Louis Mialhe

RESUMEN. Louis Mialhe (1807-1886) fue un médico y farmacéutico francés que estudió las transformaciones químicas de los cloruros de mercurio, la fabricación del éter etílico, etc., y numerosos fenómenos fisiológicos en seres humanos, entre ellos, la diabetes, los mecanismos de la asimilación de carbohidratos, grasas, y albuminoides, la acción de la saliva, pepsina, y el jugo gástrico sobre los alimentos, la acción de diversos purgantes de acuerdo con su naturaleza, etc. Sus trabajos sobre fisiología humana lo llevaron a descubrir la presencia de una diastasa en la saliva y a sugerir una teoría sobre el origen de la diabetes.

ABSTRACT Louis Mialhe (1807-1886) was a French physician and pharmacist who studied the chemical transformations of mercury chloride, the manufacture of ethyl ether, etc., and numerous physiological phenomena in human beings, among them, diabetes, the mechanism of assimilation of carbohydrates, fats, and albuminous substances, salvia action, pepsin, and gastric fluid upon food, the action of different purgatives according to their nature, etc. His work on human physiology led him to discover the presence of a diastase in saliva and suggest a theory about the origin of diabetes.

Life and career

There is no information regarding the early life and education of Louis Mialhe (Figure 1).

Fig 1: Louis Mialhe (1807-1888)

He was born in Vabre (Tarn), France, on November 5, 1807. In 1830 he was intern in the Parisian hospitals. In 1836 he received his degree of pharmacist after defending a thesis about pharmaceutical observations (Mialhe, 1836) and in 1838 his degree of doctor of medicine, after
defending a thesis about chemical and medical observations (Mialhe, 1838). He was physician and chief pharmacist of the Saint-Antoine hospital and in 1839 he was appointed agrégé at the École de Médecine after winning the competitive aggregation examination with a work about the decomposition of organized beings (Mialhe, 1839). This position opened him the possibility of an academic teaching and research career. Thus in 1839 he was appointed adjunct professor in the section of organic chemistry and pharmacology of the Faculté de Médecine of Paris, and between 1842 to 1848 he taught a course on pharmacology at the École de Médecine. In 1842 he purchased the Bonnevin pharmacy and transformed it into a successful business in Paris. In 1867 he was elected member of the Académie de Médecine.

Mialhe passed away on November 5, 1886. Mialhe received several honors and awards for his contributions to science and professional life. He was laureate of the École de Pharmacie (1833) and of the Hôpitaux (1833 and 1834); placed first in the list presented by the Chemistry Section for a place vacant in the Académie Impériale de Médecine (1848), he was elected chevalier of the Légion d’Honneur (1847); member of the commission charged with writing a new edition of the French Codex (pharmacy section) (1862); president of the Société Médicale of the IXth district of Paris (1864); and president of the Société d’Hydrologie Médicale of Paris (1866 and 1867).

Scientific work

Mialhe wrote about 90 papers, booklets, and books about his research activities in the subjects of behavior of mercury chlorides, analytical chemistry, the manufacture of ethyl ether, human physiology, food assimilation, diabetes and its causes, saliva and gastric fluids, purgatives, pharmacology, mineral waters, etc. As customary for candidates to the Académie de Médecine he wrote (twice) a booklet listing his publications and a short description of the results of his research.

Mercury chlorides

Several known chemists, such as Torbern Olof Bergman (1735-1784), Pierre-Louis Dulong (1785-1838), Pettenkofer, and Heinrich August von Vogel (1778-1867) had observed the decomposition of insoluble salts by soluble ones. Dulong had stated that all insoluble salts were decomposed by potassium and sodium carbonates, Pettenkofer, a military pharmacist of Munich, had reported that calomel (HgCl) was decomposed by an aqueous saline solution into corrosive sublimate (HgCl₂). Vogel had studied the possible decomposition of insoluble salts by cold or hot water, after noting that calomel powder alone or mixed with kermes, kermesite (golden sulfur, a red mineral species composed of oxyantimony sulfide, Sb₂S₃O), gums, or sugar, became gray black when diluted in water. His results indicated that calomel boiled in water decomposed partially into corrosive sublimate.

