

Cardiovascular and peripheral vascular disease

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'Albuminuria, a potent cardiovascular risk marker' was the opening plenary lecture by Dr. T. Deckert. This highlighted the Scandinavian experiences along with global view regarding increased morbidity and mortality in diabetic patients with micro and macro albuminuria and end stage renal diseases. The role of negatively charged heparan sulphate in pathogenesis of diabetic kidney disease, as the key mechanism was discussed (1).

'Angiogenic disease in diabetics' was the other plenary presented by J. Folkman and this paper highlighted with enormous basic data and angioscopic pictures, the fundamental factor in angiogenesis with special reference to diabetes mellitus.

'Lipoprotein, Atherosclerosis and Diabetes' was the theme of plenary lecture by D. Steinberg and it addressed itself to lipid aberrations and its role in atherogenesis in diabetes mellitus.

Symposia and Meet the Expert sessions included symposia on hyperlipidaemia in diabetes and mechanism of atherosclerosis in diabetes mellitus. Further, during the Meet the Expert session, hyperlipidaemia, hypertension, insulin resistance and diabetes (Syndrome X) was presented by and discussed with Dr. Reaven.

In various free paper sessions, the following things were extensively deliberated.

Diabetic cardiomyopathy: This was highlighted with animal and human experiments done independently and compared with each other demonstrating myocardial cell damage due to persistent hyperglycaemia without damage to coronary arteries, thus lending support to existences of a specific myo-angiopathic heart disease in diabetes (2).

IDDM patients without microangiopathy or overt clinical heart disease have small left ventricle, increased myocardial relaxation indicating a restrictive type of cardiomyopathy. In experimental rats probucol was found to help reduce plasma lipid and improve cardiac performance and may help prevent cardiomyopathy (3).

Decreased carnitine content and elevated triacyl glycerol in myocardium was found in diabetes and

propionil-L-carnitine (PC) has a therapeutic role in DM cardiomyopathy (4).

Myocardial infarction: Altered sympathetic activity in myocardium is associated with enhanced vulnerability to arrhythmias due to decreased ventricular fibrillation threshold.

In a Japanese study two types of diabetes were observed to exist with IHD. One was typical diabetes of long history accompanying microangiopathy. The other might be cardiogenic diabetes, which is reversible, without long history of diabetes and microangiopathy, with good response to insulin and normal islet cells at autopsy.

One Japanese study revealed that there is increased collagen synthesis and deposition in myocardium in diabetes (NIDDM) and these patients get abnormal thallium uptake scintigram (6).

Diabetics with borderline elevation of blood pressure may have a significant increase in LV mass together with abnormalities of LV function (5).

The diabetics have a higher incidence of early electrical and mechanical complications after acute infarction and are at a higher risk of death at the end of 1 st month. The risk of death also remains high as long as 3 years post MI as compared to controls (7).

The high mortality of diabetes with AMI may be due to increased plasminogen activator inhibitor (PAI-I) activity leading to impaired fibrinolytic activity (8).

An Indian study highlighted the significance of effects of prior glycemic control on outcome of AMI in diabetics. The mortality as well as pump failure rates were significantly lower when the glycated Hb was less than 8% (9).

Coronary Risk factor: In China the prevalence of stroke, small vessel disease and kidney disease is higher than large vessel disease (10).

In Japan the obesity in young NIDDM is one of the important risk factor for coronary artery disease (11).

There was significant correlation between insulin sen-

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sitivity index and BMI in obese diabetics. There probably exists a threshold of body weight upto which insulin sensitivity is associated with cardiovascular risk. In USA the existence of hyperlipidaemia was higher in Whites than Blacks and Mexicans, also HDL-LDL cholesterol and triglyceride showed marked variation by race which may have important implication for differential development of cardiovascular disease in US population.

Hypertension, atherogenesis and peripheral vascular disease: IDDM patients with diabetic neuropathy and antihypertensive medication had increased blood pressure and heart rate, but normal day and night variation inspite of signs of autonomic neuropathy. Whereas patients with secondary hypertension usually show decreased day and night variation in their blood pressure levels (12).

The impairment of VLDL catabolism was postulated to be playing an important role in atherogenesis from Japan. Low HDL-C and high VLDL-TG levels can serve as markers for coronary artery disease in diabetics (13).

Digitalis like substance (DLS) plays an important role in pathogenesis of hypertension and may have some role in diabetic nephropathy also (14).

In type II diabetes the occurrence of macrovascular complication is associated with bad metabolic control, insulin resistance and high prevalence of hypertension.

The Microalbuminuria collaborative study group concluded from a prospective study that hypertension and raised albumin excretion rate occurs concomitantly in patients of diabetes who progress to incipient nephropathy (15).

In diabetic rats the increased albumin escape rate occurs in short term (ST) rats, and it reflects a generalised protein leakage from intravascular space (16).

The multinational study of vascular disease in a follow up study of ten years consisting of 4746 patients found that the incidence of the five major vascular complication in diabetics e.g. CHD, gangrene, stroke, eyedisease and renal failure varied widely among the population (17).

Many workers highlighted the mechanisms of increased vascular permeability; altogether these papers established and advanced the existing knowledge about the same. It was shown that

exposure to 12.5% of glycated albumin reduced the transcapillary barrier to water in rats and when the glycated albumin reaches 25% the alterations in the capillary becomes irreversible (18).

The prevalence of peripheral vascular disease is significantly higher in Type II diabetics who have elevated albumin excretion rate and raised plasma prorenin (19). These patients have increased blood pressure and low HDL-C. Diabetes mellitus together with other coronary risk factors contribute to progression of peripheral arteriosclerosis and pathophysiological characteristics of macroangiopathy. Peripheral arterial changes may develop even in diabetics without complication, changes of peripheral vein and capillaries may be seen only in diabetics with retinopathy; venous and capillary changes occur after systemic arterial changes.

The fibrin fibre architecture is abnormal in diabetics (fibre thickness and permeability) which predisposes to increased incidence of vascular disease. This change was amenable to therapeutic modulation with gliclazide (20). There occurs increased hyaluronic acid accumulation in tunica media of aorta (21).

Oxidative stress is increased in NIDDM patients and there is further increase in stress in presence of vascular complications (both micro and macro angiopathic) (22).

One other proposed mechanism may be mediated by increased histamine synthesis acting via H₁ receptor stimulation and lipid deposition in aorta (23).

In diabetics parameters associated with possible oxidative stress are on a rise (histamine, ascorbate, GSH, glyoxalase I and II, glycated proteins).

In one paper, hyperinsulinemia was found to be the incriminated substance for high cardiovascular morbidity and mortality in Asian diabetic patients. The effect of insulin on lipids and fibrinolysis were highlighted as the causative factor (24).

Hyperinsulinemia occurs in young patients of MI but whether it is the cause or a marker of the disease remains yet to be established (25).

Altogether the papers presented further the understanding of various facts and mechanisms which are of vital importance to pathophysiology of diabetes.

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