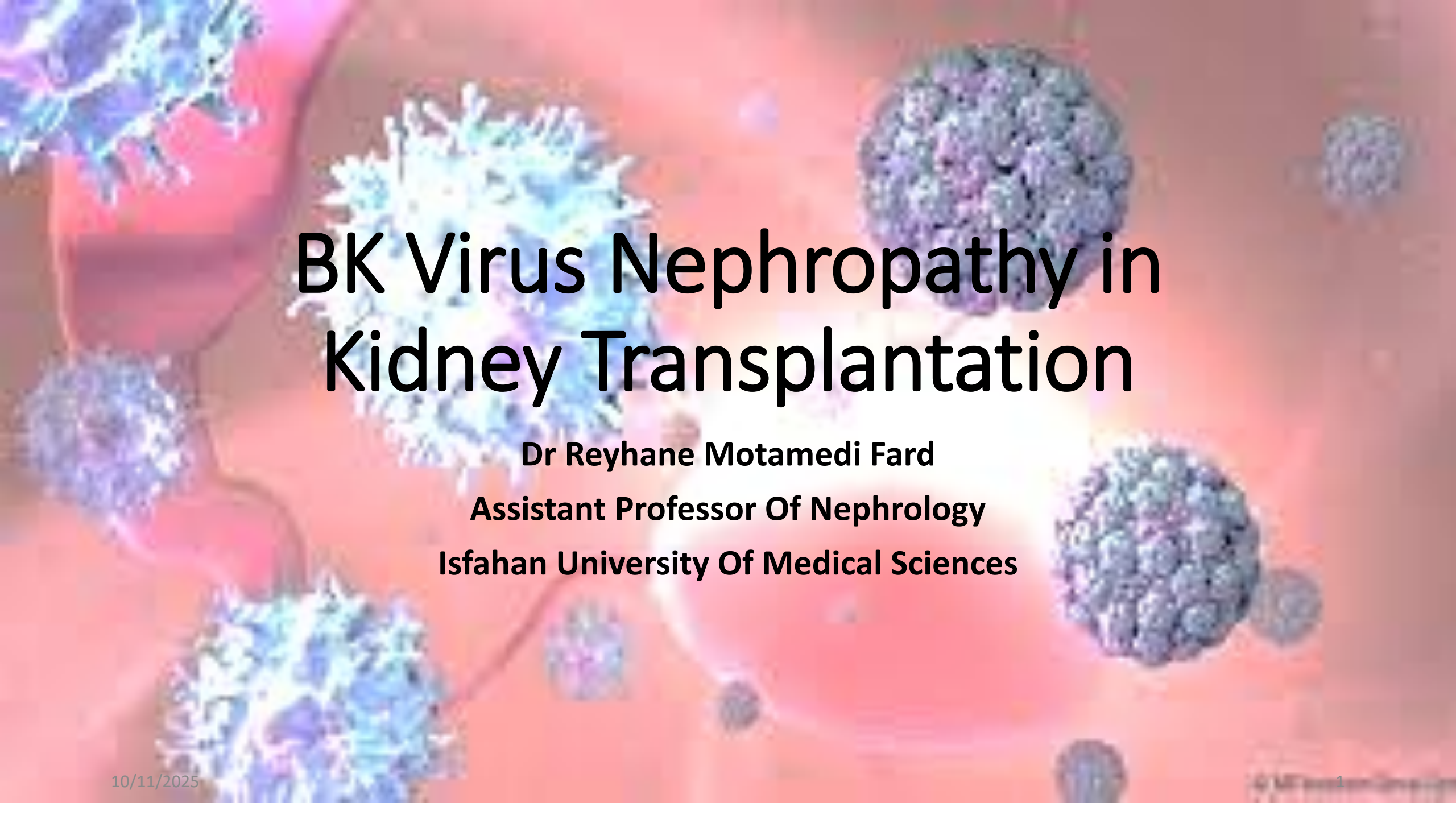


BK Virus Nephropathy in Kidney Transplantation

Dr Reyhane Motamedi Fard

Assistant Professor Of Nephrology

Isfahan University Of Medical Sciences

Introduction

- BK virus-associated nephropathy (BKVAN) is an important cause of graft loss in kidney transplant recipients.
- BKVN represents a severe infection, threatening function of the kidney graft, particularly during the first year after transplantation.
- BK polyomavirus nephropathy complicates kidney transplantation by directly and indirectly causing premature kidney allograft failure.

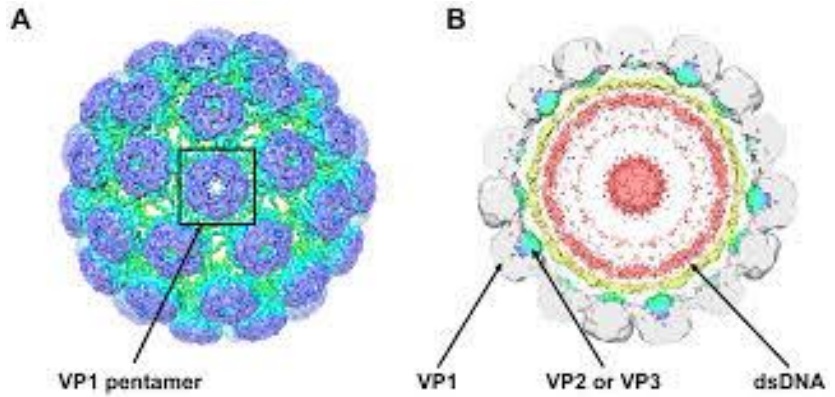
Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

History of the BK Virus

- BK virus was first discovered in a kidney transplant recipient who presented with a ureteral stricture in 1971
- In 1993 that the first definitive biopsy proven case of BKVAN was described

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Virology



- BK virus is a small, non-enveloped, icosahedral, closed circular, double-stranded DNA virus and member of the Polyomaviridae family
- The genome of the virus consists of three regions—the early coding region of the large T and small t antigens (large and small tumor antigen), the non-coding control region, and the late coding region.

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

EPIDEMIOLOGY AND PATHOGENESIS OF BKVN

- BKV is a polyomavirus, which traditionally causes nephropathy in renal allografts as a result of reactivation of latent BKV in renal tubular epithelium
- Based on the amino acid sequence of the large T-antigen, polyomaviruses are divided into 4 genera with >70 species

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

EPIDEMIOLOGY AND PATHOGENESIS OF BKVN

- The large T-antigen is important for BKV replication, recognition by the cellular immunity components and virus oncogenicity
- In the first months of life, maternal antibodies protect infants from BKV infection
- BKV infection starts to occur, as demonstrated by 10% to 30% seropositivity in infants and 65% to >90% between 5 and 10 years of age

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

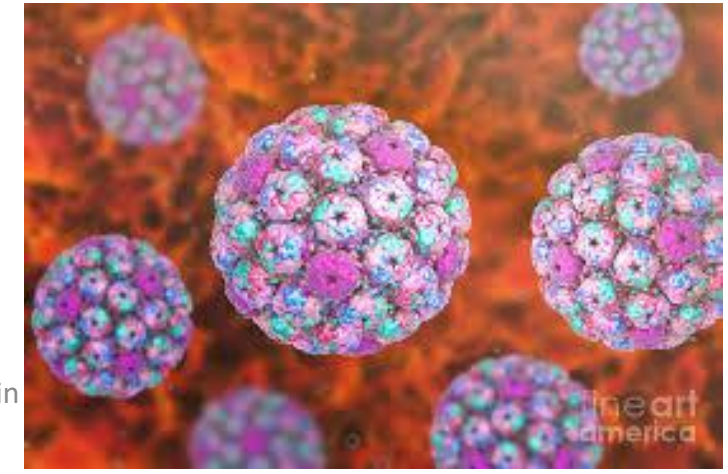
EPIDEMIOLOGY AND PATHOGENESIS OF BKVN

- Transmission is ongoing from person-to-person, foecal-oral transmission
- The primary routes for transmission of the virus are from mucosal contact including the oral, gastrointestinal, and respiratory tract.
- leukocyte-containing blood transfusion and transplacental transmission has been also reported

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

Epidemiology

- BK virus infection could be considered ubiquitous in the general population, with seroprevalence rates of over 90% by 4 years of age
- After a primary viremia, the BK virus establishes refuge in the kidney and uroepithelial cells resulting in lifelong latent/persistent infection



Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Epidemiology

- Since cellular immunity is most suppressed in the first post-transplant year as a result of induction therapy, viral replication can frequently ensue during this period.
- Clinically significant infection occurs in kidney transplant recipients via reactivation of latent infection or transmission of new infection from the donor kidney.

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Epidemiology

- The infection occurs in the following chronological stages
  - viruria, viremia, and allograft nephropathy
- Viruria and viremia are detected in approximately 30% and 12% of kidney transplant recipients
- After the onset of viruria, nearly 50% of kidney transplant recipients develop viremia during a period of 2–6 weeks

Epidemiology

- Urine BK viral loads >8 log10 c/mL predict the onset of viremia
- Plasma BK viral loads >4 log10 c/mL are associated with higher rates of biopsy-proven BKVAN
- Above 6 log10 c/mL are predictive of extensive BKVN

- Based on the most recent registry data, 1–10% of kidney transplant recipients develop BKVAN

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Viral replication risk factors

- Intensity of immunosuppression
- Recipient characteristics
- The donor–recipient interface
- Donor-related factors

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Transplant-related:

Immunosuppression

- Induction therapy (ATG)
- Type and degree of immunosuppression

Graft-related

- Prior treatment of acute rejection
- Prolonged cold/warm ischemia timing
- Delayed graft function
- Ureteric stent placement
- Renal injury (immune related,.. etc.)

Donor-related:

- Older donor age
- Donor BK virus seropositivity
- Degree of HLA matching
- ABO-Incompatibility
- Absence of HLA-C7
- Donor status (deceased versus living donor)

Recipient-related:

- Older recipient Age>50
- Gender (male recipient)
- Recipient race
- Obesity (BMI>30 kg/m^2)
- Previous graft loss due to BK nephropathy
- Diabetes mellitus
- BK seronegativity
- HLA mismatching, Absence of HLA-C7, certain HLA alleles
- High PRA titres
- Genetic factors
- Lymphocytes mean percentage (%)
- G-CSF use
- Dialysis Modality pre-transplantation
- CMV status

RISK FACTORS

- **Intensity of immunosuppression**
- **The most significant factor**
- The incidence of BK viremia is highest in the early post-transplant
- Tacrolimus may portend a higher risk of BK virus infection than cyclosporine
- mTOR inhibitors may be associated with lower risk by virtue of being less immunosuppressive than tacrolimus or cyclosporine

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

RISK FACTORS

- **Recipient characteristics**
  - Male sex and older age
  - Diabetes
  - Specific HLA-C alleles
  - Pediatric-specific risk factors are younger recipient age and obstructive uropathy as primary renal disease.

