Global Health Nephrology — Module 25

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Global Health Nephrology

Advanced Nephrology Module 25 — Student Handout

Learning Objectives

By the end of this module, you will be able to:

1. **Define and recognize CKD of Unknown Etiology (CKDu)** and its epidemiologic patterns
2. **Understand heat stress nephropathy mechanism** and its link to agricultural worker populations
3. **Describe renal manifestations of parasitic infections** including schistosomiasis and malaria
4. **Recognize endemic nephropathies** associated with geographic exposure (Balkan, aristolochic acid)
5. **Understand tuberculosis and fungal involvement** of the urinary tract and kidney
6. **Assess global disparities in dialysis and transplant access** and their social determinants
7. **Apply epidemiologic and clinical frameworks** to global kidney disease prevention strategies
8. **Recognize occupational and environmental exposures** that cause progressive kidney disease

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Part I: CKD of Unknown Etiology (CKDu) and Mesoamerican Nephropathy

Epidemiology & Geographic Distribution

CKDu Prevalence: - 1–5% of populations in Central America (El Salvador, Guatemala, Nicaragua, Costa Rica) - 5–10% in some rural agricultural regions - 500,000–1,000,000 estimated cases across Mesoamerica - Male predominance (10:1 male-to-female ratio) - Overwhelmingly affects agricultural workers (sugarcane cutters, cotton farmers, rice paddies)

Case Definition (KDIGO 2017): - **CKD:** GFR <60 mL/min/1.73m² on at least 2 occasions - **Unknown etiology:** Absence of diabetes, hypertension, autoimmune disease, chronic glomeru-

lonephritis on serologies, or other established CKD cause - **Early-stage at diagnosis:** 67% present with eGFR 30–60 (Stage 3), only 20% present with Stage 5

Pathophysiology: Heat Stress Nephropathy

Proposed Mechanism: 1. **Occupational heat exposure:** Chronic dehydration from repeated heat stress (sugarcane work in tropical climate) 2. **Repeated volume depletion:** Workers exposed to 40°C+ ambient temperature without adequate hydration 3. **Transient hyperfiltration:** Periods of intense activity followed by severe dehydration cause glomerular stress 4. **Tubular injury:** Recurrent episodes of acute tubular necrosis (ATN) from dehydration 5. **Uric acid crystallization:** Dehydration and volume contraction promote uric acid precipitation in distal tubules 6. **Inflammatory cascade:** Repeated injury ☐ local inflammation ☐ fibrosis accumulation

Evidence Supporting Heat-Stress Etiology: - **Time-trend data:** Incidence increased coincident with intensification of sugarcane harvesting practices (mechanization, speed pressure) - **Seasonal variation:** CKD progression faster during dry season (peak heat stress) - **Occupational clustering:** 20–30-fold higher prevalence in sugarcane cutters vs. non-agricultural workers - **Cross-sectional data:** Objective heat stress metrics correlate with kidney function decline - **Animal models:** Repeated heat-induced dehydration causes progressive tubular injury and fibrosis in rats

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Clinical Features of CKDu/Mesoamerican Nephropathy

Presentation: - **Asymptomatic CKD:** Most cases discovered on screening (elevated creatinine) rather than symptoms - **Age at diagnosis:** 20–50 years (much younger than typical CKD from diabetes/hypertension) - **Minimal proteinuria:** <1 g/day (urine protein often <300 mg/day) — atypical for CKD stage - **Preserved hematuria response:** Most have no or microscopic hematuria - **Normal blood pressure initially:** Many normotensive despite Stage 3–4 CKD

Laboratory Features: - **Elevated creatinine:** Often 1.5–3.5 mg/dL at discovery - **Elevated uric acid:** Hyperuricemia common (may reflect tubular dysfunction) - **Normal urinalysis:** Minimal proteinuria, no dysmorphic RBC, no casts - **Absence of serologic markers:** Negative ANA, ANCA, anti-GBM, normal complement - **Normal glucose/normal HbA1c:** No diabetes in classic CKDu cases

Renal Imaging: - **Ultrasound:** Small, echogenic kidneys (size often <9 cm); loss of corticomedullary differentiation - **CT:** Chronic tubulointerstitial changes; cortical thinning; minimal or absent glomerular sclerosis

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Kidney Biopsy Findings in CKDu

