NICE National Institute for Health and Care Excellence

Public Health England

NICE guideline

Pyelonephritis (acute): antimicrobial prescribing

NICE guideline

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www.nice.org.uk/guidance/ng111

Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guideline should be read in conjunction with NG109 and NG112.

Overview

This guideline sets out an antimicrobial prescribing strategy for acute pyelonephritis (upper urinary tract infection) in children, young people and adults who do not have a catheter. It aims to optimise antibiotic use and reduce antibiotic resistance.

See a 3-page visual summary of the recommendations, including a table to support prescribing decisions.

There is also a NICE guideline on antimicrobial stewardship: systems and processes for effective antimicrobial medicine use.

Who is it for?

- Health professionals
- People with acute pyelonephritis, their families and carers

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Managing acute pyelonephritis

1.1.1 Be aware that acute pyelonephritis is an infection of one or both kidneys usually caused by bacteria travelling up from the bladder.

Treatment

1.1.2 In people aged 16 years and over with acute pyelonephritis, obtain a midstream urine sample before antibiotics are taken and send for culture and susceptibility testing.

1.1.3 In children and young people under 16 years with acute pyelonephritis, obtain a urine sample before antibiotics are taken and send for culture and susceptibility testing in line with the NICE guideline on urinary tract infection in under 16s.

1.1.4 Assess and manage children under 5 with acute pyelonephritis who present with fever as outlined in the NICE guideline on fever in under 5s.

1.1.5 Offer an antibiotic (see the recommendations on choice of antibiotic) to people with acute pyelonephritis. Take account of:

- the severity of symptoms

- the risk of developing complications, which is higher in people with known or suspected structural or functional abnormality of the genitourinary tract or immunosuppression
- previous urine culture and susceptibility results
- previous antibiotic use, which may have led to resistant bacteria.

1.1.6 When results of urine cultures are available:

- review the choice of antibiotic **and**
- change the antibiotic according to susceptibility results if the bacteria are resistant, using a narrow spectrum antibiotic wherever possible.

Advice when an antibiotic prescription is given

1.1.7 When an antibiotic is given, as well as the general advice on self-care, give advice about:

- possible adverse effects of the antibiotic, particularly diarrhoea and nausea
- nausea with vomiting also being a possible indication of worsening pyelonephritis
- seeking medical help if:
  - symptoms worsen at any time **or**
  - symptoms do not start to improve within 48 hours of taking the antibiotic **or**
  - the person becomes systemically very unwell.

Reassessment

1.1.8 Reassess if symptoms worsen at any time, or do not start to improve within 48 hours of taking the antibiotic, taking account of:

- other possible diagnoses
- any symptoms or signs suggesting a more serious illness or condition, such as sepsis
- previous antibiotic use, which may have led to resistant bacteria.

Referral and seeking specialist advice

1.1.9 Refer people aged 16 years and over with acute pyelonephritis to hospital if they have any symptoms or signs suggesting a more serious illness or condition (for example, sepsis).

1.1.10 Consider referring or seeking specialist advice for people aged 16 years and over with acute pyelonephritis if they:

- are significantly dehydrated or unable to take oral fluids and medicines **or**
- are pregnant **or**
- have a higher risk of developing complications (for example, people with known or suspected structural or functional abnormality of the genitourinary tract or underlying disease [such as diabetes or immunosuppression]).

1.1.11 Refer children and young people with acute pyelonephritis to hospital in line with the NICE guideline on urinary tract infection in under 16s.

For a short explanation of why the committee made these recommendations, see the evidence and committee discussion on choice of antibiotic.

Full details of the evidence and the committee's discussion are available in the evidence review.

1.2 Self-care

1.2.1 Advise people with acute pyelonephritis about using paracetamol for pain, with the possible addition of a low-dose weak opioid such as codeine for people over 12 years.

1.2.2 Advise people with acute pyelonephritis about drinking enough fluids to avoid dehydration.

For a short explanation of why the committee made these recommendations, see the evidence and committee discussion on self-care.

Full details of the evidence and the committee's discussion are available in the evidence review.

