CORE CURRICULUM IN NEPHROLOGY

Viral Nephropathies: Core Curriculum 2008

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INTRODUCTION

Establishing a direct causative relationship between a virus and a specific kidney disease often is problematic. Documenting a pathogenetic role for a specific virus typically involves demonstration of viral antigens and host antibodies in blood and/or kidney tissue. Simply documenting a virus or viral particles in the kidney does not prove causation because viral particles may be present without clinical disease. Viruses are most specifically identified with glomerular diseases, but they also have been associated with the development of tubulointerstitial disease, vasculitis, and other renal manifestations. Some virus infections cause kidney diseases in individuals with previously normal immune systems or immune systems impaired as a result of the virus infection (ie, human immunodeficiency virus [HIV]), whereas others cause disease primarily in previously immunocompromised hosts, ie, as the result of transplant immunosuppression. Kidney disease can also occur indirectly as the result of systemic consequences of a virus infection, such as with hepatorenal syndrome, multiorgan failure caused by an overwhelming viral infection; rhabdomyolysis; or treatment of a virus infection.

MECHANISMS OF VIRUS-INDUCED KIDNEY INJURY

I. Glomerulonephritis (GN)
  A. Cytopathic effect of virus
    1. Direct
    2. Mediated through host inflammatory response and/or viral proteins
      a) Necrosis, apoptosis
      b) Cytokines, chemokines, adhesion molecules
      c) Altered matrix synthesis and degradation
  B. In situ immune complex formation
    1. Host antibody binding to viral antigens that are bound to glomerular structures
  C. Circulating immune complexes
    1. Viral antigens and host antiviral antibody
    2. Autoantibody directed against host antigens modified by viral injury
II. Tubulointerstitial nephritis
  A. Direct cytopathic effect
  B. Mediated through host inflammatory response and/or viral proteins

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HEPATITIS B VIRUS (HBV)

I. Virology
  A. Hepatotropic double-stranded DNA virus
    1. Envelope polypeptide contains hepatitis B surface antigen (HBsAg)
    2. Inner core contains hepatitis B core antigen (HBcAg), e antigen (HBeAg), viral DNA, DNA polymerase, other proteins
    3. Antibody response occurs with anti-HBsAg, anti-HBcAg, and anti-HBeAg antibodies

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II. Epidemiological characteristics
  A. Humans and nonhuman primates are only known hosts
    1. Endemic in parts of Asia, Africa
      a) Vertical transmission common
    2. Less common in United States, Europe
      a) Injection drug users
      b) Sexual transmission
      c) Vertical transmission
      d) Blood transfusion

III. Renal manifestations
  A. All are much less common than infection; suggests that important host immune system interaction with viral infection determines renal consequences
  B. Membranous nephropathy
    1. Membranous nephropathy most commonly reported in Far East, predominance in male children
      a) Nephrotic or non-nephrotic proteinuria, microscopic hematuria, hypertension in about 25%, chronic kidney disease (CKD) unusual in children
    2. Occurs in patients seropositive for HBsAg and antibody to HBcAg (HBcAb); most also seropositive for HBeAg; other serological patterns also seen, including rarely HBsAg negative with HBsAg in glomerulus
    3. HBsAg, HBeAg, HBcAg variably detected in glomerular basement membranes
      a) Circulating immune complexes with HBsAg or HBeAg detected with variable frequency
      b) Hypocomplementemia detected with variable frequency of up to about 65%
      c) Most cases believed to be caused by trapping of circulating HBV antigens in the glomerular basement membrane with in situ immune complex formation with antibody to HBV antigen or host antigen(s) altered by HBV
        (1) HBV antigens are not demonstrable in many cases; HBeAg most commonly detected HBV antigen in the glomerular basement membrane
          (a) HBeAg is smaller than other HBV antigens; more likely to deposit in subepithelial location with membranous pattern of nephropathy
          (b) HBsAg also common; HBcAg smaller minority of cases
    4. Pathological characteristics
      a) Subepithelial immune deposits; often also with subendothelial and/or mesangial deposits
      b) Immunofluorescence positive for immunoglobulin G (IgG), C3, IgM; IgA less common
      c) Electron microscopy (EM) shows viral-like particles in various locations; identity not clearly defined
      d) Mesangial proliferative GN or IgA nephropathy may be superimposed
      e) Combinations of membranous with IgA nephropathy or membranoproliferative GN not uncommon
      f) Immune deposits with pathological changes of early membranous nephropathy or membranoproliferative GN can be seen in patients with acute and chronic HBV infection without overt clinical manifestations of kidney involvement
    5. Resolution of glomerular disease may occur with loss of HBsAg or seroconversion to HBeAb-positive status
    6. Treatment
      a) Spontaneous remission rare in adults; common in children
      b) Corticosteroids and cytotoxic drugs
        (1) Clinical response variable; persistent remission of nephritic syndrome is uncommon
        (2) May increase viral replication and reduce clearance of HBsAg-positive status
      c) Interferon alfa
        (1) Most experience in children
        (2) Variable responses; appears to increase complete and partial remission of nephritic syn-

