In memoriam : Carl Ludwig / [William Stirling].

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CARL LUDWIG,

1816–1895.

BY

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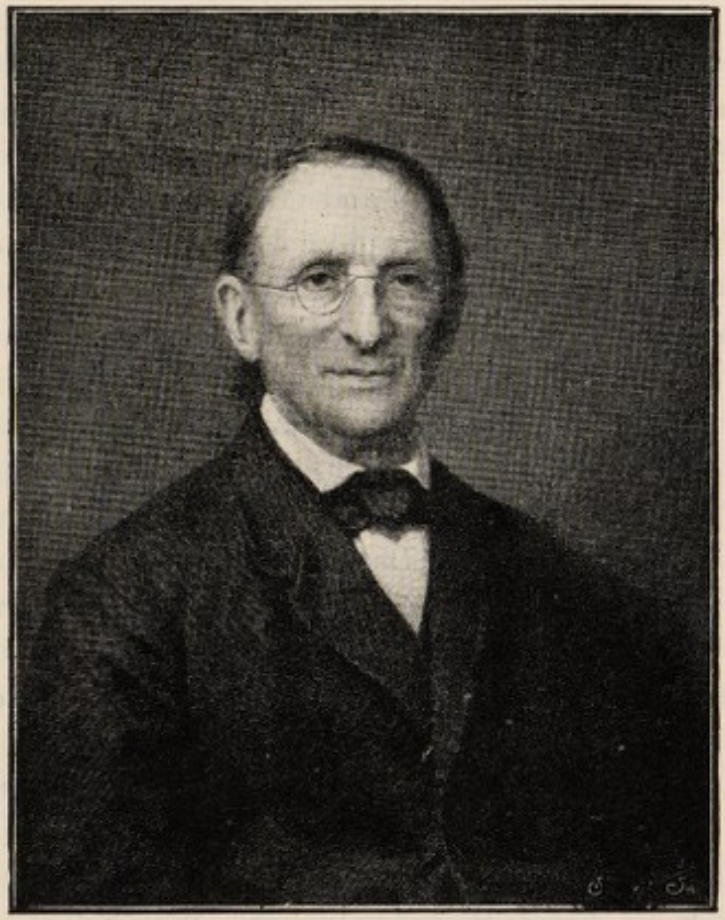
THROUGH the death of Professor C. Ludwig, which occurred at Leipzig on April 23rd, medicine has lost one of its greatest teachers of physiological science, and one whose discoveries in physiology have exerted, and will continue to exert, a lasting, beneficial, and practical influence on the science and art of medicine.



[We are indebted to the proprietors of the *Lancet* for this portrait.]

Carl Friedrich Wilhelm Ludwig—more familarly known by the simple signature of C. Ludwig—was born on December 29, 1816, in Witzenhausen, in Kurhessen. He studied in the small Hessian Univerversity of Marburg, and afterwards in Erlangen, and became Doctor of Medicine in Marburg, in 1839, at the age of 22. In the latter University he became successively Prosector in the Anatomical Department (1841), "Privat-docent" of Physiology (1842), and Professor of Comparative Anatomy (1846). In 1849 he was appointed Professor of Anatomy and

Physiology in Zurich. In 1855 he was invited to Vienna as Professor of Physiology and Zoology in the Josephinum, then a school for army surgeons, but since abolished. In April, 1865, he was called to Leipzig, and there he died in April, 1895, having spent in that old Saxon town thirty years of uninterrupted activity. On the occasion of his jubilee, on the fiftieth year of his Doctorate, he was presented with the freedom of the city of Leipzig. Year after year brilliant discoveries in physiology were made in the now famous "Physiologische Anstalt" of Leipzig, the first of its kind, and the parent of the now numerous "Anstalten" and "Instituts" which are to be found in all university towns on the Continent.

Although Ludwig "habilitirt" as a teacher of Physiology, his early training and bias led him to take a deep interest in anatomy, both human and comparative. This always reflected itself in his own work and that of his pupils. Always an anatomical and a histological investigation, where possible, formed the groundwork for the solution of a physiological problem. Dissection and microscopy were made the handmaidens and efficient coadjutors in physiological work. One has only to look at the beautifully illustrated monographs which have recently been issued from his laboratory to see how his keen insight found expression in the works of his pupils.

Take for instance: "Die Blut- und Lymphwege im Dünndarm des Hundes," by J. P. Mall;[1] "Untersuch. ü. d. papillæ foliatæ et circ. d. Kaninchens," by O. Drasch;[2] "Die Vertheilung der Blutgefässe im Muskel," by W. Spatleholz;[3] "Das reticulirte Gewebe," by F. Mall;[4] "Beiträge z. Kenntniss d. Füllung und Entleerung d. Herzens," by L. Krehl;[5] "Die Wege d. Blutstromes i. mensch. Ohrlabyrinth," by Eichler;[6] and the more recent monograph on the blood vessels of the larynx by Spiess.[7]

All these, and many previous similar contributions, inspired by his genius, show the true way of physiological investigation. Up to the time when Ludwig came to Leipzig, anatomy and physiology were still taught together by Ernst Heinrich Weber. Weber died in 1878. In 1865 physiology was separated as an independent "discipline," so that Ludwig was the first professor of physiology in Leipzig.

