

CLAUDE BERNARD

AND HIS VIEWS ON MEDICAL RESEARCH

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## BIOGRAPHICAL INTRODUCTION

Sir Michael Foster (1899), writing a decade after the death of Claude Bernard, said that the details which could be gained of Bernard's daily life were very scanty. This has been rectified, to a large extent, by the masterly volume of J.M.D. Olmsted (1939) to which many subsequent writers - including French authors - have expressed a debt.

Claude Bernard was born in 1813 in the old vine-growing province of Beaujolais in South-East France. Alexis Carrel (1939) draws attention to the fact that nearly at the same time and in the same region of France, three great men of science were born - Ampère, Bernard, and Pasteur. Perhaps he exaggerates when he says Bernard sprang from obscure peasant stock because the father of the physiologist was a vine-grower and later a school-master.

After receiving, largely at the hands of the church, an education more than commensurate with his financial position, Bernard was apprenticed to a pharmacist in Lyons in 1832. M. Millet's "thériaque" - "mélange clôtural de tous les résidus et laissés-pour-compte pharmaceutiques de l'année" (Chauvois, 1948), introduced Bernard to contemporary medicine, and the nearby veterinary college introduced him to vivisection. Almost half a century later, Bernard, in referring to "la classique thériaque", was able to say that "c'est précisément la thérapeutique qui doit le plus de progrès à la physiologie /

physiologie expérimentale" (XV:20).\*

After eighteen months, Bernard was discharged because his employer considered that his attempts at play-writing were taking up too much of his time and thoughts. A year later, Bernard took his play "Arthur de Bretagne" to Paris to Girardin, the influential critic. To Girardin is ascribed the credit for having turned Bernard's steps from drama into medicine. "The intuition of the poet by a change of application became the intuition of the scientist and ambition filled him with a fruitful discontent" (Fulton, 1932). (It is interesting that Brown-Séguard who succeeded Bernard at the Collège de France was also a dramatist (Ackerknecht, 1947)).

A student of mediocre quality, Bernard was twenty-sixth out of the twenty-nine successful candidates at the concours in 1839 to become an interne (Olmsted, 1939). While an interne Bernard entered the "service" of François Magendie who was destined to play a large part in shaping his pupil's life and work. After serving as "préparateur", and then from 1847 as substitute lecturer to Magendie, Bernard succeeded him in the Chair of Medicine at the Collège de France on the latter's death in 1855. For thirteen years Bernard held this Chair simultaneously with that of General Physiology which had been specially created for him in the Faculty of Science at the Sorbonne a year previously (1854). At the Collège de France there was only one Chair and one course and Bernard himself elaborates on "la nature spéciale de son enseignement scientifique" (XIX:137). This single "Cours de médecine" signifies that /

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\*Bernard's works are referred to by Roman numerals in order of their original appearance.

that the professor was empowered to lecture on whatever branch of medical knowledge he wished. Bernard chose physiology and utilised for his experiments "la tanière obscure et humide" (Faure, 1925).

Bernard says "L'enseignement du Collège de France est complètement désintéressé de la pratique immédiate; sa mission n'est pas d'appliquer la science médicale, mais de s'occuper exclusivement de son avancement en la représentant et en la développant toujours dans la branche qui est l'objet de son progrès actuel" (XIV:3).

We shall see later that, while the years before attaining a professorial Chair were his most fruitful in terms of academic activities, the same cannot be said for Bernard's private and financial affairs. A year after obtaining his doctorate he was unsuccessful in the competition for the position of "agrégé" (assistant professor) in the department of anatomy and physiology of the Faculty of Medicine. When, in the following year, 1845, he was not elected to the Academy of Medicine, his retreat to general practice in his native Beaujolais was averted only by the dowry of his unfortunate marriage. Though he did not obtain a formal decree of separation till 1870, his marriage was never a success. Mme. Bernard was a devout and orthodox Catholic and could not live with a husband indifferent, if not hostile, to religion. Even Millet (1945), himself a devout Catholic, says "La foi lui semblait affair d'autel et non de sacristie". But apart from religion what wife would tolerate a husband who brought home an emaciated but voracious experimental dog "having an open wound in its side and suffering from diarrhoea, /

diarrhoea, its faeces being of particular interest to the master of the house" (VII:387, quoted by Olmsted, 1939). There were three children of the marriage but the son died in infancy and the two daughters were brought up to consider their father "comme un libéral, qu'il était, comme tourmenteur de bêtes, qu'il était le moins possible et comme un athée, qu'il n'était point" (Millet, 1945).

Before becoming a professor, Bernard was awarded the Prize in Experimental Physiology of the Academy of Sciences on four occasions, and was a prominent member of the Société Philomathique and the Société de Biologie. In 1854, the same year as he became a professor in the Faculty of Science, Bernard was elected to the Academy of Sciences. His election to the Academy of Medicine was delayed till 1861. Later he was to become perpetual President of the Société de Biologie (1867), President of the Academy of Sciences (1869) and the first President of the French Association for the Advancement of Science (1872). But his greatest honour was in 1868 when, following the publication of his "Introduction à l'étude de la médecine expérimentale" (1865) he was elected to one of the forty "fauteuils" of the French Academy.

In 1861 he purchased the manor house of Châteney overlooking St. Julien and when on vacation took a great interest in its vineyard. However he also carried out experiments there - notably those on fermentation published posthumously and attacked by Pasteur.

Especially in his late forties and early fifties he was troubled by attacks of abdominal pain, but these disappeared in the /

the last decade of his life. Foster (1899) regards this illness as being due to an appendix abscess eventually discharging spontaneously.

Though Bernard's Chair at the Sorbonne was called that of General Physiology, the course dealt only with animal physiology. Bernard did not, in fact, have a Chair of General Physiology till 1868, when another new Chair was created for him - this time at the Museum of Natural History. Here he was also given a laboratory - a sine qua non of scientific experimental medicine (XVIII:97) - which he did not possess at the Sorbonne.

In the last ten years of his life, Bernard carried on a platonic friendship with Mme. Raffalovitch, a Russian Jewess from Odessa. The Raffalovitch correspondence, of almost five hundred letters, has recently been brought into prominence by Godart's edition (1950) "Lettres Beaujolaises". This correspondence does not throw as much light on the views of Bernard regarding important scientific and other issues as might have been hoped. Couitière (1938) errs grossly when he refers to Mme. Raffalovitch as Bernard's Egeria - indeed the Raffalovitch correspondence marks the beginning of the end rather than the inspiration of his work.

Though Gambetta, Berthelot, Paul Bert and many of Bernard's other friends were, in varying degree, politically minded, Bernard did not concern himself much in politics. However, by Imperial decree he was for more than a year a senator in the ill-fated and short-lived Second Empire (1869-1870). Millet (1945) quotes Bernard as having said, "Les gouvernements changent mais /

mais les personnages restent les mêmes; la comédie change de titre, les acteurs ne changent pas même de costumes".

France honoured him by making him successively a chevalier (1849), officier (1862), and commandant (1867) of the Legion of Honour.

At his death, in 1878, he was the first scientist to be accorded a state funeral.

BIBLIOGRAPHICAL INTRODUCTION /

BIBLIOGRAPHICAL INTRODUCTION

Dastre (XVII:v) emphasises that Bernard's scientific career falls into two distinct periods, the break occurring at the time of his transference from the Sorbonne to the Museum of Natural History in 1868. But in the second period, which corresponds to the last decade of his life, Bernard was interested in general biology, so that, for medicine, the first period is the more important.

Roger (1933), in "Notes Inédites", has published jottings made by Bernard between 1839 and 1843, that is, while he was still an interne. In addition to revealing remarkable intellectual maturity, these contain the germs of the major part of Bernard's life-work. Bernard was, no doubt, thinking of notes such as these when he said, "Il y a dans tout ce que j'écris certaines parties qui ne saurient être comprises par d'autres que moi. Ce sont des germes d'idées que je dépose en quelque sorte pour les reprendre plus tard" (quoted by Renan, XIX:29).

In 1843, Bernard's first work was published under the title "Recherches anatomiques et physiologiques sur la corde du tympan, pour servir à l'histoire de l'hémiplégie faciale". A few months later, the thesis for his doctorate "Du sucre gastrique et de son rôle dans la nutrition", appeared. Though their subject matter has been justly criticised, these titles are of particular interest because, built up on them, are two of Bernard's greatest contributions to physiology - the vasomotor system and the glyco-genic function of the liver. The essential details of these two discoveries were gained as early as 1850, within the first ten years /

years of his career as an investigator (Foster, 1899). From 1855 onwards, there were, in addition to papers, the "leçons", or lecture notes, which, like those of Magendie, were printed in book form. The majority of the "leçons" were published in the following circuitous way. The notes taken by a student at the lectures and demonstrations were reviewed and corrected by Bernard. The exceptions are one volume and a part of another published posthumously and three volumes written out direct by Bernard, namely "Introduction à l'étude de la médecine expérimentale" (1865), "Rapport sur le progrès et la marche de la physiologie générale" (1867) and "La science expérimentale" (1878). These last three volumes also differ from the others in that they are more theoretical and less experimental. However, in the "leçons" there is to be found, in addition to the only adequate exposition of many of Bernard's experimental results, the theoretical views expounded, especially, in the three volumes mentioned above.

