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HIV associated glomerulopathy

Pathogenesis, Clinical Manifestations, and Management

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HIV at 40: kidney disease in HIV treatment, prevention, and cure

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Glomerular Diseases

Review Article

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HIV-Associated Nephropathy in 2022

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Research Article

Histological patterns of kidney disease at Helen Joseph Hospital: a 5-year retrospective review of biopsy diagnoses

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The spectrum of kidney biopsy findings in HIV-infected patients in the modern era

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Advances in the pathogenesis of HIV-associated kidney diseases

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IN PRACTICE

Kidney Biopsy in HIV: Beyond HIV-Associated Nephropathy

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INDEX WORDS: Human immunodeficiency virus; kidney biopsy; kidney disease; proteinuria; drug toxicity.

HIV and kidney disease in sub-Saharan Africa

Fabian, J. & Naicker, S. *Nat. Rev. Nephrol.* **5**, 591–598 (2009); doi:10.1038/nrneph.2009.141

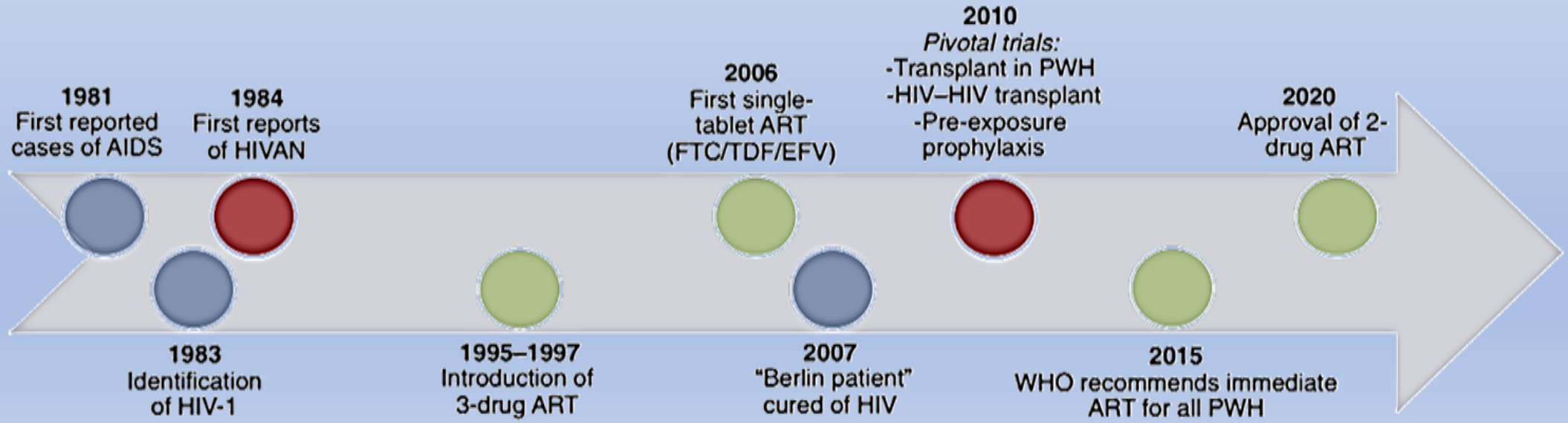
introduction

- HIV (HIV-1&2) is a retrovirus that stores its genetic material as RNA
- UNAIDS estimated in 2023, approximately 38 million people globally were living with HIV

- an association between HIV and renal disease was first reported in 1984 with individuals with HIV presenting with nephrotic range proteinuria and progressing to ESRD within 8–16 weeks (HIVAN)

- HIVAN was initially thought to be associated with advanced immunosuppression; but it was later recognized that can occur at any stage of HIV-1 infection, even before antibody seroconversion

- incidence of HIVAN in the US is estimated between 3.5% -12%
  - over 90% of patients with HIVAN are black



- worldwide prevalence of CKD in people with HIV: (GFR below 60 ml/min/1.73 m^2)
  - 18% of Chinese patients
  - 27% in India
  - 20% in Iran

- Early ART initiation was also shown to result in modestly higher eGFR and reduced proteinuria
  - prolonged life expectancy, presence of comorbid diseases of ageing and cumulative exposure to potentially nephrotoxic ART have led to an increase in the prevalence of CKD in people living with HIV (PLWH)

Spectrum of kidney diseases

3.5 – 48.5%

- AKI, electrolyte and acid–base disturbances
- Glomerulonephropathies (including HIVAN) that present as either acute-on chronic or CKD
- Renotoxic effects of treatments of HIV and its complications
- Co-morbid Disease (DM, Co-infection HCV, HTN)

Pathogenesis of kidney disease in PWH

- Multiple factors:
  1) HIV infection
  2) genetic susceptibility
  3) Treatment of HIV
  4) comorbid CKD risk factors

1) The causal relationship between direct HIV infection of the renal epithelial cells and HIVAN has been established

- renal expression of HIV genes:
  - ✓ *Nef* (negative factor)
  - ✓ *Vpr* (viral protein r)
  - ✓ *Tat* (trans activator of transcription)

  - ➢ the expression genes in kidney cells increases the expression of interferon and/or TNF within the kidney that stimulating the expression of *APOL1* G1 and/or G2 transcripts

- kidney can act as a reservoir for the virus even when viraemia is undetectable:
  - ✓ detection of HIV-1 nucleic acids in kidney biopsy samples of patients with HIVAN

2) The association between APOL1 risk variants and HIVAN is supported by a systematic review and meta-analysis:

- prevalence of APOL1 high-risk alleles (GI and G2) significantly increased the risk of HIVAN (pooled OR 16.67; n= 769, P< 0.001): 89-fold & 90% in African descent

- The APOL1 risk variants are also associated with other forms of HIV-associated kidney diseases
  - two APOL1 risk alleles: 76% had FSGS whereas 10% had hypertensive nephrosclerosis
  - one APOL1 risk allele: 47% had immune complex-mediated glomerulonephritis whereas 23% had FSGS
  - no APOL1 risk allele, 40% had immune complex-mediated glomerulonephritis and 12% had FSGS

- **Second hits**
  - Despite this strong association, not all people with HIVAN carry the high-risk APOL1 genotype, suggesting that:
    - ➢ other genes or environmental factors are required to induce inflammatory or interferon responses in kidney cells and increase susceptibility to HIVAN:

    - ✓ viruses (especially HCV or SARS-CoV-2)
    - ✓ autoimmune diseases (SLE)
    - ✓ ischemia–reperfusion injury (sickle cell disease)
    - ✓ kidney allograft rejection
    - ✓ exogenous interferon administration

