# Historical note

# Apollinaire Bouchardat (1806-1886): founder of modern Diabetology

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#### ABSTRACT

Apollinaire Bouchardat is regarded as the founder of the field of Diabetology. His contributions to the field include the first known recommendations for specific diets for the management of Diabetes Mellitus and his emphasis on patient education and self-monitoring. He was moreover a great pharmacist as well as a distinguished physician and biochemist.

Key words: Bouchardat, Diabetes diet, Diabetes mellitus, Diabetology

#### LIFE, STUDIES, CAREER

Apollinaire Bouchardat was born on July 23, 1806, in L'Isle-sur-Serein, in Burgundy, France. At a young age, he was introduced to chemistry by his father, Jean-Baptiste Bouchardat owner of a tannery. Trainee in the pharmacy of his uncle. Alphonse Bouchardat, he simultaneously completed his medical studies.

He enrolled at the School of Pharmacy in Paris. In 1832, following the defence of his medical thesis on cholera: "Sur la nature, le traitement et les préservatifs du choléra-morbus" he was appointed chief pharmacist at the Paris Hôtel-Dieu hospital. Working tirelessly, he soon earned the esteem of the Faculty of Medicine and in 1852 he received the prestigious Chair of Hygiene, subsequently following a dual career, pharmaceutical and medical, in which latter

Marianna Karamanou, MD, 4 Themidos Str., 14564, Kifissia, Athens, Greece, Tel.: +30 6973606804, Fax: +30 210 8235710, E-mail: mariannakaramanou@yahoo.com *Received: 12-07-2013, Accepted 14-11-2013*  he invariably excelled (Figure 1). He resigned from his duties at the Hôtel-Dieu at the age of 49 in order to focus on the study of nutritional hygiene. He was succeeded by Adrien Proust (1834-1903), father of the writer Marcel Proust (1871-1922).<sup>1</sup>

Member of the Academy of Medicine as from 1850, he became its President in 1866. He married Anne-Antoinette Malot (1816-1867), with whom he had two children: Jean was later to become doctormajor, and Gustave became Professor at the School of Pharmacy of Paris in 1886.<sup>2</sup> Bouchardat died in Paris on April 7, 1886.

# THE MULTIDISCIPLINARY NATURE OF THE SCIENTIFIC WORK OF BOUCHARDAT

Bouchardat's work focused on several aspects of science, namely pharmacy, biology, chemistry, toxicology, hygiene and physics. In all the scientific fields in which he was engaged he proved highly inventive and was, notably, the originator of the

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Figure 1. The eminent diabetologist Apollinaire Bouchardat.

field of diabetology. He explored the relationship between glycosuria and diabetes treatment, while in his work *Nouvelles recherches sur le diabète sucré ou glycosurie*, he proposed a therapeutic approach to diabetes based on diet.<sup>3</sup> Significantly, he stressed the role of the pancreas in the development of the disease. However, in his experimental and histological studies, he hypothesized the existence of an enzyme, named "diastase" which he assumed enabled the transformation of amide into glucose, and fruitlessly explored this erroneous theory.<sup>3</sup>

It should be noted here that Bouchardat is considered the founder of Clinical Biochemistry in France. Indeed, he measured glycosuria using the J.B. Biot's polarimeter. He also worked on the measurement of toxic substances (strychnine, morphine, mercury, copper, arsenic). During the 1830s, he did research into digestion and observed the histological changes of the pancreas in diabetes. He additionally established the causes of scurvy and advocated its treatment. In the field of pharmacology Bouchardat published the *Formulaire magistral* in 1840, which remained the most important bedside book of physicians and pharmacists for the rest of the 19<sup>th</sup> century. He described the optical properties of various natural substances such as alkali plants, glycosides, terpenes and albuminous substances.<sup>3</sup>

His scientific output includes hundreds of reports and articles. Among them we may mention in particular the following: *Traité d'hygiène publique et privée*, *Annuaire de thérapeutique et de matière médicale*, *Chimie élémentaire*, *Physique élémentaire*, *Manuel complet du baccalauréat*.<sup>2</sup>

## **BOUCHARDAT'S PLACE IN THE DEVELOPMENT OF THE FIELD OF DIABETOLOGY**

The history of the development of the field of Diabetology differs significantly from that of the other endocrine conditions. The clinical symptoms of the disease were described by Sushruta (6<sup>th</sup> century BC), Aretaeus of Cappadocia (2<sup>nd</sup> century AD) and Avicenna (980-1037), the letter stressing the abundance of diuresis, the intensity of thirst and general disorders of the condition. Eventually, the disease was definitively identified by means of the detection of the sweet taste of the urine observed by Thomas Willis (1621-1675) in 1674.<sup>4</sup>

