who direct it are incapable of realizing a defect even when their best endeavours end in a miserable failure.

Prognosis in Surgical Practice
Another aspect of the subject is shown in surgical practice. If we take a common complaint like appendicitis, there are certain signs which are held to indicate the presence of this disease. The question arises whether these signs indicate a condition which will endanger the patient’s life. In other words, what is the prognostic significance of the signs? The question is one of prime importance to the patient, for it may be a matter of saving his life if the danger is recognized and removed; on the other hand, it may be putting the patient in danger by an unnecessary operation - danger to life or of permanent damage to his health. Many a patient has had his appendix removed when there was nothing the matter with it. Everyone recognizes that appendicitis does occur, and, if not operated on, death may result. The attitude of the surgeon to-day is that, seeing that there is danger, and seeing that surgical knowledge cannot discriminate between the cases where there is danger and those where there is no danger, it is safer to operate. It is the same in the surgical treatment of gastric ulcer. I have seen patients greatly benefited by the operation; I have seen some made worse by the operation, and I have seen patients die in consequence of the operation. These results are due to an absence of a knowledge of prognosis.

Prognosis and Vaccine Therapy
The development of the bacteriological branch of medicine has resulted in the introduction of new forms of treatment by serums and vaccines. When a person is ill, and a microbe is the suspected cause, the appropriate treatment is to combat this microbe by a vaccine. But in the question, Is the patient likely to recover without treatment? If so, then the treatment is unnecessary. If the patient is in danger of death, wherein lies the danger – is it due to that microbe or to other complications?

This is not quibbling, but is essential to intelligent treatment. For instance, I have heard it seriously proposed to find the microbe of measles, and then to get a vaccine to give to patients afflicted with measles, because many people are supposed to die of measles. But the question arises, Do they die of measles? During my twenty-eight years in practice I saw numerous epidemics of measles, and only two patients died; but these did not die of measles but of complications – laryngitis and bronchopneumonia – brought on through injudicious exposure. If due care be taken, why give the vaccine? Unless the source of danger is recognized and provided against, the treatment by vaccines becomes rule of thumb, and is but a return to the empiricism of bygone times.

If treatment is to be intelligent, or even scientific, a prognosis is absolutely essential, yet in some recent textbooks on surgery and vaccine therapy I do not find the word prognosis mentioned.

Prognosis in Treatment by Digitalis
Did time permit I could illustrate in many ways how essential prognosis is to scientific treatment. Let me
give one example. For more than one hundred years it has been recognized that digitalis had a beneficial action in certain forms of heart disease, but no definite knowledge existed as to the kind of heart disease which benefited, so that every person supposed to have a heart affection was given digitalis. Careful investigation has revealed that the drug is of use in only a small percentage of cases, and that of a particular kind. We can now recognize with fair certainty the cases where it will have a good effect and those cases in which it is of no use.

The recognition of the cases that are benefited by digitalis saves us from giving it to those cases in which it is of no use. Thus, instead of an unintelligent rule of thumb treatment, we study the peculiarities of each individual case in order to find the treatment appropriate to his condition. The manner in which this knowledge was acquired will be described later.

**The Investigation of Prognosis**

It will perhaps help to get a clear idea of what I am aiming at if I describe the steps I took to obtain this knowledge in affections of the heart.

On entering general practice my knowledge was much that of a young doctor of to-day, except that perhaps we were better taught in regard to this subject. I was not long in finding out that my knowledge was limited. As an examiner for life insurance I realized that I had no real knowledge of the prospects of a candidate’s life. In dealing with my patients I would put people on treatment and restrict their work because of some vague notion that murmurs and irregular action indicated something seriously wrong. The textbooks, to which I appealed again and again, though reputed to deal with prognosis, afforded no help. Recognizing the limitation of my knowledge, I determined to see if it was possible for this knowledge to be acquired.

I saw at once that it would be necessary to watch individuals with what I considered damaged hearts for the rest of their lives to see what happened, and I started to do so. But the question soon arose, What was I to watch? I spent a long time noting with great particularity the murmurs and modified sound, and the rate of the heart when at rest and on effort. But the results were so unilluminating that I found I was getting no further. I got a sphygmograph and took records of the pulse, and spent much time measuring the height and breadth of the waves, the depth of the notches, seeking in these signs for light upon the subject of prognosis.