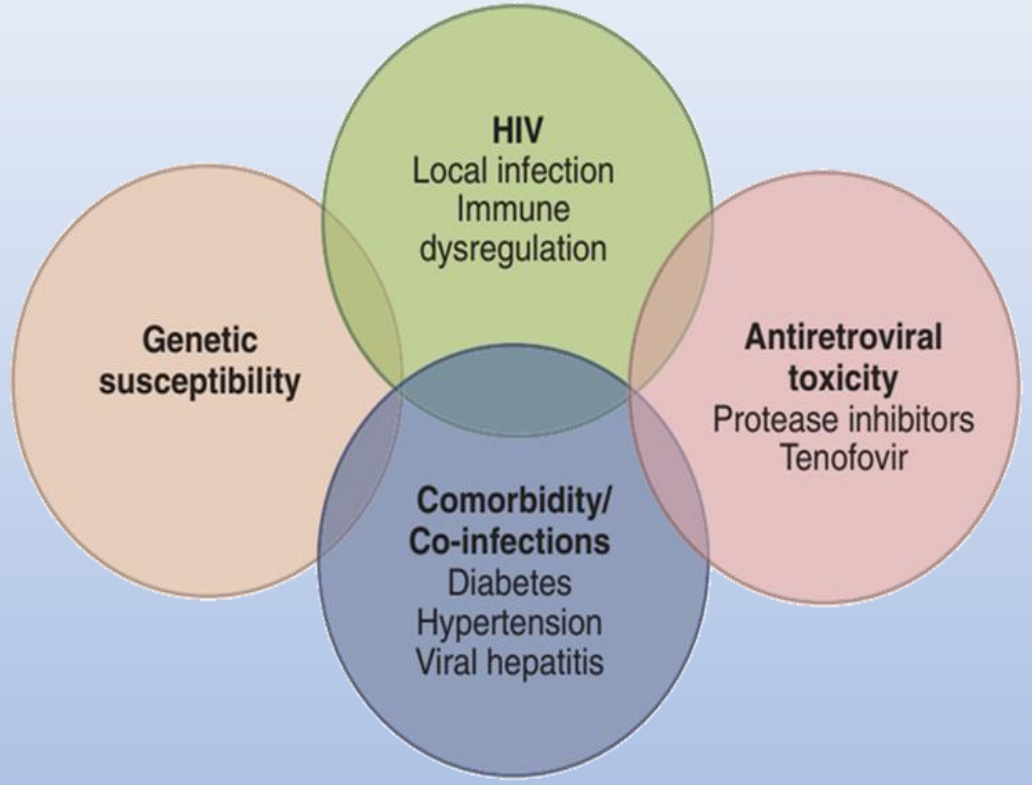
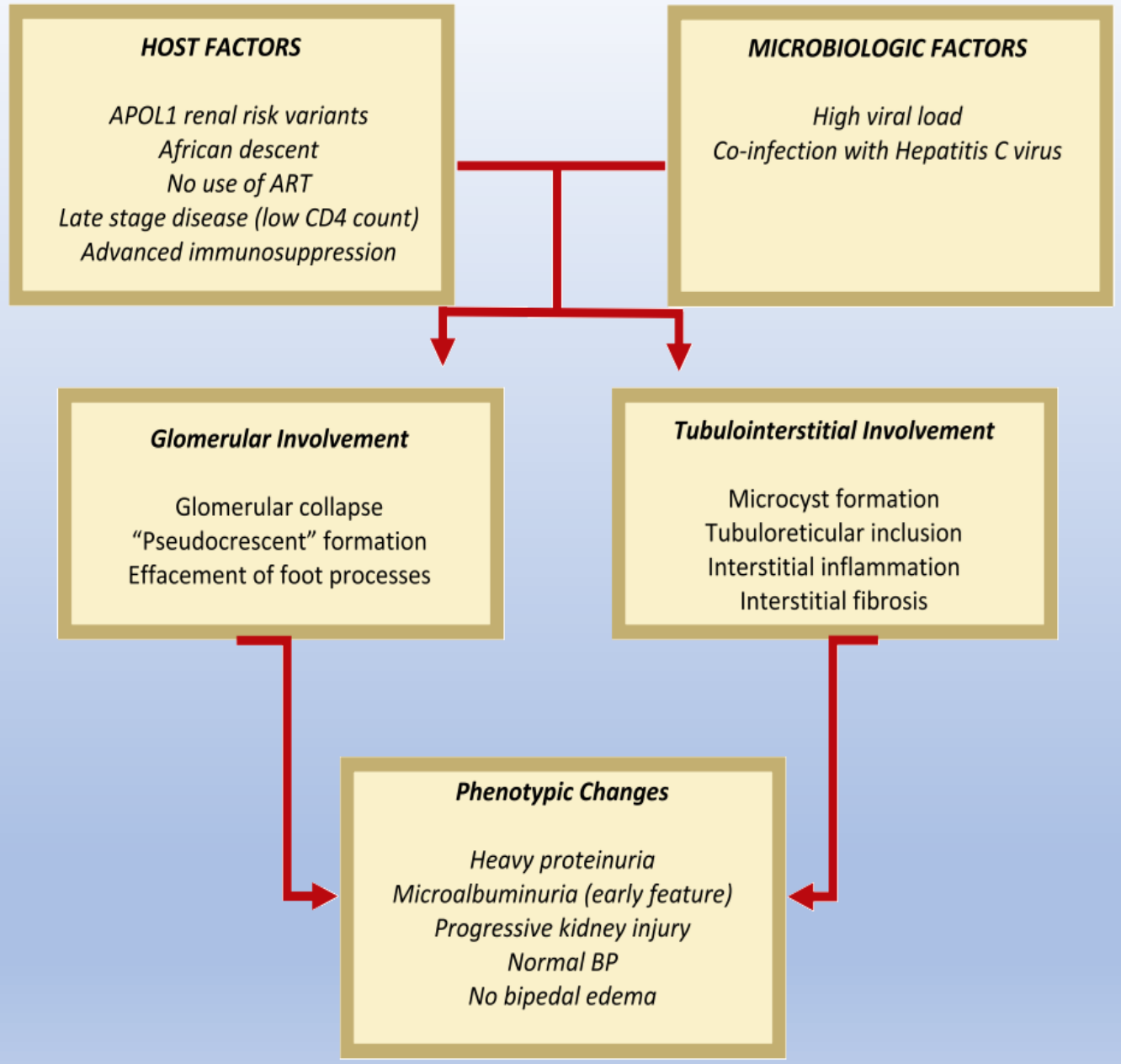


Figure 3 | Potential contributors to kidney disease in people with HIV.



