ISLET CELL ANTIBODIES IN NON-INSULIN DEPENDENT DIABETES

T H E S I S

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(M E D I C I N E)

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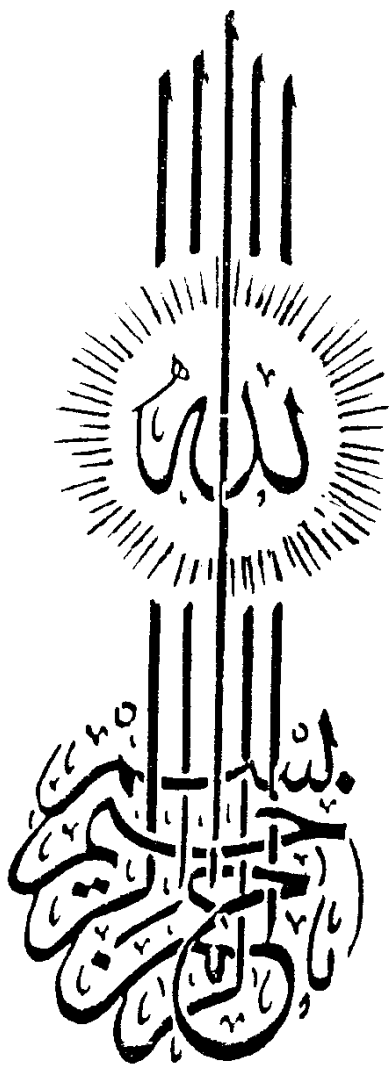

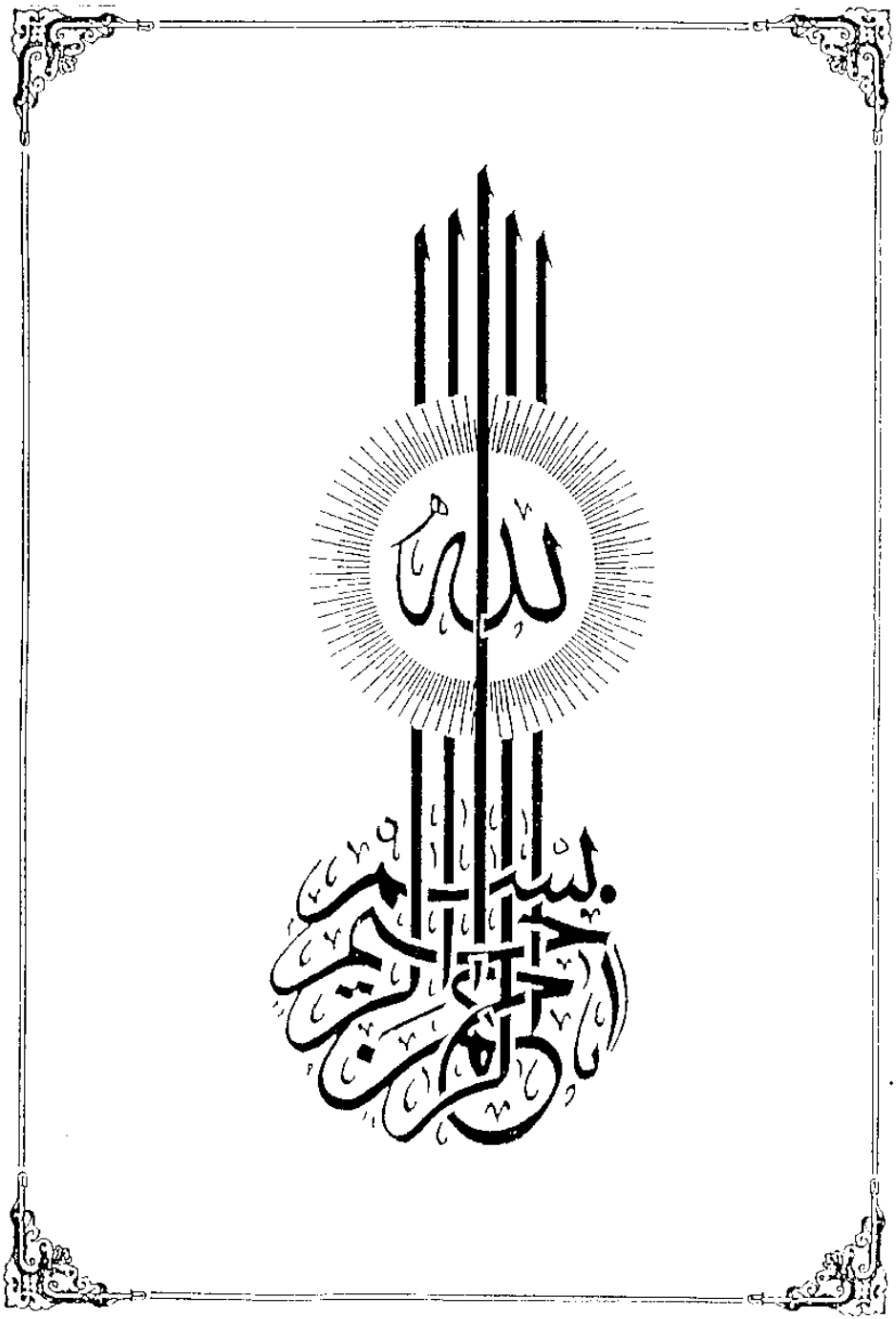

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INTRODUCTION

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Islet cell antibodies were detected frequently in insulin dependent diabetes mellitus. The frequency of the prevalence were related to the duration of the disease, prevalence of autoimmune endocrinal disorders and certain HLA phenotype. (Irvine et al., 1977 a).