The writer of the present article can well remember seeing Ernst Heinrich Weber as a man short in stature, with long silvery locks, walking about Leipzig, supported on the arm of his tall stalwart son-in-law, the late Professor Braune. Professor His was then, as now, the

[1] "Abhand. d. Math-phys. Classe d. Kön. Säch. Ges. d. Wissen." Leipzig, 1887.

[2] *Ibid.*, 1887. [3] *Ibid.*, 1888. [4] *Ibid.*, 1891.

[5] *Ibid.*, 1891. [6] *Ibid.*, 1892. [7] *Du Bois' Archiv*, 1894.

professor of anatomy, but E. H. Weber always notified in the calendar, or what corresponds to it, that he would lecture on the Anatomy of the Leech.

Ludwig was, besides being an original thinker, a great teacher, a teacher in this sense, that he trained numerous pupils in his laboratory who made physiology the basis of their future researches. Early was this characteristic phase in his teaching manifested. These pupils worked in his laboratory at original research, guided by the master mind of Ludwig. Amongst his earliest pupils were A. Fick, who succeeded him in Zurich, and who is now Professor of Physiology in Würzburg; Conrad Eckhard, Professor of Physiology in Giessen; Lothar Meyer, the distinguished chemist of Tübingen, who early under Ludwig investigated the gases of the blood; Cloëtta and Westphal.

The contributions made to physiology by Ludwig under his own name are not numerous, but they are both important and "epoch-making," to use a German phrase. His "Lehrbuch der Physiologie des Menschen" (second edition, Leipzig and Heidelberg, 1858-61), is still a standard work on the subject, but it has also an important historical interest, for in it he lays down the views which guided his methods of research, and therein he postulates his physiological faith. The book opens with the following words: "Die wissenschaftliche Physiologie hat die Aufgabe, die Leistungen des Thierleibes festzustellen und sie aus elementaren Bedingungen desselben mit Nothwendigkeit herzuleiten." His aim is to prove that "alle vom thierischen Körper ausgehenden Leistungen eine Folge der einfachen Anziehungen und Abstossungen sind." In other words, he desired to get rid of vague speculations, and sought to investigate the phenomena of living things by the methods applicable to the sciences of physics and chemistry, and to explain their phenomena by the laws of physics and chemistry, or at least to bring them into line with the phenomena of physical science. This constant reference of physiological phenomena to the facts of physics and chemistry was the key-note of his investigations, and, along with his friends Brücke, du Bois-Reymond, and Helmholtz, to whom he dedicated his "Lehrbuch," these four dealt what many considered a death-blow to the doctrine of "vital force," or "vitalismus," so strongly supported by Johannes Müller. Alas! of all the four du Bois alone survives.

The bias of his mind to explain physiological phenomena by a reference to physical facts was shown in his thesis, which he presented when he became "Privat-docent," in Marburg—"Beiträge zur Lehre von Mechanismus der Harnsecretion" (1842), in which he gave a purely physical or mechanical explanation of the process of urinary secretion, and in subsequent years he devised numerous physical experi-

ments to support his thesis, *e.g.*, "Ueber endosmotische Aequivalente und endosmotische Theorie[1]," similar experiments with his pupil Cloëtta (1851), and his own subsequent researches on this subject[2]. Between his earlier research with Goll showing the dependence of the secretion of urine upon blood pressure, and the latest researches by Thompson on the effect of atropine on renal secretion, and Grijns[3] on the temperature of the renal blood and urine, there are numerous contributions to the physiology of renal secretion, including that of Ustimowitsch,[4] who showed the effect of curare in diminishing the secretion, the effect of section of the renal nerves, and also the important fact that urea—when injected into the blood vessels, the blood-pressure being very low—caused a renewed secretion of urine. In 1890 Slosse studied the effects of ligature of the three mesenteric arteries on the secretion of urine, while in 1893 in the paper of Grijns already mentioned it is shown that "the kidneys produce heat in proportion to the water they excrete," and we have the other remarkable fact "von den ihre sonstige Leistung beherrschenden Nerven empfangen die Muskeln und Speicheldrüsen den Anstoss zur Wärmeleistung, die Niere dagegen nur dann, wenn das Blut mit harnfähigen Stoffen beladen wird"—*i.e.*, it is not nerves which determine heat production in the kidney, but the presence of urea and other "harnfähigen" substances. This fact must have some relation to that discovered by Ustimowitsch. The name of Ludwig, as well as that of Bowman, is indissolubly bound up with the theory of urinary secretion. Let any one read the article "Nieren und Harnbreitung," in "Wagner's Handwörterbuch[5]"—extending to twelve pages—and the similar chapter in his "Lehrbuch," and he will obtain some notion of the ingenuity with which Ludwig supported his thesis.

I have already spoken of his "Lehrbuch," which passed through two editions. After becoming engrossed with laboratory work in Leipzig, he found it an uncongenial task to issue a new edition, but any one who cares to look into it, will find therein much of Ludwig's subsequent work foreshadowed, as well as inspiration for the investigation of new problems.