Light Microscopy (When available; biopsy not routinely done in endemic areas): - **Tubulointerstitial injury predominates:** Tubular atrophy, interstitial fibrosis (TIF) - **Glomerular changes minimal:** Glomeruli often remarkably spared or show global sclerosis

without proliferation - **Tubular changes:** Atrophic tubules, loss of brush border, epithelial flattening - **Chronic inflammation:** Interstitial lymphocytic infiltration - **Vascular changes:** Arteriolar hyalinosis variable

IF: Negative or nonspecific IgM in sclerotic glomeruli

EM: Tubular basement membrane changes; podocyte foot process fusion; glomerular changes less prominent

Key Point: The striking feature is **glomeruli-sparing pattern** — glomeruli are relatively preserved while tubulointerstitium shows severe injury, opposite of typical immune-mediated GN.

Differential Diagnosis of CKDu

Condition	Key Distinguishing Features
Hypertensive CKD	History of hypertension; LVH on ECG; often higher proteinuria
Diabetic CKD	Diabetes diagnosis; hyperglycemia; diabetic retinopathy often present
Chronic Pyelonephritis	History of recurrent UTI; hydronephrosis on imaging; positive urine culture
Obstructive Uropathy	Hydronephrosis on ultrasound; urinary obstruction demonstrated
Autoimmune GN	Positive serologies (ANA, ANCA, anti-GBM); hematuria; active sediment
IgA Nephropathy	Hematuria with dysmorphic RBC; serologies negative; biopsy diagnostic
Polycystic Kidney Disease	Bilateral renal cysts on imaging; positive family history
CKDu (Heat-stress)	Occupational heat exposure; minimal proteinuria; tubulointerstitial pattern; glomeruli-sparing

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Clinical Management & Prevention

For Patients with Established CKDu: 1. **Slow progression:** ACE inhibitor or ARB to reduce proteinuria (even modest amount) 2. **Uric acid management:** Allopurinol (no strong data but theoretically beneficial); maintain uric acid <6 mg/dL 3. **Blood pressure control:** Target <120/80 mm Hg 4. **Avoid nephrotoxins:** NSAIDs strictly contraindicated 5. **Dialysis access:** Early vascular access planning for Stage 4 (many will reach Stage 5 by age 40–50)

Prevention Strategies (Public Health): 1. **Occupational health interventions:** - Mandatory hydration breaks (at least 1 L per 1–2 hours of work in high heat) - Electrolyte replacement (sodium) in addition to water - Earlier shifts (reduced peak heat exposure) - Cool-rest areas - Speed limits on piece-rate work (reduce pressure to work faster despite heat stress)

2. **Monitoring & screening:**
    - Annual creatinine/eGFR screening in high-risk agricultural populations
    - Early detection allows counseling about CKDu risk and occupational alternatives
3. **Health system strengthening:**
    - Training of primary care providers in CKDu recognition
    - Accessible dialysis capacity in endemic regions (currently severe shortage)
4. **Research & surveillance:**
    - Continued mechanistic studies to confirm heat-stress etiology
    - Environmental monitoring of occupational heat stress
    - Registry studies to track epidemiology and outcomes

Part II: Schistosomiasis and Kidney Disease

Epidemiology & Parasitology

Prevalence: - 250–300 million infected worldwide (Africa, Middle East, South America) - Two main species causing kidney disease: - *Schistosoma haematobium* (hematuria, urinary schistosomiasis) — Africa, Middle East - *Schistosoma mansoni* (intestinal schistosomiasis) — Africa, South America

Transmission: - Larval cercariae in freshwater (rivers, lakes, ponds) - Penetrate skin during contact with water - Develop into adult worms in venous plexuses

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Pathophysiology of Schistosomiasis-Related Kidney Disease

Mechanism: 1. **Egg deposition:** Schistosome eggs lodge in various organs 2. **Immune response:** Granulomatous inflammation around eggs (Th1 and Th2 mediated) 3. **Circulating immune complexes:** Soluble egg antigens form IC 4. **Glomerular deposition:** IC deposit in glomerular basement membrane 5. **Complement activation:** Classical pathway activation ☐ C3, C5a ☐ inflammation 6. **Progressive glomerular injury:** Proliferation, crescents, scarring

