THE ONLY EXTANT MANUSCRIPT OF CLAUDE BERNARD'S FIRST COURSE ON EXPERIMENTAL PHYSIOLOGY IN COLLÈGE DE FRANCE DURING THE WINTER OF 1847-1848

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SUMMARY

The only extant version of the first lecture course given by Claude Bernard on Experimental Physiology during the winter period of 1847-48 in Collège de France, substituting Magendie, is presented herein. The prominent Paris-graduated physician from Uruguay, Teodoro M. Vilardebó, attended the 46 lectures, wrote them down and transcribed them into a manuscript that he brought back to and kept in Montevideo in 1853. Mañé-Garzón uncovered it in 1987. These Bernard's lectures review practically all physiology at the beginning of his career, while in later courses, he covered selected themes of experimental physiology and medicine and general scientific subjects at greater depth. Comparison of Bernard's initial course with his later ones illustrates general physiology's progress in the more than 35 years of his successful scientific life. The manuscript sheds new light into Bernard's scientific activity and personality.

Introduction

In 1987, Mañé-Garzón spotted the manuscript (MS) of Bernard's first lecture course in experimental physiology in the library of the Cáceres family in Montevideo (Bernard, 1847-48). It is a 530 pages-long, ink-written manuscript, of 3 cahiers, which include 26 ink drawings. It forms a leather-bound volume, with the following inscriptions: i) in the spine, 'C. Bernard, Physiologie Expérimentale'; ii) in the first page, 'Cours de Physiologie Expérimentale de M. Cl. Bernard trimester d'hiver 1847-1848', in pencil and in Spanish; iii) 'Notes taken by T. M. Vilardebó in those lectures'; and iv) 'it belongs to Dr. Gonzalo Cáceres'. Further studies authenticated Vilardebó's MS that his grandniece had donated to the Cáceres family. Teodoro M. Vilardebó (1803-57) studied medicine in the University of Paris (1825-33) and returned to his native Uruguay after graduation. He was back in Paris in 1847 for six years. Then, he attended Bernard's lectures over the winter trimester of 1847-48, wrote down faithful literal notes and transcribed them into the ink-written MS which he brought back to Montevideo in 1853. In the middle of a brilliant career as a physician and scientist, Vilardebó died during a yellow fever epidemic in 1857 in Uruguay, while attending his patients (Bernard, 1847-48: 399-413). The Cáceres family has now presented the MS to Mañé-Garzón. We believe the MS is the only extant version of

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EL ÚNICO MANUSCRITO EXISTENTE DEL PRIMER CURSO SOBRE FISIOLOGÍA EXPERIMENTAL DICTADO POR CLAUDE BERNARD EN EL COLLEGE DE FRANCE, INVIERNO 1847-1848

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RESUMEN

Se presenta la única versión existente del primer curso sobre Fisiología Experimental dictado, en sustitución de Magendie, por Claude Bernard en el invierno 1847-1848 en el Collège de France. El destacado médico uruguayo graduado en París, Teodoro M. Vilardebó, asistió a las 46 lecciones, tomó apuntes y los transcribió a un manuscrito que trajo de vuelta en 1853 y conservó en Montevideo. Mañé-Garzón lo descubrió en 1987. Estas lecciones de Bernard revelan prácticamente toda la fisiología de comienzos de su carrera, mientras en cursos posteriores cubrió en mayor profundidad tópicos selectos de la fisiología y la medicina experimentales, así como temas científicos generales. La comparación del curso inicial de Bernard con otros posteriores ilustra el progreso de la fisiología general durante los más de 35 años de su exitosa vida científica. El manuscrito vierte nueva luz acerca de la actividad científica y la personalidad de Bernard.

O ÚNICO MANUSCRITO EXISTENTE DO PRIMEIRO CURSO SOBRE FISIOLOGIA EXPERIMENTAL DITADO POR CLAUDE BERNARD NO COLLEGE DE FRANCE, INVERNO 1847-1848

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RESUMO

Apresenta-se a única versão existente do primeiro curso sobre Fisiología Experimental ditado, em sustituição de Magendie, por Claude Bernard no inverno 1847-1848 no Collège de France. O destacado médico uruguaio graduado em París, Teodoro M. Vilardebó, assistiu às 46 lições, anotou e os transcreveu a um manuscrito que trouxe de volta en 1853 e conservou em Montevideo. Mañé-Garzón o descobriu em 1987. Estas lições de Bernard revelam práticamente toda a fisiologia do princípio da sua carreira, enquanto que em cursos posteriores cubriu em maior profundidade tópicos seletos da fisiologia e a medicina experimentais, assim como temas científicos gerais. A comparação do curso inicial de Bernard com outros posteriores ilustra o progresso da fisiologia geral durante mais de 35 anos de sua exitosa vida científica. O manuscrito verte nova luz sobre da atividade científica e a personalidade de Bernard.

