**What is ESRD?**

CKD is defined as impaired renal performance for >3 months with implications for health. ESRD is the most severe form of CKD, which is categorized (Cat 1-5) based on eGFR, BUN, creatinine, or albuminuria.

* ESRD is Stage 5 CKD is a GFR of <15 mL/min/1.73 m2
* Diabetes is the leading cause of CKD and ESRD in the United States and worldwide.
* **Risk factors:** race (disproportionately high in African American pts), DM, HTN, genetics (APOL1 mutation)
* Among initially untreated patients with mild hypertension, an elevated creatinine clearance (suggestive of glomerular hyperfiltration) at baseline has been related to a subsequent significant rise in the plasma creatinine concentration and higher blood pressure levels and to the development of moderately increased albuminuria.

**Relationship between HTN and ESRD:**

Hypertension is associated with a significant increase in risk of adverse cardiovascular and renal outcomes. These include:

●LVH

●Systolic and diastolic heart failure

●Ischemic stroke

●Intracerebral hemorrhage

●Ischemic heart disease, including MI and CAD

●CKD & ESRD



**Mechanisms & histopathology of Hypertensive Nephrosclerosis:**

Progression of most forms of CKD are largely due to secondary hemodynamic and metabolic factors. The major histologic manifestations of these secondary causes are **interstitial fibrosis** and **focal segmental glomerulosclerosis** (FSGS).

When hypertension is the primary causative mechanism, these histologic changes fall under the category of hypertensive nephrosclerosis.

Hypertensive nephrosclerosis is characterized histologically by vascular, glomerular, and tubulointerstitial involvement.

**Vascular disease** — The vascular disease consists of intimal thickening and luminal narrowing of the large and small renal arteries and the glomerular arterioles. Two mechanisms appear to contribute to the development of the vascular lesions:

●A hypertrophic response to chronic HTN that is manifested by medial hypertrophy and fibroblastic intimal thickening, leading to narrowing of the vascular lumen. This response is initially adaptive, minimizing pressure-dependent wall stress.

●The deposition of hyaline-like material into the damaged, more permeable arteriolar wall.

Renovascular disease may accelerate the development of the secondary sclerotic lesion by enhancing ischemic nephron loss.

**Glomerulosclerosis** — The glomeruli may show both focal global (involving the entire glomerulus) and focal segmental sclerosis:

●Global sclerosis is thought to reflect ischemic injury, leading to nephron loss. This can be further categorized histologically as either solidified (in which the entire tuft is involved) or obsolescent (in which the tuft is retracted and Bowman's space is filled with collagenous-type material). The solidified form is more commonly associated with African Americans than with Caucasians and might contribute to the increased prevalence of nephrosclerosis in African Americans.

●Focal segmental sclerosis is typically associated with glomerular enlargement, which can be a compensatory response to nephron loss but may also precede that loss. However, the combination of hypertrophy and a rise in intracapillary pressure in these glomeruli may gradually lead to hemodynamically mediated segmental sclerosis.

**Interstitial fibrosis and tubular atrophy** — Vascular and glomerular diseases are associated with renal interstitial changes that are often severe (but incompletely understood). Studies in experimental animals have shown that severe stenosis of the main renal artery can induce tubular atrophy and an influx of inflammatory cells. The interstitial disease in the ischemic kidney is, at least in part, an active immunologic process that may be initiated by ischemia-induced alterations in antigen expression on the surface of the tubular epithelial cells. In this model of unilateral renal artery stenosis, the contralateral kidney, which is exposed to high blood pressure but no ischemia, develops similar tubulointerstitial changes.

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