drome and seroconversion of HBV antigenemia
d) Antiviral agents
(1) Lamivudine
(a) Anecdotal reports of improvement in proteinuria and renal outcomes
(b) Emergence of drug-resistant strains limits use
(2) Adefovir dipivoxil
(a) Unproven role; nephrotoxic

C. Other glomerular lesions
1. Mesangioproliferative GN
a) Prevalence not well defined
b) IgA-dominant GN can be seen with chronic HBV infection and other liver diseases
2. Membranoproliferative GN
a) Reported prevalence of chronic HBV infection varies
b) Typically presents with nephrotic syndrome, microscopic hematuria, hypertension, CKD
c) Usually with HBsAg and HBcAb; variable hypocomplementemia and circulating immune complexes
d) Pathology of type I membranoproliferative GN with subendothelial deposits; subendothelial and mesangial deposits may also be seen

D. Classic polyarteritis nodosa (PAN)
1. Presents initially as serum-sickness–like illness with systemic vasculitis developing over subsequent weeks; most cases described in adults in United States and Europe
2. Seropositive for HBsAg or antibody to HBsAg (HBsAb); HBcAb
a) Usually occurs weeks to months after mild acute hepatitis, but may rarely precede acute hepatitis or occur years later in association with chronic active hepatitis
3. Microscopic hematuria, mild proteinuria, hypertension, acute renal failure
a) Renal manifestations caused by ischemia and infarction
b) Systemic manifestations include myalgia, palpable purpura, arthralgias, arthritis, livedo reticularis, polyneuropathy; virtually all organs may be involved
4. Renal pseudoaneurysms on angiography (renal, mesenteric, hepatic, and so on)
a) Rupture can lead to retroperitoneal and intra-abdominal hemorrhage
5. Pathophysiological mechanism believed to be related to circulating immune complexes of HBV-associated antigens (mostly HBsAg) with complement activating host immunoglobulin that deposits in blood vessel walls, synovium
a) Hypocomplementemia
b) Immune complexes in cryoprecipitates contain HBsAg, IgG anti-HBsAb, IgM
c) Spontaneous clearance of HBsAg associated with resolution of clinical manifestations
d) Antineutrophil cytoplasmic antibodies (ANCAs), mostly antimyeloperoxidase (anti-MPO), detected in about 10% of patients

IV. Renal pathological states
A. Classic PAN
1. Necrotizing vasculitis of small- to medium-sized arteries with focal transmural inflammation often at vessel branch points
a) Leukocyte infiltration, fibrinoid necrosis, fibrin deposition, aneurysm formation
2. Smaller vessels, including glomerular capillaries, are not involved in classic PAN
a) Microscopic polyangiitis (“microscopic PAN”) with focal segmental necrotizing GN very rare
3. Gross pathological characteristics
a) Nodular lesions along arteries, mostly at branch points of arcuate and interlobar arteries, because of pseudoaneurysms and inflammation
b) Infarction associated with arterial thrombus
4. Light microscopy
a) Transmural segmental fibrinoid necrosis