Mialhe referred to the subject for the first time in the thesis he presented to the École de Pharmacie. There he wrote that the inconsistency in the properties of the protochloride of mercury (HgCl, calomel) reported by a number of scientists, particularly when comparing the salt prepared by precipitation with the one prepared by sublimation, had led him to conduct his own set of experiments. His results showed there was no significant difference in the physical aspect between the chlorides prepared by both procedures; they had the same solubility in water and the chloride obtained by precipitation contained traces of sodium chloride and sometimes traces of mercurous nitrate. The latter impurity appeared when the chloride was prepared using a basic protonitrate (mononitrate) instead of a neutral one. In addition, he confirmed the correctness of Pettenkofer’s result quoted above. He continued studying the subject after reading in Vogel’s paper about a child who had died shortly after ingesting a mixture of five grains of ammonium chloride, five grains of sugar, and half a grain of calomel, with all the symptoms of poisoning by corrosive sublimate. The apothecary was charged with the death of the child on the supposition he
had erroneously substituted corrosive sublimate for the calomel. Fortunately for him he was acquitted on the basis of Pettenkofer’s finding that in presence of ammonium chloride and of water calomel was partially changed into corrosive sublimate. Mialhe conducted a series of experiments about the behavior of calomel under different conditions and concluded as follows: (1) Mercury monochloride, HgCl, under the influence of water and the chlorides of ammonia, sodium, or potassium, known to be present in the digestive system, changed partly into mercury dichloride (HgCl$_2$) and metallic mercury; (2) when the monochloride was not purged but was retained for a long time in the digestive tube, it excited an abnormal secretion from the salivary glands caused by the large quantity of corrosive sublimate produced. The same phenomena took place after a long continued use of mercury (I) chloride and for the same cause; (3) Since the quantity of HgCl$_2$ formed could only be proportional to the amount of alkaline chlorides present in the viscers, those persons who ate large quantities of common salt were more susceptible than others to salivate under the influence of a mercurial medicine; (4) The anti-syphilitic properties of calomel were actually due, totally or in part, to the sublimate and the mercury generated by its chemical decomposition. The same explanation accounted for the anthelmintic properties of calomel; its poisoning effects on the acarida was caused by the two products of its decomposition; and (5) the same conclusions were applicable to mercury (I) iodide, HgI, which under the same conditions transformed into mercury (II) iodide, HgI$_2$.

Effect of alkali chlorides

In a following publication Mialhe reported the results of his experiments on the effect of an aqueous solution of alkaline chlorides, particularly ammonium chloride, on the decomposition of calomel. He first repeated the known fact that all alkaline chlorides transformed mercury (I) chloride into mercury (II) chloride, accompanied by an equivalent amount of metallic mercury, a decomposition that ammonium chloride did more energetically than all other chlorides. He then reported the following results: (a) both oxides of mercury, Hg$_2$O and HgO, contacted with an aqueous solution of ammonium chloride, yielded HgCl$_2$, or more precisely, ammonium-mercury chloride (alembroth salt, the salt of wisdom of the alchemists). The yield from HgO was larger than the one from Hg$_2$O; (b) all the salts of Hg (I) and Hg (II) produced the same results, they generated HgCl$_2$ and the conversion of the Hg (II) salts was higher than that of the Hg (I) ones. The latter result was easy to explain: on the one hand, the reaction of ammonium chloride with a salt of mercury (II) was a double decomposition generating mercury dichloride and a new ammonium salt; on the other hand, the salts of mercury (I) generated mercury (I) chloride, which then hardly transformed into mercury (II) chloride. According to Mialhe, this fact indicated that the salts of mercury (II) were much more energetic than those of mercury (I). The latter could also be completely inoffensive; (c) metallic mercury digested with a solution of ammonium chloride, also converted partially into HgCl$_2$, a reaction allowing the transformed metal to enter the animal body; (d) the decomposing energies of alkaline chlorides were much greater than had been supposed and in many cases their action was stronger than that of certain electro-negative acids, such as HCl, etc. (e) all the above reactions occurred at room temperature, even better at body temperature, and in a very short time. Human liquids contained ammonium and sodium chlorides, accompanied or not by HCl and other acids, which could facilitate their action, hence the result of these experiments was considered likely to be of importance in modifying the use of mercury, calomel, etc. as medicines.

