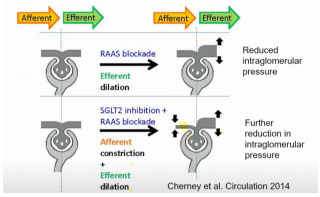
Hypertension and Chronic Kidney Disease (CKD)

Preventing the Progression of Kidney Disease

(the major factors for progression of CKD: intraglomerular hypertension and glomerular hypertrophy --> adaptive hyperfiltration --> glomerulosclerosis)

1. Aggressive BP control to target values per current guidelines
   - ACE-inhibitors, ARBs (i.e., RAS blockers) are recommended to improve renal outcomes in patients with HTN and CKD (RAS blockers inhibit Angio-II from constricting efferent arterioles and increasing hydrostatic pressure in glomerulus)
     - Monitor CKD patients on RAS blockers closely for hyperkalemia
     - If serum creatinine levels increase more than 30% from baseline after starting ACE-I or ARB, discontinue immediately
     - Avoid RAS blockers in patients with advanced kidney failure (G5)
   - Loop and thiazide diuretics are frequently used in CKD to reduce fluid retention/edema

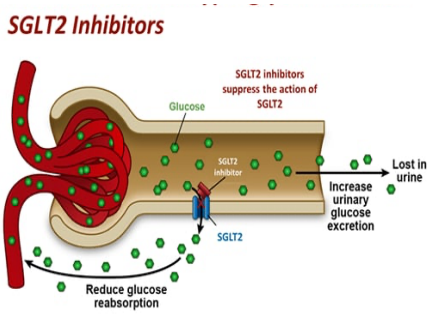


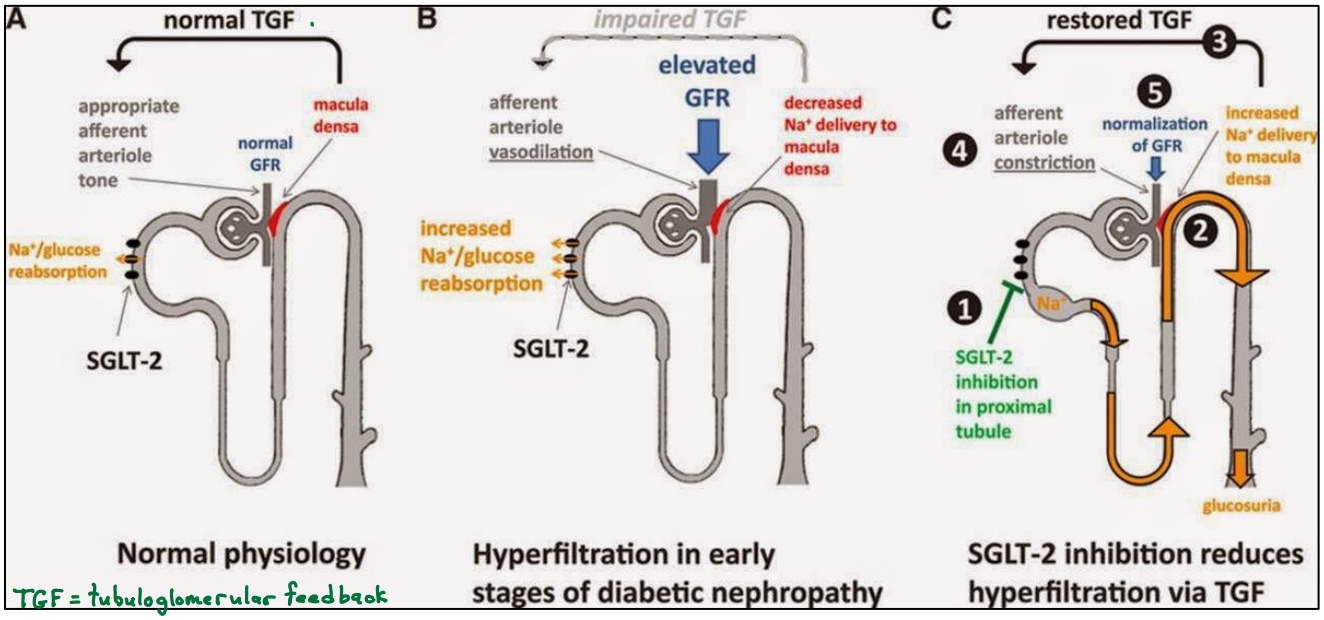
2. Aggressive glycemic control to keep HbA1C < 7 %, per ADA recommendations

3. Use ACE-inhibitors, ARBs in patients with diabetic kidney disease and proteinuria

4. Use SGLT2 (sodium-glucose cotransporter 2) inhibitors

   Dapaglifozin (Forxiga) --> blocks sodium and glucose reabsorption in proximal tubule --> increases delivery of sodium to macula densa --> constricts abnormally dilated afferent arterioles --> normalizes GFR (i.e., reduces intraglomerular pressure and reduces glomerular hyperfiltration) --> slows the progression of CKD





TGF = tubuloglomerular feedback

5. Avoid nephrotoxic drugs
   - NSAIDs, glucocorticoids --> inhibit PGI --> reduce renal blood flow (GFR)
   - aminoglycosides (e.g., gentamicin), vancomycin, IV radiocontrast media (contrast-CT)

Renal Artery Stenosis & ACE-Inhibitors / ARBs

RENAL ARTERY STENOSIS

In renal artery stenosis, a reduction in renal blood flow results in a reduction in glomerular perfusion pressure and glomerular filtration. In an attempt to reestablish glomerular filtration (i.e., GFR), the JG cells will release renin to produce angiotensin II (Ang-II). Ang-II will bind to Ang-II receptors on the glomerular efferent arterioles, causing vasoconstriction, Vasoconstriction of the glomerular efferent arterioles results in a “compensatory" increase in glomerular filtration pressure at a time when glomerular afferent arteriolar pressure is low due to renal artery stenosis. ACE-inhibitors and ARBs will inhibit the RAAS system and block Ang-II from re-establishing glomerular pressures during renal artery stenosis, resulting in a significant reduction of GFR and ultimately renal failure.

Note: Ang-II receptors only exist on the efferent arterioles, not the afferent arterioles. So, when afferent pressure is low, Ang-II selectively binds to the Ang-II receptors on the efferent arterioles to increase and maintain normal glomerular pressure and filtration.