Bernard's first lecture course. Olsmted (1938: 59) mentions Bernard's 1847-48 lectures in relation to his inaugural lecture of Dec. 1859 but we have found no information about the subjects of those lectures in several sources (Bernard, 1965; Grmek, 1967, 1973, 1991). Grmek has had access to the complete collection of Bernard's papers in *Collège de France*. Bernard also lectured during the winter periods of 1853-54 and 1854-55.

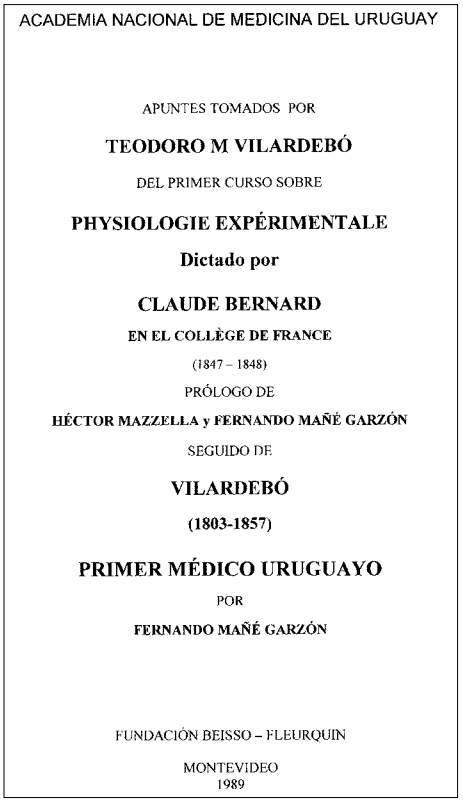
Héctor Mazzella (Professor of Physiology, Facultad de Medicina del Uruguay) and Mañé-Garzón transliterated and published the MS (Bernard, 1847-48). Its title page is shown in Figure 1. The initial 181 pages are devoted to the MS with a Table of contents (in French), a reproduction of Vilardebó's title page handwriting, the body of the MS and a name index. The following 360 pages are devoted to Dr. TM Vilardebó (Bernard, 1847-48: 183-543). The detailed contents is to be found in Table I.

Before examining *Cours de Physiologie Expérimentale de M Bernard* in detail it is useful to set up a frame of reference with only a brief glance at the lives of Bernard and of his predecessor Magendie, since they have been extensively analyzed in the context of France's 19th century experimental foundations of general physiology (Foster, 1899; Olmsted, 1938, 1944; Izquierdo, 1942; Olmsted and Olmsted, 1952; Singer and Underwood, 1962; Grande and Visscher, 1967; Schiller, 1967; Holmes, 1974; Robin, 1979).

François Magendie (1783-1855) had obtained his medical degree from *Université de Paris* in 1808. Considered the pioneer of experimental physiology in France, since he established the first Laboratory of Physiology, and was one of the founders of the *Journal de physiologie expérimentale*, he emphasized in lectures and books that experimentation is the source of knowledge (Magendie, 1909, 1916, 1836, 1837). He is known for describing the foramen of Magendie, the Magendie sign (a downward and inward rotation of the eye due to a lesion in the cerebellum), and that the dorsal root of the spinal nerves is connected with feeling and the ventral with movement (Bernard, 1847-48: 85-86; Olmsted, 1944: 93-122). His contemporary Sir Charles Bell had made similar but not so definitive findings. This observation, which constitutes the Bell-Magendie law led to bitter controversies as to the priority of the finding, as revived by Bernard in his 25th lecture of Feb. 21st (Table II; see also the last paragraph of the present paper). Magendie was perhaps the first to point out vitamin defficiencies (Magendie, 1816). Magendie was a faculty at the College of France, holding the Chair of Medicine from Apr. 4th 1831 to 1855, when he was formally succeeded by Bernard. There, he presented original investigations about the physical phenomena of life, experimenting on live animals despite opposition of anti-experimentalists and anti-vivisectionists. This shocked observers but stimulated colleagues and attracted students, such as Claude Bernard. An initiator of scientific pharmacology and toxicology, he propounded the idea that living phenomena in animals and plants were physical and chemical events accessible to experimentation (Magendie, 1837). He led an empirical approach to science, but he never abandoned vitalism completely (Olmsted, 1944: 236).

Claude Bernard (1813-78) followed under Magendie's tutelage as a brilliant, independent and creative investigator becoming France's general physiology great figure, as were his german contemporaries Johannes Müller (1801-58) and Karl Ludwig (1816-95). In 1843 Bernard obtained his *Doctorat en Mèdecine* (Bernard, 1843). He soon reached prominence in

