A. Historical Dates

G. R. Constam

Around 1500 B.C., Papyrus Ebers, Egypt; description of abnormal polyuria, possibly diabetes mellitus.

6th century B.C. The Indians differentiated the asthenic from the sthenic form of diabetes mellitus. In the Ayur Veda of Susruta, the illness is termed as “madhumeha” or “honey-urine”.

A few centuries B.C., the Chinese recognized the sweet taste of the urine.

30 B.C. to 50 A.D. Aulus Cornelius Celsus described a condition in which much urine was excreted.

30 to 90 A.D. Aretaeus of Cappadocia described a condition in which much urine was excreted.

131-201 A.D., Galen described diabetes as a weakness of the kidneys.

860-932 Rhazes, an Arabian physician, discussed the treatment of diabetes mellitus.

980~1027 Avicenna believed that the liver was particularly affected in diabetes, and observed the connection between diabetes, furunculosis, and impotence.

1621~175 Thomas Willis, in Oxford, distinguished diabetes mellitus from diabetes insipidus, and showed that the urinary sugar was increased in the former condition.

1682 Johann Conrad Brunner observed polyuria and polydipsia in a dog after removal of the pancreas.

1774 Robert Wyatt suspected the presence of a substance similar to sugar in the urine and blood. He obtained this substance by evaporating the urine.

1776 Dobson demonstrated a fermentable sugar in the urine and the sweet taste of the blood of diabetic patients.

1788 Thomas Cawley suspected a connection between diabetes and changes in the pancreas.

1796 Rollo recommended a low-calorie diet in the treatment of diabetes and described the smell of acetone.

1815 Chevreul identified the sugar in diabetes as glucose.

1806-86 Bouchardat utilized fermentation tests, the polarimeter and solutions of copper salts, for estimating sugar. He substituted fat and alcohol for carbohydrates, emphasized the value of green vegetables, of a low calory diet, and of much physical activity. He introduced days of fasting and the use of alkali, and discovered gluten bread.

1848 Hermann von Fehling described the urine test which was later named after him.

1849 Claude Bernard discovered glycogen in the liver, and the “piqure”. He made quantitative estimations of the sugar in the blood.

1869 Paul Langerhans discovered the islet cells of the pancreas.

1882 Chauvart and Hanot described the combination of pigment-cirrhosis and diabetes as “bronze diabetes”.

1889 V. Recklinghausen revealed the nature of the two pigments of “bronze diabetes”, and introduced the term hemochromatosis.

1889 O. Minkowski and J. von Mering incidentally discovered that total pancreatectomy in a suitable experimental animal produces diabetes.

1891 Giulio Vassale ligated the excretory ducts of the pancreas, which led to the destruction of the acini, but not of the islet cells.

1892 O. Minkowski produced temporary disappearance of diabetes in dogs by subcutaneous implantation of the excised pancreas.

1893 Laguesse suspected that the islet cells formed a hormone.

1895 V. Noorden developed a technique of dietary therapy, stressed the formation of sugar from protein, and introduced the course of oats as a treatment.


1906 Naunyn studied the metabolism in diabetes, particularly in diabetic acidosis. He emphasized the familial occurrence
of the disease, and the value of a just adequate nourishment in the prophylaxis and in the treatment of the metabolic disturbance.

1908 Zuelzer gained an alcoholic extract from the pancreas, which, after being injected, produced shock—probably of hypoglycemic nature—causing the trial to be discontinued.

1909 De Meyer gave the name insulin to the still hypothetical hormone of the islet cells.

1913 F. M. Allen became famous for his hunger cures. He also contributed to the knowledge of carbohydrate metabolism.

1918 C. K. Watanabe produced hypoglycemia in the animal with an injection of guanidine.

1921 N. C. Paulesco in Rumania reported "pancréine," i.e., a blood sugar-lowering extract from pancreas of dogs or cattle, which he had discovered during the First World War (1914–18).

1921 Frederick G. Banting and Charles H. Best discovered insulin.

1921 F. C. Mann and T. B. Magath showed that hepatectomy results in hypoglycemia.

1924 B. A. Housay and Magenta noticed that hypophysectomy increases sensitivity to insulin.

1924 Seal Harris suspected hyperinsulinism as a cause of spontaneous hypoglycemia.

1926 E. Frank, M. Notthmann, and A. Wagner introduced biguanidines into the treatment of diabetes which, however, was abandoned in 1940.

1926 Abel succeeded in crystallizing insulin.

1927 Wilder, Allan, Power, and Robertson published the first case of organic hyperinsulinism.

1929 Howland, Campell, Maltby, and Robinson removed an islet-cell tumor and cured a case of hyperinsulinism for the first time.

1936 H. C. Hagedorn produced the first reliable insulin with prolonged action.

1937 F. G. Young discovered meta-pituitary diabetes.

1937 H. R. Jacobs observed alloxan-hyperglycemia.

1942 Guest pointed out hypokalemia during the treatment of diabetic acidosis.

1942 M. Janbon noticed the hypoglycemic action of one of the sulfonamides recommended for the treatment of typhoid fever.

1943 Dunn, Sheehan, and MacLetchie discovered alloxan-diabetes.

1944 A. Loubañières explained the mode of action of certain hypoglycemic agents.

1945 H. Franke and J. Fuchs observed hypoglycemia produced by another sulfonamide, and suggested that it should be used therapeutically in diabetes mellitus.

1955 F. Sanger discovered the structural formula of the insulin molecule.

1957 G. Ungèr introduced phenethyl biguanide into the treatment of diabetes.

1958 S. A. Berson and R. S. Yallow measured the insulin content of the plasma by radioimmunological methods.

1964 H. Zahn in Germany, katsoYannis in U.S.A, and niu Ching-i in China (1965), all independently succeeded in synthesizing insulin.

1967 D. F. Steiner and P. Oyer isolated proinsulin.

1969 Mrs. D. G. Hodgkin discovered the three-dimensional structure of pig insulin.

**B. Embryology and Histology**

G. Tondury and G. Kistler

In the human embryo 3 to 4 mm in length, two entodermal outpocketings arise on opposite sides of the primitive duodenum. One of the epithelial buds grows out from the dorsal wall of the gut, just above the hepatic diverticulum; it forms the dorsal pancreas. The ventral pancreas, on the other hand, originates in the caudal angle between hepatic diverticulum and gut. When the embryo is about 12 mm long, the two primordia meet, and when it is about 16 mm, they fuse to produce a joint organ. With the exception of the major parts of the head and the uncinate process, which are derivatives of the ventral bud, most of the mature gland is formed by the dorsal pancreas anlage. Both primordia are crossed by an axial longitudinal duct. The duct of the dorsal anlage originates directly from the wall of the duodenum, whereas the ventral duct opens into the stem of the elongating common bile duct. When duodenal torsion has brought the two primordia into close side-by-side contact, the ventral duct taps its dorsal counterpart. The major pancreatic duct of the mature gland (duct of Wirsung) results, therefore, from the fusion of the ventral duct with the distal segment of the dorsal duct. The proximal stem segment of the dorsal duct, on the other hand, constitutes the accessory duct of Santorini, which usually retains its connection to the duodenum as well.

The islets of Langerhans develop from epithelial cells of the outgrowing pancreatic ducts. They are, therefore, of entodermal origin. Even