In efforts of this kind I spent several years, and felt inclined to give up in despair. My experience at this stage may be of some service to others who undertake similar forms of medical research. Pausing to reflect, I was struck with the resemblance of myself to one of the characters depicted by Bunyan in his Pilgrim’s Progress. He describes a man earnestly engaged in raking the mud in search for something he was not quite clear about, while above his head shines the crown of glory which was the real object of his research. I felt like the man with the “muck-rake,” and I felt certain if he were addressed in modern terms the conversation would be somewhat as follows. If asked what he was doing, he would reply he was collecting stones and twigs and straws. If it was suggested that this seemed a vain quest, he would reply that he was discovering new facts, and as a new fact was an addition to human knowledge, the quest was therefore justified. Moreover, he might add: I am the first to introduce scientific methods in this research, as I weigh the pebbles and measure the straws.

**Rules for the Investigation of Symptoms**

I saw that I must have some clearer guide in my work. I reflected that I had to deal with people in ill health, and the nature of their ill health could only be discovered by understanding the symptoms of disease. The physicians of thirty or forty years ago were, many of them, very capable men. Their minds were not distracted by the numerous methods which to-day are considered necessary for the examination of their patients, so that they cultivated their powers of observation. I had been struck during my student days, and later when I entered practice, by the rapidity and precision of diagnosis in patients who presented no physical sign, and the assurance with which they would foretell whether an illness would pursue a favourable or unfavourable course. The old doctor to whom I was assistant possessed this faculty in an eminent degree, and I often to-day reflect with admiration on the remarkable certainty of his diagnosis and prognosis. When I was considering my failure to get forward with my investigation I reflected on these matters, and I saw that this knowledge was due to the recognition of subtle signs which could only be detected and appreciated from long and careful observation. The knowledge was personal, and medicine had not advanced so far as to enable a description to be given which would convey the knowledge to others.

Seeing that disease makes itself manifest only by the symptoms it produces, I recognised that the first step in my undertaking would be to acquire a better knowledge of symptoms. In order that my inquiry should be directed in a systematic manner, I laid down three rules for guidance.

(1) To differentiate each symptom clearly, and separate it from others it might resemble.

(2) To discover the mechanism by which each symptom was produced, and to search for the laws governing the production of symptoms.

(3) To assess the value of the symptom, so far as it had a bearing on the patient’s future – the prognostic significance of the symptom.
By following these rules I hoped to get an insight into the nature of the diseases of my patients, and to find out the explanation of the older physician’s power of diagnosis and prognosis. This was all the more necessary since the vast majority of my patients had no gross physical sign of disease, the symptoms being mainly subjective, or of such a subtle and elusive kind as could only be detected by the trained senses.

Except incidentally, I do not propose to refer to the steps I took to differentiate the symptoms and to understand their mechanisms, but I propose to describe at some length how I proceeded to investigate their prognostic significance. This subject has been neglected because those engaged in research do not have its importance thrust upon them. On the other hand, experience had shown me that for intelligent practice this matter was essential, and that these two other fields were but preparatory for this, which is indeed the coping stone of all medical investigation.

As time has gone on I find that the conception of prognosis grew upon me till I now recognise it as the vital spark which endows medical investigations with life and interest, and that what rendered so much endeavour vain and futile was the absence of this life-giving conception. So far no one seems to have realized that this important field was necessary to the completion of all research in medicine.

Prognosis in Heart Affections

Guided by these rules, I continued the study of affections of the heart. The methods necessary to differentiate symptoms and study their mechanism were comparatively easy to discover, but it was a long time before it became clear how to proceed with the inquiry into prognosis. At last I put to myself the question, “What are you afraid of?” The reply was “Heart failure.” The next question then arose, “What is heart failure, and what are the symptoms by which it can be recognized?”

Were murmurs and irregularities signs of heart failure? I had to confess that, except in certain forms of heart failure where dropsy and dyspnoea occurred, I had no idea of the signs of heart failure. Again I turned to my textbooks – clinical, physiological, and pathological – for a description of the signs of heart failure, and again discovered that the knowledge did not exist. I recognized that until I knew the signs of heart failure I was incompetent to study the prognostic significance of heart affections. So I set about to acquire this knowledge and spent years in the quest. Though far from completed, I gained knowledge sufficient to enable me to recognize the importance of the subject and how it should be investigated.