5. Treatment
   a) Plasma exchange, corticosteroids, vidarabine, interferon

B. Serum-sickness–like syndrome
   1. Fever, rash, arthralgias, arthritis
   2. Rarely associated with transient proteinuria, microscopic hematuria, red blood cell casts, pyuria

C. Cryoglobulinemia
   1. Link with HBV unproven

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HEPATITIS C VIRUS (HCV)

I. Virology
   A. Small single-stranded RNA virus
      1. 6 distinct genotypes
   B. No HCV cell culture system available until recently
   C. Studies rely on chimpanzee model
   D. Immunologic basis for viral clearance and immunity not yet well defined
   E. Primarily hepatotropic

II. Epidemiological characteristics
   A. Blood-borne pathogen, endemic in most parts of the world
      1. Global prevalence estimated to be 170 million individuals infected worldwide
         a) Geographic variations in incidence and prevalence
      2. Prevalence between 10% and 20% in dialysis units in the United States, with regional variation
   B. Mechanisms of transmission
      1. Blood transfusion or transplantation from unscreened donors
      2. Shared needles
         a) Intravenous drug use
         b) Nosocomial through multidose vials in dialysis unit
         c) Accidental needle stick
      3. Perinatal transmission in about 6%
   C. Since the introduction of blood donor screening, transmission by blood transfusion is very rare (~1 in 1 million)
   D. Acute HCV infection is usually mild and frequently leads to chronic infection
   E. Major complications:
      1. Chronic liver disease (cirrhosis and hepatocellular carcinoma)
      2. Increased association with diabetes
      3. Increased mortality in patients with CKD stage 5

III. Renal manifestations
   A. Associated with proteinuria/albuminuria in population-based studies
   B. Membranoproliferative GN
      1. Frequently associated with cryoglobulinemia
   C. Mixed cryoglobulinemia
      1. 90% of afflicted patients are positive for HCV
      2. Proteinuria
      3. Microscopic hematuria
      4. Impaired kidney function
   D. Other forms of glomerular injury are uncommon, but include:
      1. IgA nephropathy
      2. Membranous nephropathy
      3. Focal segmental glomerulosclerosis (FSGS)
      4. Postinfectious GN
      5. Immunotactoid glomerulopathy
      6. Fibrillary GN

E. Post–kidney transplantation
1. Increased risk of antibody-mediated rejection
2. Recurrent membranoproliferative GN
3. Increased risk of proteinuria, new-onset diabetes, graft dysfunction, and mortality

IV. Renal pathological characteristics
A. Membranoproliferative GN
1. Lobulation of tufts
2. Splitting of capillary basement membrane
3. Capillary endothelial swelling
4. Mesangial hypercellularity
5. Inflammatory infiltrate in glomerular capillaries with mononuclear cells and polymorphonuclear leukocytes
B. Immune complex deposition in glomeruli
1. Usually subendothelial by using EM
2. Deposition of IgM, IgG, and C3

V. Diagnostic testing
A. Enzyme immunoassay for anti-HCV antibody (third generation)
B. Nucleic acid testing (qualitative or quantitative HCV RNA)
C. Complement levels useful
D. Circulating cryoglobulins
E. Kidney biopsy if active sediment or significant proteinuria
F. Before kidney transplantation
1. Liver injury panel
2. Liver biopsy for patients with detectable viremia

VI. Treatment
A. Interferon alfa or pegylated interferon
1. Half-life increases with diminished kidney function
a) Dose reduction usually required with CKD
2. May trigger rejection when used in the kidney transplant setting
B. Ribavirin
1. Usually as adjunctive therapy for interferon
2. Half-life increases with diminished kidney function
a) Dose reduction or avoidance required with CKD
C. Corticosteroids, cytotoxic therapy, and plasmapheresis for patients with systemic vasculitis

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HUMAN IMMUNODEFICIENCY VIRUS (HIV)