In 1842 Mialhe read to the Académie des Sciences a paper describing the experiments he had conducted to determine the amounts of mercury (II) chloride obtained from mercury (I) chloride under different conditions. The first series of experiments was directed to determine the possible differences between calomel obtained by sublimation and calomel obtained by precipitation. In the first experiment 10 g of distilled water, 0.6 g of common salt, 0.6 g of ammonium chloride, and 0.6 g of distilled calomel, perfectly washed, were mixed and allowed to react for twenty-four
hours at 20 °C to 25 °C. The yield was 6 mg of corrosive sublimate. Similar experiments with calomel prepared by precipitation gave analogous results. Other experiments conducted with mixtures of the same composition as above but at 40° C to 50 °C, yielded 15 mg with calomel obtained by sublimation and 17 mg with calomel obtained by precipitation, a result that confirmed the opinion of therapeutics who had always considered the calomel obtained by precipitation to be sensibly more active than the one prepared by the dry way.21

A following series of 12 experiments was directed to determine if the quantity of sublimate produced was proportional to that of the calomel employed or to that of the alkaline chloride. The results proved beyond all doubt that the quantity of sublimate formed was always in proportion to that of the alkaline chloride.21

Other experiments proved (1) that the proportion of mercuric chloride produced was in direct relation to the concentration of the alkaline chlorides put into contact with the calomel, as suggested by the theory; (2) that the presence of neutral organic bodies did not hinder the conversion of calomel into sublimate; on the contrary, dextrin favored the change; sugar and albumen probably did not modify it; and lastly, lard and gum Arabic clearly retarded it.21

Mialhe wrote that in all these experiments he had assumed that one equivalent of calomel produced one equivalent of mercury and one of sublimate. He now found that the presence or absence of atmospheric air modified the results: The reaction of calomel with alkaline chlorides in contact with air produced three times as much sublimate as when they reacted without it. He explained this result by assuming that at atmospheric temperature calomel was able to absorb a certain quantity of oxygen, as had been shown by Nicolas-Jean-Baptiste-Gaston Guibourt (1790-1867).22 At a higher temperature the absorption was greater and in Mialhe experiments it was accelerated by the presence of the alkaline chlorides. Therefore, the proportion of sublimate should be greater when air was present, since for every equivalent of oxygen absorbed an equivalent of sublimate was produced; and moreover, each equivalent of mercury dioxide formed gave by double decomposition with the alkaline chloride one equivalent of sublimate and one of alkaline oxide.21

Mialhe conducted the following experiments to check his hypothesis: (a) a mixture of 0.6 g each of calomel, common salt, and ammonium chloride, with 10 g of distilled water, was digested for twenty-four hours at temperatures between 40° and 50°C, in the absence of air. This reaction produced 4 mg of corrosive sublimate; (b) the same experiment conducted in the presence of air gave 14 mg of sublimate. These results indicated that about two-thirds of the sublimate obtained was formed by the influence of oxygen and one-third was derived from the simple conversion of calomel into metallic mercury and calomel.21

Mialhe also found calomel (obtained by sublimation or by precipitation) to be partly converted into corrosive sublimate, etc. by the influence of boiling distilled water deprived of air. Thus, the above experiment was conducted at 100°C for an hour. After cooling the water was found to contain 2 mg of sublimate. In the presence of air the quantity of sublimate produced was significantly higher, but in this case the product was a mixture of sublimate and mercury oxichloride, as shown by Guibourt.21,22

This paper ended with a description of similar experiments conducted with mercury (I) bromide, iodide, nitrate, sulfate, acetate, and tartrate, mercury (II) oxide (red oxide), iodide, cyanide, nitrate, sulfate, tartrate, black mercury oxide (a mixture of mercury and mercuric oxide), metallic mercury, etc. An important result was that all these substances decomposed producing a constant amount of corrosive sublimate, responsible for their medical proprieties.21

**Analytical procedure**

As a result of the above works Mialhe developed a new analytical method for determining the presence of mercury and other metals in aqueous solutions, based on their precipitation with
sodium hydrosulfide. The resulting sulfide was easily decomposed by an alcoholic solution of iodine. This analytical method was capable of detecting the metal in amounts down to 0.05 mg.  

