RECENT ADVANCES IN CHILDHOOD DIABETIS MELLITUS

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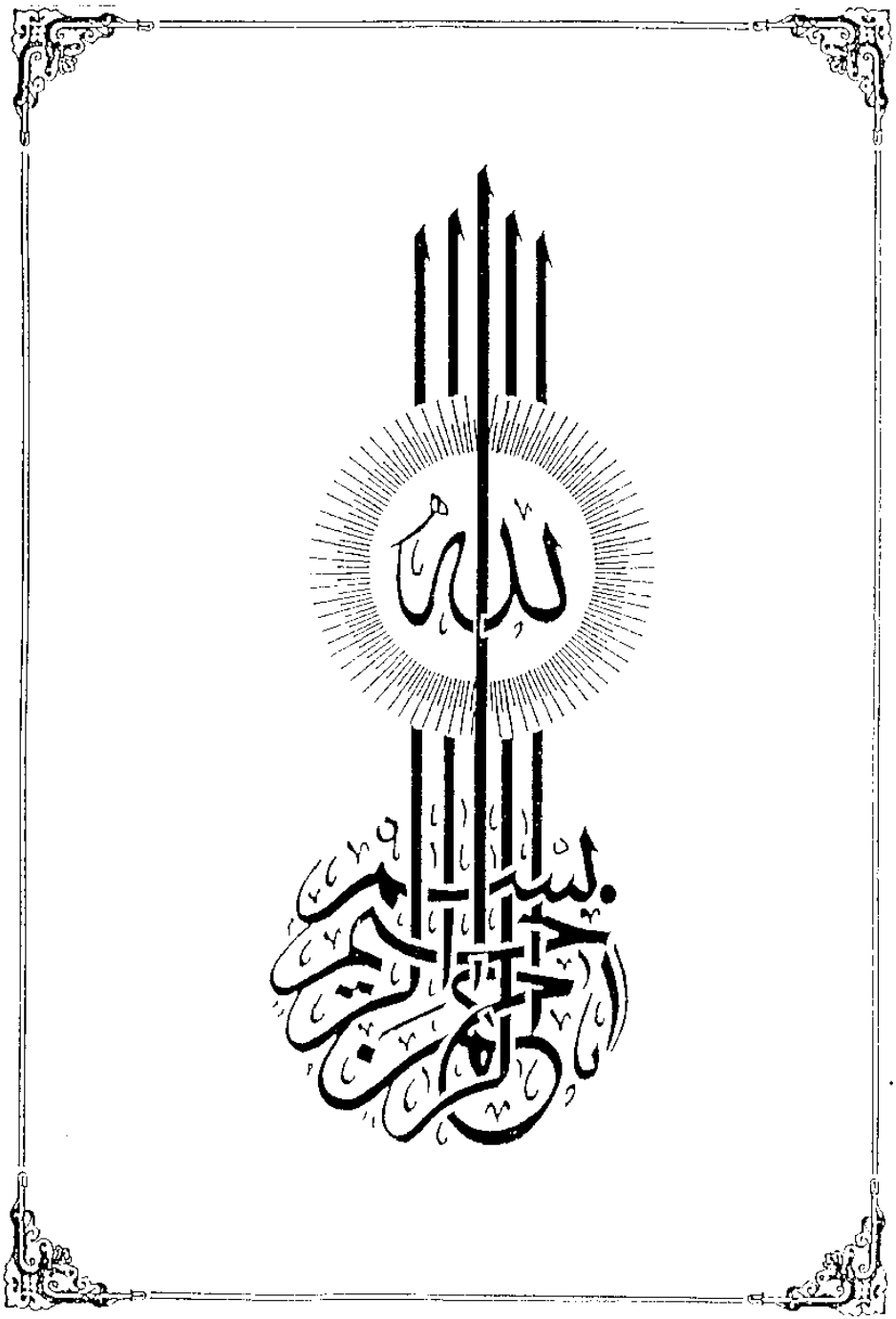

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Diabetes mellitus is the commonest endocrine disorder in childhood.

However, the pathogenesis of diabetes continues to be an engima. Furthermore, although insulin has been available now for over 50 years, yet the management continues to present an enormous challenge.

The conspicious short comings of diabetes management have generated great interest in alternative methods of insulin replacement as the use of artificial pancreas and pancreatic transplantations. However these are not likely to have a clinical application in the foreseeeable future.

A report of the National Commission on Diabetes Mellitus presented to the Congress of the United (Crofford, 1976) included the followings :

1. The chance of developing diabetes doubles with :
   - a- Every 20% of excess weight.
   - b- Every decade of life.
2. People with diabetes are :
   - a- 25 times more prone to blindness.
   - b- 17 times more prone to kidney disease.

c- 5 times more prone to gangrene.

d- 2 times more prone to heart disease.

3. Coronary heart disease is the leading cause of death.

4. Approximately 50% of children with juvenile onset diabetes die with kidney disease within 25 years from the onset of clinical disease.

All the above mentioned points provoked the stimulus for reviewing the subject of "Childhood Diabetes."

II- HISTORICAL REVIEW

II- Historical Review :

Diabetes Mellitus was first recognized in written history about 1500 B.C. in Egypt (Malone, 1977).

