Brigham and Women's Hospital
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# EARLY POST-TRANSPLANT MANAGEMENT

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  - Clinical focus: Kidney Transplantation
  - Research focus: Regulatory T cells, BK Nephropathy, Tx Genetics

# Disclosures

- Vertex: Chair, Drug Monitoring Committee, VX20-880 and VX20- 264 studies
- Amgen: Investigator Initiated Rapatha Rx in Transplant patients
- Natera: Renasight Scientific Advisory Board
- Novartis: Scientific Advisory Board
- BioHope: Scientific Advisory Board
- Sanofi: Scientific Advisory Board
- NIH: DSMB THINKER Study

# Objectives

**By the end of this session, participants should be able to:**

**1. Apply a structured early post-transplant monitoring approach** to identify and triage graft dysfunction, delayed graft function, surgical complications, infection, rejection and recurrent disease.

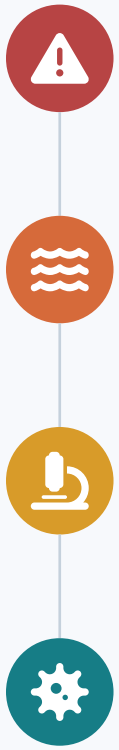
**2. Individualize early kidney-transplant management** based on recipient risk, donor-organ risk and immunosuppression strategy, including prophylaxis, biopsy decisions, biomarker use and management of common metabolic complications.

# Kidney Transplantation - the first 90 days

## Learning objectives

- **Execute a universal monitoring and prevention bundle**
- **Diagnose graft dysfunction in the correct order**
- **Tailor immunosuppression and surveillance to risk**
- **Treat DGF, rejection, TMA, recurrence, infection and metabolic complications**

## Dominant threats shift with time



**0–24 h**
Hemorrhage • arterial/venous thrombosis • hyperkalemia • shock or fluid overload

**Days 2–7**
DGF/ischemia • urine leak/obstruction • early rejection • TMA • wound/UTI

**Weeks 2–4**
Rejection • drug toxicity • recurrent FSGS • cytopenia • adherence failures

**Months 2–3**
CMV/BK/EBV • PTDM/weight gain • persistent hyperparathyroidism • anemia

**Board takeaway: time since transplant is a diagnostic test.**

Framework: KDIGO KTR guideline; AST/IDCOP Kidney Transplant Guidelines.

# Standard monitoring through day 90

| Parameter | Inpatient / week 1 | Weeks 2–4 | Months 2–3 | Escalate when… |
|---|---|---|---|---|
| **Urine output / weight / BP / temperature** | UO q1–2 h ≥24 h; daily weight and balance | Home BP/temp/weight daily; UO if unstable | Each visit + home trends | Abrupt UO fall, fever, hypotension, rapid weight change |
| **Creatinine/eGFR, K, $HCO_3$, Mg, Phos, glucose** | Daily until discharge/stable | 2–3 × / week | Weekly | Trend deviates from expected trajectory |
| **CBC** | Daily | 2–3 × / week | Weekly | Cytopenia, bleeding, hemolysis or drug change |
| **Tacrolimus trough** | Every 1–2 days until target | At early visits / dose changes | At visits until stable | Diarrhea, interacting drug, neurotoxicity or graft dysfunction |
| **Urinalysis + urine protein** | Baseline and when clinically indicated | Baseline within month 1 | Risk-based; at least quarterly in year 1 | FSGS/high recurrence risk: daily first week, then weekly ×4 |
| **Viral / alloimmune tests** | Record CMV/EBV/HBV/HCV plan | Start protocol BK/CMV strategy | Continue schedule; DSA/event-driven | After rejection therapy or increased immunosuppression |

**A “normal” creatinine is not a transplant baseline. The patient’s best stable post-transplant value is the comparator.**

KDIGO 2009. A Chandraker & M Yeung Overview of care of the adult kidney transplant recipient. In: UpToDate, A Lam (Ed), Wolters Kluwer. (Accessed on June 8, 2026.)

# Universal care bundle: the first 24 hours

### Perfusion, not “fluid matching”

- Continuous hemodynamic assessment
- Avoid hypotension and blind 1:1 replacement
- Use exam, weight, losses and cardiopulmonary reserve
- Individualize BP to chronic baseline and vascular risk
- Treat shock, bleeding and arrhythmia promptly

### Output, wound and drains

- Hourly urine output for at least 24 h
- Net balance, daily weight and edema
- Inspect graft, incision, Foley and drain output
- Record color and sudden changes
- Send drain-fluid creatinine if urine leak is possible

### Labs and drug exposure

- CBC, creatinine/BUN $Na/K/HCO_3$, Mg/Phos, glucose
- ECG and rapid treatment for severe hyperkalemia
- Tacrolimus trough once started
- Renal-dose all antimicrobials
- Recheck after dialysis, major fluid shifts or interacting drugs

### Prevention and handoff

- Immunosuppression and prophylaxis reconciled
- VTE and glycemic plans
- Avoid NSAIDs and unreviewed supplements
- Teach medication timing and emergency contacts
- Document donor/recipient serology and induction received

**Polyuria is not automatically “good graft function”- oliguria is a sign, not a diagnosis.**

KDIGO 2009

# Discharge bundle: prophylaxis, devices and safety

### PJP + bacterial coverage

TMP–SMX is preferred, typically 6–12 months. It also reduces UTI, Nocardia and toxoplasmosis risk. Watch K, creatinine and cytopenia.

### CMV strategy documented

Record D/R serostatus, induction and whether the center uses prophylaxis or preemptive PCR. Renal-dose valganciclovir and monitor CBC.

### Donor-derived infection plan

HCV/HBV consent, antiviral access, NAT schedule and specialist follow-up must be explicit before discharge.

### Devices and wound

Define Foley, drain and ureteric-stent removal plans. Minimize lines and catheters, provide wound and fever instructions.

## Medication and patient-safety checks before the patient leaves

| | |
|---|---|
| **Immunosuppression** | Exact doses/times, trough timing, food consistency, missed-dose instructions |
| **Interaction screen** | Azoles/macrolides/diltiazem/verapamil ↑ tacrolimus, rifamycins/inducers ↓ exposure |
| **Reproductive safety** | Mycophenolate is teratogenic, contraception and pregnancy planning are mandatory |
| **Home monitoring** | BP, temperature, weight, glucose when indicated, daily medication checklist |
| **Escalation pathway** | Same-day number for fever, vomiting/diarrhea, reduced urine, wound change or missed medications |

CMV: Kotton et al. Transplantation 2025. BK: Kotton et al. Transplantation 2024.

# Risk-stratify before the first creatinine returns

### Recipient / surgical

- Vascular disease, obesity, prior pelvic surgery
- Anticoagulation or bleeding risk
- Frailty, cardiac reserve, bladder dysfunction
- APS or other prothrombotic state

### Disease / genetic

- Primary FSGS vs monogenic/secondary disease
- Complement-mediated aHUS/C3G
- IgAN
- Family genetics
- Primary hyperoxaluria

### Immunologic

- cPRA, preformed DSA, crossmatch
- Repeat transplant or ABO incompatibility
- Induction and steroid plan
- Prior rejection or adherence concern

### Donor / system

- DCD, high KDPI/AKI, ischemic time, anatomy
- HCV/HBV and donor-derived infection risk
- Pharmacy coverage and lab access
- Caregiver, transport, language, housing

**More risk → more explicit monitoring, lower biopsy threshold, stronger adherence and infection planning**

# Elevated creatinine or low urine output: plumbing → perfusion → parenchyma

1

## Confirm the signal

- Repeat labs if needed
- Trend urine output and creatinine
- Check BP, weight, balance
- Review tacrolimus and new drugs

2

## Plumbing

- Doppler ultrasound
- Vascular thrombosis/kink
- Obstruction or stent issue
- Leak, hematoma or lymphocele

3

## Perfusion

- Hypovolemia or shock
- Bleeding/sepsis/cardiac failure
- Excess ultrafiltration
- Arterial inflow problem

4

## Parenchyma

- UA/UPCR and culture
- Drug toxicity or TMA labs
- BK/CMV when appropriate
- DSA ± dd-cfDNA adjunct
- Biopsy if unexplained/persistent

**Sudden anuria or abrupt graft change is a vascular/obstructive emergency until proved otherwise.**

*Do not assume "ATN" or pulse steroids before excluding a surgical catastrophe when imaging is immediately available.*

# Surgical and imaging emergencies

| Problem | Typical clue | Imaging / test | Immediate action |
|---|---|---|---|
| **Renal artery thrombosis / kink** | Sudden anuria - absent or markedly reduced perfusion | Urgent Doppler ± angiography | **Surgical/interventional rescue now** |
| **Renal vein thrombosis** | Anuria, graft swelling/pain, reversed diastolic flow on US | Urgent Doppler | **Surgical emergency** |
| **Ureteric obstruction** | Falling UO - hydronephrosis may be subtle early | US, nephrostogram if needed | Decompress - address stent/ureter |
| **Urine leak** | High drain output, perinephric collection, drain creatinine > serum | US/CT, fluid chemistry, nuclear scan selectively | Drain + stent/nephrostomy ± surgery |
| **Bleeding / compressive hematoma** | Hb fall, hypotension, pain, oliguria or “Page” effect | US/CT | Resuscitate, reverse coagulopathy, evacuate/embolize |
| **Lymphocele** | Weeks later: edema, hydronephrosis, venous compression | US/CT | Observe if small, drain/fenestrate if symptomatic |

**The graft is denervated: absence of pain does not exclude a major complication.**

# Case 1 • Sudden anuria on postoperative day 1

1

CLINICAL STEM

## RAPID-FIRE CASE 1

A 58-year-old man receives a deceased-donor kidney transplant. Urine output is initially 150 mL/hour. On postoperative day 1, he develops abrupt anuria, graft-site pain and fullness, and hypotension. The Foley catheter flushes freely and the bladder scan is empty.

