ANTOINE-BAUDOUIN POGGIALE

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RESUMEN. Antoine-Baudouin Poggiale (1808-1879) fue un médico francés que estudió en particular temas fisiológicos y toxicológicos como la generación del azúcar en organismos vivos, la diabetes, la composición de la sangre y de la leche, el uso del acetaldehído como posible anestésico, la presencia de cianuro de nitrógeno en el humo del tabaco, el envenenamiento por fósforo, etc. Sus resultados contribuyeron en forma notable a un mejor entendimiento de la diabetes.

ABSTRACT. Antoine-Baudouin Poggiale (1808-1879) was a French physician who studied physiological and toxicological subjects, such as the process of sugar generation in living organisms, diabetes, the composition of sugar and milk, the use of acetaldehyde as a possible anesthetic, the presence of hydrogen cyanide in tobacco smoke, the poisoning by phosphorus, etc. The results of his work contributed significantly to a better understanding of diabetes.

Life and career[1,7]

Antoine Baudoin Poggiale (Fig. 1)

Fig. 1: *Antoine-Baudouin Poggiale (1808-1879)*

Was born in Valle di Mezzana, near Ajaccio, Corsica, on February 9, 1808; one of the three children of a former military physician, who after retirement went into private practice. Antoine received his basic education at the local college at Marseilles and then, in 1828, entered the military teaching hospital in Strasbourg as a student pharmacist, where he graduated in 1830 as *pharmacien sous-aide* (sub-assistant pharmacist). After a short position in the French

African army he was transferred successively to the military instruction hospital in Lille and the Parisian military hospitals Gross Caillou and Val-de-Grâce (1831-1837). In Val-de Grâce he also served as *préparateur* of the chemistry course (1832).

While in Paris, he enrolled in the Faculté de Médicine where he graduated in 1833 as docteur de médicine after successfully defending a thesis about intermittent fevers.[8] The following year he won by competition the grade *pharmacien aide-major* (adjutant pharmacist) at the Val-de Grâce hospital, where he began teaching a course on analytical chemistry (1833-1836). This last position was the beginning of a fast professional and academic career: professor of physics and chemistry at the Lille hospital of military instruction (1837-1847), teaching pharmacy and botany (1837-1840) and chemistry and physics (1840-1847); promotion to pharmacien-major (1840) and to *pharmacien major de première classe* (1845); professor of organic chemistry at the École de Val-de-Grâce (1847-1850); professor of applied chemistry at the École Impériale de Médicine et de Pharmacie Militaire (1852); chief pharmacist at the Development Hospital of the Army (1847-1858); professor and *pharmacien inspecteur* in the French army, and member of the Army Health Council (1858). Poggiale was also the first professor appointed to the chair of chemistry and toxicology created at l'Ecole d'Application de Médecine et Pharmacie Militaires.

Poggiale also served in several public positions, for example, member of the Conseil d'Hygiène et de Salubrité Publique of the department of the Seine (1860) and member of the committee charged with reviewing the French Codex. During the Franco-Prussian war (1870-1871) he served as chief pharmacist of the Rhine Army at the Metz General Quarters.

In 1849 Poggiale was appointed chevalier of the Légion d'Honneur and promoted to officier in 1860 and commander in 1865; in 1856 he was elected to the Académie Impériale de Médicine (pharmacy section) and served as its treasurer. In the same year he joined the Société de Pharmacie as resident member and in 1862 served as its president.

Poggiale retired in 1872 and passed away on August 1879 after a long and painful illness. He was buried at the Montparnasse cemetery.

SCIENTIFIC WORK

Poggiale wrote over 40 papers, booklets, and books[8-12] in the areas of physiology, inorganic, organic, analytical, and mineral chemistry, medicine, public health, etc. As customary for all candidates to the Académie, he published a booklet describing his researches and achievements.[7] In addition to the subjects discussed below Poggiale investigated the properties of potable water and artesian well and mineral waters;[13-19] double haloid salts;[20] the synthesis of bromoboric acid and ammonium bromoborate;[21] new combinations of mercuric cyanide;[22] military bread;[10,23-25] the composition and equivalents of human food;[26] wine analysis;[27] phosphorus poisoning;[12] abnormal gas densities,[28] etc.