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

RISK FACTORS

- Specific HLA-C alleles

- Recipient HLA-B51 positivity and the presence of PKD have been shown to be protective factors against the development of BKVAN.
- Explain the fivefold reduction in the occurrence of BKVAN in these patients
- Absence of potentially protective HLA types or their combination (such as A2, A24, B7, B8, B13, B44, B51, Cw7, and DR15).

RISK FACTORS

- **Other recipient factors**

✓Pretransplant hemodialysis, compared with peritoneal dialysis or preemptive transplantation

✓Longer duration of dialysis

✓Duration of diabetes in simultaneous pancreas and kidney (SPK) transplantation

RISK FACTORS

- **Other recipient factors**

  - Stent placement for >3wk was associated with an increased risk of BKPyV-DNAemia whereas a stent for <3wk was no longer significant compared with no stent group

RISK FACTORS

- **The donor–recipient interface**

  - Donor positive and recipient negative for BK virus
  - ABO incompatibility
  - HLA mismatch
  - Delayed graft function
  - Rejection or ischemia of the transplanted kidney
  - Ureteral stent placement

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

RISK FACTORS

- **Donor factors**

  - Donor urinary BKPyV shedding
  - Very high donor antibody levels against BKPyV
  - BKPyV genotypes different from the recipient (mismatching)
  - the donor is BKPyV-seropositive or the donor antibody levels are high and the recipient is BKPyV-seronegative or the antibody levels are low

RISK FACTORS

Transplantation factors

- Use of tacrolimus compared with cyclosporine
- T cell–depleting agents
- Acute rejection episodes
- Higher corticosteroid exposure

RISK FACTORS

- **Transplantation factors**

➢ Alemtuzumab, thymoglobulin/ATG/ATGAM/rATG and the B cell–depleting agent rituximab has been associated with higher rates of BKPyV replication in some but not all studies.

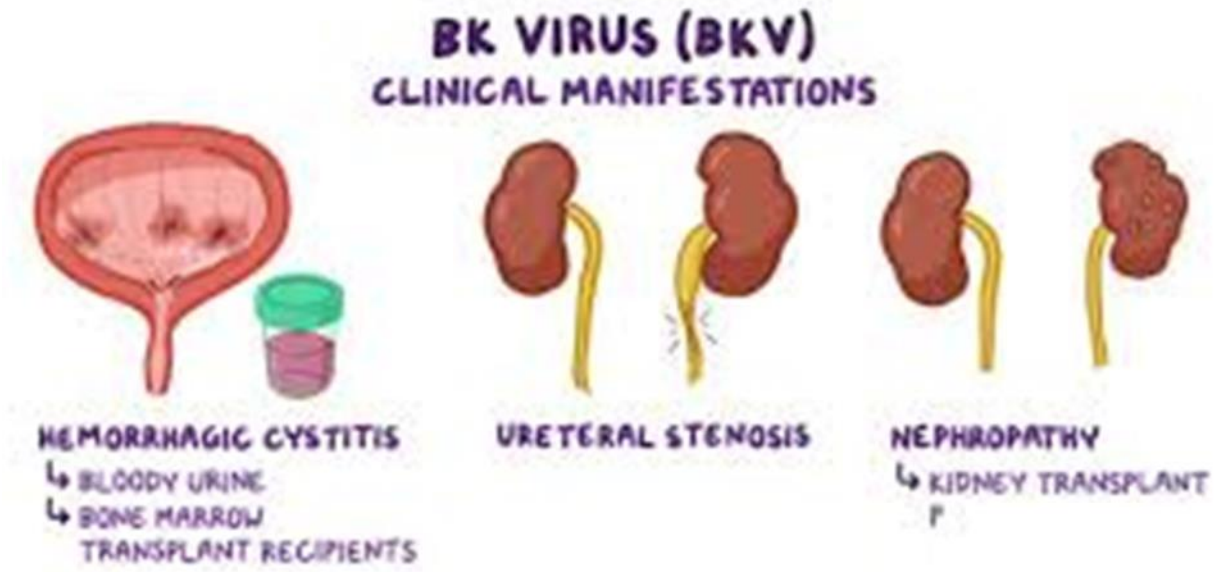
➢ It is likely that rejection is not a risk factor but is confounded by antirejection treatment and increased immunosuppression.

RISK FACTORS

- In a multivariate analysis of CMV replication events after alemtuzumab induction, a higher rate of biopsy-proven BKPyV-nephropathy was reported
- The potential interaction between CMV and BKPyV  reducing immunosuppression and the use of valganciclovir prophylaxis

Clinical Manifestations

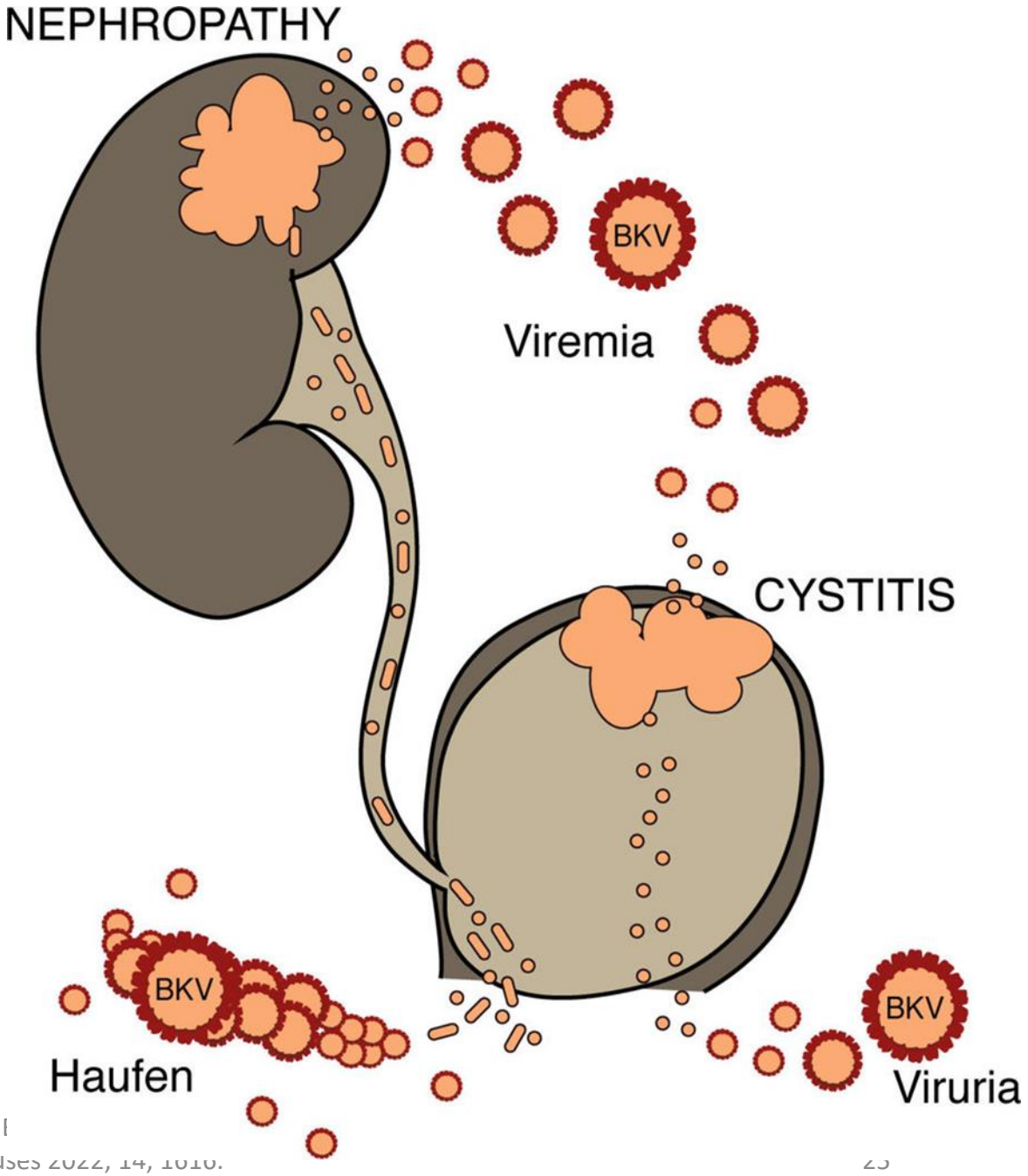
- Most clinically significant infections associated with the BK virus lack any systemic symptoms.
- viruria, viremia, and BKVAN



Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Clinical Manifestations

- Decline in renal function with or without urinary abnormalities.
- ureteral stenosis
- hemorrhagic cystitis particularly in patients after bone marrow transplantation



Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. I
Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

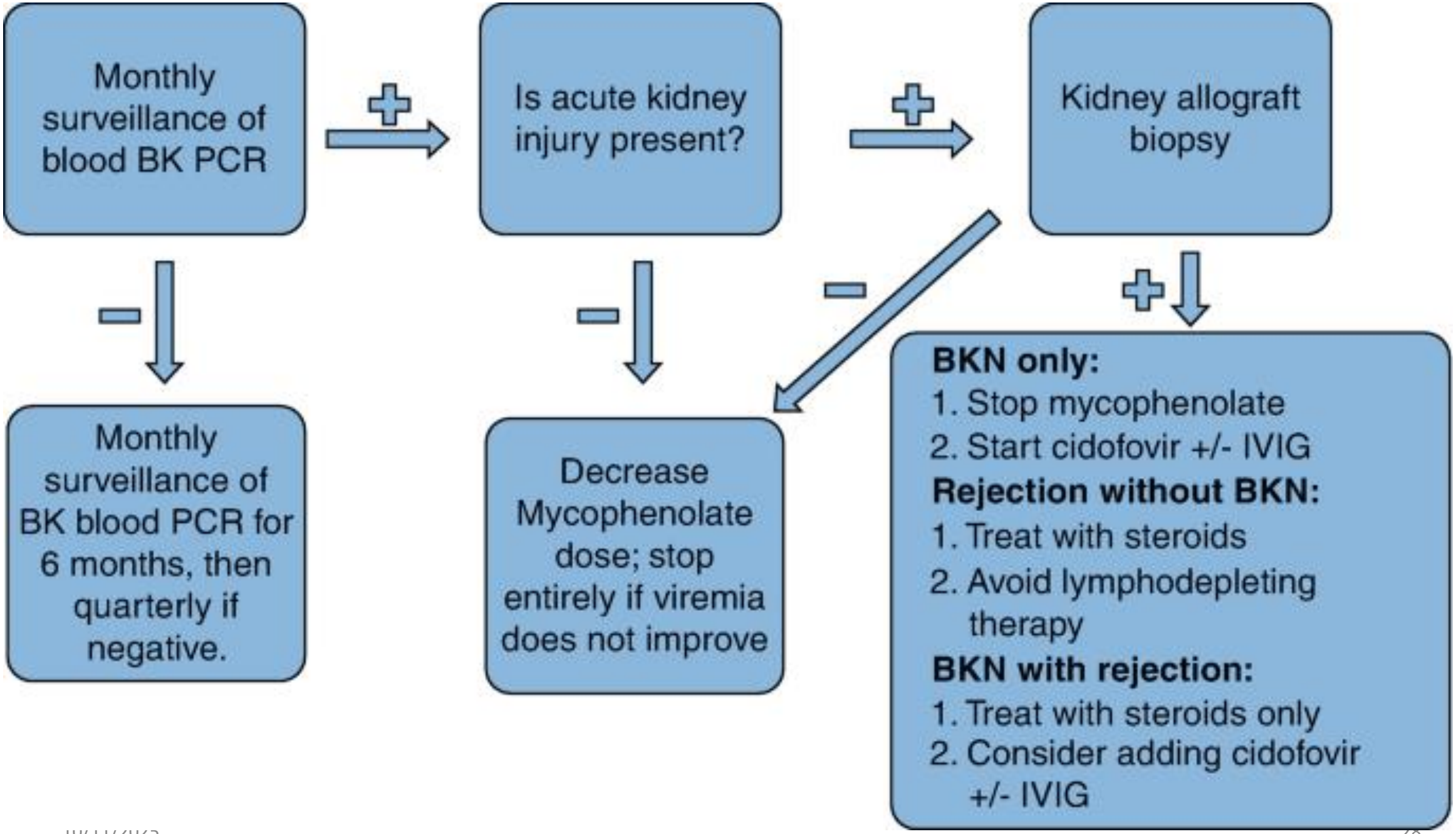
CLINICAL MANIFESTATIONS OF BKVN

Unusual manifestations	
Vasculopathy	Guillain-Barré syndrome
Retinitis	meningoencephalitis
Hepatitis	interstitial pneumonitis
SLE	