The interpretation of the sweet flavor in the urine of diabetics was confirmed thanks to the development of chemistry at the end of the  $18^{th}$  century. In 1775, Matthew Dobson (1745-1784) demonstrated that the sweetness of urine and serum in diabetics was due to the presence of sugar. In 1778, Thomas Cawley reported a case of diabetes due to stones in the pancreas, this also suggesting that "diabetes could occur due to damage to the pancreas". In 1797, the army surgeon John Rollo (?-1809) published his book, *An Account of Two Cases of the Diabetes Mellitus*, in which he was the first to apply the adjective "mellitus" to the disease thereby denoting the hyperglycemia of diabetes mellitus, or "grape sugar" as it was designated by Nicolas in 1803.<sup>5</sup>

Following Bouchardat's original contributions in the field of diabetology in 1830, the clinical knowledge of the disease was further enriched through increasing investigation into its complications. For example, Von Stosch in 1828, Proust and Grisolle in 1848, Marsh in 1854 and lastly Kussmaul in 1874 intricately described the characteristics of diabetic coma, while in 1852. Marchal drew attention to the frequency of arteritis and gangrene in diabetics and Pavy was among the first to consider the relationship between diabetes and liver impairment. In the 20<sup>th</sup> century, diabetic nephropathy was the subject of numerous studies, such as those of Rathery in France and Kimmelstiel and C. Wilson in the United States (1936).<sup>3</sup>

# BOUCHARDAT AND THE EVOLUTION OF THE DIABETES DIET

Towards the end of the 1850's, Pierre Adolphe Piorry (1794-1879), Professor of Internal Medicine in Paris, recommended that diabetics consume large amounts of sugar. However, one of his colleagues, a diabetic, was unfortunate enough to follow his advice and died as a consequence. Nevertheless, at the beginning of the 20<sup>th</sup> century, a considerable number of physicians still believed in the need to increase the consumption of sugar as a means of treating this disease. Even the most seemingly knowledgeable specialists tended to urge their diabetic patients to gain weight.

In 1910, the American physician Frederick Madison Allen (1879-1964) developed his famous "Allen starvation treatment". Considered the best therapy for diabetics before the introduction of insulin, it comprised severely restricted calorie intake (1000 calories per day) and was rich in fat and protein accompanied by 10g of carbohydrate daily.<sup>6</sup>

An important first step in the right direction was made when physicians began to adopt a position contrary to that of overeating, realizing that the surplus of food absorbed by diabetics required an extra effort of the organism, this aggravating their condition. Noting that carbohydrates appeared on the whole to be particularly harmful, they additionally recognized that, since the absorptive capacity of the diabetic organism is severely compromised, a diet poor in carbohydrates would likely be appropriate.<sup>7</sup>

Bouchardat refuted the disastrous method of Piorry, establishing his own diet specifically adapted to the needs of his diabetic patients. He experimented with periodic fasting, having noted that, during the 4-month siege of Paris in the 1870 Franco-Prussian war, those patients of his who suffered from starvation presented diminished glucose in their urine. He had also observed that exercise seemed to increase the tolerance of diabetics to carbohydrate. "You should earn your bread through the sweat of your brow", declared Bouchardat to one of his patients who had asked him to increase his food ration.<sup>8</sup> Moreover, Bouchardat sought to demonstrate the merits of his principles via their practical clinical application. He was the first to put his patients on a specific diet, thus inaugurating the clinical knowledge of diabetes and its dietary treatment.

His clinical mind and common sense impelled him to stress the importance the importance of the diabetes diet since he wrote: "...it is difficult to refrain, and to continue thus, when man so much hungers after bread. Despite the most careful monitoring, despite the assurances of these unfortunates, it is true that this food will become fatal for them, since nothing averts them from it. A little later, tired of this treatment that does not end and exhausted, more morally than physically, the diabetics resume their starchy meals; the accidents reappear....and death arrives".8 Bouchardat's work on diabetes, begun in 1830, continued for half a century. All his articles on this disease are summarized in his book De la glycosurie ou diabète sucré; son traitement hygiénique, published in 1875 in Paris and considered as the best approach to dietary treatment of diabetes.

Although a supporter of Rollo's gastric theory concerning diabetes, Bouchardat would modify it, adding the hypothesis of the presence in the gastric juice of a "diastase", an enzyme that promotes the transformation of amide into glucose. Normally carried out in the intestine, this chemical reaction was thought to occur in the stomach under certain pathological conditions; the gastric mucosa would allow a more rapid passage of sugar in the blood, hence the hyperglycemia and glycosuria.<sup>8</sup> This constituted an approach similar to that of the German physician Wilhelm Griesinger (1817-1868).