I  
II The lecture series at the Collège de France begins with "Physiologie expérimentale" in two volumes.

Before Bernard, it was believed that, in contrast to plants, animals could not synthesise organic substances within the body. This was the view expressed by Dumas and Boussingault in their classic work "Essai de statique clinique des êtres organisés" (1844). Bernard's "Physiologie expérimentale" (1855-1856) and other writings dealt this theory a blow from which it never recovered. The first volume deals with his experiments on the glycogenic function of the liver; here first appear the words "sécrétions /

"sécrétions internes"; the second volume considers digestion with special reference to the pancreas.

The next three volumes, "Substances toxiques et médicamenteuses" (1857) and, in two volumes, "Système nerveux" (1858) show the influence of Magendie.

III

Magendie's three memoirs on arrow poisons (1809) mark the beginning of experimental pharmacology. They were the first records of attempts to administer chemical substances to living organisms in a systematic way so that the effects of similar chemical agents from different sources might be compared. Bernard's name is often linked with that of his master, the two being regarded as the pioneers of experimental pharmacology but, as Olmsted (1944) points out, Bernard was not born until 1813, four years after the three memoirs were read before the Academy of Sciences. But, although Bernard believes that the results of experimental investigation of medicinal or toxic substances are applicable to human toxicology, hygiene and therapeutics (Greene:125)\*, his dominant object in studying "substances toxiques et médicamenteuses" is to use these agents in the analysis of physiological function. This aim is best explained in the "Introduction to experimental medicine" where he speaks of poisons as veritable agents of life which dissect vital units (Greene:104). Foster (1878) grasps Bernard's meaning when he asks his students "to reflect on the service which has been rendered to physiology by a knowledge of urari poisoning, viewed as a mere method of research". He goes on to ask, "if at this moment we were to blot out from our modern physiological science all /

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\*Greene, H.C. (1927). Translation of "Introduction à l'étude de médecine expérimentale".

all that has been gained, directly or indirectly, by means of urari, what would come of it?".

IV  
V

The first volume of "Système nerveux" (1858) almost constitutes a text-book of neurology, though no fewer than sixty-six pages are devoted to medullary piqûre. Contrast this with the scanty eight lines in "Comptes rendus" which was the first intimation of the experiment. Though a misinterpreted experiment (I:327) led to an incorrect notion regarding the secretory action of the vagus nerve on the liver, to the discovery of piqûre diabetes and hence to a further incorrect theory bringing the lungs into the reflex arc, Riese (1945) admirably grasps the essential significance of the work when he says, "Claude Bernard's piqûre was the decisive step of a neurophysiologist towards tracing back metabolic changes to the central nervous system as to the almighty solidum". "Claude Bernard's piqûre for the first time showed metabolic processes to be under the jurisdiction of the central nervous system. Factual evidences are now accumulating showing that autonomic functions are represented at almost all of the levels of the central nervous system, from the spinal cord to the vertex" (Riese, 1949).

VI  
VII

Unlike the previous volumes, "Liquides de l'organisme" (1859) lay entirely beyond the ken of Magendie. Bernard rightly claims to have originated the concept of "milieu intérieur", the earliest reference to "rôle général du sang" being in the first volume of "Liquides de l'organisme".

X

"L'irritabilité" and "Physiologie du coeur" are the subjects discussed in "Tissus vivants" (1866), but the chief importance /

importance of this work is that it dealt a death blow to the theory that each organ had a single function (Foster, 1899).

XI Olmsted (1939) points out that the title "Pathologie expérimentale" (1871) is rather misleading and that the volume might be said to deal with experimental pharmacology. Olmsted's point is well made but this volume also contains miscellaneous other chapters: in fact the whole work lacks the logical sequence seen in Bernard's other volumes and in consequence makes dull and disjointed reading.

XII "Anesthésiques et asphyxie" (1875) is especially notable for the theory that "anesthésie" consists in the reversible coagulation of the constituents of the nerve cell. The previous theory that anaesthesia is merely asphyxia is contested on the basis of experiments - chiefly regarding the action of chloroform on muscle and nerve. An indication of the merit of Bernard's theory is its longevity. As recently as 1930, it was supported by Bancroft and Richter and two years later contested by Henderson which shows it is still controversial.

XIII "Chaleur animale" (1876) is a good illustration of the master putting his methodology and skill to work - the rejection of Lavoisier's theory that the lungs were the seat of combustion when experiments were incompatible with it, the skill in cardiac catheterisation and the up-to-date finding that, "à la périphérie, dans la profondeur des tissus, au contact de ceux-ci avec le liquide sanguin, le siège des phénomènes chimiques qui aboutissent à la production de chaleur" (XIII:190).

XIV "Diabète", published in 1877, contains two introductory lectures /

verb?

lectures which deal with the history and function of the Chair of Medicine at the Collège de France. The principal interest of the rest of the volume is that it contains Bernard's observation that acidity is not the essential cause of rigor but only its usual accompaniment. Alluding, no doubt, to what Hill (1932) called the "revolution in muscle physiology which broke out on the last day of December, 1926", Franklin (1928) remarks, "Had his (Bernard's) observation been remembered and appreciated it would have accelerated the determination of the more essential processes of muscle metabolism during the present century".

XV "Physiologie opératoire" (1879) was published by M. Duval after the death of Bernard. The first part is a recapitulation of the physiologist's views on medical research while the other three parts deal, in amazing detail, with instruments used for various purposes in animal experimentation.

XVI The publication of "Phénomènes de la vie" (1878-1879)  
XVII occupies the second period of Bernard's scientific career which began with his assumption of the newly inaugurated Chair of General Physiology at the Museum of Natural History (1868). The two volumes of this work also show the influence of M. Rayer, Bernard's guardian and friend. It was Rayer who originated the concept of unity in biology: the research worker must therefore study all living things - vegetables, animals and man himself. In "Science expérimentale" (1878) Bernard gives his aim in writing "Phénomènes": "Mon but est de montrer que les plantes possèdent comme les animaux, au degré ou à la forme près, la sensibilité, cet attribut essentiel de la vie" (XVIII:218).

The /

The three volumes mentioned above which came direct from Bernard's pen and which embody his thoughts rather than his experiments are well named by Olmsted (1935) the "contemplative" works.

VIII Philosophical discussion swept the French medical world in the 1850's and 1860's and the "Introduction à l'étude de la médecine expérimentale" (1865) was only one of the dozens of medico-philosophical books and essays of its period (Ackerknecht, (1950). But this magnificent treatise differs from its immediate predecessors in both its higher level of reasoning and the completeness of its exposition of underlying philosophical principles as applied to medicine (Gay, 1939). It is, in fact, the methodology of a great discoverer who takes the opportunity of an enforced rest to review, in a historical light, his previous twenty-one years' labours, in order to propound his working philosophy. But in the "Introduction to experimental medicine" Claude Bernard does far more than establish the methodology of experimentation; he recognises that though vital phenomena are "doubly conditioned" the methods of discovery in both living and inorganic sciences are the same. In France, where it is still considered that no man is educated unless he has some grasp of the principles directing scientific method, the first of the three parts into which the "Introduction to experimental medicine" is divided is to this day a prescribed text for the baccalaureate.

Outside France many famous scientists have paused to acknowledge their indebtedness to this volume. Surely the greatest tribute /

tribute was paid by Professor Samson Wright (1939) who described his fascination as "akin to that of Keats on first reading Chapman's 'Homer'". Wright also made the point that the "Introduction to experimental medicine" "breathed so modern a spirit that it might have appeared the day before yesterday".

IX

The thesis of the "Rapport sur la physiologie générale" (1867) is that physiology in France never lacked genius but lacked the special material facilities necessary to allow of the study of living organisms. The work is divided into three portions - introduction and first and second parts. The introduction and the first part of the volume consist of - what the writer intended them to be - a eulogy of the French influence on physiology and the principal physiological discoveries made in France, respectively. The second part is quite different. It resembles the "Introduction to experimental medicine" or some of the essays reprinted in "La science expérimentale", treated from the national standpoint.

"Physiologie générale" (1878) is identical with the "Rapport".

XVIII

"Science expérimentale" consists of reprints of nine essays on diverse subjects originally written between 1864 and 1876 for such different purposes as publication in the "Revue des deux mondes" and delivery to the French Association for the Advancement of Science. Bernard's "Discours de réception à l'Académie française" is also reprinted in this volume. Next to the "Introduction to experimental medicine", "Science expérimentale" is the most quoted work of Bernard - perhaps because it contains in condensed form the thoughts without the experiments of several /

several of the "leçons" - such as "Chaleur animale".