**Antidotes**

Mialhe found that iron (II) sulfide, a completely inert compound, was able to decompose HgCl$_2$ instantly, generating iron (II) chloride and mercury (II) sulfide, two inoffensive compounds. This important property led him to suggest the hydrate of iron (II) sulfide as the best antidote for this poison. Mialhe wrote that whenever a few centigrams of corrosive sublimate were placed in the mouth, it immediately produced its characteristic intolerable metallic taste. It was then sufficient to wash out the mouth with hydrate of iron (II) sulfide, in the state of a thin pulp, to eliminate all the metallic taste, as if by enchantment. Interesting enough, this antidote could also be used to destroy the injurious action of many other metallic salts, particularly those of copper and lead. As described by Mialhe, the hydrate of iron (II) sulfide was easily prepared by dissolving any quantity of the dry salt in at least twenty-four times its weight of distilled water, which had been degassed by boiled; this solution was then precipitated by a sufficient quantity of sodium hydrosulfide, likewise dissolved in boiled distilled water. The resulting iron (II) sulfide was washed with pure water and preserved for use in a closely stopped bottle, completely filled with distilled water.

**Effect of HCN and cyanides**

Another research project of Mialhe was prompted by a poisoning incident, which took place in Montpellier. A physician prescribed to a young patient a medicine composed of 120 g of extract of black cherries, 30 g of syrup of Tolu, and a little of myrrh, calomel and laudanum, which the pharmacist prepared replacing the extract of black cherries by another of laurel cherries. The young man died ten minutes after ingesting the potion. An autopsy showed no particular details, except for a dark red lesion in the gastric mucosa, extending all the way to the duodenum. An examination of the medicament indicated the presence of cyanhydric acid, and consequently, the cause of death of the patient. Mialhe believed the examiners had failed to test the possibility of poisonous mercurial agents being released by the reaction of the HCN contained in the cherries with the calomel of the medicine. Initial experiments showed the medicine to be very acid, to contain a little of HgCl$_2$, and its HgCl being colored gray black.

According to Mialhe, the action of prussic compounds on calomel had been reported long ago by pharmacists but had not called the attention of chemists until 1829 when Eugène Rimbaux, a student of pharmacy, had reported that the addition of calomel to a white syrup changed its color to gray black while a black powder deposited at the bottom of the contained. These effects were absent when the preparation did not contain bitter almonds. Souberain believed bitter almonds should not be used to prepare this type of medicines because they led to the formation of mercury (II) cyanide and chloride.

Further experiments by Mialhe showed that reacting calomel with an excess of HCN led to its complete decomposition; producing in the first stage a mixture of HCl, mercury (II) cyanide, and metallic mercury. After longer contact the HCl acted on the mercuric cyanide to yield HgCl$_2$ and HCN. Further reaction led to a mixture of HgCl$_2$, HCl, HCN, metallic mercury, and traces of ammonia and formic acid. Ether readily extracted the mercury (II) chloride and HCN, leaving behind the mercuric cyanide. Mialhe found other salts of mercury (I) oxide to be similarly decomposed by HCN and the alkaline cyanides and transformed completely into mercury (II) cyanides and metallic mercury. Mialhe believed his findings proved that this formation of mercuric cyanide was responsible for several cases of poisoning which had arisen from administering mixtures containing calomel and laurel cherries. The gastric fluids decomposed the cyanide and the HCN released resulted in the death of the person.
Mercury iodides
An additional publication discussed the preparation and uses of mercury (I) iodide, a compound chemically analogous to calomel. Its physiological action was weak, as long as it did not contain mercury (II) iodide. Unfortunately, the iodide available in the commerce was mixed with considerable quantities of mercury (II) iodide, or this salt was administered in combination, or simultaneously with potassium iodide, which immediately transformed the iodide of mercury (I) into the iodide of mercury (II) and metallic mercury. Two varieties of this material were sold in the pharmacies, a yellow green one, made of neutral mercury (I) iodide, and another colored dark green, composed of basic mercury (1) iodide containing 8% of excess iodine. According to Mialhe, the latter contained substantially less mercury (II) iodide than the corresponding medicine prepared according to the Codex. In every case, Mialhe recommended removing the excess of iodine by means of alcohol washes, to make the medicine safer.\(^{27}\)