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

Screening

- ✓ 1 - 12 months post-transplantation : monthly
- ✓ 12 - 24 months post-transplantation : every 3 months
- ✓ >24 months post-transplantation : every 6 months
- ✓ Additionally:
  - post-immunosuppression intensification
  - in case of allograft dysfunction and/or biopsy


Monthly surveillance of blood BK PCR
+
Is acute kidney injury present?
+
Kidney allograft biopsy
−
Monthly surveillance of BK blood PCR for 6 months, then quarterly if negative.
−
Decrease Mycophenolate dose; stop entirely if viremia does not improve
−
+
BKN only:
1. Stop mycophenolate
2. Start cidofovir +/- IVIG
Rejection without BKN:
1. Treat with steroids
2. Avoid lymphodepleting therapy
BKN with rejection:
1. Treat with steroids only
2. Consider adding cidofovir +/- IVIG

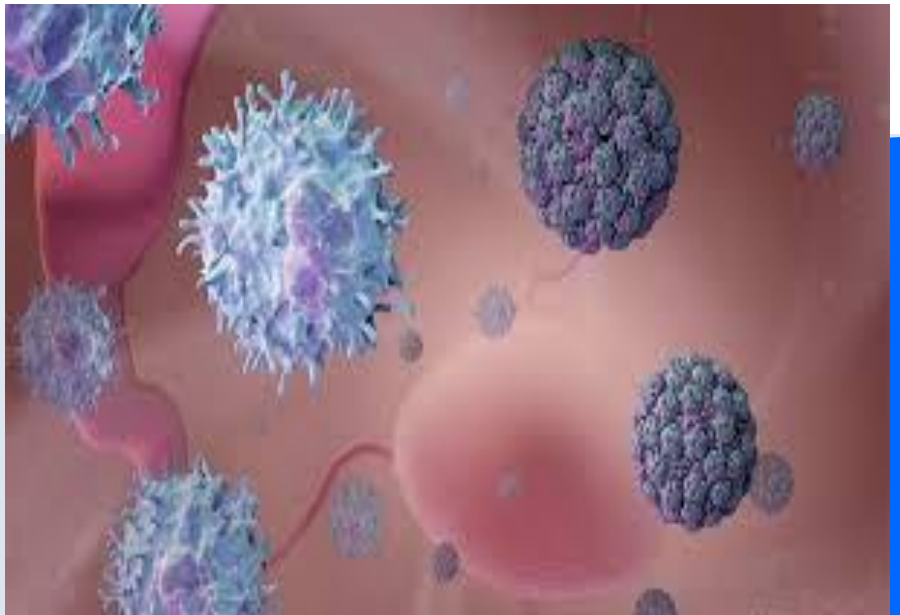
CURRENT GUIDELINES FOR GRAFT BIOPSY IN CASE OF SUSPECTED BKVN

- Biopsy should be performed before reduction of immunosuppressive therapy
- Biopsy procedure should include collection of 2 samples of the renal tissue to capture the medullary part of the parenchyma.
- 10–30% of biopsy samples may be falsely negative in case of focal distribution of changes and predominance of medullary involvement within BKVN

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

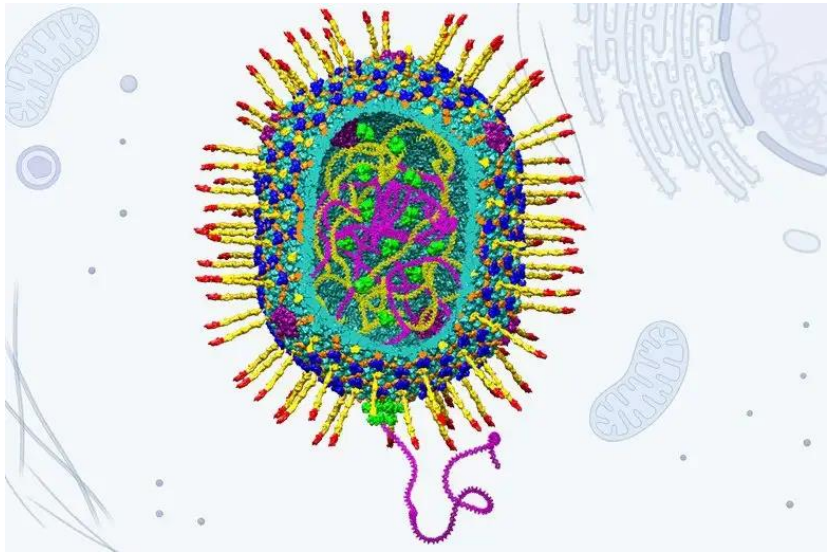
BK virus nephropathy

pegah hedayat.MD.ACP
assistant professor of Isfahan university of medical science
october2025

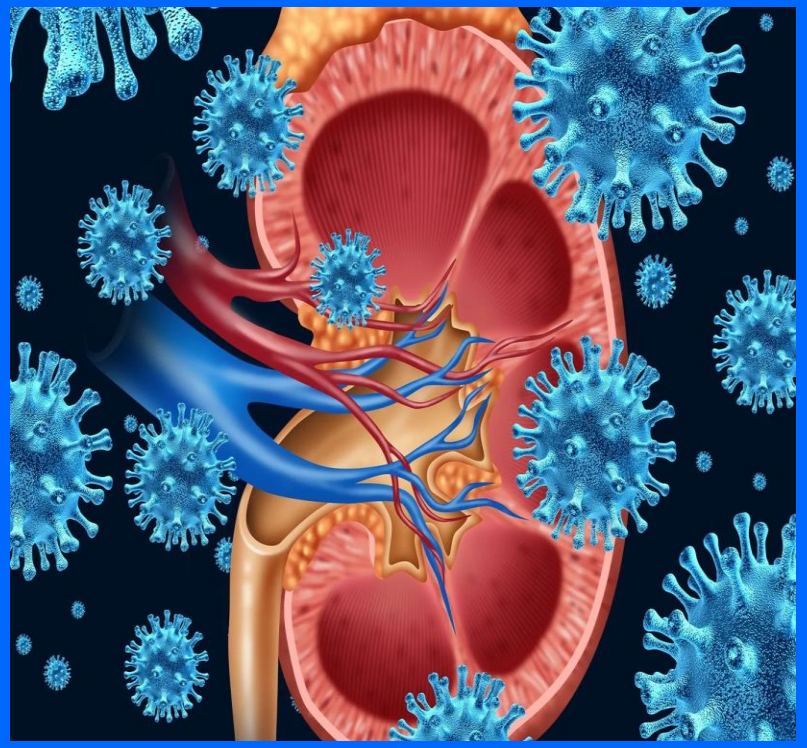


BK virus

BK virus infection is caused by a ubiquitous, opportunistic, nonenveloped double stranded DNA virus belonging to the Polyomaviridae family with a seroprevalence rate that can reach > 90% in adults



Primary infection



-virus is acquired by direct person to person contact, through contaminated surfaces, food and water Infection, which is most often subclinical,

-It is usually encountered in childhood, where after the virus remains latent in the urothelial and renal tubular epithelial cells lifelong and is kept in check predominantly by T cells.

-With immunosuppression (suppression especially of T cell immune surveillance) the virus, either the dormant one in the host or donor derived (in a portion of transplant cases), reactivates and causes viremia by crossing into the peritubular capillaries

Clinical feature

In the immunocompromised it is associated with:

-Fever

-Asymptomatic / symptomatic increase in serum creatinine levels

-Asymptomatic viruria

-BK virus associated nephropathy

-Hemorrhagic cystitis: gross hematuria

-Ureteric strictures

-Pneumonitis, retinitis, liver disease and meningoencephalitis in HIV patients and those with severe immunosuppression

diagnosis

The clinical diagnosis of BKVN utilizes measurements of BKV DNA in the **urine and/or plasma** using quantitative real-time polymerase chain reaction.

Approximately half of kidney transplant recipients with high-level viruria develop BKV viremia within 6 weeks, and of these patients, up to 50% are diagnosed with BKVN

Probable/Presumptive BK Virus Nephropathy

in 2013 and again in 2019, Hirsch and Randhawa for the American Society of Transplantation (AST) proposed a definition of possible PVN using urine:

Nevertheless, urine screening is noninvasive and has a high negative predictive value.

Therefore, the detection of **three decoy cells per high power field** or **urine BKV DNA levels greater than 1,000,000 copies/mL** continues to be used as a screening criterion to prompt further assessment for viremia.

Probable/Presumptive BK Virus Nephropathy

-Multiple studies have identified a plasma BKV level of **>10,000 copies/mL** as correlating with development of BKVN.