*Choose the next best step—not the entire eventual plan.*

ONE BEST ANSWER

### Which is the single best next step?

A **Give 2 L crystalloid and reassess in 4 hours.**

B **Obtain urgent transplant Doppler and notify transplant surgery simultaneously.**

C **Order a radionuclide renogram.**

D **Give pulse methylprednisolone for presumed rejection.**

E **Perform a percutaneous allograft biopsy.**

# Case 1 • Answer: treat as a vascular emergency

**B**

**CORRECT ANSWER**

**Urgent transplant Doppler plus simultaneous transplant-surgery notification.**

## WHY THIS IS RIGHT

- Abrupt cessation of urine after initial function, with a painful or swollen graft, is a vascular or obstructive catastrophe until proved otherwise.
- Color Doppler is the first-line test, but surgical mobilization must occur at the same time because graft salvage is time-sensitive.
- Exclude thrombosis, kinking, torsion, hematoma and obstruction before considering biopsy or empiric rejection therapy.

## BOARD LOGIC

- A fluid bolus alone delays definitive evaluation.
- Acute rejection rarely presents as abrupt anuria on postoperative day 1.
- Biopsy is not the first test when vascular compromise is possible.

## BOARD PEARL

**Sudden anuria = plumbing or vascular emergency until proved otherwise.**

Sources: KDIGO kidney-transplant recipient guideline, Chapters 8–9; contemporary transplant-ultrasound reviews.

# Delayed graft function: support the patient, protect the diagnosis

## Who is at risk?

- DCD donation and warm ischemia
- High KDPI, donor AKI or older donor
- Prolonged cold ischemic time
- Recipient hypotension, obesity or long dialysis vintage
- Technical or hemodynamic events

Risk predicts DGF—not the cause of ongoing dysfunction.

## Management

- Optimize perfusion; avoid hypotension and nephrotoxins
- Dialyze for usual indications—avoid aggressive ultrafiltration
- Dose all drugs to current function
- Maintain adequate immunosuppression; CNI timing/targets are center-specific
- Ultrasound early when the course is unexpected
- Biopsy if persistent or immunologically high risk
- No proven pharmacologic “renal rescue” agent

## What DGF can hide

- T-cell or antibody-mediated rejection
- Vascular compromise or obstruction
- CNI toxicity or TMA
- Infection or donor-derived disease
- Primary nonfunction

KDIGO suggests biopsy every 7–10 days during delayed function; current practice individualizes to risk and trajectory.

**DGF is a phenotype—not a diagnosis—and it can coexist with rejection.**

Common definition DGF: dialysis in first 7 days.

# Donor and organ risk: what changes after implantation?

## Marginal / high-risk organ features

- DCD / warm ischemia
- High KDPI / donor AKI
- Long cold ischemia
- Multiple vessels / anatomy
- Small pediatric or en bloc
- Donor-derived infection

## Post-implant implications

- Set expectations for DGF and dialysis
- Lower threshold for Doppler and biopsy if recovery is atypical
- Protect perfusion and avoid nephrotoxins
- Adjust drug doses dynamically
- Communicate vascular anatomy and preservation details
- “marginal” doe not mean universally bad

## Preservation and reconditioning

**Hypothermic machine perfusion (HMP)**
- Reduces DGF versus static cold storage in deceased-donor kidneys
- Useful for assessment and transport

**Normothermic machine perfusion (NMP)**
- Restores warm oxygenated metabolism and enables functional testing
- One-hour end-ischemic NMP was safe but did not reduce DGF in a 2023 DCD RCT

Oxygenated perfusion, NRP and therapeutic reconditioning remain active areas of development.

**Perfusion parameters add context; they are not a stand-alone discard rule or a substitute for post-transplant assessment.**

Moers et al. NEJM 2009; Niemann et al. NEJM 2023; Hosgood et al. Nat Med 2023.

# Case 2 • Delayed graft function without recovery

2

CLINICAL STEM

## RAPID-FIRE CASE 2

A 46-year-old woman with cPRA 98% receives a DCD kidney after a negative crossmatch. She requires dialysis on postoperative days 2 and 5. On day 7, urine output is 300 mL/day and creatinine is 8.1 mg/dL. Doppler shows patent vessels and no hydronephrosis; the tacrolimus trough is therapeutic.

*Choose the next best step—not the entire eventual plan.*

ONE BEST ANSWER

### Which is the single best next step?

A **Continue supportive care only because DGF is expected.**

B **Increase the tacrolimus target.**

C **Perform an allograft biopsy.**

D **Start empiric plasma exchange and IVIG.**

E **Order donor-derived cell-free DNA instead of biopsy.**

# Case 2 • Answer: biopsy the allograft

C

CORRECT ANSWER

**Perform an allograft biopsy.**

WHY THIS IS RIGHT

- Delayed graft function describes poor function; it does not establish the cause. Ischemic injury and rejection can coexist.
- Once major vascular and obstructive causes are excluded, biopsy is the decisive test for persistent unexplained dysfunction.
- KDIGO suggests biopsy at 7–10-day intervals during delayed graft function when recovery has not occurred.

BOARD LOGIC

- High cPRA raises the pretest probability of rejection but does not justify blind treatment.
- Biomarkers may complement assessment; they do not replace an indicated biopsy.
- Increasing calcineurin-inhibitor exposure may worsen ischemic injury.

BOARD PEARL

**DGF can hide rejection: image first, then biopsy when the trajectory is wrong.**

Source: KDIGO 2009 kidney-transplant recipient guideline, Chapter 9 (allograft biopsy during DGF).

# HCV- and HBV-positive donor kneys

## HCV NAT-positive donor → HCV-negative recipient

| | |
|---|---|
| **Before implant** | Informed consent; guaranteed DAA access; insurance/logistics; baseline HCV RNA/LFTs |
| **After implant** | Prophylactic, preemptive or very early reactive pangenotypic DAA according to protocol |
| **Monitor** | HCV RNA, LFTs, renal function and interactions with tacrolimus/cyclosporine |
| **Outcome** | Modern series show very high SVR and excellent short-term graft outcomes |

## HBV-positive or anti-HBc-positive donor

| | |
|---|---|
| **anti-HBc+ / HBsAg–** | Usually low transmission risk in kidney transplantation; check recipient immunity, vaccinate when possible, monitor ± prophylaxis |
| **HBsAg+ or HBV DNA+** | Specialized use: consent, potent nucleos(t)ide therapy and close HBV DNA/HBsAg/ALT follow-up |
| **Recipient factors** | HBsAb titer, prior HBV exposure, intensity of immunosuppression and local policy determine prophylaxis |
| **Do not forget** | Serology alone is not the same as donor viremia; interpret HBsAg, anti-HBc and HBV DNA together |

**U.S. PHS guidance: test all recipients with HIV, HBV and HCV NAT at 4–6 weeks after transplant.**

*Local regulation and organ-acceptance policy vary; infectious-disease and transplant-pharmacy partnership is essential.*

AASLD/IDSA HCV Guidance; KDIGO HCV 2022; AST HBV consensus; U.S. PHS 2020.

# Induction: match intensity to immunologic risk

LOWER IMMUNOLOGIC RISK — HIGHER RISK

**No DSA • negative crossmatch first transplant • low cPRA**

**Rising cPRA / repeat transplant / steroid avoidance**

**Preformed DSA • positive crossmatch ABOi • high rejection risk**

## Basiliximab (IL-2RA)

Preferred first-line induction for lower-risk recipients.

**Advantages**
- Less leukopenia and infection

**Limitations**
- Less potent for highly sensitized recipients

## rATG / lymphocyte-depleting

Use for high immunologic risk or center-specific indications.

**Monitor**
- Leukopenia, thrombocytopenia
- CMV/EBV/PJP risk
- Infusion reactions

## Early management consequence

Know exactly what was given. Induction changes:

- Rejection probability
- Steroid-withdrawal plan
- Cytopenia thresholds
- CMV/EBV surveillance
- Timing of vaccination and prophylaxis

**Induction lowers rejection risk; it does not make delayed graft function “biopsy-proof.”**

KDIGO 2009: IL-2RA first-line; lymphocyte-depleting agent for high immunologic risk.

# Maintenance immunosuppression and steroid withdrawal

## Tacrolimus

**Strength**
- Lowest acute rejection among standard CNIs

**Early toxicities**
- Nephrotoxicity, neurotoxicity
- Hyperkalemia, hypomagnesemia
- Hyperglycemia / PTDM

**Monitor**
- True trough, kidney function and interactions

## Mycophenolate

**Strength**
- Standard antiproliferative partner

**Early toxicities**
- Diarrhea and GI intolerance
- Leukopenia and infection
- Teratogenicity

Do not reflexively stop for diarrhea before checking infection and tacrolimus exposure.

## Corticosteroid

**Benefits**
- Rejection prevention and treatment

**Costs**
- Diabetes, weight, bone and mood
- Infection and wound effects

**Withdrawal**
- Consider only in selected low-risk recipients with induction; overall acute rejection risk increases.

**Common interaction traps**

Azoles / macrolides / diltiazem ↑ tacrolimus

Rifamycins / carbamazepine / phenytoin ↓ tacrolimus

Diarrhea often ↑ tacrolimus exposure

KDIGO 2009: tacrolimus + antiproliferative ± steroid; mTORi only after function/wound healing.

