Pyelonephritis

What is pyelonephritis?

Acute pyelonephritis is infection within the renal pelvis, usually accompanied by infection within the renal parenchyma. The source of the infection is often ascending infection from the bladder but haematogenous spread can also occur. The usual organisms are the same as for lower urinary tract infection (UTI) - eg, *Escherichia coli*, *Klebsiella* spp., *Proteus* spp., *Enterococcus* spp. Unusual organisms are occasionally seen - eg, mycobacteria, yeasts and fungi and opportunistic pathogens such as *Corynebacterium urealyticum*. Repeated attacks of acute pyelonephritis can lead to chronic pyelonephritis, which involves destruction and scarring of renal tissue due to repeated inflammation.

Acute pyelonephritis

Incidence

Acute pyelonephritis can occur at any age. Around 1% of boys and 3% of girls will have had acute pyelonephritis by the age of 7 years [1] . Incidence is highest in women aged 15-29, followed by infants and older people [2] . It is relatively uncommon in men. In neonates it is more common in boys and tends to be associated with abnormalities of the renal tract. Over the age of 65 the incidence in men rises to match that of women.

Risk factors

These include:

- Structural renal abnormalities, including vesicoureteric reflux (VUR).
- Calculi and urinary tract catheterisation.
- Stents or drainage procedures.
- Pregnancy.

- Diabetes.
- Primary biliary cirrhosis.
- Immunocompromised patients.
- Neuropathic bladder.
- Prostate enlargement.

Pyelonephritis symptoms

Onset of pyelonephritisis is usually rapid with symptoms appearing over a day or two. There is unilateral or bilateral loin pain, suprapubic pain or back pain. Fever is variable but can be high enough to produce rigors. Malaise, nausea, vomiting, anorexia and occasionally diarrhoea occur. There may or may not be accompanying lower urinary tract symptoms with frequency, dysuria, gross haematuria or hesitancy. The patient looks ill and there is commonly pain on firm palpation of one or both kidneys, and moderate suprapubic tenderness without guarding.

Pyelonephritis symptoms in children, especially when young, can be much less specific and culture of urine should be a routine investigation in pyrexial and unwell infants.

Differential diagnosis

- Abdominal abscess.
- Abdominal aortic aneurysm.
- Appendicitis.
- Causes of acute abdomen.
- Causes of loin pain.
- Diverticulitis.
- Ectopic pregnancy.
- Endometritis.
- Interstitial cystitis.
- Nephrocalcinosis.
- Nephrolithiasis.

- Oophoritis.
- Papillary necrosis.
- Pelvic inflammatory disease.
- Prostatitis.
- Renal corticomedullary abscess.
- Renal vein thrombosis.
- Salpingitis.
- Sexually transmitted infections.
- Urethritis.
- VUR.
- Vesicovaginal and ureterovaginal fistula.

Investigations

- **Urinalysis**: the urine is often cloudy with an offensive smell. It may be positive on dipstick urinalysis for blood, protein, leukocyte esterase and nitrite. A midstream specimen of urine (MSU) should always be sent off for microscopy and culture, although there is often poor correlation between symptoms and bacteriuria. A catheter specimen will be acceptable if a catheter is in situ, and special arrangements may be needed for collecting a sample from a child. (Clean catch, catheter or suprapubic aspiration are methods used which reduce the risk of contamination. Occasionally a collection bag or pad may be used when a sample is not obtainable by superior means.) Microscopy of urine shows pyuria.

- **Inflammatory markers**: CRP, ESR, and plasma viscosity may be raised, but the evidence base is unconvincing. Recent studies identified procalcitonin as a biological marker in diagnosing acute pyelonephritis in children, potentially more useful than white cell count or CRP[3] . National Institute for Health and Care Excellence (NICE) guidance advises CRP alone is not useful in differentiating lower UTI from pyelonephritis in chidren[4] . A Cochrane review concluded that neither came to the conclusion that there was not enough evidence that either CRP, ESR nor procalcitonin should be used in the diagnosis of acute pyelonephritis in children.
- **FBC**: this shows elevated white cell count with neutrophilia[5] .
- **Blood cultures**: these are positive in approximately 15-30% of cases[6] .