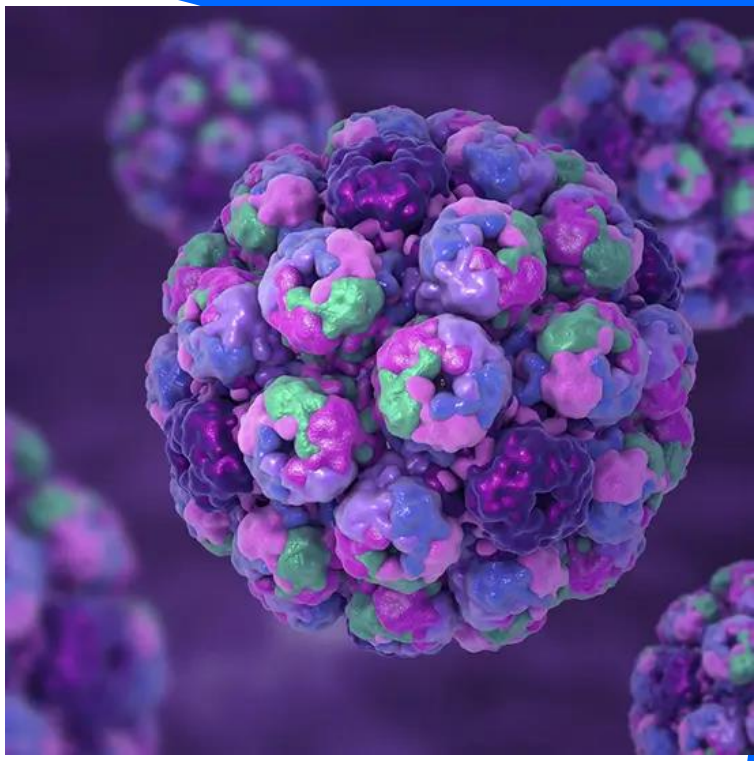
-The AST guidelines published in 2019 acknowledged this and defined probable and presumptive BKVN as **1,000 copies/mL plasma found in two measurements within 3 weeks**, and **>10,000 copies/mL in at least one of two measurements within 3 weeks, respectively**

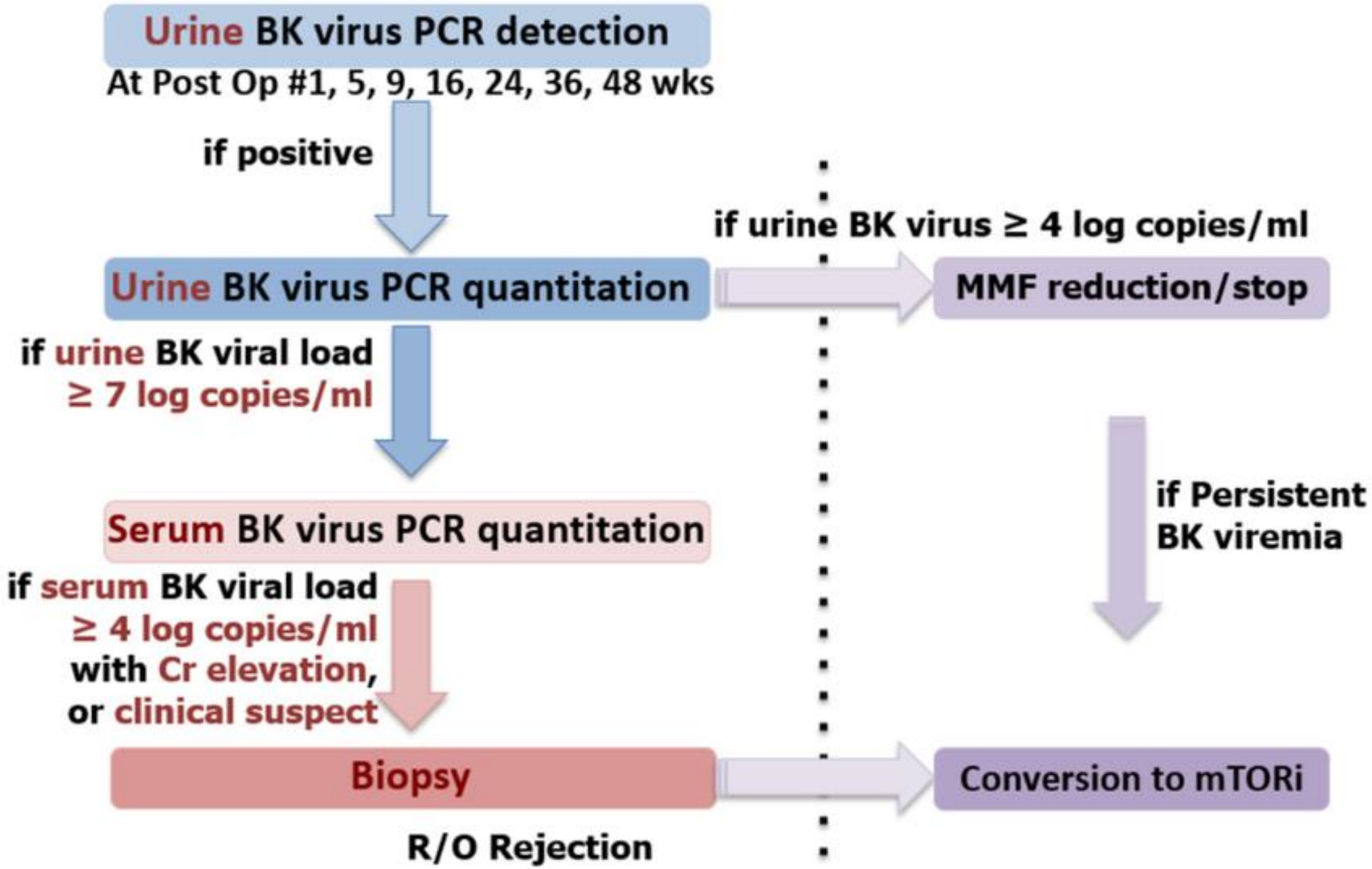
chalenges

-There may be a large variation in PCR results between laboratories.

-Using a single cut-off value in all laboratories (**4 log copies/mL in Serum and 7 log copies/mL in urine)** may reduce the sensitivity of PCR screening in BKVN diagnosis.

-PCR method should be validated and performed in certified laboratories for the diagnosis of BKVN in transplant cases. Clinicians should also be Aware of the limitations of these diagnostic tests.




Urine BK virus PCR detection
At Post Op #1, 5, 9, 16, 24, 36, 48 wks
if positive
Urine BK virus PCR quantitation
if urine BK viral load
≥ 7 log copies/ml
Serum BK virus PCR quantitation
if serum BK viral load
≥ 4 log copies/ml
with Cr elevation,
or clinical suspect
Biopsy
R/O Rejection
if urine BK virus ≥ 4 log copies/ml
MMF reduction/stop
if Persistent
BK viremia
Conversion to mTORi

Proven/Histopathologic Diagnosis of BK Virus/Polyomavirus Nephropathy

A proven diagnosis of BKVN requires viral identification on kidney biopsy, and several histologic changes are associated with intrarenal PV infection

Microscopic findings

-interstitial nephritis and tubular injury;

-these findings are focal

-Involvement is more prominent in the distal nephron, therefore evaluation of medulla is important, especially in early stage infection;

-it is recommended that 2 core biopsies be provided, at least 1 where the medulla is sampled

Microscopic findings

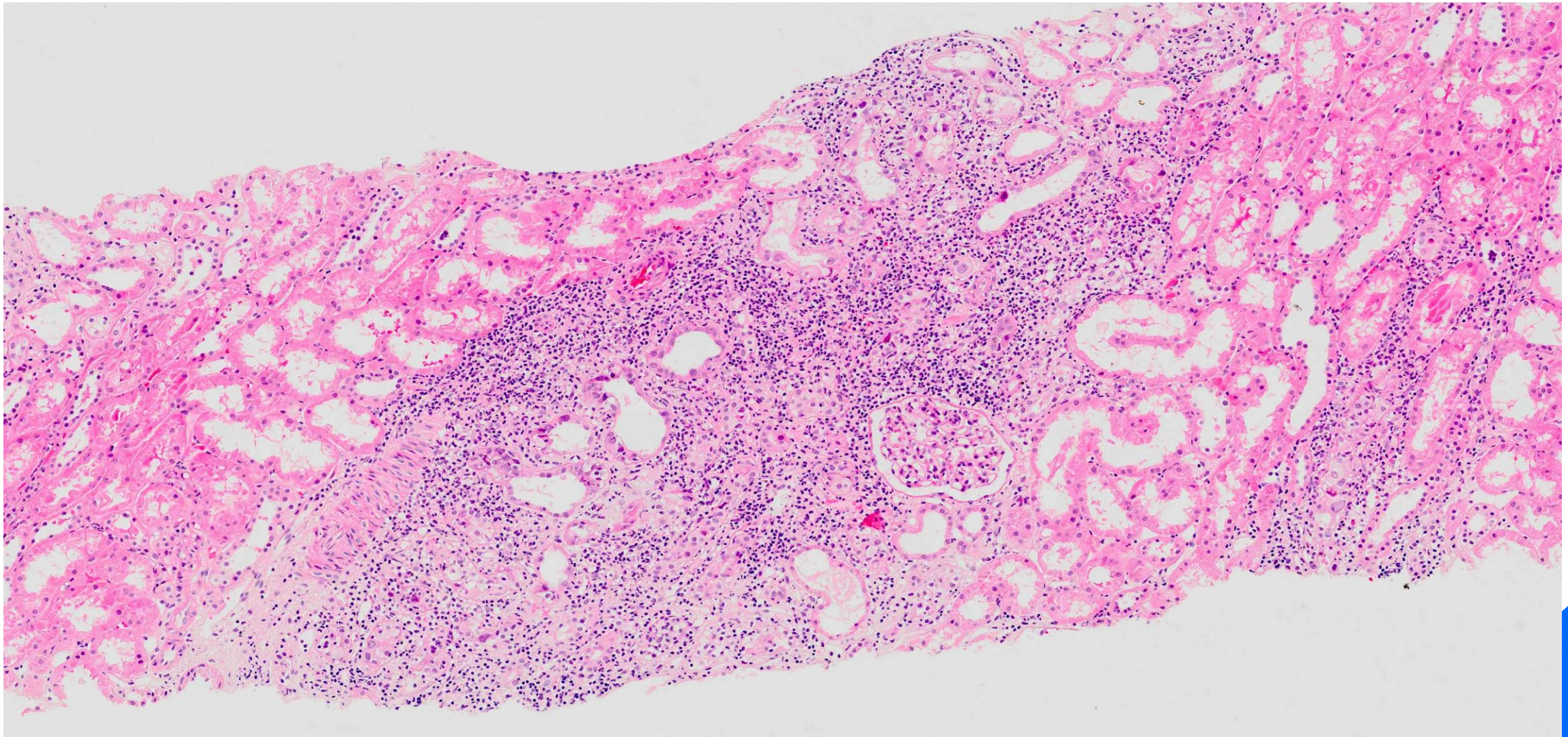
-interstitial edema and inflammation, composed predominantly of mononuclear cells, accompanied by plasma cells and less frequently eosinophils and neutrophils;

-these changes may be absent in early stages of infection

-Inflammation is patchy and associated with infected tubules,

-Tubulitis and tubular cell injury; cell necrosis / dropout, desquamation / sloughing, flattening