XIX        Although "L'oeuvre de Claude Bernard" contains nothing written by Bernard himself, its "table alphabétique et analytique" by Dr Roger de la Coudraie constitutes an invaluable dictionary for the student of Bernard. Dr Coudraie's system of reference to his published works depends on the order of their original appearance and is that utilised in the present essay. "L'oeuvre" also contains, in addition to a complete bibliography of Bernard, his "éloge" - by Renan at the French Academy (April, 1879), by Paul Bert at the "Association Scientifique de France" (February, 1879) and at his funeral by Armand Moreau on behalf of the Academy of Medicine (February, 1878).

VIEWS ON MEDICAL RESEARCH /

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"Il faudrait, pour suivre ce savant illustré partout où il a porté son investigation, tracer en quelque sorte l'histoire des sciences dont nous venons de parler depuis le commencement de ce siècle". This statement of Bernard (1856) regarding Magendie might well be applied to Bernard's views on medical research.

Physiology in France at the beginning of the nineteenth century was dominated by the views of the thirty year old Bichat. Bichat's basic idea was that the life of the body was the resultant of the combined and adjusted lives of its various tissues. But, though he thus taught that the immediate causes of the phenomena of life resided not in the soul but in the properties of the tissues, Bichat "defiled" his conception by believing the essential character of living bodies to be that, far from obeying natural laws, they maintained a perpetual struggle against them (Franklin, 1928). He held to the conception of a definite vital force: the activities of living things resulted from the conflict of this force with physico-chemical forces, the latter having full play at death but not till then (Singer, 1931). Bernard himself quotes Bichat's hackneyed axiom (XVIII:161), "La vie est l'ensemble des fonctions qui résistent à la mort" (Bichat, 1800).

Though Bernard's teacher, François Magendie (1817) regarded this idea as "one of the most childish absurdities to which the weakness of human understanding has ever given birth", Magendie's own mind was a curious suspension between the old vitalism and the new scientific determinism (Olmsted, 1944). However, clinically /

clinically, Magendie was very much in advance of his time - diet and plenty of fresh water were his chief remedial agents and he forbade bleeding. Of the many drugs included in his own "Formulatory" (1821), he himself used only morphine, quinine and Seidlitz salts (Olmsted, 1944).

Broussais, rather than Magendie, personified the "Romantisme Médical" of the early nineteenth century. Though Broussais never failed to render homage to Bichat, his megalomania led him to declaim "La Médecine c'est moi; le reste ne compte plus" (quoted by Larchier, 1938). The physiological doctrine of Broussais was that organised matter, inert by itself, was endowed with a fundamental property - "l'irritabilité" - and reacted by virtue of this property to external influences (Richet, 1928). He regarded himself as charged with a mission to apply his "diète sévère, saignées copieuses, boissons emollientes et acidulées", systematically and dogmatically, and, if necessary, despite the patient (Genty, 1938).

Renan (1879), in succeeding to Bernard's Chair at the French Academy, said, "Si Bernard n'eût pas trouvé la direction de Magendie, il est douteux qu'il eût pu surmonter les énormes difficultés matérielles que la fortune, par un jeu malin, semblait avoir semées devant lui, comme pour lui rendre méritoires les brillantes faveurs qu'elle lui réservait" (XIX:21).

While this may not be true of his experimental work, Bernard's views on medical research were certainly in large measure influenced, and even distorted, by association with Magendie.

Loeb classifies research into fundamental, basic and applied, but research in the applied sciences, including medicine, is /

is generally recognised to be a mixture of all three elements. Mayer (1946) points out that in addition to these three elements, medicine shows two sharply separated research activities. First, there is pathological and clinical research, or medical research proper, which includes the human factor and is carried out by qualified men in medical schools and hospitals. Second, experimental research incidental to medicine as performed in laboratories of allied sciences.

This distinction by Mayer echoes a similar one expressed in "Physiologie opératoire" where Bernard writes of two types of laboratory, one attached to hospitals and the other "en dehors de toute attaché clinique, prenant pour point de départ à ses recherches médicales non les faits observés sur le maladie mais bien l'étude des phénomènes physiologiques dont les faits pathologiques sont des formes dérivées" (XV:62).

### Laboratory Research

In admitting that Lavoisier made his immortal discoveries without a laboratory, Bernard points out that while a laboratory is not a necessity it saves time and greatly reduces difficulties: "Le laboratoire ne donne pas le génie mais il en facilite singulièrement les manifestations" (XV:63).

Ackerknecht says that for "physiological medicine" he would prefer the term "laboratory medicine", because it centres around the laboratories where the biological and exact sciences are used to elucidate clinical problems. Bernard's personal experience was limited to this type of laboratory. Here Bernard is at home - in the "pépinière réelle du vrai savant expérimentateur" (VIII:261). Bernard regards laboratory work as /

as an excellent training for the young medical man, because he considers that it alone can make him understand that the practical applications of the sciences to medicine are the result of previous laboratory work and also that those who profit from this work owe a tribute to their predecessors who have "péniblement cultivé l'arbre de la science sans le voir fructifier" (XVIII:98). As another argument in favour of laboratory training early in a medical career, Bernard gives his opinion that the erudition and scientific criticism of older men can bear fruit only when these men have begun (in the laboratory) their scientific initiation (Greene:225). But in addition to being trained, the young doctor should be given all the "moyens d'études" so as to give him needed opportunity (XI:475).

Bernard's attitude as to the equipping of a laboratory is coloured by his jealousy of the elaborate German physiological institutes, the first of which, that of Purkinje in Breslau, was opened in 1832. However, apart altogether from personal and political issues, his most notable passage gives, in a few lines, the via media for equipment. Today we do not need to be reminded that the solution of certain scientific questions often imperatively demands costly and complicated instruments. But we do need to be reminded that the more complicated an instrument, the more potential sources of error does it create (Greene:150).

Clinical Research /

Clinical Research

We have mentioned that Bernard's personal experience was limited to the type of laboratory "en dehors de toute attaché clinique". Indeed Bernard never practised medicine - his only clinical experience was as an undergraduate. Contrast this with Magendie who was a full physician at the Hôtel Dieu from 1830 and who in his lectures at the Collège de France took the medical implications of the title of his Chair more seriously than Bernard.

Bernard was quite out of touch with clinical medicine in general. Witness his statement, "La partie clinique de la médecine, je la suppose ..."; he assumes - he does not know (VIII:258). However, in many places in his writings, Bernard theorises excellently on clinical and pathological research which he realises must be carried on in connection with a hospital so as to receive the various pathological specimens on which scientific investigations are to be carried out (Greene: 149). In several places Bernard indicates how a clinical problem should be approached, and also says, "Si je ne fais pas ici de la médecine clinique, je dois néanmoins la soustendre et lui assigner la première place dans la médecine expérimentale. Donc si je concevais un traité dans la médecine expérimentale, je procéderais en faisant de l'observation des maladies la base invariable de toutes les analyses expérimentales" (VIII:350).

To Sir Henry Wade, the well known Edinburgh surgeon, is ascribed the saying that hospital wards are the best research laboratories. Bernard would have disagreed. He says that hospital wards are not physicians' laboratories, they are only his fields for observation, but he says that the first stage of scientific medicine /

medicine is observation and the second experimentation which depends on the first: "Je considère l'hôpital comme le vestibule de la médecine scientifique; c'est le premier champ d'observation dans lequel soit entré le médecin, mais c'est le laboratoire qui est le vrai sanctuaire de la science médicale"(VIII:258).

### Médecine expérimentale

"La médecine expérimentale n'est rien autre chose que l'état le plus avancé de la médecine considérée comme science. C'est la médecine arrivée à son développement entier, parvenue si l'on peut dire à son état adulte, c'est à dire à l'état d'une science dans lequel la pratique repose sur des théories expérimentales précises" (Principes de médecine expérimentale, 1947). But by the term "médecine expérimentale" Claude Bernard includes more than we would include today. In the "Introduction to experimental medicine" he regards "médecine expérimentale" as having three fundamental parts - physiology, pathology and therapeutics - and as containing, in addition, clinical medicine (Greene:1). Later in the same volume he expresses the same thoughts as in the above quotation from "Principes de médecine expérimentale" - namely, experimental medicine is not to be regarded as a new theory of medicine but "is one with the medicine of all people and times, in all its solid gains and sound observations" (207). However, perhaps his best exposition is in "Pathologie expérimentale" where he defines "médecine expérimentale" as "la connaissance des lois des phénomènes de la vie à l'état physiologique et pathologique" (XI:407).

