THE INFLUENCE OF CLAUDE BERNARD ON MEDICAL SCIENCE

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In this age, when new scientific discoveries follow one another with such bewildering rapidity, it may help us to retain our sense of proportion if we look back from time to time along the road which medical science has followed. We can learn much from the life and work of the great scientists of the past and it is interesting, in the light of modern knowledge, to assess their influence on the development of scientific medicine.

One of the greatest of medical scientists was the physiologist, Claude Bernard, who lived and worked in France about a hundred years ago. He performed valuable work in many and varied fields of physiology but probably his greatest gift to posterity was his philosophical approach to biology and his clear enunciation of the scope and purpose of physiology.

The science of physiology had evolved from medicine during the 17th and 18th centuries and important physiological facts had been ascertained from experiment by a number of distinguished scientists, including William Harvey and the Rev. Stephen Hales in England, Albrecht von Haller in Switzerland, and Lazaro Spallanzani in Italy, but there was still a strong tendency to accept traditional beliefs rather than put them to the test of experiment. Bernard's own teacher, François Magendie, believed in the value of experiment but applied experimental methods uncritically to a mass of investigations, with a correspondingly poor return for his efforts. Magendie's contemporary, Johannes Müller, attempted to correlate the branches of knowledge on which physiology depends. In his *Handbook of Physiology* 'the results of comparative anatomy, chemistry, and physics were for the first time systematically brought to bear on physiological problems'.[1]

BERNARD'S LIFE

Before commenting on Claude Bernard's contribution to science it is appropriate to indicate something of his personal history and background.[2,3] Claude Bernard was born in 1813 in the village of Saint-Julien in the Rhône district of France, where his father owned and worked in a vineyard. Claude was an only son; he had one younger sister. As a child he was taught at first by the local priest and then at a Jesuit College at Villefranche. From there he went to work as a pharmacist's assistant in a suburb of Lyons. Bernard's first experience of pharmacy induced in him a healthy scepticism for medical treatment. A syrup which was dispensed as a cure for all ills, and which the customers found most effective, was compounded of all the spoilt and left-over drugs in the shop. One of the young pharmacist's duties at this time was to take drugs for sick animals to the near-by veterinary college, which was one of the first in Europe. He was allowed to linger on this errand and was intensely interested in what he saw and heard at this college.

On his free evenings Bernard frequented the local theatre. Not content with the passive role of spectator he wrote a comedy, *La Rose du Rhône*, which was performed there. Encouraged by this success he proceeded to write a 5-act drama entitled *Arthur de Bretagne*. At the age of 21, armed with the manuscript of this play and with a letter of introduction to M.

Girardin, the deputy Professor of Literature at the Sorbonne, Bernard set off for Paris. Girardin read the manuscript and, finding it lacking in inspiration, advised the young author not to seek his fortune as a playwright but rather to follow up his early training in pharmacy by studing medicine.

Bernard accepted with resignation his literary failure and, as he had been advised to do, entered the Medical School in Paris. He worked hard and lived frugally, supporting himself by school teaching in his spare time. His father died about this time, leaving considerable debts; so Claude had no financial support from his family for his medical training. He was not a brilliant student, except in anatomy, where he showed great skill in dissection. Physiology had not been defined as a science clearly distinct from anatomy, and what physiology was taught was scholastic rather than scientific, the traditional views being repeated without any attempt at experimental investigation.

On the completion of his medical course, Bernard had the good fortune to be appointed *interne* to Magendie, who was Professor of Medicine at the *Collège de France.* Magendie, unlike other physicians of the period, believed in the experimental approach to medicine and had a small research laboratory, where he was studying the function of spinal nerves and the effect of cutting the anterior and posterior nerve roots in experimental animals.[4,5] Bernard proved so skilful at experimental technique that Magendie employed him as his demonstrator.