experimental science, science methodology and philosophy, due to an exceptional experimental intuition, marvelous sagacity, clear reasoning and prodigious manual and surgical abilities, as shown by his book on surgery with Huette (Bernard and Huette, 1854), extant in Viladerbo's library in Montevideo (Bernard, 1847-48: 443) and a posthumous book (Bernard, 1879; see also Rodríguez de Romo, 1989; Rodríguez de Romo and Borgstein, 1999), hard working capacity and great persistence. He solidified the concept that experimentation was indispensable to advance knowledge, working with invertebrates, amphibians, birds, herbivorous and carnivorous mammals and plants. For him, the task of general physiology was to study the phenomena of life common to animal and plant cells. As Magendie, he emphasized that laws of general biology can be derived from specific experimental data, that living phenomena are by nature physical and chemical events that should be investigated by physical and chemical methods; that living structures are harmoniously organized, interrelated and integrated in the different organs that form a living being (Bernard, 1865; Henderson, 1927; Izquierdo, 1942). Bernard spent more than 35 years of scientific activities in Paris in the *Collège de France* (until 1878), in the *Faculté des Sciences* (until 1869), and in the *Muséum d'Histoire Naturelle* (from 1870 to 1878). He collaborated with his colleagues and followed the progress of his french and foreign contemporaries not only in his own field but also in physics and chemistry (Foster, 1899; Olmsted, 1938; Singer and Underwood, 1962; Holmes, 1974).


ACADEMIA NACIONAL DE MEDICINA DEL URUGUAY

APUNTES TOMADOS POR

TEODORO M VILARDEBÓ

DEL PRIMER CURSO SOBRE

PHYSIOLOGIE EXPÉRIMENTALE

Dictado por

CLAUDE BERNARD

EN EL COLLÈGE DE FRANCE

(1847 – 1848)

PRÓLOGO DE

HÉCTOR MAZZELLA y FERNANDO MAÑÉ GARZÓN

SEGUIDO DE

VILARDEBÓ

(1803-1857)

PRIMER MÉDICO URUGUAYO

POR

FERNANDO MAÑÉ GARZÓN

FUNDACIÓN BEISSO – FLEURQUIN

MONTEVIDEO
1989

Figure 1. Title Page of Bernard, 1847-48. It would read in English: National Academy of Medicine of Uruguay. Notes taken down by Teodoro M. Vilardebó at the First Course on Experimental Physiology dictated by Claude Bernard in the Collège de France (1847-1848). Prologue by Héctor Mazzella and Fernando Mañé-Garzón. Followed by Vilardebó (1803-1857) First Physician of Uruguay by Fernando Mañé-Garzón. Beisso-Fleurquin Foundation. Montevideo. 1989.

The course on *Physiologie Expérimentale* attended by Vilardebó was the first Bernard lectured when the ageing Magendie asked him to be his substitute to the chair of experimental medicine. He was appointed Magendie's *suppléant* by the *Collège de France* (Olmsted, 1944: 243) and lectured from Dec. 14th 1847 (Table II). Twelve years later, in his opening lecture (in the winter of 1859, in lectures published in 1872) Bernard reminded his audience that in 1847 he had said: "I am in charge of teaching you scientific medicine which does not exist as yet; but we can lay its foundations by cultivating experimental physiology from which scientific medicine shall evolve, because the former is the basis for the latter" (Bernard, 1872: 456, 3rd paragraph). Bernard ended his 46th lecture on Apr. 17th, 1848 (Table II). Although he was only 34 years old, he had accumulated experimental practice: on the *chorda tympani* (Olmsted and Olmsted, 1952: 34), the action of curare (Changeux, in Robin, 1979: 73-95), he had catheterised the heart to measure the heart blood pressures and the heat production by the lungs (Cournand, in Robin, 1979: 97-121). Bernard used to work sometimes for decades on a given subject, perfecting his reasoning and interpretations until he felt his ideas had matured. He received four French Academy of Sciences' prizes between 1847 and 1854 for his many achievements; among them, his crucial finding of 1849 that pricking the 4th ventricle's floor produced diabetes. Details of Bernard's scientific life from 1850-60 are to be found in Bernard's cahier rouge (Bernard, 1965, 1967). Bernard lectured in lieu of Magendie until the death of the latter in October 1855. Elected *Professeur* of *Médecine Expérimentale* of the *Collège de France* that very December (Olmsted, 1938: 53; Olmsted and Olmsted, 1952: 90, 93) he held this position until his death in February 1878 (Olmsted, 1938: 134; Olmsted and Olmsted, 1952: 240-243).

TABLE I
CONTENTS OF BERNARD (1847-48/1989)*

i) Part devoted to Bernard	(1-181)
Portrait of Bernard	(2)
Presentation by the President of the Academy of Medicine of Uruguay**	(5-6)
Mañé-Garzón's note about the MS**	(7-8)
Mazzella and Mañé-Garzón's prologue**	(9-12)
Table of contents (see Table II)***	(13-15)
Cours de Physiologie Expérimentale de M Bernard, MS title page in Vilardebó's ink-handwriting:	(17)
Body of the MS***, with reproductions of 26 Vilardebo's ink hand-drawings	(19-175)
Name index***	(179-181)
ii) Part devoted to Vilardebó**	(183-543)
Biography by Mañé-Garzón, Vilardebo's scientific contributions and writings, his life's chronology	(189-435)
Catalogue of his library	(443-457)
Vilardebo's Bibliography	(459-465)
Appendix with documents	(467-524)
Name and content indices	(525-543)

*Pages in parentheses. **In Spanish. ***In French.