Well demarcated inflammation



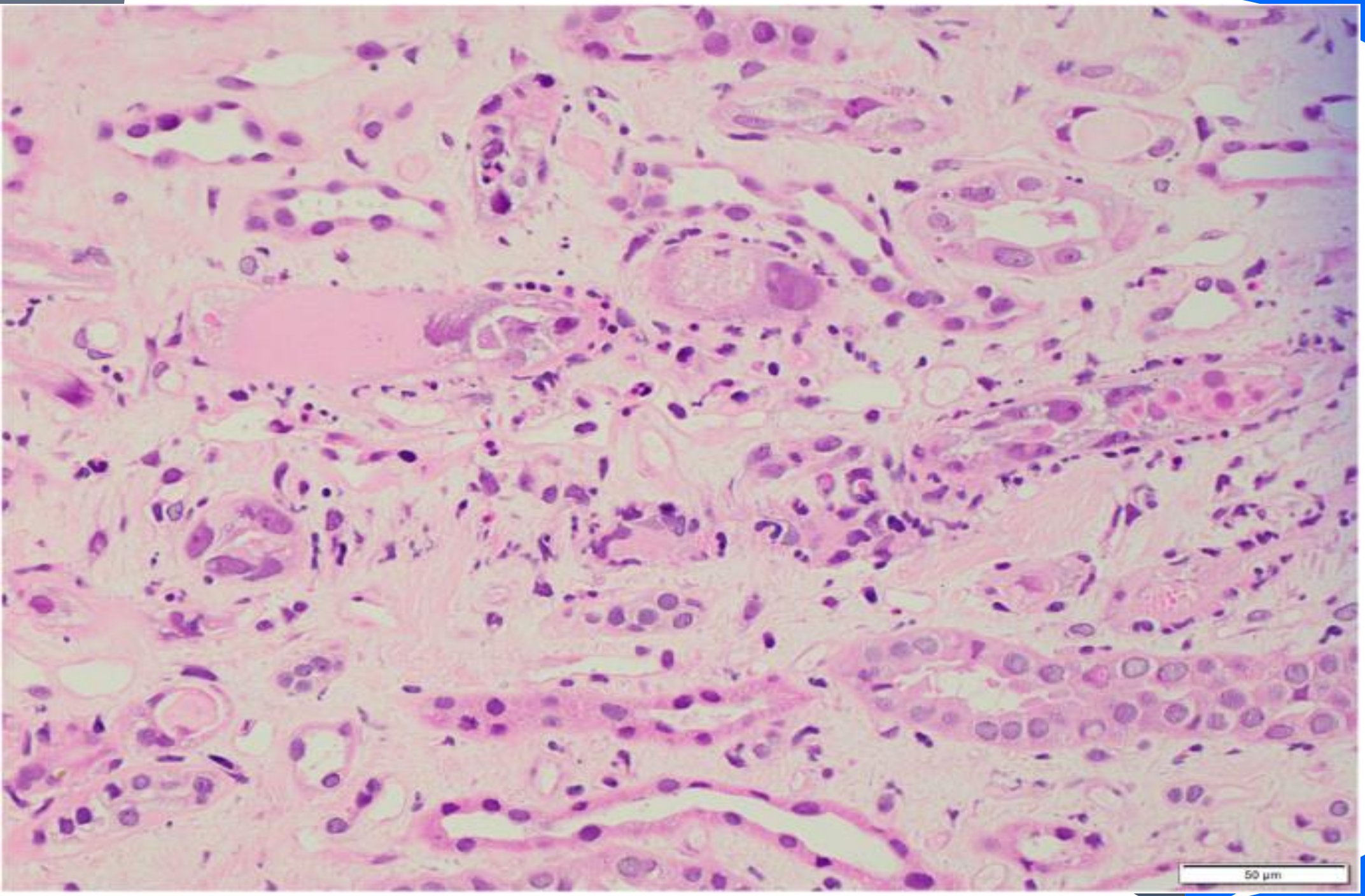
Microscopic findings

-Tubular epithelial cell cytopathy; maybe absent in early stages of infection:

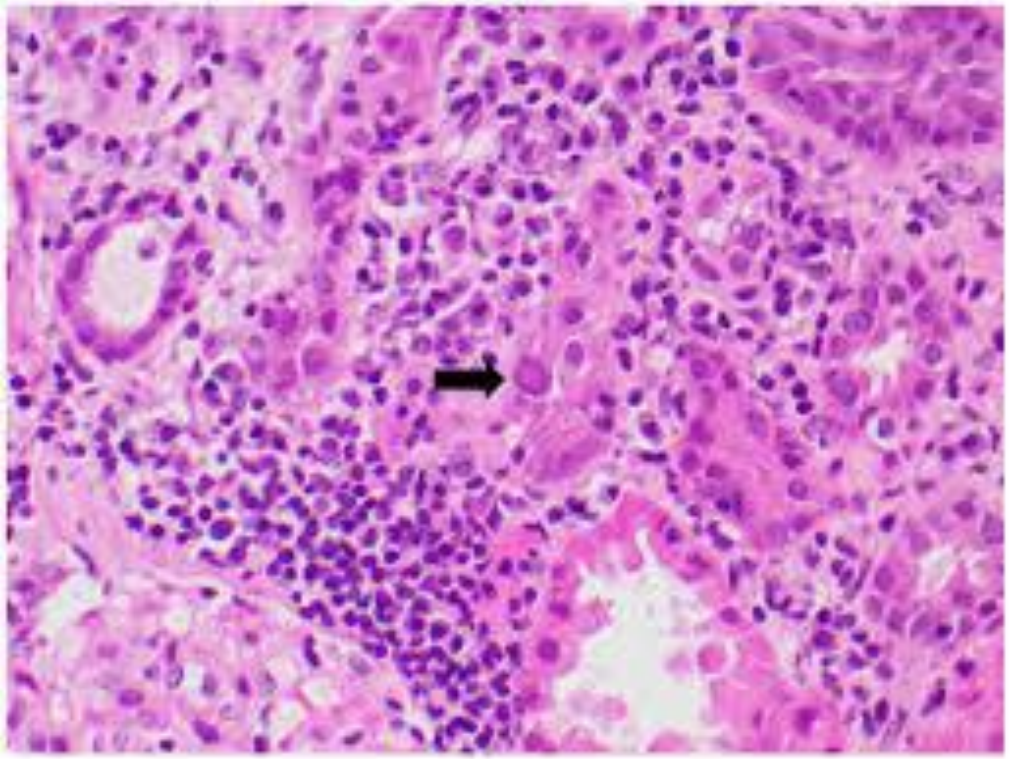
*Cell enlargement

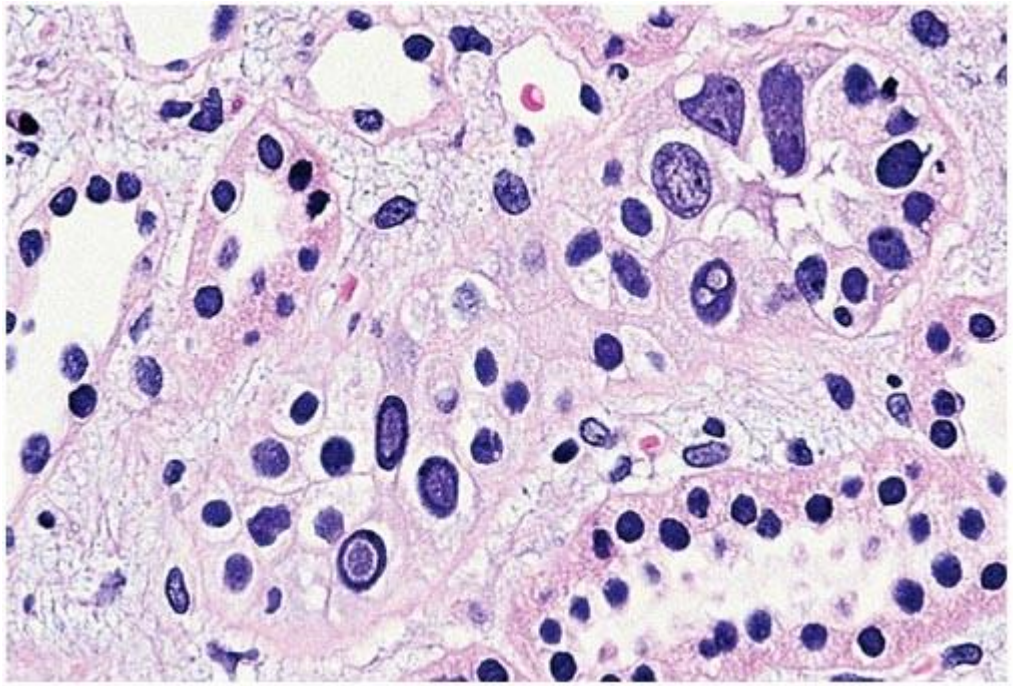
*Nuclear hyperchromasia and anisonucleosis

*Intranuclear inclusions: basophilic granules, ground glass appearance or clearing, no halo; chromatin changes: smudging, clumping or peripheral margination