1.3 Choice of antibiotic

1.3.1 When prescribing an antibiotic for acute pyelonephritis, take account of local antimicrobial resistance (AMR) data from Public Health England and follow:

- table 1 for non-pregnant women and men aged 16 years and over
- table 2 for pregnant women aged 12 years and over
- table 3 for children and young people under 16 years.

1.3.2 Give oral antibiotics first line if the person can take oral medicines, and the severity of their condition does not require intravenous antibiotics.

1.3.3 Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

Table 1 Antibiotics for non-pregnant women and men aged 16 years and over

Treatment	Antibiotic, dosage and course length
First-choice oral antibiotics	**Cefalexin**: 500 mg twice or three times a day (up to 1 to 1.5 g three or four times a day for severe infections) for 7 to 10 days **Co-amoxiclav** (only if culture results available and susceptible): 500/125 mg three times a day for 7 to 10 days **Trimethoprim** (only if culture results available and susceptible): 200 mg twice a day for 14 days **Ciprofloxacin** (**only if** other first-choice antibiotics are unsuitable): 500 mg twice a day for 7 days See the MHRA January 2024 advice on restrictions and precautions for using fluoroquinolone antibiotics because of the risk of disabling and potentially long-lasting or irreversible side effects. Fluoroquinolones must now only be prescribed when other commonly recommended antibiotics are inappropriate

Treatment	Antibiotic, dosage and course length
First-choice intravenous antibiotics (if vomiting, unable to take oral antibiotics, or severely unwell). Antibiotics may be combined if susceptibility or sepsis a concern.	**Co-amoxiclav** (only in combination or if culture results available and susceptible): 1.2 g three times a day **Cefuroxime**: 750 mg to 1.5 g three or four times a day **Ceftriaxone**: 1 g to 2 g once a day **Gentamicin**: Initially 5 mg/kg to 7 mg/kg once a day, subsequent doses adjusted according to serum gentamicin concentration Therapeutic drug monitoring and assessment of renal function is required (BNF information on gentamicin) **Amikacin**: Initially 15 mg/kg once a day (maximum per dose 1.5 g once a day), subsequent doses adjusted according to serum amikacin concentration (maximum 15 g per course) Therapeutic drug monitoring and assessment of renal function is required (BNF information on amikacin) **Ciprofloxacin** (**only if** other first-choice antibiotics are unsuitable): 400 mg twice or three times a day See the MHRA January 2024 advice on restrictions and precautions for using fluoroquinolone antibiotics because of the risk of disabling and potentially long-lasting or irreversible side effects. Fluoroquinolones must now only be prescribed when other commonly recommended antibiotics are inappropriate
Second-choice intravenous antibiotics	Consult a local microbiologist

See the BNF for appropriate use and dosing in specific populations, for example, hepatic

impairment, renal impairment and breastfeeding, and administering intravenous antibiotics.

Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.

Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

Table 2 Antibiotics for pregnant women aged 12 years and over

Treatment	Antibiotic, dosage and course length
First-choice oral antibiotic	**Cefalexin**: 500 mg twice or three times a day (up to 1 g to 1.5 g three or four times a day for severe infections) for 7 to 10 days
First-choice intravenous antibiotic (if vomiting, unable to take oral antibiotics, or severely unwell)	**Cefuroxime**: 750 mg to 1.5 g three or four times a day
Second-choice antibiotics or when combining antibiotics if susceptibility or sepsis a concern	Consult local microbiologist

See the BNF for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment, and administering intravenous antibiotics.

Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.

Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

Table 3 Antibiotics for children and young people under 16 years

Treatment	Antibiotic, dosage and course length
Choice for children under 3 months	Refer to paediatric specialist and treat with intravenous antibiotics in line with the NICE guideline on fever in under 5s