Diabetes
In 1844 Mialhe published a short note describing his theory about the causes of this illness, which he had conceived as the result of some doubtful chemical analysis of sugars. Contrary to the prevailing opinion of among chemists, he had found that grape sugar (glucose, or diabetes sugar) was unable to reduce cupric oxide, under hot or cold conditions. Glucose acquired this capability only after being chemical changed by an alkaline substance, free or as carbonate. This simple and remarkable fact explained the failure of the Karl Fromherz’s (1797-1854) assay for properly detecting the presence of glucose in blood and urine.\(^ {28}\) Mialhe believed the effect of morbid illnesses on organized subjects was the result of a chemical perturbation or an abnormal chemical reaction. The results of his experiments indicated that carbohydrate foods such as grape sugar, gum, starch, or dextrin did not undergo assimilation until the alkalis of the blood had transformed them into new products; among them was one possessing a very vigorous deoxygenating power, able to easily reduce iron (III) oxide to iron (II) oxide, all iron (II) salts to iron (II) salts, etc., the nature of which had not yet been examined. As a result, the urine of a healthy person would not contain sugar. If this transformation did not take place, the original materials would undergo no changes and, consequently, would be excreted by the kidneys. It was known that diabetic individuals did not perspire or did it slightly; since the secretions of the skin were acid, it followed that when they were suppressed, the presence in the blood of free alkalis or their carbonates became impossible, being neutralized by the acids not excreted. Consequently the carbohydrate matter would leave the body unchanged. Diabetes should then be considered a defect of assimilation; sugar, instead of promoting the organic chemical changes taking place in the body would act as a foreign body, which the economy would try to eliminate insistently. The exaggerated saccharification (hydrolysis) of amylaceous matter would then be only an insignificant phenomenon, which did not explain the passive intoxication experimented by diabetes patients. This fact suggested diaphoretics and well-diluted alkaline preparations as the curative means for diabetes (more below).\(^ {28}\)

Saliva and its diastase
In a following publication Mialhe provided new data to justify his hypothesis regarding the causes for diabetes. He now added that the essential base of animal feeding was composed of three very different bodies: albuminous, fatty, and carbohydrate substances, which were not immediately assimilated. To be assimilated they had to reside in the gastric and intestinal cavities and through the action of the liquids they met, experiment a sort of fluidization or fermentation, which Mialhe named digestion.\(^ {29}\) Present knowledge indicated that albuminoidal substances were assimilated with the help of the gastric juice, which swelled nitrogenous substances, and by pepsin, a true ferment (enzyme), which liquefied them. This phenomenon was similar to the action of diastase on starch. Bile made fatty substances assimilable. Unfortunately, no such
definite information was available for feculent or starch materials. Mialhe reported he had discovered that this particular group of substances were decomposed by the weak diluted alkaline solutions present in vital fluids, either immediately (e.g. glucose, dextrin, and lactose), or going first into a preliminary transformation (e.g. sugar cane into glucose, and starch into dextrin or glucose). According to Mialhe these transformations were conducted exclusively through an active principle contained in the saliva. This principle was a white or gray white amorphous solid, insoluble in alcohol, and soluble in water and diluted alcohol. Its aqueous solution was tasteless, neutral to test papers, and not precipitable by lead subacetate. Left alone, in contact or not with air, it promptly became acid; the resulting acid was the butyric or one very closely allied to it. The principle did not act upon nitrogenous substances such as fibrin, albumen, casein, gelatin, gluten, cane sugar, inulin, gam Arabic, and lignin, but exerted an extraordinary effect on starch.\textsuperscript{30}

