ACUTE PYELONEPHRITIS

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- **Clinical pyelonephritis** is characterized by any or all of the following: abdominal, back, or flank pain; fever; malaise; nausea; vomiting; and, occasionally, diarrhea
- Newborns can show nonspecific symptoms such as poor feeding, irritability, jaundice, and weight loss.
- Pyelonephritis is the most common serious bacterial infection in infants <24 mo of age who have fever without an obvious focus
- Involvement of the renal parenchyma is termed *acute pyelonephritis,* whereas if there is no parenchymal involvement, the condition may be termed *pyelitis.* Acute pyelonephritis can result in renal injury, termed *pyelonephritic scarring.*
- If bacteria ascend from the bladder to the kidney, acute pyelonephritis can occur. Normally the simple and compound papillae in the kidney have an antireflux mechanism that prevents urine in the renal pelvis from entering the collecting tubules. However, some compound papillae, typically in the upper and lower poles of the kidney, allow intrarenal reflux.
- Infected urine then stimulates an immunologic and inflammatory response. The result can cause renal injury and scarring Children of any age with a febrile UTI can have acute pyelonephritis and subsequent renal scarring, but the risk is highest in those <2 years of age
- UTI may be suspected based on symptoms or findings on urinalysis, or both; *a urine culture is necessary for confirmation and appropriate therapy*
- suprapubic aspirate is ideal but midstream culture is a reasonable alternative
- Pyelonephritis is **confirmed with with DMSA scan**, eventhogh it is usually not done
- In acute febrile infections suggesting **pyelonephritis,** a 10- to 14-day course of broad-spectrum antibiotics capable of reaching significant tissue levels is preferable.
- Children who are dehydrated, are vomiting, are unable to drink fluids, are ≤1mo of age, or in whom urosepsis is a possibility should be admitted to the hospital for IV rehydration and IV antibiotic therapy.
- **Parenteral treatment with ceftriaxone (50-75 mg/kg/24 hr, not to exceed 2 g) or cefotaxime (100 mg/kg/24 hr), or ampicillin (100 mg/kg/24 hr) with an aminoglycoside such as gentamicin (3-5 mg/kg/24 hr in 1-3 divided doses**) is preferable.
- The potential ototoxicity and nephrotoxicity of aminoglycosides should be considered, and serum creatinine and trough gentamicin levels must be obtained before initiating treatment, as well as daily thereafter as long as treatment continues. Treatment with aminoglycosides is particularly effective against *Pseudomonas* spp, and alkalinization of urine with sodium bicarbonate increases its effectiveness in the urinary tract.
- The main consequences of chronic renal damage caused by pyelonephritis **are arterial hypertension and end-stage renal insufficiency;** when they are found they should be treated appropriately

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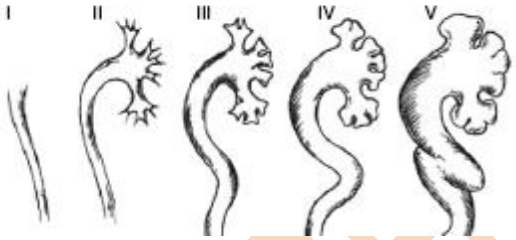
Asymptomatic Bacteriuria

- **Asymptomatic bacteriuria** refers to a condition in which there is a positive urine culture without any manifestations of infection. It is most common in girls.
- The incidence is <1% in preschool and school-age girls and is rare in boys. The incidence declines with increasing age. This condition is benign and does not cause renal injury, except in pregnant women, in whom asymptomatic bacteriuria, if left untreated, can result in a symptomatic UTI.
- Some girls are mistakenly identified as having asymptomatic bacteriuria, whereas they actually are experiencing day or night incontinence or perineal discomfort secondary to UTI

Vesicoureteral Re fl ux

- Vesicoureteral re fl ux (VUR) is seen in 40–50 % infants and 30–50 % children with UTI. Its severity is graded using the International Study Classi fi cation, from grades I to V, based on the morphological appearance of the urinary tract on VCUG
- Lower grades of re fl ux (grades I–III) are more likely to resolvethan higher grades.
- VUR may be primary or secondary to bladder out fl ow obstruction (e.g., posterior urethral valves), neurogenic bladder dysfunction, or functional voiding disorder.
- The presence of moderate to severe VUR is an important risk factor for pyelonephritis and renal scarring, with subsequent risk of hypertension, albuminuria, and progressive kidney disease.
- The risk of scarring is highest in the fi rst year of life. The presence of intrauterine VUR has been associated with renal hypoplasia and/or dysplasia.