# When to convert: belatacept or an mTOR inhibitor?

| Belatacept: CNI-free costimulation blockade | | Sirolimus / everolimus: mTOR pathway inhibition | |
|---|---|---|---|
| **Consider** | CNI nephrotoxicity/TMA or intolerance; unstable exposure; long-term renal-function preservation | **Consider** | CNI minimization, selected malignancy/skin-cancer contexts, or specific center protocols |
| **Requirements** | EBV seropositive only; reliable monthly IV attendance; center experience | **Do not start early** | Wait until graft function is established and the wound is healed |
| **Trade-offs** | More early acute cellular rejection; PTLD/CNS risk; infection surveillance; cost/logistics | **Avoid / caution** | Proteinuria, DGF, wound problems, dyslipidemia, cytopenia, edema, mouth ulcers, pneumonitis |
| **Timing** | Usually conversion after the immediate postoperative period; urgent early use is specialized (for example CNI-associated TMA) | **Monitor** | Drug trough, urine protein, lipids, CBC, wound and pulmonary symptoms |

**Conversion should follow a diagnosis and a goal—not a reflex response to one creatinine value.**

Belatacept: FDA label and conversion trials. mTORi timing: KDIGO 2009.

# Case 3 • BK DNAemia at week 8

3

CLINICAL STEM

## RAPID-FIRE CASE 3

Eight weeks after transplant, a 55-year-old asymptomatic recipient has stable creatinine at 1.4 mg/dL. Surveillance plasma BK PCR rises from 2,800 to 15,000 copies/mL on the same assay over 2 weeks. Tacrolimus trough is 9.4 ng/mL; urinalysis and ultrasound are unremarkable.

*Choose the next best step—not the entire eventual plan.*

ONE BEST ANSWER

**Which is the single best initial management step?**

**A** Start intravenous cidofovir.

**B** Add leflunomide and continue current immunosuppression.

**C** Reduce maintenance immunosuppression stepwise and repeat plasma BK PCR.

**D** Give IVIG.

**E** Give pulse methylprednisolone.

# Case 3 • Answer: reduce immunosuppression

**C**

**CORRECT ANSWER**

**Reduce maintenance immunosuppression stepwise and repeat plasma BK PCR.**

## WHY THIS IS RIGHT

- Plasma BK DNAemia above approximately 10,000 copies/mL on a validated assay is presumptive BK nephropathy and warrants prompt action.
- The treatment cornerstone is protocolized reduction of net immunosuppression, with serial viral-load and creatinine monitoring.
- Cidofovir, leflunomide, fluoroquinolones and routine IVIG are not standard first-line therapy.

## BOARD LOGIC

• In a stable-function adult, biopsy is not mandatory unless immunologic risk or diagnostic uncertainty is high.

• Pulse steroids can amplify viral replication when rejection has not been demonstrated.

• Use the same assay and follow trends every 2–4 weeks.

## BOARD PEARL

**For BK, treat the net state of immunosuppression—not the virus with an unproven antiviral.**

Source: Second International Consensus Guidelines on BK Polyomavirus, Transplantation 2024.

# Acute allograft dysfunction: biopsy is the pivot

**Classic biopsy indications**

### Clinical trajectory

Creatinine, urine output, proteinuria, time after transplant

### Alloimmune data

DSA, crossmatch history, adherence and C4d/microvascular injury


### Competing diagnoses

Ischemia, CNI toxicity, infection, recurrence, TMA, obstruction

### Adjunctive biomarkers

dd-cfDNA, viral PCR and molecular tissue tools—context, not replacement

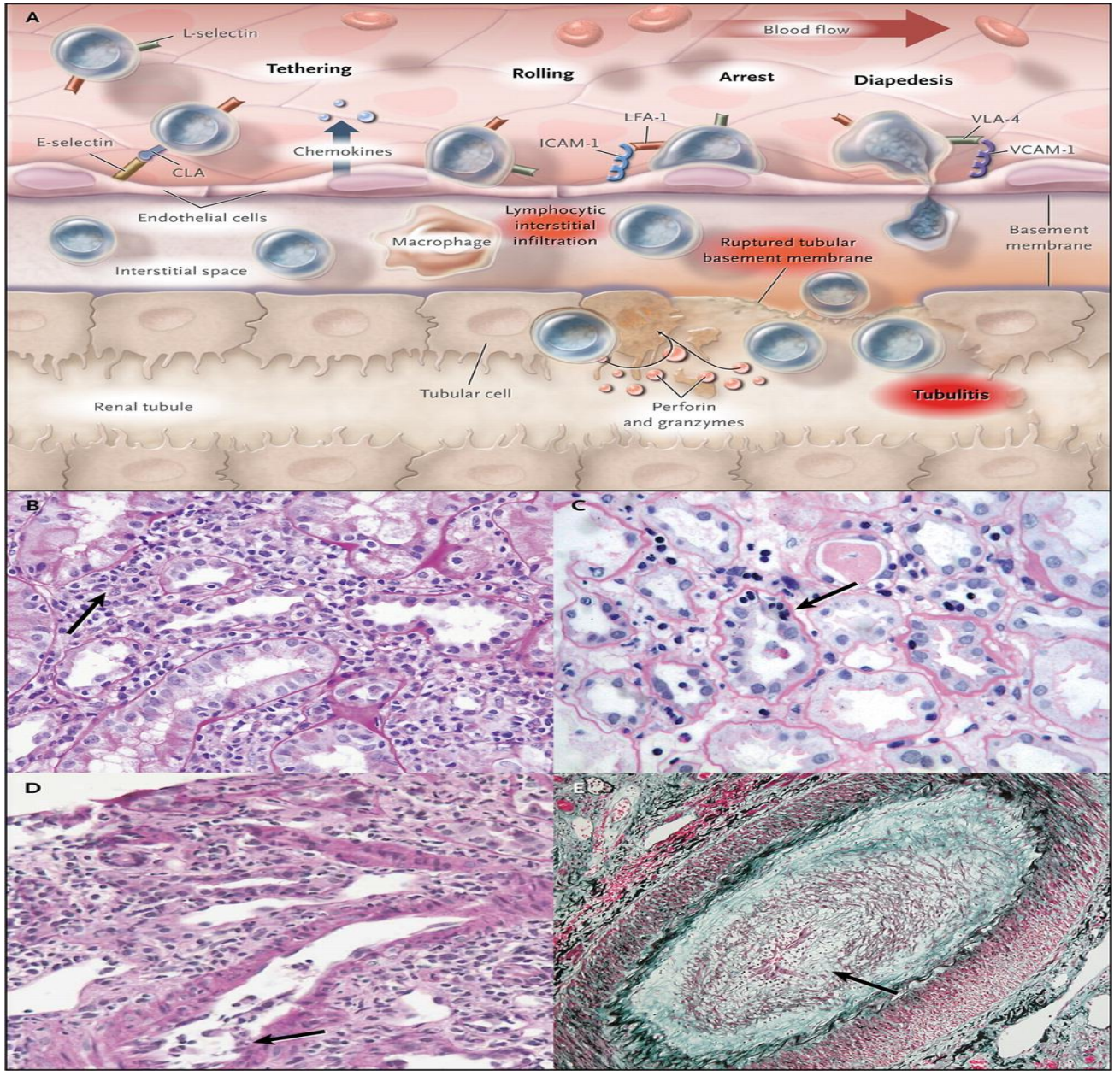
**Persistent unexplained creatinine rise • New proteinuria • DGF with slow/atypical recovery • Failure to return to baseline after treatment**

**Not every microvascular-inflammation pattern is classic DSA-positive AMR; use the Banff reasoning framework.**

Banff 2024 made (no classification changes from 2022)

# Acute T cell-mediated rejection

- T cell transport into the allograft after activation in the lymphoid organs
- T cells invading tubules causing T cell mediated rejection – Tubilitis
- Early reversible rejection no impact on long term
- Protocol biopsies have shown evidence of ‘rejection’ with stable kidney function
- Cell Free DNA not always elevated with acute rejection