Bernard's first scientific publication was a paper on the comparative anatomy and physiology of the chorda tympani.[6] He found the course and distribution of this nerve very constant in different mammals and he found no chorda tympani in birds or in reptiles. He showed also that the main effect of section of the nerve in dogs is loss of taste sensibility on the corresponding side of the tongue, and he linked this observation with the diminished appreciation of taste often encountered in human facial palsy. This paper was followed in the same year (1843) by a thesis for the Doctorate of Medicine on the subject of gastric juice and its role in nutrition. Thus, from the very beginning of his academic career, Bernard's interests lay in the application of physiology to medical problems.

In 1845 Bernard married Marie Françoise Martin, the daughter of a wealthy physician in Paris. They had 4 children, 2 sons who died in childhood and 2 daughters who outlived their father. The marriage was not a happy one. Mme. Bernard was not only quite uninterested in her husband's intellectual pursuits but actively opposed to the experiments on animals which were a feature of most of his research work.

Domestic difficulties, however, did not impair Bernard's academic activity. In 1847 he was appointed assistant lecturer to Magendie at the *Collège de France.* In 1848 he was elected to membership of the *Académie des Sciences* and was a founder member of the *Société de Biologie.* In the same year he was appointed to a new chair of general physiology created for him at the *Sorbonne.* In 1849 his scientific work received public recognition when he was created *Chevalier* of the *Légion d'honneur.*

The next decade was the most active of Bernard's career. He worked unsparingly at experimental research and teaching and yet found time to take an active part in the meetings of scientific societies. His fame spread, and students from many countries attended his lectures and his demonstrations of experimental technique. His students remarked on the number of phenomena which Bernard demonstrated in the course of experiments, details which nobody else had noticed although they were quite obvious when pointed out. 'He made discoveries as easily as other people breathe.'[7]

In 1853 Bernard was awarded the degree of Doctor of Natural Sciences for a thesis on the glycogenic function of the liver. In 1855 he succeeded Magendie as professor of medicine at the *Collège de France.*

And then in 1860, when 47 years old and at the height of his research career, Bernard's health began to fail. While he contrived to continue his teaching and some other professional commitments, the active experimental research which had been the main interest of his life was interrupted for some years and thereafter was never pursued with the same vigour. During remissions of his illness he did continue some research work; for instance in 1863 he collaborated with Pasteur in experiments on the putrefaction of blood and of urine, but towards the end of that year illness once again compelled him to leave his work and retire to the country, where he had purchased a house in the district where he was born. We have no exact information about the nature of this illness except that he suffered much abdominal pain and recurring attacks of fever. It has been suggested that the lesion was an appendix abscess.

Although Bernard was ill for many years he did not spend the time in idleness. It was during this period that he wrote one of the greatest books in the literature of science, the *Introduction to the Study of Experimental Medicine.*[8] He also managed to maintain his contacts with scientific societies and to appear at court, where he made a very favourable impression on the Emperor Napoleon III. In subsequent years Bernard used his influence with the Emperor to obtain better research facilities for laboratories throughout the country.

By 1869 Bernard's health was greatly improved and he resumed his teaching and administrative duties with full vigour although he was less active than before in the field of research. At this time in his public life honour after honour was showered upon him but his private life was lonely; after a long period of domestic unhappiness M. and Mme. Bernard had finally parted and the two daughters were living with their mother. In his professional work, from this time on, Bernard's interests became more and more philosophical rather than experimental and his clear intellect was applied as successfully to philosophy as it had been to experimental science. His teaching also was of a high order and he still attracted to his classes gifted young men from many countries who later furthered the cause of science in many fields besides that of pure physiology. In the last year of his life Bernard was still actively teaching and contributing original papers to scientific meetings, and he was engaged in research into the chemical processes involved in fermentation. Bernard realized that fermentation might depend on a soluble enzyme, acting outside the cell, and he hoped to find the enzyme.[9] On his death-bed he said, 'What a pity; it would have been nice to finish it.'[7]*

Claude Bernard died in the year 1878. He had received many honours during his life and at his death he was mourned as a national hero. Bernard was the first scientist in France to be accorded a state funeral. The funeral orations leave no doubt that he was honoured as a great scientist, and his name is still revered, particularly in his own country.