Grading of VUR

- Grade 1: Re fl ux of urine in a non dilated ureter
- Grade 2: Re fl ux into renal pelvis and calyces without dilatation
- Grade 3: Mild dilatation of ureter, pelvis, and calyces with blunting of fornices
- Grade 4: Dilatation of ureter, pelvis, and calyces and blunting of fornices
- Grade 5: Ureteral tortuosity, gross dilatation of ureter and calyces, and loss of papillary impressions

- Conventional therapy for VUR includes antibiotic prophylaxis and surgical intervention.A recent systematic review on patients with dilating re fl ux concluded that the outcomes following surgical repair versus prophylaxis were similar in terms of the number of breakthrough UTI and risk of renal scarring.

- The management of patients with VUR depends on the patient age, grade of re fl ux, and whether there are any breakthrough infections

Indications for Surgical Treatment

- Persistent grade IV/V re fl ux
- High-grade re fl ux in a single functioning kidney
- Deterioration of renal function due to UTI while on chemoprophylaxis

Management of VURa VUR grade Management **Grades II** Antibiotic prophylaxis until 1 year old Restart antibiotic prophylaxis if breakthrough febrile UTI	**Grades III–V** Antibiotic prophylaxis up to 5 years of age Consider surgery if breakthrough febrile UTI **Beyond 5 years**: prophylaxis continued in children with bowel bladderdysfunction a Derived from the revised Indian Society of Pediatric Nephrology 2011 guidelines	

SYMPTOMATIC BACTERIURIA

LIST FOUR TESTS TO SUSPECT UTI

- The gold standard for diagnosis of UTI is the urine culture. The urine sample needs to be appropriately collected and evaluated for bacterial growth. The presence of >5 white blood cells/high power fi eld (HPF) in a centrifuged sample and 10 white cells/HPF in an uncentrifuged sample of urine is seen in the majority of patients with UTI.

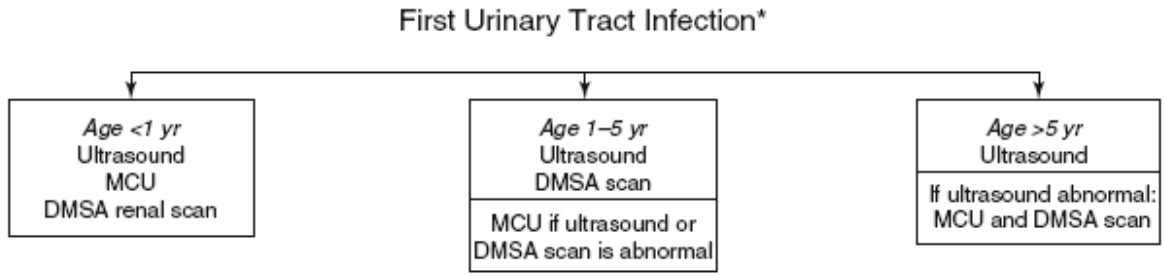
Tests That Help Improve the Predictive Value of UTI

- *Nitrate reductase test* : The principle behind this test is reduction of nitrate to nitrite by nitrate reductase enzyme present in bacteria. This test has a sensitivity of 53 % and speci fi city of 98 % in detecting UTI.
- *Leukocyte esterase test* : This test has 83 % sensitivity and a speci fi city of 78 % to detect UTI.
- The combination of leukocyte esterase and nitrite tests has a sensitivity of 72 % and speci fi city of 96 % for diagnosing UTI

Method of collection	Colony count	Probability of infection (%)
Suprapubic aspiration	Any number of pathogens	99
Urethral catheterization	$>5 \times 10^4$ CFU/ml	95
Midstream clean catch	$>10^5$ CFU/ml	90–95

NAME TWO TESTS YOU DO AFTER TREATING IN CHILD OF 8 MONTHS

DMSA
MCU



*All patients with recurrent UTI need detailed evaluation with ultrasonography, DMSA scan and MCU.