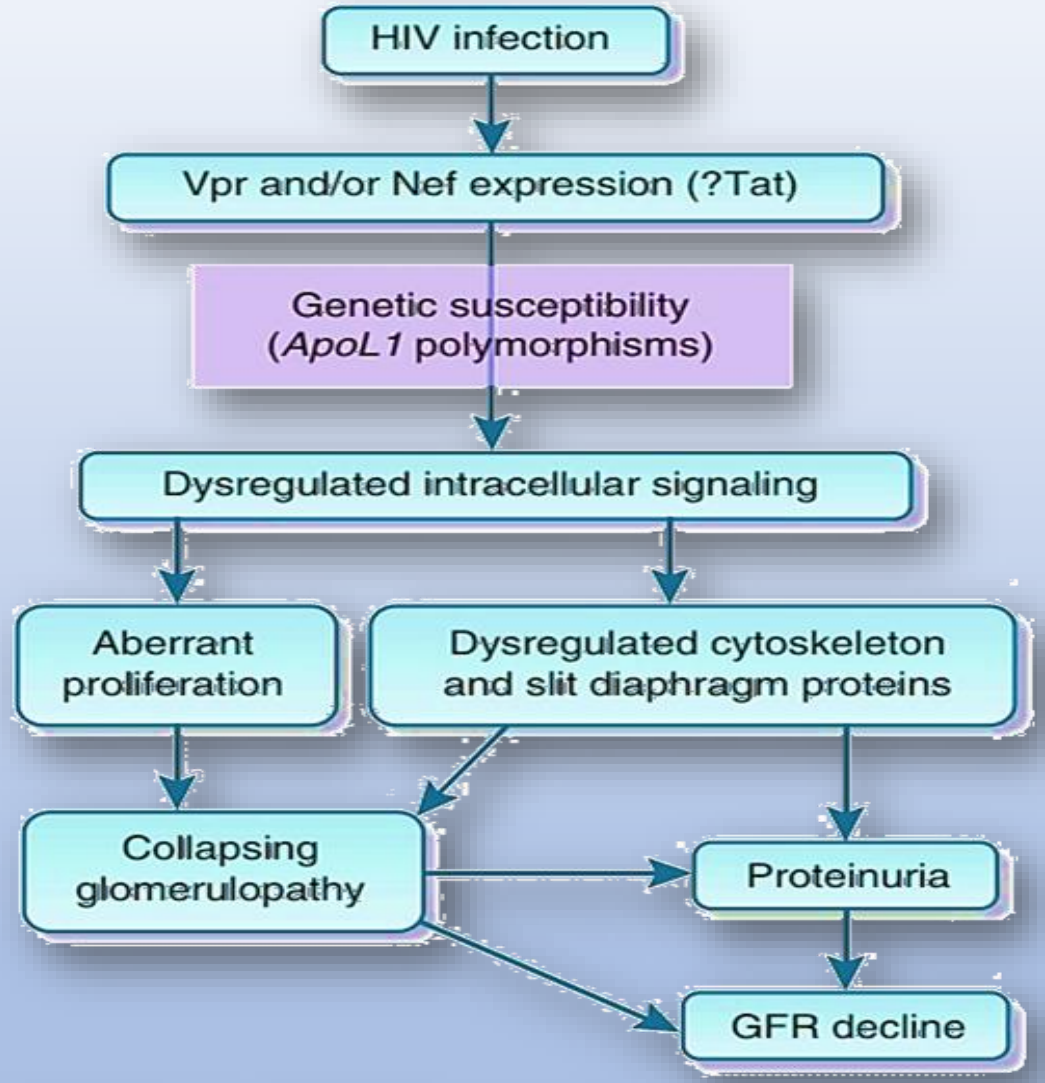


Figure 3 | Diagram depicting general mechanisms by which HIV infection of podocytes can promote glomerular injury. GFR, glomerular filtration rate.

Acute Kidney Injury

- AKI in hospitalized patients with HIV can be community or hospital acquired
  - ➢AKI acquired in the hospital is associated with worse outcomes and 5–10 times more common
  - ➢the most common is ATN secondary to:
    - ✓Sepsis
    - ✓Hypotension
    - ✓Dehydration
    - ✓exposure to nephrotoxins
- predominant risk factor is severe immunosuppression
  - $CD4^+$ T-cell count <200 cells/mm3
  - HIV RNA level >10,000 copies/ml

HIV-Associated CKD

- Prevalence: 6% to 45%

- Shift in kidney disease presentation with ART:
  - ➢While HIVAN remains present, its prevalence has markedly decreased due to the effective suppression of viral replication

  - ➢This shift now includes a higher incidence of:
    - ✓comorbid kidney diseases in an aging population of HIV-infected individuals
    - ✓ART-related nephrotoxicity

Classification of Kidney Disease in HIV

- Consensus Classification of Kidney Disease & Histology in HIV has been proposed to:

  - reduce variability in biopsy interpretations

  - divides kidney diseases into distinct histological categories based on the compartments affected within the kidney

Table 1 | Kidney Disease: Improving Global Outcomes classification of kidney pathology in people with HIV

I. Glomerular-dominant[a]

a. Podocytopathies (all characterized by extensive foot process effacement)[b]
   i. Classic HIVAN
   ii. FSGS (NOS) in the setting of HIV
   iii. Minimal change disease in the setting of HIV
   iv. Diffuse mesangial hypercellularity in the setting of HIV
   v. Other podocytopathy in the setting of HIV

b. Immune complex–mediated glomerular disease[a]
   i. IgA nephropathy in the setting of HIV
   ii. Lupus-like glomerulonephritis in the setting of HIV
   iii. Lupus nephritis in the setting of HIV
   iv. Membranous nephropathy in the setting of HIV
      - Indicate whether HBV-positive, HCV-positive, PLA2R-positive (should not preclude workup for other secondary causes)
   v. Membranoproliferative pattern glomerulonephritis in the setting of HIV
      - Indicate whether HCV-positive (should not preclude workup for other secondary causes)
   vi. Endocapillary proliferative and exudative glomerulonephritis in the setting of HIV
      - Post-streptococcal, staphylococcal-associated, other
   vii. Fibrillary or immunotactoid glomerulonephritis in the setting of HIV
   viii. Other immune complex disease in the setting of HIV

II. Tubulointerstitial-dominant[a]

a. Tubulointerstitial injury in the setting of classic HIVAN
   i. Hyaline droplet tubulopathy
   ii. Tubular microcysts
   iii. Tubulointerstitial inflammation

b. Acute tubular injury or acute tubular necrosis
   i. Ischemic
   ii. Toxic (associated with ART vs. other)

c. Drug-induced tubulointerstitial nephritis (other than ART)
   i. Antibiotics
   ii. Proton pump inhibitors
   iii. NSAIDs
   iv. Other

d. Direct renal parenchymal infection by pathogens (bacterial, viral, fungal, protozoal, etc.)

e. Immunologic dysfunction–related tubulointerstitial inflammation
   i. Diffuse infiltrative lymphocytosis syndrome
   ii. Immune reconstitution inflammatory syndrome