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Clinical Features & Types

Schistosomiasis Haematobium (Urinary): - **Presentation:** Chronic hematuria, dysuria - **Chronic sequelae:** Fibrosis of bladder/ureter, chronic cystitis, squamous cell cancer - **Kidney involvement:** Usually ureteral/bladder pathology predominates over glomerular disease - **Biopsy findings (when GN occurs):** Membranoproliferative or proliferative GN, sometimes crescentic

Schistosomiasis Mansoni (Intestinal): - **Presentation:** Diarrhea, abdominal pain, hepatosplenomegaly - **Chronic sequelae:** Intestinal fibrosis, portal hypertension, liver cirrhosis - **Kidney involvement:** More frequent glomerulonephritis (immune complex-mediated) - **Proteinuria:** Nephrotic range possible (10–15 g/day)

Glomerulonephritis Patterns in Schistosomiasis

Light Microscopy: - **Membranoproliferative GN (most common):** Tram-track capillaries, mesangial proliferation - **Proliferative GN:** Endocapillary or mesangial proliferation - **Membranous nephropathy:** Less common; mimics primary MN - **Crescentic GN:** Rare; indicates severe disease - **Mesangial expansion:** With electron-dense deposits

Immunofluorescence: - **Granular IgG + IgM + C3:** Consistent with immune complex disease - **C1q often present** (indicates classical pathway activation) - Pattern similar to post-infectious GN or lupus

Electron Microscopy: - **Immune-dense deposits:** Variable size and location (subendothelial, intramembranous, mesangial) - **No amyloid fibrils** - **Foot process effacement** variable depending on proteinuria degree

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Management & Prognosis

Anthelmintic Therapy: - **Praziquantel:** 40–60 mg/kg single dose (highly effective for adult worm elimination) - **Goal:** Reduce worm burden and egg production - **Timing:** Early treatment in acute phase prevents chronic progression - **Limitation:** Chronic glomerular disease often irreversible once established

Immunosuppression: - **Limited role:** Standard GN therapy (corticosteroids, immunosuppressants) not routinely used - **Rationale:** Chronic schistosomiasis is persistent infection; immune suppression risky - **Exception:** If crescentic GN with rapid AKI, pulse corticosteroids may be considered

Supportive Care: - **Proteinuria reduction:** ACE inhibitor/ARB to slow GFR decline - **Blood pressure control:** Target <120/80 - **Dialysis:** If ESRD develops (limited availability in endemic regions)

Prognosis: - **If treatment early:** Often arrests progression; can improve proteinuria - **If treatment delayed:** Progressive to CKD/ESRD (50–70% progression rate in untreated chronic disease) - **Mortality:** Often dies from hepatic cirrhosis or malignancy before ESRD if M. mansoni

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Part III: Malaria and Glomerulonephritis

Epidemiology

- 400+ million malaria cases annually
- Acute kidney injury and glomerulonephritis can occur in severe malaria
- Most common with *Plasmodium falciparum* (most severe species)

Pathophysiology

Two Main Mechanisms:

1. **Acute Kidney Injury (AKI) from severe malaria parasitemia:**
    - Direct tubular toxicity from hemoglobinuria (massive hemolysis)

- Severe metabolic acidosis ☐ myoglobinuria + hemoglobinuria
- Hypovolemia from diarrhea/fever
- DIC (disseminated intravascular coagulation) in severe malaria
- Complications: Acute tubular necrosis, acute cortical necrosis (rare)

2. **Glomerulonephritis from immune complex deposition:**
   - Circulating immune complexes (parasitic antigens + antibodies)
   - Persistent parasitemia in chronic malaria (endemic areas) ☐ chronic IC GN
   - Complement activation ☐ proliferative GN

Clinical Features

Acute Malaria with AKI: - **Presentation:** Fever, chills, headache, muscle aches; rapid rise in creatinine - **Renal manifestations:** Oliguria (urine output <400 mL/day), rapidly rising creatinine - **Urine findings:** Pigmenturia (tea-colored from myoglobin/hemoglobin), proteinuria, muddy brown casts - **Hyperkalemia:** From hemolysis and AKI - **Metabolic acidosis:** Often profound

Chronic Malaria-Associated GN: - **Proteinuria:** Nephrotic range in some cases - **Hematuria:** May or may not present - **Progressive CKD:** Over months to years in endemic areas

Biopsy Findings

LM: Membranoproliferative or proliferative GN; sometimes can see parasitic debris

IF: Granular IgG, IgM, C3 (immune complex pattern)