NAME FOUR COMPLICATIONS OF UTI

- RENAL SCARRING
- RENAL ABSCESS
- PERIRENAL ABSCESS
- AKI

NEPHROTIC SYNDROME

Define remission,relapse in nephrotic syndrome

- Urinary remission Urine albumin nil or trace (or proteinuria <4 mg/m 2 /h) for three consecutive days
- Relapse Urine albumin 3+ or 4+ (or proteinuria >40 mg/m 2 /h) for three consecutive days, having been in remission previously

Define steroid sensitive,steroid resistant nephrotic syndrome and frequent relapse

- Glucocorticoid (steroid) dependence (SDNS):Two consecutive relapses during alternate-day prednisone therapy or within 14 days of its discontinuation
- Glucocorticoid resistance (SRNS) :Persistent proteinuria (>2 g/g creatinine) despite high-dose prednisone therapy with 60 mg/m 2 (2 mg/kg) daily for 4 weeks, in the absence of infection or nonadherence to medication

What is the pathology in MCNS AND FSGS?

- MCNS is characterized by the lack of histological changes by bright-fi eld and immuno fl uorescence microscopy. Electron microscopy reveals generalized effacement of podocyte foot processes.
- The term FSGS refers to sclerotic lesions that initially affect some glomeruli while sparing others (“focal”). Glomeruli are partially affected (“segmental” sclerosis), but the lesions may progress to global sclerosis with progressive nephron loss. Immuno fl uorescence is negative. In contrast

to MCNS, foot process effacement is not generalized. Up to 25 % of patients with FSGS may not present with nephrotic syndrome

LIST FOUR INVESTIGATIONS IN NEPHROTIC SYNDROME

- **URINE PROTEIN**
- Urinalysis and microscopy. Microhematuria is noted in up to 30 % of patients with INS and does not predict poorer outcome. Mild "sterile" pyuria can be present.
- Urine protein to creatinine ratio (Upc) or 24-h (timed) urine protein estimation.
- Serum albumin, total protein, cholesterol, and creatinine.
- Infectious disease workup including PPD (Mantoux) skin test and chest X-ray

What are the indications for renal biopsy?

Indications for Renal Biopsy in Patients with Nephrotic Syndrome

- Age <12 months or >12 years at presentation
- Glucocorticoid resistance
- Proteinuria associated with malformations or "syndromes" (e.g., nail patella syndrome, Lowe syndrome)
- Persistently low plasma C3 and/or C4
- Sustained hypertension not related to glucocorticoid or calcineurin inhibitor therapy
- Serum creatinine elevation (renal failure) for >1 week, not attributable to intravascular volume depletion
- Secondary nephrotic syndrome with features of systemic disease (e.g.,SLE, SHP, HIV infection, hepatitis B or C)

TREATMENT OF IST EPISODE

- Prednisone (or prednisolone, used interchangeably): 60 mg/m 2 once daily or in 2–3 divided doses (~2 mg/kg/day, max. 60 mg/day) for 4–6 weeks followed by 40 mg/m 2 (~1.5 mg/kg, max. 40 mg) on alternate days as a single morning dose for the next 6 weeks with or without SLOW taper.
- Some authors recommend prolonged glucocorticoid therapy for 6 months after the initial, intense therapy
- A focus of infection must always be searched and treated. Control of underlying infection can achieve remission in some cases

HOW DO YOU TREAT RELAPSE?

- Prednisone remains the only medication to effect remission quickly in patients with glucocorticoid-sensitive, relapsing INS. Prednisone 60 mg/m 2 per day () usually achieves urinary remission within 7–10 days. Once urine is protein- free for three consecutive days, daily prednisone is switched to a single morning dose of 40 mg/m 2 (~1.5 mg/kg) on alternate days for 4 weeks and then stopped

HOW TO TREAT FRNS OR STEROID RESISTANCE

- Upon achieving remission with daily high-dose prednisone, patient is switched to alternate-day prednisone as above. However, there is no clear consensus about the best long-term approach.