f. Other tubulointerstitial inflammation in the setting of HIV

III. Vascular-dominant[a]

a. Thrombotic microangiopathy in the setting of HIV

b. Arteriosclerosis

IV. Other, in the setting of HIV infection

a. Diabetic nephropathy

b. Age-related nephrosclerosis

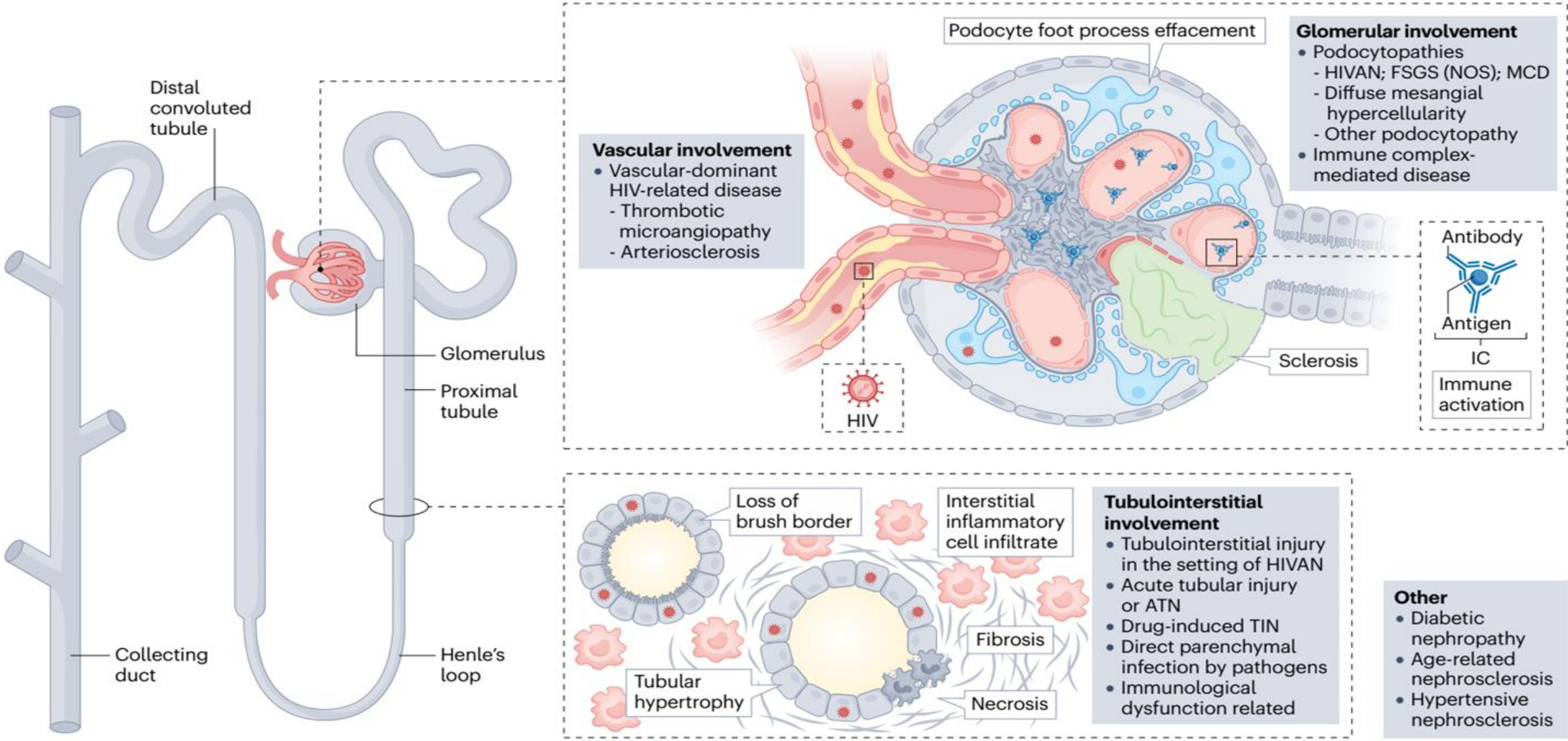
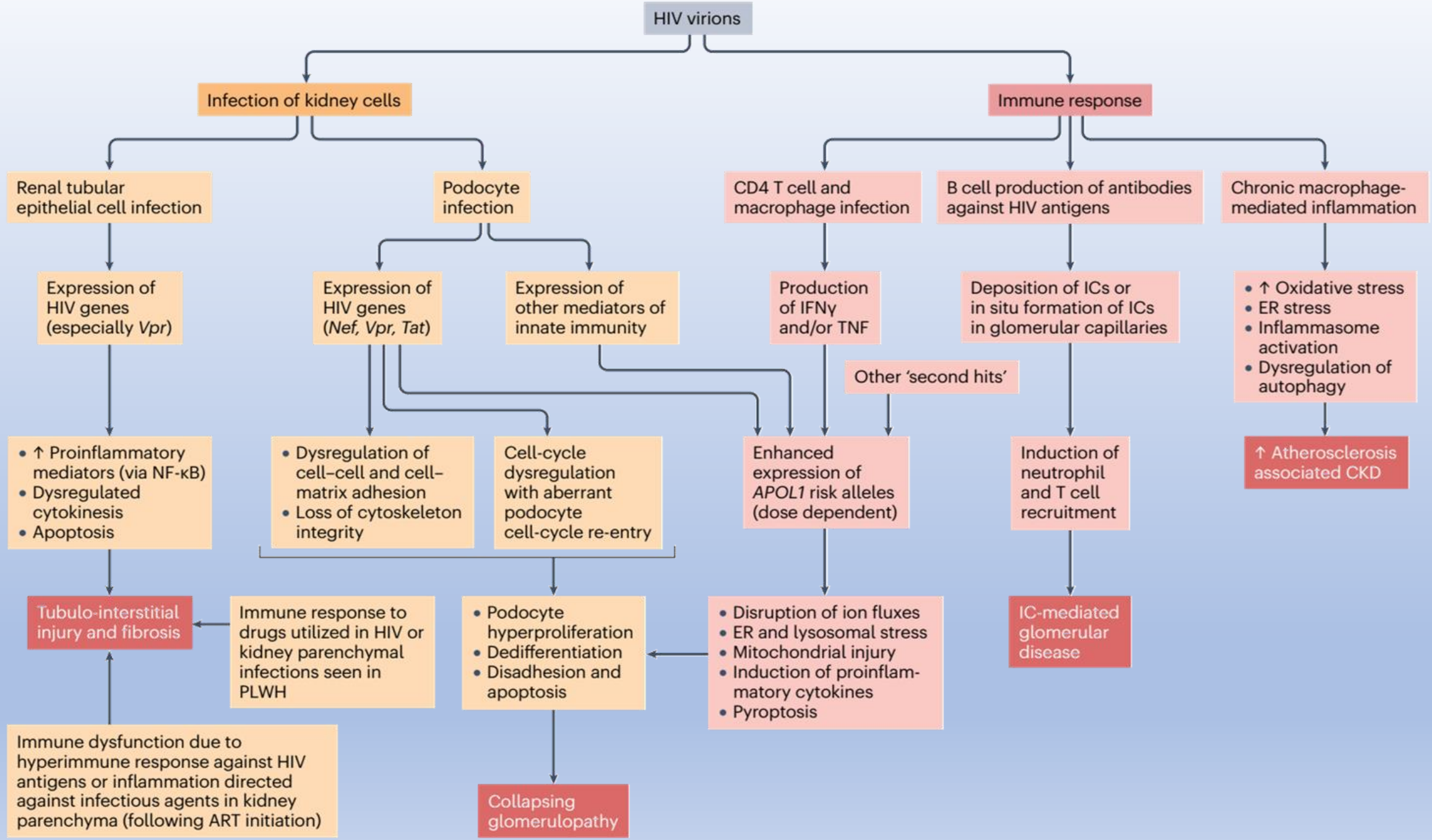


Fig. 2 | Pathological classification of HIV-associated kidney disease. HIV infection can affect all compartments of the kidney. The pathological classification of HIV-associated kidney diseases proposed by KDIGO is based on the major tissue compartment involved. The four main categories are: glomerular dominant, tubulointerstitial dominant, vascular dominant and other in the setting of HIV. The schematic view shows the location and subtypes in each main category. ATN, acute tubular injury; FSGS (NOS), focal segmental glomerulosclerosis (not otherwise specified); HIVAN, HIV-associated nephropathy; IC, immune complex; MCD, minimal change disease; TIN, tubulointerstitial nephritis.