Sarsaparilla

In 1824 Galileo Pallotta (1797-1885) announced the discovery of a new salifiable base present in the roots of the plant sarsaparilla, of the smilax Genus.[31] Pallotta exhausted the powdered roots with boiled water, filtered the amber brown decoctions and treated them with limewater until they acquired alkaline properties. The resulting grey precipitate was washed, dried, and boiled repeatedly for two hours with alcohol of 40 ºC Bé (specific gravity 0.817), until all the solutes were taken up. The alcoholic extracts were filtered and distilled until they became turbid and started depositing a white pulverulent substance. The solid deposit, which Pallotta named *pariglina*, was dried in a stove at 31.3 ºC and stored in an appropriate vase. Pallotta described pariglina as a white, light, pulverulent solid, not altered by exposure to the air, having a peculiar smell and a bitter and sharp taste, slightly astringent and nauseous. It was insoluble in cold water, slightly soluble in hot water and in cold concentrated alcohol, and soluble in boiling water. It fused when heated to 257 °C, becoming black and partly decomposing. Pariglina turned red turmeric paper and combined with diluted acids forming the corresponding salts.[29]

Pallotta tried the effects of pariglina upon himself several days, in the morning with an empty stomach, in doses increasing from 2 to 13 grains (0.13 to 0.84 g). The higher doses occasioned nausea, vomiting, diminished the rapidity of the pulse, and acted as a sudorific. According to Pallotta, pariglina should be considered debilitating medicine acting particularly on the lymphatic system.[29]

In the same year Giacomo Folchi treated an infusion prepared from the inner parts of the roots with animal carbon and observed that the spontaneous evaporation of the filtrate resulted in the deposition of small yellow crystals, almost tasteless and giving a green color to syrup of violets (alkaline reaction). Folchi named this new substance *smilacin* and reported that the exterior of the root contained much more active matter than the interior one.[30] Later work resulted in the separation of two additional substances: Thubeuf used alcohol to separate a new substance, which he named *salseparine*. Salseparine was a white tasteless solid, soluble in alcohol and water, communicating a soapy property to its aqueous solution. According to Thubeuf, salseparine contained, by weight, 62.84% carbon, 9.76% hydrogen, and 27.40% oxygen, a composition corresponding to the formula C_3H_6O.[31] In 1833 Johann Baptista Batka separated from this plant an acid, which he named *parillinic acid*; this acid appeared in the solid state as fish scales, was soluble in alcohol and sparingly soluble in cold water; it combined with alkalis yielding soluble salts; the solutions of the latter were highly foaming.[32]

Analysis of the available information indicated that the four compounds had been obtained using similar experimental procedures; this fact led Poggiale to analyze the possibility that they were the same principle.[33] In the first stage he prepared a substantial amount of pariglina, smilacin, salseparine, and parillinic acid. He had no problem separating the pariglina of Pallotta but this was not the case with the smilacin of Folchi: the yield was substantially lower when using only water as the solvent. Poggiale carefully separated the cortical substance of the medullar part present in 5 kg sarsaparilla roots and after maceration in water obtained a very small amount of smilacin; this substance was hardly discolored by carbon, but treated first with alcohol and then with animal carbon yielded a substance having all the properties of the pariglina. These results led Poggiale to examine if the active properties of sarsaparilla resided in the bark root or in the central part (meditullium). The results indicated that they were present in both sections.[33]

Poggiale followed Thubeuf's procedure and once again obtained a substance identical with pariglina. Batka's procedure was complicated and Poggiale simplified it by adding HCl to a concentrated decoction of sarsaparilla. According to Poggiale, Batka's product was acid because it still contained part of the acid used to separate the active principle. Poggiale mentioned that he had found that salseparine or pariglina could be easily prepared by means of KOH, magnesia, sulfuric acid, etc., and in every case the final substance was the same. The four principles were all white, inodorous when deprived of water, bitter and nauseous to the taste when dissolved in water or alcohol, insoluble in cold water, slightly soluble in boiling water, very soluble in boiling alcohol and less in cold alcohol, soluble in boiling ether in volatile oils, and less soluble in fixed oils. They slightly turned red turmeric paper and green the syrup of violets. Their water solutions foamed strongly when agitated (today we know the foaming is caused by the saponins present in the root). KOH, NaOH, and ammonia solubilized them easily.[33]

Poggiale proposed that all four substances be known under the name *salseparine* because it recalled the raw material used for their preparation. An elemental analysis of the four substances yielded a percentage composition corresponding to the formula $C_8H_{15}O_3 + (H_2O)$.

