PedsCases Podcast Scripts

This podcast can be accessed at www.pedscases.com, Apple Podcasts, Spotify, or your favourite podcasting app.

APPROACH TO PEDIATRIC CHRONIC KIDNEY DISEASE

Developed by Alexis Filyk and Dr. Michelle Ruhl for PedsCases.com.
April 10, 2025

Introduction:

Hi everyone, thanks for tuning into this PedsCases Podcast episode. My name is Alexis Filyk and I am a medical student at the University of Alberta. This podcast was created with the help of Dr. Michelle Ruhl, a pediatric nephrologist at Stollery Children's Hospital in Edmonton, Alberta.

The aim of this episode is to explain the relationship between Acute Kidney Injury and Chronic Kidney Disease and to understand the pathophysiology of Chronic Kidney Disease. Additionally we want to help explore the differential diagnoses relevant in a child presenting with kidney injury, as well as walk through tests and imaging that might be ordered, clinical management strategies and hypothetical disease progression.

Objectives:

1. To understand the timeline of acute kidney injury and chronic kidney disease
2. To understand that acute kidney injury has a variable natural history of recovery. Depending on cause of AKI, patients may recover to normal renal function or may be left with reduced renal function (chronic kidney disease)
3. To learn about common causes of chronic kidney disease in children.

Etiology:

The most common causes of chronic kidney disease in children are

- congenital anomalies of the kidney and urinary tract (CAKUT), including obstructive uropathy, renal hypoplasia or dysplasia and reflux nephropathy
- glomerular diseases; and
- cystic kidney disease.

Okay, now let's dive into our first case and learn more about how CKD may present acutely.

Case 1.

When a patient presents with acute kidney injury, it is not always clear how long standing the injury is, and how likely there is to be renal recovery.

A 13-year-old female presents to the Emergency Department accompanied by her mother. She noticed brown urine two weeks ago and came in today when it happened again. On further history, she has had several recent episodes of epistaxis. She is a high level athlete, dancing 4-5 times per week, and she has been feeling more tired lately, with a chronic cough over the last month.

The emergency physician orders a urinalysis and serum chemistry (electrolytes, creatinine, urea, glucose). Urinalysis results are positive for hematuria and proteinuria; negative for nitrite and leukocytes.

Plasma creatinine comes back at 150 umol/L, urea 12 mmol/L. Serum sodium and potassium are within normal limits.

After hearing this case, what do you think could be going on with this patient? What is your differential?

The plasma creatinine stands out as elevated for age. The usual range for a 13yo female would be around 50-60 umol/L, but hers is 150 umol/L. It is also important to consider the timeline of symptoms. She describes a month of cough/epistaxis. Both this timeline of less than 3 months of symptoms as well as elevated creatinine support a diagnosis of acute kidney injury.

The findings of hematuria and proteinuria, together with AKI, are highly suspicious for glomerulonephritis.

The differential for glomerulonephritis in this 13yo girl includes post-infectious glomerulonephritis, IgA vasculitis (previously called Henoch Schonlein purpura), especially if typical rash is present, as well as serious autoimmune diseases such as lupus nephritis and ANCA vasculitis.

Now that we have a differential, what are the next steps we should take to narrow down a diagnosis?

There are other serum markers that can be ordered to narrow down the causes of acute glomerulonephritis. These include C3, C4, ASOT (for infection-associated glomerulonephritis), antinuclear antibodies, anti-dsDNA (for lupus) and ANCA antibodies (MPO - myeloperoxidase and PR3 - proteinase 3) for ANCA. A kidney biopsy can also clarify the pattern of glomerular injury, confirming the diagnosis.

Her renal biopsy shows features of pauci-immune glomerulonephritis with severe crescentic disease, consistent with ANCA vasculitis. Pauci-immune means that immunofluorescence staining was negative. This stands in sharp contrast to lupus, which usually shows extensive deposition of complement and immunoglobulin in the glomerulus, and infection-associated GN, in which comseplement deposition is expected.

Developed by Alexis Filyk and Dr. Michelle Ruhl for PedsCases.com.
April 10, 2025.

In case you haven't heard of ANCA vasculitis before, or need a refresher on this disease, ANCA stands for antineutrophil cytoplasmic antibody. This is a group of autoantibodies that target neutrophils in the blood. There are three types of ANCA-associated vasculitis:

- Microscopic polyangiitis, causing inflammation of the small vessels in the kidneys and sometimes the respiratory tract, without causing granulomas
- Granulomatosis with polyangiitis, where vasculitis involves the kidneys, respiratory tract including lungs, trachea, nose and ears, and granulomas are present.
- Eosinophilic granulomatosis with polyangiitis, which tends to present with allergic rhinitis or asthma-like pulmonary involvement

ANCA vasculitis can affect any system of the body, in some patients presenting as rash, arthritis, rhinosinusitis, epistaxis, hearing loss, ENT cartilage destruction, cavitary lung lesions/nodules/hemorrhage, and mononeuritis multiplex.