Lecture Series 1847-48: *Physiologie Expérimentale*

In *Physiologie Expérimentale* (Bernard, 1847-48), our MS of interest, Bernard covered practically all the physiology of the time emphasizing on the experimental approach and on giving proofs for what he had asserted during lectures (underlined in Table II). Table II can be sum-

TABLE II
ABBREVIATED TABLE OF CONTENTS OF BERNARD`S
PHYSIOLOGIE EXPERIMENTAL (1847-1848)*

		Première cahier
1st	Dec 14	Gastric secretion
2nd		Composition
3rd		Effects on digestion
4th	Dec 23	Gastric secretion mechanisms
5th	Dec 27	Saliva
6th	Dec 29	Pancreatic fluid
7th	Jan 2	Gastric fluid, bile and chyle absorption
8th	Jan 6	Starchy and sugary substances
9th		Potassium cyanide
10th		Urine: composition
11th	Jan 19	Urine: continued
12th		Urine, urea, uric acid; curare, Boussingault and the contribution of America
13th		Digestion and age; milk and starch digestion; after lecture experiments
14th		Chyle, comparison between carnivores and herbivores, intestinal digestion, experiments
15th	Jan 29	Potassium cyanide and ferrous lactate
16th	Jan 31	Experiments on digestion; circulation, properties of blood
17th	Feb 3	Blood circulation: speed
18th		Its origin
19th	Feb 7	Gastric digestion experiments; arterial circulation; blood pressure modifiers: coffee, alcohol, opium; capillary circulation
20th	Feb 10	Capillary circulation; capillary wall absorption: endosmosis and exosmosis; gas absorption; experiments of Magendie
21st	Feb 12	Experiments; venous circulation: origin; portal circulation
		Deuxième cahier
22nd	Feb 14	*Experiments*; blood, chemical composition
23rd	Feb 18	Ozone; *Schönlei's experiments*, substances introduced into the blood; heart movements; heart contractions, theories
24th	Feb 19	Bile; heart contractions; *experiments: injections of potassium cyanide and ferrous lactate*
25th	Feb 21	Nervous system; sensory and motor nerves; Bell and Magendie; cranial nerves; classification according to sensory and motor roots
26th	Mar 2	Cranial nerves: the pneumogastric and Willis accessory nerves
27th	Mar 4	*Experiments with toads; galvanism*; muscular irritability, nervous excitability: theory of Marshall Hall
28th	Mar 6	PneuPneumogastric and Willis accessory nerves; anastomosis of the pneumogastric nerve; distribution; superior laryngeal nerves
29th	Mar 9	Pneumogastric nerves section
30th	Mar11	Its effects on the heart, digestion, circulation and respiration
31st	Mar13	Dedicated to experiments: section of pneumogastric and of Willis' accessory nerve
32nd	Mar 16	Human anatomical piece to show Willis' accessory nerve; Bell and the sensitivity of the face; Magendie's experiments; demonstration in the rabbit
33rd	Mar 18	Continue Magendie's experiments; ophthalmic branch of the trigeminal nerve; oculomotor nerves; section of facial nerve; taste; *chorda tympani*
34th		Progress of physiology due to organic chemistry: Haller, Réaumur, Spallanzani, Dumas, Chaussier; gastric juice composition; experiments of Chevreul and Beaumont; works of Müller and Blondlot
		Troisième cahier
35th	Mar 21	Nerves: glossopharyngeal, hypoglossal, the grand sympathetic
36th	Mar 23	Nervous system: disposition of the membranes; cerebrospinal fluid: quantity, composition, uses
37th	Mar 25	*Experiments*; properties of pancreatic juice; functions of: *medulla spinalis*
38th	Mar 27	*Medulla oblongata*; Flourens vital node; annular protuberance; *pons cerebri*; cerebellum; *corpus callosum*; optic thalamus; *corpora striata*; *corpora quadrigemina*
39th	Mar30	Experimental toxicology (Humboldt); strychnine
40th	Apr 1	Experiments with strychnine: nux vomica: five experiments
41st	Apr 3	Nicotine; cyanide; carbonic oxide
42nd		Curare, opium, digitalis, alcohol
43rd	Apr 8	Action of ether on the nervous system; medicaments; quinine
44th	Apr 10	Arsenic and arsenious acid, mercury and compounds, curare, lead, antimony
45th	Apr 13	Substances that act on the blood: putrid substances; ferments; extreme heat and cold; counterpoisoning
46th	Apr 17	Mechanical action of some substances: ergot, ergotine; curare, digitalis

Translated from the French of Vilardebo's MS. Experiments and demonstrations are underlined.
Lecture number, date and subjects (shortened) are given.

marized as follows: a) Digestion, psychic gastric acid secretion (a finding that preceded Pavlov by decades), chemical aspects, destination of ingested glucose, history and methodology of studies on digestion. In his first lecture of Dec. 14th, he mentions how Beaumont's studies in Alexis St' Martin's gastric fistula stimulated his developing artificial fistulas to experiment on digestion (Beaumont, 1833; Bernard, 1847-48: 19). b) Blood. c) Circulations, arterial, venous and portal; Poiseuille and Magendie's experiments; heart. d) Nervous system, peripheral, cranial nerves, brain, central and autonomous nervous system. e) Excitability, muscle. f) Kidney, urine and urea, uric acid. g) Drugs, poisons, toxics, medicaments. h) Contributions of America to Europe. i) Contributions of chemistry to physiology.