Poggiale remarked that Pallotta should be considered the true discoverer of salseparine.[33]

Digitalis purpurea (foxglove) and hyoscyamus (henbane)

In 1835 Brault and Poggiale reported that in many situations principles assumed to be active were simply a mixture of inorganic salts, As examples they considered the principles supposedly obtained from the plants foxglove and henbane, particularly as reported by Auguste Le Royer, Charles Louis Pauquy (1800 -1854), and Johann Planiává.[34] In 1824 Auguste Le Royer read to the Société de Physique et d'Histoire Naturelle of Genève a memoir on the active principle of *Digitalis purpurea*, which he had succeeded in isolating, and its effects on several animals. Le Royer digested the dry leaves of *digitalis purpurea* in ether and from the concentrated solution separated an acid salt having a peculiar alkaloid basis, which he named *digitalina*. The purified alkaloid was a brown butter-looking substance, intensively bitter, acting weakly as an alkali upon litmus paper reddened by an acid, soluble in alcohol, ether, and water, and leaving the tongue, upon tasting, insensitive in a manner similar to aconite. When dissolved in alcohol and dried on a glass plate, it formed highly deliquescent microscopic crystals. Le Royer dissolved a grain of this substance in a small quantity of water and injected it into the abdomen of a middle sized rabbit, which was very speedily killed, without experiencing any convulsions; half a grain injected into the veins of a cat killed it in fifteen minutes; a solution containing 1.5 grains injected into the jugular vein of a dog killed it in fifteen minutes.[34]

Pauguy boiled the leaves of foxglove in distilled water acidulated with sulfuric acid, treated the resulting brew with calcined magnesia, and extracted the dry precipitate with alcohol. On evaporation the alcoholic extract precipitated small needles of white crystalline and acrid substance, soluble in alcohol, having a clear alkaline reaction, and forming crystallizable salts with acids. Planiává exhausted the watery extract with ether and separated the chlorophyll by steam distillation. The watery residue was treated with powdered lead oxide, evaporated to dryness, extracted again with ether, and evaporated to a transparent yellow non-crystallizable mass.[34,35]

Brault and Poggiale repeated the Le Royer process and found, as reported, a heavy brown substance possessing an extremely acrid bitter taste (the digitalin of Le Royer). The extract was treated with water acidulated with sulfuric acid in order to precipitate most of the chlorophyll. The filtrate was evaporated to a syrupy consistency and then repeatedly treated with cold water to precipitate the remaining chlorophyll. The corresponding filtrate was evaporated and then left to cool. The resulting brown precipitate was found to have all the properties of a resin. Extraction with ether separated a fatty matter. Additional tests indicated the presence of different salts of calcium and potassium; their presence justified the deliquescence reported by Le Royer.[34]

Brault and Poggiale concluded that the leaves of foxglove were composed of chlorophyll, resin, fatty matter, starch, vegetable fiber, gum, tannin, calcium and potassium salts, volatile oil, and potassium oxalate. Without asserting the non-existence of a peculiar principle called digitalin, they believed that the purgative and diuretic effects of foxglove were actually attributable to the joint effect of all the substances that composed it, especially the resin. This resin had a bitter taste, and was acrid and almost corrosive. A small portion of it placed on the tongue produced a very painful sensation of heat and constriction in the throat. Two grains of this resin swallowed, irritated strongly the stomach. A further proof of the main action of the resin was the fact that the alcoholic extract of foxglove presented the same properties of the raw material.[34]

In 1824 Friedlieb Ferdinand Runge (1795-1867) reported that the aqueous solutions of the acetate derivative of the narcotic base of belladonna were completely deactivated by diluted solutions of alkalis; the resulting liquid was incapable of dilating the pupil. He also found that alkalis acted in the same manner on the aqueous solutions of henbane (hyoscyamus) and datura (angel trumpet, *datura stramonium*).[36] Rudolph Brandes (1795-1842) found that hyoscyamus contained a volatile alkali (hyosciamine) combined with an acid, having physical and chemical properties very similar to those of nicotine and atropine. The active principle was obtained by precipitation of aqueous solutions of hyoscyamus with an alkali, followed by drying of the precipitate and washing with alcohol. Evaporation of the alcoholic extract yielded the active principle as prismatic crystals, capable of forming salts with nitric and sulfuric acids.[37]

