CASE STUDY: Chronic Kidney Disease (CKD)

A.L. is a 44-year-old, African American woman (Wt: 79.5 kg, Ht: 5'5") with a 20-year history of Type II DM and a 2-year history of declining kidney function. She presents to the diabetes clinic for her quarterly checkup. She has been noncompliant with regular appointments and her blood glucose levels has generally remained greater than 200 mg/dL on prior evaluations, with a HgA1c of 10.1% two months ago (goal: HgA1c < 7%). Lately A.L. complains of general nausea, malaise, and poor appetite. The workup reveals the following pertinent lab values:

Na = 143 mEq/L (135 – 145)
K = 4.7 mEq/L (3.5 – 5.2)
Cl = 106 mEq/L (98 – 106)
CO_2 = 18 mEq/L (22 – 29)
sCr = 2.9 ng/dL (0.6 – 1.2)
BUN = 63 mg/dL (7 – 18)
BG = 289 mg/dL (70 – 115)
Beta-hydroxybutyrate < 0.5 mmol/L (< 0.5)

Physical examination reveals a BP of 160/102, HR of 88 bpm, 2+ pedal edema, mild pulmonary congestion, and a 10 LB weight gain. Additional lab studies show the following results:

Phosphate = 6.8 mg/dL (2.7 – 4.5)
Calcium = 9.6 mg/dL (8.4 – 10.2)
Albumin = 3.8 gm/dL (3.5 – 5.5)
Mg = 2.8 mEq/L (1.3 – 2.1)
Uric Acid = 8.5 mg/dL (F: 2.6 – 6.0; M: 3.5 – 7.2)
HGB = 9.2 g/dL (F: 12 – 16; M: 13.5 – 17.5)
HCT = 28% (F: 35 – 45%; M: 39 – 49%)
WBC = 9.6K (4.5 – 11K)
PLT = 155K (150 – 450K)
RBC indices are normal.

A.L.'s UA showed 4+ proteinuria, later quantified as a urinary albumin of 700 mg/24 hours.

<u>Questions</u>
(1) What is the cause of A.L.'s CKD?
(2) What is the significance of A.L.'s albuminuria?
(3) How should A.L.'s kidney disease be managed?

Stratify A.L.'s CKD

CrCl = (140 - Age) (IBW) / (72) (sCr)

= (140 - 44) (57) / (72) (2.9)

$CrCl_{(female)}$ = (26.2 ml/min) x 0.85

= 22.3 ml/min

Albuminurea: 700 mg/24 hrs

A.L.'s CKD Classification: G4/A3

Chronic kidney disease classification based upon glomerular filtration rate and albuminuria

GFR stages	GFR (mL/min/1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60 to 89	Mildly decreased
G3a	45 to 59	Mildly to moderately decreased
G3b	30 to 44	Moderately to severely decreased
G4	15 to 29	Severely decreased
G5	<15	Kidney failure (add D if treated by dialysis)
Albuminuria stages	**AER (mg/day)**	**Terms**
A1	<30	Normal to mildly increased (may be subdivided for risk prediction)
A2	30 to 300	Moderately increased
A3	>300	Severely increased (may be subdivided into nephrotic and nonnephrotic for differential diagnosis, management, and risk prediction)

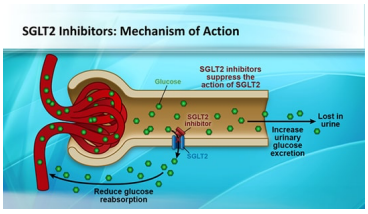
The cause of CKD is also included in the KDIGO revised classification but is not included in this table.

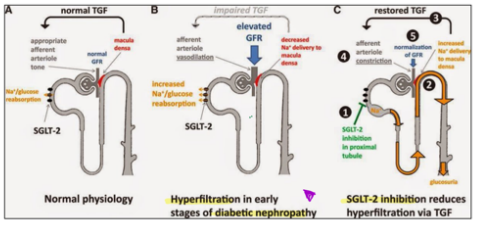
GFR: glomerular filtration rate; AER: albumin excretion rate; CKD: chronic kidney disease; KDIGO: Kidney Disease Improving Global Outcomes.