In Vienna he became the fast friend of Brücke, for whom he always entertained the warmest regard. Here, too, he knew Hyrtl, and numerous were the anecdotes that he sometimes told of the peculiarities of the Vienna anatomist. So great was Ludwig's fame as a teacher and investigator, that in Vienna he soon formed a school of physiology, and amongst others whose names are household words, not only in physiology, but other departments of medicine, he had as pupils Czermak, at that time working with Türck on the laryngoscope; Politzer, who worked

[1] *Zeitsch. f. rat. Med.*, VIII. [2] "Sitzungsb. d. Wiener Akad," XX., 1856. [3] *Du Bois Archiv*, 1893. [4] Arbeiten, V. 1870, p. 199. [5] Vol. II., p. 628, 1844.

on the movements of the ear ossicles; von Recklinghausen, Kühne, Stephan, Jendrassik of Buda-Pesth, Setschenow of Odessa, Einbrodt, Preyer, Holmgren of Upsala, and many others. Thus his fame as a teacher and as an investigator was spread throughout Europe, although at that time apparently it was not the custom for Englishmen to study in foreign laboratories, although they frequently enough visited the various cliniques.

One of the most epoch-making inventions of Ludwig was the recording of the oscillations of the blood pressure in animals by means of his "kymograph." Although the blood pressure had been measured in the horse in terms of a column of blood by the Rev. Stephen Hales, of Teddington, in 1727, and although Poiseuille in 1828 had used a Hg-manometer to measure the arterial blood pressure, the oscillations of the column of mercury being observed by the eye, it remained for the genius of Ludwig to convert the hæmodynamometer of Poiseuille into a kymograph, by which the oscillations were recorded on a cylinder moved by clock-work. The kymograph, or kymographion[1]—as he called it, was invented in 1847, when Ludwig was still in Marburg. The original description of this instrument is given in his paper in the *Archiv* already referred to, entitled "Beiträgen zur Kentniss des Einflusses der Respirationsbewegungen auf den Blutlauf im Aortensysteme." Here is the simple yet classical description of this instrument, which has become a necessity in all physiological and many other laboratories, and which was the parent of the sphygmograph and many other instruments of precision now employed in medicine. "Um durch ihn (Poiseuille's Quecksilbermanometer) nun gute Druckzahlen unter allen Umständen und zugleich Zeitbestimmungen für die Dauer und Folge der einzelnen Druckgrössen zu erhalten, setzt man auf das Quecksilber einen stabförmigen Schwimmer, versieht ihn am oberen Ende mit einen Feder und lässt diese Schwankungen auf eine Flache zeichnen, welche sich mit gleichförmiger Geschwindigkeit an der Feder vorbei bewegt. Auf diese Weise erhält man Curven, deren Höhe ein Ausdruck für den Blutdruck, deren Breite eine Bestimmung der Zeit enthält." This was indeed an epoch-making invention, and it is characteristic of the man to note in what terms he describes this apparatus in his "Lehrbuch."[2] There one finds a figure of the original form of the instrument, with a description of it in small type, and he states that "it depends on a principle which was first employed by the celebrated Watt."

Later, by a simple method, his pupil, v. Kries, now Professor of Physiology in Freiburg, measured the blood pressure in the capillaries.[3]

Thus he founded the graphic method, and gave it back in an improved form both to Physics and Meteorology. With the invention of the

[1] J. Müller's *Archiv*, 1847. [2] Lehrbuch, p. 123. Second Edition. [3] Arbeiten, X., 1875.

kymograph a new territory was opened up, and consequent on this followed numerous investigations by Ludwig and his pupils. The whole hydrodynamics of the circulation had still to be investigated, and, with Stephan, he carried out a purely physical investigation—"Ueber den Druck, den das fliessende Wasser senkrecht zu seiner Stromrichtung ausübt."[1] This apparatus, composed of metal tubes, with vertical manometers—designed to show how the variations of pressure and velocity could be accounted for by physical means—Ludwig used to show regularly in his lectures, and he has figured the apparatus, and recorded his results in his "Text book."

Ludwig and his pupils published many researches on the variations of the blood-pressure in different parts of the vascular system in different animals, the effect of the respiratory movements of the chest wall (Einbrodt), and other conditions on the blood stream.

The influence of the nervous system on the blood stream was investigated by Ludwig and Thiry in a most important and classical paper, entitled "Ueber den Einfluss des Halsmarks auf d. Blutstrom."[2] Besides other important facts stated in this paper he showed that the portal system by its varying and variable capacity largely regulated the blood pressure in the branches of the aorta. In his inaugural address at Leipzig, his subject was "Die physiologische Leistungen des Blutdrucks."[3] In this address he gave a sketch of all that he and his pupils had done up to that time, and foreshadowed a plan for future investigations.

In 1871 Owsjannikow ascertained the position from which the vasomotor nerves in the rabbit obtain their tonic excitement to be 1—2 mm. below the corpora quadrigemina and 4—5 mm. above the calamus scriptorius, *i.e.* in the direction from above downwards in a space of 4 mm.

In 1873, with C. Dittmar, he defined more precisely the position of the vasomotor centre in the medulla oblongata.

In 1867 appeared the first volume of the famous "Arbeiten aus der physiologischen Anstalt zu Leipzig," issued under the unassuming title "mitgetheilt durch C. Ludwig," in which there is recorded a mass of work of the highest physiological and practical value, such as the writer of this notice believes has never been issued from any one laboratory, the guiding, inspiring spirit contenting himself in many cases with the simple "communicated by."