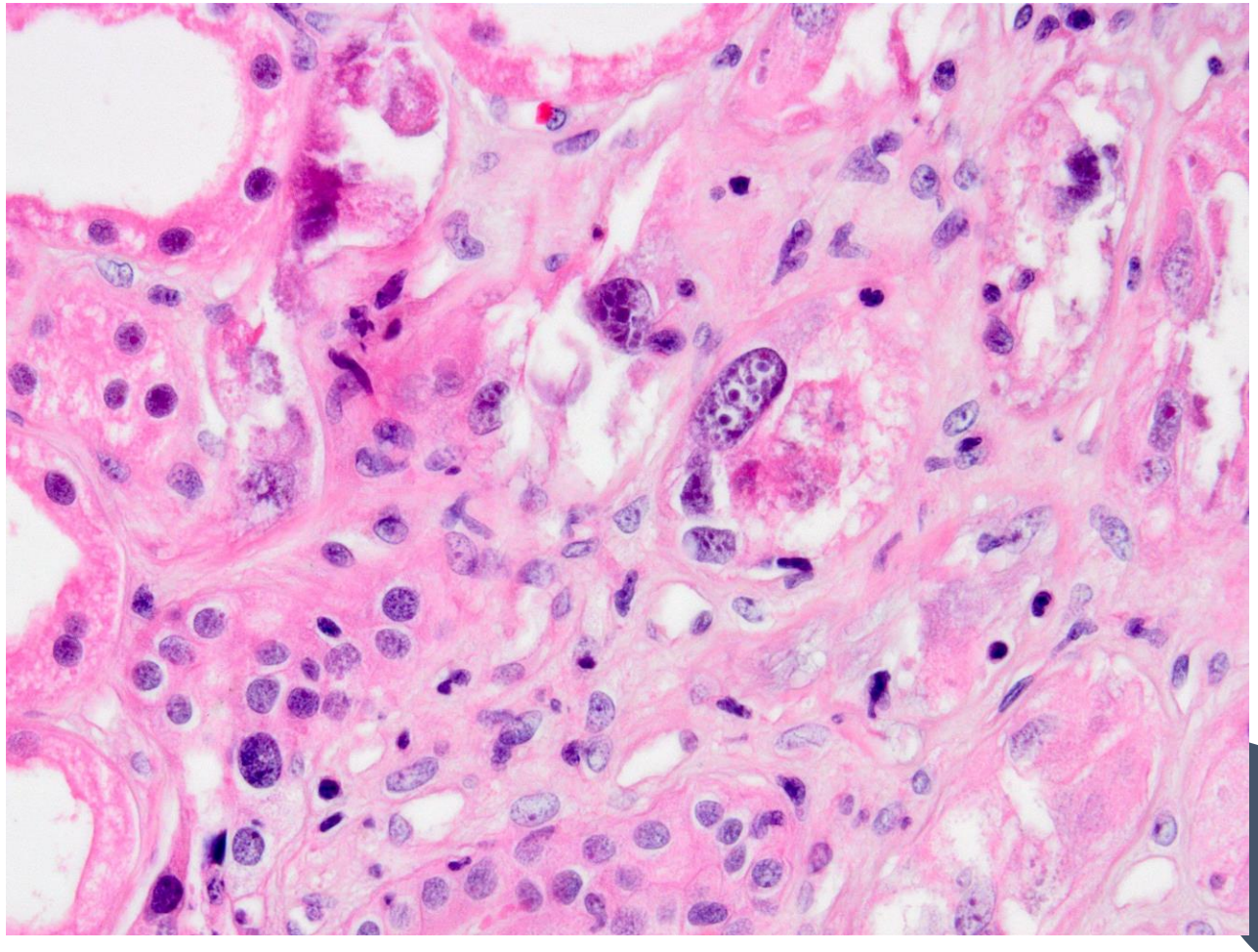

50 µm

tubulitis





Intranuclear basophilic inclusion

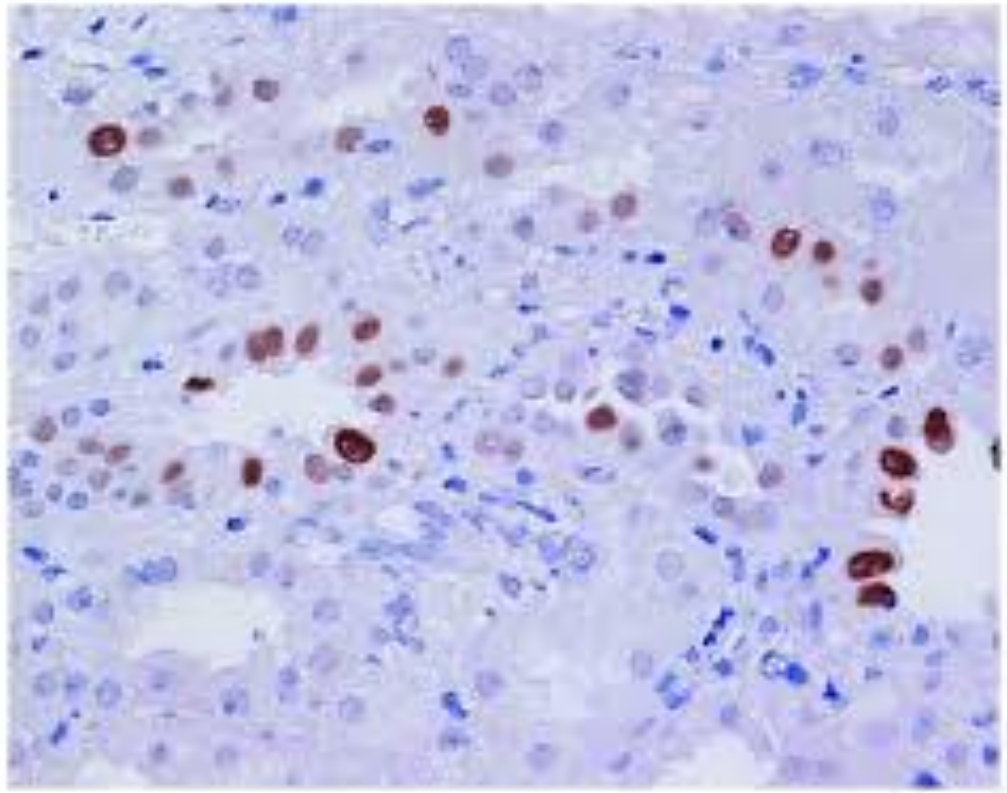


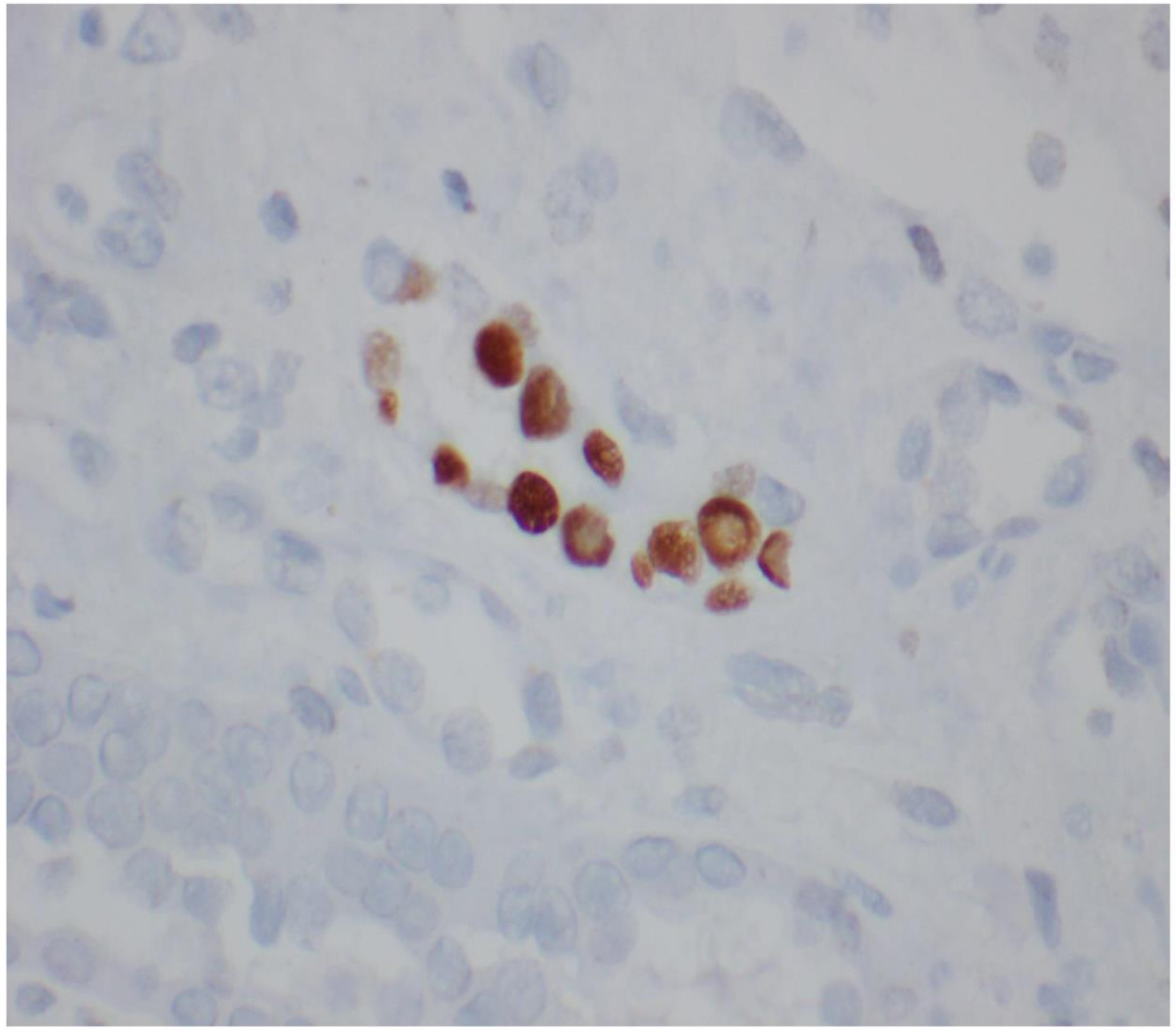
Early and late stage

-in early stage infection, morphological findings are only present in scattered cells, mostly in the medulla and may even be characterized by only a handful of SV40 positive cells without discernable cytopathy

-Interstitial fibrosis and tubular atrophy: late stage disease

Positive SV40 IHC





Histologic scoring

Scoring of polyomavirus replication load / level (pvl): percentage of positive tubules / ducts by morphologic assessment of cytopathy or SV40 immunohistochemistry in the entire biopsy (cortex and medulla)

pvl 1: 1%

pvl 2: 1 - 10%

pvl 3: > 10%

Histologic classification

Histologic classification system: consisting of polyomavirus replication load / level (pvl) score and Banff score for interstitial fibrosis (ci):

PVN class 1: pvl 1; ci ≤ 1

PVN class 2:

- **pvl 1; ci ≥ 2**
- **pvl 2; any ci score**
- **pvl 3; ci ≤ 1**

PVN class 3: pvl 3; ci ≥ 2

BK virus in urine cytology

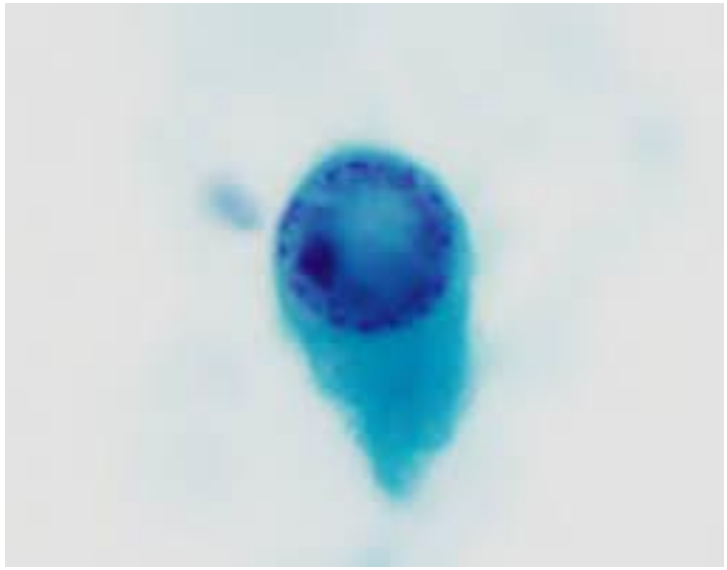
Urine cytology: **decoy cells** (resemble cells in uroepithelial cancer); BK virus infected tubular epithelial cells that have been shed into the urine

Rounded basophilic nuclei larger than the average transitional and tubular epithelial cells

Nuclei have **viral inclusions** appearing as dense granular basophilia and no halo

Dirty background: transitional, tubular and inflammatory cells and clumps of amorphous basophilic material (harder to appreciate in slides prepared with thin layer methods)

Cytology grading



Graded as :