1. What is the cause of A.L.'s CKD?
   A. Diabetic nephropathy is a microvascular complication of DM, resulting in albuminuria, glomerular structural changes, and a progressive decline in kidney function.
   B. Hypertension: Elevated and uncontrolled BP (160/102) → CKD

2. What is the significance of A.L.'s albuminuria (700 mg / 24 hours)?
   A. Albuminuria is the earliest sign of kidney impairment in patients with DM that correlates with CKD.
   B. Albuminuria indicates irreversible kidney damage.
      - A.L.'s lab data suggest that she has substantial CKD (G4/A3) and associated complications of CKD.
      - Although the progression to ESRD is generally beyond prevention at this stage, appropriate intervention can slow the progression to ESRD.
      - Albuminuria indicates renal damage and correlates with cardiovascular morbidity and mortality.
   C. Since A.L.'s CKD is not reversible, the primary goals are to delay the need for dialysis therapy as long as possible to manage complications.

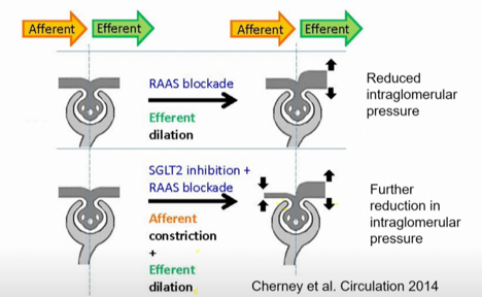
3. How should A.L.'s kidney disease be managed?
   A. Improve Glycemic Control to maintain HgA1c < 7 %.
      - Consider Humalog (Lispro) / Lantus (Glargine) insulin regimen for improved glycemic control.
      - Implement Humalog Sliding Scale Regimen (ACHS) to assess daily insulin requirement, then give 30% of daily insulin requirement as once daily Lantus dose.
      - Consider SGLT-2 inhibitor to improve glycemic control and reduce progression of CKD.



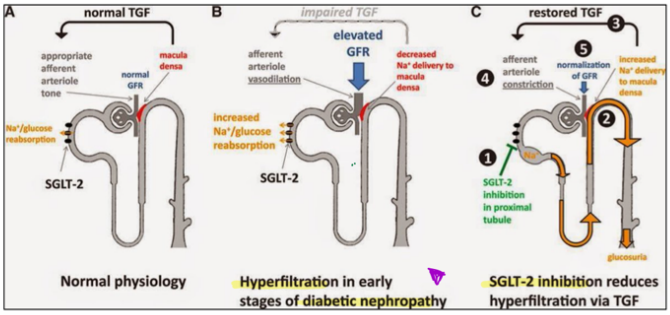


B. Improve Blood Pressure Control (A.L.'s BP: 160/102).

- Consider 2+ pedal edema, mild pulmonary congestion → diuretic.
- Consider ACE-I/ARB to reduce intraglomerular pressure → reduce "adaptive hyperfiltration" → delay progression of CKD
- Consider SGLT-2 inhibitor (dapaglifozin, canaglifozin) in DM and CKD.
    - In the treatment of DM, SGLT-2 inhibitors block glucose reabsorption in proximal tubule → reduce hyperglycemia.



- In the treatment of CKD, SGLT-2 inhibitors block glucose and Na^+ reabsorption in proximal tubule → increases delivery of Na^+ to macula densa → constrict abnormally dilated afferent arterioles
  → reduce intraglomerular pressure
  → reduce "adaptive hyperfiltration"
  → delay the progression of CKD



C. Reduce Dietary Protein Intake.

- Schedule patient counseling with nutritionist to assist in managing DM and to reduce protein intake. Approx. 0.8 gm/kg/day of protein intake is recommended to reduce the rate of further progression of albuminuria and CKD.

D. Avoid Nephrotoxic Drugs: NSAIDs, glucocorticoids, aminoglycosides (Gentamicin, Tobramycin) vancomycin, and IV radiocontrast media (contrast CT).

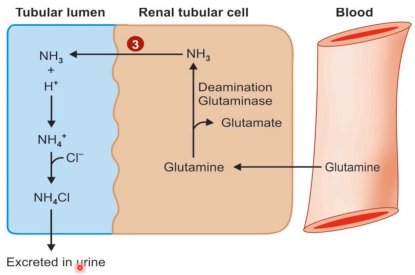
E. Closely monitor for hyperkalemia, especially after starting an ACE-I/ARB and a Loop diuretic (furosemide). A.L.'s serum K = 4.7 mEq/L.

