

CAUSES AND HISTORY OF THE ORIGIN OF DIABETES

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Annotation: Clinical features similar to diabetes mellitus were described 3000 years ago by the ancient Egyptians. The term "diabetes" was first coined by Araetus of Cappodocia (81-133AD). Later, the word mellitus (honey sweet) was added by Thomas Willis (Britain) in 1675 after rediscovering the sweetness of urine and blood of patients (first noticed by the ancient Indians). It was only in 1776 that Dobson (Britain) firstly confirmed the presence of excess sugar in urine and blood as a cause of their sweetness. In modern time, the history of diabetes coincided with the emergence of experimental medicine. An important milestone in the history of diabetes is the establishment of the role of the liver in glycogenesis, and the concept that diabetes is due to excess glucose production Claude Bernard (France) in 1857. The role of the pancreas in pathogenesis of diabetes was discovered by Mering and Minkowski (Austria) 1889. Later, this discovery constituted the basis of insulin isolation and clinical use by Banting and Best (Canada) in 1921. Trials to prepare an orally administrated hypoglycemic agent ended successfully by first marketing of tolbutamide and carbutamide in 1955. This report will also discuss the history of dietary management and acute and chronic complications of diabetes.

Key words: Mering, Minkowski, history, diabetes, Claude Bernard.

The condition known today as diabetes (usually referring to *diabetes mellitus*) is thought to have been described in the Ebers Papyrus (c. 1550 BC). Ayurvedic physicians (5th/6th century BC) first noted the sweet taste of diabetic urine, and called the condition *madhumeha* ("honey urine"). The term *diabetes* traces back to Demetrius of Apamea (1st century BC). For a long time, the condition was described and treated in traditional Chinese

medicine as *xiāo kě* (消渴; "wasting-thirst"). Physicians of the medieval Islamic world, including Avicenna, have also written on diabetes. Early accounts often referred to diabetes as a disease of the kidneys. In 1674, Thomas Willis suggested that diabetes may be a disease of the blood. Johann Peter Frank is credited with distinguishing diabetes mellitus and diabetes insipidus in 1794.

In regard to *diabetes mellitus*, Joseph von Mering and Oskar Minkowski are commonly credited with the formal discovery (1889) of a role for the pancreas in causing the condition. In 1893, Édouard Laguesse suggested that the islet cells of the pancreas, described as "little heaps of cells" by Paul Langerhans in 1869, might play a regulatory role in digestion. These cells were named Islets of Langerhans after the original discoverer. In the beginning of the 20th century, physicians hypothesized that the islets secrete a substance (named "insulin") that metabolises carbohydrates. The discovery and purification of insulin for clinical use between 1921–1922 by a group of researchers in Toronto—Frederick Banting, J.J.R. Macleod, Charles Best, and James Collip—paved the way for treatment. The patent for insulin was assigned to the University of Toronto in 1923 for a symbolic dollar to keep treatment accessible.

In regard to *diabetes insipidus*, treatment became available before the causes of the disease were clarified. The discovery of an antidiuretic substance extracted from the pituitary gland by researchers in Italy (A. Farini and B. Ceccaroni) and Germany (R. Von den Velden) in 1913 paved the way for treatment. By the 1920s, accumulated findings defined diabetes insipidus as a disorder of the pituitary. The main question now became whether the cause of diabetes insipidus lay in the pituitary gland or the hypothalamus, given their intimate connection. In 1954, Berta and Ernst Scharrer concluded that the hormones were produced by the nuclei of cells in the hypothalamus.