HIV virions
Infection of kidney cells
Immune response
Renal tubular epithelial cell infection
Podocyte infection
CD4 T cell and macrophage infection
B cell production of antibodies against HIV antigens
Chronic macrophage-mediated inflammation
Expression of HIV genes (especially Vpr)
Expression of HIV genes (Nef, Vpr, Tat)
Expression of other mediators of innate immunity
Production of IFNγ and/or TNF
Deposition of ICs or in situ formation of ICs in glomerular capillaries
• ↑ Oxidative stress
• ER stress
• Inflammasome activation
• Dysregulation of autophagy
Other 'second hits'
• ↑ Proinflammatory mediators (via NF-κB)
• Dysregulated cytokinesis
• Apoptosis
• Dysregulation of cell–cell and cell–matrix adhesion
• Loss of cytoskeleton integrity
Cell-cycle dysregulation with aberrant podocyte cell-cycle re-entry
Enhanced expression of APOL1 risk alleles (dose dependent)
Induction of neutrophil and T cell recruitment
↑ Atherosclerosis associated CKD
Tubulo-interstitial injury and fibrosis
Immune response to drugs utilized in HIV or kidney parenchymal infections seen in PLWH
• Podocyte hyperproliferation
• Dedifferentiation
• Disadhesion and apoptosis
• Disruption of ion fluxes
• ER and lysosomal stress
• Mitochondrial injury
• Induction of proinflam-matory cytokines
• Pyroptosis
IC-mediated glomerular disease
Immune dysfunction due to hyperimmune response against HIV antigens or inflammation directed against infectious agents in kidney parenchyma (following ART initiation)
Collapsing glomerulopathy

Glomerular-Dominant Diseases

- primarily divided into two major subcategories:

a) Podocytopathies

b) HIV immune complex-mediated glomerular or kidney diseases (HIVICK)

a) Podocytopathies: five main subtypes and characterized by:

- foot process effacement
- significant proteinuria
- minimal or absent of immune complex deposition

1) Classic HIVAN (HIV-associated nephropathy):

- prototypical form of HIV-related kidney disease
- characterized by:

✓collapsing glomerulopathy

✓microcystic tubular dilatation

✓tubulointerstitial inflammation

✓podocyte effacement

✓severe proteinuria

✓strongly associated with uncontrolled HIV infection, and its prevalence has decreased significantly with the advent of ART

- **prevalence of classic HIVAN has significantly declined since the introduction of ART:**
  - ✓ Columbia University Study (2011–2018): 76% in 1987 to 14% in 2018
  - ✓ Cape Town, South Africa (2016–2020 vs. 2005–2009): from 45% during 2005-2009 to 29% during 2016-2020
  - ✓ Johannesburg Cohort: from 43.4% to 22.8%

- **classic HIVAN has not been eradicated:**
  - ✓ Undiagnosed HIV infections: In regions where HIV testing and treatment coverage are insufficient
  - ✓ Incomplete ART coverage
  - ✓ Non-adherence to ART
  - ✓ Genetic diversity of PLWH

2) Focal Segmental Glomerulosclerosis - Not Otherwise Specified (FSGS-NOS) or Non-HIVAN podocytopathies:

- often appears in HIV-infected individuals, particularly those on ART
- more common diagnosis in the current era of ART
- represent a partially treated or attenuated form of HIVAN, with a potential pathogenic contribution of age-related factors
- Patients are older and more likely to have undetectable viraemia than those with a histological diagnosis of HIVAN
- HIV is presumed to be the causative factor **when secondary causes of FSGS have been excluded:**
  - ✓ other viral causes of FSGS (cytomegalovirus, parvovirus, simian virus 40 infection)
  - ✓ drug-induced disease
  - ✓ Hypertension
  - ✓ diabetes or obesity
- Differentiating HIV-related FSGS from secondary FSGS is challenging:
  - ✓ Molecular approaches are not yet available in clinical practice

3) **Minimal Change Disease (MCD)**: rare

- podocyte effacement without significant glomerular changes
- typically responsive to corticosteroid therapy

4) **Diffuse Mesangial Hypercellularity**: characterized by increased mesangial cell proliferation

5) **Other Podocytopathies in HIV**: include atypical forms of podocyte injury or diseases that do not fit neatly into the classical definitions but still result in significant kidney dysfunction in the setting of HIV

b) Immune Complex-Mediated Glomerular Diseases

- characterized by the deposition of immune complexes in the glomeruli, which can trigger an inflammatory response
- Limited evidence linking HIV directly to immune complex-mediated kidney disease

- possible causal role for HIV in these conditions:
  - ➢ In a small cohort of PLWH, HIV antigens and specific HIV antibodies were found in glomerular immune deposits
  - ➢ presence of a **ball-in-cup** type of **subepithelial immune deposit** observed in kidney biopsies from South Africa
    - ✓ not pathognomonic for HIV-related immune complex glomerulopathy and has also been observed in other forms of immune complex diseases

- **IgA nephropathy**: can coexist with HIV infection, but whether this is due to the deposition of IgA against HIV antigens or is merely co-incidental remains unclear
  - ➢ higher rates observed in certain populations (e.g., Caucasian Americans)

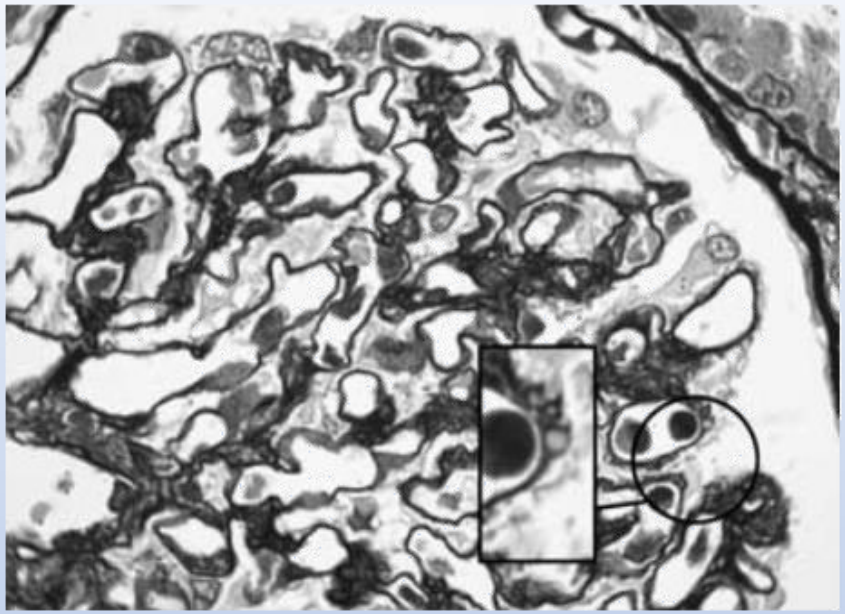


Figure 4 | Subepithelial eosinophilic deposits in relation to the glomerular basement membranes, with a 'ball-in-cup' reaction pattern (see encircled and enlarged tuft with capillary loop). Silver–methenamine stain, original magnification, × 1000 (oil-immersion).