In Vol. I. of the "Arbeiten" we have a record of the work done in the small temporary laboratory, which includes two classical researches relating to the circulation, one the discovery of the "depressor nerve," under the title E. Cyon and C. Ludwig, "Die reflexe eines d. sensiblen Nerven des Herzens auf d. motorischen der Blutgefässe," accompanied by a drawing of the nerves of the neck in the rabbit, itself a testimony

[1] Sitzb. d. Wiener Akad., 1858. [2] "Sitzb. d. Wiener Akad., 1864. [3] Leipzig, 1865.

to the anatomical instinct of Ludwig. In the depressor nerve—a sensory or afferent nerve from the heart, which is connected with the bulb—he found a nerve which when its central end was stimulated greatly lowered the tone of the vaso-motor centre, and "durch ihn vermag der wesentlichste Motor des Blutlaufs (das Herz) die Wiederstände zu regeln, die er selbst überwinden soll." Whatever drawings or illustrations appeared in the "Arbeiten" had to be both accurate and artistic. In the same volume we have Lovén's paper, "Uëber d. Erweiterung von Arterien in Folge einer Nervenerregung," to wit, the effect of stimulation of the auricular nerves or nervus dorsalis pedis, which produce reflex dilatation of vessels, and the discovery of the action of the nervi erigentes. The influence of temperature on the heart beat by Cyon and several other classical papers, including that on the lymphatics of the central tendon of the diaphragm, by Schweigger-Seidel and himself, and Dybkowski's paper on "Absorption from the pleural cavity," make up the record of work done in the small temporary laboratory during one year.

From this time forward uninterruptedly a series of memoirs on the vascular system were issued from his laboratory and published by his pupils. Here Lauder Brunton[1] studied more fully the action of amyl nitrite on the blood stream. In 1874 A. Mosso ("Ueber einigen neuen Eigenschaften der Gefässwand"[2]), under the inspiration of Ludwig, began those researches on the excised kidney which proved that the blood vessels of peripheral organs may undergo variations in size independently of the central nervous system, and which led to the recording of the volume of an organ by various forms of plethysmograph, which have proved so valuable in the investigation of the functions of other organs. Schmiedeberg's[3] classical paper, "Einige Giftwirkungen am Froschherzen," showing the action of muscarin, opened up a new sphere of investigation, viz., the action of drugs on the heart.

In no laboratory has the physiology of the heart been so thoroughly investigated as in that of Leipzig, for with Ludwig this was ever a "Lieblingsthema." The arrangement of the muscular fibres of the heart wall early attracted his attention, and continued to do so throughout. The paper already referred to by Krehl, and that by Ludwig and Hesse on the shape of the heart in systole and diastole, are but an extension of the same subject. The same subject crops up again in 1884, when Conrad Gompertz[4] investigated the arrangement of the muscular fibres of the heart of the frog. Ludwig often spoke of the masterly manner in which Gompertz carried out this thema. The stereoscopic pictures of the arrangement of the muscular fibres in the interior of the frog's heart are really works of art.

[1] Arbeiten IV., 1869, p. 101. [2] Arbeiten IX., 1874. [3] Arbeiten V., 1870. [4] *Du Bois Archiv*, 1884, p. 244.

Ludwig, in his inaugural address, had foreshadowed a method which has been most fruitful in its results, not only in physiology, but in pharmacology, viz., the circulation of blood or other fluid through an "excised" organ, or through the blood vessels of "excised surviving organs" (*i.e.*, "Ueberlebender Organe"), *i.e.*, the process of "perfusion." Using the excised heart and the frog-manometer, H. P. Bowditch ("Ueber die Eigenthumlichkeiten d. Reizbarkeit, welche die Muskelfazern d. Herzens zeigen") showed that the frog's heart-muscle, quite independently of the strength of the stimulus, always gave a maximal contraction, *i.e.*, it either contracted or it did not, and when it did contract its beat was always maximal, or, as it has recently been put, "all or nothing." Kronecker conclusively proved that the heart muscle could not be tetanised. It is interesting in this connection to refer to Ludwig's own words, who, in speaking of the peculiarities of cardiac excitability,[2] says that "induction shocks which are sufficient to throw every other nerve muscle into tetanus only cause the normal heart, through which blood is circulating, to beat faster; *i.e.*, the condition of excitability of the heart prevents it from passing into tetanus." There are numerous researches on the excised frog's heart by Schmiedeberg (1870), Luciani ("Periodic Function of the Frog's Heart," 1872), Rossbach (1874), Merunowicz (1875), Kronecker, and many others.

Coats[3] showed how the work of the heart varied with stimulation of the vagus. With Dogiel,[4] Ludwig devised a method of measuring the amount of blood flowing out of the vessels—"Die Ausmessungen d. strömenden Blutvolumina"; and herein is described the famous "Stromuhr." A year later—"Ein neuer Versuch über den ersten Herzton"—Ludwig and Dogiel devised those classical experiments which showed the importance of the cardiac muscle in the production of the first sound of the heart, a view returned to later by Ludwig and Krehl[5] in 1888. The latter also investigated the mechanism of closure of the tricuspid valve. Later, in 1886,[6] we have Stolnikow measuring the velocity of the blood in the aorta of the dog by another modified and extremely ingenious "Stromuhr."

