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Wellcome Silver Medal, 1926.

The Discoveries

associated with

The Name
of
Claude Bernard

and their

Results.

Welcome Prizes in the History of Medicine. 1926.
A Competitive Essay.

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Introduction.

Of Explorers and Discoveries in general.

Throughout the ages, one of the most fascinating features of History is that which deals with exploration. The expeditions into unknown and savage lands, the scaling of formerly inaccessible peaks, the charting of formerly mysterious and unfathomable seas, the hardships endured under a torrid sky or in the icy grip of the bitter polar regions; the dangers, the adventures, the toils, the misfortunes the hopes, the fears, the great and glorious successes or the terrible and heart-breaking defeats of many early pioneers into unknown realms make a wonderful picture in the varied and vivid gallery of a country's history.

The Scientist as an Explorer.

Yet how much more fasinating still is the tale of many an heroic explorer in the realm of Science in earlier days. The extraordinary difficulties he had to overcome, the obstacles placed in his path by an obtuse, conservative and reactionary generation, the wretched conditions under which he had to work, the brilliant discoveries made, the far reaching results attained, powerfully affecting all humanity, the laying of a foundation on which others might build, in short, the triumph of a genius over great difficulties.

Such a man was Claude Bernard.

Claude Bernard.

He was a native of France, but like every true scientist he was not animated by any selfish, national or patriotic spirit. The results of his experiments were for the benefit of mankind in general, for suffering humanity in the world at large, and they were crowned with a brilliant and enduring success.

The personality of the Scientist.

The mere chronicle of bare facts can never be very interesting. In reading of those who seek after truth and of their discoveries, the personality and life of the seeker is a dominant factor, and a fa[r] greater appreciation of his works is found when something of the life of a scientist [is] known. Therefore, though primarily concerned with the discoveries of Claude Bernard and their results, a short space may be allowed in this paper dealing with h[is] early life. His discoveries will then be narrated, thereafter a few incidents of his latter years when he had become the greatest physiologist of last century, an[d] finally the results of his labours.

__His Early Life.__

In the village of St Julien near the town of Villefranche in the south of France there was born on July 12, 1813 one who was to become a great physiolog[ist] of world wide fame, Claude Bernard.

His early Education.

His home was on a small estat[e] where his father carried on the occup[ation] of a wine grower, and his early teach[ing] was in the hands of the local curé. Later he became a pupil at the Jesuits' school in Villefranche.

From there he went to Lyons, b[ut]

Life in Lyons.

in that city his education was neglected, possibly owing to the pecuniary difficulties of his family, and he thus became a chemist's assistant. He soon observed the rascally methods of the ugly chemist who indulged in a little "hocus pocus" at the expense of his customers, selling them a "cure all" ointment and a syrup which was a concoction of all the bad drugs in his shop. Perhaps this was the cause of that doubt which afterwards nearly always made Bernard cautious of accepting the teachings and time-honoured doctrines of his medical professors.

An excursion into literature.

He now turned to literature, and, having earned a little money through the acceptance of a comedy, he determined to go to Paris. In 1834 he arrived in that city armed with an historical drama which he had recently written, and which he showed to Girardin, the great dramatic critic of his day. Medicine owes something to Girardin for he it was who advised Bernard to become a disciple of Aesculapius, and leave literature for his spare moments. "Study Medicine," said he, "you will thereby much more surely gain a livelihood.

Early Hardships.

He thereupon threw himself with great assiduity into his medical studies. Barely "making ends meet" he struggled on, living in a garret in the Quartier Latin, giving lessons and studying hard. To him may be applied the words of Augustine:-

"The heights by great men reached
and kept
Were not attained by sudden flight
But they, while there companions slept.
Were toiling upwards in
the night."

Bernard now became an expert anatom[ist] and his interest in physiology increa[sed].

Comparison of Anatomy and Physiology at that period.

Knowledge of Anatomy was clear cut and concise at that period, but with referen[ce] to Physiology Sir Michael Foster says:- "In place of light there was darknes[s] and in place of clear and distinct guidance, uncertainty and dubious discuss[ion]. He next started a little laboratory f[or] experimental work near the Collége de France, but the fees did not pay h[is] rent or the cost of the rabbits, accordingly the laboratory was closed. In his medical studies his logical mind and clear intelligence soon saw the faults in his teachers' reasoning. and he began to think out many problems for himself.

His work under Magendie.

In 1839 he became an "interne" at the Hôtel Dieu and came under the influence of Magendie, at that time th[e] leading physiologist of France. The latter was also Professor of Medicine at the Collége de France. This ancient college founded in 1530 by Francis I had held up to that period an old tradition. In effe[ct] that all its professors should use their position for research purposes and to expoun[d] new theories to advanced students instead of giving the usual type of lecture to the ordinary student.

The gruff Magendie was soon attracted by the skill in dissection of young Bernard, and appointed him his préparateur at the College. This involved Bernard's assisting him in his experiments in research or in demonstrations to his classes. Gone were now his literary aspirations, he never looked back, and in that year, 1841, the career of Bernard as a physiologist began.

The Position of Physiology in the year 1840.

An approaching change in physiological methods.

The coming of Bernard into the realm of physiology was an epoch making one, for he it was who put experimental physiology on a sound scientific basis. The far-reaching results of his experiments can only be fully realized when some consideration is given to the very limited advance which Physiology had made up to that period, that is, about the year 1840.