Let me explain how this was done. I had first to watch, in people with failing hearts, the appearance of symptoms, and re-educate myself in the examination of the patient so as to differentiate the symptoms clearly.

This, to a certain extent, had been done in regard to murmurs and modified sounds, but the equally common symptoms of irregularity had been neglected. After many years I was able to differentiate the irregularities. I had also to study with care the sensations of the patient, for, as I ultimately found, this was the key which brought the solution of the problem. I thus found out the sensations that indicated heart failure. I found, among other things, that the first signs of heart failure were not to be detected in the heart itself, but were shown in the disturbed function of organs remote from the heart. Then I had to see people before the heart was affected; I had to watch the circumstances that weakened the heart; I had to see the effects of hard work, of pregnancy, of intercurrent diseases, and I had to detect the onset of the earliest sign and watch the progress till death. I had to find out the mechanism by which the various symptoms were produced, and to do this I had frequently to resort to the physiologist for help. By the knowledge thus acquired I was able to distinguish those signs which were of significance from those which were of no significance. It will be seen that to understand the subject of prognosis the observer has first to undertake a long training, and then he has to have the opportunity of studying not only acute cases, but cases that proceed gradually for ten or twenty years or longer.

It is impossible for those who have not undertaken this kind of research to understand its difficulties. Let me describe one phase of the subject. One object I had in mind was to understand where lay the danger of pregnancy in a woman with a damaged heart. This is a problem which confronts, time and again, every general practitioner, and it is one of very serious moment to those concerned. The references to this subject in the most recent books on obstetrics have not advanced beyond those published over forty years ago. To undertake this part of the inquiry I had, as I have said, first to train myself to detect the early signs of heart failure. Then I had to study the changes in the circulation and search for the causes producing them, during pregnancy, during confinement, and during the puerperium which occurred in healthy women; I had to watch the changes that took place in women with different forms of heart disease, examining them before pregnancy and at all the subsequent stages. This meant attending them during labour, taking careful observations during the pains and when free from the pains. These observations were not made in a comfortable ward with plenty of help, but often after a hard day’s work, during the night in poor cottages, where I had to do the duties of the doctor and nurse, give chloroform, apply the forcepts. Yet this work had to be done, and in no other way could the knowledge be acquired.

It will be seen that a matter like prognosis, so essential to medical practice, requires methods and opportunities of a particular kind, but so backward is the state of medicine that neither the methods for
acquiring this knowledge nor the value of the knowledge when acquired is understood.

**Guiding Principles in Prognosis**

It was necessary not only to seize the opportunity and make a note of symptoms, but to have a clear guiding principle. I want you to grasp this point, for it was the want of this principle that caused me to spend years in “muck-raking”. I remember examining repeatedly a man suffering from angina pectoris and failing to detect any physical sign of disease, yet he could not walk 200 yards without being pulled up by an excruciating pain. When he died I found the myocardium extremely atrophied and the coronary arteries blocked. I saw that this condition must have been coming on for many years, and this caused me to reflect on the effects of the damaged muscle. When the man was at rest he was quite well, mentally active, and complained of nothing, but when he made an effort he was pulled up. So I dimly conceived that the symptoms were only produced in response to effort.

I therefore made a long investigation into this response to effort, considering first what happened to people in health. In childhood the response to effort is small, for the child stops after running a few yards. In boyhood it is much greater, and reaches its greatest amount in the heyday of youthful vigour; after that it gradually declines till the old man reaches the limits of his childhood. I compared these results with what happened in disease, and found that the response to effort was restricted in exactly the same way. Then I asked, What are the signs of this limitation? And for a time, being under the delusion that instruments were the most scientific method, I spent much time in recording the rate of the heart, and studying the changes in the character of the pulse by graphic records and blood-pressure instruments. These did not help. Then it occurred to me to ask of the individual, healthy and ailing, “Why have you to stop,” and they all replied, “Because of a feeling of distress.” This gave a new turn to my inquiry, and I then investigated this sensation of distress. At first it was difficult to get a clear conception, for I was too ignorant to interpret the answer. After a time I got a little understanding, and gradually the nature of the distress became perfectly clear. The reason why I failed, and, indeed, why the medical world fails to-day, to understand the symptoms of heart failure is because of their extreme simplicity. When we search for the rec- ondite and the obscure we fail to recognize the simple and the obvious.