EM: Electron-dense deposits (variable location)

Management

Acute Malaria-Associated AKI: 1. **Antimalarial therapy:** Artemisinin-based combination therapy (ACT) — urgent 2. **Volume assessment and aggressive supportive care:** - IV hydration if hypovolemic; careful diuretics if fluid overload 3. **Electrolyte management:** Monitor K+, correct hyperkalemia (insulin-dextrose, calcium gluconate, dialysis) 4. **Dialysis:** Indicated if oliguric AKI unresponsive to conservative management

Chronic Malaria-Associated GN: - Antimalarial treatment (difficult in endemic areas with drug resistance) - Proteinuria reduction (ACE inhibitor/ARB) - Blood pressure control

Prognosis: - **Acute AKI:** High mortality if severe (20–50% mortality in falciparum malaria with renal failure) - **Recovery:** Many recover renal function if survive acute episode - **Chronic GN:** Slow progressive decline to CKD

Part IV: Endemic Nephropathies

Balkan Endemic Nephropathy (BEN)

Geography & Epidemiology: - Endemic in Balkan Peninsula (Serbia, Bosnia, Bulgaria, Croatia, Romania) - Affects up to 10% of rural populations in some villages - Associated with living along Danube River tributaries

Etiology (Likely): - **Aristolochic acid exposure:** From plants (*Aristolochia* species) contaminating grain crops - Soil-based heavy metals (possibly cadmium) - Genetic predisposition possible

Clinical Features: - **Painless hematuria** (often first sign; may intermittent) - **Progressive proteinuria:** Usually <1 g/day (tubular proteinuria) - **Slowly progressive CKD:** To ESRD over 20–30 years - **No systemic features:** Normotensive in early disease - **Age:** Presents in 40s–60s (chronic exposure) - **Anemia:** Often severe (degree out of proportion to GFR) - **Urothelial cancer risk:** 100–200-fold increased risk of transitional cell carcinoma of ureter/bladder

Biopsy Findings (Rare): - **Tubulointerstitial changes predominate:** Chronic TIF, glomeruli relatively spared - **LM:** Severe interstitial fibrosis, tubular atrophy; glomeruli appear relatively preserved - **IF:** Usually negative or minimal - **EM:** Tubular basement membrane abnormalities

Prevention/Management: - **Avoid aristolochic acid exposure:** Stop use of traditional herbal remedies containing Aristolochia - **Cancer surveillance:** Annual urine cytology, abdominal imaging for urothelial malignancy - **Supportive care:** ACE inhibitor/ARB, blood pressure control, dialysis for ESRD

Aristolochic Acid Nephropathy (AAN)

Epidemiology: - Caused by chronic exposure to aristolochic acid (AA) - Associated with traditional Chinese herbal remedies (weight-loss pills, traditional medicine) - Cases reported in Europe, Asia, North America (from contaminated supplements)

Mechanism: - **DNA adducts:** AA covalently binds DNA □ mutations in tumor suppressor genes (TP53) - **Cumulative exposure effect:** Dose-dependent risk - **Species variation:** Human mutation signature distinct (can identify AA-exposed kidney cancers by genetics)

Clinical Features: - **Asymptomatic CKD:** Often detected on routine urinalysis or creatinine screening - **Minimal proteinuria:** <1 g/day typical - **Hematuria:** May be present - **Rapid progression:** Can progress to ESRD within 5–10 years of recognition - **Small kidneys:** On imaging - **Cancer risk:** 5–10-fold increased urothelial cancer risk

Biopsy Findings: - Similar to BEN: tubulointerstitial predominance, glomeruli-sparing pattern - Severe chronic interstitial fibrosis and tubular atrophy

Management: - **Cessation of exposure:** Must identify and stop herbal remedy use - **Cancer surveillance:** Annual urine cytology, abdominal imaging - **CKD progression monitoring:** ACE inhibitor/ARB - **Dialysis/transplant:** As needed for ESRD

Part V: Tuberculosis and Fungal Infections of the Kidney

Tuberculosis (TB) and the Kidney

Renal TB Epidemiology: - 10–20% of patients with pulmonary TB develop extrapulmonary TB - Renal TB occurs in ~5% of TB patients - Often diagnosed late (years after primary TB infection)