Physiology in Germany.

Though German influence was the most dominating in Physiology during last century, yet when Bernard joined Magendie those great physiologists Ludwig, Helmholtz and du Bois-Reymond had not yet begun their work. Johannes Müller, a leading light in the physiological firmament at that time, upheld the "Vitalistic Theory," a view which was widely and strongly supported. To explain the phenomena of life the vitalists supposed the existence

The Vitalistic Theory.

of some organic or vital principle of force "the action of which is not independent of certain conditions". This was contradicted by the physico-chemical outlook which explained these phenomena as being "the result, manifestation or property of a certain combination of elements." Müller, however, considered the vitalistic view as one of academic interest, and in his teaching he nevertheless advocated the solving of physiological problems on a physico-chemical basis. Other leading physiologists such as Weber, Henle, Tiedemann, and Volkmann did likewise, and the precepts of their inquiries were the same for living as for non-living phenomena. But if their analysis failed they then fell back on the "vitalistic" theory.

The Physico-chemical Theory.

Experimental Physiology.

The birth of experimental physiology had taken place shortly before the coming of Bernard. Ludwig was to become a brilliant exponent of it in Germany. In England Marshall Hall and Reid were studying the action of the nervous system by experimental methods, and the foreseeing Sharpey was continuing research on lines similar to those of today. Bowman was making Histology a powerful ally of Physiology. In France the influence of Cuvier, who had died a few years previously, and who was a great supporter of the "vitalistic" theory was still strongly felt.

French influence in Physiology.

Magendie, Bernard's master and the leading physiologist in France at that tim

Magendie's Views.

combined the two great prevailing views of that period. He held that certain living phenomena were beyond experimental inquiry, but these phenomena which are the result of chemico-physical causes are open to experiment. He, however, carried experiment to excess. Many of his investigations had excellent results, but others were misleading and useless, and he ended by almost substituting experiment for thought. From his chief Bernard heard that all theory and reasoned discussion were ridiculous, and that experiment was the great essential in Physiology, outweighing any or every other consideration.

Bernard escapes the cult of his master.

Bernard here showed that genius which ever attended his actions. He struck out on a line of his own, and he made experiment "the servant and not the master of reasoned speculation".

His Discoveries.

His first communication

Bernard's first work of any importance was published in May 1843 in the form of a communication entitled "Recherches anatomiques et physiologiques sur la corde du tympan pour servir à l' histoire de l' hémiplégie faciale." This was followed later in the same year by his thesis for the Doctorate in Medicine with the title - "Du suc gastrique et de son rôle dans la nutrition."

His Thesis for the Doctorate

These two earlier works cannot be disregarded as they were the beginning of a long series of investigations which led to brilliant discoveries, the work on the gastric juice ultimately leading to the discovery of Glycogen and the glycogenic function of the Liver. The thesis also contained the record of what has since become a classical experiment. He demonstrated that the acid of the gastric juice makes its appearance on the surface and not in the depths of the gastric glands. This was shown by the simultaneous injection of potassium ferrocyanide and ferrous sulphate.

Demonstration of the Gastric Juice.

When investigating the differences in digestion between Herbivora and Carnivora in 1846 he made an observation which was the beginning of his first remarkable discovery. He noted that when fat was introduced into a rabbit's stomach, the fat passing on from the stomach was not altered until it had reached a certain distance from the stomach at a point much lower than that at which a similar change occurs in dogs. Similarly in absorption, he noted that the lacteals in the rabbit became white and opaque due to fat being present at some distance from the pylorus, while in dogs the change was observed at the commencement of the duodenum. What was the cause of this difference? In the dog the pancreatic juice is discharged into the intestine close to the pylorus; in the rabbit, however, the chief pancreatic duct opens into the intestine thirty centimetres below the

Action of the Pancreatic Juice.

opening of the biliary duct. The difference therefore coincided with a difference in the entrance of the pancreatic duct. This started Bernard's researches on the functions of the pancreas.

In 1856 he published his memorable treatise entitled, "Mémoire sur le pancreas et sur le rôle du suc pancréatique". In it Bernard pointed out the three actions of the pancreatic juice. First, it emulsified and split up into fatty acids and glycerine the neutral fats which had entered the duodenum from the stomach. Secondly, he proved that the juice acted on starch converting it into sugar. Thirdly, he exposed its action on "proteid matters". The bile precipitated the products of gastric digestion of proteins and stopped peptic changes. The pancreatic juice also acted on these precipitated products as well as on the proteins of a meal which had escaped solution in the stomach. Bernard declared that the digestion of nitrogenous substances is far from being completed in the stomach though that was the view of his day. He showed that gastric digestion only paves the way for the action of the pancreatic juice in the intestine. The method of the artificial gastric fistula now a commonplace in experimental physiology was made practicable by Bernard in this discovery. For this remarkable work the Académie des Sciences awarded

Three functions of the Pancreatic Juice.

Gastric digestion, a preliminary to action of the pancreatic juice.

him the prize of Experimental Physiology.

