NORTHWEST AIDS EDUCATION AND TRAINING CENTER

# HIV and the Kidney

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NW AETC ECHO
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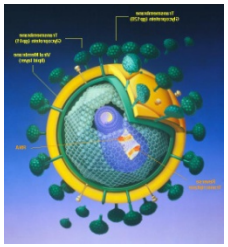
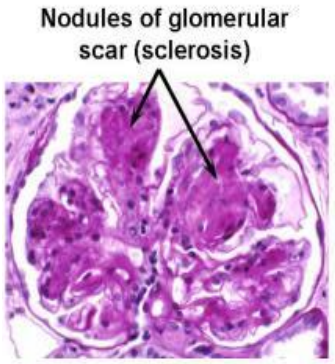
# Etiology of renal disease in HIV

- 1985- The virus



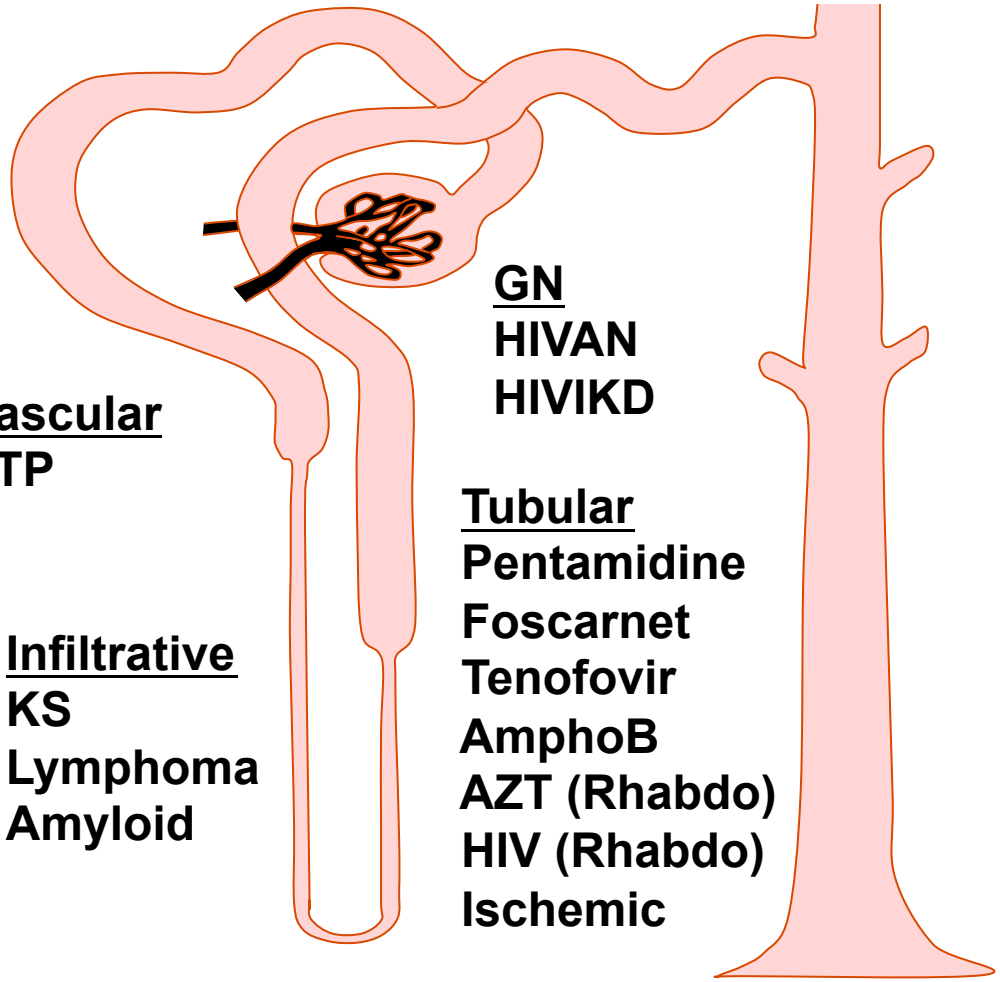
- 1995- The antivirals


- 2005- The usual
  (diabetes and HTN)