Treatment	Antibiotic, dosage and course length
First-choice oral antibiotic for children aged 3 months and over	**Cefalexin**: 3 months to 11 months, 12.5 mg/kg or 125 mg twice a day for 7 to 10 days (25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections) 1 year to 4 years, 12.5 mg/kg twice a day or 125 mg three times a day for 7 to 10 days (25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections) 5 years to 11 years, 12.5 mg/kg twice a day or 250 mg three times a day for 7 to 10 days (25 mg/kg two to four times a day [maximum 1 g per dose four times a day] for severe infections) 12 years to 15 years, 500 mg twice or three times a day (up to 1 g to 1.5 g three or four times a day for severe infections) for 7 to 10 days **Co-amoxiclav** (only if culture results available and susceptible): 3 months to 11 months, 0.25 ml/kg of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 1 years to 5 years, 0.25 ml/kg of 125/31 suspension or 5 ml of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection) 6 years to 11 years, 0.15 ml/kg of 250/62 suspension or 5 ml of 250/62 suspension three times a day for 7 to 10 days (dose doubled in severe

Treatment	Antibiotic, dosage and course length
	infection) 12 years to 15 years, 250/125 mg or 500/125 mg three times a day for 7 to 10 days

Treatment	Antibiotic, dosage and course length
First-choice intravenous antibiotics (if vomiting, unable to take oral antibiotics or severely unwell) for children aged 3 months and over. Antibiotics may be combined if susceptibility or sepsis a concern	**Co-amoxiclav** (only in combination or if culture results available and susceptible): 3 months to 15 years, 30 mg/kg three times a day (maximum 1.2 g three times a day) **Cefuroxime**: 3 months to 15 years, 20 mg/kg three times a day (maximum 750 mg per dose), increased to 50 mg/kg to 60 mg/kg three or four times a day (maximum 1.5 g per dose) for severe infections **Ceftriaxone**: 3 months to 11 years (up to 50 kg), 50 mg/kg to 80 mg/kg once a day (maximum 4 g per day) 9 years to 11 years (50 kg and above), 1 g to 2 g once a day 12 years to 15 years, 1 g to 2 g once a day **Gentamicin**: Initially 7 mg/kg once a day, subsequent doses adjusted according to serum gentamicin concentration Therapeutic drug monitoring and assessment of renal function is required (BNFC information on gentamicin) **Amikacin**: Initially 15 mg/kg once a day, subsequent doses adjusted according to serum amikacin concentration Therapeutic drug monitoring and assessment of renal function is required (BNFC information on amikacin)

Treatment	Antibiotic, dosage and course length
Second-choice intravenous antibiotics for children aged 3 months and over	Consult a local microbiologist

See the BNF for children for appropriate use and dosing in specific populations, for example, hepatic and renal impairment, and administering intravenous antibiotics. See table 2 if a young woman is pregnant.

The age bands apply to children of average size and, in practice, the prescriber will use the age bands in conjunction with other factors such as the severity of the condition being treated and the child's size in relation to the average size of children of the same age.

Check any previous urine culture and susceptibility results and antibiotic prescribing, and choose antibiotics accordingly. Where a child or young person is receiving prophylactic antibiotics, treatment should be with a different antibiotic, not a higher dose of the same antibiotic.

Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total of 10 days. If intravenous treatment is not possible, consider intramuscular treatment if suitable.

For a short explanation of why the committee made these recommendations, see the evidence and committee discussion on choice of antibiotic, antibiotic course length and antibiotic route of administration.

Full details of the evidence and the committee's discussion are available in the evidence review.

Summary of the evidence

The recommendations in this guideline are based on the evidence identified, which was mainly for people with acute pyelonephritis. Some studies also included people with a complicated urinary tract infection (UTI; associated with a structural or functional abnormality, or underlying disease, which increases the risk of a more serious outcome or treatment failure) or urosepsis (a systemic response to a UTI).

Self-care

- No systematic reviews or randomised controlled trials (RCTs) of any non-antimicrobial treatments were identified that met the inclusion criteria.

Committee discussion on self-care

- There was no evidence for the use of oral analgesia in acute pyelonephritis. However, paracetamol has a well-established efficacy and safety profile for managing pain. The committee agreed that it was reasonable to advise people about paracetamol for self-management of pain. A low-dose weak opioid, such as codeine, could be taken with paracetamol by adults and young people over 12 years for more severe pain.
- Non-steroidal anti-inflammatory drugs, such as ibuprofen, are generally not recommended for people with acute pyelonephritis because of concerns about renal safety.
- The committee discussed the need for an adequate intake of fluids to ensure a high urine output, which is believed to help resolve acute pyelonephritis through a mechanical flushing of bacteria from the kidney. No evidence was found for this and there was no evidence of what constitutes adequate hydration. However, based on committee experience that dehydration is often cited as a cause of UTIs, the committee agreed that people should be advised about drinking enough fluids to avoid dehydration.