There are also papers on "The effect of the vagus and accelerans on the heart," Baxt (1875); "Intra-cardiac Pressure," Waller (1878); on "The accelerans cordis," Münzel (1887), Pawlow (1887), Hüfler (1888), Johannson on "Vasomotor Nerves," chiefly the influence of stimulation of the splanchnic nerves on the aortic blood pressure; F. Mall in 1892 showed the influence of the portal vein on the distribution of blood (1891); Krehl (1892), Öhrwall (1893); and on "The pulse," v. Frey and Krehl (1890).

[1] "Ludwig's Arbeiten," VI., 1871. [2] "Lehrbuch," p. 91, Second Edition. [3] "Ludwig's Arbeiten," IV., 1869. [4] "Ludwig's Arbeiten," II., 1867. [5] *Du Bois Archiv*, 1888, p. 253. [6] *Ibid*, 1886.

Besides the mechanical relations of the circulation, the exchange of gases between the blood and the air in the lungs on the one hand and the lymph on the other, together with the source and composition of the lymph itself, were also favourite subjects of investigation.

The analysis of the blood-gases begun under Ludwig by Lothar Meyer, in Zurich, carried forward by Setschenow,[1] in Vienna, and the construction of a gas-pump for the extraction of the blood-gases, gave a new impulse to the study of the gaseous exchanges taking place in the body. In 1865 Ludwig published in the *Wiener medicinischen Jahrbüchern* a "Zusammenstellung der Untersuchungen über Blutgase." These were followed by the researches of Kowalewsky, Ludwig, and Alexander Schmidt, "Uber CO_2 in d. Blutkörperchen,"[2] "Die Athmung innerhalb d. Blutes,"[2] "Das Verhalten d. Gase, welche mit d. Blut. d. d. reizbaren Säugethiermuskeln strömen;"[3] and by J. J. Müller,[4] "Uber die Athmung in d. Lunge," all of which are classical researches on gaseous exchanges. The CO_2 excreted by a passive and active muscle was investigated by Minot (1876); the CO_2 in the lymph by Hammarsten (1871), Tschiriew (1874), and by Buchner (1876); the O- tension in asphyxiated blood by Manille Ide, in 1893; and the action of sugar on the blood gases by V. Harley (1894). How thoroughly Ludwig investigated a problem can be seen from even one example: the respiratory exchanges of the blood and lymph, a problem begun in the early sixties, and one still being worked out by his pupils to the end. In .the paper by Slosse the fundamental proposition is laid down, "If one wishes to understand the process of respiration, then one must employ or search for methods, which will enable us to determine the contributions made to the respiratory exchanges by the individual organs and tissues." On this follows immediately the paper by Franz Tangl, wherein it is shown that directly after ligature of the mesenteric arteries the general respiratory exchanges are diminished by 30 per cent.

As to lymph secretion, we have not yet heard the last of his "mechanical theory," indeed the latest observations of Starling strongly support Ludwig's contention. The numerous experiments on lymph secretion, beginning with those of Tomsa, are classics in this chapter of physiology. Schweigger-Seidel and Dogiel showed the communication between the peritoneal cavity and the lymphatic system in the frog (1866); Genersich (1870) the absorption of lymph by tendons and fasciæ; Lesser (1871) showed how large quantities of lymph are to be obtained by movements of a limb; Paschutin (1872) studied the outflow in the forearm of the dog, while Emminghaus (1873) showed the dependence of lymph production on increased venous pressure; Budge

[1] "Ludwig's Lehrbuch d. Phys.," p. 473. Second Edition, 1860. [2] "Arbeiten," II., 1867.
[3] *Ibid.*, III., 1868. [4] *Ibid.*, IV., 1869.

(1874) investigated the lymphatics of the liver, which was followed by a paper by Fleischl (1874) on liver-lymph, while Merunowicz (1876) demonstrated the influence on abdominal lymph of muscarin, nicotin, and veratrin.

To Ludwig we owe the "Puncture," or "Einstich" method of injecting the lymphatics, by means of which he and Schweigger-Seidel were enabled to inject the lymphatics of fascia and tendon, and their results they published jointly in a beautifully illustrated monograph, "Die Lymphgefässe d. Fascien und Sehnen." (Leipzig, 1872.)

There are also numerous investigations on the general physiology of muscle and nerve by Kronecker (fatigue and recovery of muscle), in 1871; by Tiegel (1875); by v. Kries and Sewall (1881); "On the Heat Formation in Muscle," by Meade Smith (1881); Lujankow and P. Starke (1890); Ch. Bohr on "Tetanus" (1882); Tigerstedt on "Latent Period of Muscle" (1885); v. Frey on "Compound Contractions" (1888); and Bowditch on "The Non-fatigue of Nerves" (1890); by Sobieranski, Buckmaster, Lee, and others.

Many contributions were also made to the histology and physiology of the sense organs by his pupils, Prussak ("Blood Vessels of the Membrana Tympani," 1868), Schweigger-Seidel ("Cornea," 1869), J. J. Müller ("Elastic Vibrations, Sensation of Depth," 1871), Paschutin ("Olfactory Region," 1872), Klug ("Temperature Sense," 1876), Drasch, Eichler, and others.