The sensations of distress which indicate the limitation of the heart’s power are of two kinds – breathlessness with its associated phenomena, and pain with its associated phenomena. When you come to think of it, a failing organ does not itself necessarily show its impaired efficiency; rather the symptoms will be shown by the organs which are affected by the diseased organ’s failure. Health is the harmonious working of all the organs. The disordered or impaired function of one organ upsets the others, and the signs of ill health are found, not in the inefficient organ, but in the others.

**The Estimation of the Functional Efficiency of Organs**

That is a principle which is of universal application, and should be applied to the study of the functional efficiency of every organ.

In regard to the heart, its failure affected structures which did not receive a sufficient supply of pure blood. The respiratory system is the most sensitive, and possesses a mechanism which causes distress when its blood supply is inefficient – so we get breathlessness. The heart muscle, when forced to increased effort, requires more blood, and if it fails to receive an adequate supply it gives expression to its exhaustion by pain, a symptom belonging to the nervous system.

I cannot here explain the steps by which this conclusion was reached, nor show you what a flood of light it has thrown upon that darkest of fields in medicine – the evidences of functional inefficiency of organs. While for many years I have used this knowledge in practice, the full meaning of it was not understood until, in St. Andrews, we had carried the inquiry further, and discovered the mechanism by which such symptoms and the vast majority of other symptoms were produced.

If you reflect, common sense will tell you that the response to effort is the only means by which the efficiency of the heart can be recognized. It is now many years since I called attention to it, yet its significance is not grasped. You can see this failure to grasp it in the medical forms for life insurance. Questions are asked about the size of the heart and its sounds, its rate and its rhythm, but not a single question as to the response to effort. Some companies have an elaborate series of questions for suspected hearts, but in none of these is there any reference to its functional efficiency. People are to-day rejected for life insurance or penalized because of an innocent murmur and irregularity – a mistake which would never occur if insurance examiners understood the response to effort. Other people are passed as fit who would never be accepted it the answer to a simple question was skillfully interpreted. I have on many occasions been consulted by men who had a few months before been insured for large sums, who suffered from such advanced disease of the heart that they died shortly after. There was no physical sign, but their replies to my inquiries as to their response to effort revealed the extreme gravity of their condition.

It requires much experience to use this method, but when the knowledge is acquired it is easy. The testing
The Keeping of Records

Did it ever occur to you why records of patients are kept? Every hospital keeps them as a routine, but it is doubtful if the reasons are understood. The chief purpose of records is to lay the basis of prognosis – that is, to obtain a knowledge of a patient’s complaint from data drawn from patients presenting similar symptoms whose progress has been observed. The real purpose of records is to show this progress. They can be used for other purposes, but these are subsidiary. To-day they fail in usefulness because of the absence of a knowledge of prognosis. If you consider the enormous amount of record-taking and record-keeping in all the hospitals and private note-books in the world, with the enormous number of life insurance records, and reflect that if one wished to know what was the significance of some simple sign, such as a heart murmur or irregularity, the information could not be obtained, you will appreciate the futility of record-taking as understood to-day. The records taken to-day are not a bit more helpful than those taken fifty years ago. I know this will be disputed, for there is a belief that medicine has made such gigantic strides that signs and symptoms are now detected that were never before recognized. Thus a physician who has had some laboratory training in biochemistry includes in his notes the chemical constitution of some fluid. Another who has studied the blood will reflect his speciality in his records. If he has studied bacteriology the records will describe the various bacteria found, while blood-pressure records and electro-cardiograms will show the bent of others, and so on. Each one finds his justification in the belief that in recording facts he is adding to the sum of human knowledge, whereas he is but adding to that enormous mass of chaotic details which darkens and confuses medicine to-day.

The Purpose of Records

The real purpose of record-taking is to relate the life-history of disease in a number of people so that the signs which reveal the disease and show its progress and those which indicate danger can be recognized.

Prognosis is the motive which inspires note-taking with the breath of life, making the notes a perennial source of knowledge that can be applied in the practice of medicine. To obtain records of value, opportunity must be had of seeing disease from its onset till its end, while knowledge of a particular kind is required in order that out of the mass of symptoms those that are essential only are recorded.