In his first treatise on diabetes (1830), Bouchardat proposed the presence of a "diastase" in the stomach

of diabetic patients. Later, he carried out numerous experiments to study in depth the digestion of starches in both physiological and pathological conditions. The results of these investigations were recorded in various publications dealing with "*la fermentation* glucosique", presented at the Academy on January 13, 1845, "*la digestion des aliments sucrés et féculents*" and "*les fonctions du pancréas*", presented to the Academy of Sciences on January 20, 1845.<sup>3</sup>

The following question occurred to him: "Does there exist in the gastric juice a specific substance that plays an important role in the disease?" Italian and German medical authors of the same period who had written on diabetes reported the existence of the diastase in normal gastric juice. However, though Bouchardat experimented on the action of normal gastric juice on intact starch, on jelly starch and on bread, he could never discern the least specific debilitating action. He thus concludes: "To my mind, the existence in the gastric juice of a substance that transforms the starch into glucose in the stomach of diabetics concerns a "pathological" fact and not a "physiological" one, and it is none other than the diastase". This was Bouchardat's theory, inspired by that of Rollo. He summarized his ideas saying, "... abundant glycogenic food, production of an overly energetic diastatic ferment, excess of glucose in the blood: these are the main conditions defining diabetes mellitus pathogenesis"<sup>8</sup> (Figure 2).

## BOUCHARDAT, PROMOTER OF THE FIRST DIET FOR DIABETES IN THE CONTEMPORARY AGE

Despite some unresolved questions and the unsoundness of his "diastase" theory, the fact remains that Bouchardat was the first physician to formulate a dietary treatment and should therefore be viewed as the originator in the present age of a diet tailored to diabetes. He recommended the substitute of carbohydrate fats and advocated alcohol which, according to him, was a valuable source for diabetics of considerable amounts of calories. He was opposed to milk consumption because of its richness in lactose, while he recommended green vegetables and gluten bread. He also demonstrated the importance for diabetics of a moderate degree of undernutrition combined with physical exercise.<sup>9</sup>



Figure 2. Frontispiece of Bouchardat's manuscript on diabetes mellitus.

In his book, *De la glycosurie ou diabète sucré*, Bouchardat devotes seventeen pages to enumerating both forbidden and permitted foods. He begins by offering general advice on the alimentation of diabetics such as the following: "Eat moderately and slowly, chewing the food thoroughly; the amount of urine in 24 hours needs to be over one liter and a half; drink the least possible; two meals a day are advised: one at 10 o'clock, the other at 6 o'clock; avoid resting, and especially sleeping, after meals; a good walk out of doors is recommended; sleep only four to five hours after the last meal; refrain from smoking".<sup>8</sup>

In the list of forbidden foods he includes starches and sugars and anything which contains "all fruits" and "jams of all kinds". Also prohibited are bread, regardless of the cereal, carrots, turnips, rape and other farinaceous roots, or sweet onions, radishes, beans, peas, lentils, beans and chestnuts. This list additionally incorporates honey, milk, beer, cider, wines sparkling or sweetened, carbonated water, soft drinks and other beverages, especially when they are sweet, and also sorrel soup. All these foods are prohibited because they are not used by the body and, moreover, will produce sugar in the urine.<sup>9</sup>

The list of permitted foods is very long, including gluten bread and many others. Providing more specific advice about meals, he writes: "...you can add egg volks and cream in the last soups and in chocolate". Concerning meat, he said: "...all the meats and deli meats, smoked or salted, are acceptable; they can be served dry in slices or with olive oil and herbs on them". Concerning pastry entries: "...all these dishes should be prepared with gluten flour instead of regular flour". Regarding wines: "...during the 24-hour day, a liter of wine suffices for a man and 0.5 liter for a woman". He advocates old wine (white or red) and adds: "...wine is very useful to animate the body's forces, but when these are diminished by the design of the regime and moderate exercise, it is appropriate to eliminate them from the diet".<sup>8</sup>

In general, the recommended foods were meat (beef, lamb, veal), fish fried or with sauce, cheese, eggs, cream. Preference was given to animal and vegetable fats, in order to replace banned carbohydrates, and alcohols. He suggests that "you can add to coffee and tea infusions either a dash of rum or brandy, kirsch, pure glycerin or a dollop coffee instead of sugar cream".<sup>8</sup> Bouchardat believed that the diabetic's sugar in the urine was "grape sugar" (glucose). To detect glycosuria, he used the fermentation test, the polariscope and solutions of copper.

Bouchardat's contribution to the dietary treatment of diabetes was noteworthy and is still appreciated today. His clinical work was inspired through his medical intuition, since the metabolism of diabetics was as yet unknown during his time.<sup>10</sup> Subsequent to Bouchardat's pioneering prescription of dietary treatment for diabetes, there followed similar initiatives by Carl Harko von Noorden, Frederick Madison Allen and Wilhelm Falta.

#### CONCLUSION

Bouchardat's firmly scientifically based work on diabetes resulted in the improvement in the health of numerous diabetics. His efforts were characterized by originality and innovativeness. He passed away in 1886 at the age of 80, living in relative poverty in a small apartment near the Hôtel-Dieu hospital, continuing to treat and tend his patients, until his very last days. A truly dedicated Physician and Scientist.

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