EXPERIMENTAL RESEARCH

From the year 1843, when he graduated Doctor of Medicine, Bernard devoted himself to research in experimental physiology. He investigated the spinal accessory and vagus nerves[10, 11] and continued his studies in digestion with an investigation of differences in nutrition and digestion between herbivora and carnivora.[12] His first really important contribution to science arose from this latter investigation and may well be reported in a translation of his own words since these show his ability to follow up chance observation with a logical theory based on the observation and then to proceed to experimental proof of the theory.

'We had observed that when we introduced fat into the stomach of rabbits the fat leaving the stomach was not altered until it had reached a certain distance from the pylorus much lower than the point at which the change took place in dogs. The absorption of fat by the lacteals showed the same difference, for we saw that lacteals containing fat appeared in the rabbit only at a considerable distance from the pylorus, whereas in dogs they appeared at the beginning of the duodenum. When we had confirmed the difference between dogs and rabbits in the site of digestion and absorption of fat it was natural to look for the cause in some special disposition of the intestines. We now noticed that the difference coincided with a difference in the site of entry of pancreatic juice into the intestine. In dogs the pancreatic juice is discharged into the intestine quite close to the pylorus whereas in rabbits the main pancreatic duct opens into the intestine 30 to 35 centimetres below the orifice of the bile duct. It was precisely at this point that the change in the fat occurred and that the lacteals could absorb the fat.'[13]

Bernard cannulated the pancreatic duct of some of his animals in order to collect pure pancreatic juice and he went on to show that this juice emulsified fat and split it into fatty acids and glycerol.[14] He also demonstrated that pancreatic juice converts starch to sugar.[15] The revolutionary nature of these discoveries can be appreciated when we realize that nothing was known before this about digestion in any part of the alimentary canal beyond the stomach.

Although Bernard's experimental investigations were never limited to one theme, his main interest at this time was in liver function. Magendie had shown that starch injected into the veins of a rabbit was rapidly converted to sugar.[16] Bernard and Barreswill demonstrated sugar in liver even when the animals had been fed exclusively on meat.[17] It appeared then that the liver could make sugar and this opened up an entirely new field of physiology. Previously it had been believed that food material could be formed only by plants; animals could not synthesize complex chemical substances, but could only derive energy from breaking them down.

Bernard set to work to test this theory of formation of sugar by the liver. He starved some dogs and fed others on meat alone; he sampled blood from different veins and found sugar in the blood leaving the liver even when it was not detectable in blood from the mesenteric, pancreatic or splenic veins. Finally he detected sugar in an extract of liver and showed that this sugar had the properties of glucose.[18] In the course of this work he observed that puncture of a particular region of the floor of the fourth ventricle caused sugar to appear in the urine.[19] He went on to show that this glycosuria was associated with hyperglycaemia and he made the correct inference that sugar production in the liver is controlled by the nervous system.[20]

Bernard continued his investigations on liver function at intervals during the rest of his active life. He found that an excised liver, from which all sugar had been washed out, could still form sugar during the next 24 hours but if the liver were boiled no more sugar was formed.[21] He later succeeded in isolating the substance from which the sugar was produced and in demonstrating its chemical properties.[22] He showed that this substance, which later came to be called glycogen, was formed only by living tissue but could be broken down to sugar, even after death, by the 'ferments' of saliva, of pancreatic juice, or of blood.

In a subsequent investigation Bernard found that the placenta of many mammals contained glycogen, which seemed to be the main source of sugar for the foetus until the liver commenced its glycogenic activity.[23]

Another major investigation undertaken while the liver research was still in progress was into the function of vasomotor nerves. Most physiologists of the time were firmly convinced that the blood vessels are incapable of active contraction, but some sympathetic motor nerves had been traced to arteries and a few scientists argued that these must stimulate the smooth muscle of the arteries to contract, in the same way as somatic motor nerves are responsible for the contraction of skeletal muscle. No experimental proof was attempted until Bernard showed that division of the cervical sympathetic on one side in a rabbit resulted in a rise of temperature of that side of the head and neck associated with dilatation of the superficial arteries in the region.[24] He did not believe however that the rise in temperature could be attributed entirely to vasodilatation but thought that some local increase in metabolism was involved. Later he showed that electrical stimulation of the upper portion of the divided sympathetic chain reduced the circulation through the blood vessels of the head and neck.[25] In another paper he described active dilatation of the blood vessels of the submaxillary gland when the branch of the lingual nerve supplying the gland was stimulated, and he showed that stimulation of the sympathetic nerve-supply caused active constriction of these vessels.[26] He concluded that the individual blood-supply of each part of the body is determined by nervous control of its blood vessels.