- **Imaging**[7] :
  - Imaging is useful if the clinical picture or biochemical markers are ambivalent, as structural problems are not uncommon. Ultrasonography is usually the first-line investigation. Whether advised for all varies between guidelines. Imaging is normally recommended in men and children; it is mandatory in patients with recurrent pyelonephritis and may help to identify obstruction or stones[8] .
  - Contrast-enhanced helical/spiral CT (CECT) scan is the best investigation in adults where diagnosis is in doubt, improvement does not occur after 72 hours of treatment, or deterioration occurs. Non-contrast helical/spiral CT scans will pick up moderate-to-severe disease but may be normal in milder cases. In pregnant women, ultrasound or MRI is preferred.
  - In children, where imaging is required, ultrasound is the first-line investigation as dictated by NICE guidance[4] . See the separate Urinary Tract Infection in Children article for details.
  - Dimercaptosuccinic acid (DMSA) scan is mainly used for detailed renal cortical views in recurrent cases, to detect scarring.
  - MRI is also useful in detecting scarring but may require sedation in children. In adults, it is increasingly used where renal infection, masses and urinary obstruction are suspected but its use is limited by cost and availability.
- Renal biopsy is occasionally employed to exclude papillary necrosis.

Pyelonephritis treatment and management

- **Support**: rest, adequate fluid intake and analgesia are important.

- **Hospital admission**: many patients can be managed in the community, providing they are otherwise healthy. Guidelines generally recommend considering admission for pregnant women, due to the risk of complications [9] . Other indications for admission include:

    - Severe vomiting.
    - Comorbidity such as diabetes.
    - Signs of sepsis (eg, tachypnoea, tachycardia, hypotension).
    - Dehydration or inability to take fluids/medication.
    - Severe pain or debility.
    - Urinary tract obstruction.
    - Oliguria or anuria.
    - Suspected complications (see 'Complications', below).
    - Uncertain diagnosis.
    - Social issues.
    - Non-concordance with treatment.
    - Inadequate access to follow-up.
    - Relapse of symptoms as soon as antibiotics have been stopped.

    All babies aged under 3 months should be admitted. For older children, the decision where to treat will depend on the severity of the illness and whether there are any conditions inhibiting the absorption of antibiotics (eg, diarrhoea or vomiting).

- **Antibiotics**[10] : start empirical antibiotic treatment whilst awaiting culture and sensitivity. For adults, current UK protocols recommend that the first-line antibiotic should be either ciprofloxacin or co-amoxiclav for seven days (500 mg bd or 500/125 mg tds respectively). Trimethoprim may be used if culture confirms sensitivity (200 mg bd for 14 days). For children, co-amoxiclav is recommended as first-line treatment, with cefixime second-line. There is a theoretical concern that children who are not treated with early intravenous antibiotics could develop renal scarring. However, studies increasingly suggest that most cases in children over the age of 1 month can be managed with oral therapy[11] .
- **Surgery**: this may rarely be required to drain renal or perinephric abscesses, or to relieve obstructions causing the infection (eg, stones).

Complications[9]

Potential complications include:

- Sepsis.
- Perinephric abscess (more common if there is urinary tract abnormality).
- Renal abscess, including emphysematous pyelonephritis (rare, life-threatening form with tissue necrosis and accumulation of gas in the renal parenchyma, perinephric space and collecting systems - particularly occurs in obese, elderly women who have diabetes and develop urinary tract obstruction).
- Acute papillary necrosis, which is more likely in the elderly and those with diabetes (suggested by associated symptoms of renal colic).
- Pregnancy - tends to produce a more complicated course with significant risk of premature labour.
- Impaired renal function or renal damage potentially leading to acute kidney injury or chronic kidney disease (CKD).

Risk factors for complications include:

- Severe illness.
- Age over 65.

- Renal tract structural abnormality, or foreign bodies within the renal tract (including calculi and stents).
- Diabetes mellitus.
- Pregnancy.
- Renal transplant (especially the first three months).
- AIDS and other immunocompromised states.

Prognosis

Premature labour can occur in pregnant women. In other cases, there is usually uncomplicated recovery, providing there are no significant comorbidities.

