

Milestone 5

A pioneering study of diabetes complications



By the middle of the twentieth century, the link between diabetes and degenerative conditions such as neuropathy, retinopathy and nephropathy was already well established. However, the precise relationship between these complications and glycaemic control was not fully appreciated until the publication of a ground-breaking longitudinal study, which was initiated by the Belgian physician Jean Pirart in 1947 and continued for over three decades.

“In 1947, I had the good fortune to take up practice at the Cesar de Paepe Clinic in Brussels, which treated hundreds of diabetic patients,” explained Pirart in a key paper charting the first 25 years of the study, which was first published in French in 1977 and was translated into English in 1978. “The faithful attendance of these patients and the quality of their files over the preceding years gave me the idea to attempt a longitudinal study, which I have been able to follow for more than 30 years because of my long association with the clinic.”

The 1977 paper included data from 4,398 patients with diabetes, each of whom underwent a series of examinations, including blood

tests and neurovascular evaluations, at least once a year for a period of up to 25 years. In total, around 21,000 such examinations were conducted over the first 25 years of the study. At each assessment, the patients were rated according to their level of glycaemic control (good, fair or poor).

In light of the frequent co-occurrence of neuropathy, retinopathy and nephropathy, Pirart adopted the practice of referring to these manifestations as a ‘diabetic triopathy’, as originally proposed by Root and colleagues in 1954. The risk of developing one or more components

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of this triopathy correlated robustly with long duration of diabetes and poor glycaemic control, particularly in the year leading up to the examination. By contrast, the degree of glycaemic control seemed to have little influence on other vascular manifestations, such as coronary and peripheral atherosclerosis.

Owing to a meticulous approach and a high level of patient engagement, Pirart’s study was unprecedented in terms of size and duration. Earlier studies often relied on single measurements taken at baseline to determine diabetes severity, but the longitudinal assessments performed by Pirart and his colleagues reflected the true dynamic nature of glycaemic control status and raised the prospect of modifying this status to reduce the risk of degenerative complications.

Pirart acknowledged that his data could not prove the existence of a causal link between long-term hyperglycaemia and the diabetic triopathy. However, his work laid the foundations for further investigations, such as the UK Prospective Diabetes Study, which set out to determine whether improved glycaemic control could prevent the development of complications from type 2 diabetes. Researchers are also exploring the mechanisms underlying glucose-mediated vascular damage, including defects in the mitochondrial electron transport chain.

“Our study ... conclusively proves that diabetic triopathy and not atherosclerosis is a function of the duration and intensity of diabetes and more precisely of hyperglycaemia,” concluded Pirart in his paper. “Of course, this can be lessened by treatment. This fact should encourage physicians to strive toward normoglycaemia in diabetes therapy, while at the same time recommending various methods of hygiene which could slow down the development of atheromatosis and of hypertension.”

Heather Wood Chief Editor,
Nature Reviews Neurology

Milestone studies

Pirart, J. Diabetes mellitus and its degenerative complications: a prospective study of 4,400 patients observed between 1947 and 1973. Part 1. *Diabetes Care* **1**, 168–188 (1978) | Pirart, J. Diabetes mellitus and its degenerative complications: a prospective study of 4,400 patients observed between 1947 and 1973. Part 2. *Diabetes Care* **1**, 252–263 (1978)

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