While that is the ideal, only those who have recognized it and have striven to attain it understand its difficulties. This ideal, it is to be observed, differs greatly from the practice of to-day when there is too often but a dreary record of undigested symptoms during a passing phase of disease.

The Records of Mitral Stenosis

In order to convey some idea of the method and purpose of record-taking, let me cite my observations on mitral stenosis. It is over fifty years since the presystolic murmur was recognized as indicating stenosis of the mitral valve. If you turn to most textbooks you will find that since that day no progress has been made in our knowledge of this murmur, or indeed of any other murmur – that is to say, for fifty years auscultation has not progressed, and notwithstanding all the alert minds that have been engaged in clinical
medicine, no conception existed as to how progress should be made. But as soon as I was possessed of the idea to find what happens to the individual with a presystolic murmur, new life was breathed into my work, and a way of progress opened up. Early in my career as a general practitioner I found that the presence of mitral stenosis was associated with danger to pregnant women as well as to others. It was necessary to know wherein lay the danger. To understand this it was necessary to know the life-history of people with this trouble. I therefore began a series of observations on patients with rheumatic fever or who had had rheumatic fever. I kept in contact with them for many years, and watched the progressive changes that took place in the sounds of the heart. In this way I discovered that the murmur peculiar to mitral stenosis – the presystolic – did not occur during the causative attack but at variable times afterwards – usually several years. The murmur at first was short in duration and was not always present. As time went on it became of longer duration and constant. By-and-by another murmur appeared, diastolic in time. This increased in length until it ran into the presystolic, so that during the diastole of the ventricle there was a continuous murmur. When such patients died the mitral orifice was reduced to a mere slit. One infers that the cicatrizing process is gradual, and that these changes in the murmur are due to increase of the cicatrizing process which narrows the orifice. But the point of importance is that you are given an idea of the stage of narrowing that has been reached. Moreover, the rate of progress varies greatly; some only reach a certain stage and remain stationary. The recognition of this gives a further guide to prognosis. It is necessary, for instance, in advising as to a woman’s fitness for child-bearing to know whether the stenosis is stationary or advancing rapidly, and this knowledge is obtained by recognizing the peculiar features of the murmur, whether short or long, or whether a diastolic murmur is present, with a knowledge of the time of the causal attack. Thus, a short presystolic murmur with a history of rheumatic fever ten or fifteen years before would indicate a favourable prognosis, while a presystolic and diastolic murmur with a history of four or five years would give a much graver outlook. To-day, amongst obstetric physicians, there is much confusion, for, while one group says mitral stenosis is a very dangerous complication, others declare it not to be of serious significance, the reason being that each speaks of the cases that come within his own experience, none recognizing the principle that should guide them.

But in this inquiry I was struck with the great diversity of phenomena that arose. Thus some patients suffered from severe heart failure and died while yet the stenosis was slight in degree. Others pursued laborious occupations when the stenosis was far advanced. I therefore recognized that there were other factors, the chief of which I found to be a coincident damage to the heart muscle. Sometimes this could be made out by the changes in the size of the heart, or by the presence of partial heart-block, but the most instructive indication was the response to effort. This meant that the mitral stenosis was but one factor in assessing the functional efficiency of the heart, and that it was necessary to consider the associated phenomena and particularly the response to effort.

Many instructive phenomena, which explained features that had puzzled clinical observers (to some of these I will refer later), came under notice during this research. But the most striking and most dramatic was the sudden onset of extreme heart failure that every now and again overtook some of these patients. One, whom I had watched for seventeen years, and who had lived a useful and industrious life as a nurse, was suddenly seized with great breathlessness, and the heart became rapid in its rate and dilated. She was cyanosed, the liver was enlarged, and dropsy set in. On taking graphic records I found that the rhythm was very irregular and the auricular wave had disappeared from the jugular and liver pulses. On listening to the heart the presystolic murmur, which had been present, had disappeared. Thus all signs of auricular activity had disappeared. My attention being arrested by these signs I sought for similar conditions and found that these cases were frequent and occurred independent of mitral stenosis, so that I was able to recognize a definite and distinct type among heart cases. Indeed, I found that between 80 and 90 per cent. of cases of heart failure with dropsy and enlarged liver were of this type. I then proceeded to watch these cases to see what happened, and I found that on the onset of this abnormal rhythm the heart failure set in with such severity that some died within a few days, others within a few weeks, others led a crippled existence for months or a few years, while others lived comfortably at a lower level for many years, and in a few the onset was not accompanied by any limitation of the heart power. Seeing these very diverse results I set about a long inquiry into the reasons. I found that in those who did well after the onset, though the heart rhythm became irregular, the rate did not alter. On the other hand, in those who did badly the rate became increased, sometimes greatly. In watching them I found that if the rate slowed the patient improved, so I looked for means for slowing the rate and naturally turned to digitalis. I gave the digitalis at first timidly, as we were brought up to look upon it as a dangerous though useful drug, then more and more boldly, till I found the quantity that would slow the heart. When I had acquired a knowledge of the drug and how to administer it, I was able to give speedily the greatest relief to many patients who were apparently in extremis. But I found that as soon as the drug was stopped the patients relapsed, so I set about...
discovering how to give the drug so as to keep the pulse at a moderate rate, and at last devised a method by which many people who were apparently hopelessly broken down were enabled to resume their occupations.

