When I joined Professor Dacie's department, at the Royal Post Graduate School in London, as a trainee in hematology in 1959, he suggested that I should investigate the abnormal red cell morphology he and others had observed in patients with malignant hypertension, uremia, and metastatic carcinoma. It soon became apparent that the degree of morphological abnormality did not correlate with the height of the blood urea. Before joining Dacie, I had worked at the London Hospital where Professor Clifford Wilson and his colleagues were interested in the pathogenesis of malignant hypertension. This made me aware of a highly relevant observation made there by Verel and his co-workers. They had observed shortened red cell survival in a young patient with malignant hypertension with normal renal function in whom the red cell survival returned to normal when the malignant phase of hypertension had been treated. Although they did not comment upon red cell morphology, their observation suggested to me that the hemolytic anemia and the red cell fragmentation might be due to reversible arteriole necrosis. It thus seemed possible that the hemolysis in patients with malignant hypertension, the hemolyticuremic syndrome, thrombotic thrombocytopenic purpura, and in some patients with metastatic carcinoma, might have a common pathogenesis due to microvascular disease; the association with uremia being due to renal vascular disease and not uremia per se.

"We were not the first to describe the abnormal morphology nor, indeed, did we claim credit for the suggested mechanism. In 1953, Monroe and Strauss had observed schizocytes in the blood vessels of sections obtained at necropsy from two patients who had died of thrombotic thrombocytopenic purpura. These authors suggested that the abnormal blood vessels might be the site of red cell fragmentation and destruction. This perceptive observation and hypothesis was not pursued by the authors, nor did it receive the recognition it warranted.

Our hypothesis received independent support from the observation, made at about the same time, that red cell fragmentation and hemolysis followed the insertion of prosthetic materials to correct intracardiac defects and to replace malfunctioning heart valves. More direct evidence has come from a number of experimental studies in animals undertaken by myself with various colleagues, and independently by a number of other workers. Finally, it must be acknowledged that the initial pursuit of ideas is more dependent upon the stimulus provided in an academic environment than upon research funding; as none was sought, received, nor required for this study to be undertaken. This may serve to emphasize how important it is to encourage and support young investigators in the pursuit of their ideas, which at the outset may well make few or little demands on the resources of many academic institutions."