Some years prior to this Magendie, in his experiments on the anterior and posterior nerve roots of spinal nerves, he sometimes found the anterior sensitive. This irritability of the anterior root was he found dependent on the posterior root & and not inherent - "recurrent sensibility". The phenomena were very inconstant, however, sometimes the anterior root was sensitive at other times it was not; and Magendie's discovery fell into disrepute. Bernard, with that genius which led him to more brilliant discoveries, decided that those different results must be due to ignorance of the conditions under which the experiment should be conducted. He determined to discover the conditions and as a result he showed later what conditions favoured, and what conditions hindered the development of "recurrent sensibility".

Vindication of Magendie's Theory of "recurrent sensibility".

The Discovery of Glycogen.

The greatest of Bernards discoveries was that in which he demonstrated the glycogenic function of the liver. Prior to Bernards discovery the whole question of the chemistry of nutrition was in a very disordered condition. The prevalent view as postulated by Dumas was that the animal body never built up or manufactured fats, carbohydrates or proteins, that these were brought to the animal body in its food. This had however been questioned, and th

Views of that period.

chemist Payen had shown that the fat in the bodies of fattened geeze very much exceeded the amount of fat given in their food.

Bernard had intended to study the three classes of foods, fats, carbohydrates and proteins, but this was too great a task, and consequently he never got beyond the study of carbohydrates. He was particularly interested in the excess of sugar found in diabetes, and he therefore began his researches on the sugars.

Bernard takes up the study of carbohydrates.

He had already shown that all carbohydrates may be considered as passing into the blood in the form of dextrose, and he now determined to trace the dextrose introduced into the body from the alimentary canal. What become of it? Where was it transformed? In answer to these questions it must be traced from the alimentary tract along the portal vein to the liver, and from the liver to the heart and lungs. Then, finally it must be traced from the lungs through the heart to the other regions of the body. "At one or other of these stations I shall find that the dextrose disappears, is destroyed or is in some way or other changed. If, having found the station of destruction, I am able to suppress the activity of the station, sugar will accumulate in the blood and a condition of diabetes will result. If I can thus artificially produce diabetes, the way

His investigation into the ultimate fate of Dextrose will be opened for the discovery of curative means."

Experiments on Dogs.

First of all, then, he fed a dog on a rich sugar diet and examined the blood leaving the liver by the hepatic veins to see if there was destruction of sugar in the liver. Bernard found sugar in the hepatic veins. He now asked himself whether or not this sugar was the same as that which had entered the portal blood through the food. Taking another dog he fed it on meat only, having made certain that there was no dextrose present in the alimentary tract or portal blood. To his astonishment he now found that there was still abundant sugar in the hepatic vein. He was now practically certain that he had come upon the production of sugar, that the liver produces sugar.

The liver produces Sugar.

"If the result which I have just got is confirmed on repetition of the experiment the liver is a sugar producing tissue, it manufactures sugar out of something which is not sugar, and within it lies the secret of diabetes." This confounded the prevalent theory of that day. The liver does construct dextrose.

He thereupon tried many tests. Killing a dog in full digestion he placed ligatures on the veins from the pancreas, the splenic vein, the portal vein near the liver and on the mesenteric veins from the intestine. There was no sugar found in any of these veins except in the portal blood between the ligature and the liver. In this case the sugar had regurgitated from the liver. Therefore the liver, and not the spleen, the pancreas or the food in the alimentary tract was the source of the sugar. He found that a decoction of liver substance contained sugar in every case, and that dogs which had been starved and dogs fed on meat also for some time, in both cases had sugar in the blood of the Right Heart and in the portal vein close to the liver. He also determined that the sugar in question was dextrose. This action of the liver at once seemed to him analogous to the act of secretion by a secretory gland, and might therefore be called an "internal secretion". In 1849 he gave a full account of these discoveries to the Société de Biologie, and in 1850 to the Académie des Sciences.

Experiments to prove that the liver produces sugar.

By examining the livers of many animals he confirmed this discovery that the sugar of the liver is furnished by the liver itself through a mechanism similar to a secretory process "at the expense of the elements of the blood which traverse the hepatic tissue"; but he also noted that this hepatic sugar was influenced as regards quantity by the nature of the food taken. It was diminished by starvation;

The nature of the food taken the quantity of hepatic sugar formed.

it was very little increased if at all by fats but was much increased by carbohydrates. These explanations were put forward in his thesis for the Doctorate of Science which was published in 1853.

The "Diabetic Puncture" Experiment.

He also discovered in these researches that puncture of the floor of the fourth ventricle produces temporary diabetes. He argued that this internal secretion of the liver would, like other secretions be controlled by some particular nerve. The relations of the vagus to digestion and his earlier observations led him to think that the nerve in question was the Vagus. He expected that by stimulating the Vagus trunks with the electric current an increase in the sugar of the liver would result. This experiment did not meet with success. He then thought of puncturing the floor of the fourth ventricle at the point where the vagus has its origin. He was led to this by the fact that in his investigations on the trigeminal nerve he had produced secretory effects by puncturing the nerve at its origin in the brain.

Success of this experiment.

The vagus experiment was successful and the glycogenic function of the liver was excited, the excess of sugar in the blood being removed through the Urine.

Conclusions.

Bernard, none the less, realized that the vagus is not the secretory nerve governing the secretion of hepatic sugar; and that some other influences must govern the changes in the liver secretion when stimulated by puncture of the 4th Ventricle.

The "Mother-Substance" of Hepatic Sugar.