In some the digitalis or other drugs would not slow the rate, and these invariably drifted and died. In others in whom the heart slowed, the symptoms of heart failure were not relieved – these also speedily sunk and died. The post-mortem examination in these cases invariably revealed such extensive damage of the heart muscle that one could infer that such hearts, embarrassed by the abnormal rhythm, were inconsistent with life.

I need not go into the numerous interesting points that arose from this inquiry. One I may mention was that the particular kind of rapid heart for which digitalis is the remedy stood now clearly revealed, as I have already said. If you have grasped the significance of the methods I adopted for getting the prognosis you will at once see what a powerful weapon has been placed in our hands, and with what confidence we are now able to give a clear prognosis based upon accurate observation and sound principles.

Many years after, this condition was discovered from experimental search to be due to fibrillation of the auricle, and it is a curious illustration of the lack of perception of the essentials of medicine that the discovery of this condition is frequently assumed to have occurred only when it was demonstrated in the laboratory. All that work which revealed its clinical symptoms, which laid the basis of a sound prognosis, and which indicated rational lines of treatment, is practically ignored. The research in the laboratory has indeed helped to a partial understanding of the mechanism, and to differentiate this condition from others it resembled, but it has not added one iota to the knowledge necessary to clinical practice. Indeed, so little is the significance of this inquiry realized that in books and articles written by cardiologists you seldom find any appreciation of the basis for a rational treatment, let alone a rational prognosis.

I do not quote this in order to disparage laboratory work or to praise myself, but to demonstrate the blindness to what is essential in medical inquiry – to illustrate the limitations of laboratory investigations into diseased states. While we recognize the presence of auricular fibrillation, we do not know the conditions which induce it, nor is there the slightest expectation that laboratory experiment will reveal it. I have a poor woman who suffers from haemorrhages, which occur spontaneously under the skin. It would not throw any light upon her ill health to give a man a black eye. It is vain to expect to discover a process of disease by applying to a healthy organ a stimulus of a kind which nature never employs. A disservice is thus done to experimental work, inasmuch as it is asked to reveal that which it cannot reveal.

### New Fields Opened up by the Study of Symptoms

In watching the life-history of patients with mitral stenosis a great number of instructive incidents occurred. By keeping in mind the rules I had adopted of differentiating the symptoms and recognizing their mechanism and their prognostic significance a light was thrown beyond the immediate object of research and opened up other fields of inquiry. There was revealed, for instance, the nature of many functional abnormalities, which could not be shown by experiment or by the study of dead organs. Thus one man whom I attended for rheumatic fever in 1880 was left with a damaged heart and a systolic murmur. It was ten years later before I detected a presystolic murmur. Later I recognized that this murmur became separated from the first sound by a short pause – a feature which had been described as a mid-diastolic murmur. Records of the jugular pulse showed that at the time of this mid-diastolic murmur there was a wave in the jugular vein due to the contraction of the right auricle, and there was an increase in the interval after the wave before the carotid pulse appeared. By-and-by I was able to recognize that this meant a delay in the transmission of the stimulus from the auricle to the ventricle, and from this I inferred that the bundle connecting auricle and ventricle had been damaged. So that we can now recognize that a mid-diastolic murmur means not only mitral stenosis but a partial heart-block. With the recognition of this delay between the auricular and ventricular systoles we caught the early stage of that condition which goes by the name of Stokes-Adams syndrome.