# Renal Disease in the HIV positive patient

**Pre-renal**
Diarrhea
Sepsis



**Vascular**
TTP

**Infiltrative**
KS
Lymphoma
Amyloid

**GN**
HIVAN
HIVIKD

**Tubular**
Pentamidine
Foscarnet
Tenofovir
AmphoB
AZT (Rhabdo)
HIV (Rhabdo)
Ischemic

**Interstitium**
TMP-SMX
Rifampin
MAI
Plasmocytic IN
DILS

**Post-Renal**
Crystalline
Indinavir
Tumors
Fungus balls
Mycobacteria
Retro. Fibrosis

# Renal disease in HIV
## Up to 10% have impaired GFR

**Risks**

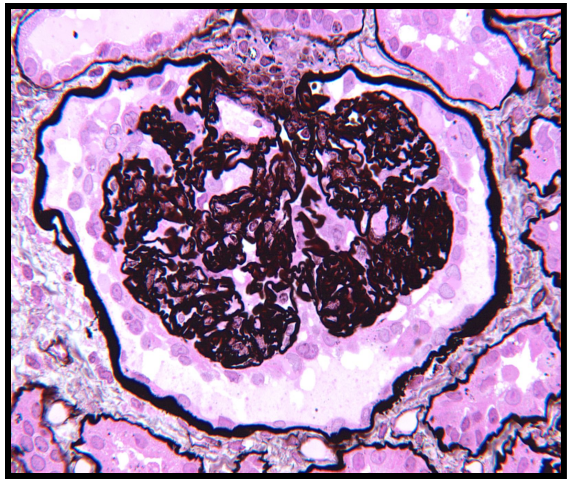
- HepC
- HTN
- Diabetes
- Black race
- Low CD4 count/high viral load
- HAART (TDF, Indinivir, atazanivir?)
- Age
- Low muscle mass
- Pre-existing CKD