# Acute T cell-mediated rejection

**BANFF criteria**

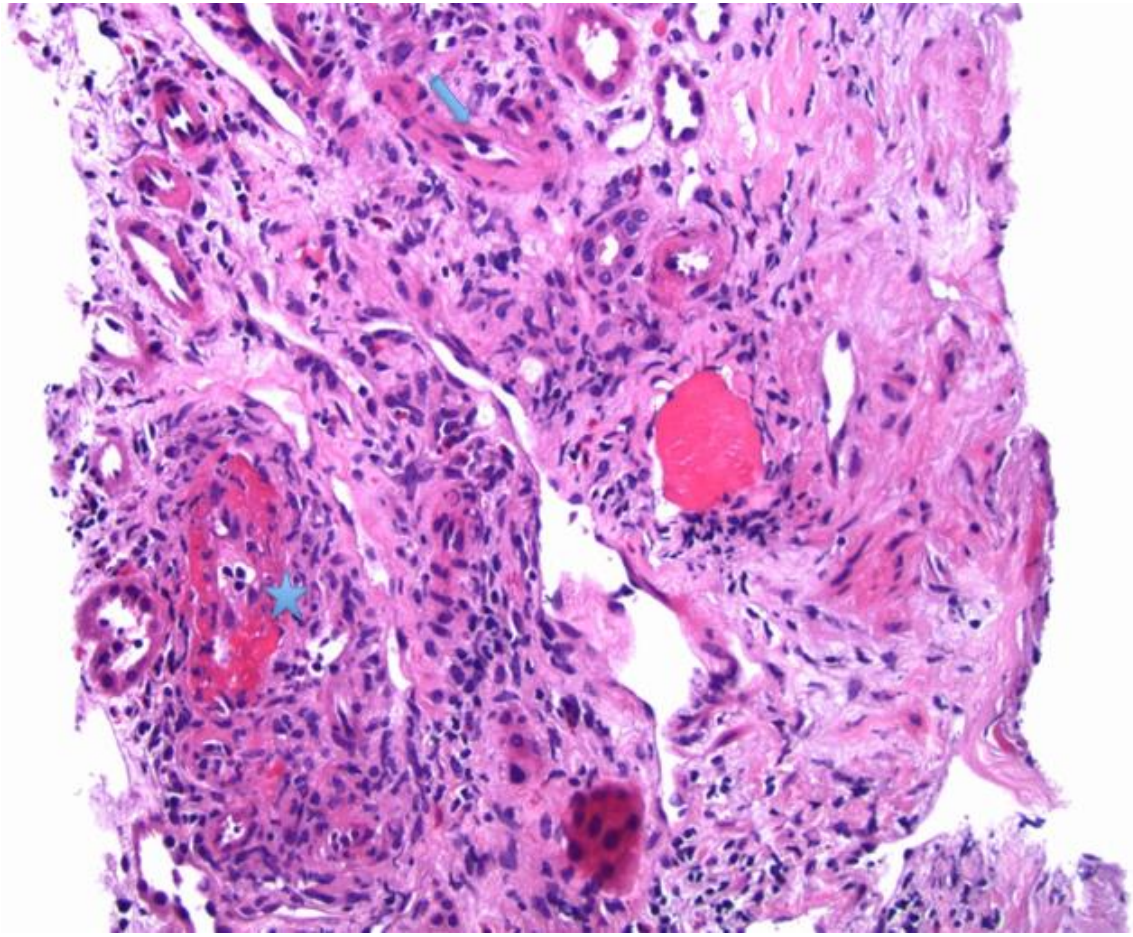
**Type IA** — Significant interstitial inflammation (>25 percent of parenchyma affected) and moderate tubulitis (>4 cells/section).

**Type IB** — Significant interstitial inflammation (>25 percent of parenchyma affected) and severe tubulitis (>10 cells/section)

**Type IIA** — Mild to moderate arteritis found in at least one arterial cross section.

**Type IIB** — Severe arteritis, which is associated with greater than 25 percent loss of luminal area

**Type III** — Transmural arteritis, and/or arterial fibrinoid alterations, and necrosis of medial smooth muscle cells occurring in association with lymphocytic inflammation of the vessel.



Necrosis indicates BANFF type 3 cellular rejection

# T-cell–mediated rejection (TCMR)

| Biopsy phenotype | Usual early treatment | What else to do | Board caution |
|---|---|---|---|
| **Borderline** | Treat if graft dysfunction or high-risk context, surveillance lesions are individualized | Review adherence, tacrolimus exposure, infection and maintenance regimen | “Borderline” is not synonymous with harmless |
| **Banff IA / IB** | IV methylprednisolone pulse, optimize baseline immunosuppression | Check response, tacrolimus, mycophenolate tolerance and missed doses | Biopsy, not creatinine alone, distinguishes rejection from BK/toxicity |
| **Banff IIA / IIB / III** | Lymphocyte-depleting therapy (commonly rATG) ± steroids | Evaluate for concomitant AMR, monitor cytopenia and infection | Vascular lesions imply greater severity |
| **Steroid-resistant / recurrent** | Lymphocyte-depleting therapy, re-biopsy when course is atypical | Reassess diagnosis, adherence, drug exposure and mixed rejection | Persistent creatinine rise may be irreversible injury or a different process |

### After treatment

Follow creatinine, urine protein and drug levels, biopsy if function fails to recover.

### Infection tension

Steroids/rATG worsen viral risk, resume intensified BK/CMV surveillance.

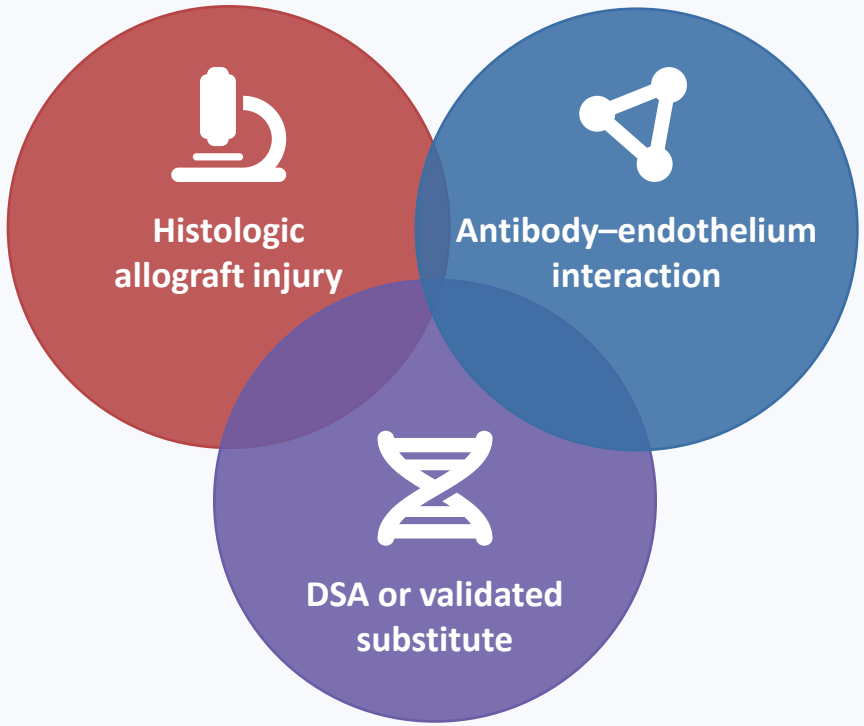
### BK tension

TCMR can occur during BK immunosuppression reduction—confirm the diagnosis.

Treatment framework: KDIGO 2009; Banff 2024.

# Antibody-mediated rejection (AMR)

## Diagnosis: integrate three domains




**There is no single FDA-approved standard AMR drug; treatment is phenotype- and center-dependent.**

## Early active AMR: common treatment backbone

1. Optimize baseline immunosuppression and adherence; treat concurrent TCMR
2. Plasma exchange + IVIG
3. Corticosteroids
4. Consider rituximab or other adjuncts case-by-case

### Chronic active AMR

Optimize tacrolimus/mycophenolate, adherence, BP/proteinuria and cardiovascular risk. Evidence for repeated PLEX/IVIG or novel agents is limited; use center-specific protocols and trials.

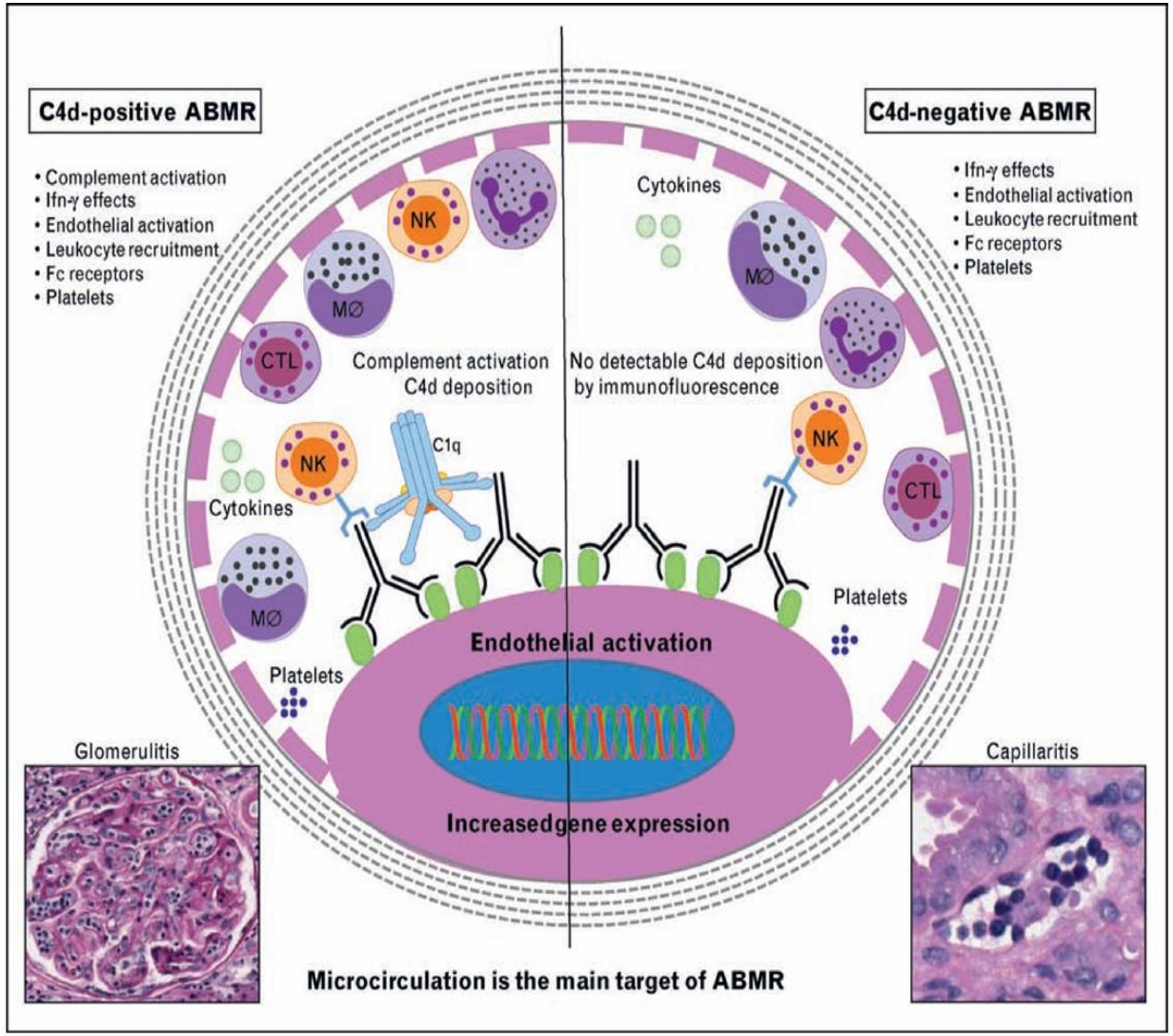
*Banff 2022/2024 reminder: "probable AMR" and MVI/DSA–/C4d are distinct categories but increasingly treated the same*

TTS expert consensus: Transplantation 2020

# Acute antibody-mediated rejection (AMR)

- The central feature is endothelial injury within the microvasculature.