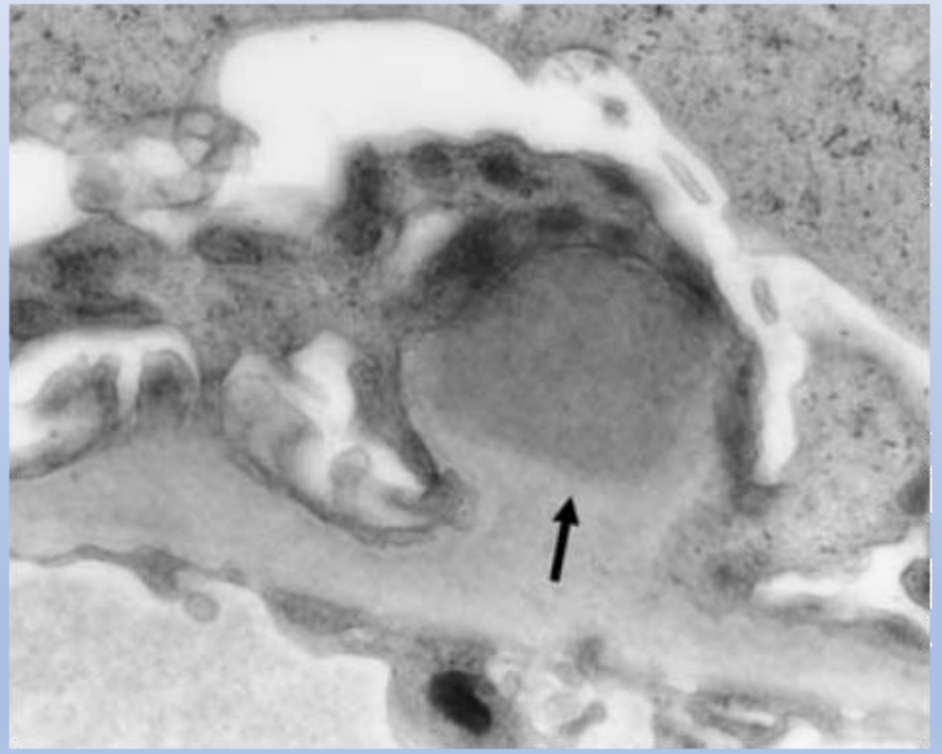


Figure 5 | Electron microscopy depicting a subepithelial 'ball-in-cup' deposit (see black arrow).

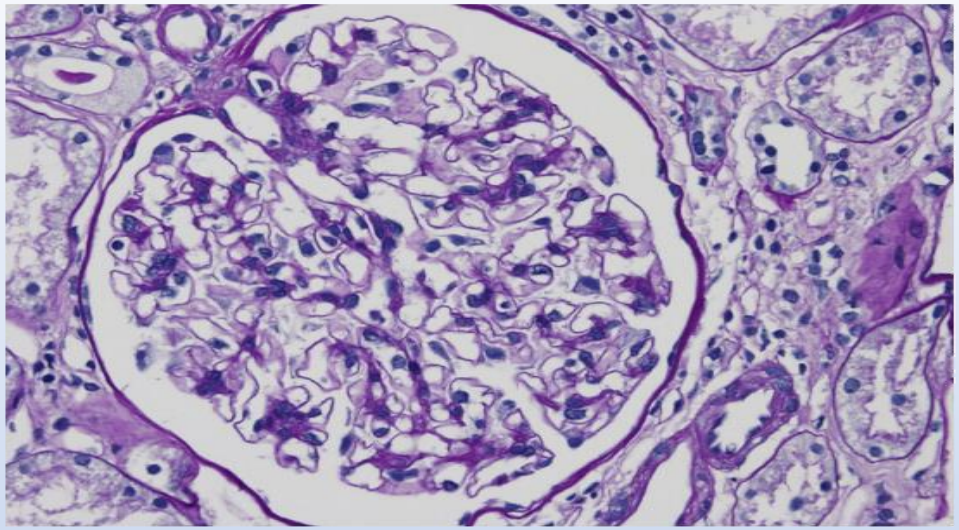


Figure 1. HIV-associated immune complex kidney disease with mesangial proliferation (periodic acid–Schiff stain).

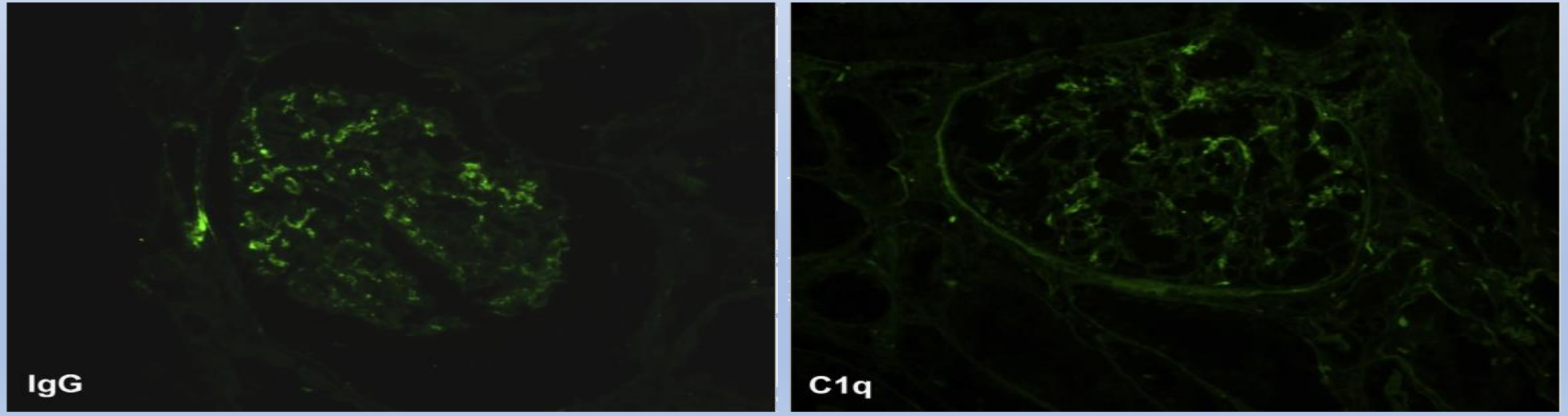


Figure 2. HIV-associated immune complex kidney disease with "full-house" staining in the mesangium (immunofluorescence microscopy, IgG and C1q).

Comorbidities and CKD in PLWH

- ART has transformed HIV into a chronic disease, and with the longevity of PLWH, kidney disease is increasingly associated with age-associated comorbidities, such as:
  - metabolic syndrome
  - obesity, diabetes mellitus
  - chronic inflammation
  - Arterionephrosclerosis

- Hypertension, type 2 diabetes and vascular disease are now common causes of CKD in these individuals
  - Activation of the immune system through HIV infection leads to increased atherosclerosis and cardiovascular risks, even among those with viral suppression

- association between HIV infection and type 2 diabetes are contradictory:
  - In a large Danish cohort study from 2021, the adjusted odds ratio of type 2 diabetes in PLWH was 1.77 (95% CI 1.23 – 2.54; *P* = 0.002) compared with matched uninfected controls
  - Risk factors included higher age and BMI
  - **HIV-specific risk factors**, including CD4 count, duration on ART, use of older ART and previous AIDS-defining illnesses, were **not associated** with the increased risk of type 2 diabetes
  - The proposed contributing mechanisms included:
    - ✓ ART regimen, co-infection with HCV or tuberculosis, growth hormone deficiency, lipodystrophy and mitochondrial dysfunction, leading to insulin resistance

