Robert's Review of Pediatric Nephrology

Third Edition

Update #1 – November 2026

This document contains updates, corrections and supplemental information.

20. Maintenance and replacement fluids

- Clarification: On Table 20.1, the units are mEq/L.

28. Hypokalemia

Combined therapeutic hypothermia and barbiturate coma

- Therapeutic hypothermia and barbiturate coma *each* cause hypokalemia in >80% of patients due to intracellular potassium movement
  - When used in combination, the effects are amplified
- Patients may also develop a rebound hyperkalemia when either therapy is withdrawn

29. Hyperkalemia

Causes of artifactual hyperkalemia

- Severe leukocytosis
  - Patients with extremely high WBC counts may have falsely elevated potassium results due to cell fragility and damage during the transport and centrifugation process
  - Suspect this when a patient has very high potassium result without any EKG changes
    - The easiest way to avoid this is to use whole blood (uncentrifuged) specimens, such as a point-of-care blood gas analyzers (which usually measure electrolytes as well)
    - This can also be done by using serum from a clotted specimen (using an anticoagulant-free or serum separator tube) but most laboratories are not set up to do this
  - Of course, patients with very high WBC counts may have true hyperkalemia due to tumor lysis syndrome

65. Kidney structure/function assessments

On page 67, regarding cystatin C, the phrase "Still under investigation and not widely available for clinical use" should be deleted. Cystatin C is readily available at most laboratories, is commonly used, and is endorsed by guidelines.

68. Hematuria and proteinuria

Other genetic causes of proteinuria

- Biallelic variants in *CUBN* may cause significant albuminuria, without hematuria
  - The proteinuria may be nephrotic-range, but is rarely associated with edema or decreased serum albumin
  - Renal biopsies are generally normal or show only minimal foot process effacement
  - This disorder does not appear to be progressive, does not lead to loss of GFR, and does not respond to treatment with RAS inhibition or immunosuppression
  - Early genetic diagnosis may prevent unnecessary biopsy and treatment

69. Congenital and infantile nephrotic syndrome

Galloway-Mowat syndrome [ar]

- Not all cases have identified genes

- Most common gene is *WDR73*
- At least 10 subtypes have been identified
- Associated genes include *OSGEP, LAGE3, TP53RK, TPRKB, WDR4, NUP107, NUP133, GON7, YRDC*

70. Introduction to nephrotic syndrome

- **Obinutuzumab** (Gazyva™) is now FDA-approved "to reduce the risk of relapse in adult and pediatric patients 2 years of age and older with frequently relapsing or steroid dependent childhood-onset idiopathic nephrotic syndrome who are in complete remission." Obinutuzumab is a fully humanized anti-CD20 monoclonal antibody. (Rituximab is chimeric; it is part mouse and part human antibody, hence the higher risk of allergic reactions.) It is also approved to treat adults with primary membranous nephropathy.
- **Sparsentan** (Filspari™) is now FDA-approved for FSGS in patients 8 years and older, without nephrotic syndrome
  - The IgA nephropathy indication remains limited to adults
  - The FSGS dose is twice that of the IgAN dose

85. Granulomatosis with polyangiitis

In table 85.1, the term "Goodpasture syndrome/disease" should be replaced with the newer preferred nomenclature, anti-GBM disease, with or without pulmonary hemorrhage.

90. IgA nephropathy

This field continues to evolve so quickly, it's very hard to stay up to date. Nothing is new in pediatrics, but several new drugs have been approved for adults. KDIGO has released a 2026 "commentary[a]" that is not really a guideline update, but it does open the door to the newer therapies they previously did not endorse at all. These include:

- Iptacopan (Fabhalta™): Oral complement inhibitor, FDA approved for IgAN in adults
- Ravulizumab (Ultomiris™): IV complement inhibitor, FDA approved for IgAN in adults
- Atrasentan (Vanrafia™): Oral endothelin A receptor inhibitor, FDA approved for IgAN in adults
  - This class is called ERAs (**E**ndothelin **R**eceptor **A**ntagonists)
  - Sparsentan is called a DEARA (**D**ual-acting **E**ndothelin and **A**ldosterone **R**eceptor **A**ntagonist)
- Atacicept (Trutakna™): APRIL/BAFF inhibitor
- Povatacicept (No brand name): Expected approval any day now – APRIL/BAFF inhibitor
- Sibprenlimab (Voyxact™): APRIL inhibitor
- Still, none of these are approved for pediatrics

[a]Rovin BH, Barratt J, Cook HT, et al. Complement inhibitors and B cell-modifying agents for IgA nephropathy-a Kidney Disease: Improving Global Outcomes (KDIGO) commentary. *Kidney Int* 2026 Sep;110(3):502-507. PMID: 41895685.

