INTERNATIONAL SYMPOSIUM ON EPIDEMIOLOGY OF DIABETES MELLITUS

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Today the scope of epidemiology has become wide based. Besides providing the distribution and determinants of health and disease, the methods of clinical evaluation, and study of the natural history of diseases have been made objective, and inferences are based on statistical evaluation.

An international symposium on epidemiology of diabetes mellitus supported by International Diabetes Federation and attended by eminent scientists from different parts of the world in this field has just concluded in Bangkok.

The contributions consisted of 8 plenary lectures, 48 oral presentations and 28 poster displays, over 2 days. A resume of the scientific deliberations that provide new information is presented herewith.

Plenary Sessions

Two of the plenary sessions were devoted to etiogenesis of diabetes mellitus (IDDM and NIDDM). The sequence for IDDM seemed to consist of :

(i) Genetic predisposition (relating to chromosome 6 HLA type DR3-DR4).

(ii) Environmental determinant (Beta cell cytotropic virus).

(iii) Beta cell function destruction (based on autoimmunity).

Mode of inheritance still seemed undeterminable, though penetrance was greater in familial cases than in sporadic cases. Beside virus, chemicals or IL-I could also initiate the beta cell injury. ICA or ICSA were not corroborative in all instances of IDDM. Antigen specific T-cell response was greater in DR4 than in DR3 haplo-types.

With regard to NIDDM, three stage development was defined :

1. Genetic susceptibility.
2. Insulin resistance.
3. Impaired glucose tolerance.

Pima Indian studies have shown frequency of HLA-A2 and now RFLP indicate 1-1 53%, 1-3 47 % and 3-3 3%. Pedigree studies have shown a dominant inheritance.

Mixed racial groups show intermediate prevalence than that observed in the individual ethnic populations. Presently insulin resistance studies, using euglycaemic clamp show impaired glucose utilization in NIDDM indicating that with existing hyper-insulinemia, there is

reduced insulin mediated glucose disposal. This insulin resistance precedes detectable abnormalities in the glucose homeostasis, sequential to insulin resistance. Thus sequence of factors for NIDDM are :

(i) Hyperinsulinaemia.

(ii) Glucose intolerance.

(iii) Hypertriglyceridemia.

(iv) Increase in VLDL.

(v) Hypertension.

(vi) Obesity, especially involving upper body segment.

Impaired glucose tolerance was categorised as :

(i) Non-obese.

(ii) Obese IGT.

(iii) IGT associated with other conditions.

Rate of worsening of glucose tolerance was related to initial degree of glucose value, body mass index and plasma insulin value.

Again Whitehall studies have shown 95% percentile IGT had substantial risk of CAD (18,000 cases, 100 deaths per 10 yr.).

Two other presentations relating to natural history of diabetes and complications were based on Japanese data.

Time course of complications worked out was different for IDDM and NIDDM:

Time (yr)	*IDDM*	*NIDDM*
5	Neuropathy (5.0)	Neuropathy (6.3)
10	Simple retinopathy (8.6) Intermittent proteinuria (11.9)	Simple retinopathy (7.4) Intermittent proteinuria (9.5)
15	Proliferative retinopathy (12.3)	Proliferative retinopathy (13.5)
20	Persistent proteinuria (15.7)	Persistent proteinuria (16.0)

The duration of diabetes was longer and progression of complications slower in NIDDM. Multivariate analysis showed that the factors correlating to development of the microvascular diseases were age, blood glucose, duration, hypertension, age of onset. The ranking order of the factors was different in different organ involvement and according to the treatment.

In Japanese diabetics HDLc changes are not observed, while IDL is proving a significant atherogenic factor. Of recent, the ratio of actual death over expected deaths from coronary artery disease had increased to 1.6 in this country.

In Scandinavia, incidence of diabetic nephropathy had been employed to determine as to the quality of the treatment provided. Those with strict control had 6 times lower mortality. With modern amenities for transplatantion, 50% of diabetics who had undergone this procedure were working full time and another 17% working half time. Again overall cost of transplant was less than repeated haemodialysis or CAPD procedures.

Oral Presentations :

In pathogeriecity of diabetes role of environment factors was gaining greater significance.

This was evident as regards IDDM from the population studies, migrants from Japan to Hawali and France to Canada. IDDM has also doubled in Finland and Poland.