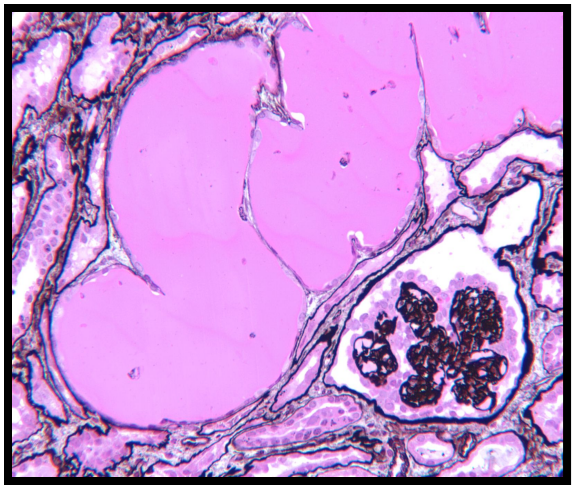
**Consequences**

- Vascular disease
- Increased Mortality

# HIV -associated Nephropathy
# HIVAN

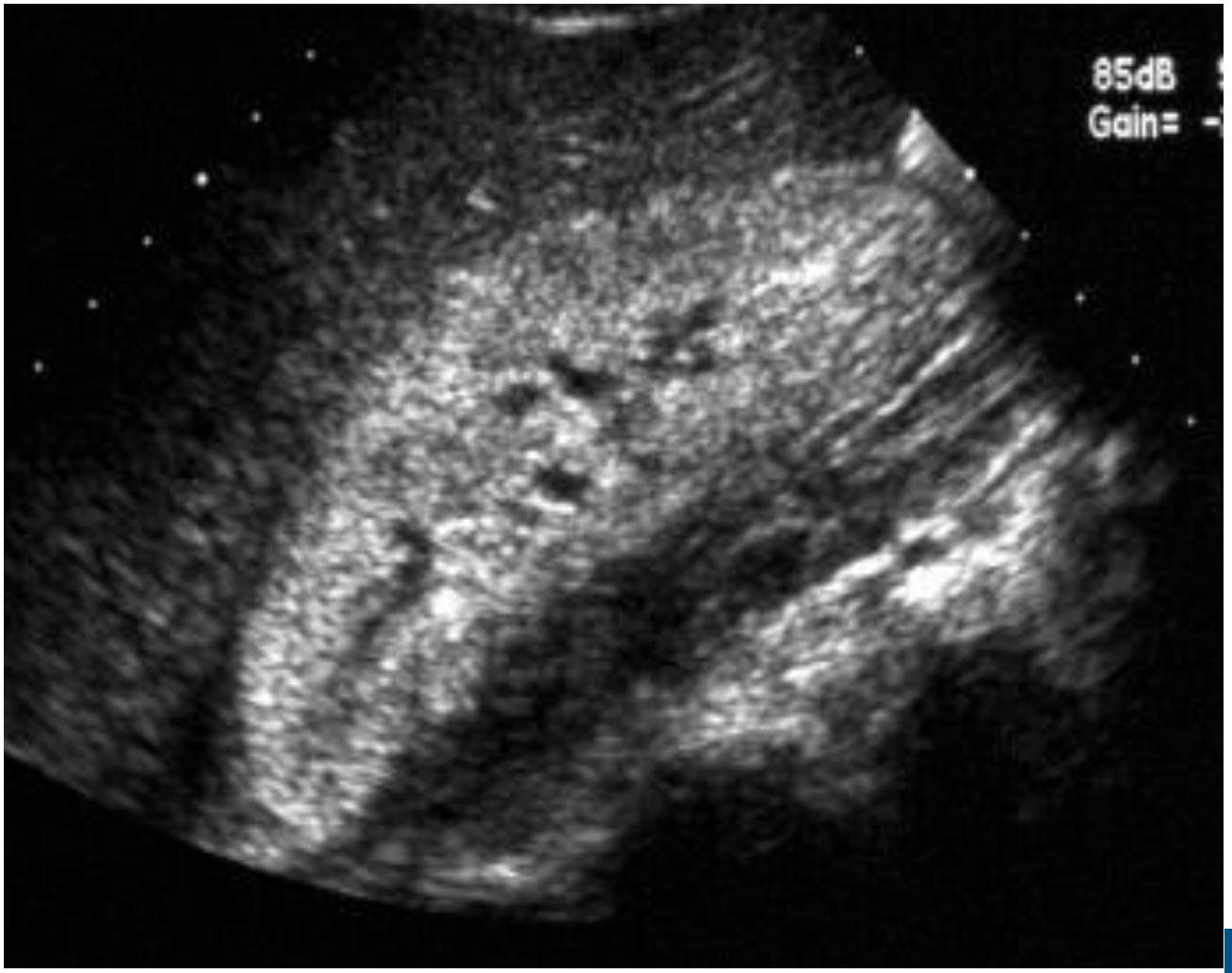
- Initially described in 1984  (New York, Miami)
- To date: 90% cases reported in blacks
- HIV infects glomerular and tubular cells
- Collapsing FSGS and cystic tubules





Courtesy of Charles Alpers, MD UWMC

# HIV Nephropathy



# HIV associated Nephropathy

| ERA | Pre-HAART | Post HAART |
|---|---|---|
| **Incidence/1000pt years** | 26 | 7 |
| **Presentation** | **Nephrotic syndrome:**<br>Edema<br>>3.5 gms proteinuria<br>Hypoalbuminemia<br>Lipiduria<br>Large echogenic kidneys | **Subnephrotic proteinuria**<br>Slow rise in creatinine<br>Normal renal ultrasound |
| **Time to ESRD** | 3-4 months | Years, ?never |

# HIVAN: Significance

- HIVAN is the most common finding at renal biopsy among HIV- infected patients
- HIVAN occurs almost exclusively in Black patients and is the 4th most common cause of ESRD among African American men age 20-64
- HIVAN is an indication to start HAART *regardless of viral load*