93. Alport syndrome

Figure 93.3 should be corrected as follows:



Figure 93.3: For comparison, this normal GBM (yellow box) is noticeably thinner, with a much more uniform appearance. *Courtesy of David Milford, MD*

98. Human immunodeficiency virus-associated nephropathy

- Note that **dolutegravir** and **rilpivirine** inhibit creatinine secretion, falsely elevating serum creatinine and lowering eGFR
  - Cystatin C is not affected, and will give more accurate representation of renal function in these patients

106. GLP-1 agonists

- Correction: GLP-1 agonists **stimulate**, not inhibit, GLP-1 production.
- Semaglutide (Ozempic™) injection (not tablets) is now FDA-approved for risk reduction of sustained eGFR decline, end-stage kidney disease, and cardiovascular death in adults with type 2 diabetes mellitus and chronic kidney disease. The approval is brand-specific and it is the first and only GLP-1 medication approved for this use
- Semaglutide (Wegovy™) injection (not tablets) is FDA-approved to treat metabolic dysfunction-associated steatohepatitis (MASH) in adults with liver fibrosis

116. Nephrotoxic agents

Principles and mechanisms of nephrotoxicity

- Kidneys are at high risk because:
  - They receive 20-25% of cardiac output, so large amounts of circulating drugs pass through kidneys
  - They actively participate in drug metabolism and excretion
  - They concentrate drugs to levels above serum concentrations through filtration and reabsorption
- Mechanisms of injury (note some drugs may have more than one mechanism)
  - Direct tubular injury
    - Most common mechanism
    - May involve mitochondrial dysfunction, oxidative stress, disruption of cellular transporters such as sodium-potassium ATPase, and/or intracellular accumulation
    - Aminoglycosides, cidofovir, cisplatin, carboplatin, lead, mercury, amphotericin B

- Crystal precipitation and tubular obstruction
  - Acyclovir, sulfamethoxazole, sulfadiazine, methotrexate, ciprofloxacin, indinavir, triamterene, ethylene glycol
- Hemodynamic alterations
  - NSAIDS: Inhibit prostaglandin synthesis, causing afferent arteriole vasoconstriction
  - ACE inhibitors/ARBs: Block angiotensin II formation, reducing efferent arteriole tone
  - Cyclosporine, tacrolimus: Cause afferent arteriole vasoconstriction
- Tubulointerstitial nephritis
  - Cephalosporins, penicillins, NSAIDs, many others – see chapter 139, Acute and chronic tubulointerstitial nephritis
- Thrombotic microangiopathy
  - Cyclosporine, chemotherapy agents

- Factors which make toxicity worse
  - Dehydration
  - Concurrent use of multiple nephrotoxins
  - Pre-existing CKD
  - Other comorbidities, such as diabetes mellitus
  - High or frequent dosing
  - Pharmacogenetic risk factors: Slow metabolizers may accumulate high levels of drug

124. Hemoperfusion and poisoning

Planning dialysis to treat poisoning

- This varies tremendously depending on the specific poison and individual patient circumstances. Consult references, toxicologists and/or poison control for guidance. Key questions:
  - Is toxin removed by hemodialysis?
    - Best candidates for hemodialysis are low-molecular weight molecules that are water soluble with minimal protein binding (<80%) and low endogenous clearance and volume of distribution
    - Common toxins treated with hemodialysis include ethanol, ethylene glycol, methanol, metformin, salicylates and lithium

Substances for which hemodialysis is NOT recommended

- Toxins with high molecular weight, significant lipophilicity, high protein binding (>80%) or large volumes of distribution will *not* be removed effectively by hemodialysis

Table **Error! No text of specified style in document.: Substances NOT treated with hemodialysis**

Substance	Preferred treatment
Chloroquine, hydroxychloroquine, and quinine	Supportive care
Tricyclic antidepressants	Supportive care, sodium bicarbonate
Digoxin	Antidote: Digoxin F_{ab} fragments
Benzodiazepines	Antidote: Flumazenil

148. Cystinuria

- The older phenotype-based classification into Types I, II and III is largely obsolete now, and gene-based classification is preferred
- Cystinuria is caused by variants in *SLC3A1* and/or *SLC7A9*
  - Since this is autosomal recessive, patients can have variants in both copies of one gene, or in one copy of both genes (biallelic)

180. Skeletal

Definitions (per KDIGO[a])

- **Chronic kidney disease-metabolic bone disorder (CKD-MBD)**
  - A systemic disorder of mineral and bone metabolism due to CKD manifested by one or more of the following:
    - Abnormalities of calcium, phosphorus, PTH, or vitamin D metabolism
    - Abnormalities in bone turnover, mineralization, volume, linear growth, or strength
    - Vascular or other soft-tissue calcification
- **Renal osteodystrophy**
  - An alteration of bone morphology in patients with CKD
  - One measure of the skeletal component of the systemic disorder of CKD–MBD that is quantifiable by histomorphometry of bone biopsy

194. Hemodialysis

Dialysis water

- The current standard for dialysis water is defined in ANSI/AAMI/ISO 13959, from 2014
  - This standard allows dialysis water to contain up to 100 CFU bacteria/ml and up to 0.25 units of endotoxin /ml
  - The previous standard, from 2004, is AAMI RD52, which allows up to 200 CFU bacteria/ml and 2 units of endotoxin/ml
    - Although a newer standard exists, the 2004 standard is still the minimum required by CMS for dialysis centers in the USA
    - Even by the newer 2014 standards, in a typical 4-hour treatment with dialysate flow of 500 ml/min, a patient could conceivably be exposed to 12 million CFU of bacteria and 120,000 units of endotoxin without violating the standards. Using the 2004 standards, those values would double.

199. Ethical problems

ASN has released detailed guidelines on conservative care in chronic kidney disease:

Wong SPY, Schell JO, et al.; ASN Kidney Health Workgroup on Conservative Kidney Management. ASN Kidney Health Guidance on Conservative Management in People with Kidney Failure. *J Am Soc Nephrol* 2026 Apr 1. Epub ahead of print. PMID: 41848800.

213. Complications of renal transplantation

Post-transplant erythrocytosis

- Persistently, markedly elevated hemoglobin in post-transplant patients
- Etiology is not understood
- Treatment with ACE inhibitors or ARBs is usually very effective
  - How these work in this condition is also not understood