By his classical researches on the sub-maxillary gland, "Neuen Versuche über d. Beihilfe d. Nerven z. Speichelabsonderung," Ludwig completely modified the theory of salivary secretion and of secretion in general. By his pupils, Becher, Rahn, Spiess, and Giannuzzi—and later Gaskell and Novi—the doctrine of secretion was placed on a new basis, Ludwig having shown that secretion could not be directly dependent on blood pressure, as secretion might take place when the pressure in the salivary duct was greater than that in the carotid artery, and moreover secretion might be made to take place in a decapitated head, provided the lymphatic vessels contained lymph. One of the most interesting chapters in the "Lehrbuch"[1] is that on the secretion of saliva, where Ludwig points out that saliva "belongs to the juices which flow out only when the nerves going to the gland are stimulated directly or are excited reflexly." Still desiring to know more of the forces concerned in salivary secretion, he set Novi[2] the task to investigate "Die Scheide-kraft d. Unterkieferdrüse," in 1889.

Under his direction too, numerous were the contributions to physiological chemistry. Cloëtta discovered inosit and uric acid in animal tissues.

[1] *Loc. cit.* p. 328. [2] *Du Bois Archiv*, 1889.

Pribram determined the presence of lime and phosphoric acid in the blood by a new method, while the digestion and absorption of fat and fatty acids and their fate in the economy were the subject of numerous investigations by Röhrig[1], Zawilski[2], and were continued by Cash[3] ("D. Antheil d. Magens u. d. Pancreas a. d. Verdauung d. Fettes"), and v. Frey[4] ("Die Emulsion d. Fettes im Chylus"). The papers of Ogata[5] and v. Anrep[6] on allied subjects, Zebedeff[7], v. Walther[8], and Frank, all extended these researches on fat absorption.

Schmidt-Mulheim[9] proved that after complete occlusion of the thoracic duct, the digestion and absorption of proteids, as well as their transformation into urea, takes place just as when the thoracic duct is free. Ogata showed that digestion of proteids took place in the dog after excision of the stomach (1883).

There is a whole series of memoirs on absorption of various substances from the alimentary canal, *e.g.*, sugar, and the channels by which they are absorbed, beginning with v. Mering's[10] paper "Die Abzugswege d. Zuckers a. d. Darmhöhle," which showed conclusively that the chyle is not essentially concerned in the absorption of sugar, that lymph contains sugar nearly in the same proportion as blood, while the blood itself—even after starvation has caused glycogen to disappear from the liver—still contains sugar. Brasol[11] showed that after excess of sugar is injected into the blood even after two minutes some has disappeared, while in two hours the blood contains its normal amount of sugar. Some at least of the sugar passes into the tissues, and some is excreted by the urine. Meade Smith[12] returned to the subject of absorption of sugar and proteids from the stomach, while Weyert[13] traced the presence of the sugar in the different tissues and juices of the body. Even in 1868 Scheremetjewski had investigated the effect on the respiratory exchanges of introducing into the blood bodies which are readily oxydisable, *e.g.*, the sodium salts of lactic, acetic, and formic acids, grape sugar, and glycerine. A similar subject was investigated by Harley in 1893. Lépine, now professor in Lyons, in 1868 investigated the origin and distribution of the animal sugar-forming ferment. It is interesting to note that even after a quarter of a century Lépine is still making contributions to a subject which he began to study under Ludwig. Klikowicz[14] investigated the fate of salts injected into the blood and the means by which the quantity of salts in the blood is regulated. We have numerous researches on the bile by Schmulewitsch (1868), Asp, Fleischl, Kufferatt (1880), and Vaughan Harley (1893), and on the secretion of pancreatic juice by N. O. Bernstein (1869).

[1] *Arbeiten*, IX., 1874. [2] *Ibid.*, XI., 1876. [3] *Du Bois Archiv.*, 1880, p. 323. [4] *Ibid.*, 1881, p. 382. [5] *Ibid.*, 1881, p. 515, and p. 504. [6] *Ibid.*, 1882, p. 488. [7] *Ibid.*, 1890, p. 329. [8] *Ibid.*, 1892, p. 497. [9] *Ibid.*, 1877, p. 549. [10] *Ibid.*, 1877, p. 379. [11] *Ibid.*, 1884, p. 211. [12] *Ibid.*, 1884, p. 481. [13] *Ibid.*, 1891, p. 187. [14] *Ibid.*, 1886, p. 518.

Following naturally on absorption of proteids came the researches of Schmidt-Mulheim[1] showing the remarkable effects produced by injecting so-called "peptones" directly into the blood; of Fano[2] on the action of peptone and tryptone on blood and lymph; of Lahousse (1889), Blachstein (1891), and Grandis (1892) on the diminution of the CO_2 in peptone-blood and the causes thereof.

Worm-Müller[3] and Lesser studied the effect of transfusion of blood, while Tscheriew[4] studied the fate of blood introduced into the alimentary canal, or rather the daily excretion of urea from proteids in the form of blood introduced either into the blood vessels or the alimentary canal; and Kunkel[5] the fate of the sulphur in combination taken with the food. In 1892, Geelmuyden found that consequent upon a great excess of blood being introduced into the vascular system, more nitrogen was excreted in the urine than was taken in the food, that this N-elimination lasted several days, and that the excess of red blood corpuscles was destroyed within the vessels themselves.

Wooldridge also from 1881 onwards produced a series of remarkable papers on the chemistry of the blood corpuscles, the coagulation of the blood and intra-vascular clotting (1883-88).

Gaglio investigated the lactic acid of the blood (1886), and Siegfried the presence of this acid in other tissues (1894). Lactic acid was proved to exist in the "surviving" liver (1887), while Rochwood found it in the urine (1895).