Antibiotics

- Acute pyelonephritis is a bacterial infection needing treatment with an antibiotic that reaches therapeutic concentrations in the kidney.
- Gram-negative bacteria are the most common causative pathogens in acute pyelonephritis, with Escherichia coli (E. coli) causing 60 to 80% of uncomplicated infections. Other gram-negative pathogens include Proteus mirabilis (responsible for about 15% of infections) as well as Klebsiella (approximately 20%), Enterobacter and Pseudomonas species. Less commonly, gram-positive bacteria such as Enterococcus faecalis, Staphylococcus saprophyticus and Staphylococcus aureus may be seen.
- Complications of acute pyelonephritis include impaired renal function or renal failure, sepsis and preterm labour in pregnancy.

Choice of antibiotic

Efficacy of antibiotics

- An intravenous cephalosporin (ceftolozane/tazobactam or ceftazidime) was compared with an intravenous fluoroquinolone (levofloxacin or ciprofloxacin) in 2 RCTs (Wagenlehner et al. 2015 and Pasiechnikov et al. 2015) in adults with acute pyelonephritis, acute obstructive pyelonephritis or complicated UTI. Moderate quality evidence found that ceftolozane/tazobactam was significantly more effective than levofloxacin for improving composite cure (clinical cure and microbiological eradication and microbiological cure; 76.9% versus 68.4%, number needed to treat [NNT] 12 [range 7 to 43]) but there was no significant difference between antibiotics for clinical cure. Ceftazidime had a significantly higher rate of clinical cure compared with ciprofloxacin (88.9% versus 73.8%; NNT 7 [range 4 to 62]; very low quality evidence).
- An intravenous cephalosporin (ceftriaxone or ceftazidime/avibactam) was compared with an intravenous carbapenem (ertapenem or imipenem/cilastatin) in 2 RCTs (Park et al. 2012 and Vazquez et al. 2012) in adults with acute pyelonephritis or complicated UTI. Very low to high quality evidence found that these cephalosporins and carbapenems were equally effective.
- Very low quality evidence from a small single RCT (Moramezi et al. 2008) in pregnant women with acute pyelonephritis found no significant difference between intravenous

cephalothin and intravenous ampicillin plus gentamicin in the duration of lower UTI symptoms or costovertebral angle pain. The mean time to end of fever was reduced with ampicillin plus gentamicin compared with cephalothin (mean 11 hours lower, p=0.01; very low quality evidence).

- One RCT (Peterson et al. 2008) compared different fluoroquinolones (levofloxacin and ciprofloxacin: intravenous or oral) for acute pyelonephritis and complicated UTI in adults and found no significant differences in clinical or microbiological outcomes at follow-up (high quality evidence).
- One RCT (Talan et al. 2000) compared oral ciprofloxacin with oral co-trimoxazole for acute pyelonephritis in adult women. Low to moderate quality evidence found that ciprofloxacin was significantly more effective for clinical cure (96.5% versus 82.9%; NNT 8 [range 5 to 18]) and microbiological cure (99.1% versus 89.1%; NNT 10 [range 7 to 28]) than co-trimoxazole.
- Low quality evidence from 2 RCTs (Wagenlehner et al. 2015 and Park et al. 2012) found no difference between antibiotics (ceftolozane/tazobactam versus levofloxacin, and ertapenem versus ceftriaxone) for treating bacteraemia secondary to complicated UTI or acute pyelonephritis in adults.
- The evidence for children is based on 1 systematic review (Strohmeier et al. 2014) in acute pyelonephritis. No evidence from systematic reviews or RCTs was identified for children with complicated UTI. This systematic review did not find major differences in clinical effectiveness between different antibiotics compared in the studies (third- and fourth-generation cephalosporins, aminoglycosides, co-amoxiclav and co-trimoxazole; very low to moderate quality evidence).