- Risk factors for AMR:
  - Elevated PRA
  - Prior transplantation
  - Historically positive crossmatch,
  - Female sex.
  - No correlation with HLA match
  - Ischemic time, or donor characteristics.




Microcirculation inflammation (peritubular capillaritis and glomerulitis; bottom microscopic pictures) and damage (multilayering of basement membrane – dashed lines in the schematic capillary figure – and/or glomerular double contours, transplant glomerulopathy) are the typical histological lesions in allografts exposed to antibody-mediated injury (periodic acid–Schiff reagent staining, original magnification ×400). ABMR, antibody-mediated rejection; CTL, cytotoxic T lymphocytes; Mø, monocytes–macrophages; IFNγ, interferon-gamma; NK, natural killer.

# Clinical criteria of diagnosis of acute AMR

Morphologic evidence of tissue injury:

- **Type I: ATN-like histology with minimal inflammation**
- **Type II: capillary glomerulitis with margination and/or thrombosis**
- **Type III: arterial-transmural inflammation/fibrinoid changes**

Immunopathologic evidence for antibody mediated action:

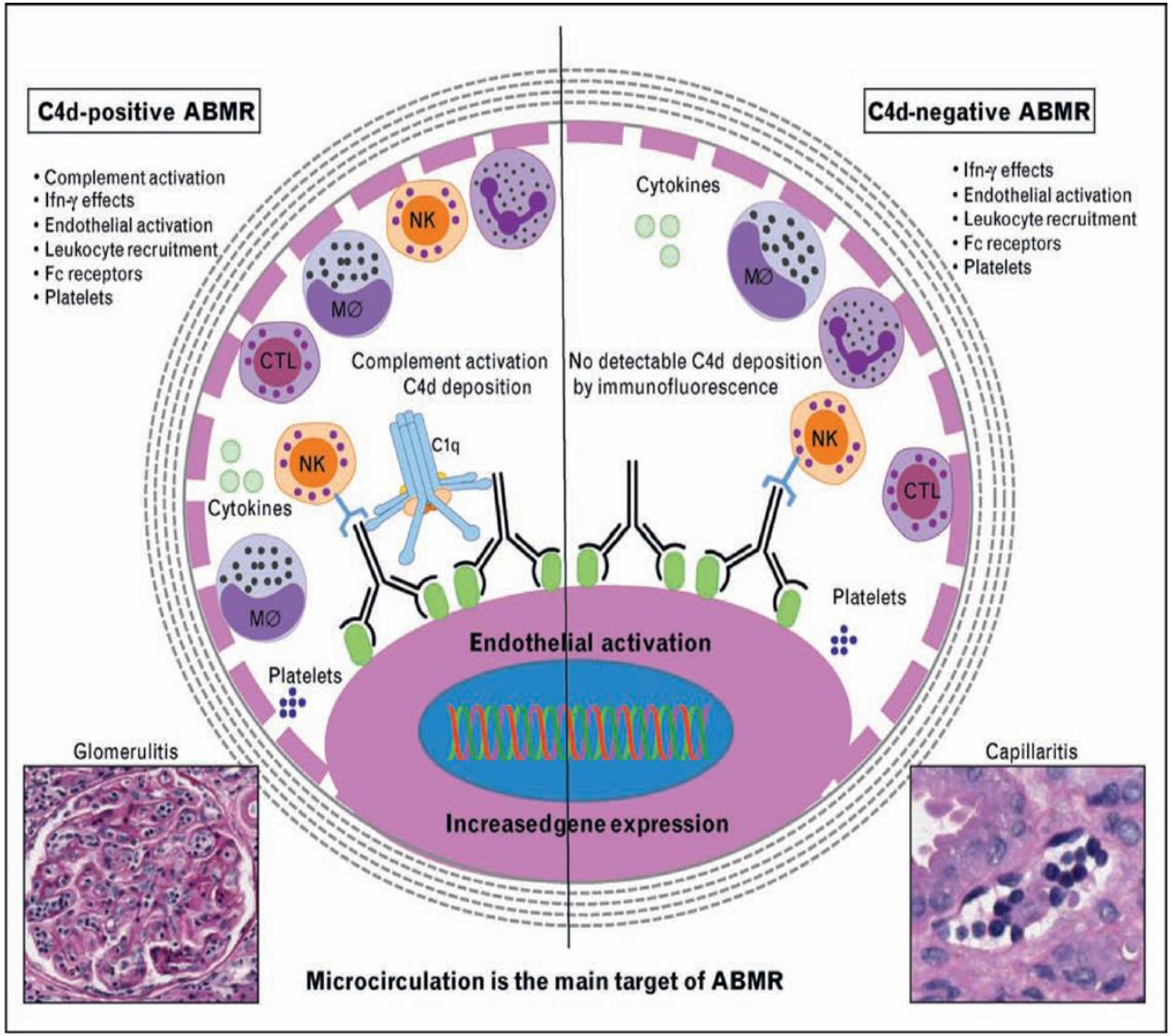
- **C4d deposition of the peritubular capillaries that can be diffuse or focal**

Serologic evidence for circulating antibodies to

- **Donor HLA**
- **Donor endothelial antigens.**

***Chronic* antibody-mediated rejection:**

- **Morphologic features of transplant glomerulopathy,**
- **C4d deposition in proximal tubular cells**
- **Presence of DSA**

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# Incidence and Prognosis of AMR

- Antibody mediated rejection resulting in graft dysfunction is estimated to occur in **3 to 10 % of high risk renal transplants**
- In general: antibody-mediated immunologic processes portend **a worse prognosis**
- In addition- recent studies suggest that chronic immune injury mediated by anti-donor antibodies may account for the **majority of graft losses**

# Treatment for Antibody Mediated Rejection

| Treatment | Mechanism | Approval Status (U.S.) |
|---|---|---|
| Plasmapheresis | Removes DSAs | Standard use; not FDA-approved for AMR |
| IVIG | Immunomodulation | FDA-approved (not for AMR) |
| Rituximab | B-cell depletion | Off-label |
| Bortezomib | Plasma cell depletion | Off-label |
| Eculizumab | Complement inhibition | Off-label for AMR |
| Tocilizumab | IL-6 pathway inhibition | Off-label |
| Imlifidase (IdeS) | IgG cleavage | EU-approved (desensitization); under study in U.S. |

# Experimental Agents for Treatment of AMR

| Agent | Target | Stage | Notes |
|---|---|---|---|
| Felzartamab | CD38 (plasma cells) | Early-phase trial | M-PLACE study |
| Clazakizumab | IL-6 | Phase 3 | IMAGINE trial for chronic AMR |
| Daratumumab | CD38 | Case series | Used off-label |
| Belatacept | Co-stimulation | Investigational | Also used in maintenance |
| C1-INH | Complement | Case reports | Not routinely used |
| Inebilizumab | CD19 | Preclinical | More potent B-cell depletion |
| CAR-T | CD19/BCMA | Preclinical | Experimental |

# Post-transplant TMA and catastrophic APS: act before the label is perfect

## Recognize the syndrome

- Graft dysfunction ± hypertension
- Falling platelets
- LDH ↑, haptoglobin ↓, schistocytes
- Hemolysis may be absent in kidney-limited TMA
- Biopsy may show acute TMA or microvascular injury

Do not wait for the full pentad of TTP.

## Same-day etiologic work-up

- CBC/smear, LDH, haptoglobin, bilirubin, reticulocytes
- Coagulation profile, creatinine, urinalysis, tacrolimus level
- DSA/C4d/biopsy; infection testing
- ADAMTS13 before plasma therapy if possible
- Complement history/genetics and antiphospholipid antibodies when indicated

## Treat by mechanism

**CNI / ischemia / infection / AMR**
- Remove trigger, reduce/switch CNI, treat infection or AMR

**TTP**
- Urgent plasma exchange + steroids ± caplacizumab

**Complement-mediated TMA**
- C5 blockade in a compatible phenotype

**Catastrophic APS**
- Therapeutic anticoagulation + high-dose steroids + PLEX and/or IVIG; treat trigger

**CAPS = rapidly progressive multiorgan thrombosis - known APS requires an explicit perioperative anticoagulation plan.**

Mechanism-directed treatment; CAPS “triple therapy” supported by EULAR/registry guidance.