The 45 Lecture Series 1854-55 were the first that Bernard published (Bernard, 1855-56). They were delivered just after Magendie's death. He opened them with an *homage* to Magendie (Bernard, 1856a). In addition, in these lectures he analyzed the following subjects: i) He compared the style of lectures given in the University with those given in the *Collège de France*, describing how in the former they were recitative, as plain speeches to the audience; while they were more experimentally based in *Collège de France.* In the latter Bernard always showed new results, new extended views; chats interspersed with experiments: were public demonstrations and discussions of results, since the lecture hall in the *Collège de France* was an extension of Bernard's laboratory (Foster, 1899; Olmsted, 1938; Olmsted and Olmsted, 1952). ii) The links between physiology and pathology. iii) Diabetes and sugars, production of sugars and starch and glycogen by the liver, and by plants and animals; the "diabetic" center in the floor of the 4th ventricle. iv) Digestion. v) Blood, portal and hepatic venous blood; blood temperature in right and left heart. vi) Secretion *vs* excretion.

vii) Excitation and irritation. viii) The great sympathetic. ix) Curare (Bernard, 1856b). Establishing a clear cut difference with the 1847-48 lectures, in this and in future lecture series Bernard covered, in each course, few successively selected subjects but at a great depth. Thus, he lectured on curare; toxics and medicaments (Bernard, 1857), animal heat (Bernard, 1876), pancreas, diabetes, liver and glycogen synthesis (Bernard, 1853, 1877), *chorda tympani* and salivary secretion (Bernard, 1866), nervous system physiology and pathology, the great sympathetic nerve system (Bernard, 1858), fluids of the organism (Bernard, 1859), concepts of internal secretion and internal milieu and on general scientific subjects (Grmek, 1967: 248-264). Bernard published hundreds of papers and more than 20 book-volumes, some posthumous (Bernard, 1878, 1878-79, 1879, 1947, 1954, 1965). Many are available at www.claude-bernard.co.uk/. As Vilardebó had done in 1847-48, Bernard's lectures were noted down by his assistants and edited and published by Bernard or his colleagues (Olmsted, 1938: 52, 55; Omsted and Olmsted, 1952: 94-95), a procedure initiated by Magendie (Olmsted, 1944: 202).

Bernard's famous methodological text *Introduction à l'Étude de la Médecine Expérimentale (Bernard, 1865) was written during his long illness and convalescence (*Olmsted and Olmsted, 1952, *ch. 11, 12). It was translated s into Spanish (Bernard, 1880, 1900, 1959; Izquierdo 1942) and later into German (Bernard, 1960). L.J.* Henderson (1878-1942) stimulated its English *translation* (Bernard, 1927) writing an Introduction (Henderson, 1927). Henderson, who greatly admired Bernard, "originated" one of the papers of his long series "Blood as a Physicochemical System" (Henderson and Murray, 1925) in the "Claude Bernard Laboratory, Névache, France", actually the hotel they were at while writting the paper. In *Introduction à l'Étude...* Bernard underscored: a) the logical steps in the scientific method; b) that in biology, as in physics or chemistry, a well controlled and performed experiment ought to give the same result when repeated (Bernard, 1865: 219); c) that the experimental results should be quantified, since ideally laws of all phenomena should be mathematically expressed; at that time it was believed by some that biological experiments were not necessarily reproducible, making a difference with those of physics and chemistry; d) that in science there is no absolute truth on a given subject, because what looks like truth at one time may be later modified by new evidence; and e) the importance of the experimental doubt. This book *had been in Bernard's mind at least since December 1856, when he opened his course lecturing about: "The experimental method; difficulties of experimentation...; the art of experimentation,..." (Bernard, 1858a, Vol. 1: 1-19, also published as Bernard, 1858b).*

Bernard had planned that his *Principes de Médecine Expérimentale* should follow *Introduction à l'Étude... (cf. Bernard, 1865: 27;* Bernard, 1947: xi; Grmek, 1967: 35-40), but it was published 80 years later (Bernard, 1947). Bernard strongly influenced the biomedical environment of his time: for example, his last lecture course *Leçons sur les Phénomènes de la Vie Communs aux Animaux et aux Végétaux* of 1874, with the concept that "the constancy of the milieu interieur is required for free life", was out of the presses within a fortnight of his death (Bernard, 1878-1879). In addition, *Introduction à l'Étude... also* produced great impact among the *intelligentsia* of the time (Tenney, 1991). For example, Zola, wrote an "experimental" novel (Zola, 1880) and characters Mitia and Alioscha in The Brothers Karamazov speak of a "Carl" Bernard and of science in a rather derogative way (Dostoievski, 1879).