The kidney biopsy has clarified the cause of this patient's acute glomerulonephritis and we can proceed with treating our patient for ANCA vasculitis.

Treatment plan:

She is treated with high-dose (pulse) methylprednisolone and Rituximab, with a slow steroid taper planned over 6 months. At the end of 6 months, she no longer has active signs or symptoms of ANCA vasculitis, but her serum creatinine remains elevated at 100 umol/L. She continues to be regularly followed by a nephrologist, and requires dietary potassium restriction to keep her serum potassium level in the normal range.

When elevation in creatinine from an acute kidney injury persists beyond three months, a patient is diagnosed with chronic kidney disease. For this patient, ANCA vasculitis caused kidney injury that did not fully recover, even with treatment. Sometimes the cause, or the severity, of acute kidney injury can be a sign that a patient is more likely to be left with long-term renal sequelae of chronic kidney disease.

Acute kidney injury is defined as a decline in renal function, present for less than 3 months. Our patient presented initially with acute kidney injury, but as her renal function has not returned to normal after her initial 6-month treatment course, she would now be diagnosed with chronic kidney disease. Chronic kidney disease is reduced renal function that has been present for at least 3 months. Renal function is measured by glomerular filtration rate (GFR) - the total rate of filtration of the blood by all the glomeruli in both kidneys. GFR is normalized to body surface area and is typically between 90 and 120mL/min/1.73m2 in a normal individual with completely functional kidneys.

Key takeaways for this case:

- Severe AKI can result in chronic kidney disease
- Definitions of AKI vs. CKD, divided by time course

Developed by Alexis Filyk and Dr. Michelle Ruhl for PedsCases.com.
April 10, 2025.

Case 2.

Sometimes the risk for chronic kidney disease is recognized even before birth, which brings us to case 2. In this second case, an antenatal ultrasound has shown bilateral hydroureteronephrosis, trabeculated bladder and dilated posterior urethra for a male fetus.

His mother is referred to see a Pediatric Urologist, who discusses that the baby will likely require surgery after birth to resect posterior urethral valves. She is also referred to the Pediatric Nephrologist to discuss some of the long-term complications that come with this condition.

The Pediatric Nephrologist discusses that many patients with posterior urethral valves will have difficulty concentrating their urine. This is a common finding in patients with posterior urethral valves because high pressure during tubular development damages renal response to ADH, causing ADH resistance. Patients also often have chronic kidney disease.

The baby is born by uncomplicated vaginal delivery and named Gabriel (nickname Gabe)

After birth, Gabe is admitted to the Neonatal Intensive Care Unit and a foley catheter is placed immediately. The foley catheter pushes aside the valve tissue so the urethra is no longer obstructed and the bladder can drain. Follow up ultrasound 3 days later shows some decompression of hydroureteronephrosis, but kidneys appear echogenic and there is still some cortical thinning noted. These findings reflect damage to functioning renal tissue during development and do not always resolve once the urinary system is decompressed. Voiding cystourethrogram (VCUG) confirms presence of posterior urethral valves.

The surgeon books him for urgent resection of posterior urethral valves on day 5 of life. Gabe develops post-obstructive diuresis lasting just over 24h. With careful monitoring in the NICU and supplemental IV fluid, he does not become dehydrated or suffer an acute kidney injury.

Gabe has been doing well for two years. He required supplemental sodium bicarbonate starting at one month old to replace urinary losses, but he has been growing and developing well. At two years old, his Nephrologist calculates his renal function by eGFR (typical equations such as Schwartz and CKiD are validated for children 2yo and over). It is 56 mL/min/1.73m2, which puts him at stage 3 chronic kidney disease.

To visualize the stress that chronic kidney disease places on the kidneys, hold out both of your hands and imagine that each hand is a healthy kidney, with the five fingers representing nephrons. The metabolic demands of your body only require the clearance provided by 6 of your 10 finger nephrons. This means there is renal reserve present, with the kidneys easily able to compensate during times of increased metabolic stress.

Developed by Alexis Filyk and Dr. Michelle Ruhl for PedsCases.com.
April 10, 2025.

In chronic kidney disease, nephron function is permanently lost. To simulate CKD stage 1, put down 2 fingers on each hand. Both kidneys will have three functioning nephrons. The kidneys are still able to meet the metabolic demands of the body (which required 6 finger nephrons), so creatinine will be normal if measured, but there is no longer renal reserve present. Each of the nephrons must work all the time to provide the clearance the body needs.

Now imagine that chronic kidney disease has progressed, and more nephron function has been lost. To simulate CKD stage 3, put down two more fingers on your left hand and one on your right. There are only three finger nephrons remaining. The kidneys are not able to meet the metabolic demands of the body (which required 6 finger nephrons), so serum creatinine will be elevated if it is measured. The nephrons left are working all the time, and during times of metabolic stress, will be driven to increase clearance further. This increases the risk of the remaining nephrons becoming injured and eventually failing. In patients with moderate to severe kidney disease, progressive worsening of kidney function is common due to the strain on the remaining nephrons.