# HIVAN: Treatment

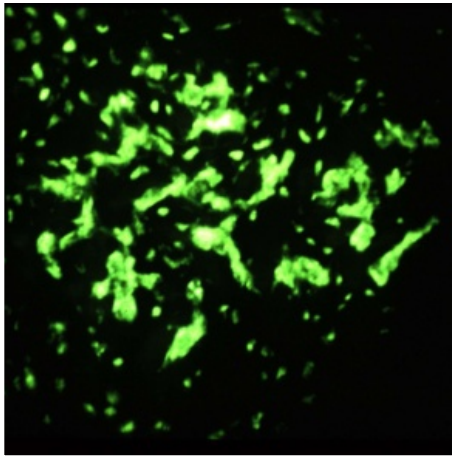
- FIRST BIOPSY!!
- Diagnosis of HIVAN is an indication for ART: Dramatic reduction in incidence of HIVAN and some reversibility of CKD with HAART
- ACE inhibitors
- “Nephrotic hygiene” – watch for hypercoaguable events, encapsulated organisms, hyperlipidemia
- Treat HTN to < 130/80
- Optimize co-existent conditions- e.g. diabetes
- Discourage smoking, cocaine use

# “HIVIKD”
# HIV immune kidney disease

- IgA Nephropathy
- Postinfectious glomerulonephritis
- “Lupus-like” glomerulonephritis
- MPGN (Hep C with cryoglobulins)
- Membranous GN (HepB)
- Immunotactoid GN

# IgA Nephropathy in HIV

- IgA levels commonly elevated in HIV
- Autopsy studies among Caucasian Europeans with HIV show 8% have mesangial IgA deposits
- IgA-p24 HIV containing immune complexes eluted from glomeruli of HIV patients
- Idiotypic IgA antibodies also described:  IgA-IgG-gp120



Mesangial deposits of IgA

Courtesy of Gerald Appel, MD

# HIV immune kidney disease
## presentation/diagnosis

- Nephritic syndrome
- Hematuria
- Proteinuria
- Acute or chronic kidney disease
- HTN
- Fluid overload
- Suggested labs: ANA, RF, cryoglobulins, C3, C4, hepatitis serologies

# HIVIKD: Management

- Biopsy first (60% of pts thought to have HIVAN actually have an HIVIKD)
- Efficacy of HAART not clear
- Consider immunosuppressives depending on pt safety

Examples:

MPGN with cryoglobulins:  rituximab, treat HepC

IgA nephropathy: steroids, cyclophosphamide

# HAART Nephrotoxicity

- Tenofovir: Fanconi Syndrome, AKI, CKD
- Indinivir: Stones, interstitial nephritis
- Atazanivir: Stones

# HAART
## Is tenofovir nephrotoxic?

- ✓Subclinical tubular defects
- ✓Fanconi Sydrome: glycosuria, phosphaturia, aminoaciduria, RTA
- ✓ATN (reversible)

**CKD:**

- Ø Randomized control trials
- Ø Industry sponsored
- ✓ Observational

# Rates of Discontinuation Due to Renal Impairment in early TDF Studies

| Study | TDF Pts (N) | Percent (%) Discontinuation TDF Control | | Follow-up (weeks) | Reference |
|---|---|---|---|---|---|
| **Boosted PI-Based** | | | | | |
| Abbott 418 | 185 | **1** | **NA** | 96 | IAS 2005 |
| BMS 045 | 243 | **0.4** | **NA** | 96 | Glasgow 2004 |
| **EFV-Based** | | | | | |
| GS-903 | 299 | **0** | **0** | 144 | JAMA 2004 |
| GS-934 | 257 | **0** | **0** | 48 | IAS 2005 |
| **Cohort Studies** | | | | | |
| RECOVER | 1193 | **0.4** | **NA** | 36 | IAC 2004 |
| Chelsea-Westminster | 1058 | **0.9** | **NA** | 49 | JAIDS 2004 |
| CHORUS | 1625 | **1.2** | **NA** | >24 | CROI 2005 |

Overall Discontinuation Due to TDF Renal Events (0- 1%)