The passing of frequent and large quantities of urine was recorded in the papyrus Ebers, a copy of an Egyptian medical journal. Celsus (30 B.C. 38), wrote concerning polyuria without pain but with emaciation and danger. Aretaeus (30 - 90 AD) described diabetes and gave it the Ionic Greek name meaning "to run through a siphone". A Chinese physician, Tchang Tchonking (200 AD), described diabetes as the disease of thirst.

The arabian doctor Avicena (980 - 1037 AD), gave the first description of diabetic gangrene.

Willis (1621-1675) observed that the urine of the diabetic patient was wanderfully sweet as if imbedded with honey or sugar.

Morton (1637-1698) was the first to make clear the heriditary characteristics of diabetes.

In (1788) Cawley gave the first description of a fatal case of diabetes with abnormal changes in the pancreas.

Cullen (1712 - 1790) added the adjective "mellitus" to the disease in order that it might be distinguished from diabetes insipidus.

The odour of decaying apples - doubtless acetone - was noted on the breath of a young diabetic patient by Marshall (1798).

Cherreul (1815) found that the sugar present in the urine of diabetic patients was identical with glucose.

Trommer reported his qualitative test for sugar in the urine in 1841 and Fehling reported a quantitative test in 1850.

Peteres (1827) obtained from the urine of a patient in diabetic coma positive reactions for acetone, but it was Kussmaul in (1874) who gave the first detailed clinical description of diabetic coma.

Rollo (1796) treated diabetes by restriction of the diet to animal food and few green vegetables of low food value, occasionally permitting some milk and little bread. Drugs were given to decrease the appetite. Bouchardat (1806 - 1886) revived the Rollo treatment but

modified it by substituting fat and alcohol for carbohydrates.

Duncan (1963) stated that Baunel was first to set up the hypothesis that all types of diabetes are pancreatic in origin.

Langerhans, in 1869 discovered islet formation in the pancreas which bears his name.

Von Mering and Minkowski (1889) discovered diabetes in a dog following pancreatectomy. They established the hypothesis of the internal secretion of the pancreas.

Naunyn (1906) introduced the term acidosis and recognized clinical renal glycosuria.

Duncan (1963) stated that the swelling of the beta-cells of Langerhans, formerly designated hydropic degeneration, was first observed by Weichselbaum and Stangle but it was (Opie, 1901) who first put forward the hypothesis that diabetes is due to alterations in the islets of Langerhans.

Allen (1914) demonstrated the advantages of undernutrition in the treatment of diabetes.

Duncan (1963) mentioned that Rousston and Woodytt used high fat diet, but Joslin (1949) found that by decreasing the fat content of the diet the patient's health was improved.

Allen (1914-1921), investigated diabetic therapy by experiments on partially depancreatized dogs on the permise that diabetes is a disorder of the total metabolism and not of carbohydrate utilization alone and that the maintenance of the entire body mass constituted a load upon the internal secretion of the pancreas.

A great triumph had been obtained by the discovery of insulin by Banting in (1921).

Houssay and Magenta (1924) found that the removal of the pituitary gland from a dog increased the animal's sensitivity to insulin. Later, Houssay and Biostti (1930), found that in toads and dogs hypophysectomy diminished the severity of diabetes produced by pancreatectomy.

A transitory diabetes was provoked by giving normal animal an injection of anterior pituitary extract (Evan et al, Bauman and Marini, 1932) and diabetes was made more severe by treatment with anterior

pituitary extract (Biasotti and Haussy, 1936).

Long and Lukens (1936) attenuated the diabetes by removing the adrenal cortex from depancreatized cats.

Lukens and Dohan (1938), by giving large doses of cortin, aggravated the diabetic state in depancreatized and adrenalectomized dogs.

Abel (1927) obtained insulin in a crystalline form.

Hagedorn (1936) succeeded in reducing the immediate effect and in prolonging the action of insulin by adding protamine. The resulting product, protamine insulin, was relatively unstable, but Scott and Fisher (1936) by adding small amounts of zinc, prolonged its activity and made the product more stable. Zinc insulin crystals in solution were made commercially available in 1938. Globin insulin, the first commercial insulin with an intermediate action was made available by Reiner et al in 1946. A modification of protamine zinc insulin, in Hagedorn's laboratory led to production of (NPH) insulin (N = neutral, P = protamine, H = Hagedorn).

Haist et al (1940) have found that the production

of diabetes by injection of the anterior pitutary extract is prevented if large doses of insulin are given at the same time as the pituitary extract. They also found it impossible to provoke diabetes by injection of the pituitary extract if the animal was on a starvation regimen.

The hypoglycemic effect of certain sulfonamides when taken orally was observed by Janbon and his colleagues (1942) and was further explored and developed by Loubatiers (1946).

The lent insulin, semilent and ultralent were developed by Moller and his associates (1951). They contain no added protein and yet possess a spectrum of activaties - rapid - intermediate and long effects.

The concept of subclinical diabetes is not new, attention has been attracted to the possibilities of preventing clinical diabetes by treating the prediabetic pregnant women (Hoet, 1954), and the prediabetic relatives of diabetes (Conn and Fajans, 1961) as thought they had mild diabetes.

Intermittent periods of 4 to 14 days of total fasting have been introduced and extended for the correction and control of intractable obesity complicating diabetes (Duncan et al, 1962).