Safety of antibiotics

- Antibiotic-associated diarrhoea occurs in 2 to 25% of people taking antibiotics, depending on the antibiotic used (NICE clinical knowledge summary on diarrhoea – antibiotic associated).
- About 10% of the general population claim to have a penicillin allergy; this is often because of a skin rash that occurred while taking a course of penicillin as a child. Fewer than 10% of people who think they are allergic to penicillin are truly allergic. See the NICE guideline on drug allergy for more information.
- People with a history of immediate hypersensitivity to penicillins may also react to

cephalosporins and other beta-lactam antibiotics (BNF information on phenoxymethylpenicillin).

- Trimethoprim has a teratogenic risk in the first trimester of pregnancy (folate antagonist; BNF information on trimethoprim). The manufacturers advise that it is contraindicated in pregnancy (trimethoprim summary of product characteristics).
- Fluoroquinolones are generally not recommended in children or young people who are still growing (BNF information on ciprofloxacin). The manufacturers advise to avoid in pregnancy (ciprofloxacin summary of product characteristics). Tendon damage (including rupture) has been reported rarely in people receiving fluoroquinolones (BNF information on ciprofloxacin), and the European Medicines Agency's Pharmacovigilance Risk Assessment Committee in a press release (October 2018) has recommended restricting the use of these antibiotics following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons and bones and the nervous system. Fluoroquinolones remain an option in acute pyelonephritis, which is a severe infection.
- Aminoglycoside doses are based on weight and renal function, and whenever possible treatment should not exceed 7 days (BNF information on aminoglycosides).
- Overall there did not appear to be major differences in adverse effects between antibiotics based on the included studies, although these were not well reported (very low to low quality evidence).
- See the summaries of product characteristics for information on contraindications, cautions and adverse effects of individual medicines.

Committee discussion on choice of antibiotic

- Based on evidence and experience, the committee agreed that acute pyelonephritis is a bacterial infection needing treatment with antibiotics that reach therapeutic concentrations in the kidney. Antibiotics that don't achieve adequate levels in renal tissue, such as nitrofurantoin, fosfomycin and pivmecillinam, are to be avoided.
- A urine sample should be sent for culture to confirm susceptibility of the bacteria and inform treatment choice.
- The committee reviewed the available evidence comparing different antibiotics in adults and children and agreed that it was limited by its setting (most studies in adults were undertaken in a hospital, and in children the setting of the studies was not reported). The studies included various different antibiotics, which may not reflect those chosen in UK practice. The committee discussed the evidence for a benefit of the intravenous third-generation cephalosporins, ceftolozane/tazobactam or ceftazidime, over an intravenous fluoroquinolone, but this was mainly limited to a benefit for composite cure (which included clinical cure, microbiological eradication and microbiological cure) and the absolute benefits were small.
- The committee agreed, based on experience, that several oral and intravenous antibiotics should be available for people with acute pyelonephritis. This enables antibiotics to be selected based on the severity of illness, antibiotic susceptibilities from culture results when available, local resistance patterns, risk of resistant bacteria, the setting, and known patient factors (such as whether the person has a higher risk of developing complications). In line with antimicrobial stewardship, narrower-spectrum antibiotics should be used wherever possible.
- Nationally for England, resistance of E. coli (the main causative organism of acute pyelonephritis) in laboratory-processed urine specimens to the following antibiotics is:
  - cefalexin: 9.9% (varies by area from 8.1 to 11.4%)
  - ciprofloxacin: 10.6% (varies by area from 7.8 to 13.7%)
  - co-amoxiclav: 19.8% (varies by area from 10.8 to 30.7%)

  - trimethoprim: 30.3% (varies by area from 27.1 to 33.4%).

    (Public Health England. Antimicrobial resistance quarterly surveillance: March 2018)

- The committee also discussed that prescribers should be aware of their local antimicrobial prescribing data, because resistance rates do vary by area.
- The committee agreed that any recent previous urine culture and susceptibility results, and antibiotic prescribing, should be reviewed before choosing an antibiotic.
- Based on experience, the committee agreed that if the results of urine culture suggest the bacteria are resistant to the antibiotic given, people with acute pyelonephritis should be contacted and the antibiotic changed regardless of whether symptoms are improving or not. The committee agreed that acute pyelonephritis is a serious infection and antibiotics should be changed to ensure cure.