Brault and Poggiale repeated several times the procedure described by Brandes and obtained, in every case, a white deliquescent powder, composed of the sulfates, acetates, phosphates, and chlorides, of potassium, calcium, and magnesium. Tests with concentrated sulfuric acid proved that this powder contained only inorganic material. Additional chemical exams indicated that hyoscyamus also contained a fatty substance, a particular resin, gum, and ligneous fiber. From their results they concluded that the active principle hyosciamine was yet to be isolated and that the white substance assumed to be hyosciamine was simple a mixture of many salts. They believed that the narcotic-acrid properties of hyoscyamus were actually the result of the combined action of the substances they had identified in it, which originated its characteristic bad odor, taste, and brown color.[34]

Acetaldehyde as anesthetic agent

In 1774 Carl Wilhelm Scheele (1742-1786) noted that an ethereal odorous substance was formed when ethanol was oxidized with manganese dioxide and sulfuric acid.[38] In 1821 Johann Wolfgang Döbereiner (1780-1849) repeated this experiment and isolated a compound, which he named *Sauerstoff Äther* (oxygen-ether).[39] In 1835 Justus von Liebig (1803-1883) reported that the ether separated by Döbereiner could also be prepared by reacting diluted ethanol with chromo-sulfuric acid. The ether was described as a colorless liquid, of specific gravity of 0.79 and boiling point 22.2 ^{o}C. Its odor resembled that of sulfuric ether (diethyl ether), but was more suffocating; it was neutral, inflammable, and burned with a pale flame; it easily mixed with water, alcohol, and ether; it spontaneously changed when long kept, and converted into two substances, a solid and a fluid (metaldehyde and elaldehyde); and was decomposed and blackened by sulfuric acid. Liebig named it *aldehyde*, a name he formed from the expression *alcohol dehydrogenatus* (alcohol dehydrogenated), and also determined its composition and formula, C_2H_4O.[40]

In 1848 Poggiale reported to the Académie des Sciences that he had discovered that the inhalation of the vapors of aldehyde was promptly followed by the most complete insensibility.[41] The stupefying action of the compound was more prompt and energetic than that of diethyl ether and chloroform. He had submitted several dogs to the action of aldehyde and noticed that after 45 seconds they had become completely insensitive; their eyes became fixed, the muscles completely relaxed, and the pupils dilated and immoveable. After three minutes the animal, although still insensible, turned over, and experienced some involuntary movements. After eight minutes, respiration became normal and the skin regained its sensibility. No particular incidents were observed during the process. During two experiments the inhalation of the vapor was continued for ten minutes: the animal remained insensible and motionless, only the muscles of respiration continuing to act. When exposed to a free current of air, the head of the animal was thrown back; respiration first became almost convulsive and subsequently regular. Lastly, the dog raised itself upon its fore feet, drew after it its abdominal members, which still were paralyzed, and was completely recovered in about 15 minutes. The arterial blood had the strong and peculiar odor of aldehyde.[41]

Poggiale remarked that if the powerful odor of aldehyde would allow the surgeons to apply it to human subjects, the liquid could become a very economical substitute for chloroform: large amounts of it could be prepared rather cheaply by distilling a mixture of alcohol and manganese dioxide with diluted sulfuric acid, and subsequent rectifying the product in the presence of calcium chloride. The resulting aldehyde boiled at 28 to 29 ^{o}C, and contained only small quantities of alcohol and formic ether.[41]

Blood

In 1845, Louis Figuier (1819-1894) published a new procedure for analyzing blood based on the fact reported many years ago by Berzelius that when defibrinated blood was mixed with a solution of a neutral salt the globules hardly passed through filtering paper. Figuier reported he had been able to retain all the globules by mixing two parts of a solution of sodium sulfate of density 1.125 to 1.141 with one part of blood. The fibrin was eliminated by beating fresh blood with a small bundle of whalebone switches, followed by filtering, drying, and weighting. The globular mater was eliminated from the filtrate by addition of the solution of sodium sulfate, and the albumen coagulated by heating the new filtrate. Figuier used this method to determine that blood was composed, by weight, of 80.29% water, 13.06% globules, 0.39% fibrin, 5.96% albumen, and 1.2% inorganic salts.[42]

In 1847 Poggiale reported that he had found Figuier's procedure appropriate for analyzing the blood of mammals but not so for animals having elliptical blood globules. Mixing 50 to 80 g of blood from chicken of pigeons with 3 or 4 volumes of a solution of sodium sulfate of specific gravity 1.141 turned the mixture so viscous that it was impossible to filter it completely. The resulting filtrate was slightly colored and after a few hours it turned into a transparent gel. A microscopic examination showed that the sulfate solution had profoundly changed the elliptical

globules. Further experiments showed that a sugar solution retained on the filter the elliptical globules in the same manner that a sodium sulfate solution did with those globules of mammals.[43]