- Option 1: identifi cation of a “threshold” dose of prednisone. Alternate-day prednisone is tapered to 0.5 mg/kg every 48 h. If stable, taper is continued until a dose is reached that still prevents relapses. When a relapse occurs, aim at a maintenance dose just above the last dose where the patient relapsed and continue this dose for 6 months.
- Option 2: introduction of second-line agent, usually in conjunction with prednisone tapering, intended to minimize long-term glucocorticoid adverse effects

LIST 4 SECOND LINE DRUGS IN NEPHROTIC SYNDROME

CYCLOSPORINE
LEVAMISOLE
MYCOPHENALATE
TACROLIMUS

GIVE THE DOSE AND ONE SIDE EFFECT OF 2 ND LINE DRUGS

LEVAMISOLE	2-2.5MG/KG	Neutropenia, fl u-like symptoms, skin rash, gastrointestinal symptoms
CYCLOSPORINE	5-7 MG/KG	Nephrotoxicity, hypertension, hepatotoxicity, hyperkalemia, hypomagnesemia, gingival hyperplasia, hirsutism
MYCOPHANLATE	600-1200MG/M2/KG	Gastrointestinal (colitis, oral aphthous ulcers), anemia, neutropenia
CYCLOPHOSMAMIDE	2-3 MG/KG	Neutropenia, anemia, gonadal toxicity
TACROLIMUS	,1-.2 MG/KG	Nephrotoxicity, hypertension, hepatotoxicity, impaired glucose tolerance,

LIST 4 COMPLICATIONS OF NS

Infections

- In the pre-antibiotic and pre-steroid era, many children with nephrotic syndrome died of infection and/or malnutrition. Bacterial infections, commonly due to encapsulated gram-positive and or gram-negative bacteria, speci fi cally *S* . *pneumoniae* , *H* . *influenzae* , *E* . *coli* , and *K* . *pneumoniae* , have been attributed to the urinary loss of IgG and complement components. They present as spontaneous bacterial peritonitis, septicemia, cellulitis, diarrhea, upper and lower respiratory, or urinary tract infection
- **Hypercoagulopathy-** Nephrotic syndrome increases the risk of thrombosis and thrombosis-related complications, such as deep venous thrombosis, renal venous thrombosis, pulmonary emboli, and cerebral infarction.
- **Acute Kidney Injury-** May be due to intravascular volume depletion (prerenal failure) or renal hypoperfusion, use of nephrotoxic drugs, renal venous thrombosis, or sepsis.
- **Electrolyte Disturbances -** Spurious hyponatremia may be seen due to hyperlipidemia or where the laboratory measures electrolytes by fl ame photometry. True hyponatremia may develop due to diuretics
- DRUGS –CAN CAUSE HPA AXIS SUPPRESSION

HOW WILL YOU IMMUNIZE A CHILD WITH NS

- Live vaccines are contraindicated in children receiving immunosuppressive or cytotoxic medication (e.g., varicella, measles, mumps, rubella, rotavirus, oral polio)
- **Live vaccines should be deferred until**

– Prednisone dose is <1 mg/kg/day (<20 mg/day) or <2 mg/kg/dose on alternate days (<40 mg/dose)
– More than 3 months after the last cyclophosphamide or chlorambucil dose
– More than 4 weeks after the last calcineurin inhibitor or mycophenolate dose

Immunosuppression is not a contraindication for inactive (killed) vaccines, but the vaccine response is likely to be reduced.

- *Hepatitis B* vaccine should be given to all unvaccinated or non-immune children– Higher glucocorticoid doses at the time of immunization appear to diminish the short-term, but not the long-term vaccine response
- Immunization, particulalry against encapsulated bacteria including *H. infl uenzae*, *S. pneumoniae* and *N. meningitidis* should be initiated, if they have not been obtained previously.
- *Pneumococcal* vaccine: Unimmunized children up to 2 years of age should receive 2–4 doses of the 13-valent (or at least the 7-valent) conjugate pneumococcal vaccine.
- For previously unimmunized children between 2 and 5 years old, give two doses of the available conjugate vaccine 4–8 weeks apart, followed 8 weeks later by administration of one dose of the 23-valent polysaccharide vaccine.
- Children older than 5 years receive a single dose of the 23-valent polysaccharide vaccine. Revaccination every 5 years should be considered for children who continue to have active nephrotic syndrome.
- Not all pneumococcal serotypes are included in the vaccines, and antibody levels may fall during a relapse; hence, previously vaccinated children may develop pneumococcal peritonitis and sepsis, as well as infections by other pathogens, despite having been vaccinated.
- *Seasonal In fl uenza vaccines* are given to patient and family to reduce preventable relapses and morbidity.
- *Varicella* vaccine is given as 2 doses, 1–3 months apart.
- Defer *o ral polio vaccine* (OPV) to patients and to siblings unless patient is in stable remission off immunosuppressants or can be isolated from vaccinated family members.