Non-pregnant women and men with acute pyelonephritis

- Based on evidence, their experience and resistance data, the committee agreed to recommend a choice of first-line **oral antibiotics**, at usual doses for acute pyelonephritis. These are:
  - **cefalexin** (a first-generation cephalosporin); based on its broad spectrum of activity and acceptable levels of resistance
  - **co-amoxiclav** (a penicillin with a beta-lactamase inhibitor); which is only suitable if culture results are available and bacteria are susceptible, because resistance rates are high
  - **trimethoprim;** which is only suitable if culture results are available and bacteria are susceptible, because resistance rates are high
  - **ciprofloxacin** (a fluoroquinolone); based on its broad spectrum of activity and acceptable levels of resistance (particularly for people who have had previous treatment with penicillins, or cannot tolerate or are allergic to penicillins).

- The committee noted that use of broad-spectrum antibiotics, such as later-generation cephalosporins, fluoroquinolones or co-amoxiclav, can create a selective advantage for bacteria resistant to these second-line broad-spectrum agents, allowing such strains to proliferate and spread. And, by disrupting normal flora, broad-spectrum antibiotics can leave people susceptible to harmful bacteria such as Clostridium difficile in community settings. However, these antibiotics are appropriate for the empirical treatment of acute pyelonephritis, where coverage of more resistant strains of common bacterial pathogens is required.
- The committee was aware of the European Medicines Agency's Pharmacovigilance Risk Assessment Committee recommendation to restrict the use of fluoroquinolone antibiotics following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons and bones and the nervous system. However, they discussed that fluoroquinolone antibiotics are a valuable option for the treatment of acute pyelonephritis, which is a severe infection, and it is appropriate to reserve fluoroquinolone use for such conditions. Resistant gram-negative organisms are a particular concern in acute pyelonephritis, and the committee agreed that ciprofloxacin should remain a first-choice option to cover what can be a complex infection. The committee was keen to point out, however, that cefalexin, co-amoxiclav and trimethoprim are also first-choice options, and antibiotics should be chosen on an individual patient basis, taking fluoroquinolone safety concerns, as well as susceptibility and resistance, into account.
- Based on evidence, experience and resistance data, the committee agreed to recommend a choice of first-line **intravenous antibiotics**, at usual doses, for people with acute pyelonephritis who are unable to take oral antibiotics due to vomiting, or are more severely unwell. These are:
  - **co-amoxiclav** (only in combination or if culture results are available and bacteria are susceptible)
  - **cefuroxime** (a second-generation cephalosporin) or **ceftriaxone** (a third-generation cephalosporin)
  - **ciprofloxacin** (taking safety concerns into account)

  - **gentamicin** or **amikacin** (aminoglycosides); which may be appropriate for some people with acute pyelonephritis, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed at 48 hours. Gentamicin is the preferred aminoglycoside in the UK, but shortages of certain antibiotics may result in the use of alternatives; for example, amikacin in place of gentamicin.

- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist, taking into account local antimicrobial resistance data.

Pregnant women with acute pyelonephritis

- Based on experience and resistance data, the committee agreed to recommend **cefalexin** (a first-generation cephalosporin) as the first-choice oral antibiotic for pregnant women who don't require intravenous antibiotics, and **cefuroxime** (a second-generation cephalosporin) as the first-choice intravenous antibiotic.

- Ciprofloxacin and trimethoprim are not recommended because they should be avoided in pregnancy. Co-amoxiclav was not recommended because of high resistance levels nationally and the risks of treatment failure in pregnancy.

- The committee agreed, based on experience, that local microbiologists should be consulted for advice on second-choice antibiotics, or combining antibiotics if susceptibility or sepsis is a concern.

Children and young people with acute pyelonephritis

- The committee was aware that the NICE guideline on urinary tract infection in under 16s makes recommendations on diagnosing acute pyelonephritis and considering referral to a paediatric specialist.

- Based on evidence, their experience and resistance data, the committee agreed to recommend **cefalexin** or **co-amoxiclav** (only if culture results are available and bacteria are susceptible) at usual doses for acute pyelonephritis, as first-choice **oral antibiotics**.