Prevention

Consider prophylactic treatment in women with at least three symptomatic infections a year. Trimethoprim is widely used. In children, the current approach is to reserve antibiotic prophylaxis for those who are at highest risk of complications (eg, demonstrable VUR, recurrent infections or renal scarring on imaging) [4] [12] .

Chronic pyelonephritis

Chronic pyelonephritis is a characteristic scarring on the kidney which occurs after recurrent or persistent infections.

Epidemiology

There are few data available. VUR, which is a common risk factor, is found in up to one third of children investigated for UTI [13] . A meta-analysis revealed that the prevalence of reflux was 31.1% in children who were evaluated for a UTI and 17.2% in those with normal kidneys who had voiding cystourethrogram for other indications, such as the diagnosis of hydronephrosis [14] . Children who have recurrent episodes of infection or VUR are most likely to develop renal scarring.

Risk factors

- Any structural renal tract anomalies, obstruction or calculi.
- VUR.

- Intrarenal reflux in neonates.
- Diabetes.
- Any factors predisposing to recurrent urinary infection - eg, neurogenic bladder.

Chronic pyelonephritis symptoms

Chronic pyelonephritis is often asymptomatic. There may be features of acute or recurrent infection, or of complications of significant renal damage:

- Fever
- Malaise
- Loin pain
- Nausea
- Vomiting
- Dysuria
- Hypertension
- Failure to thrive
- Features of CKD

Investigations

- **Urine microscopy, culture and sensitivity**: this may be helpful in identifying the organism involved in recurrent infection but negative urine culture does not exclude diagnosis.

- **Imaging**:

    - Renal ultrasound may show small kidneys with a thin cortex.
    - Intravenous pyelogram (IVP) may show small kidneys, ureteric and caliceal dilatation/blunting with cortical scarring.
    - Micturating cystourethrogram (MCUG) may help to identify reflux.
    - Ultrasound and KUB X-ray may show stones but are not sensitive for reflux nephropathy.
    - Technetium-^{99m} Tc-DMSA scan is the most sensitive for demonstration of renal scars.
    - Renal biopsy may be required to rule out other causes of damage.

Chronic pyelonephritis treatment and management

Aims of management are to control active or recurrent infection and to treat/correct any underlying causes.

- Blood pressure should be controlled to slow the progression of chronic kidney disease. Ideally angiotensin-converting enzyme (ACE) inhibitors should be used.
- Supervening UTI may require lengthier courses of antibiotics than are normally given.
- Severe underlying VUR diagnosed in children may require antibiotics prophylactically until puberty or until the reflux resolves (see 'Prevention', below).
- Calculi may need removal.
- Surgical re-implantation of the ureters may be needed in severe cases but, in most cases, surgical management is not superior to medical.
- In severe cases, there may eventually be a need for dialysis or renal transplantation.

As with all other forms of CKD, the patient should be monitored for the development of hyperlipidaemia, hypertension, diabetes and deteriorating renal function [15] .

Complications

- Progressive renal scarring with reflux nephropathy and CKD.
- Secondary hypertension.
- Pyonephrosis.
- Focal glomerulosclerosis.
- Urea-splitting organisms can lead to staghorn calculi - the usual culprit is *Proteus* spp.

Prognosis

Adults with chronic pyelonephritis generally have good prognosis with preserved renal function if treated promptly.

Many children with VUR do not develop renal scarring, although data are lacking [16] . Higher grades of VUR correlate with higher rates of renal scars.

Prevention

- On the assumption that most pyelonephritis is caused by ascending infection, its prevention is based on preventing UTI. If children have structural abnormalities of the renal tract they require assessment with a view to correction.
- The use of prophylactic antibiotics to prevent renal scarring in children is controversial but the evidence suggests that it is unnecessary unless the child has more than two episodes of febrile UTI [17] .
- The evidence for the preventative benefits of cranberry juice is increasingly weak [18] .

- A Cochrane review of antibiotic treatment of asymptomatic bacteriuria in pregnancy found it effective in reducing the risk of pyelonephritis in pregnancy but that the estimate of the effect is very uncertain due to poor-quality evidence. Antibiotics lead to a reduction in low birth weight and preterm birth but the conclusion was that this should be interpreted with caution [19] .

Further reading

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