Mialhe conducted a series of experiments with several sweet substances under different conditions and stated that the results clearly proved that all carbohydrates (e.g. grape sugar, starch, gum or dextrin, etc.), did not undergo assimilation until after they had been transformed by the alkalies of the blood into new products, such as potassium saccharate, ulmin, and formic acid (an acid known to have strong deoxidizing properties). The results led to the following conclusions: (1) Glucose appeared in the urine of individuals in whom all the fluids had a neutral or even acid character, (diabetic patients); (2) this amount of glucose decreased or became nil when the patients were subjected to an alkaline treatment; (3) their urine and feces became colorless because no ulmin was formed (a substance which, in the normal state, colored these two excretions); (4) the urine of patients who had ingested red potassium ferrocyanide showed the presence of yellow potassium ferrocianyde, proving that a reduction process had taken during the passage of the original chemical through the body. Mialhe believed that this chemical action was due to the products resulting from the decomposition of glucose by alkalies, and particularly by the formic acid; and (5) the formic acid and the other deoxidating bodies produced during the ingestion of amylaceous and sweet substances, exercised a salutary reducing effect, similar to respiration. The absence of these compounds in the blood of diabetic patients produced a harmful disruption in their circulation, resulting from an oxygenation over and above that of the protein elements that this fluid contained.\textsuperscript{30,31}

Mialhe finished his paper commenting that carbohydrate matters performed an important part in the process of nutrition and did not serve solely for the support of respiration. Since some of them participated in the vital chemical reactions ruling over the incessant organic changes, it resulted that if their assimilation was destroyed, (chronic diabetes) or simply vitiated, (acute diabetes) abnormal molecular decompositions were brought into being, at the expense of the living fluids and tissues. These disorders led to two physiological consequences: (1) a general perturbation of the fluids of the system owing to a deficiency of alkalinity, originating a weakness of sight, of the capillaries, and pulmonary tuberculization; and (2) a profound alteration of nutrition, leading to weakness, sleepiness, and weight loss. These two physico-pathological facts led invariably to the fatal end of diabetic affections.\textsuperscript{31}

Mialhe described in detail the action of this principle on starch, under different conditions, and indicated this action was very similar to the one exerted by diastase, the active principle discovered by Anselme Payen (1795-1871) and Jean-François Persoz (1805-1868).\textsuperscript{32} Mialhe proposed naming animal diastase the principle present in saliva and vegetable diastase the one active on cereals, and gave a detailed description of the process for obtaining animal diastase from saliva: The saliva was first filtrated and then treated with five to ten times its weight of absolute alcohol; the addition of alcohol was stopped when no more precipitation of white flakes was observed. The flakes were filtrated, dried over a glass plate by a current of air at 40\textdegree{} to 50\textdegree{}C, and then stored in a tight closed flask. According to Mialhe, saliva contained about 2/1000 wt. of a diastase similar to the one present in germinated barley.\textsuperscript{30}
These two papers by Mialhe gave place to an extensive polemics with Apolinaire Bouchardart (1808-1888) and Sandras, and Jean-Louis Lassaigne (1800-1859), regarding the priority of the discovery of the possible causes of diabetes and the role played by saliva and its diastase in the assimilation of feculent and starchy bodies. 29,33-38

**Albuminose**

Mialhe then discussed in detail the assimilation of albuminoidal substances; he mentioned that all of these materials were transformed by pepsin into a final product, which he named *albuminose*, presenting the same chemical reactions, although its composition could be slightly different depending on the original body. 39 Albuminose was a solid substance, white or yellow white, having a slightly odor and taste, very soluble in water and completely insoluble in absolute alcohol. Heat, the bases, the acids, or even pepsin, did not coagulate the aqueous solution, but it was precipitated by a large number of metallic salts, (i.e. those of lead, mercury, and silver), by chlorine, tannin, and nitric acid. Yet, albuminose played a critical role in animal nutrition similar to the one played by glucose on amylaceous foods; albuminose alone was able to carry on the process of assimilation, as could be illustrated by the following two experiences: (1) injection in the veins of an animal of albumin or casein not modified by pepsin, resulted in their elimination by the urine in a natural form; and (2) injection in the veins of an animal of fibrin dissolved in acid water and not modified by pepsin, resulted in immediate death by congestion of the lung capillaries. 39

