Synopsis from Recent Literature

GENETICS OF DIABETES

Understanding the genetics of diabetes has many intrigues. Carbohydrate intolerance being the only common factor, the present day recognition qualifies that diabetes is heterogenous and not a single entity. This renders genetic etiology per se possible only in a subset of diabetics.

At present studies in identical twins and of the HLA antigen provide us understanding of the genetic attributes in diabetes. Insulin dependent diabetes mellitus (IDDM) appears to be genetically distinct, linked with genes in the HLA region of the sixth chromosome. Non-insulin dependent diabetes mellitus (NIDDM) on the other hand, may be related to the molecular structure of insulin as coded on chromosome eleven.

The concordance rate in identical twins for IDDM is 50% and for NIDDM 90% (WHO, 1985).

HLA specificity for diabetes in a population varies from 5% (DR4) to 15% (DR3) when compared with control populations of the same ethnic background. This, however, only signifies the immunosuceptibility and not metabolic aberration. 1n IDDM associated with poly-endocrine autoimmunity the HLA allele specificity indicates further relationship with BW8 and DR3 (Irvine, 1980). Multiplex family studies on IDDM siblings are controversial to indicate if HLA identical or haplotypes are inherited as simple autosomal or recessive characteristics. With these limitations HLA typing. cannot be applied as a routine method in clinical practice.

Studies using- DNA restriction endonuclease enzymes may provide greater insight in this area in the future.

Unlike IDDM, NIDDM is not HLA associated. There is evidence, though not unequivocal, that a large DNA fragment flanking the insulin gene on chrosmosome eleven may be associated with NIDDM. Likewise, insulin response (C-peptide) to glucose is genetically modulated and serves as a marker for susceptibility to NIDDM.

Recent population studies comparing pure natives with admixed population bring out new information on the genetic profile of NIDDM (Serjeatson et al 1983). Nauru population with ancestral foreign admixture had a protective effect against diabetes, compared to pure natives. The protection was most marked in the older population. Among person aged 60 and over, 83% of full blooded Nauruans in the genetic sample had diabetes, compared to only 17% in part Nauruans. The association is believed to be genetic, for there was no difference in the diet, life styles or body mass index of the two groups. A study of Mexican Americans has also shown similar results.

Prevalence of diabetes in Pima Indians (who have 100°/a native American genes) is 50%, Barrio Mexican Americans (native American admixture 46%) 15%, Trans Mexican Americans (admixture 27%) 10% and Anglos (adimixture 0%) 5%. Thus, the native American gene seems to contribute to the greater prevalence of NIDDM, which declines with admixture (Lytt et al, 1984).

The entity maturity onset diabetes of the young (MODY) is inherited as a dominant trait (Tattersall, 1974). Many other genetic syndromes, mostly involving the neuromuscular system, inborn errors of metabolism or pancreatic degeneration are transmitted as dominant or recessive modes and are associated with impaired glucose tolerance or clinical diabetes mellitus. Inheritance of diabetes is thus polygenic.

References

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