Courtesy of Gilead Pharmaceuticals

# Department of Veteran Affairs TDF study

## Subjects

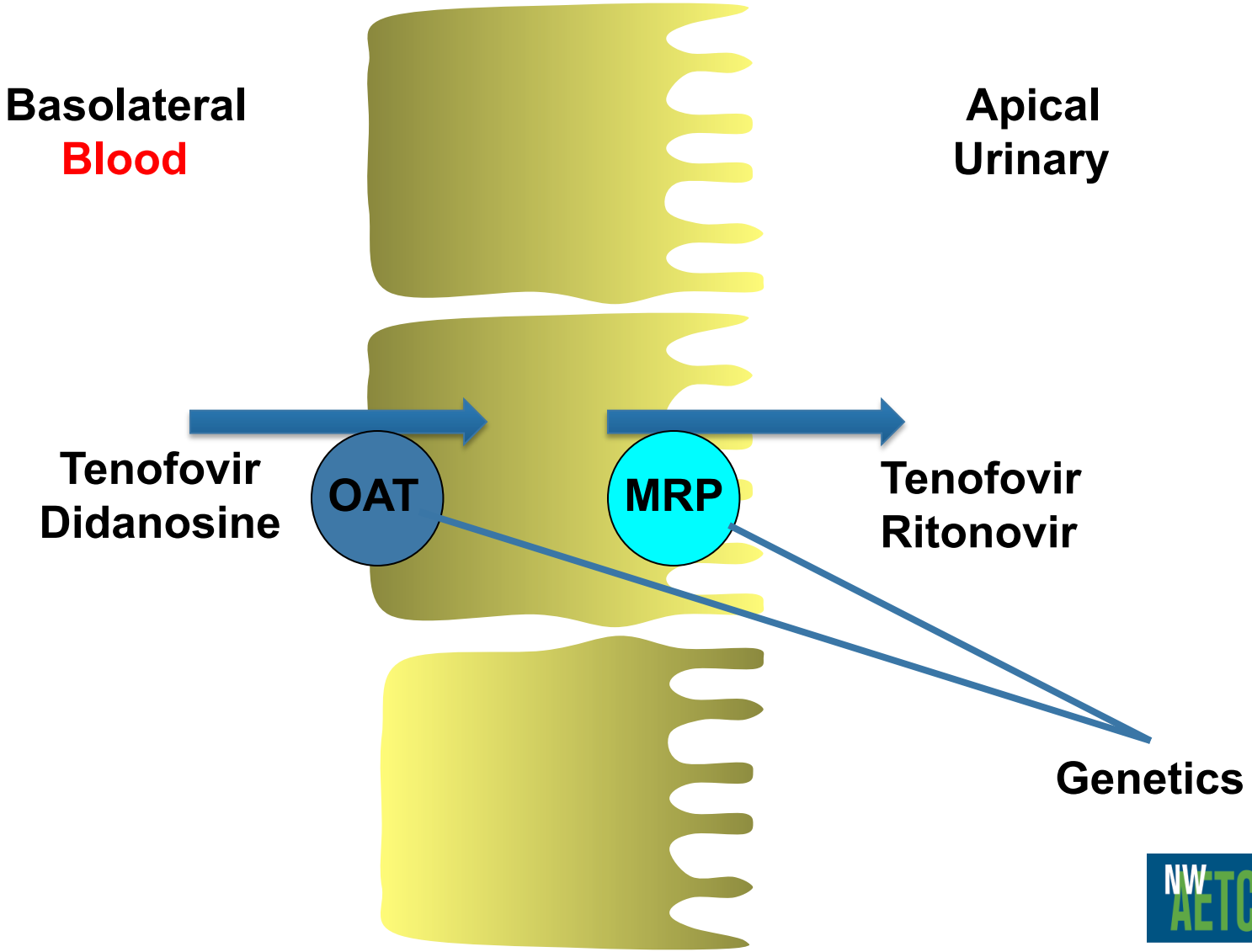
- 10,842 HAART naïve veterans 1997-2007
- Exclude: advanced CKD
- 4303 exposed to TDF for mean of 1.3 years (max 6.3 years)