Poggiale used standard analytical procedures to determine the amount of water, globules, albumen, fibrin, fatty matter, salt, and extractive matter (salts soluble and insoluble in water) present in human blood and in that of beef, cow, veal, sheep, rabbit, dog, cat, chicken, and pigeon. He also tested the composition of human blood before and after the patient had ingested sodium chloride and found that this salt induced a profound change in the composition, as shown by the following table (weight %):[43]

Food	Normal	10g/day NaCl
Water	77.992	76.760
Globules	13.009	14.3
Albumen	7.743	7.400
Fibrin	0.210	0.225
Fatty matter	0.113	0.131
Salts	0.933	1.184

According to Poggiale and Charles Jacob Marchal (1815-1873) chemists and physiologists were in disagreement regarding the differences in composition between arterial and venous blood. In other to provide further information they carefully analyzed blood samples taken from the temporal artery from the arm of a patient affected with erysipelas (red skin) and cerebral inflammation, and obtained the following results:

Blood	arterial	venous
Water	82.246	81.839
Fibrin	0.617	0.608
Albumen	6.603	6.137
Globules	9.746	10.605
Fatty matter	0.110	0.120
Salts	0.678	0.691

showing that arterial blood contained more water, more fibrin, more albumen, and less globules than venous blood.[44]

Milk

Poggiale published a series of papers regarding the analysis and properties of milk.[11,45-48] In his first publication he wrote that he had developed the first fast and rigorous procedure for determining the richness of milk, based on Charles Louis Arthur Barreswil (1817-1870) finding that a mixture of a concentrated solution of grape sugar with another of cupric sulfate reacted forming a bluish white quantitative precipitate of a complex formed by the two solutes.[49] According to Poggiale, the sugar of milk (lactose) reacted in the same manner. The decomposition of the complex provided a quantitative measurement of the amount of sugar present in the milk. He analyzed 10 different samples of milk and determined that their average composition was (by weight) 86.28% water, 4.38% butter, 3.8% caseum (casein), and 0.27% salts.[45]

According to Poggiale, the testing liquor was prepared by adding potassium bitartrate (potassium hydrogen tartrate) to a solution of cupric sulfate and dissolving the resulting precipitate with KOH. The intense blue of filtrate of this solution served as the testing liquor. Its titer was fixed by the amount of a sugar of milk employed to decolorize a known volume of it. The first step in the analytical procedure consisted in separating the casein and fatty material by coagulation: A few drops of acetic acid were added to 50 to 60 g of the milk sample and the mixture heated to 40° or 50 °C. The filtered whey was placed in a graduated dropping tube, marked each 0.2 cm^3, and added drop by drop to 20 cm^3 of the testing liquor contained in a small flask, until complete disappearance of the blue tint. The number of divisions of whey required to produce this change were noted and the weight of sugar in 1000 parts of whey calculated by the rule of three. Poggiale wrote that his procedure allowed a fast detection of milk falsification.[45]

Shortly thereafter Poggiale published a second paper on the subject, this time advocating the use of a polarimeter for determining the richness of milk. This method was based on the fact that a solution of clear whey acted upon polarized light.[46] The milk tested was coagulated by means of acetic acid at the temperature of 40° or 50 °C and the filtrate treated with a few drops of lead acetate. The new filtrate, perfectly transparent, was introduced in a tube 20 cm long and the closed tube placed in the polarimeter for measuring the degrees of deviation. Poggiale provided a table giving the value of the sugar content of 1 liter of milk for deviations varying between 18^0 (36.34 g) and 31^0 (64.60 g). He mentioned that commercial milk gave a reading of 19^0 (36.34 g) to 23^0 (46.43 g), a value below the average he had previously determined (52.7 g).[46]