To sum up, the present paper draws attention to a transcendental manuscript of Bernard's first lecture course on experimental physiology that remained unknown for 140 years (Bernard, 1847-48: 7-8). It sheds further light on the early period of Bernard's scientific career and contributes to show that when Bernard was substituting Magendie, he lectured during several winter periods, and not only during the summer as has been hinted (Olmsted, 1944: 243). It establishes many new details of Bernard's scientific career. For example, as already mentioned, in his 25th lecture Bernard vindicated Magendie's demonstration that the anterior roots in the medulla are motor and the posterior sensitive, as superior and clearer than Bell's, who, according to Bernard, "never opened the rachis" (Bernard, 1847-48; lecture 25, Table II) a view shared by others (Foster, 1899: 59-60; Olmsted, 1938: 201). At the time of his lecture, Bernard had already published on the subject (Bernard, 1847). Vilardebó's MS shows that in March 1848, Bernard was beginning his experiments on the action of the vagus nerve on the heart (Bernard, 1847-1848; lectures 29-31, Table II), as well as his studies on the poisonous action of carbon monoxide (Bernard, 1847-1848; lecture 41, Table II). It is widely accepted that Bernard contributed to build general physiology particularly on i) pancreatic functions, a subject which has been reexamined in studies that reaffirm Bernard's great manual dexterity (alluded to above) and show Bernard's deductions related to the function of the pancreas as correct (Rodríguez de Romo, 1989; Rodríguez de Romo and Borgstein, 1999); ii) glycogen and other carbohydrate-related functions of the liver and carbohydrate metabolism in plants and animals (Bernard, 1877; Robin, 1979: 96-97) including histochemical methods (Bernard, 1859b, c); iii) the idea of internal secretions (Robin, 1979: 91); iv) the nervous system control of vasomotor activity; iv) poisons, curare and carbon monoxide; and v) the idea that anaesthetics work in animals and in plants. *Introduction à l'Étude....(Bernard, 1865)*, Phenomena of Life.... (Bernard, 1878-79, 1974), his views on philosophy (Bernard, 1954; Dhurout, 1939; Roll-Hansen, 1976; Sertillanges, 1944) became classic landmarks that unified science, foreshadowing by many decades the development of 20th century biology (Forster, 1899; Izquierdo, 1942; Pi-Sunyer, 1944; Singer and Underwood, 1962; Schiller, 1967; Houssay, 1972).

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REFERENCES

Beaumont W (1833) *Experiments and Observations on the Gastric Juice and the Physiology of Digestion.* Facsimile ed. New York, USA. 1959 pp.

Bernard C (1843) *Du Suc Gastrique et de son Rôle Dans La Nutrition. Thèse Presentée a la Faculté de Medecin de Paris pour le Doctorat en Mèdecine par Claude Bernard. 7 Dec. 1843.* Rignoux, Imprimeur de la Faculté de Medicine. Paris, France. 34 pp.

Bernard C (1847) Recherches sur les causes qui peuvent faire varier l'intensité de la sensibilité récurrente. *C. R. Hebd. Acad. Sci. 25*: 104-106.

Bernard C (1847-48) *Physiologie Expérimentale* (1847-1848). Apuntes tomados por Teodoro M Vilardebó del primer curso sobre *Physiologie Expérimentale* dictado por Claude Bernard en el *Collège de France* (1847-1848). Prólogo de Héctor Mazzella y Fernando Mañé-Garzón. Seguido de Vilardebó (1803-1857) Primer médico Uruguayo, por F Mañé-Garzón. Academia de Medicina del Uruguay y Fundación Beisso-Fleurquin. Talleres Gráficos Barreiro. Montevideo, Uruguay. 1989. 540 pp.

Bernard C (1853) *Recherches sur une Nouvelle Fonction du Foie Considéré comme Organe Producteur de Matière Sucrée Chez l' Homme et les Animaux. Thèse pour le Grade de Docteur ès Sciences Naturelles.* Martinet. Paris, France. 97 pp.

Bernard C (1855-56) *Leçons de Physiologie Expérimentale Appli-*

quée à la Médecine. Baillière. Paris, France. 2 vols. 520 pp., 510 pp.

Bernard C (1856a). *Magendie, Fr. Leçon d'ouverture du Cours de Médecine du Collège de France.* Baillière et Fils. Paris, France. 36 pp.

Bernard C (1856b) Analyse physiologique des propriétés des systèmes musculaires et nerveux au moyen du curare. *C. R. Hebd. Acad. Sci. 43*: 825-829.

Bernard C (1857) *Leçons sur les Effets des Substances Toxiques et Médicamenteuses*. Baillière. Paris, France. 488 pp.

Bernard C (1858a) *Leçons sur la Physiologie et la Pathologie du Système Nerveux*. Baillière. Paris, France. 2 vols. 520 pp., 560 pp.