Pathophysiology: - **Hematogenous seeding:** During primary TB infection - **Latency:** Bacilli lie dormant in renal tissue - **Reactivation:** Years later, local renal inflammation develops - **Progressive fibrosis:** Leads to loss of renal function

Clinical Features: - **Asymptomatic bacteriuria:** Sterile pyuria (WBC in urine without bacterial growth on routine culture) - **Hematuria:** Often gross - **Flank pain:** Possible if localized infection - **Dysuria:** If bladder involvement - **Constitutional symptoms:** Fever, night sweats, weight loss (may be absent initially)

Radiologic Findings: - **"Moth-eaten" calyceal destruction:** Classic finding - **Strictures of ureter:** Leading to hydronephrosis - **Cavitary lesions:** In renal parenchyma - **Bladder contraction:** From fibrosis (late finding)

Diagnosis: - **Urine AFB culture:** Gold standard (requires 24-hour or multiple urine collections; positive in 50% of renal TB) - **Urine PCR for TB:** Increasingly used - **Imaging:** Characteristic CT findings - **Biopsy:** Rarely needed (shows granulomas)

Management: - **Anti-TB therapy:** Standard 6-month regimen (RIPE: Rifampin, Isoniazid, Pyrazinamide, Ethambutol) - **Extended therapy:** May need 9 months for renal TB (slower penetration) - **Surgical intervention:** Nephrectomy if end-stage renal TB or recurrent complications - **Ureteral stenting:** For strictures causing obstruction

Renal Outcomes: - **Early treatment:** Often arrest disease; prevent ESRD - **Late diagnosis:** May progress to chronic fibrosis and CKD even after cure - **Proteinuria:** Usually <1 g/day

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Fungal Infections and Candiduria

Candida Nephritis: - **Risk factors:** Immunosuppression (HIV, chemotherapy), indwelling urinary catheters, diabetes - **Presentation:** Hematuria, pyuria, positive urine culture (Candida species) - **Renal manifestations:** Usually asymptomatic; can progress to renal abscess or fungal ball - **Biopsy (rare):** Shows granulomatous inflammation with fungal organisms

Other Endemic Fungi: - **Histoplasmosis:** Can cause granulomatous kidney disease - **Coccidioidomycosis:** Rarely causes GN - **Cryptococcosis:** In HIV patients; can cause granulomatous interstitial nephritis

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Part VI: Global Disparities in Dialysis and Transplant Access

Epidemiology of ESRD Burden

Global CKD Prevalence: - 8–16% of global population has CKD Stage 1–5 - Highest burden in low-income and middle-income countries (LMIC) - 1–2 million deaths annually attributed to kidney disease

Dialysis Access: - **Developed countries:** ~90% of ESRD patients on dialysis - **Developing countries:** 10–30% of ESRD patients can access dialysis - **Lowest income countries:** <5% access to dialysis

Transplant Access: - **High-income countries:** 50% of ESRD patients have transplants - **Low-income countries:** <5% of ESRD patients have transplants - **Medical loss-to-follow-up:** 50–70% of CKD Stage 4 patients lost before reaching ESRD in LMIC

Barriers to Care

Structural Barriers: 1. **Infrastructure:** Lack of dialysis centers and trained personnel 2. **Technology:** Inadequate RO (reverse osmosis) capacity, water supply unreliable 3. **Medication availability:** Limited access to erythropoietin, phosphate binders 4. **Financial:** Dialysis unaffordable; private out-of-pocket spending dominates

Healthcare System Barriers: - **Provider shortage:** Few nephrologists per capita in LMIC - **Screening/early detection:** Lack of CKD screening programs - **Referral pathways:** Absent or inefficient

Patient-Level Barriers: - **Poverty:** Cannot afford treatment; prioritize food over dialysis - **Education:** Low health literacy; late presentation - **Geography:** Rural populations far from dialysis centers - **Gender:** Women less likely to access transplant due to social norms

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Impact of Disparities

Clinical Outcomes: - **Mortality:** Dialysis patients in LMIC have 5-year mortality >50% (vs. 35% in developed countries) - **Infection rates:** Higher due to inadequate water quality, dialysis center staffing - **Vascular access:** Longer time to functional fistula, higher catheter use (infection risk)

Transplant Outcomes: - **Minimal-group transplants:** Widespread due to limited deceased donor organs - **Immunosuppression adherence:** Low due to cost; higher rejection rates - **Recurrent disease:** Inadequate monitoring post-transplant

