

Letter to the Editor

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DIABETES AND CARDIOVASCULAR DISEASE

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A recent issue of the Philippine Journal of Internal Medicine featured H.B. Calleja's lengthy, highly informative and well documented article about Diabetes and cardiovascular disease.¹

In essence it stresses again what I often hear in medical meetings especially from the Dean of Diabetologist, Dr. Ricardo Fernando, that Diabetes is heart disease or words to that effect. I am almost a permanent fixture in medical symposia and round table discussions in Metro Manila to learn and to react in a contributory manner to the speaker.

In the article prediabetes was discussed lengthily. Patients with early onset of cardiovascular disease and hypertension among others may eventually develop overt carbohydrate intolerance. These patients are prediabetics. I think it is safe to say that the most extensive studies on prediabetes was made by Dr. Jerome Conn.²

In 1958 he was honoured by the American Diabetes Association to deliver the Banting Memorial Lecture. In his lecture on prediabetes he mentioned that he had been working on it since the late thirties or about 20 years ago. In later years he relegated much of his researches to his able associate Dr. Stefan Fajans. They introduced the cortisone provocative glucose tolerance test among patients with stigmata of diabetes or the prediabetics.³ Is the test reliable? A comparison was made with normal subjects without prediabetes and the result showed a significant difference.

A study based on needle biopsies of the kidney done in the late fifties by researchers from Baylor University in Houston, Texas and headed by reknowned Diabetologist, Dr. Harold Dobson, on prediabetic subjects without clinical and laboratory evidence of kidney disease was compared with a similar group of overt diabetics showed findings essentially the same by light and electron microscopy.⁴ The study demonstrated that renal microvascular changes can antedate the onset of overt carbohydrate intolerance.

A kidney biopsy study by the prodigious group of Kark Gellman *et al* among overt diabetics in the late fifties showed that the functionally significant lesion in diabetes is the diffuse type of glomerulo-Sclerosis and not the nodular type.⁵ These investigators suggested dropping the eponym Kimmelstiel-Wilson's syndrome because the clinical manifestations are not due to the nodular lesion but the diffuse type of glomerulosclerosis. Dr. Calleja alluded to hypertension as more correlative with the diffuse lesion was in agreement to their findings. Thus their study suggested that the eponym Kimmelstiel-Wilson's disease be confined only to the histopathology which is the nodular lesion. Many investigators to this day consider the Kimmelstiel-Wilson's lesion as pathognomonic of diabetes mellitus.

The development of macro and microvascular disease is an inherent sequel of diabetes. In the midnineties Nasser *et al* investigated diabetics without clinical and laboratory evidence of heart disease compared with normal (non-diabetic) subjects.⁶ Adenosine and papaverine were injected in the coronary ostia during cardiac catheterization and found abnormalities in blood flow and ability to dilate in contrast to normal subjects which responded normally.

A 15-year follow-up study by Danish researchers headed by Gaede *et al* showed an almost 50% reduction in macro and micro vascular disease in diabetics with microalbuminuria when prescribed the following regimens namely behavioural modifications, intensive glucose control, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, statins, aspirin and micronutrients such as ascorbic acid, vitamin E, Chromium picolinate and folic acid.^{7,8}

Schrier and Bogaert were so impressed by the results of the Steno study of the Danish researchers that they suggested a huge randomized controlled trial prescribing the 3 defining elements used in the study namely angiotensin blockers, statins and spirin aside from behavioural modification in patients at risk such as diabetics, obese, hypertensive, dyslipidemic, those with premature vascular diseases, etc. The trial would last for years, perhaps decades.⁹

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More recently 3 studies are working on endothelial function aimed in enhancing oxidative metabolism.^{10,12} The earliest of the 3 was based on the works of Murad who devoted most of his time on research regarding endothelial dysfunction. Preliminary data based on his work showed encouraging results on laboratory animals by feeding them L-Arginine whereas the results in humans were scanty to be conclusive and more data are awaited. Arany *et al* and Eremina *et al* working along the same lines of improving oxygenation of disease vascular tissues have shown promising preliminary results. These three works constitute what is referred to as therapeutic angiogenesis. This is the future of vascular disease. In much the same way as new drug discoveries have significantly reduced the incidence of invasive approaches to prostate, heart and other organs it is hoped that in some future date therapeutic angiogenesis will also reduce invasive cardiovascular treatments.

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