## Empiricism

Bernard defines "empiricism" as "l'expérience inconsciente ou non raisonnée acquise par l'observation journalière des faits" (VIII:37). He points out that the very word "empiricism", from its Greek derivation, means "expérience", illustrating that the experimental method itself originated from empiricism. It is important to appreciate that the French "expérience" includes not only what we now call "experiment" but also that which comes haphazardly by the whim of chance. Francis Bacon also understood "experience" in the happy, inclusive sense of the French "expérience" (Gay, 1939). In discussing the use and abuse of empiricism in medicine, it is instructive to compare the views of Bernard with, for example, those of Trousseau. Trousseau regarded physiology as a "science de luxe", incapable of giving the explanation of the most simple illness (Trousseau et Pidoux, 1862). Bernard was, no doubt, thinking of men like Trousseau when he said, "il en est qui admettant qu'on possède la médecine par une sorte de science infuse qu'on appelle le tact médical que le médecin ne doit pas être un savant mais un artiste" (VIII:339). But the gap between these two medical men is narrowed when we recall that Trousseau proclaims himself as an empiricist precisely because he does not regard medical science as being sufficiently advanced to be applied clinically, while Bernard admits that the medical man of his day can only reasonably be a scientist, or in the meantime, an empiricist. He entirely understands a physician's saying that he cannot always rationally account for what he is doing, and accepts his conclusion that medical science is still groping in the shades of empiricism, but if the physician goes on to proclaim his medical tact /

tact or his intuition as a criterion which he means to impose on others without further proof, that is, in Bernard's opinion, wholly unscientific (Greene:193). Bernard admits that experience may be a valuable aid to the physician, largely due to the accumulation of empirical knowledge, but what he castigates is the physician who remains in the empirical state and does not try to escape from it. He affirms that Hippocratic, empirical and experimenting physicians do not differ in the nature of their knowledge but only in the point of view from which they each carry medical science somewhat further (Greene:208). In "Principes de médecine expérimentale" (1947) Bernard asks whether scientific medicine should be separated from "médecine professionnelle". His own answer is that "si la théorie doit diriger la pratique, la pratique à son tour doit donner des enseignements et fournir des matériaux précieux à la science pure".

#### Principle of Scientific Determinism

Though Descartes has been regarded as the founder of the determinist school (Guthrie, 1950), it was Magendie who, in 1809, made his scientific debut by being the first to enunciate clearly the "principle of scientific determinism" later to be so firmly established by Bernard.

The concept of the "principle of scientific determinism" is carefully defined by Bernard. By "determinism" he means simply that a given experiment perfectly carried out will always give the same results. He says that "principles" are scientific axioms and that as absolute truths they are an immutable criterion (Greene:172). He distinguishes sharply between scientific /

scientific determinism and the philosophical determinism of which Leibnitz was the exponent. Bernard says "Fatalism assumes that the manifestation of any phenomenon is necessary and independent of its conditions, while determinism is the condition necessary to a phenomenon whose manifestation is free" (Greene:219). He nowhere undertakes to discuss the ultimate as opposed to the empirical validity of his determinism (Olmsted, 1935).

The principle of determinism renders the vitalism of his contemporaries unnecessary because if vital phenomena were no longer to be regarded as unstable, the practical ground for insisting upon the distinction between physical and vital phenomena would no longer exist (Olmsted, 1944).

#### The Experimental Method

Though the principle of scientific determinism is taken for granted today, Bernard was obliged to stress it because even a prominent Professor of Surgery, Gerdy, told him in 1845, that "toutes les fois que la vie intervient dans les phénomènes on a beau être dans des conditions identiques, les résultats peuvent être différents" (VIII:315). Magendie, though considering the physico-chemical elements of the body to be within his experimental field, regarded "vital force" as being beyond the reach of experiment. Thus even he accepted the division of living phenomena into two groups: those which could be approached experimentally and those which, because of their native vitalism, could not (Petersen and Saucier, 1935). Bernard, on the other hand, in the evolution of his work did not recognise this division but approached all problems in which he was interested in /

in the same way. "There is but one expression of life", he said "one physiology embracing all things". The important fact in Magendie's vitalism was that it did not deter him from studying what he regarded as the physico-chemical elements of the body by experimental means. His firm belief in experiment encouraged the young Bernard to deify the experimental method. "Man can do a great deal by observation and thinking but with them alone he cannot unravel the mysteries of nature" (Sir W. Osler).

Bernard was under no illusions that he himself was either the founder of the experimental method or the first experimenter. He believed that, as great orators preceded all treatises on rhetoric, so great experimenters appeared before all precepts of experimentation. Consequently he did not consider that Bacon invented the experimental method, since Galileo and Torricelli had admirably practised it previously (Greene:51). Richet (1928) points out that though physiologists, especially Magendie, and before Magendie, Galen, Haller and John Hunter, had developed the idea of experimental medicine, they had not succeeded in persuading the doctors. This was left for Bernard.

Sigerist (1944) remarks that the "Introduction to experimental medicine" is still fully alive since the experimental method expounded is still our chief method of research. The eminent historian goes on to say that this is only part of the truth because more important than any particular effect is the general effect of Bernard's teaching on the philosophy of medicine. Sigerist, like A.W. Franklin (1928), approvingly quotes Michael Foster's answer to his own rhetorical question, "what has been the distinguishing token of the physiology of the nineteenth /

nineteenth century?" - "Experimental investigation, the application of chemical and physical knowledge and methods to the solution of biological problems" (1878).

### Scientific Discipline

A consequence of the principle of determinism and the use of the experimental method is that without an exact definition of the modus faciendi it is impossible to arrive at results comparable with other experiments (XV:2). Bernard realises what is even more true today - "Ce qu'il faut aujourd'hui, ce n'est plus établir la nécessité des expériences, c'est constituer une discipline expérimentale qui précise et les circonstances et les conditions de toute bonne recherche"(XV:6).

### Induction and Deduction

In the preface to his "Précis élémentaire de physiologie" (1816) Magendie writes that his principal object is to help to introduce the Baconian method of induction into physiological science. Bernard does not believe that induction and deduction are two distinct forms of reasoning (VIII:41) - indeed he sees no distinction between Baconian induction and the syllogism.

The principle of determinism and the value of the experimental method are thoroughly appreciated today and Bernard's laboured contrast between the scholastic and experimental approach to a problem is not relevant now. Similarly his pains to distinguish between observation and experiment seem unnecessary to the present-day research worker. On the other hand, the views of Bernard on the use of the preconceived idea and the hypothesis in experimentation are still as fresh today.

### Preconceived Ideas /

### Preconceived Ideas

Bernard regards the domain of "l'expérimentation rationnelle" as being the via media between "la vérification obstinée d'une idée préconçue" and the opposite extreme approached by Magendie (XV:7). In another passage he defends the attitude of his former teacher, saying that Magendie's spontaneous reaction to his period was very useful to physiology (IX:6). Bernard says categorically that it is impossible to devise an experiment without a preconceived idea. His argument is that devising an experiment is akin to putting a question, and we never put a question without having an idea which invites it (Greene:22). During the experiment the idea is to be neglected. Observing with preconceived ideas leads to bad observation and the risk that mental conceptions be taken for reality (Greene:32).

### Hypotheses

Bernard's definition of an "hypothesis" is significant. It is defined as a scientific idea that we submit to experiment. Indeed he goes so far as to say that "La méthode expérimentale, en tant que méthode scientifique repose tout entière sur la vérification expérimentale d'une hypothèse scientifique"(VIII:39). Bernard regards hypotheses and theories as "indispensables comme les échafaudages sont nécessaire pour construire une maison" (VIII:90). Scientific invention consists in the creation of fortunate and fertile hypotheses (Greene:220). "We usually think of discovery", says Bernard, "as the recognition of a new fact but I think that the idea connected with the discovered fact is the real discovery" (Greene:33). In the "Introduction to /

to experimental medicine" Bernard gives his research leading to the discovery of vasomotor nerves, as an example of how a hypothesis served as a starting point.

After noting the results of the experiment like those of an ordinary observation, the mind of the experimenter has to decide whether his experimental hypothesis is verified or disproved by these results (Greene:22). Beveridge, in his "Art of Scientific Investigation" (1950), suggests that some research institutes deliberately destroy records of "negative experiments". He considers that it is a commendable custom usually not to publish investigations which merely fail to substantiate the hypothesis they were designed to test. It is certain that Bernard would have disagreed with this course of action. No one knew better than he that even mistaken hypotheses and theories are of use in leading to discoveries (Greene:170). Bernard recognises that the hypothesis which is not verified disappears, but he recognises that "les faits mêmes qui la démentent deviennent aussitôt le point de départ d'une nouvelle ère de recherches" (XV:39).

By his connection with Magendie, Bernard could not help noticing the fate of one who had little use for the hypothesis, the results of Magendie's experiments being inevitably and apparently contradictory. But Magendie's empiricism was too narrow to satisfy the bounds of reason, so that he was content with contradictions (Olmsted, 1944). Raymond Millet (1945) ably differentiates the weakness of Magendie from the strength of Bernard. Magendie: "Avec sa méthode, la recherche scientifique allait un peu au hasard; elle évitait mille causes d'erreur; mais elle se dispersait; et elle réduisait les chances /

chances de multiplier les découvertes ou de pousser chacune d'elles jusqu'au bout". Bernard: "Au lieu d'expérimenter un peu au hasard, il acceptait, afin d'orienter ses expériences, des hypothèses ou des raisonnements provisoires, qu'il soumettait au contrôle des faits, sans parti pris ni pour ni contre".