According to Mialhe gastric fluid was composed of two main agents, an acid and ferment. The acid swelled, hydrated, and prepared the food for further processing. The ferment was unique; pepsin, rennin, and gasterase were one and only one principle. On the one hand, pepsin transformed only albuminous matter, on the other hand, the diastase contained in saliva, completely different from pepsin, transformed only amylaceous matter; yielding albuminose as the final product. Diastase and pepsin allowed animals to digest simultaneously starchy and albuminous foods. As a result of chemical and physiological phenomena this double digestion took place in three stages: the first one involved disaggregation and hydration, the second the production of an intermediate substance (chyme from albuminous matter, and dextrin from starchy matter). The last stage was the transformation of the intermediate substance into two other, glucose and albuminose, totally soluble, movable along all the system, and appropriate for nutrition. 39

In another publication, Mialhe and the physician J. E. Pressat discussed the different states assumed by albumin during the assimilation process. 40 They stated they had already shown that “no substance could enter into the economy or leave it, without being in a state of solution which gave it the property of moistening, soaking, penetrating, and traversing the membranes, and arriving in the interior of the tissues, to be there, according to its ultimate destination, assimilated, destroyed, or burned, in order to aid in the formation of the organs or to pass out by the secretions.” Surprisingly enough, albumen was the only exception to a law, which seemed universal; although albumen had all the appearances of ordinary liquids it behaved as an insoluble body. In the normal state of health, it never appeared in the excretions; the albuminous liquids were thus found in different conditions from ordinary aqueous liquids. Mialhe and Pressat went on to demonstrate that the mechanism by which this apparently insoluble and non-osmotic body penetrated the economy, involved a series of transformations, which rendered it soluble. To do so albumin had to possess a globular organization similar to the one held by other non-osmotic substances, such as fibrin, casein, and starch, which were suspended in the liquids that transported them. Albumin was modified by pepsin into a soluble substance able to traverse membranes with no difficulty. The transformation of albumin into albuminose, the ultimate state, took place in three successive stages, having very distinct physical and chemical properties: (1) The first one was *normal, physiological albumen*, one of the principal elements of the blood, identical with the
albumen of white of egg, insoluble and incapable of traversing membranes, precipitable by heat and by nitric acid, and insoluble in an excess of acid; (2) the following stage was amorphous caseiform albumen resulting from the first modification of the albuminous foods under the influence of the gastric juices. This albumen was capable of traversing the membranes but incapable of being assimilated; it was imperfectly precipitated by heat and nitric acid; the precipitate was insoluble in an excess of acid. While being modified it began to resemble albuminose, of which it assumed the characters and properties; (3) the last stage was albuminose, the ultimate product of the transformation of the albuminous foods by the act of digestion. Albuminose was soluble, osmotic, and assimilable, and capable of being transported by all the apparatus of secretion and organic composition (i.e. blood, milk, saliva, perspiration and urine), almost in an scarcely appreciable quantity. It furnished the principal elements of nutrition; it was not precipitated either by heat or by nitric acid, but only by the reagents, which detected all animal matters.

According to Mialhe and Pressat, these three states of albumen constituted one and the same substance, which, in being modified, acquired new properties. They were chemically isomeric, and no analysis could detect the slightest difference in their elementary composition. Although retaining their common character of being precipitated by the salts of lead, silver and mercury, creosote, tannin, alcohol, etc., they were perfectly distinguishable from each other by the manner in which they acted with heat and nitric acid.

The discharge of albuminous matters in the urine was a pathological state long regarded as the result of a special affection of the kidneys; nowadays it was known the urine could contain albuminous matters in certain dropsical disorders, affections of the heart, after diseases of the skin, etc., without alteration of the kidneys. The three states of albumin could be found in the urine, each associated with a particular pathological cause. Thus, normal albumin was connected with a profound alteration of the renal glands; amorphous albumen with an alteration of physiological fluids; and albuminose, with the absence of assimilation, or with the cholera illness.

In 1860 Mialhe and Pressat published a booklet describing in more detail pepsin and its digestive properties. Pepsin (a name derived from the Greek πεψις = digestion) was the active principle present in the gastric fluid; its nature was similar to ferments and “operated by means of a particular force conveniently named catalytic”. Its physiological function was the transformation of albuminous substances into a soluble substance, osmotic, and appropriate to satisfy the different needs of organic composition and decomposition. Pepsin existed in the gastric fluid, in the mucus that covered the internal membrane of the stomach, and in the tissue of this membrane. It could be extracted from gastric fluid or from the liquids obtained by maceration of the mucous membranes of the stomach. After filtration, these liquids were treated with 10 to 12 times their volume of absolute alcohol; this caused the precipitation of pepsin as a flaky substance, corresponding to about one percent of the gastric fluid employed. This pepsin was already very pure and quite active; its activity could be doubled by redissolving it in water and precipitating again with alcohol.