Diagnosis of kidney disease in HIV

- **kidney biopsy**
  - Estimating the prevalence of kidney histological diagnoses in the setting of HIV from biopsy data has its limitations
    - selection bias
    - facility is not available
  - histological findings on the biopsy core may not be representative of the disease within the kidney
  - clinical parameters, including genotyping for *APOL1*, can't accurately predict histological diagnosis in HIV infection and **kidney histology is the gold standard** for diagnosis to **aid therapy and prognostication** of HIV kidney disease

- **Biomarkers of kidney disease**
  - serum and urinary biomarkers can be helpful
  - The most common and reliable biomarkers for CKD progression are:
    - **Glomerular Filtration Rate (GFR)** :
      - ✓ All PLWH are at an increased risk of developing CKD and should receive frequent monitoring of GFR
      - ✓ Although there are potential concerns with the use of cystatin C in the setting of ongoing systemic inflammation, $eGFR_{Cys}$ and $eGFR_{Cr}$ appear to have similar performance in PWH on stable ART
      - ✓ $eGFR_{Cys}$-EPI has been shown to be a stronger predictor of adverse outcomes in PWH
    - **Proteinuria/Albuminuria**

- Biomarkers that are used predominantly in research settings and are **increased** in the **urine** of patients with HIV-associated kidney diseases include:
  - urine kidney injury molecule-1 (KIM-1)
  - liver-type fatty acid binding protein (L-FABP)
  - alpha-1-microglobulin (α1m)
  - B2-microglobulin (B-2M)
  - Neutrophil Gelatinase-associated Lipocalin (NGAL): Patients with HIVAN express four-fold higher levels of urinary NGAL than those with other glomerulopathies, reflecting the cystic tubular dilation that is a feature of HIVAN
  - N-acetyl-beta-D-glucosaminidase (NAG)

- Biomarkers associated with disease progression include increased:
  - urine albumin
  - IL-18
  - KIM-1

  correlated with more rapid eGFR decline over 8 years of follow-up in women with HIV infection in one study

Management of CKD in PWH

- In PWH with suppressed HIV viral load, a diagnosis of CKD should prompt evaluation and optimized management of traditional CKD risk factors
- Kidney biopsy is strongly recommended for definitive diagnosis in PWH with albuminuria
- Current therapies for CKD do not specifically target the pathways and/or genetic factors that contribute to HIV-related CKD progression
- PLWH should be started on ART (if not already initiated) and assessed for reversible factors that may increase their risk of kidney disease progression:
  - Hyperglycaemia
  - Hyperuricaemia
  - Hyperlipidaemia
  - Hypertension
  - lifestyle factors
  - co-infections

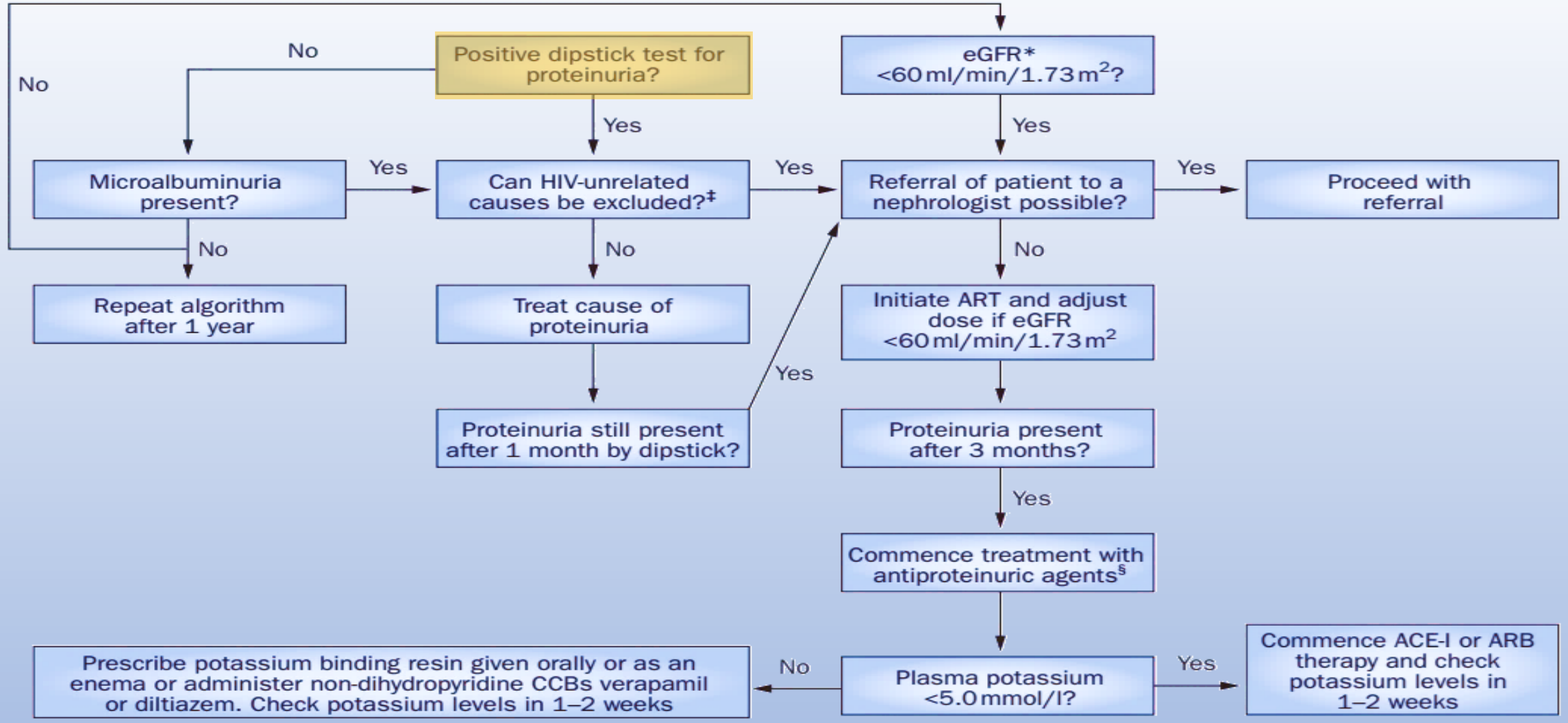


Figure 1 | Algorithm for the screening of chronic kidney disease in all antiretroviral therapy-naïve patients upon diagnosis of HIV. *Calculate eGFR by measuring serum creatinine. ‡Alternative causes for proteinuria include fever, infection (urinary tract infection, sexually transmitted infection and tuberculosis), pregnancy, uncontrolled diabetes, uncontrolled hypertension, cardiac failure. §Antiproteinuric agents can only be used with caution in normotensive individuals with gradual uptitration of dose depending on tolerance and severity of proteinuria. Abbreviations: ACE-I, angiotensin-converting-enzyme inhibitor: ARB, angiotensin 2 receptor blocker; ART, antiretroviral therapy; CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate.