He soon discovered that the sugar was not ~~formed~~ at once out of the elements in the blood which reached the liver, but that some substance already in the hepatic tissue - some glycogenic substance - produced the sugar. This was what he described as the "mother substance" of the sugar. ~~He~~ also proved this by taking a fresh liver and sending a stream of water through ~~it~~ until the water coming through the hepatic vein contained no sugar. If the liver, thus washed out and free of sugar, were left in a warm atmosphere for some hours a subsequent stream of water sent through the vessels was loaded with sugar. The sugar had previously been washed out, but not the glycogenic substance which manufactured the sugar. Moreover, he discovered that this process was arrested when the ~~(sugar)~~ liver was boiled, but that if an infusion of fresh unboiled liver was added to a decoction of boiled liver the latter gave rise to sugar. The process was essentially a kind of fermentation.

A preparation of powdered liver.

He now prepared an impure powdered liver - a glycogenic substance - which was converted by fermentation into dextrose. These results were reported to the Académie des Sciences in 1855. Two years later he definitely isolated the substance Glycogen by the potash-alcohol process. He pointed out that the formation of glycogen takes place early under conditions of life, the conversion of glycogen to dextrose is independent of life. Bernard also noted the the blood contains a ferment capable of performing this action and he indicated that the nervous system, in causing an increase of sugar in the ~~blood~~ puncture of the fourth ventricle, acts in an indirect way and modifies the circulation.

The Nervous System and the Production of Sugar.

Histological investigation aided chemical investigation in these discoveries. For instance, through it the "port wine" colour which glycogen shows when treated with Iodine was clearly demonstrated. In these researches Bernard who had no particular aptitude for the technique of histology was aided by the German physiologist Kühne who later became one of the most brilliant scientists of his day. His old chief had made a special note of the granules in the secreting pancreatic cells, and Kühne in his brilliant research work on the pancreas called them "Bernard's Granules.

Bernard assisted by Kühne.

The Discovery of the Vaso-motor Nerves

The Vaso-motor System.

It was in the years 1850-58 that Bernard pursued the researches which lead to his second great discovery, that of the vaso-motor nerves. It is interesting to note in this connection that others than himself first recognised the vaso-motor function of the cervical sympathetic.

A Divergence from the original line of Inquiry.

In this case as in that of glycogen he was looking for something else when he found it. In his discovery of glycogen he began, carried out and almost completed that discovery by his own researches, whereas in this case it would appear as if he had not noticed the significance of his results, and was inclined to hold to his original line of inquiry.

Views of the Period.

Up to that period Müller, the German physiologist had done much work on the study of muscle. He had recognised two kinds of muscle, the striated and the unstriated. He had definitely postulated the non-existence of muscular contractility in arteries. He declared that they possessed physical elasticity but not muscular contractility. He had no conception of the idea of a vaso-motor system at all. Yet physiologists realized that the nervous system must govern the blood vessels in some way for sympathetic nerves were often traced to blood vessels. Henle had, in 1840, concluded that the middle coat of arteries was partly muscular but of a different type from either skeletal muscles or the unstriated muscle of the "organic life." Stilling had also in 1840 introduced the word "Vaso-motor."

Henle's Views.

Stilling introduces the word "Vaso-motor".

His conclusions were that motor nerves not subject to the will but acted on by sensory impulses determined the blood movements and he called them "Vaso-motor nerves."
In 1846 Kölliker demonstrated that plain

muscular tissue was present in the blood vessels made up of minute spindle shaped cells aggregated together. No one proved the existence of vasomotor nerves, however, until Bernard made his discovery.

The intentions of Bernard in his experiments on the Cervical Sympathetic.

Bernard intended to study the relation of the nervous system to animal heat, and to observe what changes in temperature occurred in different parts of the body when the nerves supplying these parts were divided. He started with the sympathetics because they were often traced to blood vessels and had possibly some connection with the changes between the blood and the tissues, determining the development of heat and therefore the temp of the particular area.

He divided the cervical sympathetic in the neck, and, already believing that the control exercised by this nerve caused chemical changes producing the liberation of heat, he expected that division of the nerve would remove the control and cause a loss of temperature. It was, however, quite otherwise. When he divided the sympathetic in the rabbit on one side of the neck he was amazed to find that the temperature of that side of the head and neck rose considerably and the parts felt warm to the touch. Together with this he noted an increased sensibility of the side of the head on which he had operated. The flushing of the delicate skin of the rabbit's ear was the most marked feature of the experiment.

His first communication was read in 1851 to the Société de Biologie with the title, "Influence du grand sympathique sur la sensibilité et sur la calorification". The next year he gave a similar communication to the Académie des Sciences. But in neither did he discuss the question of the blood vessels. He does not attempt to explain "whether the vascular changes are the cause or the effect of the rise of temperature"; but he notes that the part of the head which becomes hot after division of the nerve is also the "seat of a more active circulation". He notes the state of the arteries. They "seem fuller and appear to pulsate more forcibly, this is very distinctly seen in the case of the rabbit in the vessels of the ear".

Certain Communications to learned Societies.

Bernard's discovery was the first definite proof of what is known as the vasomotor functions of the nervous system. Yet he himself considered it a contribution to the knowledge of animal heat. Other observers had divided the cervical sympathetic but had been engrossed in watching the result of this section on the pupil, namely, its constriction. They noticed nothing else. It may be said that Bernard was looking for animal heat. Undoubtedly, but he nevertheless saw the vascular changes and referred to them so that they could not be ignored afterwards. It was in every way Bernard's

The work of other observers compared with Bernard on this subject.

discovery.