- Based on evidence, experience and resistance data, the committee agreed to recommend a choice of first-line **intravenous antibiotics**, at usual doses, for children and young people who are unable to take oral antibiotics due to vomiting, or are more severely unwell. These are:
  - **co-amoxiclav** (only in combination or if culture results are available and bacteria are susceptible); which can be given intravenously
  - **cefuroxime** (a second-generation cephalosporin) or **ceftriaxone** (a third-generation cephalosporin); which would be suitable alternatives to co-amoxiclav
  - **gentamicin** or **amikacin** (aminoglycosides); which may be appropriate for some children and young people with acute pyelonephritis, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed at 48 hours.
- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of children and young people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist, taking into account local antimicrobial resistance data.

Antibiotic course length

- The evidence for antibiotic course length in the treatment of acute pyelonephritis in adults comes from 2 systematic reviews (Eliakim-Raz et al. 2013 and Kyriakidou et al. 2008) and 1 RCT (Ren et al. 2017). No significant differences were found for clinical, microbiological or safety and tolerability outcomes between short courses and longer courses of antibiotics (7 days or fewer compared with 10 days to 6 weeks in 1 systematic review, and 7 to 14 days compared with 14 to 42 days in the other systematic review [very low to moderate quality evidence]). There were no significant differences between a short course (5 days) of intravenous levofloxacin (750 mg once daily) and a longer course (7 to 14 days) of intravenous and then oral levofloxacin (500 mg once daily; moderate quality evidence).
- There were some significant differences in clinical effectiveness between different antibiotic course lengths in 1 systematic review in children with acute pyelonephritis

(Strohmeier et al. 2014). However, this was limited to 1 RCT comparing 10 days of oral sulfafurazole with 42 days (moderate quality evidence), with other studies in the review finding no differences in outcomes (very low quality evidence). Safety and tolerability outcomes were not reported.

Committee discussions on antibiotic course length

- The committee agreed that the shortest course that is likely to be effective should be prescribed to reduce the risk of antimicrobial resistance and minimise the risk of adverse effects.
- Based on evidence, the committee agreed that a short course of antibiotics was generally as effective as a long course of antibiotics for acute pyelonephritis, but the definition of short and long course differed depending on the clinical trial definition and the antibiotic used.
- In line with the NICE guideline on antimicrobial stewardship and Public Health England's 'Start smart – then focus' toolkit, the committee agreed that the use of intravenous antibiotics should be reviewed by 48 hours (taking into account the person's response to treatment and susceptibility results from urine culture) and switched to oral treatment where possible.

Non-pregnant women and men with acute pyelonephritis

- Based on evidence, experience and resistance data, the committee agreed that, for oral treatment, a 7-day course of ciprofloxacin was sufficient to treat acute pyelonephritis in non-pregnant women and men. However, because there was no evidence for 7-day courses of cefalexin or co-amoxiclav, a range of 7 to 10 days was recommended for these antibiotics. For trimethoprim, a 14-day course was recommended because there was no evidence for course lengths shorter than 14 days.
- For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible, for a total of 7 days.

Pregnant women with acute pyelonephritis

- Based on evidence, experience and resistance data, the committee agreed that, for oral treatment, a 7- to 10-day course of cefalexin was required to treat acute pyelonephritis in pregnant women. For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible, for a total of 7 days.

Children and young people with acute pyelonephritis

- Based on evidence, experience and resistance data, the committee agreed that a 7- to 10-day course of oral antibiotics was required to treat acute pyelonephritis in children and young people. For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible, for a total of 10 days.

Antibiotic dose frequency

- No systematic reviews or RCTs that compared the frequency of antibiotic dosing in adults were identified that met the inclusion criteria.
- Evidence from 1 systematic review in children with acute pyelonephritis (Strohmeier et al. 2014) found no significant difference in the clinical effectiveness of aminoglycosides with once-daily administration compared with 8-hourly administration (moderate quality evidence). There were no significant differences in the number of children with hearing impairment or kidney dysfunction (very low quality evidence).