GLOMERULONEPHRITIS

WHAT is hematuria?
List 4 causes of hematuria.

- **Hematuria is defi ned as presence of more than 5 RBCs/HPF in a centrifuged specimen of urine**

- Postinfectious GN (poststreptococcal GN)*
- Uti
- IgA nephropathy
- Tumor (Wilms,

Name 4 causes of red urine

- Hemoglobin
- Myoglobin
- Urate
- Beetroot/black berry

How do you suspect acute nephritis

- Poststreptococcal GN is most common in children aged 5-12 yr and uncommon before the age of 3 yr. The typical patient develops an acute nephritic syndrome 1-2 wk after an antecedent streptococcal pharyngitis or 3-6 wk after a streptococcal pyoderma. The history of a specific infection may be absent, because symptoms may have been mild or have resolved without patients receiving specific treatment or seeking the care of a medical provider.
- The severity of kidney involvement varies from asymptomatic microscopic hematuria with normal renal function to gross hematuria with acute renal failure. Depending on the severity of renal involvement, patients can develop various degrees of edema, hypertension, and oliguria. Patients are at risk for developing encephalopathy and/or heart failure secondary to hypertension or hypervolemia. Hypertensive encephalopathy must be considered in patients with blurred vision, severe headaches, altered mental status, or new seizures.

Name Tests to dx acute glomerulonephritis

- Urinalysis demonstrates red blood cells (RBCs), often in association with RBC casts, proteinuria, and polymorphonuclear leukocytes. A mild normochromic anemia may be present from hemodilution and low-grade hemolysis. The serum C3 level is significantly reduced in >90% of patients in the acute phase and returns to normal 6-8 wk after onset. Although serum CH50 is commonly depressed, C4 is most often normal in APSGN, or only mildly depressed.
- Confirmation of the diagnosis requires clear evidence of a prior streptococcal infection. A positive throat culture report might support the diagnosis or might simply represent the carrier state. On the other hand, a rising antibody titer to streptococcal antigen(s) confirms a recent streptococcal infection. The antistreptolysin O titer is commonly elevated after a pharyngeal

infection but rarely increases after streptococcal skin infections. The best single antibody titer to document cutaneous streptococcal infection is the anti-deoxyribonuclease (DNase) B level

How do you treat acute glomerulonephritis?

- Management is directed at treating the acute effects of renal insufficiency and hypertension.
- Although a 10-day course of systemic antibiotic therapy with penicillin is recommended to limit the spread of the nephritogenic organisms, antibiotic therapy does not affect the natural history of GN.
- Sodium restriction, diuresis usually with intravenous furosemide, and pharmacotherapy with calcium channel antagonists, vasodilators, or angiotensin-converting enzyme inhibitors are standard therapies used to treat hypertension
- Dialysis, although rarely indicated, is needed for severe AKI with oligoanuria,uncontrolled hyperkalemia, or fl uid overload unresponsive to loop diuretics.
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What are the complications?

- Acute complications result from hypertension and acute renal dysfunction.
- Hypertension is seen in 60% of patients and is associated with hypertensive encephalopathy in 10% of cases.
- Although the neurologic sequelae are often reversible with appropriate management, severe prolonged hypertension can lead to intracranial bleeding.
- Other potential complications include heart failure, hyperkalemia, hyperphosphatemia, hypocalcemia, acidosis, seizures, and uremia.
- Acute renal failure can require treatment with dialysis

What is the prognosis?

- Complete recovery occurs in >95% of children with APSGN. Recurrences are extremely rare. Mortality in the acute stage can be avoided by appropriate management of acute renal failure, cardiac failure, and hypertension.
- Infrequently, the acute phase is severe and leads to glomerulosclerosis and chronic renal disease in <2% of affected children.