# Recurrent disease and genetic risk: surveillance starts immediately

| Disease | Earliest clue / timing | Risk discriminator | Early management |
|---|---|---|---|
| **Primary FSGS** | Hours–days: abrupt nephrotic proteinuria | Primary circulating-factor phenotype high risk monogenic/secondary forms usually low recurrence | Daily UPCR/albumin in high risk, prompt PLEX ± rituximab - not proven for treatment/prophylaxis |
| **Complement-mediated aHUS** | Hours–months: TMA, graft. dysfunction, hypertension | Complement variant and prior recurrence history | Peri-/post-transplant C5 blockade for selected high-risk patients; urgent treatment of recurrence |
| **IgA Nephropathy** | Hours-years: Often visible on histology | Course of native IgA Nephropathy | Maybe reason to avoid early steroid withdrawal, conventional IgA therapies |
| **C3G / immune-complex MPGN** | Proteinuria/hematuria - can be early but often later | Complement / monoclonal driver | UA/UPCR, complement/monoclonal work-up and biopsy; mechanism-specific therapy |
| **Alport anti-GBM (rare)** | Weeks–months: hematuria and rapidly worsening function | COL4A5 phenotype and antibody formation | Biopsy; anti-GBM treatment approach |

**APOL1 is a donor-genotype is potentially an allograft risk— but not recurrence of recipient 'APOL1-related risk'**

KDIGO recurrence screening; genetic diagnosis refines recurrence probability and prophylaxis.

# Case 4 • Hemolysis, thrombocytopenia and graft dysfunction

4

CLINICAL STEM

## RAPID-FIRE CASE 4

On day 10 after transplant, creatinine rises from 1.9 to 3.4 mg/dL. Hemoglobin falls from 10.2 to 7.9 g/dL, platelets from 210 to 55 $\times 10^9$/L, LDH is high, haptoglobin is undetectable, and schistocytes are present. Tacrolimus trough is 14 ng/mL and a new class II DSA is detected.

*Choose the next best step—not the entire eventual plan.*

ONE BEST ANSWER

**Which is the single best next step?**

**A** **Treat as immune TTP with plasma exchange alone.**

**B** **Give platelets and observe.**

**C** **Evaluate TMA urgently - biopsy if safe, reduce or hold tacrolimus and treat the trigger.**

**D** **Start eculizumab in every case.**

**E** **Continue tacrolimus and give steroids only.**

# Case 4 • Answer: diagnose the TMA mechanism

**C**

CORRECT ANSWER

**Urgent TMA evaluation, biopsy if safe, calcineurin-inhibitor adjustment and mechanism-directed treatment.**

WHY THIS IS RIGHT

- Post-transplant TMA is a syndrome with multiple causes: calcineurin-inhibitor toxicity, AMR, TTP, complement-mediated TMA, infection, APS and ischemic injury.
- Send hemolysis studies, ADAMTS13 and targeted complement/infectious testing; biopsy can define graft-limited TMA and support an AMR diagnosis.
- Remove or reduce the provoking drug and treat the driver—AMR therapy, urgent plasma exchange for likely TTP, or complement blockade when indicated.

BOARD LOGIC

• Not every TMA is TTP, and not every TMA requires eculizumab.

• If clinical suspicion for TTP is high, plasma exchange should not await the ADAMTS13 result.

• Avoid platelet transfusion unless there is major bleeding or a procedure-related need.

BOARD PEARL

**TMA is a syndrome: identify and treat the mechanism before the label becomes perfect.**

Sources: Banff/TTS AMR framework; contemporary post-transplant TMA reviews and mechanism-directed algorithms.

# Case 5 • Nephrotic proteinuria on postoperative day 3

5

CLINICAL STEM

## RAPID-FIRE CASE 5

A 32-year-old man with kidney failure attributed to primary FSGS had nephrotic syndrome before dialysis and no pathogenic podocyte-gene variant. On postoperative day 3, creatinine is 1.2 mg/dL, but edema develops, serum albumin is 2.3 g/dL, and UPCR is 9 g/g. Doppler is normal.

*Choose the next best step—not the entire eventual plan.*

ONE BEST ANSWER

**Which is the single best next step?**

- **A** **Observe, this is expected ischemic tubular injury.**
- **B** **Start an ACE inhibitor alone.**
- **C** **Start prompt plasma exchange for presumed recurrence; obtain biopsy and EM in parallel.**
- **D** **Give pulse methylprednisolone for TCMR.**
- **E** **Convert tacrolimus to sirolimus.**

# Case 5 • Answer: treat recurrent primary FSGS

**C**

CORRECT ANSWER

**Treat presumed recurrent primary FSGS promptly with plasma exchange; obtain biopsy/electron microscopy in parallel.**

## WHY THIS IS RIGHT

- Recurrent primary FSGS often presents within hours to days as abrupt nephrotic-range proteinuria despite preserved graft filtration.
- Early biopsy may show diffuse podocyte foot-process effacement before segmental sclerosis is visible on light microscopy.
- Plasma exchange is the usual first-line treatment; rituximab or other adjuncts are center-specific and supported by lower-quality evidence.

## BOARD LOGIC

- RAAS blockade is useful later as adjunctive antiproteinuric therapy, not as sole acute treatment.
- Monogenic and secondary forms generally have much lower recurrence risk.
- mTOR inhibitors may worsen proteinuria and are unattractive during early wound healing.

## BOARD PEARL

**Very early nephrotic proteinuria after transplant = recurrent primary FSGS until proved otherwise.**

Sources: KDIGO recurrence guidance; international clinical-practice recommendations for recurrent FSGS.

# Infection prevention by time after transplant

## 0–1 month

**Surgical / nosocomial / donor-derived**

- Bacterial UTI, wound and line infection
- Pneumonia, C. difficile, candiduria
- Donor-transmitted HBV/HCV or unusual pathogens
- Technical complications that mimic infection

## 1–6 months

**Peak net immunosuppression**

- CMV, BK and EBV
- PJP, Nocardia, herpesviruses
- Invasive fungi or TB in epidemiologic risk
- Prophylaxis toxicity and breakthrough disease

## >6 months

**Community pattern if stable**

- Respiratory and urinary infections
- Opportunistic infection after rejection therapy or overimmunosuppression
- Malignancy-related viral disease

## Prevention bundle

### TMP–SMX

PJP prophylaxis but also UTI/Nocardia/toxo benefit

### CMV

Prophylaxis or preemptive PCR by D/R and induction

### Devices

Remove lines/Foley promptly and defined stent plan

### Vaccines

No live vaccines post-transplant; update inactivated vaccines when timing permits

# Viral surveillance: what to test, when and why

| Virus | Who / schedule | Action threshold or strategy | Key limitation / pitfall |
|---|---|---|---|
| **BK polyomavirus** | All KTRs: plasma PCR monthly to month 9, then q3 months to 2 years | 1,000–10,000 copies/mL: confirm in 2–3 weeks persistent >1,000 or >10,000: stepwise immunosuppression reduction | Use same specimen/assay; no established antiviral leflunomide/cidofovir/quinolone/ IVIG treatment not routine |
| **CMV** | D+/R− kidney: 6 months prophylaxis or preemptive; R+: 3 months prophylaxis or preemptive testing | Preemptive strategy requires approximately weekly PCR and rapid treatment at center threshold | Renal-dose valganciclovir, leukopenia, assay thresholds for treatment are center-specific |
| **EBV / PTLD risk** | Serial EBV DNA in high-risk D+/R−, pediatric, T-cell–depleted or belatacept patients, especially first year | Rising DNAemia → clinical evaluation and usually immunosuppression reduction | No universal viral-load threshold, plasma vs whole-blood results are not interchangeable |
| **HHV-8 / KSHV** | Jurisdiction- and risk-based, consider donor/recipient epidemiology and syndromic monitoring | Unexplained fever, cytopenia, adenopathy, effusions or Kaposi lesions → urgent testing/oncology | Practice varies -UK deceased-donor screening vs risk-based approaches elsewhere inc USA |

**After rejection treatment or a major increase in immunosuppression, restart intensified viral surveillance.**

BK consensus 2024; CMV consensus 2025; AST IDCOP EBV/PTLD.

# Protocol biopsy and emerging surveillance tests

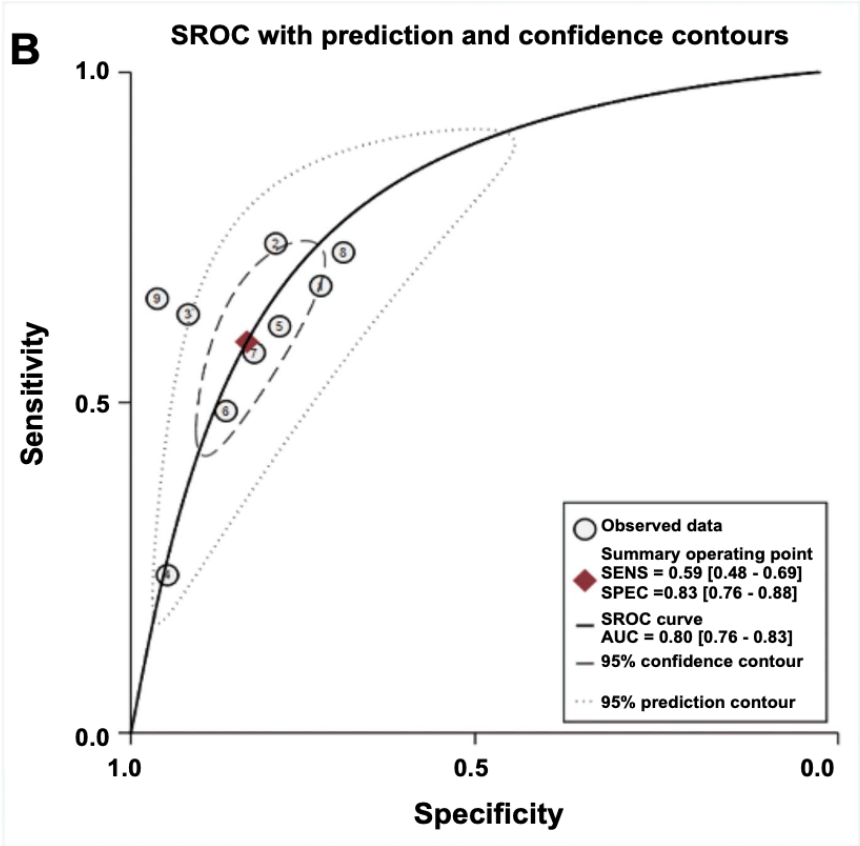
| Tool | Best use | Strength | Limitation / board interpretation |
|---|---|---|---|
| **DSA** | **Alloimmune risk and AMR context** | **Mechanistically relevant, serial change can matter** | **Antibody is not the same as tissue injury, interpret with biopsy/clinical data** |
| **Protocol biopsy** | **Subclinical rejection, BK, recurrence and chronic injury** | **Direct tissue diagnosis** | **Bleeding, sampling and interobserver variability, outcome benefit is center/population dependent** |
| **Blood gene expression (TruGraf / OmniGraf)** | Immune quiescence or subclinical-risk assessment in stable recipients | Noninvasive and repeatable | No guideline currently recommends routine use to diagnose/exclude rejection, platform-specific evidence |
| **Urine CXCL9 / CXCL10** | Inflammation signal in stable or dysfunctional grafts | May be promising for tubulointerstitial inflammation | Infection confounds, assay standardization, and availability more limited |
| **dd-cfDNA (AlloSure, Prospera, TRAC)** | Adjunct for graft injury, strongest signal for AMR, serial monitoring in selected programs | Negative value in some contexts, adds information beyond creatinine | Ischemia, infection and other injury can elevate, low result does not exclude TCMR, does not replace biopsy |
| **Biopsy transcriptomics (MMDx)** | Adjunct in complex or discordant biopsies | Quantitative molecular phenotype | Requires tissue, cost/availability, complements rather than replaces histology |