In a study of BMI in Finland, risk of Diabetes (NIDDM) had a U shaped association with the 25 year average BMI. Amongst American born Japanese, early life urban environment represented adverse development factor for NIDDM. Family history had a promotive influence while educational achievement had a protective effect.

Beta lymphocyte clone of islet cell antibodies (ICB) were now identified in ICA negative IDDM. The Japanese workers had earlier reported 100% ICA positivity in IDDM if blood samples are collected within 6 months after the onset of diabetes. ICA positivity in Chinese IDDM is rather low (10%.)

Autoimmune thyroid disease patients had 4.5% prevalence of diabetes mellitus and nearly half of these were insulin dependent. All of these were ICA positive and 70% of these ICSA positive as well, which persisted throughout the follow up period.

Again heterogeneity of ICSA has been demonstrated, ICSA found in the earlier phase of IDDM is involved in the development of the disease, but found in aged subjects, either diabetic or non-diabetic appear to result from autoimmunity which is not specific from diabetes but caused by ageing process itself.

Repeat studies *in prevalence* in some populations of South East Asia are showing distinctive increase, e.g.

Singapore	(1975)	(1.99%)	(1986)	(5.30%)
Delhi	(1975)	(4.0%)	(1986)	(7.30%)
Papua New Guinea (Urban)	(1978)	(1.7%)	(1986)	(4.00%)

In the *diagnostic criteria*, fasting blood glucose values were found to be unimodal, slightly skewed and to increase significantly with age and body mass index in both sexes as observed in 1152 of the Thiai population. 2 hour blood glucose was assessed for its accuracy as a diagnostic test for diabetes. 2 hour blood glucose value of 11 mmol/1 (200 mg/dl) judged with standard OGTT has sensitivity of 69.2% (confidence interval 44.1-94.3%) specificity 97.4% (confidence interval 95.1-99.77) and positive predictive value 64.3% (confidence interval 39.2-89.4%). There was no difference in sensitivity of fasting, 2 hour post-glucose or HbA_1C value. It may therefore provide a reasonable estimate of prevalence of DM but individual diagnosis requires confirmation by OGTT. Fructosamine provide, correlation coefficient of 0.74 with fasting blood glucose and 0.7 with glycosylated haemoglobin. In comparison with other methods the predictive value of a positive (65.0%) and negative (85%) test results, make serum fructosamine a useful method for excluding or confirming the diagnosis of diabetes mellitus.

Interpretation of *blood glucose values during pregnancy* seemed controversial. W.H.O. has applied standard blood glucose values for diagnosis of gestational diabetes (disregarding O' Sullvians criteria) and introduced another term of impaired glucose tolerance during pregnancy (GIGT). Its acceptability and significance remains controversial.

Natural *history* of diabetes and rate of progression of diabetic complications, especially microvascular disease have been studied in various centres.

Urinary albumin/creatinine ratio (ACR) was of higher level >4, 2½ times in Indians than the European diabetics in a study in London. Amongst instances of diabetic nephropathy, in South India 55% had diabetes <10 yrs, and only 5.5% had the disease >20 yrs.

In 22% retinopathy was absent. Concomitant large vessel disease was observed as follows : coronary artery disease in 33.5%, cerebrovascular disease in 7.4% and peripheral vascular disease in 4.0%. 50.7% of Chinese diabetics (Hongkong) with 10 yrs. duration of diabetes were found to have significant retinopathy. In Japan retinopathy seems to progress in young onset diabetes readily. Proliferative retinopathy in IDDM is 9.5% while for NIDDM it is 12.9%. In India, background retinopathy has been reported in 24.3% and proliferative retinopathy in 4.2%.

Pittsburg had done a prospective study on a cohort of diabetic children. Glycemic control (glycosylated Hb%) related to the development of microaneurysm and urinary albumin excretion (effect was less striking in males).

In Japanese NIDDM who had retinopathy, proteinuria and hypertension, mortality was about 4 fold of that in general population and causes of death were mainly vascular complications (50% of total deaths). MODY as interpreted by Madras group as well seem susceptible to vascular complications and they seemed similar to the observations in the NIDDM patients except for lower rate of background retinopathy or complete absence of cerebrovascular disease.

In recording mortality data, diabetes did not get mention in upto 40-50% of case reports. In countries such as Nauru (West Pacific), Prince Edward Island (Canada) wherein complete death- registry data has been available, diabetes now ranks as the third leading cause of mortality.