### Scientific Theories

Bernard says that facts in themselves are never scientific; only generalisation can establish science. But here there is a double stumbling block; if excess of detail is antiscientific, excessive generalisation creates an ideal science no longer connected with reality (Greene:91). A theory is defined as a scientific generalisation or scientific idea which sums up the present state of our knowledge. Thus, since theories are only relative truths, they are destined to change with the progress of science (Greene:173).

Selye echoes the view of Bernard when he says in his Heberden Oration (1950) "Facts must be true, but a theory need not be entirely true. The value of the theory lies in its capacity to weld together isolated facts into a whole greater than the sum of those facts and in its capacity to stimulate research". But theories must be in accord with facts. Bernard stresses that when we meet a fact which contradicts a prevailing theory we must accept the fact and abandon the theory, even when the theory is supported by great names and generally accepted (Greene:164). Bernard's "Introduction à l'étude de la médecine expérimentale" is often compared with Descartes' "Discours de la méthode". Claude Bernard reckoned René Descartes

as "au nombre des promoteurs de la physiologie moderne" (XVIII:368), though this did not deter him from stating that the opinions of Descartes regarding the functions of the brain could not bear the slightest physiological examination. Chauvois (1948) points out the difference in the attitude of the two geniuses. In the "Discours" Descartes examines the work of William Harvey and accepts the concept of the circulation of the blood. However, because his mathematical mind is satisfied by the pre-Harveian theory regarding the movements of the heart during the cardiac cycle, he rejects the experiments of Harvey in favour of the theories of the ancients. In this problem Descartes was confronted with a choice between Harvey's experiments and "l'opinion commune des autres médecins, et le jugement ordinaire de la vue" (Descartes, 1637), and took the logical way out, which happened to be wrong.

Though it is generally admitted that Bernard's strength lay in his ability to discard ruthlessly an incorrect theory once its experimental bases were found to be questionable, Olmsted (1939) and others, have criticised his statements regarding the liver and its place in carbohydrate metabolism. Young (1937, 1946) is fairer to Bernard. Bernard found that though sugar was plentiful in the hepatic veins of a meat-fed or fasting dog, there was no sugar in the portal blood of such an animal. Even after the latter finding had been disputed, Bernard did not consider it necessary to repeat his work though he did take the trouble to use the new quantitative method of sugar estimation to confirm the observation of M. Chauveau that arterial blood generally contained more sugar than venous blood. But /

But Olmsted, who criticises Bernard on this score, does not mention that at the same time as confirming M. Chauveau's work, Bernard corrected his previous mistaken assertion that sugar was lacking in portal blood. Having reaffirmed that there is more sugar in the blood leaving the liver than in that entering it, Bernard defends himself on the just grounds that his earlier results were valid for the conditions under which they had been obtained and that they were now merely refined by the application of more precise conditions.

Indeed he takes the opportunity to drive home the moral that "Toutes ces rectifications et ces corrections ne sont donc que l'expression même d'une science qui avance. Autrement des idées fixes seraient l'expression de systèmes a priori" (XIV:346).

Young (1937) also tells how neither Pavy nor Pfluger, who also studied the liver's relationship to carbohydrate metabolism, was as willing as Bernard to part with their preconceived notions. Pfluger allowed himself to be prejudiced by his belief that protein could not be converted into sugar in the body and said quite frankly "my aim has been to find the origin of sugar in sugar itself and not in any other substance" (Pfluger, 1907).

Olmsted (1939) also criticises Bernard because he was "completely unjustified" in making deductions from his original experimental data, shown above to have been at least misleading in addition. But Bernard did not decide definitely that the liver absorbs sugar delivered from the gut and converts it into glycogen. He points out that he is carefully refraining from making a definite decision as he realises that the matter is /

is not as simple as it might appear. "Le fait qui est indubitable, c'est que l'injection du sucre de canne augmente considérablement le contenu glycogénique du foie; mais comment le sucre agit-il dans ce cas, comme excitant nutritif ou comme principe directement transformable en glycogène? Je penche, je dois le dire, pour la première opinion jusqu'à plus ample informé"(XIV:322).

### Fact and Judgement

Bernard emphasises the difference between a fact and an opinion. In "Physiologie expérimentale" (II:482) he tells how Magendie passed beyond the bounds of fact when he concluded that since pancreatic juice was coagulated by heat it must contain a protein. Bernard also found that pure pancreatic juice was coagulated by heat, but took care to show that this phenomenon could be accounted for on other grounds, and indeed showed that pancreatic juice did not contain protein in solution. His comment is, "Dès qu'il cesse de dire, 'tel liquid a été coagulé par la chaleur', 'ce liquide est albumineux', il n'exprime plus le fait pur et simple, et exprime un jugement" (XV:47).

### Doubt and Scepticism

Bernard repeatedly tries to draw the dividing line between doubt and scepticism. Ironically enough, his feelings are well expressed by Magendie who, in this instance, did not practise what he preached. "Doubt", he said rhetorically in one of his lectures, "and I do not speak of that scepticism which questions even what has been proved, doubt which is applied only to facts still obscure, to suppositions bare of truth - doubt, I say, is /

is the seal of true wisdom" (Magendie, 1839, quoted by Olmsted, 1944). But it was only Bernard who practised what both himself and Magendie preached. Magendie's weakness was that his obsession to avoid hypotheses and preconceived notions and his distrust of theory made him a sceptic. He was proud of his scepticism because he considered it to be scientific, and as Olmsted (1944) remarks, "His scepticism may be granted; it was the scepticism which germinated into scientific medicine". Bernard was no doubt thinking of Magendie when he says that a sceptic finds it impossible to build up a science because he has no foundation on which to establish his criteria (Greene:52). Renan (1879) in his Eloge at the French Academy, expressed the opinion that Bernard was "sceptique a l'égard de l'autel qu'il desservait" (XIX:20). This scepticism is illustrated by the following quotation of Godart (1950) from "Principes de médecine expérimentale" (1947). Here Bernard says "Beaucoup soutiennent qu'on ne change pas, par la médecine la loi des naissances et la loi de la mortalité des peuples. Mais on peut changer celle des individus et il est certain qu'on guérit des individus qui seraient morts: la compensation se trouve, peut être, dans ceux qui sont tués par le médecin".

#### "Control" Experiments

Though even today the necessity for careful "control" experiments is not fully realised, in 1865 Bernard was so well aware of this necessity that he went a step further. He is at great pains to distinguish between "contre-épreuve" or "contre-expérience" and "expérience comparative". Counter-proof is defined as a counter-judgement dealing with the experimental conclusion /

conclusion and forming one of its necessary terms (Greene:56). "It has not the slightest reference to sources of error that may be met in observing facts, is concerned only with experimental reasoning and has in view only judging whether the relation established between a phenomenon and its immediate cause is correct and rational" (126). On the other hand, Bernard defines the comparative experiment as a comparative observation resorted to, in complex circumstances, to simplify phenomena and to forearm oneself against unforeseen sources of error (56). Unlike counter-proof "it bears solely on notation of fact and on the art of disengaging it from circumstances or from other phenomena with which it may be entangled" (127). However, despite Bernard's labours in distinguishing them, the usefulness - and even the validity - of distinction between counter-proof and comparative experiment is doubtful and many modern writers on medical logic, for example (Gay, 1939), use the terms interchangeably. The "control" experiment - in the sense of the "expérience comparative" of Bernard - is in the process of assuming the importance in medical research that Bernard wished it would, namely, a sine qua non of scientific experimental medicine (XVIII:97).

The care with which Bernard worked out "control" experiments is instanced by his own comment regarding a statement by Pinel. The latter said in his clinic "This year we will observe diseases without treating them, and next year, we will treat them". Bernard comments that scientifically we ought to adopt Pinel's idea without, however, accepting the long-range comparative experiment which he proposes, because diseases vary in severity from year to year (Greene:194). Only now is therapeutic research /

research beginning to attach to this principle the importance it deserves.

But Bernard wishes also to have "controls" in the study of disease. He says that since science can be established only by the comparative method, knowledge of pathological or abnormal conditions cannot be gained without previous knowledge of normal states (Greene:2). In other words, he does not consider that we shall ever have a science of medicine as long as we separate the explanation of pathological from the explanation of normal vital phenomena (146).

### Vivisection

"Though by no means cruel in his nature, he was greatly in favour of vivisection; and he more than once said that, though the operation might be cruel, it was necessary for the enlightenment of science which should not be stopped merely on considerations of affected sentimentality" (Brit. med. J., 1878). This obituary notice of Bernard expresses contemporary English opinion regarding experiments on animals. During Bernard's life popular opposition to vivisectional experiment was so strong in Britain that Foster (1899) wonders whether Bernard would even have been allowed to carry out his experiments in England. It is difficult to conceive of the discovery of the glycogenic function of the liver, or any other of Bernard's epoch-making discoveries as having been made without vivisectional methods. Bernard himself tells how, especially in his early days, the Paris populace disliked his experiments (IX:144).