**Persistent graft dysfunction still gets an indicated biopsy—even when a commercial biomarker is reassuring.**

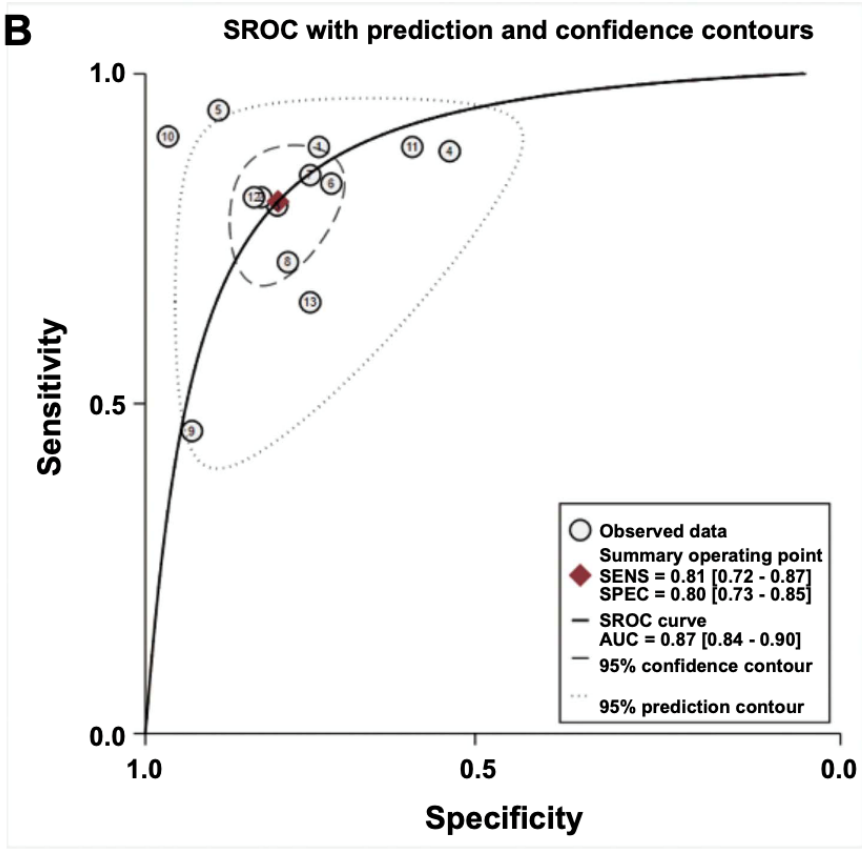
ESOT consensus: Park et al. Transpl Int 2024.

# sROC with Prediction and Confidence Contours of dd-cfDNA in Acute Kidney Transplant Rejection

## Cellular Rejection




## Antibody Mediated Rejection




Xing Y, et al Donor-derived cell-free DNA as a diagnostic marker for kidney-allograft rejection: A systematic review and meta-analysis. Biomol Biomed. 2024

natera™

# Electrolytes, bone-mineral and hematologic problems

## Hyperkalemia

CNI + TMP–SMX + DGF + acidosis ± RAAS blockade.

ECG and standard acute therapy; review triggers. Binders or fludrocortisone are selected options—not substitutes for diagnosis.

## Hyponatremia

Assess volume and tonicity. Consider hyperglycemia, SIADH, polydipsia, diuretics and adrenal insufficiency after rapid steroid change. Correct safely as in nontransplant patients.

## Mg / phosphate

Tacrolimus causes Mg wasting; persistent PTH/FGF23 drives phosphaturia. Replace cautiously and monitor GI tolerance and calcium.

## Hypercalcemia / PTH

Check Ca, phosphate, PTH and 25-OH vitamin D. Many improve over months, use cinacalcet for significant persistent hypercalcemia and surgery for severe/refractory disease.

## Anemia and cytopenia

Bleeding, DGF, iron/B12/folate, hemolysis/TMA, CMV/parvovirus and marrow suppression from MMF/valganciclovir/TMP–SMX. Avoid unnecessary transfusion and sensitization.

## Hyperlipidemia

Check a fasting profile around 2–3 months and after major therapy change. Statins are commonly indicated; choose dose with CNI interactions in mind—especially cyclosporine.

## When the pattern is wrong

Hyperkalemia + thrombocytopenia + LDH rise → TMA.
Persistent hypercalcemia + graft dysfunction → nephrocalcinosis/volume effects.
Pancytopenia + fever → infection or drug toxicity.

**Do not “normalize the number” without explaining the mechanism; many abnormalities are the first clue to drug toxicity, infection or TMA.**

# PTDM, weight gain, lipids and kidney-protective drugs

**Immediate postoperative instability** → **Stable graft / wound / intake / infection status**

## Early hyperglycemia

- Insulin is preferred while steroid dose, intake and GFR fluctuate
- Do not rush to label permanent PTDM in an unstable patient
- HbA1c is unreliable early with anemia, transfusion and rapid metabolic change
- Reassess after the early postoperative period

## GLP-1 receptor agonist

**Best fit: obesity and diabetes after stabilization.**

- Observational transplant data suggest weight and glycemic benefit
- Slow titration; GI intolerance is common
- Monitor tacrolimus when intake or gastric emptying changes

## SGLT2 inhibitor

**Use once graft function is stable.**

- Consider heart failure/CKD benefit
- Avoid during acute illness, fasting, volume depletion or significant urosepsis risk
- Watch euglycemic DKA and early catheter/stent context

## RAAS blockade / MRA

**ACEi/ARB**

- Proteinuria/HTN after K and creatinine stabilize

**MRA / finerenone**

- Hyperkalemia concern
- Transplant outcome evidence remains limited; not routine early postoperative therapy

**Novel CKD drugs are usually “stable-graft decisions,” not postoperative day-3 decisions.**

International PTDM consensus: Sharif et al. Nephrol Dial Transplant 2024.

# Psychological and systems risk is graft risk

## Patient factors

- Delirium, depression, anxiety or cognitive impairment
- Health literacy and language
- Substance use or unstable psychiatric disease
- Steroid psychosis, sleep loss or tacrolimus neurotoxicity
- Grief, guilt and unrealistic expectations

## Regimen factors

- Teach-back of exact medication times
- Pillbox, written calendar and one pharmacy
- Plan for vomiting, diarrhea and missed doses
- Reconcile every external prescription
- High tacrolimus variability = interaction, absorption or adherence signal
- Simplify when safe

## System factors

- Caregiver and transport
- Pharmacy coverage and copay burden
- Lab access, phone/internet and secure housing
- Interpreter and culturally safe education
- Same-day transplant contact pathway
- Multidisciplinary pharmacy, social work and psychology support

**A “nonadherent patient” may have an inaccessible regimen.**

# Case 6 • Early post-transplant hyperglycemia

6

CLINICAL STEM

## RAPID-FIRE CASE 6

Four weeks after transplant, a 61-year-old recipient with BMI 36 kg/m² has fasting glucose 180–220 mg/dL and post-meal values 280–340 mg/dL while receiving tacrolimus and tapering prednisone. eGFR fluctuates between 28 and 42 mL/min/1.73 m², oral intake is variable and the ureteral stent remains in place.

*Choose the next best step—not the entire eventual plan.*

ONE BEST ANSWER

**Which is the single best initial treatment?**

A **Start empagliflozin now.**

B **Start semaglutide now.**

C **Begin basal–bolus insulin, reconsider other agents after graft and urologic stability.**

D **Stop tacrolimus and prednisone.**

E **Defer treatment until HbA1c is checked at 3 months.**

# Case 6 • Answer: insulin during instability

**C**

**CORRECT ANSWER**

**Begin basal–bolus insulin and defer other agents until the graft, volume, intake and urologic status are stable.**

## WHY THIS IS RIGHT

- Early post-transplant glycemia changes rapidly with steroid dose, kidney function, nutrition and acute illness, insulin is immediately titratable.
- Do not compromise essential anti-rejection therapy solely to control glucose; adjust immunosuppression only through a transplant-risk framework.
- SGLT2 inhibitors and GLP-1 receptor agonists may be considered later in stable recipients after individualized assessment.