## Results

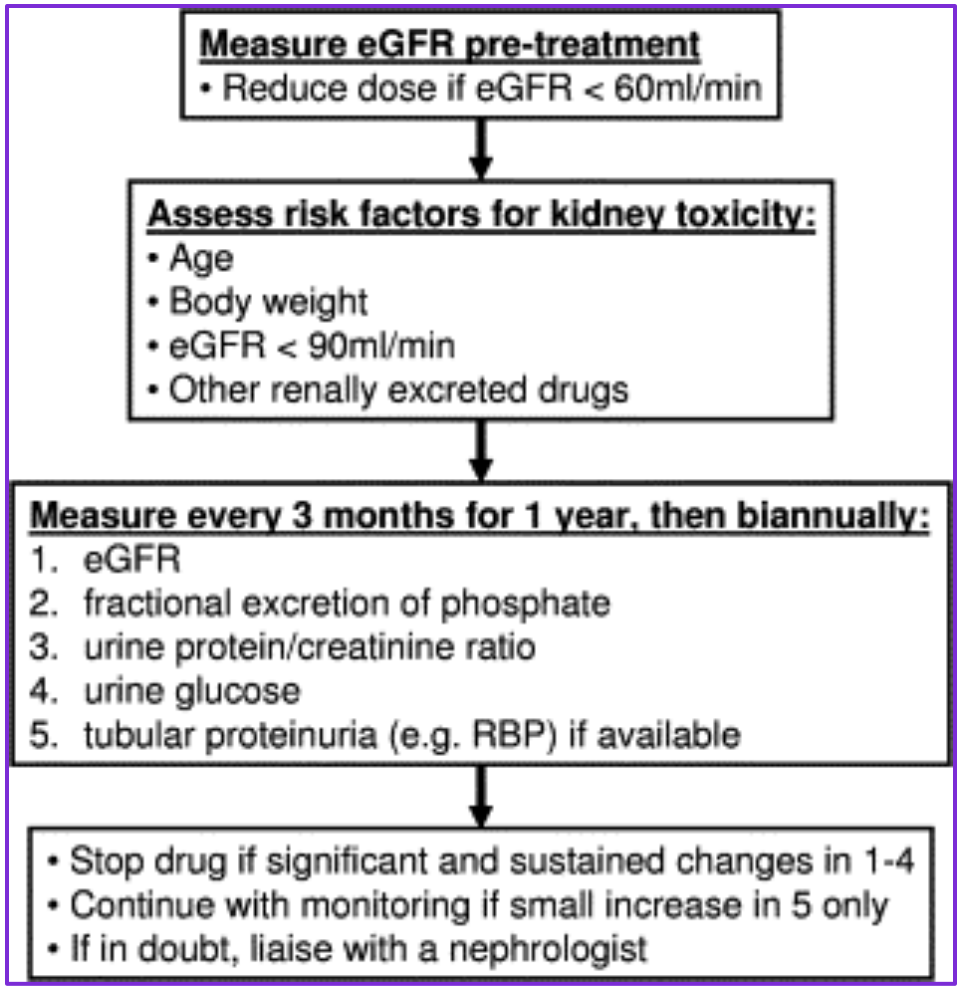
- 30% increased risk of proteinuria per year of exposure
- 11% increase risk of rapid decline in renal function
- 10% increased risk of creatinine doubling
- 33% increased risk of GFR < 60.
- **NO increased risk of GFR < 30**

Scherzer, AIDS, 2012

# Vulnerability to TDF nephrotoxicity



# Recommended monitoring protocol for TDF nephrotoxicity




Hall et al AJKD 2011

# HAART in ESRD

- HAART medications can be used safely in dialysis patients, and are probably underutilized
- PIs do not require dose adjustments
- NNRTIs do not require dose adjustments
- NRTIs require 3-7 fold reduction in dose EXCEPT abacavir
- Tenofovir is given only once weekly after hemodialysis