Bernard also studied the effect of drugs on his experimental animals. He obtained a supply of curare from Brazil and showed that its action was to paralyse motor

* All the quotations from Claude Bernard in this paper are translated from the original French.

nerves, although the muscles themselves still responded to direct stimulation.[27] Before this discovery it had been believed that muscle had no inherent power of contraction but was entirely dependent on the nerve fibres supplying it: Bernard demonstrated that curarized muscle is in fact more sensitive than normal muscle to direct stimulation. Working with Pelouze he showed that curare, although not toxic when administered orally, is lethal by parenteral injection even after prolonged incubation with gastric or pancreatic juice. Curare was not absorbed from mucous membranes but was rapidly absorbed from subcutaneous tissue or from the lung.[28] That Bernard's imagination was no less vivid for being kept strictly under control is revealed by his comment on poisoning with curare:

> 'Can one conceive of suffering more horrible than that of a mind aware of the successive withdrawal of all the organs destined to serve it and finding itself buried alive in a corpse?'[29]

Bernard also demonstrated the pharmacological action of the several alkaloids of opium on experimental animals.[30] He came to the conclusion that crude opium, having a very variable action, should be replaced in therapeutics by the alkaloid appropriate to the condition to be treated.

Another fundamental discovery made by Bernard was connected with the mechanism of poisoning with carbon monoxide. It had been accepted only a short time previously that oxygen and carbon dioxide are transported in the blood but it was still quite unknown how this was achieved and it was commonly attributed to simple solution of the gases in plasma. Bernard exposed animals to carbon monoxide and observed that the venous blood became red and would not take up oxygen. He observed also that arterial blood exposed to carbon monoxide gave up oxygen and took up carbon monoxide; this property could be used to ascertain the oxygen content of samples of blood.[31] From these observations he deduced that carbon monoxide poisoning is due to displacement of oxygen from the erythrocytes by carbon monoxide and he reached the further and much more important conclusion that the oxygen is normally carried in the erythrocytes.

In his last research, on fermentation, Bernard showed that cane sugar is converted to glucose by the action of a soluble enzyme formed by yeast, even when the yeast itself is inactivated by ether.[29]

Apart from these major discoveries Bernard made many lesser contributions to medical science in the field of digestion,[32] salivary secretion,[33] and neurology.[34] His lectures in the *Collège de France* and at the *Sorbonne* were published in several volumes and these books contained, not only details of his research work, but also the wider picture of the fundamental principles of physiology which were suggested by his experimental findings. Probably the most important general principle which he enunciated was the concept of an internal environment, consisting of the blood and tissue fluids in which the cells inside the body live. According to Bernard, constancy of this internal environment is a condition of free life; in other words higher animals like ourselves are free to move about in a variety of external environments because of carrying with them an unchanging internal environment in which the vast majority of the body cells are living. As he put it,

> 'All the vital mechanisms, varied as they are, have only one object, that of keeping constant the conditions of life in the internal environment.'[35]

PHILOSOPHY

Not content with his numerous publications on various aspects of physiology, Claude Bernard in his later years attempted to analyse the general principles underlying experimental research. During the enforced interruption of experimental work occasioned by his long illness he wrote the book which is now acknowledged to be his masterpiece, *Introduction to the Study of Experimental Medicine*.[8] The importance of physiology to medicine was not appreciated at the time, and so we find it mentioned again and again in this book; for instance:

> 'The scientific basis of experimental medicine is physiology . . . without it no medical science is possible.'