When /

When he began his experimentation there were no anaesthetics but as soon as anaesthetics were introduced he began to use them (XV:74). But in addition to the aesthetic opposition to animal experiments, renowned scientists like Cuvier in France and Sir Charles Bell in Britain, questioned the validity of the results obtained.

Today it is generally realised that experiments in animals are necessary for the advance of science, and Bernard concurs with this view when he says, "La véritable, la seule raison que nous ayons à donner, c'est que les vivisections font marcher la science" (XV:74). Bernard's spirited defence of vivisection is one of his finest literary passages. The sincerity and earnestness of the author are strikingly obvious. "A cowardly assassin", he says, "a hero and a warrior each plunges a dagger into the breast of his fellow. What differentiates them unless it be the ideas which guide their hands?" (Greene:103). Bernard realises that results obtained in the lower animal orders are often not applicable to man, but he exaggerates when he claims that investigations of medicinal or of toxic substances in the higher animals are wholly applicable to man save for differences of degree (125).

### Anatomy

Though Bernard was an excellent anatomist he realised the limitations of anatomy in medical research. He distrusts theories as to function arrived at by anatomical inference. In the "Introduction to experimental medicine" he states that while anatomy is the study most immediately necessary to physiology, it is insufficient in itself. "On s'est demandé pendant bien /

bien longtemps, et l'on se demande encore, 'a quoi sert la rate, la thyroïde, etc. Je ne pense pas que ce soit en posant la question de cette manière qu'on arrivera jamais à quelque découverte nouvelle sur ces organes"(II:19).

In "Science expérimentale" he expresses the same thought and concludes by saying "en un mot, la physiologie n'est point une déduction de l'anatomie"(XVIII:107). In another volume he says "Bichat fut le plus grand anatomiste des temps modernes mais à cause de cela même il ne fut point un physiologiste complet dans l'acception précise et plus vaste qu'il donne à ce mot" (IX:5).

However, significantly enough, it is in his opening lecture at the Museum of Natural History that he gives his best exposition of the role of anatomy in research. He begins by distinguishing two chief periods in the development of physiology. The first from Galen to Haller and the second from Haller to his own times. In the first period, physiology was regarded as a simple corollary of anatomy but from the beginning of the nineteenth century it was realised that anatomy was insufficient to explain physiological phenomena. He says that anatomy is to physiology as geography is to history, and as it is not enough to know the topography of a country to understand its history so it is not enough to know the anatomy of the organs to understand their functions. When comparing anatomy and physiology to geography and history, Bernard may have been thinking of a passage from the "Medicina" of Jean Fernel (1497-1558). But Fernel, on the contrary, says here that anatomy is to physiology as geography is to history - that is it describes the theatre in which the action takes place.

Bernard approvingly quotes Mery who compared anatomists to commissioners of the police in large towns who know the name of the streets and the numbers of the houses but who do not know what happens inside these houses. Foster (1899) remarks that Bernard did not seem to have the same facility in histological as in other physiological inquiries. But although Bernard carried out very little histological work, he appreciated the significance of that of other workers, for example, that of Kühne on the secretory granules of the pancreas.

Manual Dexterity

In addition to having a profound knowledge of anatomy the research worker - again especially when engaged in animal research - must be skilful with his hands. In the "Introduction to Experimental Medicine" Bernard says that one of the three qualities which the experimenter must possess is manual dexterity - the other two being ideas and unbiased observation (quoted by Millar, J.L., 1935, from VIII).

The protocols of Bernard's experiments themselves vouch for his dexterity. However, the tendency of many authors to compare his technical ability so favourably with that of Magendie is regrettable, because though not the equal of Bernard in manual dexterity, Magendie's experiments were technically most skilful. Bernard considers the research worker must have technical ability in his specialty "Il faut même être maître dans cette science et être capable d'expérimenter par soi-même et en faire mieux que ceux dont on discute les opinions"(VIII:142).

Statistics /

## Statistics

Bernard's criticisms of the abuse of statistics in medical research should be read by all medical men. Unfortunately, two points are often forgotten which must be kept constantly in mind when reading such views.

Bernard was living in the third quarter of the nineteenth century, and the second quarter was the golden age of the "méthode numérique", introduced by Louis in 1825.

It was not till the twentieth century that Pearson, Fisher and others established the notion of "Probability" on a sound scientific basis.

In opposing the application of the numerical method to physiology and medicine, Bernard joined with such unwonted allies as Trousseau, Cruveilhier and Ricord. Underwood (1951) quotes the following sentence from Trousseau (1861), which might well have been said by Bernard, "Je ne reproche pas à la méthode numérique de compter, car on ne peut systématiser sans compter; mais je lui reproche de compter seulement, en un mot, de s'en tenir au résultat rigoureux, comme le mathématicien". Bernard was so imbued with the spirit of determinism in biology that he considered the concept of "error" in the modern statistical sense of that term - inapplicable in his epoch.

In some passages where he confuses statistical probability with indeterminism Bernard is grossly mistaken, for example, when he says "La statistique n'a de raison d'être que par la nature indéterminée des faits auxquels on l'applique" (XV:50).

In several places in his writings Bernard expresses the truism that "La statistique ne peut donner qu'une probabilité, mais /

mais jamais une certitude"(VIII:239). However he shows that he appreciates that a known probability can be useful when he says that statistics can guide physicians to predict the outcome of a disease by teaching them the proportion of mortal cases (Greene: 213). Bernard emphasises the importance of a link between the collection and interpretation of data when he says that statistics in, for example, pathology, can be valid only when collected by the statistician himself (361). This means that the medical research worker must include a knowledge of statistics in his training.

But Bernard's fundamental misgiving is often disregarded today. He welcomes every possible application of calculation, provided, and only provided, the physiological conditions are accurately defined (Greene:135). Underwood (1951) expresses Bernard's objection when he says, "In effect Bernard was hitting at those who sought to employ the numerical method without remembering that the facts with which they were dealing were biological facts and could therefore be subject to precise numerical definition only when the associated factors were unaltered". Many modern workers are deluded by a superficial knowledge of statistics into believing that their complicated statistical calculation itself counters the objection raised by Bernard. Nothing could be farther from the truth. If the physiological conditions are inaccurately defined, their definition is no more accurate because, for example, in addition to the "moyenne" or simple arithmetic mean used by Bernard, the trouble is taken to calculate the standard error of that mean. The /

The standard error merely measures the scatter of the observations about the mean.

Bernard is correct when he points out that statistics cannot with validity be applied to a small number of cases. Addison's discovery of the disease which now goes by his name was based on eleven cases, some of which are doubtful. Apropos of this Young (1951) remarks - and Bernard would have been in agreement - "The world of biology and particularly of medicine, rarely displays the mathematical regularity and platonic perfection that allows a statistician to assess the significance of the result of the small number of observations that alone are often possible".

Bernard says he believes that the most useful path for physiologists and physicians to follow during his life, is to seek to discover new facts instead of trying to reduce to equations the facts which science already possesses, and that qualitative study must necessarily precede quantitative assessment of phenomena. Have we reached the quantitative stage now? Surely if the application of mathematics to natural phenomena is the aim of all science, medical knowledge has progressed to the stage when many phenomenal laws can be mathematically expressed (Greene:129).

Reading /

## Reading

"It is that which we do know which is the great hindrance to our learning of that which we do not." Thus said Bernard to Gambetta (quoted by Tjomsland, 1947). Yet his personal library contained more than a thousand scientific volumes. Bernard saw danger in both excessive and in too little reading but felt obliged to emphasise the former: he was acutely aware that the shadow of the dark ages after Galen was still not far behind.

While he admits that libraries should be considered as part of a laboratory, he regards them only as places from which new experiments can be formulated - he inveighs against seeking ready-made opinions instead of making new experiments. Bernard agrees with Maistre who says that those who make the most discoveries in science know Bacon least, while those who read and ponder him, like Bacon himself, have poor success (Greene: 225). He realises the fact that often less clever workers have a better knowledge of literature, "souvent même les hommes médiocres sont ceux qui possèdent le plus de connaissances acquises" (VIII:74). While recognising the superiority of great men, he thinks that they are necessarily more or less a function of their time (Greene:224), and that the more science advances, the more it takes on an impersonal form and detaches itself from the past (Greene:42).

In his opinion the study of old scientific literature is a waste of time because, he says, unlike literary and artistic productions, it reveals only the history of the human mind (142). On the other hand, up-to-date literature is certainly to be studied, but not to excess in case it stifles originality (145).

This /

This echoes the saying of Lord Byron "to be perfectly original, one should think much and read little" (quoted by Beveridge, 1950). It is interesting that the importance of originality in research is stressed by modern writers. Mayer (1946) says, "Since the result of true research is always either a new truth or a new interpretation of relationships, originality is its essence. Efficiency of research facilities and research institutions, like efficiency of individual workers, should be evaluated by the criterion of originality alone, without any regard to the usefulness of the result".