## BOARD LOGIC

- HbA1c is unreliable early after transplantation because of anemia, transfusion and rapid glycemic change.
- Unstable eGFR, variable intake and an indwelling stent increase practical concerns with immediate SGLT2 or GLP-1 initiation.
- Treat clinically important hyperglycemia now; formal PTDM classification can wait for stability.

## BOARD PEARL

**Stage-gate metabolic drugs: stabilize the graft, volume, intake and infection risk first.**

Source: International Consensus on Post-Transplantation Diabetes Mellitus, NDT 2024.

# Rapid-fire board cases 7-11

**7** **POD 5: urine output falls as clear drain output rises; drain creatinine 28 vs serum 2.1.**

BEST NEXT STEP

Maintain bladder decompression; urgent transplant-urology review for ureteric stent and/or nephrostomy.

**8** **Week 4: 10-cm lymphocele causes leg edema, hydronephrosis and a creatinine rise.**

BEST NEXT STEP

Percutaneous catheter drainage; fenestrate if the collection persists or recurs.

**9** **POD 16: tremor, K 6.1 and AKI; tacrolimus trough 24 after fluconazole.**

BEST NEXT STEP

Hold/reduce tacrolimus, reassess the azole, treat hyperkalemia and monitor trough and creatinine closely.

**10** **CMV D+/R- recipient receives rATG; the center uses universal prophylaxis.**

BEST NEXT STEP

Use renally adjusted valganciclovir for **6 months.**

**11** **Month 2: EBV D+/R- after rATG; rapidly rising DNAemia without PTLD symptoms.**

BEST NEXT STEP

Reduce net immunosuppression; repeat EBV NAT and perform close clinical assessment.

# Rapid-fire board cases 12-16

**12** **POD 2: HCV-negative recipient of an HCV NAT-positive kidney; stable, RNA still negative.**

BEST NEXT STEP

Start a pangenotypic direct-acting antiviral now; do not wait for recipient viremia.

**13** **Immune recipient (anti-HBs 185) is offered an HBsAg-negative, anti-HBc-positive, NAT-negative kidney.**

BEST NEXT STEP

Proceed without routine antiviral prophylaxis; continue post-transplant HBV surveillance.

**14** **Retransplant candidate: cPRA 98%, preformed DSA and a negative flow crossmatch.**

BEST NEXT STEP

Use lymphocyte-depleting induction such as rabbit ATG, balancing infection and cytopenia risk.

**15** **First transplant, no DSA, low immunologic/recurrence risk; induction plus tacrolimus/MMF planned.**

BEST NEXT STEP

Appropriate candidate for steroid discontinuation in the first week with close monitoring.

**16** **POD 10: obese diabetic recipient; draining wound and large lymphocele; tacrolimus tremor.**

BEST NEXT STEP

Defer sirolimus/everolimus until the wound and lymphocele resolve and graft function is established.

# Rapid-fire board cases 17-21

**17** **Month 3: severe calcineurin-inhibitor neurotoxicity; recipient is EBV seronegative.**

BEST NEXT STEP

Do not use belatacept; EBV seronegativity is a contraindication.

**18** **Week 3: creatinine rises; ultrasound is normal; biopsy shows Banff IA T-cell-mediated rejection.**

BEST NEXT STEP

Give pulse intravenous corticosteroids and optimize maintenance immunosuppression.

**19** **Day 10: sensitized recipient; graft dysfunction, microvascular inflammation, C4d positive and rising DSA.**

BEST NEXT STEP

Plasma exchange plus IVIG and corticosteroids; optimize baseline immunosuppression.

**20** **Unexplained creatinine rise; donor-derived cell-free DNA is low and DSA is negative.**

BEST NEXT STEP

AMR is less likely, but TCMR and non-rejection injury remain possible; biopsy if dysfunction persists.

**21** **Deceased-donor kidney has prolonged cold ischemia and a high predicted risk of DGF.**

BEST NEXT STEP

Use hypothermic machine perfusion where available; it lowers but does not eliminate DGF.

# Rapid-fire board cases 22-26

**22** **Pathogenic CFH variant; a previous allograft was lost rapidly to recurrent complement-mediated aHUS.**

BEST NEXT STEP

Plan perioperative eculizumab with transplant/hematology and meningococcal infection prevention.

**23** **Month 2: resistant hypertension, bruit and ACEi-associated AKI; focal anastomotic stenosis confirmed.**

BEST NEXT STEP

Perform percutaneous angioplasty, with stent placement when indicated.

**24** **Month 3: calcium 11.6, phosphate 1.8 and PTH 760; hydration ineffective and surgery delayed.**

BEST NEXT STEP

Start cinacalcet; pursue parathyroidectomy if severe or medically refractory.

**25** **CMV treatment: DNAemia falls on renal-adjusted valganciclovir; ANC 900 on MMF and TMP-SMX.**

BEST NEXT STEP

Maintain effective antiviral dosing if possible; adjust other myelosuppressants and consider G-CSF.

**26** **POD 1-7: triple-positive APS, anticoagulation interrupted; multiorgan thrombosis plus MAHA.**

BEST NEXT STEP

Therapeutic heparin plus high-dose steroids plus plasma exchange/IVIG; treat triggers urgently.

# Day 0–90 checklist

## Every encounter

□ BP, weight, temperature, edema

□ Medication reconciliation and trough timing

□ Wound, urine, Foley/stent/drain status

□ Adherence, side effects and access barriers

□ Creatinine trend—not just value

## Core laboratory panel

□ Creatinine/eGFR, BUN

□ Na, K, $HCO_3$, Mg, phosphate, Ca, glucose

□ CBC; LFTs when indicated

□ Tacrolimus trough

□ UA and urine protein

## Risk-based tests

□ BK and CMV per protocol

□ EBV high-risk surveillance

□ DSA after dysfunction or high-risk protocol

□ Hemolysis/TMA panel

□ HCV/HBV NAT and liver tests

□ Disease-specific recurrence tests

## Escalate today

□ Abrupt anuria or graft change

□ Fever or sepsis physiology

□ Severe K/acidosis/volume overload

□ Rising creatinine without explanation

□ New nephrotic proteinuria

□ Platelet fall + hemolysis or thrombosis

Use as a one-slide clinic or ward checklist; adapt to local protocol.

# High-yield tacrolimus interactions

| Effect on tacrolimus | Examples | Clinical response |
|---|---|---|
| **Markedly increases exposure** | Azole antifungas, clarithromycin/erythromycin, ritonavir/cobicistat, grapefruit, some calcium-channel blockers | Preemptive dose reduction or avoidance, frequent troughs and renal/electrolyte monitoring |
| **Decreases exposure** | Rifampin/rifabutin, carbamazepine, phenytoin, phenobarbital, St John's wort | Avoid when possible, specialist dose strategy and close trough monitoring |
| **Absorption / metabolism changes** | Inflammatory diarrhea often raises exposure, vomiting or poor intake causes unreliable dosing, major weight change can alter kinetics | Check a true trough and clinical status before changing dose |
| **Additive nephrotoxicity or hyperkalemia** | NSAIDs; aminoglycosides; amphotericin, TMP–SMX; ACEi/ARB/MRA, contrast in high-risk settings | Avoid unnecessary combinations; monitor creatinine, K, Mg and BP |
| **(Mycophenolate issues)** | Antacids/binders reduce absorption, cholestyramine reduces exposure, acyclovir/valganciclovir increase marrow toxicity | Separate dosing when appropriate, monitor CBC and clinical efficacy |

**A new prescription, diarrhea or abrupt kidney dysfunction is an indication to recheck tacrolimus—not merely to "watch the creatinine."**

# Summary: biopsy and viral surveillance pearls

## When biopsy is the answer

- Persistent unexplained creatinine rise
- DGF with slow or atypical recovery
- Failure to return to baseline after rejection treatment
- New or unexplained significant proteinuria
- Suspected mixed rejection, recurrent disease or graft-limited TMA

Biopsy after excluding urgent vascular/obstructive causes.

## BK essentials

- Plasma PCR monthly to month 9; q3 months to year 2
- 1,000–10,000 copies/mL: repeat in 2–3 weeks
- Persistent >1,000 or >10,000: reduce immunosuppression
- Same laboratory/assay when following trends
- No routine leflunomide, cidofovir, fluoroquinolone or IVIG

## CMV essentials

- Kidney D+/R−: 6 months prophylaxis or rigorous preemptive strategy
- R+: 3 months prophylaxis or preemptive strategy
- Preemptive monitoring is approximately weekly
- Renal-dose valganciclovir; monitor CBC
- After lymphocyte-depleting rejection therapy, re-establish prevention/monitoring

# Take Home Messages

1. Time since transplant narrows the differential.
2. Trend urine output and creatinine—never one isolated value.
3. Sudden anuria is a vascular/obstructive emergency.
4. DGF can hide rejection - image, then biopsy when unexplained.
5. Risk-match induction and tacrolimus + mycophenolate ± steroid is the default.
6. Early AMR commonly uses PLEX + IVIG + steroids; adjunct evidence is limited.
7. TMA is a syndrome—find and treat the mechanism.
8. BK: monthly to month 9-12. CMV prevention follows donor/recipient risk.
9. Biomarkers complement,they do not replace an indicated biopsy.
10. Start SGLT2/GLP-1/RAAS/MRA therapy only after graft, potassium, volume and infection status stabilize.

The early transplant recipient is managed by a team—but the nephrologist must recognize the emergency, the biopsy indication and the risk trade-off.

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Thank you for your attention

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