Take a minute to brainstorm what roles a healthy kidney has in your body. Chronic kidney disease comes with many sequelae or comorbidities because the kidney has many diverse physiologic functions. As chronic kidney disease progresses, patients tend to require support for many of these physiologic roles.

Aspects of normal renal physiology:

The kidneys maintain bone health through their key role in body calcium and phosphate balance. Along with the liver, the kidneys turn vitamin D into activated vitamin D. In chronic kidney disease, bone and mineral disorder develops.

Kidneys also produce erythropoietin, a hormone that works on bone marrow to produce new red blood cells. Your body also doesn't absorb, transport or store iron normally in advanced chronic kidney disease. Many patients with chronic kidney disease will have anemia, and both abnormal iron handling and erythropoietin deficiency can contribute to this. Patients may need treatment with iron supplementation and darbepoetin, which is given by subcutaneous injection.

The kidneys are important for normal growth and development. Children with chronic kidney disease often have slower growth, caused by a number of factors including reduced pituitary GH secretion, GH insensitivity, poorer nutrition due to nausea or dietary restrictions, and chronic inflammation. Recombinant human growth hormone is often given to kids with kidney disease to aid in their growth.

In our case, Gabe is now 6 years old. He continues to require sodium bicarbonate supplementation for treatment of acidosis and is on long-term iron supplementation. Despite iron supplementation, his hemoglobin levels have fallen over the last two measurements. When his labwork is reviewed at his next visit, eGFR is now 35 mL/min/1.73m2. He has also developed anemia of CKD, requiring treatment with darbepoetin.

Developed by Alexis Filyk and Dr. Michelle Ruhl for PedsCases.com.
April 10, 2025.

With this decline in renal function, he is booked to see his Pediatric Urologist to review bladder function. Urodynamic studies are completed, but do not show significant voiding dysfunction.

Gabe's nephrologist ensures his risk factors for progression of chronic kidney disease are well controlled, including monitoring for hypertension, treating acidosis and preventing recurrent urinary tract infections by managing constipation and voiding dysfunction. Despite optimized medical management, he continues to have slow decline in renal function.

At age 12, Gabe's renal function by eGFR is 14 mL/min/1.73m2- which now puts him at stage 5 CKD. At this point, accumulation of the uremic toxins the kidney is unable to clear will often cause patients to feel unwell. The early manifestations of uremia include brain fog, early-morning nausea, anorexia, altered taste and fatigue. Later manifestations of vomiting, weight loss, peripheral neuropathy, pruritus, and in extreme cases encephalopathy, seizure, and serositis.

Gabe is beginning to experience some early-morning nausea. Gabe's nephrologist begins a discussion around renal replacement therapy and recommends insertion of a peritoneal dialysis catheter to start home dialysis. Gabe has several family members who are interested in kidney donation, so he is also referred for transplant workup.

Gabe has been on peritoneal dialysis for four months when his father learns that he has completed his donor workup and will be able to proceed with kidney donation. A final crossmatch is booked and Gabe and his father are scheduled for living-donor renal transplantation.

When he wakes up after transplant, Gabe's transplant team is happy to share with the family that everything has gone well. His peritoneal dialysis catheter was removed during the transplant surgery as it is no longer required. He will continue to take immunosuppressive medication life-long, but Gabe no longer requires all the medications he was taking for renal failure. His eGFR is now 87 mL/min/1.73m2, nearly normal for age. And that concludes this case.

Conclusion and Take-Home Points:

To recap, the most common causes of chronic kidney disease in children are congenital anomalies of the kidney and urinary tract, glomerulonephritis, and hereditary kidney disease. This concludes our podcast on the approach to pediatric chronic kidney disease, thanks for listening!

Developed by Alexis Filyk and Dr. Michelle Ruhl for PedsCases.com.
April 10, 2025.

References:

Ikhuoriah T, Oboh D, Abramowitz C, Musheyev Y, Shamsian E. Posterior urethral valve: A case report in an older Nigerian child. *Radiol Case Rep*. 2023;18(5):1715-1720. Published 2023 Feb 27. doi:10.1016/j.radcr.2023.01.077

Urinary tract obstruction. (n.d.). UCSF BCH Fetal Treatment Center - Urinary Tract Obstruction. https://fetus.ucsf.edu/urinary-tract-obstruction/#what_is_urinary_tract_obstruction

CKD Evaluation and Management. (2024). KDIGO. https://kdigo.org/guidelines/ckd-evaluation-and-management/

Developed by Alexis Filyk and Dr. Michelle Ruhl for PedsCases.com.
April 10, 2025.