Irvine et al.,(1977 b & 1979) were able to estimate islet cell antibodies in 86% of patients treated with oral hypoglycemic agents, shifting to insulin dependency, and the prevalence of islet cell antibodies in non insulin dependent diabetics are considered as a marker for hypoglycemic therapy failure.

The aim of the work is to study the incidence of islet cell antibodies in non insulin dependent diabetics treated with oral hypoglycemic agents, in various duration of the disease. By indirect immunofluorescence technique on small sections of guinea pig pancreas.

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REVIEW

DIABETES MELLITUS

It has been clearly established in recent years that diabetes mellitus is a genetically and clinically heterogenous group of disorders that share glucose intolerance in common. Diabetes is however , the most common serious metabolic disease of humans.

The disease is characterized by either fasting hyperglycemia or levels of plasma glucose during an oral glucose tolerance test above defined limits. It is characterized also by a series of hormone - induced metabolic abnormalities,by long-term complications, and by a microvascular lesion demonstrable by electron microscopy. In recent years it has become clear that a variety of syndromes are subsumed under the general term diabetes and that they differ in both clinical manifestations and patterns of inheritance, (Foster, 1984).

CLASSIFICATION OF DIABETES MELLITUS

Traditionally, diabetes was classified according to patient's age at onset of symptoms into juvenile onset and adult onset diabetes mellitus.

In 1979 National diabetes data group has classified diabetes. The classification system had to fulfill the following requirements :

1. The classification should be defined so as to be exclusive, that is , an individual at any given time in his life can be placed in only one class.

2. The classification should require only simple clinical measurments or descriptive observations that are readily obtainable and have biologic significance.

3. The classes should be as precise and well defined, so that each class contains a population as homogeneous as possible.

4. The terminology should be precise and well defined and should describe the phenotypic expression of the abnormality as much as possible.

5. The classification should be adaptable and able to incorporate new research findings on the

etiopathology of diabetes.

The classification includes three clinical classes : diabetes mellitus; impaired glucose tolerance and gestational diabetes. In addition the classfication includes stages that may be part of the natural history of diabetes in which there are no abnormalities of carbohydrate metabolism, namely, previous abnormality of glucose tolerance and potential abnormality of glucose tolerance.

C L A S S	Former Terminology
I. Diabetes mellitus.	
a. Insulin dependent Type I	Juvenile diabetes, ketosis prone
b. Non insulin dependent Type II	Adult onset, maturity onset, ketosis resistant, stable diabetes.
- Non obese	
- Obese	
c. Other Types .	
Including diabetes associated with certain conditions and syndromes.	Secondary diabetes .
1.Pancreatic diseases. 2.Hormonal . 3.Drugs or chemical induced. 4.Insulin receptor abnormality. 5.Certain Genetic syndromes.	
II.Impaired glucose tolerance.(IGT)	Asymptomatic diabetes, chemical diabetes, subclinical diabetes, border line diabetes.
- Non obese	
- Obese	
- IGT associated with certain conditions and syndromes as	
- Pancreatic disease.	
- Hormonal .	
- Drug or chemical induced.	
- Genetic syndromes.	
III. Gestational diabetes.	Gestational diabetes.
IV. Previous abnormality of glucose tolerance (Pre AGT).	Latent diabetes, prediabetes.
V. Potential abnormality of glucose tolerance.	Potential diabetes, prediabetes.

[National diabetes Data group,1979].

TYPE I DIABETES

INSULIN DEPENDENT DIABETES MELLITUS (IDDM)

This Type of diabetes mellitus is usually characterized clinically by abrupt onset of symptoms, insulinopenia and dependence on injected insulin to sustain life, and proneness of ketosis.

Classically, this type of disease occurs in juveniles, so it was formerly termed juvenile onset diabetes. However, it can be recognized and become symptomatic for the first time at any age , hence, diagnosis based on age at onset is inapropriate.

In natural history of the disease there may be preketotic non insulin dependent phase, for example, by testing of siblings of insulin dependent diabetics with normal fasting plasma glucose levels but with abnormal glucose tolerance who progress rapidly to the ketotic form, usually within 2 years or longer.

Insulin dependent diabetes mellitus appears to be heterogenous in terms of genetics and environmental factors that precipitate the disease (Rotter and Rimoin, 1978).

Genetic determinants are thought to be important in most patients. As expressed by the associated increased or decreased frequency of certain histocompatibility antigens (HLA) on sixth chromosome (Cudworth and Woodrow , 1976).

Abnormal immune responses and auto immunity are also thought to play an etiologic role, and islet cell antibodies are frequently present at diagnosis in this type (Delperte et al.,1977).

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TYPE II DIABETES

NON INSULIN DEPENDENT DIABETES MELLITUS (NIDDM)

Persons in this subclass are not insulin dependent or ketosis prone, although they use insulin for correction of symptomatic or persistent hyperglycemia and they can develope ketosis under special circumstances such as episodes of infection or stress.

In the majority of cases, onset is after age of 40 but NIDDM is known to occur at all ages.

Serum insulin level may be normal, elevated or depressed (Genuth, 1973). About 60-90% of NIDDM subjects are obese, in those patients glucose tolerance is often improved by weight loss(Genuth,1982). Hyperinsulinemia and insulin resistance characterize patients in this subclass (National Diabetes data group ,1979). Patients with NIDD may be asymptomatic for years and show only slow Progression of the disease.

However, the typical chronic associations and complications of diabetes, namely, microangiopathy,