F. Treat hyperphosphatemia (Phos = 6.8) with a phosphate binder. Consider the following benefits and risks …

- Sevelamer carbonate may be a good option since it lowers LDL and does not lower serum bicarbonate levels (like Sevelamer HCl) in patients predisposed to metabolic acidosis.
- Mg Hydroxide / Mg Carbonate are not a good choices since A.L. is slightly hypermagnesemic (Mg = 2.8).
- Iron-based Binders (sucroferric oxyhydroxide / ferric citrate) may provide benefit in anemic patients with CKD who require iron supplementation.
- Aluminum phosphate binders should be avoided in advanced CKD → risk of aluminum accumulation in CKD (G4/A3) → osteomalacia / encephalopathy.
- Calcium-containing binding agents (calcium carbonate) offers a benefit in CKD patients who are hypocalcemic (A.L.'s Ca = 9.6)

G. Treat A.L.'s Metabolic Acidosis (CO_2 = 18 mEq/L).

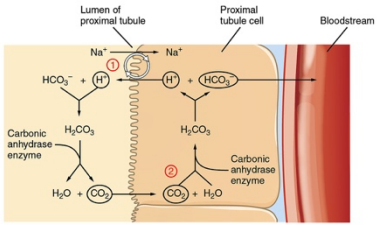
- The kidneys are responsible for absorption of bicarbonate and excretion of H^+ ions through buffering by ammonia (produced by the kidneys); therefore, reduced reabsorption of bicarbonate and impaired production of ammonia by the kidneys are major factors responsible for accumulation of serum H^+ ions and metabolic acidosis in advanced CKD.

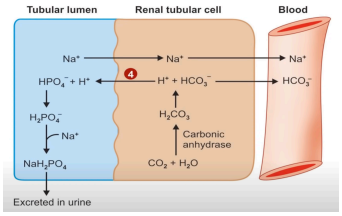


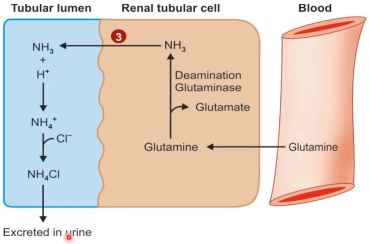
Formation of ammonia and excretion of ammonium ions in the urine.

Renal conservation of $HCO3^-$ and excretion of acid (H^+) occur through 4 key mechanisms in the kidneys.

1. Exchange of H^+ for Na^+ of tubular fluid.
2. Reabsorption of bicarbonate from tubular fluid.
3. Formation of ammonia and excretion of ammonium ion (NH_4^+) in the urine.
4. Excretion of H^+ as $H_2PO_4^-$ in the urine.







- Sodium bicarbonate 650 mg tablets: 2 to 4 tabs (8 mEq Na^+ / 8 mEq bicarbonate per tablet) per day normalizes serum plasma bicarbonate concentration.
- Closely monitor A.L.'s Na^+ and fluid status after initiating sodium bicarbonate tabs.

H. Treat Chronic Anemia in CKD with Iron Supplementation (A.L.'s Hgb = 9.2)

- Before initiating ESA therapy, A.L.'s iron indices should be determined (TSAT and ferritin): TSAT < 30% and ferritin is < 500 ng/ml (per KDIGO Guidelines).
- If iron deficiency is the cause of anemia, A.L. may benefit from oral iron supplementation alone, without ESA therapy to increase Hgb levels.
    - Rx: Ferrous sulfate 325 mg PO TID with meals.
- If A.L.'s condition does not respond to oral iron replacement, as indicated by either persistent iron deficiency based on iron indices, then IV iron supplementation should be implemented.

Table 3. Treatment Options for Anemia of CKD

IV Iron Therapies	
Iron dextran	One-time test dose 25 mg IV 100 mg IV or IM daily for 10 doses OR 250-100 mg slow IV infusion Alternatively: dose (mL) = 0.0442 (desired Hgb–observed Hgb) × LBW + (0.26 × LBW)
Iron sucrose	200 mg IV × 5 doses in 14 days OR 500 mg slow IV infusion on days 1 and 14 OR 300 mg, 300 mg, 400 mg IV infusion, all 14 days apa
Sodium ferric gluconate	250 mg slow IV infusion[a]
Ferumoxytol	510 mg IV × 2 doses 3-8 days apart

I. Initiate ESA therapy for anemia in CKD, if there is no response to IV iron.
    - KDIGO guidelines recommend intiating an ESA when hemoglobin (Hgb) is below 9 g/dL and targeting treatment to 10-11 g/dL. Higher Hgb levels increases the risk of stroke and other cardiovascular events.
        - ESA: Epogen / Procrit 50 UNITS/kg (3000-4000 UINTS/dose) SC once or twice weekly
    - The goal of ESAs is to reduce the risk of blood transfusion, which imparts negative consequences for subsequent transplantatin due to allosensitization.