Some years later, Poggiale reported again his previous findings and added some more information, for example, a table giving the composition of the milk (% solid matter, and weight of casein, butter, sugar of milk, salts, and water in one liter of milk) obtained from 2 to 15 months after parturition.[47] The amount of solid matter was determined by evaporation of the milk in a dry vacuum; the fatty matter was isolated by extraction with ether; the amount of lactose

by means of the Fehling reagent and that of salts by ordinary processes. Poggiale also gave a detailed description of the process for preparing the test liquor, preparation and testing of the whey, and the determination of the sugar by means of polarimetry. He also remarked that if the milk was adulterated by albuminoidal substances such as Arabic gum, dextrin, starch, emulsions of starchy seeds, etc., the fraud could be determined by estimating the lactose, because this could only be made by adding water to the milk.[47]

In 1867 Justus von Liebig (1803-1883) published a paper discussing the high mortality of infants in places where the mother had to work in order to help the family economy.[50] Most German physicians attributed the death to the fact that in this situation the infants were fed with porridge made of flour and milk instead of the mother's milk. Among other shortcomings, wheat flour did not allow the infant to receive the amount of alkali that was necessary for the formation of blood. These reasons led Liebig to develop artificial milk containing skimmed milk, wheat flour, germinated barley, and potassium bicarbonate. The milk was prepared by boiling 16 g of dry wheat flour with 160 g of skimmed milk until it became a homogenous porridge. Immediately thereafter were added 16 g of crushed germinated barley, 32 g of cold water, and 3 g of a solution of potassium bicarbonate containing 2 parts of the salt in 11 of water. The resulting mixture was heated until it turned into a creamy liquid, and then filtered. The resulting matter contained plastic and respiratory elements in a proportion similar to maternal milk. Liebig reported that several well-known physicians had tested his artificial milk and given a very positive opinion.[50]

Liebig's paper was sharply criticized by Poggiale.[48] He mentioned that natural milk contained three main ingredients: casein, lactose, and butter. The first one helped generate tissues, and the other two were sources of energy. In addition, butter contained six different fatty components. Furthermore, milk contained salts, particularly those of calcium, which were indispensable for the formation of blood in infants. Natural milk was a comprehensive substance, which provided all the food needed by an infant during the first months of its life. No other substance could replace it without danger. It was reckless to claim that Liebig's artificial milk was a perfect substitute of natural milk.[48]

Poggiale went on to compare the components of both fluids and concluded that the physical and chemical properties, and the flavor, odor, color, and consistency of Liebig's artificial milk completely differed from maternal milk; hence it could not be assumed that it played the same physiological role as the natural product.[48]

Sugar in the organism

In 1855 Poggiale published an extensive memoir describing his efforts to discover the pathway of sugar formation in the organism. He wanted to discern between the possibilities that it was formed at the expense of nitrogenous foods or fatty materials or in default of starchy substances, or it was manufactured in the liver or in the circulatory torrent by the digestive process.[51] According to common knowledge, human and animal food was composed of organic matter, nitrogenous or not, fatty substances, and mineral ones. The nitrogenous substances maintained the organs, produced strength, and assisted in the development of animals. Fatty, sugary, and starchy material activated respiration; the carbon and the hydrogen combined with atmospheric oxygen and maintained the animal temperature. Poggiale thought that these ideas were not rigorously exact; if starchy material transformed easily into sugar, then it seemed logical to accept that the nitrogenous and fatty materials followed the same course.[51]

In the first stage Poggiale tested the possibility that sugar was formed *at the expense* of nitrogenous or fatty materials. For this purpose he conducted two experiments. In the first one he examined the milk of female dogs subjected successively to two feeding regimes: (a) flesh and bread and (b) only flesh, for 21 days. Analysis of the milk, carried on by the procedures he had developed and previously published[45.46] gave the following results:

Regime	(a)	(b)
Water	73.41	71.21
Fatty material	8.18	12.04
Casein	13.04	12.89
Lactose	2.89	1.82
Salts, soluble and insoluble	2.08	1.63
Loss	0.40	0.41

These results showed that a feed based only on flesh resulted in a decrease in the amount of sugar.

In the second experience a dog was fed only cooked flesh for 15 consecutive days. It was then anesthetized and blood samples taken from the femoral artery, inferior vena cava, and the hepatic veins. These samples were found to contain 0.055, 0.148, and 0.154 g sugar/100 g blood, respectively. A set of additional experiences dismissed the possibility that the flesh fed to the dog already contained sugar.[51]

According to Poggiale, all the above experiments left open the possibility that sugar could form at the expense of nitrogenous or fatty matter. Lack of starchy or sugary material would force the organism to decompose the main albuminoidal materials into sugar and urea and other substances, which would then be burned. Consequently, animals, the same as vegetables, were able, under specific conditions, of generating immediate principles, and their role was not only the destruction of those provided by vegetables.[51]