I. Virology
A. RNA retrovirus; transcribed to proviral DNA by viral reverse transcriptase, then to viral RNA by host RNA polymerase
B. Frequently mutates, allowing virus to resist host immunity and antiviral agents

II. Renal manifestations
A. HIV-associated nephropathy (HIVAN)
1. Clinical manifestations
a) Typically presents with variable proteinuria, including microalbuminuria; often nephrotic-range proteinuria with nephrotic syndrome
b) Hypertension relatively uncommon (~20% to 40%)
c) CKD common at presentation

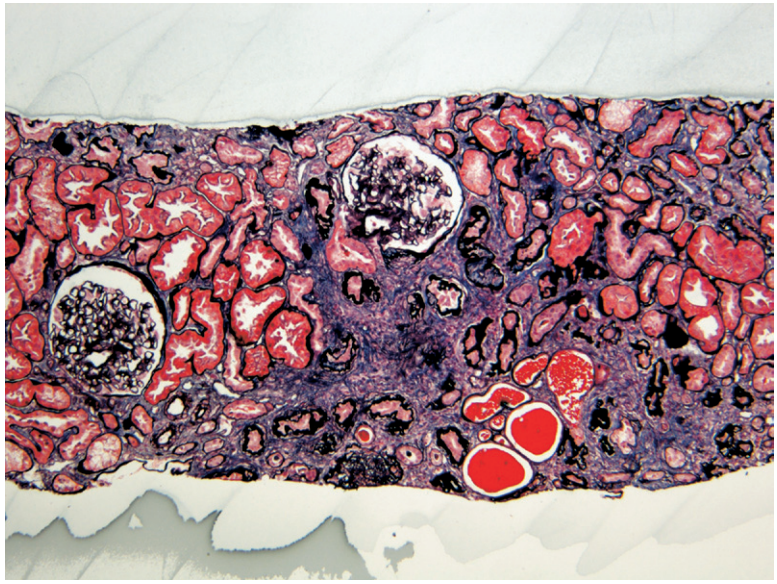

Figure 1. Human immunodeficiency virus–associated nephropathy with focal segmental glomerulosclerosis, areas of tubulointerstitial fibrosis with tubular atrophy, and dilated tubules with proteinaceous casts. (Original magnification ×10.) (Courtesy of Dr John Tomaszewski, Department of Pathology, University of Pennsylvania, Philadelphia, PA.)

(1) Rapid progression to end-stage renal disease (ESRD); often in less than 6 months
(2) Course appears to be slowed and survival prolonged with angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and highly-active antiretroviral therapy (HAART)

d) CD4 count usually low, but may present at any stage of HIV infection, often without acquired immunodeficiency syndrome (AIDS)
e) Renal ultrasound typically shows normal- to large-sized kidney with markedly increased echogenicity

2. Epidemiological characteristics
   a) Third leading cause of ESRD in US African American adults
   b) Rare in non–African Americans
   c) Occurs in all age groups, including children; not specifically associated with a particular route of HIV acquisition
3. Pathophysiological characteristics
   a) HIV infects podocytes and tubular epithelial cells
   b) Expression of specific HIV genes causes similar lesion in transgenic animal models, ie, *nef* and *vpr*, without systemic infection or immunodeficiency
   c) Infection induces podocyte cell-cycle dysregulation and proliferation, loss of podocyte morphological features and differentiation markers, expression of immature podocyte markers
   d) Mechanism of viral entry into renal cells uncertain
   e) Cytokine activation proposed, but unproven
4. Pathological characteristics (Figs 1 and 2)
   a) FSGS with global or segmental tuft collapse
      (1) EM: glomerular collapse, glomerular basement membrane wrinkling, sclerosis
         (a) Immune deposits minimal
         (b) Tubuloreticular inclusions ("interferon footprints") common in glomerular and vascular endothelial and other cells
         (c) Nuclear bodies in tubular and interstitial cells
   b) Podocyte hyperplasia and proliferation
   c) Tubular epithelium flattened, atrophic; formation of microcysts from