But much more was learnt. I had found that one effect of digitalis was to increase this delay, so that at times the stimulus from the auricle failed to reach the ventricle, and a beat would drop out, and thus was explained one effect of digitalis that had hitherto baffled interpretation.

The continued observation of this patient revealed other important changes. He used to come and see me every two or three weeks. In April, 1904, I found for the first time that his pulse was irregular. On further examination, I found that the mid-diastolic murmur had disappeared, while the auricular wave also was absent from the jugular tracing – that is to say, all evidence of activity of both auricles had disappeared – the disappearance of the murmur was a sign of cessation of activity of the left auricle, and the disappearance of the wave in the jugular a sign of the cessation of activity of the right auricle.

This condition continued for a week; then one day I found both murmur and auricular wave had returned and the rhythm had become quite regular. The heart continued thus until the following November, when the irregularity returned with the cessation of auricular activity. This condition persisted till his death ten years later.
One instructive point was this: I had observed, as I have said, that when these events happened heart failure usually set in, sometimes speedily. This man was unconscious of the changes, and he continued his laborious work – that of a mechanical engineer - with no signs of heart failure. On seeking for a reason, I found that in his case though the rhythm had become irregular the rate had not increased; both before and after the rate was about 60.

The reason for this was no doubt the presence of the partial heart-block. I had recognized that digitalis acted on the bundle and produced heart-block. The cases that did badly and suffered from heart failure after the onset of auricular fibrillation had the rate of the heart greatly increased. It occurred to me, if I could imitate his heart-block by using digitalis, the ventricle in these cases might be kept slow and heart failure prevented. This was found to be correct, and in this way was found that treatment which has robbed auricular fibrillation of much of its peril.

The Basis of a Scientific Therapy

A matter which strikes everyone who gives it attention is the curious difference between theoretical therapy and practical.

We have the experimental pharmacologist demonstrating to the student with precision the effects of remedies by animal experiment. The student as soon as he enters the wards of the hospital finds a different atmosphere – drugs are administered without any reference to their experimental effects, and he finds the knowledge he has acquired in his pharmacological course of no use.

The pharmacologist scoffs at the clinician as unscientific and as employing empirical methods. The clinician replies that the laboratory teaching is academic and unpractical.

I have already remarked that the action of digitalis on the human heart was not understood, and when I made the observations on the effects of digitalis during this inquiry into mitral stenosis, I was struck by the variety of results I obtained. In one patient digitalis would produce dropping out of beats due to heart-block; in another it would cause the whole heart to stand still for two or three seconds, and then the ventricle would start off by itself; in another great slowing would result, and so on. When I looked at these patients individually, I found they all suffered from damaged hearts, but there were differences in the kind of damage, and I therefore formulated the theory that the action of digitalis is modified by the nature of the disease. It is manifest that the pharmacologist could never find this out, and his results were different, therefore, from that of the clinician. On the other hand, the knowledge of the heart irregularities was so defective that the clinical observer could not recognize them, but saw that they were different from the description given by the laboratory observer. That is the reason of the failure for the pharmacologist to explain the action of digitalis on the human heart, and the reason why the clinician could not recognize it.

This principle, at first dimly perceived, holds out the possibility of directing therapeutical research on lines based upon sound principles. One of the least creditable fields of knowledge is the therapeutic. While many drugs are usefully employed, it must be confessed that our knowledge of the action of remedies is sadly lacking in accuracy. To this defect must be attributed that wide diversity of opinion as to the action of the simpler remedies and that confusion which bewilders the student. This inquiry into the nature of symptoms led us at St. Andrews to recognize that a great mass of symptoms is due to disturbances of normal reflexes. When a man falls ill, due, say, to the invasion of his body by a microbe, the toxins of this microbe produce the ill health by upsetting the normal reflexes, and we recognize these disturbances in the signs of disease.

The administration of a drug such as atropine acts in the same way by disturbing certain reflexes. Indeed, the effect of atropine may be described as an imitation disease. One of its effects is to paralyse the peripheral ends of the vagus and cause an increase in the heart rate. If digitalis is given it is without effect, because digitalis stimulates the vagus, and under atropine it is paralysed.