### Specialisation

Though he rejects specialisation in the theory of science, Bernard regards practical specialities as a necessity and as an excellent thing for science. But the research worker must realise the connections in other fields to avoid "l'anarchie scientifique" (VIII:350). In other words, men devoting themselves to the investigation of a special part of medicine must also have a grasp of experimental medicine as a whole and appreciate the place occupied in that whole by their speciality (Greene:217).

Since physiology is his chosen study, Bernard takes this as his example and says that physiologists call to their aid all the sciences - anatomy, physics and chemistry, which he regards as allies and providing indispensable tools for investigation (Greene:111).

"... pendant que l'homme de recherches s'occupe à sa tâche dans un coin de l'édifice que la science contemporaine élève avec tant de rapidité, il n'est pas nécessaire qu'il embrasse le plan de /

de cet édifice auquel collaborent tant d'autres études que les  
siennes. Cependant c'est à réaliser ce plan qu'il travaille  
d'une manière consciente ou inconsciente, comme maçon ou comme  
architecte" (XVII:391).

PHILOSOPHICAL TENDENCIES /

PHILOSOPHICAL TENDENCIES

"Nous dirons avec Descartes: on pense métaphysiquement mais on vit et on agit physiquement!" (XVIII:212).

While still an externe, in 1839, Bernard found time to read Gall (1822) but he read only the first one hundred and twenty pages of the first of the five volumes (Genty, 1939). We learn from the Raffalovitch correspondence that, when on vacation at St. Julien, he tried with little enthusiasm or success to read Descartes, Leibnitz and Pascal.

Bernard considers philosophy to be an excellent mental exercise (Greene:50).

"C'est une distraction utile pour l'esprit de causer philosophie après avoir travaillé. Comme c'est une distraction d'aller faire une promenade après être resté longtemps à travailler dans son laboratoire" ("Philosophie", 1938).

However, he recognises that philosophy has systematic and scholastic tendencies, in spite of itself, which he considers harmful to men of science properly so-called (Greene:50). Bernard says that since experimental medicine should not go beyond phenomena it does not need to be tied to any system. Experimental medicine is simply the science which tries to reach the immediate causes of vital phenomena in the healthy and in the morbid state and therefore has no reason to encumber itself with systems - none of which, he believes, can ever embody the whole truth (Greene:219). On the other hand, as Bernard cannot accept a philosophy which tries to assign boundaries to science so he cannot accept a science which claims to suppress philosophic truths which he considers to be at present /

present outside its own domain (223). In answer to the question whether Bernard was a philosopher, Bourquin (1945) makes the excellent point that "de l'oeuvre scientifique de Claude Bernard l'on peut tirer des conclusions d'ordre philosophique".

No writer's words should be considered apart from their context, but in Bernard's case one must take into account not only the context but also the special circumstances under which the words were written. Olmsted (1939) was provoked into saying this because unfortunately writers on Claude Bernard have seized upon some fragment from his writings, torn it from its context and used it in support of their own system or ends - despite Bernard's statement that the best philosophic system consists in having none (Greene:221).

Driesch, Bergson and Sertillanges have ignored Bernard's paradox that philosophy should not be systematic and his statement that "on veut toujours être matérialiste ou spiritualiste comme si la vérité ne pouvait être que dans ces deux opinions extrêmes. La vérité est au contraire dans ces deux vues réunies et convenablement interprétées" (quoted by Roger, 1935).

Driesch (1914) describes Bernard as a "critical vitalist" and with some justification, because indeed, like Lotze, Bernard is for the most part tilting at windmills when he criticises what to Driesch is an exaggeration of the vitalistic doctrine. Driesch claims Bernard would have agreed with the views of Blumenbach and Wolff.

Bergson (1928) uses the statement that "systems do not exist in nature but only in men's minds" to make Bernard appear as the fore-runner of his own philosophical system. The position /

position of Bergson brings us to Sertillanges and to an interesting new departure. Bernard's views on philosophy have been partially elucidated in recent years by the publication of such fragments as "Pensées" (1937), "Philosophie" (1938) and, especially, "Cahier rouge" (1942). Up till a decade ago Catholic writers were content to regard Bernard as being hostile to religion. Since then a more moderate view has been supported by the work of the erudite Thomist Dominican, Fr. R.P. Sertillanges (1944) and of the popular writer Raymond Millet (1945). The efforts of Sertillanges, especially, have been induced by the recent increased interest in France in scientific philosophy in general and in that of Bernard in particular - witness the (exaggerated) statement of M. Pierre Lamy that all recent French philosophy of science, from Lachalier through Henri Poincaré down to Meyerson, takes its rise in Claude Bernard (quoted by "Times Literary Supplement", 1942).

Sertillanges makes Bernard a disciple of Aristotle and of Aquinas, "si avec plus de verité on lui prôte un 'spiritualisme nouveau' encore faut-il ajouter, que ce spiritualisme est aussi fort ancien; car c'est celui de saint Thomas d'Aquin voire celui d'Aristote". Millet triumphantly remarks "si sa position jusqu'à l'heure de sa mort demeure un mystère, elle semble pourtant éclairée par ce jugement impartial et net du R.P. Sertillanges". But the scholarly Sertillanges supports his judgement with greater frankness than either Criesch or Bergson: "C'est à nous philosophes professionnels, d'achever ce que le savant ne peut qu'amorcer ou même seulement suggérer comme aboutissement normal de ses thèses".

The whole tendency of Bernard's biological generalisation  
ran /

ran counter to a strict Roman orthodoxy. Bernard could not have agreed with Pasteur's credo "Metaphysics does nothing but translate within us the dominating notion of the infinite" (quoted by Moschowitz, 1948). It is interesting to note, however, that Bernard's posthumous attack on Pasteur can be construed as the via media between the materialism of Berthelot and the views of Pasteur, and twenty years after his death Buchner proved Bernard to have been correct.

But Bernard's fame does not rest on the theoretical view of life that he propounded. It is as a methodologist and as a practical pioneer in the sphere of experimental biology that he has acquired so great a name (Nordenskiöld, 1929). Bernard himself says that no one asks whether Harvey or Haller were spiritualists or materialists, that we know only that they were great physiologists and that it is their observations and experiments which have been handed down to posterity.

So let it be with Claude Bernard.

Though Bernard continually distinguished between first causes and immediate causes or conditions he was astute enough to praise the cortical function theory of Gall "qui avait eu le mérite de ramener les qualités morales au même siège, au même organe que les facultés intellectuelles" (XVIII:412). Perhaps the most fitting conclusion to the scientific philosophy of Bernard is given in his obituary in the "British Medical Journal". "In his researches among the circumvolutions of the brain it was not the soul he sought, for he knew it was not to be found there, it being the invisible and immaterial part of man and perhaps of animals; but it was its modus vivendi with the body. The problem however of the manner in which the soul and body are connected was not for him to solve".

VIEWS ON EVOLUTION

While Bernard is to be excused for not taking sides in philosophical discussion he might be reproached for not doing so in the scientific controversy engendered by Darwinism (Olmsted, 1939). If the French anti-Darwinists be divided into the disciples of Cuvier and of Comte, Bernard belonged to the latter. He had little sympathy for the speculative and hypothetical elements of the "Origin of Species" (1858) (Nordenskiöld, 1929). His emphasis on exactness of method, clarity of expression, and, especially, the importance of experiment, undoubtedly allies him with Comte. Doubt enters where an attempt is made to define Bernard's own ideas of evolution. Bernard asserted that we must look to the organism itself - not to any force outside it - if we wish to discover the final cause of any physiological process: that every living organism is an end unto itself and is subject to the inner laws of its own being, (Rádl, 1930).

Riese (1949) links Bernard to Goethe's doctrine of metamorphosis and Jackson's law of evolution of nervous function on the ground that he traces back the influences modifying the type and producing diversities to "differentiation". The only evidence for this link is provided in the recently published "Principes de médecine expérimentale" (1947) where Bernard expounds his belief that although it is the true criterion of science to derive the particular from the general, variations from a single though only hypothetical type, he is most anxious not to lose contact with the perceptible reality which the experimenter wants to explore and to transform. Reality, however /

however, offers no types, but only individuals. The physician, he says, is not the physician of the human species, but of an individual, even of a given individual under most specialised conditions. What matters is to analyse the influences modifying the type and producing diversities (Greene:92).

Claude Bernard was more interested in the development of a single individual than in the evolution of the race. He groups the manifestations of life under the following headings

"Organisation, Generation, Nutrition, Evolution". Of these he finds the last to be both the most characteristic of life and the most difficult to explain from the purely mechanical point of view (Nordenskiöld, 1929).