The reflex functions of the spinal cord were successively investigated by Sanders-Ezn (1867), W. Baxt (1871), Stirling (1874), Ward (1880), Walton (1882), and as bearing on this we have the results of laborious work by Birge, under the direction of Gaule, who counted the number of nerve fibres and cells in the spinal cord and nerve roots of the frog[6]; W. P. Lombard[7] (reflex muscular contractions); Sirotinin (1887) and De Boeck (1889) on punctiform stimulation of the cord. The long disputed question as to whether the grey matter of the spinal cord is directly excitable, Ludwig settled in the affirmative by means of limited mechanical stimulation of the cord.

The course of the afferent and efferent spinal impulses was investigated by Miescher,[8] now Professor of Physiology in Basel, "Zur Frage d. sensiblen Leitung i. Rückenmark," by Nawrocki,[9] Woroschiloff and Owsjannikow.[10] The influence of vaso-motor nerves on the circulation was investigated by Slavjansky (1873) and v. Basch (splanchnic area, 1875) G. Johannson (1891) and F. Mall (vena porta, 1892). The course of the vaso-motor nerves was investigated

[1] *Ibid.*, 1880, p.33. [2] *Ibid.*, 1881. [3] Arbeiten, VI., 1871. [4] *Ibid.*, VIII., 1873. [5] *Ibid.*, X., 1875. [6] *Du Bois Archiv*, 1882, p. 435. [7] *Ibid.*, 1885. [8] Arbeiten V., 1870. *Ibid.* VI., 1871. [9] *Ibid.*, V., 1870. [10] *Ibid.*, IX., 1874.

by Nicolaides,[1] while Hafiz and Gaskell (1876) investigated the influence of nerves on the blood vessels, or rather the changes in the blood stream in muscles by stimulation of their nerves, while v. Frey studied the mode of action of the vaso-dilator nerves of the sub-maxillary gland.

The exact peripheral distribution of nerves was always of interest to Ludwig, and he often quoted the remarkable researches of Türck[2] of Vienna on the sensory nerves of the dog. Indeed he reproduces Türck's figures in his text book. In them one sees foreshadowed the recent work of Sherrington. He had the highest regard for Türck as an accurate observer.

On only one or two subjects do I not remember to have seen any detailed researches, viz., on the physiology of the cerebrum and cerebellum. Whether it was he thought the methods used were too crude, or for whatever cause, investigations on cerebral physiology as at present conducted—viz., chiefly by electrical stimulation and excision—did not, so far as I recollect, engage much of his attention.

The strongly morphological bias of Ludwig's mind has already been referred to. As early as 1848 he discovered the presence of ganglionic nerve cells in the auricular septum of the frog's heart, and these ganglia still bear his name, while his memoir on the histology of the kidney in Hermann's Handbuch is still the standard article on this subject. With many of his pupils he carried out histological researches, *e.g.*, on the salivary glands (Giannuzzi), eye (Leber, 1865), ear (Prussak, 1868, Eichler, 1893), pancreas (Ogata), liver (Budge, Fleischl), testicle (Mihalkowicz), skin (Stirling), cerebellum (Beevor), muscle, intestinal vessels (Heller, 1872, Mall, 1888), blood parasites or Würmchen (Gaule); in fact, on almost every organ in the body.

Many of these histological researches were carried out under the superintendence of his able histological assistants, Schweigger-Seidel, Schwalbe, Flechsig, Gaule and Drasch, while the chemical side was under the direction of Drechsel, and, latterly, of Siegfried. Kronecker, v. Kries, and v. Frey, in their capacity as assistants, gave most valuable aid to those working in the laboratory, more especially in the physical department. The present writer has specially to thank Professor Kronecker for much valuable aid in carrying on his researches, and also for instruction in that knowledge of many methods which is specially valuable to one who intends to devote his life to physiology. Not to be forgotten is the invaluable aid of Salvenmoser when apparatus had to be devised and fitted up.

It was while Flechsig was assistant to Ludwig that he carried out that series of investigations on the time when nerve fibres become medullated, which have made his name famous.

[1] *Du Bois Archiv*, 1882. [2] p. 160, Second Edition.

On reviewing Ludwig's work one sees in it not only the directing hand, but also how it was planned by a master mind, so that pupil after pupil amplified and extended the work of his predecessors, and thus secured that continuity of investigation which has produced such prolific results. It was only with great difficulty that he overcame his dislike to operating upon animals, and he did so only under the firm conviction that the results thereby obtained are and would be beneficial to humanity at large. He was most strongly opposed to any unnecessary torture or operations upon animals, and for twenty years he was president of the Leipzig Society for the Protection of Animals, and he remained to the end a member of this society.

Apart from the separate publications cited above, the work of Ludwig and his pupils will be found in the following publications: J. Müller's *Archiv* (1843-49); Henle and Pfeufer's *Zeitsch. f. rat. Med.* (1844-55); *Verhandl. d. Züricher Natur. Gesellsch.* (1852-55); *Sitzb. d. Wiener Akad. d. Wissensch.* (1856-64); *Ber. d. k. Sächs. Gesellsch. d. Wissensch. zu Leipzig* (1865-94). During the years 1866-77 the work of Ludwig, which was always communicated to the "Sächische Akademie," was reproduced separately as the famous "Arbeiten aus der physiologischen Anstalt zu Leipzig," *i.e.*, for eleven years (Jahrgang 1—11), and in these will be found many standard papers on the subjects to which these papers relate. These memoirs were always well illustrated, for the "Akademie" has a fund left by J. Alexander Jablonowski for the publication of scientific works. Ludwig was a member of this society for thirty years, and in its work and publications he took the deepest interest. He rarely missed attending a meeting, and for eleven years he acted as secretary, and generally conducted the affairs of the society.