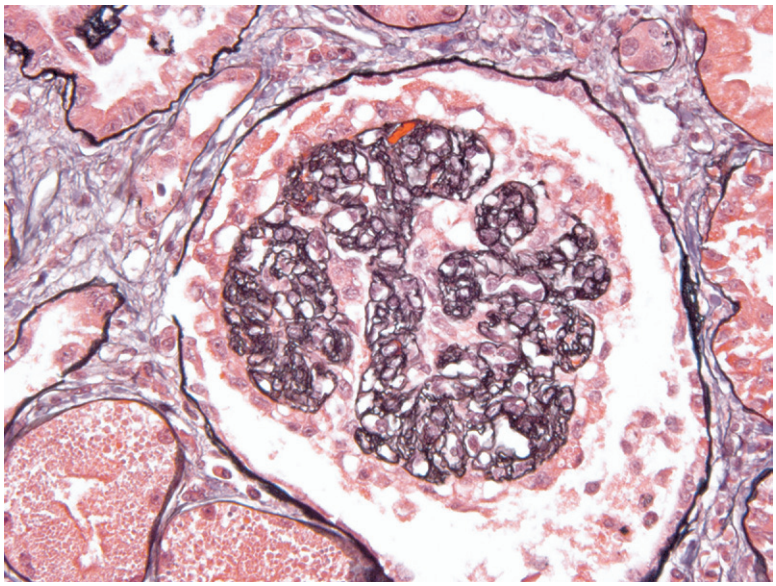

Figure 2. Human immunodeficiency virus–associated nephropathy with collapsing glomerulosclerosis. (Trichrome methenamine silver stain.) (Courtesy of Dr John Tomaszewski, Department of Pathology, University of Pennsylvania, Philadelphia, PA.)

dilated tubules with proteinaceous cast material
- d) Interstitial edema and mononuclear (lymphocytic) infiltrate

5. Treatment
   - a) Corticosteroids
     - (1) Benefit suggested in uncontrolled studies
     - (2) May increase risk of opportunistic infection, especially if not on HAART
   - b) ACE inhibitors and ARBs
   - c) HAART
     - (1) Benefit suggested by isolated reports of clinical and pathological improvement with HAART and retrospective cohort studies; no large-scale controlled trials
     - (2) Complicated by nephrotoxicity of some antiretroviral agents (Table 1)
     - (3) Increased survival of HAART-treated HIV-infected patients expected to increase number of patients with CKD and ESRD
   - d) Transplantation
     - (1) Generally performed by experimental protocol
     - (2) Requirements
       - (a) Life expectancy longer than 5 years
       - (b) No detectable HIV viremia

Table 1. Renal Toxicities of Antiretroviral Agents

Drug Class	Drug	Renal Toxicity
Nucleotide/nucleoside reverse-transcriptase inhibitor	Class effect	Lactic acidosis, proximal tubule dysfunction, Fanconi syndrome, AKI
	Tenofovir	Distal RTA
	Abacavir	AIN (rare)
	Didanosine, stavudine, lamivudine	Nephrogenic diabetes insipidus (rare)
Protease inhibitor	Indinavir	Crystalluria, nephrolithiasis, obstructive uropathy, AIN, hypertension, AIN, nephrogenic diabetes insipidus (rare)
	Nelfinavir, saquinavir	Nephrolithiasis (rare)
	Ritonavir	AKI (rare)

Abbreviations: AKI, acute kidney injury; RTA, renal tubular acidosis; AIN, acute interstitial nephritis.