Brown Séquard's Researches.

Brown Séquard was about that time studying the affects of cervical sympathetic section. He noted that on stimulating the upper portion of the divided nerve by the galvanic current, the ear cooled, the responsibility and sensibility diminished, and the vessels of the face and ear resumed their normal condition.

Bernard later in the same year - 1852 - made the same discovery independently of Brown-Séquard's result. He says, "the circulation from becoming active becomes feeble; the conjunctiva, the nostrils and the ears which were red become pale".

Bernards views on the subject.

It is worthy of note that Bernard considered the importance of his experiment on the sympathetic began in the proof they afforded that the nervous system did act directly on the chemical changes in the tissues, and intervened in the development of heat. This was the thing which was to his eyes of the greatest importance. The vascular changes he regarded as of secondary interest. Even after his experiments on the submaxillary gland, though he admitted and in fact supplied the mechanical explanation of the change in the colour of the ~~blood~~ as the result of the widening or narrowing of the arteries yet he never even to the end abandoned his first position, that the rise of temperature following section of the sympathetic is not to be explained as the fuller rush of blood through the wider vessels. There was in his opinion a direct action of the nerve in the tissue changes which formed the local source of heat. Even to within a year of his death he still held this view, and gave expression to it in certain of his papers.

Work on the Submaxillary Gland.

It was in 1858 that Bernard communicated the results of his work on the submaxillary gland. He showed that the blood coming from it, that is the venous blood, is not dark in colour but bright red or arterial in an actively secreting gland. He then noted that this was the result of stimulation of the chorda tympani. When the sympathetic which also supplies the gland was stimulated the venous blood was very dark. There were therefore antagonistic nerves in the gland. His opinion on these phenomena was that the chorda tympani dilates the vessels. The blood rushes rapidly through the gland and does not lose its arterial colour. The sympathetic constricts the vessels, and therefore the flow of blood is slow, consequently the exchange of oxygen and carbon dioxide is abnormally increased.

The Discovery of the Vaso-constrictor and Vaso-dilator Nerves.

He says:- "The sympathetic nerve is the constrictor of the blood vessels, the tympanico-lingual is the dilatator."

This was, then, the great discovery of the vaso-constrictor and vaso-dilator nerves. Claude Bernard made known the two fundamental facts in vaso-motor physiology.

Minor Discoveries.

By far the greatest of Bernards' discoveries were those of glycogen, the functions of the pancreatic juice and vaso-motor nerves. Yet he made other discoveries which cannot be neglected though of minor importance.

He was early interested in poisons, not from their toxicological history, but from their importance as "vital reagents"[1] He realized that they could be used to "analyse the anatomical elements of the living body" and as such were of great use to the physiologist.

Investigations on Curari.

He first investigated Curari, the South American arrow poison. In 1850 he published a communication on this investigation. In it he describes how the drug is not absorbed from the alimentary canal into the blood, and is therefore harmless when swallowed. In a second paper he noted that the drug destroys the reflexes, renders the nerves, both motor and sensory unexcitable, but leaves the muscles quite excitable. This statement was important because Bernard thus

Independence of Muscular Irritability.

showed that the irritability of muscular tissue is independent of the nervous tissue which supplies it. In fairness it must be said that this was proved even more distinctly by other physiologists. He was now led to make a combined experiment on the muscles of the same animal. He had noted that the muscles of the frog poisoned with Curari are more irritable than normal muscles. He experimented in the following manner. He ligatured the blood vessels of one leg before he introduced the curari into the blood stream. The muscles in the leg supplied with blood and with poison were more irritable than the muscles in the ligatured leg. He also noted that the ligatured leg, that is the one protected from the poison, not only remained sensitive but movements occurred in it when the skin on the poisoned parts of the body was stimulated. He therefore concluded that the motor nerves were paralysed by the poison but that the sensory nerves and the central nervous system escaped. He showed, by what are now common experiments, that not only the motor nerves to the muscles but other efferent nerves e.g. the vagus to the heart are also paralysed by Curari. Moreover, he realized that the limits of the action of the drug were determined by the dose; a small quantity in the blood affected only the motor nerves of the skeletal muscles, a larger quantity affected the vaso-motor nerves also.

Experiments with Curari.

The action of Curari

During the '50s Bernard took up another problem, the action of Carbon Monoxide Gas. Hitherto its action and the cause of death in cases poisoned by it were unknown. Magnus had shown in 1838 that both arterial and venous blood contained Oxygen and Carbon Dioxide, that arterial blood contained more oxygen and less carbon dioxide than venous, and that respiration consisted in blood gaining oxygen and losing carbon dioxide in the lungs

Investigations into the Action of Carbon Monoxide Gas.

and vice versa in the tissues. He maintained that the gases were simply dissolved in the blood. Meyer in 1857 refuted this view of Magnus by concluding that the blood gases exist in a loose combination from which they may be set free. This he showed to be the case as regards Oxygen. What was the substance with which the gas combined? The red corpuscles were supposed to be concerned. The connection between haematin in the blood and oxygen absorption had not been established.

Views of the Period.