Bernard C (1858b) De la Méthode Expérimentale, de l' Expérimentation et de ses Perfectionnements, de la Critique Expérimentale. Malteste. Paris, France. 24pp.

Bernard C (1859a) *Leçons sur les Propriétés Physiologiques et les Altérations Pathologiques des Liquides de l'Organisme*. Bailliere. Paris, France. 2 vol. 524 pp., 476 pp.

Bernard C (1859b) De la matière glycogène considérée comme condition de développement de certains tissus, chez le fœtus, avant l'apparition de la fonction glycogénique du foie. *C. R. hebd. Acad. Sci. 48*: 673-684.

Bernard C (1859c) Remarques à l'occasion de la communication précédente (M. Schiff): «De la nature des granulations qui remplissent les cellules hépatiques - amidon animal». *C. R. hebd. Acad. Sci. 48*: 884-886.

Bernard C (1865) *Introduction à l'Etude de la Médecine Experiméntale*. Baillière. Paris, France. 398 pp. Trans. into Spanish, Bernard, 1880, 1900, 1959; English, Bernard, 1927; and German, Bernard, 1961.

Bernard C (1866) *Leçons sur les Proprietés des Tissus Vivants*. Baillière. Paris, France. 492 pp.

Bernard C (1872) *Leçons de Pathologie Expérimentale*. Baillière. Paris, France. 604 pp.

Bernard Claude (1876) *Leçons sur la Chaleur Animale, sur les Effets de la Chaleur et sur la Fièvre*. Baillière. Paris, France. 471 pp.

Bernard C (1877) *Leçons sur la Diabète et la Glycogenèse Animale*. Baillière. Paris, France. 576 pp.

Bernard C (1878) *La Science Expérimentale*. Baillière. Paris, France. 440 pp. It includes lectures on Bernard by JB Dumas and P Bert, and Bernard's incorporation speech to the French Academy with his laudatio to Flourens, his predecessor at seat Nº 24 in *L'Académie Française.*

Bernard C (1878-79) *Leçons sur les Phénomènes de la Vie Communs aux Animaux et aux Végétaux*. Ballière. Paris, France. 2 vols, 404 pp., 564 pp. Trans. into English, Bernard, 1974.

Bernard C (1879) *Leçons de Physiologie Opératoire*. Posthumous. Baillière. Paris, France. 614 pp.

Bernard C (1880) *Introducción al Estudio de la Medicina Experimental. Traducción por el doctor Antonio Espina Cano.* 78 pp. Cit. Izquierdo, 1942.

Bernard C (1900) *Introducción al Estudio de la Medicina Experimental. Versión española de don Carlos García.* Imprenta de la E. Industrial Militar. A cargo de A B Cortés. Cit. Izquierdo, 1942. 78. pp.

Bernard C (1927) *An Introduction to the Study of Experimental Medicine*. Trans. Greene HC, with an Introduction by Henderson LJ. MacMillan. New York, USA. 226 pp.

Bernard C (1947) *Principes de Médecine Expérimentale*. Presses Universitaire de France. Paris, France. 308 pp.

Bernard C (1954) *Philosophie. Manuscripte inedite*.Chevallier J (Ed.) Paris, France. With Chevalier's essay, "La philosophie de Claude Bernard". Préface de J Godard. Boivin. Paris, France. 62 pp. This book as well as Dhurout (1939) contains reflections Bernard wrote as he was reading Cousin's translation of Tennemann's gigantic *Manuel d' Histoire de la Philosophie*, and Comte's *Cours de Philosophie Positive*.

Bernard C (1959) *Introducción al Estudio de la Medicina Experimental. Introducción de L. J. Henderson. (Traducción de Bernard 1927)*. Ateneo. Buenos Aires, Argentina. 271pp.

Bernard C (1960) *Einführung in das Studium der Experimentellen Medizin*. Translation by Szendro P. Introduction by Rothschuh KE, Barth JA. Leipzig, Germany. 350 pp.

Bernard C (1965) *Cahier de Notes 1850-1860. Édition intégrale du "Cahier Rouge"*. Grmek MD (Ed.). Gallimard. Paris, France. 315 pp.

Bernard C (1967) *The Cahier Rouge of Claude Bernard*. (Translit. Into English, tr. by Hoff HH, Guillemin L, Guillemin R). Cambridge, MA, USA. Also printed in Grande and Visscher (1967) Schenkman. Cambridge, MA, USA. 120 pp.

Bernard C (1974) *Phenomena of Life Common to Animals and Vegetables.* (Tr. by Cook RP, Cook MA). Burns & Harris. Dundee, Scotland, UK. 206 pp.

Bernard C, Huette C (1854) *Précis Iconographique de Médecine Opératoire et d'Anatomie Chirurgicale*. Méquignon Marvis. Paris, France. 495 pp. This book was in Viladerbo's library in Montevideo. Tr. (1861) by van Buren WH, Isaacs CE as *Illustrated Manual of Operative Surgery and Surgical Anatomy.* Bailliere. New York, USA. 513 pp.