(c) CD4 count greater than 200/μL
(d) No history of opportunistic infections or cancer
(3) Immunosuppression
(a) Increased risk of infection with depleting antibody therapies
(b) Calcineurin inhibitors, antimetabolite therapies, and tapering steroid dosages appear to be tolerated
(c) Antiretroviral therapies interact with calcineurin inhibitors
(4) Outcomes
(a) Short-term patient and graft outcomes are good
(b) HIV-infected kidney recipients have increased rates of acute rejection compared with uninfected counterparts
(c) Patients coinfected with HCV may do worse

B. Other renal disorders associated with HIV infection
1. Epidemiology
a) Occur in all racial/ethnic groups
b) Accounts for greater percentage of kidney disease in white and Hispanic populations compared with HIVAN
2. Clinical manifestations
a) Varies; proteinuria, hematuria, acute kidney injury (AKI), CKD
3. Pathological states
a) Membranoproliferative GN
b) IgA nephropathy
c) Others: minimal change, membranous, amyloidosis, lupus-like acute GN, postinfectious GN, interstitial nephritis, acute tubular necrosis

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PARVOVIRUS B19

I. Direct causation of kidney disease not definite
II. Virology
A. Single-stranded DNA virus
B. Humans are only known host
1. Highly trophic for erythroid progenitor cells
III. Epidemiological characteristics
A. Asymptomatic infection common in childhood and adulthood
1. Inhalation of aerosol droplets most common
2. Vertical transmission, blood products, bone marrow and solid-organ transplantation
IV. Renal manifestations
A. Acute GN
1. Nephritic features with hypocomplementemia
a) May follow prodrome with rash, fever, arthritis
b) Most patients with spontaneous recovery
(1) Some with persistent proteinuria, CKD
B. Nephrotic syndrome

1. Associated with aplastic crisis in sickle cell disease
2. Hematuria and other nephritic features also present
   a) Chronic sequelae with persistent proteinuria, CKD common
3. Renal transplant dysfunction, acute rejection
   a) Symptomatic infection may occur posttransplantation
      (1) Acute and chronic red blood cell aplasia most common
      (2) May present with collapsing FSGS, thrombotic microangiopathy
   b) Causal link with acute rejection and chronic allograft dysfunction not definite
      (1) May be transient AKI associated with acute infection
4. Less common associations: thrombotic microangiopathy, hemolytic uremic syndrome, Henoch-Schönlein purpura, microscopic polyarteritis, Wegener granulomatosus

V. Renal pathological characteristics
   A. Endocapillary or mesangial proliferation
      1. Subendothelial deposits; C3 and IgG in mesangium and capillary walls
   B. FSGS
   C. Collapsing glomerulopathy
   D. Viral antigens and genome detectable in glomeruli (podocytes, parietal epithelial cells)
      1. Tubular reticular inclusions
      2. Intact virions have not been detected in kidney tissues

VI. Diagnostic testing
   A. Serological testing not helpful
   B. Polymerase chain reaction (PCR) testing for viral DNA in blood, tissues

VII. Treatment
   A. No antiviral therapy
   B. Intravenous immune globulin (IVIG) used for aplastic disease

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POLYOMAVIRUS

I. Kidney disease most commonly occurs in renal allograft recipients

II. Three known human polyomaviruses
   A. BK virus (BKV)
   B. JC virus (JCV)
   C. Simian Virus 40 (SV40)

III. Virological characteristics
   A. Nonenveloped double-stranded DNA virus
   B. Humans are natural hosts
   C. Virus may establish latent or lytic infection
   D. JCV resides in uroepithelium and rarely causes nephropathy

IV. Epidemiological characteristics
   A. BKV is acquired during childhood
      1. Fecal-oral or respiratory route
      2. May be transmitted from donor tissue
   B. BKV is by far the most common polyomavirus that causes kidney disease; JCV and SV40 infection seldom associated
   C. 60% to 80% of recipients are BKV seropositive before transplantation
   D. BKV-specific antibodies do not prevent posttransplantation infection
   E. BKV replicates during states of immunosuppression
   F. Reactivation leads to cell-to-cell spread
   G. BKV infection progresses through viruria to viremia and then nephropathy
      1. BK viremia occurs in up to 13% of kidney recipients
      2. BK nephropathy occurs in up to 8% of kidney recipients

V. Renal manifestations
   A. Tubulointerstitial nephritis

1. BKV nephropathy is unusual in the absence of viremia
2. Appears to be related to net state of immunosuppression
3. Patients typically are asymptomatic
4. Present with worsening kidney function
5. Results in worsening chronic graft dysfunction, especially if untreated or treatment is initiated late in the course
6. Rare in nonkidney organ recipients