- Expert guidelines recommend screening and early identification of CKD in PLWH
  - The diagnosis of CKD should prompt immediate initiation of ART in PWH who are not currently treated, regardless of CD4 cell count
  - In patients with asymptomatic HIV, a diagnosis of ICGN should prompt consideration of immunosuppressive therapy as determined by the specific histologic diagnosis and the severity of the clinical presentation
- Unique considerations in the management of CKD in PWH are largely related to:
  - ➢the need for lifetime suppressive ART
  - ➢potential for nephrotoxicity, drug–drug interactions, and polypharmacy

Treatment of CKD in HIV-positive patients

- HIV-related proteinuric CKD should be treated with an angiotensin-converting-enzyme (ACE) inhibitor or an angiotensin-receptor blocker (ARB)
  - Patients with persistent proteinuria despite treatment with an ACE inhibitor or ARB may benefit from the addition of a sodium–glucose cotransporter 2 (SGLT2) inhibitor

- Dose adjustment of renally excreted medications should be performed and nephrotoxic agents avoided

- Such an approach is important in order to coordinate CKD treatment, prepare for dialysis and list the patient for kidney transplantation

- APOL1 inhibitors such as INAXAPLIN offer the potential of a ‘precision medicine’ approach for *APOL1*-associated kidney diseases

Table 2 | Antiretroviral agents: special considerations for the diagnosis and management of people with HIV and chronic kidney disease (CKD)

Antiretroviral drug class		Inhibition of tubular creatinine secretion	Recommended dose adjustment in CKD[a]	Relevant drug–drug interactions[b]
Nucleos(t)ide reverse transcriptase inhibitors	Emtricibine	None reported	CrCL <50 ml/min: TDF, Emtricitabine, Lamivudine	No relevant DDI
	Lamivudine			
	TDF			
	TAF		CrCL <15 ml/min: TAF (approved in HD), Zidovudine (rare use)	
	Abacavir		No dose adjustment: Abacavir	
	Zidovudine			
Non-nucleoside reverse transcriptase inhibitors	Efavirenz	Modest effect[c]: Rilpivirine	Not required: Doravirine, Efavirenz, Etravirine, Rilpivirine	Moderate DDI with calcineurin inhibitors: Efavirenz, Etravirine, Nevirapine; Mild DDI with calcium channel blockers, statins
	Nevirapine			
	Doravirine			
	Delavirdine			
	Rilpivirine			
	Etravirine			
			Extra dose after HD: Nevirapine	Same as above
Protease inhibitors	Atazanavir/cobicistat	None reported	Not required	Significant DDI with eplerenone; Boosted PIs only
	Atazanavir/ritonavir			Significant DDI with lovastatin, simvastatin, atorvastatin
	Lopinavir/ritonavir			Moderate DDI with calcineurin inhibitors
	Darunavir/ritonavir			Mild DDI with beta-blockers, calcium channel blockers, other statins
	Darunavir/cobicistat			

Table 2 | Antiretroviral agents: special considerations for the diagnosis and management of people with HIV and chronic kidney disease (CKD)

Antiretroviral drug class	Inhibition of tubular creatinine secretion	Recommended dose adjustment in CKD[a]	Relevant drug–drug interactions[b]
Integrase inhibitors	Prominent effect Dolutegravir Elvitegravir/cobicistat	Not required	Severe DDI with eplerenone, lovastatin, simvastatin, atorvastatin Elvitegravir/cobicistat only
	Modest effect Bictegravir Raltegravir Cabotegravir/rilpivirine		Moderate DDI with calcineurin inhibitors Elvitegravir/cobicistat only
Other antiretroviral classes Maraviroc	None reported	CrCL < 30ml/min Maraviroc No dose adjustment	No relevant DDI
Mavaviroc with CYP3A inhibitor			
Enfuvirtide		Enfuvirtide	
Ibalizumab		Ibalizumab	
Fostemsavir			
Lenacapavir			
Pharmacoenhancers	Prominent effect Cobicistat *In vitro* effect Ritonavir	Not required	Severe DDI with eplerenone, lovastatin, simvastatin, atorvastatin Moderate DDI with calcineurin inhibitors

HD, hemodialysis; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

[a]Dose adjustment or discontinuation is recommended below the calculated creatinine clearance (CrCl) listed in the table. Readers are encouraged to review the package insert for detailed dosing recommendations.

[b]Drug–drug interactions (DDI) of particular relevance to patients with chronic kidney disease, including antihypertensive therapy, lipid-lowering therapy, and immunosuppressive therapy. This is not a comprehensive listing of all potential interactions.

[c]Agents with a modest effect on tubular secretion of creatinine result in an average increase in serum creatinine of 0.1 mg/dl, whereas agents with a prominent effect on tubular secretion of creatinine result in larger increases of 0.2 mg/dl or greater. An effect of ritonavir on tubular secretion has been observed *in vitro* but has not been reported to impact serum creatinine or the performance of creatinine-based glomerular filtration rate (GFR) estimates. Updated information is available online at clinicalinfo.hiv.gov/en/guidelines.

- add-on corticosteroids for HIVAN:
  - significant increase in eGFR **without** a significant reduction in proteinuria at last follow up
  - increased adverse events including risk of infections and all-cause mortality in the group treated with ART and adjuvant corticosteroids
  - reduced interstitial inflammation seen on repeat biopsy

- Renal transplantation in PLWH
  - Transplant and HIV outcomes in recipients who received HIV-positive donor kidneys were excellent
  - The recurrence of HIVAN was **not** considered to be a clinical problem in a multicentre trial of 150 kidney transplant recipients living with HIV in the USA

Table 2. Glomerular Disease in Patients With HIV

Disease	Classic Features	Treatment
HIVAN*	Rapid progression of AKI, high-level proteinuria, detectable viral load	HAART ± ACE inhibitors ± steroids
HIV-related immune complex disease*	Variable presentation including AKI, proteinuria, and/or hematuria	HAART
Thrombotic microangiopathy*	AKI, proteinuria, hematuria with microangiopathic hemolytic anemia and thrombocytopenia	HAART, possibly plasmapheresis
HCV-related MPGN/cryoglobulinemia	Variable: proteinuria and/or hematuria (nephritic, ⅓; nephrotic, ⅓; mixed picture, ⅓)	Treat HCV, if possible, immunosuppression if cryoglobulinemia
Postinfectious glomerulonephritis	AKI and hematuria, variable proteinuria, frequently nephrotic	Treat infection and supportive management, possible steroids in severe cases
Classic FSGS	Variable rates of AKI, proteinuria often nephrotic, hypertension, most common cause of NS in African Americans	ACE inhibitors (alone in mild cases), possibly steroids and/or other immunosuppression (usual treatment)
Diabetic nephropathy	Proteinuria (microalbuminuria to nephrotic); proteinuria and GFR decrease proportional to severity	Diabetes control, ACE inhibitors
Amyloidosis	Primary: older patients, monoclonal gammopathy on SPEP or UPEP (AKI may be due to myeloma casts), Secondary: injection drug users, usually nephrotic with gradual progression of renal failure	Treat myeloma/plasma cell dyscrasia, if present; no specific treatment otherwise
Membranous glomerulopathy	NS with or without slowly progressive renal failure, Primary: idiopathic, Secondary: associated with HBV or cancer	Treat HBV or malignancy, if present, ACE inhibitors, immunosuppression in severe idiopathic disease
Minimal change disease: primary or secondary	NS, AKI due to AIN if NSAID is the cause	Stop NSAIDs, steroids if idiopathic disease
IgA nephropathy	Variable: hematuria with or without renal failure and/or proteinuria; proteinuria can be nephrotic	ACE inhibitors, fish oil, and/or immunosuppression may benefit

Thanks for attention