When Bernard took up the matter he observed that in animals poisoned with carbon monoxide the blood from the right side of the heart, on exposure to an atmosphere containing a known quantity of oxygen did not take up oxygen like normal blood. He also noted that normal blood exposed to a carbon monoxide atmosphere gave up oxygen as it absorbed carbon monoxide in equal parts. He now concluded that the different colours of arterial and venous blood must be due to the behaviour of the red cells, and that they were responsible for the retention of the above gases in the blood. He therefore demonstrated exactly how carbon monoxide poisons the animal body.

Bernard's Observations.

"This gas rapidly poisons animals because it instantly displaces the oxygen of the red corpuscles and cannot itself be subsequently displaced by oxygen. The animal dies because the red cells are, as it were, paralysed and circulate as inert

His Conclusions.

bodies devoid of the power of sustaining life."

At that period there was a great controversy regarding the question of "spontaneous degeneration."

A Contribution to the Question of "Spontaneous Degeneration."

Bernard showed that growths which appear in a gelatin and dextrose solution exposed to air, do not appear if the solution is supplied only with air which has passed through a red hot pipe. He therefore postulated that the growths were not spontaneous but were due to air-borne germs which in the experiment where they passed through the pipe were killed on their way to the solution. Pasteur's work in this connection was on the lines of Bernard's experiment.

Bernard also played a part in another discovery, that of Inhibition. Here he was forestalled by the brothers Weber who originated the theory of inhibition by their experiment in which they showed that stimulus of the vagus nerve caused stoppage of the heart beat.

Work on Inhibition.

This discovery was made in 1846. Quite independently Bernard came upon the same results in the same year, but he did not pursue his investigations in this matter. He observed that on auscultating a dog while the vagus nerve was being stimulated the heart stopped and the sound ceased to recur; as soon as the electric stimulus was removed the action was resumed. He does not, however, appear to have been much interested in this work on inhibition.

Later Life.

It is not the purpose of this essay

to enter into much detail regarding the life and character of Claude Bernard, but

Declining Years.

before dealing with the results of his discoveries a few facts of his later life when success had placed him on a high pinnacle of fame may not be out of place.

His difficulties in carrying on his experimental work were extraordinary yet he overcame them. In 1847 he was appointed Magendie's Deputy at the Collége de France. His domestic relations were unhappy and he therefore buried himself in his scientific

Recognition.

studies. He was soon to occupy the new chair of Physiology in the faculty of Science of the University of Paris, and in 1855 he succeeded Magendie to the full professorship at the Collége de France. It was during the next few years that he demonstrated to the world those startling discoveries which have been already discussed.

Interview with Louis Napoleon.

It was in 1864 that Bernard met the Emperor, Louis Napoleon; and so impressed was the latter with his brilliant gifts that he caused two well equipped laboratories to be established in order that Bernard and his fellow scientists might work under better surroundings. In 1868 he was

An "Immortal"

admitted into the Académie Francaise and took his seat as one of the Immortals. One of his most intimate friends was Pasteur whose genius and great researches he noted with keen appreciation.

Having reached a renowned position in the world of science, and having received the highest honours which his country could bestow he still continued his work with as great assiduity as ever. In the December of

His Death.

1877 he caught a chill, the onset of a severe illness affecting the kidneys from which he never recovered, and to which he finally succumbed on the 10th of February 1878. The whole nation mourned for him and he was buried with all the ceremonial of a public

A National Tribute.

funeral at the expense of the state. This was an unprecedented event in itself for France had previously shown such a proof of national esteem only to her great princes, soldiers or statesman.

In 1886 a statue was erected to him in the Collège de France where he had laboured long and brilliantly, and another statue was erected in 1894 in the city of Lyons in the court of the Faculty of Medicine and Science.

Memorials to his Memory.

There is a picture by Lhermitte in the Luxembourg Gallery at Paris in which the artist depicts Claude Bernard in his laboratory surrounded by his friends and demonstrating to them an experiment. The experiment appears to be the effects of the sympathetic on the rabbit's ear. Surrounded by his friends, M.M. Gréhant, Dumontpellier, Malassez, Paul Bert, D'Arsonval and Dastre, he appears as a stately gentleman with a noble head, an intellectual face, kindly and expressive eyes and a distinguished demeanour. Truly a striking figure.

A man of remarkable and varied gifts, Bernard was beloved by his pupils and by his fellow scientists. They gave eloquent testimony to this at his death. He was a brilliant conversationalist though he rarely exercised his powers in that direction. He had an almost uncanny dexterity in his experimental work, and throughout his life he showed that genius which enabled him in all his researches to realize the importance or insignificance of side issues. Whenever it seemed to him necessary he would leave his original line of inquiry and follow up some new research with brilliant results. He had an extraordinary ability for, as it were, separating the wheat from the chaff. He never allowed himself to be led down some side track which would only end in a morass of doubt and uncertainty. This was the secret of his genius and success and the dominant characteristic of a truly great mind.

The Stamp of a Genius.

The Results of His Discoveries.

The Results

His "classical" works.

Whenever the student of physiology opens any standard text book on the subject he finds that in almost every reference to the discoveries associated with Bernard's name a certain word appears with oft repeated emphasis. That is the word "classical". It occurs so often that the student realizes that the discoveries of this physiologist must have been epoch-making, and their results far-reaching, and he would be correct in his surmise. For example he would read such phrases as:- "the great significance attached to this classical experiment of Claude Bernard; or "the results of Claude Bernard classical discovery; or "Claude Bernard's classical research in which etc."