VI. Renal pathological characteristics (Fig 3)
- A. Intranuclear viral "inclusion bodies" in epithelial cells of cortex and/or medulla are pathognomonic
- B. Three histological patterns:
  1. Pattern A: viral cytopathic changes with minimal inflammation or tubular atrophy (early disease)
  2. Pattern B: viral cytopathic changes with varying inflammation, tubular atrophy, or interstitial fibrosis
  3. Pattern C: less prominent cytopathic changes, more extensive tubular atrophy and interstitial fibrosis (late disease)
- C. May coexist with acute rejection and be difficult to differentiate histologically, helpful adjunctive testing includes:
  1. Negative C4d staining
  2. Absence of arteritis
  3. Positive serum and urine virological study results
- D. Concomitant histological changes include:
  1. Glomerular crescents
  2. Calcineurin-inhibitor toxicity
  3. Plasma cell infiltration

VII. Diagnostic testing
- A. Transplant kidney biopsy is "gold standard"
- B. Viral DNA testing by PCR of blood and urine
- C. Urine cytology; presence of decoy cells
- D. Urine EM for viral particles
- E. Urinary studies lack specificity
- F. Routine screening for viremia may lead to early detection and prevention of clinically significant nephropathy

VIII. Treatment
- A. Reduction in immunosuppression is primary approach
  1. Often ineffective after advanced histological injury or allograft dysfunction has developed
  2. Requires monitoring for clearance of viremia by BKV PCR
- B. Because immunosuppression reduction may precipitate rejection, an individualized approach is needed

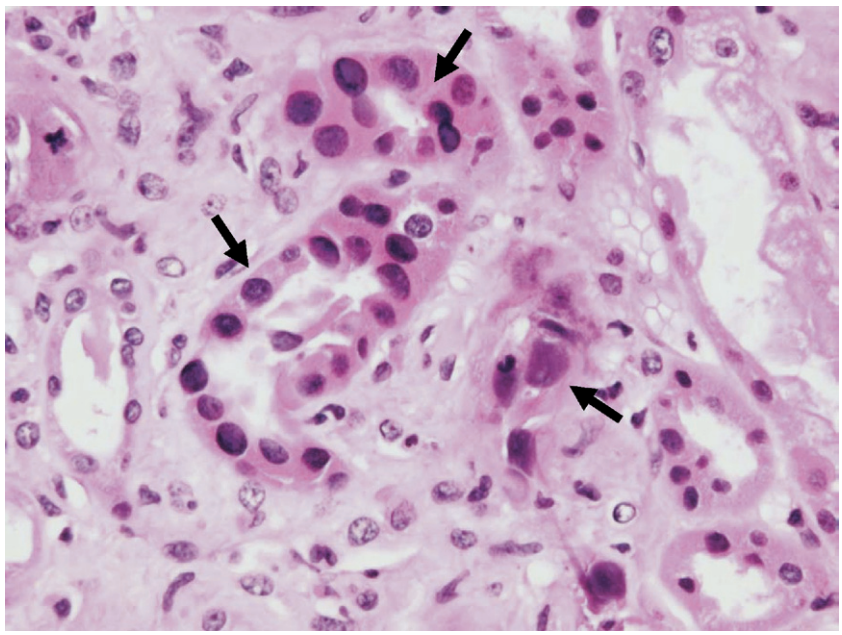

Figure 3. Histological features of viral cytopathy in a kidney recipient with BK virus nephropathy, including tubules containing epithelial cells with nuclear enlargement and granular intranuclear inclusions (arrows). Surrounding tubules show some degenerative changes and sloughing. (Courtesy of Dr John Tomaszewski, Department of Pathology, University of Pennsylvania, Philadelphia, PA.)