Dhurout E (1939) *Claude Bernard. Extraits de son Œuvre. Avec an Exposé de sa Philosophie Emprunté à l'œuvre de Henri Bergson*. With Henri Bergson's address at the centenary celebration of Bernard's birth (12/30/1913) at *Collège de France*. Presses Universitaires de France. Paris, France. 140 pp.

Dostoievski FM (1879-1880) *Los Hermanos Karamázov*. Aguilar. Madrid (1949). pp 467-468.

Foster M (1899) *Claude Bernard*. Fisher Unwin. London, UK. 245 pp.

Grande F, Visscher MB (Eds.; 1967) *Claude Bernard and Experimental Medicine*, *Symposium commemorating the centenary of the publication of An Introduction to the Study of Experimental Medicine, and the first English translation of Bernard's The Cahier Rouge,* Cambridge, MA. The Symposium forms the 1st. part of this book; (210 pp.); The *Cahier Rouge*, the 2nd. (120 pp). Schenkman. Cambridge, Mass.

Grmek MD (1967) *Catalogue des Manuscrits de Claude Bernard. Avec la Bibliographie de ses Travaux Imprimés et des Études sur son Oeuvre*. Collège de France. Masson. Paris, France. 420 pp.

Grmek MD (1973) *Raisonnement Expérimental et Recherches Toxicologiques chez Claude Bernard.* Droz. Genève-Paris. 474 pp.

Grmek MD (1991) *Claude Bernard et la Méthode Expérimentale*. Payot. Paris, France. 192 pp.

Henderson LJ (1927) *Introduction* to Bernard, 1927, pp. v-xii.

Henderson LJ, Murray CD (1925) Blood as a physicochemical system. III. *J. Biol. Chem. 65*: 407-417.

Holmes FL (1974) *Claude Bernard and Animal Chemistry. The Emergence of a Scientist*. Harvard University Press. Cambridge, MA, USA. 541 pp.

Houssay BA (1972) El significado de la obra de Claude Bernard**.** *Medicina e Historia. 14*: 1-26.

Izquierdo JJ (1942) *Bernard, Creador de la Medicina Científica. Estudio Crítico de su Labor Científica Seguido de una Versión Castellana de su Introducción al Estudio de la Medicina Experimental*. Imprenta Universitaria de México. 329pp.

Magendie F (1809) Examen de l'action de quelques végétaux sur la moelle épinière. *Nouv. Bull. Scient. Soc. Philomat. 1*: 368-405.

Magendie F (1816) Mémoire sur les propriétés nutritives des substances qui ne contiennent pas d'azote. *Bull. Soc. Philomat. 4*: 137.

Magendie F (1836) *Precis Elementaire de Physiologie*. 4ème éd. (The 1st ed. was published in 1816-1817). Mequignon-Marvis. Paris, France. Vol I, 456 pp; vol II, 628 pp.

Magendie F (1837) *Leçons sur les Phénomènes Physiques de la Vie Professées au Collège de France*. Hauman, Cattoir. Bruxelles, Belgique. Facsimile reprint (2002) of the original edition as Elibron Classics by Adamant Media. Boston, MA, USA. 347 pp.

Olmsted JMD (1938) *Claude Bernard, Physiologist*. Harper. New York, USA. 272 pp.

Olmsted JMD (1944) *François Magendie: Pioneer in Experimental Physiology and Scientific Medicine in XIX Century France. Preface by John F. Fulton*. Schuman. New York, USA. 290 pp.

Olmsted JMD, Olmsted EH (1952) *Claude Bernard and the Experimental Method in Medicine*. Schuman. New York, USA. 277pp.

Pi-Sunyer J (1944) *El Pensamiento Vivo de Claude Bernard*. 2ª ed. (1965). Lozada. Buenos Aires, Argentina. 231 pp.

Robin ED (Ed.; 1979) *Claude Bernard and the Internal Environment*. Dekker. New York, USA. 299 pp.

Rodriguez de Romo AC (1989) Tallow and the time capsule: Claude Bernard's discovery of the pancreatic digestion of fat. *Hist. Philos. Life Sci. 11*: 243-274.

Rodriguez de Romo AC, Borgstein J (1999) Claude Bernard and Pancreatic Function revisited after 150 years. *Vesalius 1*: 18-24.

Roll-Hansen N (1976) Critical teleology: Immanuel Kant and Claude Bernard on the limitations of experimental biology. *J Hist. Biol. 9*: 59-91.

Schiller J (1967) *Claude Bernard et les Problèmes Scientifiques de son Temps*. Éd. du Cèdre. Paris, France. 231 pp.

Sertillanges AD (1944) *La Philosophie de Claude Bernard*. Aubier. Paris, France. 256 pp.

Singer C, Underwood EA (1962) *A Short History of Medicine*. 2nd ed. Oxford University Press. Oxford, UK. 854 pp.

Tenney SM (1991) Physiology and literature. *News Physiol. Sci. 6*: 45-47.

Zola E (1880) *Le Roman Expérimental*. Flammarion (2006). Paris, France. 460pp.