One of the results of Bernard's experiments was that his discoveries marked a new epoch in physiological history and with his results as a basis, succeeding physiologists have perfected or advanced on his work. Yet it was Bernard who as it were laid the foundation of much of our more modern physiology of today. The significance of some of his discoveries has been altered slightly by some of his successors but the broad principles have been little changed. He was a pioneer. Brilliant results in Science are not attained by travelling along a "royal road", or "hitting" suddenly on some brilliant new discovery. They are rather the result of much patient experimental study over which men have devoted their lifes and which often do end in brilliant success. The discovery of Insulin in 1922 by Banting and Best thrilled the lay world; nevertheless it was the result, not of a sudden brilliant feat, but the culmination of a devoted and laborious study of the pancreas which many physiologists had taken part in and whose history was a long one.

A remarkable change in physiology.

We now have a distinct knowledge of the several functions of the pancreatic juice and of the great importance of this fluid, not only in intestinal digestion, but in digestion as a whole. As a result of Bernards' discovery other physiologists studied the subject and more recently his views were enlarged. He

Results of his discoveries in connection with the pancreatic juice.

considered that the proteolytic function of the juice was unimportant, but, as Starling points out, this was because Bernard had worked with fresh pancreatic juice. Later Corvisart, Kuhne and Pawlow followed up his discovery and showed that fresh pancreatic juice secreted normally from the pancreas contains no trypsin but a percursor of trypsin, trypsinogen. The trypsinogen is converted into trypsin by the action of a ferment enterokinase furnished by the mucus membrane of the intestine.

Later Researches by his Successors.

Again, the view of Bernard supported by Heidenhain, Pawlow and Foster regarding the flow of pancreatic juice occurring when acid chyme passed into the duodenum was that the phenomenon took place through a reflex arc. By experiment, however, Popielski, Wertheimer and Page showed that the introduction of acid into the Duodenum still excites pancreatic secretion after section of both vagi and both splanchnic nerves, or after destruction of the spinal cord, or even after extirpation of the solar plexus. The conclusion was that a local reflex action occurs, the centres for which are in the scattered ganglia found throughout the pancreas.

Conclusions.

Even allowing for these researches, one must realize how deeply the present knowledge of the various actions of the pancreatic juice has affected our ideas, not only of digestion but also of the process of nutrition through this discovery of Bernard's. It was the foundation and in large part the structure of the present knowledge on this question.

Bernard himself quite recognised, after his "diabetic puncture" experiment, that the vagus is not the secretory nerve governing the secretion of hepatic sugar. But as a result of his discovery great interest was stimulated, and subsequent research workers continued his investigations. Their observations have tended to alter the significance attached to Bernard's experiment. It was soon found that puncture of the fourth ventricle excited glycosuria by setting up some nervous irritation which was believed to act directly on the liver. Then it was noted that previous section of the splanchnic nerves or painting nicotine on the ganglia concerned prevented the usual effects of the puncture. It now appears that the nervous impulses excited pass, not to the liver direct, but to the adrenals and the pituitary gland causing them to throw more of their secretion into the circulation. That is, puncture glycosuria is adrenal or pituitary glycosuria. This result brings in the questions of internal secretion; it was Bernard who first used the term "internal secretion" and the result of his great discovery was to throw open a new branch of physiology.

The results associated with his experiment on the 4th Ventricle.

Modern conclusions based on his work.

Bernards discovery of Glycogen had the most brilliant results. It was a contribution to the discovery and study of sugar in the animal body and it solved special problems of digestion and nutrition. It destroyed

The Results of the Glycogenic discovery.

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the prevalent theory at that time which was that the animal body in contrast to the plant could only destroy and not construct. It completely upset the theory of functions which was held in those days. They then regarded each organ as having its own special appropriate function and when that was found there was no need for further investigation. But the most important result of all was the idea suggested by Bernard, that of "internal secretion". As Swale Vincent points out in his work on the "Internal Secretions", Bernard first gave to the world the phrase "internal secretion". The glycogenic function of the liver is not at the present time included among the internal secretions. It is rather a special arrangement for the storing of food material. The glycogenic function of the liver is however intimately related to certain internal secretions notably those of the pancreas and suprarenals.

Origin of the term, "Internal Secretion".

It cannot be denied that since Bernard's time there has been much loose writing and loose thinking regarding the subject of internal secretion. There is a tendency to listen to unwarrantable conclusions and "in physiology many processes really imperfectly understood have been prematurely classed among the internal secretions." The failure or discordance of those secretions which alter the blood passing through the various tissues entails disease. Their study is an extraordinarily fascinating one

Internal Secretions supposed to explain everything.

As Foster puts it. "The study of these internal secretions constitutes a path of inquiry which has already been trod with conspicuous success and which promises to lead to untold discoveries of the greatest moment, the gate to this path was opened by Bernard's work." These words are prophetic. The study of internal secretion has in recent years made great advances; its most brilliant result so far being the discovery of Insulin in 1922 by Banting and Best. No one has played a greater part in the study of these secretions, the foundation of which was laid by Claude Bernard, than that renowned scientist and leading physiologist in the world today, that doyen of physiological scholars, Professor Sir Edward Sharpey Schafer, of whom the Medical School of Edinburgh is justly proud.

