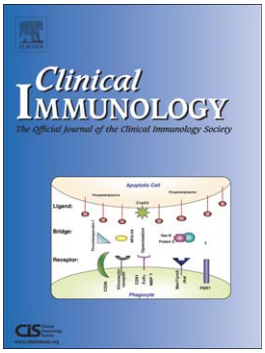

Pathogenesis of Proliferative Lupus Nephritis from a Historical and Personal Perspective

Shu Man Fu, Hongyang Wang, Chao Dai, Sun-sang J. Sung, Felicia Gaskin

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Introduction.

In a historical perspective for lupus nephritis (LN) from 1968 to 1998, JS Cameron provided an excellent brief review of lupus nephritis up to 1998 (1). Since then, there has been significant progress in our understanding of the pathogenesis of lupus nephritis. However many issues remain to be debated. Some of these issues are the subject of this perspective with an emphasis on the data generated from the authors' laboratory. This review will address selective aspects of the pathogenesis of proliferative lupus nephritis.

Multiple immune complex systems are involved in lupus nephritis.

Figure 1 shows the pathology of class IV diffuse proliferative lupus glomerulonephritis (PLGN). On light microscopy, wire-loop lesions first described by Baehr et al (2) are evident in H&E stained renal biopsy sections (figure 1A). Masson trichrome stain highlights the wire-loop subendothelial deposit (figure 1B). Immunofluorescence (IF) studies show Ig and complement deposits (figure 1C). By electron microscopy (EM), the dense deposits in subendothelial and subepithelial spaces (figure 1D) correlate with the presence of wire-loops. The nature of the deposits in the wire-loops seen by light microscopy and the dense deposits in EM has been the subject of extensive investigation for many decades.

The dense deposits were shown to be immune complexes (IC) by Vazquez and Dixon (3). With circulating anti-nuclear Ab (ANA) demonstrated to be a dominant Ab in systemic lupus erythematosus (SLE) and the description of anti-DNA Ab to be a component of ANA by Holman and Kunkel (4), ANA and anti-DNA Ab were shown to be enriched in the eluates of post mortem kidneys from patients with LN (5-7). *Although*