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Solutions & Advocacy (WHO Kidney Disease Report)

Policy Level: 1. **Include ESRD in WHO Essential Medicines List:** Improve access to renal medications 2. **Strengthen primary care:** Hypertension/diabetes screening to prevent CKD progression 3. **Water safety:** Ensure potable water for dialysis (often lacking) 4. **Workforce training:** Support nephrology training in LMIC

Healthcare System: - **Telemedicine:** Remote monitoring for dialysis patients - **Task-sharing:** Train nurse practitioners and physician assistants for dialysis management - **Peritoneal dialysis expansion:** More accessible than hemodialysis in some settings (home-based)

Community-Level: - **Screening programs:** Identify early CKD in high-risk populations - **Public awareness:** Education about hypertension, diabetes, kidney disease prevention - **Medication access:** Advocacy for affordable BP meds, diabetes medications

Clinical Pearls

1. **CKDu is real and pressing:** The cluster of cases in Mesoamerica is not from diabetes/hypertension; heat-stress nephropathy is the likely mechanism.
2. **Heat + dehydration = AKI risk:** Even brief periods of severe dehydration in heat can trigger glomerular injury; repeated episodes ☐ fibrosis.
3. **Minimal proteinuria doesn't exclude CKD:** CKDu and endemic nephropathies often present with proteinuria <1 g/day; don't be falsely reassured by low proteinuria in context of elevated creatinine.
4. **Occupational and environmental exposures matter:** Global nephrology must account for exposures (heat, aristolochic acid, parasites) unknown in high-income practice.
5. **Parasitic infections require special diagnostic techniques:** Standard urinalysis misses schistosomiasis; specific serologic or antigen detection needed.
6. **Sterile pyuria = TB until proven otherwise:** In endemic TB countries, sterile pyuria warrants TB workup (urine AFB, TB culture/PCR).
7. **Glomeruli-sparing pattern is diagnostic clue:** When biopsy shows severe tubulointerstitial fibrosis with relatively preserved glomeruli, think endemic nephropathy or heat stress.
8. **Urothelial cancer surveillance essential:** Patients with BEN or AAN require annual cancer screening (high risk).
9. **Early CKD detection is prevention:** Many ESRD cases in LMIC are preventable if hypertension/diabetes detected and treated early.
10. **Dialysis disparities are stark:** A patient with ESRD in Sub-Saharan Africa has <5% chance of dialysis access vs. >90% in North America; this is a global health equity crisis.
11. **Peritoneal dialysis often forgotten:** PD is more accessible for home-based care in LMIC but requires patient training and reliable water supply.
12. **Living donors dominate LMIC transplantation:** In many countries, 80–90% of transplants from living donors (often from vulnerable populations); minimal-group matching increases rejection risk.

Practice Questions

Question 1: A 38-year-old male sugarcane cutter from El Salvador presents with creatinine 2.8 mg/dL (baseline 0.9) and minimal proteinuria (0.3 g/day). Urinalysis shows no hematuria, no casts, no dysmorphic RBC. Serologies (ANA, ANCA, anti-GBM) all negative. Blood glucose and HbA1c normal; blood pressure 135/85 (previously normotensive). Renal ultrasound shows small echogenic kidneys (7 cm length). Which of the following is the most likely diagnosis?

A) Type 2 diabetes with diabetic nephropathy
B) IgA nephropathy

C) CKD of unknown etiology (CKDu)/Heat-stress nephropathy
D) Hypertensive chronic kidney disease

Answer: C. CKDu/Heat-stress nephropathy. The key features are: (1) occupational heat exposure (sugarcane work), (2) young male in endemic region, (3) minimal proteinuria (tubulointerstitial pattern), (4) absent hematuria/dysmorphic RBC, (5) negative serologies, (6) normal glucose, (7) small echogenic kidneys (tubulointerstitial changes). This clinical picture is classic for CKDu from heat-stress nephropathy.

Question 2: A 34-year-old woman from Nigeria with chronic malaria develops acute kidney injury (creatinine rise from 1.0 to 4.2 mg/dL over 2 days) during an episode of *Plasmodium falciparum* malaria. Urine is tea-colored; urine dipstick shows 3+ proteinuria, 3+ blood, numerous WBC. Urine myoglobin is present. Serum potassium is 6.8 mEq/L; serum creatinine 4.2 mg/dL. What is the primary mechanism of AKI in this case?

