IgA Nephropathy: 50 years on

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Fifty years have lapsed since the original description of IgA nephropathy (IgAN) in 1968 by the French pathologist Jean Berger (1930 – 2011). While a lot has been learnt about this condition over the past 50 years, much is still unknown about this heterogeneous condition as reflected by its lack of specific therapy to date. While there have been a number of histological descriptions and classification systems, the most recent of which is the Oxford Classification that has been validated in different populations over the last 10 years. From an epidemiologic and genetic perspective, IgAN is more frequent in Asian populations than in Caucasians, and certainly extremely rare in Africans. Population-based genome-wide association studies (GWAS) have discovered nearly 20 IgAN risk loci, but there is a distinct difference between those from the West and the East. The autoimmune nature of the disease is explained by a multi-hit pathogenesis model, wherein overproduction of aberrantly glycosylated IgA1, galactose-deficient in some O-glycans, by IgA1-secreting cells leads to elevated levels of circulatory galactose-deficient IgA1. Emerging evidence also implicate the spleen tyrosine kinase pathway, tubulointerstitial injury via mesangial-podocytic-tubular crosstalk mechanisms and the gut-kidney connection to play important pathogenetic roles. Finally, there is an evolution of different therapeutic approaches over time that culminate in the 2012 KDIGO Clinical Practice Guideline for Glomerulonephritis that is presently being updated to embrace data from recent clinical trials across the globe.