With reference to Glycogen, it was Flint the noted American physiologist who reconciled the views of Bernard and Pavy. Those accepting the experiments of Bernard as conclusive assumed that the substance of the liver and the blood in the hepatic veins always contained sugar. Dr Pavy of Guy's Hospital professed to have demonstrated that neither the liver or the hepatic blood contained sugar during life but that sugar found in these situations was the result of a post mortem change of the "amyloid matter" of the liver. Flint reconciled those views by his experiments.

The path first was opened up.

This brilliant investigator in endocrinology.

Researches by Flint based on Bernard's Work.

He showed that a substance glycogen was present in the liver, that the liver has a glycogenic function which consists in the formation of sugar out of glycogen, and that during life the liver contains only glycogen and no sugar, for the mass of blood passing through the liver washes out the sugar as fast as it is formed.

Conclusions

All that has since been added, however by others to Bernard's own results amounts compared with them to very little. It was remarkable that he should bring his discovery so far to completion, and there have been few alterations by subsequent inquir[ers] on the views he left behind him.

Before dealing lastly with the results of his discovery of the vasomotor nerves, reference may be made to the results of his minor researches.

Modern Use of Curari.

As a result of his work on Curari, the latter poison has become in the hands of the physiologist an instrument similar to the anaesthetic of a surgical operation. He is now able to abolish temporarily the movements of skeletal muscles, and it has thus aided him in making observations which could not have been made at all or at anyrate with difficulty. This result is due to the work of Bernard.

The action of Carbon Monoxide and its connection with Red Cells.

Regarding carbon monoxide poisoning, Bern[ard's] remark that "the gas instantly displaces the oxygen of the red corpuscles and cannot of itself be subsequently displaced by oxygen" has been questioned.

Some authorities hold that under pressure maintained at a high level oxygen can again replace the carbon monoxide in the corpuscle. Haldane has pointed out that an animal can live for some time even when carbon monoxide has completely replaced the oxygen in the corpuscle, because of the oxygen present in the blood plasma.

The results of experiments based on Bernard's discovery.

Be this as it may, the results of Bernard's discovery were a great gain. He explained how carbon monoxide acted and thus found or paved the way for a remedy in cases poisoned by the gas. He also brought in a method of measuring the quantity of available respiratory oxygen in any given quantity of blood, and he formed a correct view of the process of respiration. This view led him on to the functions of the blood and incidentally to the discovery of the vaso-motor nerves.

Conclusions.

The Results of the Vasomotor Discovery.

The results of that great discovery of the vasomotor nerves were manifold. The importance of the discovery was immense. As a result there was a great widening of all physiological and pathological conceptions, of medical practice, and of human life. The vaso-motor system dominates physiology; it is always appearing in a thousand different problems. Vaso-motor factors appear in all branches of physiological science; in the temperature regulating mechanism of the body, in the blood control to the brain subject to the conditions of the individual's environment, in the processes of secretion and in the

Far reaching Effect.

energy of muscle. In ill health where pathological processes, the results of physiological disorders of function are in progress vaso-motor influences play a part; in fevers, in inflammation and in any or every disease. Bernard's discovery made this far more scientific conception of disease a possibility. Medical men got away from those old and extraordinary ideas about "humours" and "vapours." These notions make very interesting, in fact romantic reading but they are not scientific. The immense gain to clinical work can hardly be exaggerated. Attention had been drawn to cases where there was some connection between changes of the vascular system and affections of the nerves, but the whole problem was obscure. The results of Bernards' discovery drew the veil aside and exposed many things previously hidden from the eyes of the keen enquirer. To this discovery of Bernard's modern medicine and particularly modern clinical scientific medicine owes an almost incalculable debt.

Influence of this Discovery.

A Great Debt.

The power of the healer to cure or lessen disease or to prevent or lessen pain has grown with a marvellous rapidity. This is due to the wider view of vaso-motor action now held. These views have their origin in Bernard's initial experiment.

Thus it is seen that the results of this brilliant investigator were no less momentous than his discoveries. A great seeker after the truth, he did those things for the benefit of his fellow men, and with this knowledge as part of his armour the doctor of today goes out into practice and into the world like some knight of old to fight against that powerful dragon, Disease. The physician cannot get away from physiology; it is one of the strong foundations of his art. As Mr Miles says in his recent little volume on "The Study of Medicine", "The Doctor must ever think along the lines of Physiology." The practical physician seeks in physiology facts in explanation of pathological phenomena, and by knowing the true state of affairs he is led to employ proper medical resources. Cooperation between physician and physiologist is necessary. Pawlow, himself a renowned physiologist, has himself put it :- "Frequent interchange of thought between the physiologist and the physician should be the rule, in order that the common goal of physiological science and of medical art will be most quickly and rapidly and safely reached".

The influence of Claude Bernard's discoveries and their results on Medicine and on physiology will be felt for many years to come. Nay more, that influence will be an enduring and lasting one, for future generations in Medicine, appreciating the wonderful advances made in our knowledge of the functions of the human body and its relations to disease now and in the future, will realize that many of these advances had their genesis in the work of Claude Bernard. The works of great physiologists in the future will still refer to his discoveries as "classical".

Conclusion.

His achievements will live in the world of science for many days to come, though the earthly form has long since dwindled into dust.

In conclusion it may be said of him with all due reverence, esteem, and respect:—

"He being dead, yet liveth".

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