C. Several adjuvant antiviral therapies have been used; however, overall efficacy and benefit not clearly established
   1. Cidofovir
   2. Quinolones
   3. IVIG

D. Retransplantation of patients with BK nephropathy in prior transplant
   1. Safe in the absence of active viremia
   2. BKV monitoring required after transplantation

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Several other viruses can be associated with a variety of renal manifestations (Table 2).

Table 2. Renal Manifestations of Other Viruses

Virus	Primary Clinical Manifestations	Histopathologic Features
Cytomegalovirus	Systemic infection in immunocompromised host with fever, malaise, arthralgias, bone marrow suppression, hepatitis, colitis, and so on; renal allograft dysfunction with AKI, volume contraction, thrombotic microangiopathy, transplant glomerulopathy, glomerulonephritis	Viral intranuclear and cytoplasmic inclusions in tubular, endothelial, urothelial cells; AIN uncommon; acute GN with glomerular viral inclusions rare
EBV	Major cause of PTLD; rare cause of AIN, acute GN, AKI with primary EBV infection	PTLD with interstitial infiltrate with atypical lymphoid cells, plasma cells with nuclear atypia in some cases, tubulitis and venulitis may mimic acute rejection; $CD20^+$ B cells
Hantavirus	Hemorrhagic fever with renal syndrome or nephropathia epidemica: febrile multisystem acute illness; hematuria, proteinuria, oliguric AKI	AIN with hemorrhage, inflammatory infiltrate; ATN; mesangial hypercellularity, expansion
Hepatitis A	Kidney disease mostly with fulminant hepatitis and hepatorenal syndrome or AKI with ATN; proteinuria, microscopic hematuria	AIN with lymphocytic infiltrate; mesangial proliferative GN with subendothelial and mesangial deposits; may be IgA, IgG, or IgG dominant or codominant with C3 and/or C1q
Adenovirus	AKI, hemorrhagic cystitis; typically in immunocompromised host (renal transplant, HIV infected)	AIN with hemorrhage, ATN, intranuclear inclusions, “smudge cells” in tubular epithelial cells
Mumps	AKI, proteinuria, microscopic hematuria; prenrenal azotemia caused by mumps myocarditis; acute hemolysis and hemoglobinuric AKI	AIN with mononuclear infiltrate, mesangial proliferative GN with IgA, IgM, C3
Measles	Oliguric AKI	AIN, proliferative GN
Dengue fever	AKI with ATN caused by shock and multiorgan failure, rhabdomyolysis, hemolysis with hemoglobinuria, proteinuria, thrombotic microangiopathy	ATN, mesangial hyperplasia

Abbreviations: AKI, acute kidney injury; AIN, acute interstitial nephritis; PTLD, posttransplantation lymphoproliferative disorder; ATN, acute tubular necrosis; GN, glomerulonephritis; HIV, human immunodeficiency virus; EBV, Epstein-Barr virus; IgA, immunoglobulin A.

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Update

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Erratum

In "Viral Nephropathies: Core Curriculum 2008" (Berns & Bloom, *American Journal of Kidney Diseases*, 52:370-381, 2008), the legend for Fig 3 contained an error. The sentence "(Courtesy of Dr John Tomaszewski, Department of Pathology, University of Pennsylvania, Philadelphia, PA.)" should have appeared as "Reproduced with permission from Weiss M, Liapis H, Tomaszewski JE, and Arena LJ, *Heptinstall's Pathology of the Kidney* (ed 6), Jennette JC, Olson JL, Schwartz MM, and Silva FG (eds), copyright Lippincott Williams & Wilkins, 2006." The full legend in its corrected form follows:

> Figure 3. Histological features of viral cytopathy in a kidney recipient with BK virus nephropathy, including tubules containing epithelial cells with nuclear enlargement and granular intranuclear inclusions (arrows). Surrounding tubules show some degenerative changes and sloughing. Reproduced with permission from Weiss M, Liapis H, Tomaszewski JE, and Arena LJ, *Heptinstall's Pathology of the Kidney* (ed 6), Jennette JC, Olson JL, Schwartz MM, and Silva FG (eds), copyright Lippincott Williams & Wilkins, 2006.