A large number of other experiences led Poggiale to conclude as follows: (1) sugar may form at the expense of nitrogenous foods and, perhaps, also from fatty materials; (2) a nutrition based completely on fat is unable to decrease the level of sugar in the organism; (c) the digestive process is able to transform starchy food into sugar; (d) in animals fed with starchy substance, the blood transported by the portal vein contains a significant amount of sugar; (e) in animals fed flesh, the blood of the portal vein does not carry sugar, but sugar is carried in significant amounts by the blood of the hepatic veins, the lower vena cava, and arterial blood; (f) sugar is not present in the blood of the portal vein of fasting animals; and (g) sugar is produced in the liver of animals fed with nitrogenous and fatty substances.[51]

In a following work Poggiale tested the hypothesis that the presence of alkali was necessary for the destruction of sugar in the body, an assumption, which led to attributing diabetes to a deficiency of alkali in the blood. For this purpose he carried a series of experiments in which animals were partly fed on flesh and partially on starch or sugary substances, mixed enough sodium bicarbonate to make the urine strongly alkaline.[52]

The results of the experiments proved conclusively that alkaline carbonates did not act upon glucose and that the temperature of the mixture had to be raised to about 95 ºC for this action to take place. They also dismissed the belief that when blood, for any cause whatever, lost its alkaline properties, its non-burned sugar passed into the urine, hence the medical recommendation of introducing into the systems alkalis to restore the normal state.[52]

Glycogen

In a paper about glycogen Poggiale recalled that the physiologist Claude Bernard (1813-1878) had long established the presence of sugar in normal blood. Bernard had written that there were two possible sources for the sugar material present in human beings and animals, an internal one, originating from a normal function of the liver and significantly more important than the external one, which depended of the variable conditions of the food intake. The formation of sugar occurred by transformation of an amylaceous substance discharged by the liver, a *true animal starch* (glycogenic substance), present only and only in this organ. The formation of sugar in carnivores took place by a mechanism completely analogous to the one known in vegetables. The experimental evidence proved conclusively that the glycogenic function was completely independent of the nourishment. According to Bernard, treating the liver tissue with an excess of glacial acetic acid easily and neatly isolated the glycogen present. Alcohol was less efficient because it also separated the albuminoidal material.[53,54]

Bernard ideas did not go unchallenged, shortly thereafter, André Sanson (1826-1902) communicated to the Académie des Sciences that the blood of abdominal circulation and the tissues of the main organs of animal economy contained a substance analog to dextrin, able to convert into glucose under the influence of diastase. The dextrin present in the blood of herbivorous animals originated from the action of the saliva on the main starchy material of their food; in carnivorous animals it was already available in the meat they ate. In other words, the liver did not secrete sugar or glycogenic matter.[55]

These discrepancies led the Académie des Sciences to appoint a committee composed of Henri Bouley (1814-1885), Poggiale, and François-Achilles Longet (1811-1871) to examine the two communications and carry on the necessary experiments to resolve the question regarding the formation of glycogen.[54]

The report of the commission addressed the following questions: (a) what is the appropriate procedure for extracting the glycogenic material? (b) What is the nature of this substance? (c) In carnivorous, is it found only in the liver and what is the origin of the one present in this organ? (d) Is it formed only by the liver or it originates from the starchy material present in the food? And (e) does it exist in all the organs of the herbivorous and how its production is influenced by the food?

The report mentioned that initially Bernard had extracted the glycogen contained in the liver by an elaborate procedure based on washing the liver tissue with boiling water to avoid the transformation of the glycogenic matter into sugar by its own ferment (enzyme), followed by extraction of the filtrate with absolute alcohol, washing the impure glycogen with concentrated KOH, more washing with water, and precipitation with alcohol. The precipitate was washed with water to eliminate the remaining potassium carbonate, and a second precipitation with alcohol. This procedure was the source of errors because the use of the alcohol and a strong reagent (KOH) resulted in the extraction of albuminous matter and the production of a small amount of substance that transformed into sugar. This led Bernard to switch the procedure to one based on treating a concentrated decoction of the organ (liver and muscles) with a large excess of glacial acetic acid. The albuminoidal substances dissolved in the acid leaving the glycogenic matter as a white precipitate. The committee found that mixing this substance with saliva led to its immediate transformation into sugar and that the resulting transparent solution was able to ferment and react with Fehling's liquor. For these reasons the committee adopted this procedure for their further work.[54]