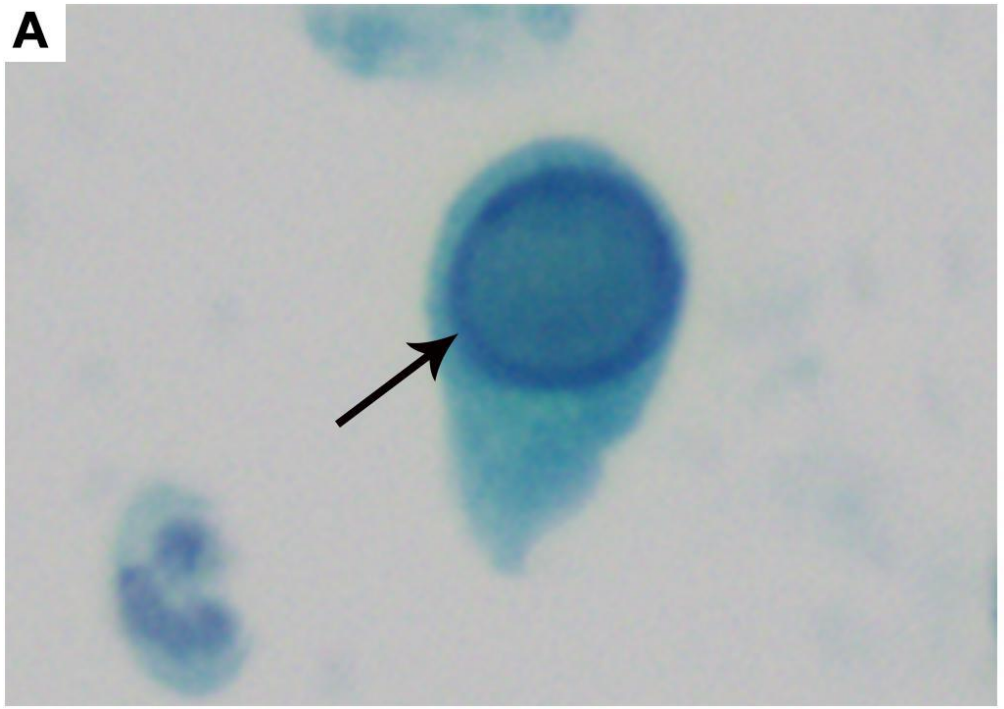
-rare,

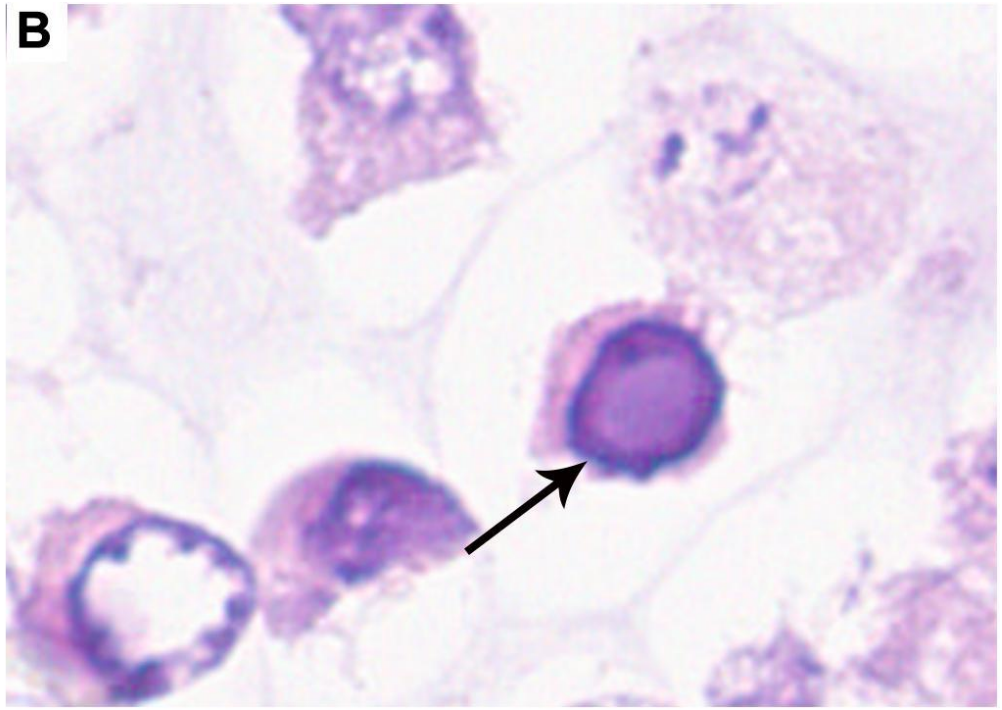
-up to 4 per cytospin

-10 per cytospin;

when rare cells are present with lack of inflammation, chances of positive infection in biopsy sample is low

Decoy cell

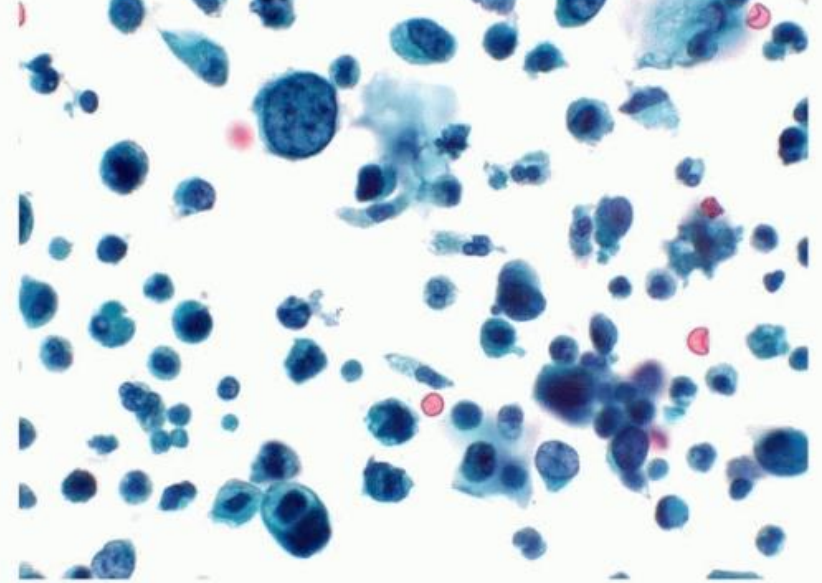




Differential diagnosis

1-JC infection

2-high grade TCC



BK virus	TCC
Hyperchromasia less pronounced Smudgy chromatin Homogeneous, opaque nucleus Absence of cell clusters	Hyperchromasia more prominent Coarse chromatin Eccentrically located nucleus Presence of cell clusters

3-acute Tcell mediated rejection

BK virus:	**Acute T cell mediated rejection:**
Cytopathic changes Tubulitis less prominent Inflammation patchy, well demarcated, more B cells (Transplantation 2001;71:896) No edema No vasculitis Neutrophils may be present	Cytopathic changes absent but degenerative regenerative changes may be confused with cytopathy Tubulitis more prominent Inflammation less demarcated, more T cells (Transplantation 2001;71:896) Edema positive Vasculitis may be present Neutrophils rarer

DDX

4-Acute tubular injury:

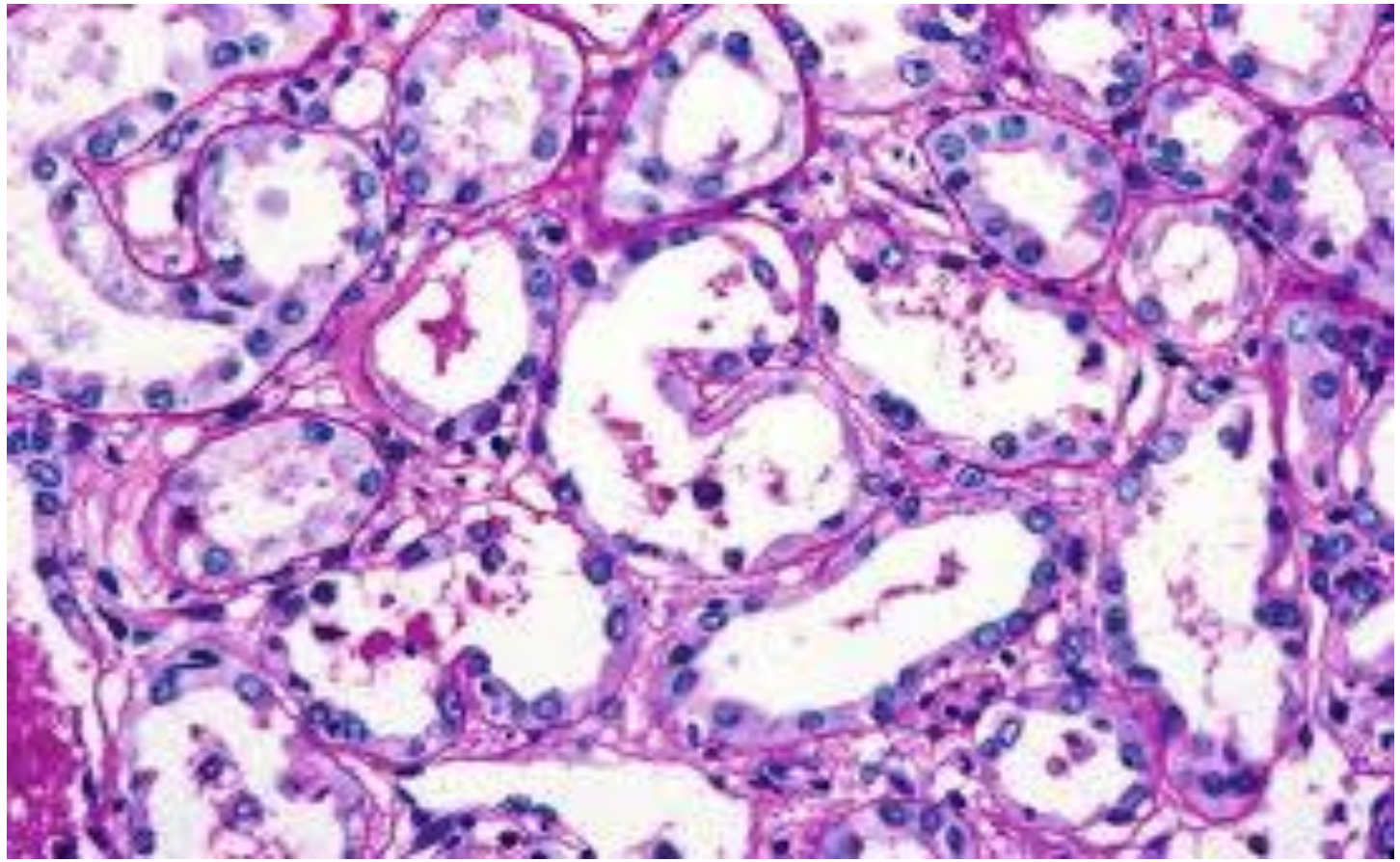
-Nuclear degenerative / regenerative changes that accompany acute tubular injury may resemble viral cytopathy;

-the nuclear changes, however, are usually not as exaggerated, are composed of nucleolar enlargement and hyperchromasia and less often show chromatin changes that resemble intranuclear inclusions

-Moreover, inflammatory infiltration is not prominent, as that which accompanies viral infection