Antibiotic route of administration

- The evidence for route of antibiotic administration in acute pyelonephritis is based on 1 systematic review of 15 RCTs in adults and children (Pohl 2007). This review addressed different modes of administration of antibiotics, which cover:
  - sequential intravenous then oral treatment compared with intravenous or intramuscular treatment
  - sequential intravenous then oral treatment compared with oral treatment
  - oral treatment compared with intravenous or intramuscular treatment
  - single-dose intravenous or intramuscular treatment then oral treatment compared with sequential intravenous then oral treatment.
- Overall, this review found that oral antibiotics were as effective as other routes of

administration in treating symptomatic severe UTI (including pyelonephritis) in both adults and children. Intravenous or intramuscular antibiotics were significantly better for bacteriological cure than oral antibiotics at the end of treatment, but this is based on 1 small RCT (NNT 4 [range 3 to 15]; low quality evidence).

- There were no significant differences in adverse effects between different routes of administration of antibiotics (very low quality evidence).
- Further evidence is available from 1 systematic review in children with acute pyelonephritis (Strohmeier et al. 2014), which compared different routes of administration, which cover:
  - oral treatment compared with sequential intravenous then oral treatment
  - sequential intravenous then oral treatment (short course of 3 to 4 days) compared with intravenous treatment (longer course of 7 to 14 days)
  - single-dose intramuscular then oral treatment compared with oral treatment
  - oral treatment compared with rectal treatment.
- Overall, this review found no significant differences in the clinical effectiveness of oral antibiotics (cephalosporins or co-amoxiclav) in children with acute pyelonephritis compared with other routes of administration (very low to moderate quality evidence).
- Safety and tolerability outcomes were poorly reported in the RCTs included in Strohmeier et al. 2014, but there did not appear to be any significant differences between different routes of administration of antibiotics (very low quality evidence).

Committee discussions on antibiotic route of administration

- Based on evidence, the committee agreed that, overall, oral antibiotics were as effective as other routes of administration for treating acute pyelonephritis in adults and children.
- The committee agreed, based on evidence and experience, that oral antibiotics should be given first line when people can take oral medicines and the severity of their condition does not require intravenous antibiotics.
- The committee agreed, based on evidence and experience, that intravenous antibiotics can be used for people who are unable to take oral antibiotics due to vomiting, or are more severely unwell, in line with Public Health England's 'Start smart – then focus' toolkit.

See the full evidence review for more information.

Other considerations

Medicines adherence

Medicines adherence may be a problem for some people with medicines that require frequent dosing (for example, some antibiotics) or longer treatment duration (see the NICE guideline on medicines adherence).

Resource implications

- One small randomised controlled trial (RCT; Moramezi et al. 2008) in pregnant women with acute pyelonephritis found no significant difference in length of hospital stay in women taking a cephalosporin compared with ampicillin plus gentamicin (p=0.22; very low quality evidence).
- One RCT (Talan et al. 2000), which compared ciprofloxacin with co-trimoxazole in adult women with acute pyelonephritis, found that resource use (hospital stay, visits and telephone contacts, laboratory tests and prescription costs) was higher in the co-trimoxazole group (no analysis reported). The only exception was for radiological procedures, which was slightly higher in the ciprofloxacin group (no analysis reported). One systematic review (Eliakim-Raz et al. 2013), which compared antibiotic course lengths in adults with acute pyelonephritis and included the Talan et al. (2000) study, noted a shorter duration of hospital stay with a short course of antibiotics (7 days or fewer) compared with a longer course (10 days to 6 weeks).
- One RCT in the systematic review by Strohmeier et al. (2014) in children with acute pyelonephritis found that giving sequential intravenous then oral antibiotics reduced the duration of hospital stay compared with a longer duration of intravenous antibiotics (4.9 days compared with 9.8 days).
- Recommended antibiotics are available as generic formulations, see the Drug Tariff for costs.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE topic page on antimicrobial stewardship.

For full details of the evidence and the guideline committee's discussion, see the evidence review. You can also find information about how the guideline was developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put this guidance into practice.

Update information

Minor changes since publication

September 2024: We updated table 1 to reflect the new safety advice on fluoroquinolones.

September 2019: Minor wording changes were made and a footnote was updated in table 1 to reflect new restrictions and precautions for the use of fluoroquinolone antibiotics.

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