With the foundation of *Du Bois Reymond's Archiv* in 1877, Ludwig agreed to publish his work and that of his pupils in that journal, so that the famous "Arbeiten" ceased to be sold as a separate work, and the fruits of his labours and those of his pupils must therefore be sought for in that journal from 1877 onwards.

It is sincerely to be hoped that all his works, and those of his pupils, will be reproduced in a permanent and easily accessible form.

On the 15th October, 1874, Ludwig celebrated his silver jubilee as Professor of Anatomy and Physiology, on which occasion, as is usual in Germany, some of his pupils presented him with the well-known *Beiträge z. Anatomie und Physiologie* als Festgabe dedicated to Carl Ludwig. Few who were present at the subsequent dinner will ever forget the reunion of old friends and pupils that took place on that day. Again, on his seventieth birthday, he was the recipient of a similar honour.

He visited England twice, the first time along with Kronecker, who acted as his guardian and friend, and on the second occasion he came to London to receive the Copley Medal of the Royal Society. Ludwig always professed himself as unable to stand the sea voyage. Besides numerous honours conferred on him by learned societies abroad, and by the King of Saxony, he was a Foreign member of the Royal Society and an honorary member of the Physiological Society, while his paper with Cyon on the depressor nerve was "crowned" by the Paris Academy.

In his latter years he was fond of making models to illustrate his lectures, and ever and anon one saw the strongly pronounced mechanical bias crop up in the construction of apparatus for the solution of some problem or other.

As a teacher of physiologists he stood *facile princeps*. To use the words of his former assistant, Professor Hugo Kronecker, of Berne—"No physiologist ever had so many pupils of all nationalities as Ludwig; more than three hundred scientific men owe to him at least a part of their scientific education, and each one of them fell under the influence of his enchanting personality." "Der Zauber seiner Persönlichkeit ermuthigte die Zaghaften und Zähmte die Rohen" (Kronecker). In every country of the world is to be found some one who has worked in his laboratory, and from 1865 onwards there was to be found a constant succession of English and Americans and other nationalities who either wished to become physiologists, or who wished physiology to be the basis of their future pursuits in practical medicine. "Amongst his English and American pupils may be mentioned, in the order of time, Lauder Brunton, Coats, Bowditch, Rutherford, Moseley, Ray Lankester, Stirling, Minot, Gaskell, Ward, Waller, Cash, Sewall, Meade-Smith, Wooldridge, Walton, Beevor, Buckmaster, Carslaw, F. S. Lee, F. Mall, W. H. Thompson, and Vaughan Harley."[1]

The record of pupils has no reference to the ordinary students of medicine who listened to his lectures, but refers to those who, after completing their medical education, came to Leipzig to carry out original researches under his guidance, and to perform those fundamental experiments in physiology, many of which, owing to well-known reasons, could not be performed in this country. Moreover, in a laboratory like that of Ludwig's, where, perhaps, ten men at a time were carrying on different researches, it was an education to have the privilege of working there.

When one remembers that Ludwig's services were open to all who came to his laboratory inspired with the desire to do original work, and when one also remembers that laboratory fees or fees for apparatus were unknown, one can form some idea of his goodness and kindness. Moreover, when one recollects the pains he took to instil into one those

[1] *Lancet*, May 11, 1895.

precise methods of experimenting, and the necessity for the frequent confirmation of an observation, and the self-sacrifice on his part that all this involved, one cannot wonder that all his pupils revered him and honoured him as few teachers have ever been honoured or revered. There was a fascination about his manner and his discourse which was quite bewitching. For him the study of physiology was something more than the pursuit of a subject whose results had a direct practical bearing on the progress of medicine, and therefore on the material well-being of humanity; he prized it, also, for its relations to the fine arts, to music, to the doctrine of colour, and to progress in the study of language itself.

To listen to his talk on subjects outside physiology, whether on matters social, political, personal, or anecdotal, was to some of us a rare intellectual treat. Personally I shall ever retain an undying recollection of all his goodness and kindness. For many years it has been my privilege to visit him once a year, and, to the writer, both happy and profitable were the few days we annually spent together. He had always something new to show or to tell one. Often while we were talking would Salvenmoser, his attached and valued steward—be preparing some experiment which had been worked out during the previous year. His unfailing courtesy was known to all, while his indefatigable energy remained unimpaired until the last. To few men is it given to have a record of almost uninterrupted academic activity for fifty-six years. Five weeks before he passed away—from failure of the heart, following an attack of influenza—he conducted the examinations for the degree. This was the last act of his academic life. "Die Uhr stand still, der Zeiger fiel. Es war vollbracht." One may, with Kronecker, apply to him his own words, uttered in respect of his predecessor, E. H. Weber, "Jetzt, da er von uns geschieden, hat er uns ein reiches Erbe gelassen, aber unschätzbar Güter sind mit ihm ins Grab gesunken."

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