-SV40 immunohistochemistry also aids diagnosis

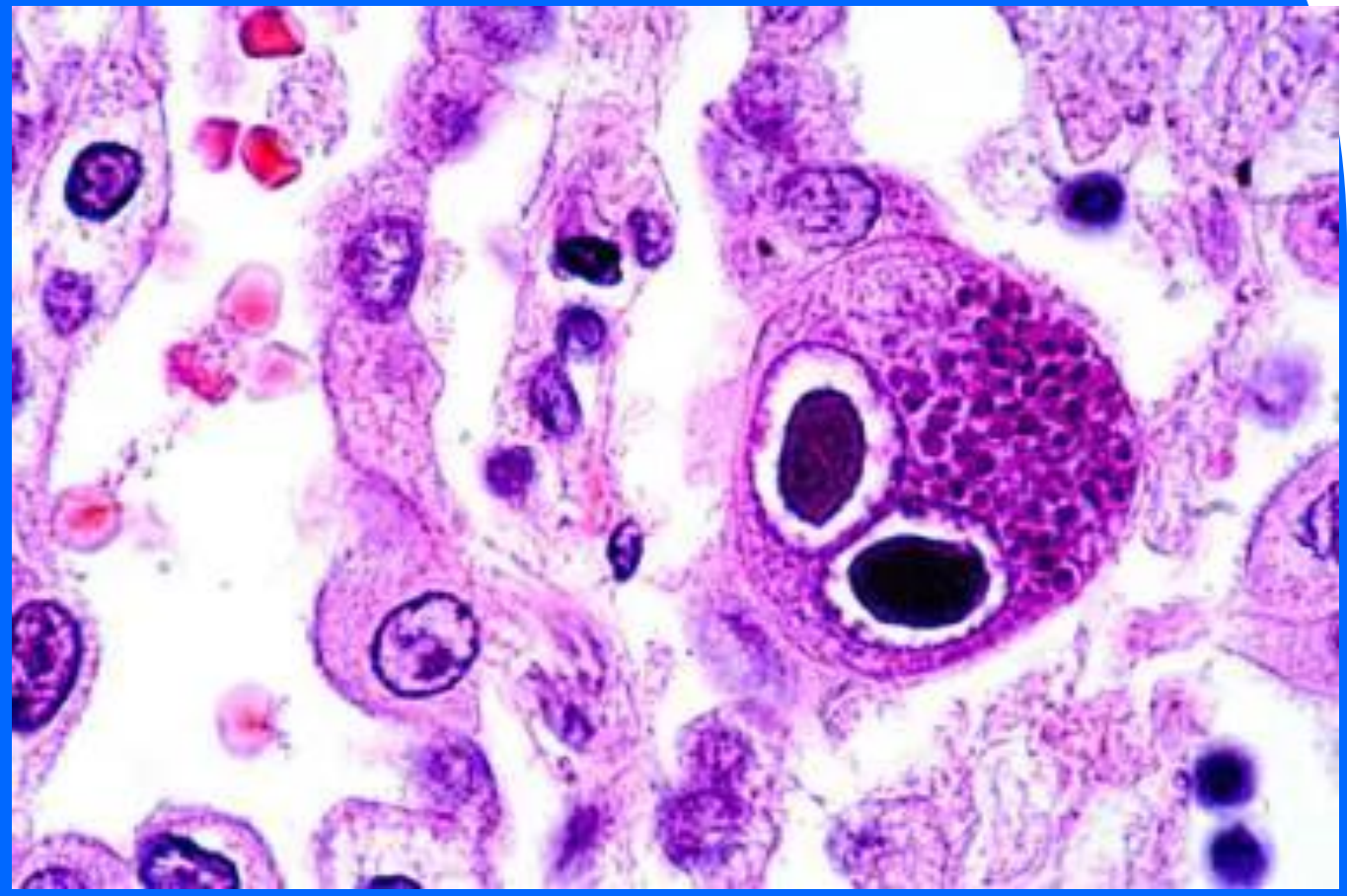
Acute tubular necrosis



DDx:

5-Other viruses may have similar cytopathic changes, such as **cytomegalovirus** (presence of both intranuclear and intracytoplasmic inclusions and perinuclear halo may aid histologic diagnosis)

adenovirus and human **herpes simplex virus**



Treatment

- 1. Reduce dose of antimetabolite by half while continuing on the same doses of calcineurin inhibitor and/or prednisone.
- It is imperative to monitor serum creatinine and serial plasma BK PCR levels from the same laboratory (to reduce inter-assay variability) every 2 weeks

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Treatment

- 2. If viral loads continue to be at similar levels or increase, proceed with complete cessation of anti-metabolite.
- 3. The next step is to reduce calcineurin-inhibitor trough goals if viral loads do not reduce over 4 weeks despite cessation of anti-metabolite (4–6 ng/mL for tacrolimus and 50–100 ng/L for cyclosporine).

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Decrease immunosuppression and assess creatininemia and viremia every 2-3 weeks

STEP 1 : MMF daily dose equivalents ≤ half the daily maintenance dose.

STEP 2 : if no decrease in BK viremia, reduce CNI (TAC trough levels <6 ng/ml, cyclosporine 50-100 ng/ml).

STEP 3 : if no decrease in BK viremia, STOP MMF and switch to low-dose CNI + mTORi.

STEP 4 : Administration of IVIG 400 mg/kg, for a total of 5 days (total of 2 g/kg).

CURRENT GUIDELINES FOR BKV VIRAEMIA AND BKVN THERAPY

- Immunosuppressant level targets should be < 6 ng/ml for tacrolimus, < 150 ng/ml for cyclosporine, < 6 ng/ml for sirolimus; mycophenolate should be administered in a half or lower dose.

- Complementary therapy based on conversion of tacrolimus to low-dose cyclosporine, CI to sirolimus or mycophenolate replacement with leflunomide may be considered.

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

Quinolones

- Despite demonstrating anti-viral properties in vitro, randomized trials failed to show efficacy as prophylaxis in the immediate post-transplant period or treatment for BK viremia
- In the levofloxacin prophylaxis trial, a higher incidence of resistant bacterial infection was seen in the quinolone group

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Cidofovir

- Studies have shown no benefit with cidofovir use, notwithstanding that a significant risk of kidney dysfunction was noted
- Cidofovir has already been shown to be associated with proteinuria, proximal tubular dysfunction, and kidney disease
- Prophylaxis with newer less toxic brincidofovir may yet prove effective

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Leflunomide

- A prodrug that converts to an active metabolite, A77 1726, which has demonstrated both immunosuppressive and anti-viral properties
- Pharmacodynamic and prospective open-label study showed no benefit .
- Another metabolite, FK778, did not demonstrate efficacy in a phase 2, proof-of-concept, randomized, open-label, parallel-group, 6-month study in kidney transplant patients

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

POSSIBILITIES OF IMMUNOTHERAPY IN BKVN

- BKV SPECIFIC T CELL IMMUNOTHERAPY

A phase II clinical trial showed that administration of BKV-specific T cells manufactured from a patient's stem cell donor or unrelated donors could reduce symptomatic infection and BK viral load effectively in HSCT and solid organ transplant recipients

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

POSSIBILITIES OF IMMUNOTHERAPY IN BKVN

- Virus-specific T cells therapy

➢In this study was safe with no infusional toxicity, GVHD , or graft rejection

➢A phase II of trial with either high or low levels of BK viraemia is also currently underway

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

ANTIBODIES IN THE TREATMENT OF BK VIRUS

- MAU868 is a human monoclonal antibody (IgG1), which binds to viral capsid protein VP1 and blocks the binding of the virus to the host cell surface.
- It could be the first effective therapy for BKV infection.

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

BKV VACCINE DEVELOPMENT

- Administration of a multi-epitope VLP vaccine

- A prospective phase II multicenter study to evaluate the tolerability and safety of BD03, a DNA vaccine administered intramuscularly for the prevention of CMV and BKV reactivation in kidney transplant recipients, is currently in progress

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

RNA-BASED THERAPY (HYBRIDIZE'S THERAPEUTICS)

- A direct acting anti-viral therapy is designed to target the viral mRNA, work intra-cellular and protect the cells from within and therefore provides for low off-target effects.
- RNA antisense oligonucleotides discontinues the splicing process, preventing viral synthesis and replication .

Acta Medica (Hradec Králové) 2022; 65(4): 119–124
https://doi.org/10.14712/18059694.2023.1

Kidney Re-Transplantation

- Retransplantation of recipients has been associated with an increased risk of BKPyV-DNAemia in some but not all studies.
- Transplant nephrectomy of the failed allograft did not protect against recurrent BKPyV-DNAemia or BKPyVnephropathy.

Kidney Re-Transplantation

- Failed transplant or native nephrectomy is not recommended

- Consideration for lower immunosuppression should be balanced with the risk of rejection.
- Allograft survival in patients who receive re-transplantation is 98% and 94% at 1 and 3 years

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

Kidney Re-Transplantation

- In comparison to re-transplanted patients for graft failure from other causes, five-year death-censored graft survival rates were 91% for the BKVAN group and 84% for the non-BKVAN group.
- There was no significant difference in the rates of acute rejection or patient survival at one year

Citation: Kant, S.; Dasgupta, A.; Bagnasco, S.; Brennan, D.C. BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review. Viruses 2022, 14, 1616.

viruses

MDPI

Review

BK Virus Nephropathy in Kidney Transplantation: A State-of-the-Art Review

Sam Kant [1,2,*], Alana Dasgupta [3], Serena Bagnasco [3] and Daniel C. Brennan [1,2]

Current Status, Prevention and Treatment of BK Virus Nephropathy

Ester Kurašová[1,*], Jakub Štěpán[1], Karel Krejčí[1], František Mrázek[2], Pavel Sauer[4], Jana Janečková[5], Tomáš Tichý[3]

Reviews

OPEN

The Second International Consensus Guidelines on the Management of BK Polyomavirus in Kidney Transplantation

Camille N. Kotton, MD,[1] Nassim Kamar, MD, PhD,[2] David Wojciechowski, MD,[3] Michael Eder, MD,[4] Helmut Hopfer, MD,[5] Parmjeet Randhawa, MD,[6] Martina Sester, PhD,[7] Patrizia Comoli, MD,[8] Helio Tedesco Silva, MD, PhD,[9] Greg Knoll, MD,[10] Daniel C. Brennan, MD,[11] Jennifer Trofe-Clark, PharmD,[12,13] Lars Pape, MD, PhD,[14] David Axelrod, MD, MBA,[15] Bryce Kiberd, MD,[16] Germaine Wong, MBBS, MMed, PhD,[17,18,19] and Hans H. Hirsch, MD[20,21]; on behalf of The Transplantation Society International BK Polyomavirus Consensus Group*

Incidence, Risk Factors, and Outcomes of Kidney Transplant Recipients With BK Polyomavirus-Associated Nephropathy

Ryan Gately[1], Elasma Milanzi[2], Wai Lim[3], Armando Teixeira-Pinto[4], Phil Clayton[5], Nicole Isbel[1,2,6], David W. Johnson[1,2,6], Carmel Hawley[1,2,6], Scott Campbell[1,2,8] and Germaine Wong[4,7,8]


Thank
you