In certain infections the heart rate is increased because the toxins act like atropine, and digitalis does not slow the heart because the vagus is paralysed, and that is the reason why digitalis does not slow the heart in a great many febrile and other conditions.

In auricular fibrillation the increased pulse rate is due to a totally different mechanism. Here the ventricles are stimulated to increased rate by a shower of stimuli from the fibrillating auricle. The vagus is unaffected, and so the digitalis, when given, acts as we have seen on the bundle which converts the stimulus from auricle to ventricle, and it is probably in this way that digitalis is so effective in slowing the heart rate in auricular fibrillation.

The First Step in Investigating Disease

Many visitors come to see our institute at St. Andrews, and they go away disappointed at what they see. Our work is not spectacular – our chief method is seen to be a general practitioner quietly asking questions of a patient who has little the matter with him. A learned physician one day was being shown over the institute. He came to the general practitioner engaged in his work. He looked at the notes and said, “Ah! Applying hospital methods to general practice?” “No,” I replied, “we are training ourselves how to examine patients. We find that students are never trained to examine patients so as to fit them for general practice.” “Oh, nonsense!”
said he; “they are well enough trained.” “Well,” I replied, “you have been teaching students at least for twenty-five years?” “Yes,” said he. Then I asked him: “Can you tell me the symptoms of which the majority of people complain when they fall sick?” After some consideration he said, “No,” I said, “The most common complaint is exhaustion. Can you tell me what is exhaustion?” He again, after a little consideration, said “No.” “So,” I said, “here is a symptom of the most common kind, a symptom which, when understood, throws a flood of light upon the patient’s state, and yet you, who reckon to be able to teach students how to examine patients, have never given it the slightest consideration.” I quote this incident to show what should be the first step in investigating disease, and the only individual whose opportunity permits him to take it. The necessity that the general practitioner should participate in other fields of research is obvious as soon as a real perception of medical research is obtained.

I know quite well that these views at present will fail to carry conviction. All I wish you to do is to pause from time to time and ask whether they are true.

Commentary: A thesis that still warrants defence and promotion

Blair H Smith,1* Bruce Guthrie,2 Frank M Sullivan3 and Andrew D Morris4

1Population Science, Medical Research Institute, University of Dundee, Dundee, Scotland, UK 2Primary Care, Medical Research Institute, University of Dundee, Dundee, Scotland, UK 3General Practice, Medical Research Institute, University of Dundee, Dundee, Scotland, UK and 4Diabetic Medicine, Medical Research Institute, University of Dundee, Dundee, Scotland, UK

*Corresponding author. Tayside Centre for General Practice and Medical Research Institute, University of Dundee, Mackenzie Building, Kirsty Semple Way, Dundee DD2 4BF, UK. E-mail: b.z.smith@dundee.ac.uk

Accepted 24 September 2012

Introduction

Sir James Mackenzie (1852 to 1925) is known as ‘the father of general practice-based research’.1 His eponymous legacy includes the Chairs of General Practice at the Universities of Aberdeen and Edinburgh, and the building where the authors of this commentary pursue their research, as well as the principal annual lecture of the Royal College of General Practitioners. From humble agricultural origins in rural Perthshire, Mackenzie overcame early social and educational hurdles to study medicine in Edinburgh, then pursued a career in general practice in Burnley. During this full-time clinical post, he initiated the systematic observation of his patients that led to his stellar research career, including an established international reputation in cardiology, discovery of novel and important insights into heart rhythms and the use of digitalis, appointment as a Fellow of the Royal Society and a knighthood.

At St Andrews University, the Chair of Public Health and Social Medicine is also named after Mackenzie, and it is at St Andrews University that his heart remains (literally, in the anatomy department).2 Although he had re-located his professional and academic base to London when his career took off, he left there at its height, at the age of 64 years, to establish the Institute for Clinical Research in St Andrews. This is where he was based at the time he presented the accompanying re-printed article.3 Although the institute was ultimately short lived, surviving only briefly after Mackenzie’s death, it was innovative in bringing together all the General Practitioners (GPs) working in the town, for the purposes of collecting and using clinical data for research. These included the systematic recording of routine observations, which were used in longitudinal studies, and the development of record-keeping systems that eventually influenced national policy. By working with general practice colleagues in St Andrews, he made real his key insight: that systematic observation and recording of symptoms and signs in a whole population could provide essential