BERNARD AND POSTERITY /

BERNARD AND POSTERITY

Claude Bernard is famed for his discoveries and for his writings, rather than for his merit as a teacher. In comparing him with Pasteur, Tzanck (1933) says "Bernard n'a créé ni école, ni caste, et craignant par avance les cadres trop rigides, il répétait sans cesse à ses élèves: 'Démolissez-moi, mais créez'". The French pupils of Bernard provided little more than technical assistance to their master. The famous painting by Lhermitte demonstrates how the "disciples" are merely engaged in experimental details to which they have delegated themselves. How different from the establishments of the German physiologists - especially that of Ludwig, whom Franklin (1949) calls "the greatest physiological teacher of all time". In Ludwig's laboratory the experiments going on simultaneously were singular in their diversity. Bernard, himself, would doubtless have laid the responsibility for the failure of his French pupils at the door of the French treasury. Samson Wright (1939) is in agreement with this view and states that lack of money and space were the fundamental obstacles which prevented Bernard from giving his country world leadership in his subject in his own generation. During Bernard's lifetime - by 1860 (Osler, 1894) - Germany had become the centre of the medical world. However, a German pupil of Bernard became a scientist of first rank: though Kühne was also a pupil of Virchow and of Helmholtz, the major part of his work - that concerning the intermediate products of digestion - shows the influence of his French teacher. The position of Kühne is important in that, in addition to his own work, his pupil Chittenden founded the first definite laboratory of physiological /



physiological chemistry in the New World at the Sheffield School of Science of Yale University. The Yale laboratory became the centre for the spread of physiological chemistry in the United States (Castiglioni, 1947).

Appropriately enough, the first publication of Bernard's lectures in book form was by the American, Atlee (1854). The current English translation of the "Introduction to experimental medicine" is also, of course, by an American (Greene, 1927).

In Britain, Bernard has never attained prominence, though the value of his discoveries was appreciated from the first. As early as 1851, Kirkes and Paget, in preparing the second edition of their "Handbook of pathology", repeated the reference to the chorda tympani from the first edition, and added sections on the pancreas and on the newly discovered function of the liver, abstracted from Bernard's paper published in the preceding year (Franklin, 1928).

Claude Bernard is quoted by Vallory-Radot (1911) as having said, "We shall not live to see the blossoming out of scientific medicine; those that sow on the field of science are not destined to reap the fruit of their labours". Though since Bernard's death the importance of many of his views has increased, this is especially true of the concepts of "sécrétions internes" and "milieu intérieur".

"L'histoire du foie établit maintenant d'une manière très nette qu'il y a des sécrétions internes, c'est à dire des sécrétions dont le produit, au lieu d'être déversé à l'extérieur est transmis directement dans le sang" (quoted by Miller and Larkey, 1935). Though such was the first appearance of the actual words, long before Bernard there were hints of the same concept. It was Neuberger /

Neuberger (1903) who first emphasised the credit due to Théophile de Bordeu for the comment in his "Recherches sur les maladies chroniques" (1775) that each organ gives off emanations which are necessary and useful to the whole body. Bordeu's views, however, were not based on observational or experimental evidence and had little general effect in his time. Though just before Bernard, T. Wilkinson King, George Gulliver and, especially, A.A. Berthelot, were strengthening the concept, it was still novel and not generally accepted till clearly demonstrated by Bernard in 1850. In this year the discovery of the glyco-genic function of the liver was reported in the "Comptes rendus". This epoch-making paper, in addition to furthering the renown of its author, gained for him the prize in Experimental Physiology of the Academy of Sciences for the third time (1851). The same matter constituted the thesis defended for the Doctorate of Natural Sciences in 1853. It is ironic that today, neither is the liver considered to be an endocrine organ nor is glucose regarded as an internal secretion. Bernard clearly states, "Le foie présente les deux espèces de sécrétions: celle de la bile qui est une sécrétion externe et celle du sucre qui est une sécrétion interne" (VII :412).

There is a tendency to regard Bernard's conception of "milieu intérieur" as being one of his later achievements, but at latest, the basic principle must have been grasped by 1857, because the earliest reference in his published lectures regarding "Rôle général du sang" is in that year (VI). He first regarded the plasma of the blood as the sole internal environment /

environment, but the conception is elaborated in the "Introduction to Experimental Medicine" with the important advance that instead of only the plasma, "tous les liquides circulant, la liqueur du sang et les liquides intra-organiques constituent en réalité ce milieu intérieur" (VIII:109). Finally, in "Phénomènes de la Vie" Bernard refers to the internal environment as the totality of the circulating fluids of the organism.

In 1878, Sir Michael Foster told his students that the teaching of physiology at Cambridge was built up on the conception that the blood is the great internal medium on which and in which and by which the tissues live, and also that the above "picturesque and far-reaching phrase we owe to Bernard". Fulton (1932) claims that in Foster's book on Bernard (1899) no mention is made of the conception of the internal environment, because at that time, no one realised the full significance of Bernard's idea. Though Foster, admittedly, makes insufficient reference, he does state that in "Liquides de l'organisme" Bernard develops his "pregnant idea of the blood as the internal medium on which the tissues live".

Fifty years after the death of Bernard, Henderson (1928) was able to state that subsequent discoveries and the introduction of physico-chemical methods into physiology had proved the master's theory well-founded. "There can be no doubt that the cells of warm blooded animals are bathed by liquids of quite exceptional stability of composition and of physico-chemical properties so that their protoplasm is, in general, not obliged to protect itself, if one may use that expression".

J.S. Haldane, in his Donnellan Lectures (1930), quotes the conclusion of Bernard that "Tous les mécanismes vitaux, quelque variés qu'ils soient, n'ont toujours qu'un but, celui de maintenir l'unité des conditions de la vie dans le milieu intérieur" (XVI:121). Though Haldane claims "no more pregnant sentence was ever framed by a physiologist", he rejects Bernard's general conclusion regarding a common internal environment, substituting the phrase "a common element in environment", on the grounds that the environment of each cell depends on the influence of other cells.

Twenty years ago, Fulton (1932) pointed out that Bernard looks on the nervous system as a regulator of metabolism, but that he had obtained only scant evidence regarding the possible central mechanism concerned. In "Phénomènes de la vie", Bernard dismisses the question in a single prescient sentence. "Seulement chez l'animal perfectionné à vie indépendante, le système nerveux est appelé à régler l'harmonie entre toutes ces conditions" (XVI:114). Fulton considers that in this forecast that the central nervous system is called upon to regulate the harmony existing between all parts of the body, lie the greatest problems of physiology and medicine of the immediate future.

W.B. Cannon, of Harvard, (1932), in his volume "The Wisdom of the Body", makes the statement "le système nerveux est l'agent de l'équilibre de toutes ses conditions" (XVI:115) the starting point for the development of his "Principle of Homeostasis".

Barcroft (1934) seizes upon the statement that "La fixité  
du /

du milieu intérieur est la condition de la vie libre, indépendante" (XVI:113), and makes this the foundation of his discussion regarding "Features in the Architecture of Physiological Function". While acknowledging that the works of Haldane, Henderson and Cannon have elucidated both the mechanisms which secure the constancy of the internal medium and the exactness with which these mechanisms operate, he endeavours to ascertain at what disadvantage, if any, the organism was while as yet the internal circulating media were variable. He concludes that the intellect is the bodily function most readily affected by variations in the internal environment and that the high intellectual development is conditioned by the fixity of the internal environment.

The biochemists Schoenheimer and Young furnish a more biochemical interpretation of the internal environment. Schoenheimer expresses a conventional modern viewpoint in his "Dynamic State of Body Constituents" (1942). He visualises a kind of metabolic reservoir, the maintenance of whose level is an expression, not of stagnation, but of "steady states" in numerous dynamic equilibria. Constant controlled change is thus regarded as the body's secret of gaining the needed degree of freedom from its internal environment. F.G. Young (1951) stresses the part played by the endocrine system in the internal environment. He criticises Bernard as not being free from "the obfuscating effects of the prevailing tendency to regard the nervous reflex as of immediate and dominating significance in physiological phenomena". Young brings Bernard up to the hour by hypothesising that "Cortisone does not in general influence directly a toxin or a noxious stimulus but depresses the reaction /

reaction of the cells of the body to the stimulus. ... This ability is conferred on a cell by the action of adrenal steroids such as cortisone to withstand abnormality in the internal environment".

In tracing the concept of "milieu intérieur" up to the present time, one realises that the possibilities and implications of at least one of Bernard's ideas are still being recognised. As Henderson (1928) says, "Claude Bernard, when he died fifty years ago, left behind a program for the new science that he himself had gone far to carry out". The attempts of J.L. Faure (1925) and of Pierre Mauriac (1927) to deify the spectacular Louis Pasteur at the expense of Claude Bernard are nullified by A.W. Franklin's eulogy (1928): "He was neither burned at the stake like Servetus, nor left to die unknown like Mayow; his discoveries neither revolutionised science like Harvey's circulation, nor hindered progress like Stahl's phlogiston. He lived a simple life, of fixed purpose, sometimes a general sometimes a humble warrior in the army of science, always filled with a sublime faith in its power to benefit humanity, seeking for himself nothing, for the world the truth which never perishes."

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