The importance of experimental work on animals is stressed:

> 'It cannot be gainsaid that this is the most delicate and difficult branch of biological investigation: but I deem it the most fruitful and perhaps the most immediately useful for the advancement of experimental medicine.'

The great dispute of the day in physiology was philosophic rather than scientific, between vitalists and mechanists. The vitalists affirmed that life depends not on the same laws as other sciences but on a specific vital force inherent in the living cell and inaccessible to investigation; any attempt to study and explain the phenomena of life would therefore be foredoomed to failure. The mechanists, on the other hand, affirmed that living processes are no different from other physical and chemical phenomena and can be adequately explained in terms of these. Bernard considered such disputes irrelevant; in the *Introduction* he says:

> 'Experimental medicine, that is physiology, belongs to no medical doctrine and to no philosophic system.'

Bernard expounded the philosophic basis not only of physiology but of science in general. He said:

> 'Fundamentally all sciences reason in the same way and aim at the same object. They all try to reach knowledge of the law of phenomena so as to foresee, vary or master phenomena.'[8]

To put it another way, the value of science to mankind depends on the power it gives us to foretell future events and to control some of these events.

Bernard described very clearly the fundamental method involved in the scientific approach to a problem:

> 'The true scientist is one whose work includes both experimental theory and experimental practice. (1) He notes a fact; (2) apropos of this fact an idea is born in his mind; (3) in the light of this idea he reasons, devises an experiment, and imagines and brings to pass its material conditions; (4) from this experiment new phenomena result which must be observed, and so on and so forth. The mind of a scientist is always placed, as it were, between two observations: one which serves as starting-point for reasoning, and the other which serves as conclusion.'[8]

Science depends on the formulation of theories, not on dogma, and the scientist must keep an open mind, especially on his own favourite theories. As Bernard puts it:

'In science indeed we must not only try to criticise others but every man of science must always be a severe critic of himself. Whenever he proffers an opinion or proposes a theory he must be the first to try to control it by criticism and to base it on well observed and accurately determined facts.'[8]

That Bernard realised the limitations of the experimental approach is shown by another passage from the same book:

'The nature of our mind leads us to seek the essence or the *why* of things. Thus we aim beyond the goal that it is given us to reach; for experience soon teaches us that we cannot get beyond the *how*.'[8]

In his book, *Experimental Science*, published in the last year of his life, Bernard says:

'Philosophy represents the eternal aspiration of the human mind to understand the unknown.'[29]

Science, according to Bernard, is concerned with the known and the knowable but not with truths which cannot be submitted to the test of experiment. In his view the function of an experimenter is to influence matter, animate or inanimate, by providing the conditions under which the desired reactions will take place. The object of experiment is to find these conditions and to observe the reactions.[29]

One subject on which Bernard's view differs radically from that of most modern scientists is statistics. Bernard held a very low opinion of the value of statistics, a view which was probably justified by the very imperfect statistical methods practised at the time. Also he saw no advantage for medical science in the establishment of laws of probability, which give no information about the particular case.

CONCLUSIONS

In retrospect we see that many of the physiological concepts now incorporated in medical science are attributable in the first instance to Claude Bernard. These include the processes of digestion and absorption in the small intestine, the formation of glycogen in the liver and its utilization, the nervous control of blood vessels and of salivary secretion, the pharmacology of a number of important drugs, the mechanism of gas transport by the blood, and the nature and significance of the 'internal environment' of the cells of the body.

What were the qualities which made Bernard great? I think these were an alert imagination and thoroughness in carrying out the ideas which this suggested to him. We all notice things we are looking for and fail to observe things we are not looking for or do not know about, but it is given to only a few gifted individuals like Bernard to notice unexpected details and to follow up such chance observations with thorough, planned investigation. Bernard was thorough; the second-best was never good enough for him. His observations were meticulously accurate and the conclusions he drew from them were careful and critical. It was never enough merely to observe; he had to look beneath the surface of individual results for the fundamental principles on which they depended.

Not only was Bernard a brilliant experimental scientist but he also gave clear expression to the principles on which he and other scientists should work. Not only physiology but science as a whole owes him a great debt.

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