Dried over a glass plate, it appeared as transparent yellow white scales, having a mordant and nauseous taste, soluble in water and diluted alcohol and totally insoluble in anhydrous alcohol. The aqueous solution, heated to 100°C, became turbid, without coagulating and without all its specific power. Pepsin was different from all other organic matter by its ability to coagulate milk in the absence of an acid. On the one hand, all the acids present in the gastric fluid had no digestive properties; on the other hand, with the exception of casein, pepsin, free of acids, did not act upon albuminous substances. Hence, the combination of an acid and pepsin was indispensible for digesting albuminous foods. Mialhe and Pressat believed that the following series of phenomena took place in the stomach and afterwards: the albuminous food ingested activated the secretion of the gastric fluid; the acid contained in the latter swelled, softened, and disintegrated
the food turning it into a semi liquid gelatinous mass, upon which pepsin began to act. The first effect was precipitation of this jelly mass as a white or reddish coagulate (the chyme), which redissolved under the action of more pepsin becoming the albuminose, a soluble, osmotic, and assimilable product, which passed into the circulation system to be absorbed by all the organs of organic composition and decomposition. Albuminous foods, which left the stomach without experimenting all the necessary transformations to make them absorbable, were not lost. Upon entering the intestine they came under the action of new fluids (pancreatic and intestinal), which completed their transformation into albuminose. Albuminose and albumin had one important difference; the former, injected in the veins, was perfectly assimilated without appearing in the urine; the latter, dissolved in acid water, had no nutritive power and reappeared in all the secretions.

Laxatives

In 1848 Mialhe read to the Académie de Médecine a memoir about the physiological and chemical mode of action of purgatives and the results of their action. A purgative was defined as a substance producing diarrhea, that is, an excessive secretion from the surface of the intestinal mucus. Purgatives were divided into two large groups: (1) insoluble substances unable to react with animal fluids and acting by mechanical irritation or simple contact (e.g. carbon, silica, crushed glass, etc.), and (2) substances normally insoluble but able to dissolve in the animal economy by reactions caused by principles contained in animal liquids (e.g. magnesia, resins, etc.). Some of these purgatives acted locally because the principles were usually located in specific parts of the digestive tube.

The soluble substances subdivided in two groups depending if they had or not coagulating properties. Saline substances were non-coagulating; salts such as the sulfates of sodium potassium and magnesium, and potassium sodium tartrate, exerted a double effect depending on the way they were administered: the salt was totally absorbed if ingested highly diluted in water; administered in high dose and as a concentrated solution, it acted as a purgative. Two effects caused purgation: (a) absorption of the salt by osmosis and (b) strong sapidity (e.g. aloe, quinine sulfate, etc.). The latter effect caused a powerful stimulation of the mucous membranes with the resulting abundant secretion in the mouth and in all the digestive tube. Soluble coagulating substances produced a local effect by their immediate absorption and possible combination with the tissues of the membranes. The consequent irritation resulted in a flow of liquid towards the injured zone. According to Mialhe, the above characteristics allowed classifying purgatives in five groups: (1) soluble and coagulating substances combining directly with the tissue and irritating it (i.e. mercuric chloride, castor oil, etc.); (2) soluble and non-coagulating substances, acting by osmosis or sapidity (i.e. magnesium citrate or sulfate, potassium sodium tartrate, mannitol, and sodium phosphate); (3) soluble and non-coagulating substances acting only by sapidity and strongly stimulating the mucous membrane and producing symphatetic secretion (i.e. colchicum and colocynth); (4) naturally soluble bodies solubilized by a chemical reaction (i.e. mercurous chloride and resins); and (5) insoluble bodies, acting by mechanical irritation (i.e. magnesia and carbon). A detailed description was given of the mode of action of each of these purgatives, advice about the proper selection, influence the diet, of the food, and the amount of water ingested.

REFERENCES