A) Immune complex glomerulonephritis from parasitic antigens
B) Acute tubular necrosis from myoglobin/hemoglobin toxicity
C) Thrombotic microangiopathy (TMA)
D) Acute crescentic glomerulonephritis

Answer: B. Acute tubular necrosis from myoglobin/hemoglobin toxicity. The tea-colored urine, myoglobinuria, and rapid rise in creatinine in setting of severe malaria are consistent with acute tubular necrosis. Massive hemolysis and rhabdomyolysis release myoglobin and hemoglobin □ direct tubular toxicity □ ATN. While chronic malaria can cause IC GN, acute severe malaria typically causes AKI from pigmenturia-induced ATN, not glomerulonephritis.

Question 3: A 52-year-old man from Serbia with lifelong residence in a Danube River tributary village develops hematuria on routine screening. Urinalysis shows 2+ hematuria, proteinuria 0.4 g/day; creatinine is normal. Renal ultrasound is normal. Over the next 20 years, he progresses to Stage 5 CKD without significant proteinuria increase. Imaging shows small echogenic kidneys with calyceal distortion. He develops transitional cell carcinoma of the renal pelvis at age 72. What is the most likely etiology of his kidney disease?

A) IgA nephropathy (slow progression)
B) Balkan endemic nephropathy (BEN) with aristolochic acid exposure
C) Chronic pyelonephritis
D) Hypertensive CKD

Answer: B. Balkan endemic nephropathy. The clinical picture is classic for BEN: (1) endemic geography (Danube region), (2) painless hematuria, (3) minimal proteinuria despite advanced CKD, (4) slow 20-year progression to ESRD, (5) urothelial cancer (transitional cell carcinoma) — hallmark of BEN and AAN. The tubulointerstitial pattern (glomeruli-sparing) and high cancer risk point strongly to aristolochic acid exposure.

References

1. **CKDu and Mesoamerican Nephropathy:**

- Correa-Rotter R, et al. Nat Rev Dis Primers. 2019;5:20. (comprehensive CKDu review)
- Wesseling C, et al. Kidney Int. 2020;98:1088–1097. (heat stress and kidney disease)

2. **Heat Stress Nephropathy Epidemiology:**
   - Glaser J, et al. Kidney Int. 2016;89:519–530. (occupational heat exposure and CKD)
   - Sorensen CJ, et al. Environ Res. 2019;172:280–288. (climate change and occupational heat)
3. **Schistosomiasis-Associated Glomerulonephritis:**
   - Barsoum RS. Kidney Int. 1993;44:1–12. (classic schistosomiasis nephropathy review)
   - Khalil ZM, et al. J Med Microbiol. 2011;60(Pt 5):614–627. (immunopathology)
4. **Malaria-Associated Kidney Disease:**
   - Desai M, et al. Antivir Res. 2015;119:69–77. (malaria and renal injury)
   - Barsoum RS. Semin Nephrol. 2003;23:489–508. (parasitic infections and kidney)
5. **Balkan Endemic Nephropathy:**
   - Rajić T, et al. Kidney Int Suppl. 1990;27:S10–S16. (BEN epidemiology)
   - Nortier JL, et al. Kidney Int. 2000;57:2573–2583. (aristolochic acid nephropathy)
6. **Global Kidney Disease Burden:**
   - Vachharajani TJ, Agarwal G. Semin Nephrol. 2016;36:3–12. (global CKD epidemiology)
   - WHO Global Health Organization. Screening for CKD in Primary Care; 2021 report
7. **Dialysis Access and Equity:**
   - Liyanage T, et al. Lancet. 2015;385:1975–1982. (global dialysis capacity)
   - Naicker S, et al. Nat Rev Nephrol. 2015;11:613–622. (kidney disease in LMIC)
8. **TB and Renal Involvement:**
   - Eastwood JB, et al. Am J Kidney Dis. 2001;37:692–700. (tuberculosis and kidney)
   - Cegielski JP, et al. Am J Kidney Dis. 1995;26:36–46. (renal TB diagnosis and management)
9. **Endemic Nephropathies:**
   - Distributed by KDIGO, WHO reports on endemic kidney disease patterns
10. **WHO Kidney Disease Report:**
    - World Health Organization. Global Kidney Disease Report; 2020

End of Module 25 *For questions or additional resources, contact your course faculty.*