The glycogenic substance was described as a pulverulent and neutral white matter, insipid, inodorous, and soluble in water and insoluble in alcohol and acetic acid. It was not reduced by Fehling's liquor and did not ferment in the presence of beer yeast but in the presence of hot diluted mineral acids, diastase, or saliva, transformed into sugar and was able to ferment and reduce copper salts. All the properties examined placed glycogen between starch and dextrin.[54]

The report described the series of experiments that were carried on to answer the target questions and the pertinent conclusions: (1) the best procedure for extracting the glycogenic matter is the one based on glacial acetic acid; (2) a concentrated decoction of liver, muscular tissue, etc., mixed with saliva and slightly warm, ferments in the presence

of beer yeast if it contains glycogenic matter, as long as it been shown not to contain sugar; (c) the properties of glycogenic material place it between starch and dextrin; (d) in dogs fed only with meat, the glycogenic material is present only in the liver. In the present state of science, it can only be stated that this substance is produced only in the liver; (e) the glycogenic material is abundantly found in the liver of herbivorous. It is found in other organs only when these animals are fed with food rich in amylaceous substances, and (f) the result of a large number of experiments has shown only once the presence of glycogenic matter in meat coming from butchery. In other experiments it has always been found in the muscular tissue of healthy horses, but this fact does not prove that the glycogenic matter is always provided by food.[54]

Presence of HCN in tobacco smoke

In 1857 Augustus Vogel (1778-1867) and C. Reischauer announced that they had detected the presence of hydrogen sulfide and hydrogen cyanide in tobacco smoke. Hydrogen sulfide was identified by blowing the smoke of the cigar upon a piece of paper moistened with lead acetate, and HCN by the standard iron test (formation of Prussian blue after the smoke has been bubbled through a concentrated solution of KOH, followed by treatment with ferrous sulfate and chemically pure HCl).[56] Vogel and Reischauer found that except of a very old tobacco, the smoke of all the other samples tested showed the presence of HCN. One important consequence was that the mode of combustion of the tobacco (cigar or pipe) appeared to influence the formation of the acid. Some years later, Vogel suggested that Christian Schönbein's (1799-1868) reagent [1] was a simpler process for identifying the presence of HCN.[57,58]

Poggiale and Jean Hippolyte Marty (1835-1918) decided to test Vogel' suggestion because they thought that Schönbein's reagent was not reliable enough; it also gave a blue coloration with compounds such as ammonia.[59] For this purpose they conducted a series of experiments in which samples of 200 g of tobacco were slowly and carefully burned in the bowl of a large pipe and the resulting smoke sucked by means of aspirators and bubbled through three washing bottles in series, kept in a large vase full of water. The water absorbed the soluble components and condensed the tarry and oily products present in the smoke. After each experiment, the liquids were tested with Schönbein's reagent and found to give a decreasing blue coloration when going from the first to the third vase.[59]

Poggiale and Marty conducted an additional series of tests with the liquid to examine the possibility that the blue color originated from ammonia components in the smoke: (a) treatment of 100 g of the absorbent liquid with ferric-ferrous sulfate resulted only in the precipitation of the corresponding iron oxides, which dissolved in HCl and did not color blue or green the strip of paper; (b) treatment 100 g of the same liquid with silver nitrate produced a voluminous precipitate, mostly soluble in diluted nitric acid. The precipitate was insoluble in boiling concentrated nitric acid; (c) another 100 g were boiled with 29 g of ammonia sulfide until disappearance of the sulfurous vapors. The resulting solution was evaporated to dryness and the resulting residue treated with alcohol, filtered again, and dissolved in water. The aqueous solution did not react with ferric chloride, indicating that it did not contain ammonium thiocyanide; and (d) 900 g of the liquid were treated with 20 g of mercury dioxide (HgO) and left to react for several days. The filtrate was evaporated to dryness and the residue subject to a series of operations that proved it did not contain Prussian blue. According to Poggiale and Marty the results of these experiments proved that that tobacco smoke did not contain HCN and that Schönbein's reagent was unreliable for recognizing the presence of this acid.[59]

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[Schönbein's reagent is prepared impregnating strips of filter paper with tincture of guaiac, followed by drying and humidifying the paper with cupric sulfate. The wet paper is contacted with the liquid being tested for HCN: appearance of a blue color indicates the acid is present.]

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