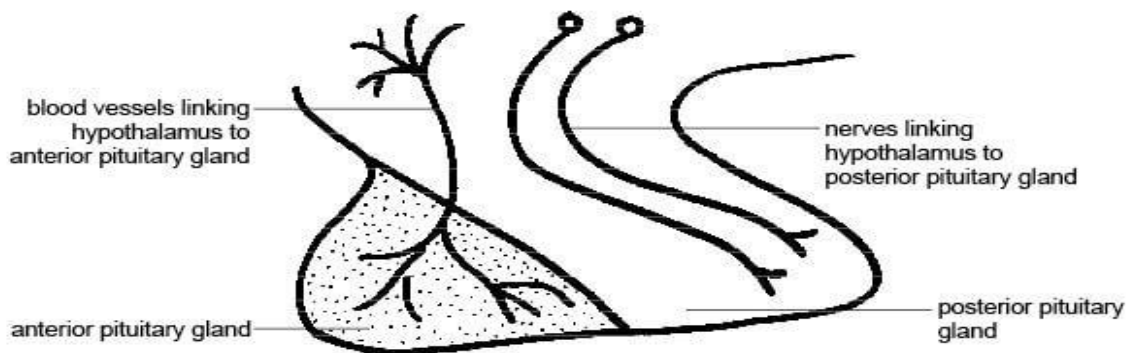
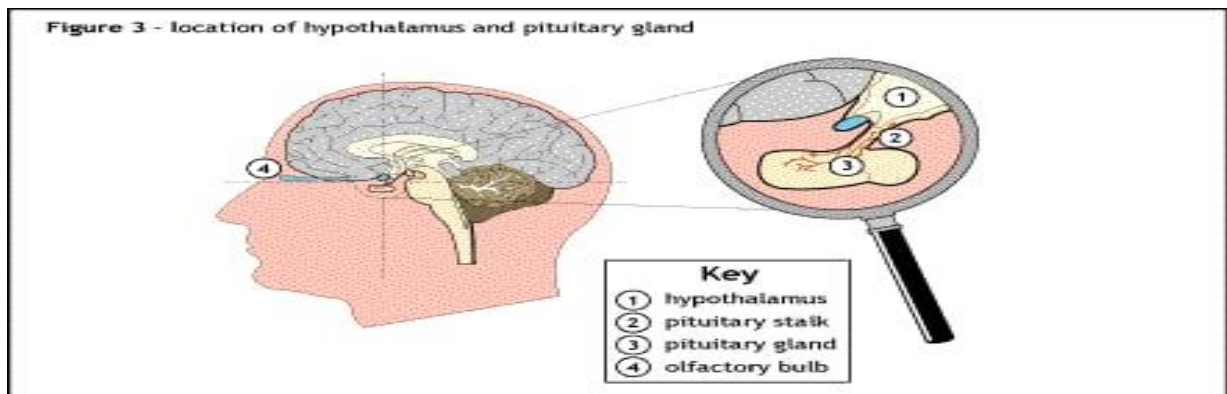
The Ebers Papyrus is among the oldest and most important medical papyri of Ancient Egypt. Written circa 1550 BC, it was likely copied from a series of much earlier texts, and contains a passage from the First Dynasty (c.

3400 BC). The document is named after Georg Ebers, who purchased the document in 1872 in the city of Luxor, the site of Thebes (known to Ancient Egyptians as Waset). Thebes was the most venerated city of Ancient Egypt in its heyday during the Middle Kingdom and New Kingdom.

The Ebers Papyrus is thought to contain the first known medical reference to diabetes, by the phrase: "...to eliminate urine which is too *asha*". The crucial word *asha* can mean both "plentiful" and "often". It is unclear whether the condition described was excessive urine (polyuria), which may have been symptomatic of diabetes, or increased frequency of urine, very often due to urinary tract infection.

Zhang's specialized chapter on *xiāo kě* is found in *Shānghán Lùn* and *Jīnguì Yàoliùè*. Nine subsections and nine formulae (herbal remedies) on wasting-thirst were recorded. The text proposed a theory of "three wasting-thirsts": upper- (associated with the lungs), middle- (associated with the stomach), and lower- (associated with the kidneys), all three of which shared excessive urine and thirst as symptoms. This theory was later expanded through the works of Liu Wansu (1120–1200 AD) and Wang Kentang (1549–1613 AD). According to Liu, "lower wasting-thirst" attributed to "kidney-yin deficiency" was associated with sweet urine (glycosuria).^[17] This may indicate differentiation akin to modern-day differentiation of diabetes mellitus and diabetes insipidus.

In 1794, Johann Peter Frank gave a relatively clear description of diabetes insipidus, as a "long continued abnormally increased secretion of non-saccharine urine which is not caused by a diseased condition of the kidneys".^[68] This remained the general state of knowledge for another century. William Osler, in the first edition of his textbook (1892), summarized the pathophysiology of the condition as follows: "The nature of the disease is unknown. It is doubtless of nervous origin. The most reasonable view is that it results from a vasomotor disturbance of the renal vessels... giving rise to continuous renal congestion.



In 1912, Alfred Eric Frank, then working on diabetes mellitus in the department of Oskar Minkowski in Breslau, reported a specific link to the pituitary gland upon observing a case of a man who had survived after shooting himself in the temple. Morris Simmonds drew the same connection in 1913. Thereafter, numerous reports documented cases of diabetes insipidus associated with pituitary lesions, steadily accumulating evidence favouring the hypothesized connection.

George Oliver and Edward Albert Schafer were among the first researchers to document its endocrine functions.^[71] In the first two decades of the 20th century, however, a number of conflicting reports on the diuretic versus anti-diuretic properties of the pituitary extract caused confusion in the field.

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