Acute prostatitis: antimicrobial prescribing NICE guideline

Draft for consultation, May 2018

This guideline sets out an antimicrobial prescribing strategy for acute prostatitis. It aims to optimise antibiotic use and reduce antibiotic resistance.

See a 2-page visual summary of the recommendations, including tables to support prescribing decisions.

Who is it for?

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

The guideline contains:

- the draft recommendations
- summary of the evidence.

Information about how the guideline was developed is on the <u>guideline's</u> <u>page</u> on the NICE website. This includes the full evidence review, details of the committee and any declarations of interest.

Recommendations

1.1 Managing acute prostatitis

- 1.1.1 Be aware that acute prostatitis:
 - is a bacterial infection of the prostate needing treatment with antibiotics
 - is usually caused by bacteria entering the prostate from the urinary tract

- can occur spontaneously or after medical procedures such as prostate biopsy
- can last several weeks
- can cause complications such as acute urinary retention and prostatic abscess.

Treatment for acute prostatitis

- 1.1.2 Obtain a midstream urine sample before prescribing antibiotics for people with acute prostatitis and send for culture and susceptibility testing.
- 1.1.3 Offer an antibiotic (see the recommendations on <u>choice of</u> <u>antibiotic</u>) to people with acute prostatitis. Take account of:
 - the severity of symptoms
 - the risk of developing complications or having treatment failure, particularly after medical procedures such as prostate biopsy
 - previous urine culture and susceptibility results
 - previous antibiotic use, which may have led to resistant bacteria.
- 1.1.4 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

- 1.1.5 When an antibiotic is given, give advice about:
 - the usual course of acute prostatitis (several weeks)
 - possible adverse effects of the antibiotic, particularly diarrhoea and nausea
 - seeking medical help if symptoms worsen rapidly or significantly at any time, do not start to improve within 48 hours of taking the antibiotic, or the person becomes systemically very unwell.

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Reassessing symptoms

- 1.1.6 Reassess at any time if symptoms worsen rapidly or significantly, taking account of:
 - other possible diagnoses
 - any symptoms or signs suggesting a more serious illness or condition, such as acute urinary retention, prostatic abscess or sepsis
 - previous antibiotic use, which may have led to resistant bacteria.

Referring to hospital

- 1.1.7 Refer people with acute prostatitis to hospital if they have:
 - a severe systemic infection (any of the high risk criteria from the NICE guideline on <u>sepsis</u>), or
 - complications, such as acute urinary retention or suspected prostatic abscess, or
 - symptoms that are not improving 48 hours after starting the antibiotic.

See the evidence and committee discussion on antibiotics.

1.2 Self-care

- 1.2.1 Consider paracetamol (with or without a weak opioid, such as codeine) or, if preferred and suitable, a non-steroidal anti-inflammatory drug (NSAID) for pain in people with acute prostatitis.
- 1.2.2 Advise people with acute prostatitis about the intake of adequate fluids.

See the evidence and committee discussion on self-care.

1.3 Choice of antibiotic

- 1.3.1 When prescribing antibiotic treatment for acute prostatitis follow table 1 for adults aged 18 years and over.
- 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.
- 1.3.4 Review antibiotic treatment after 14 days and either stop the antibiotic or continue for a further 14 days if needed, for example, based on the person's history, symptoms, recent examination, urine or blood tests.

Antibiotic ¹	Dosage and course length ²
First choice oral antibiotic (guided by susceptibilities when available) ³	
Ciprofloxacin	500 mg twice a day for 14 days then review ⁴
Ofloxacin	200 mg twice a day for 14 days then review ⁴
Alternative first choice oral antibiotic for adults unable to take a quinolone (guided by susceptibilities when available) ³	
Trimethoprim	200 mg twice day for 14 days then review ⁴
Second choice oral antibiotic (after discussion with specialist)	
Levofloxacin	500 mg once a day for 14 days then review ⁴
Co-trimoxazole ⁵	960 mg twice day for 14 days then review ⁴
Intravenous antibiotic (if unable to take oral antibiotics or severely unwell; guided by susceptibilities when available). Antibiotics may be combined if sepsis a concern ^{3,6}	
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Table 1. Antibiotics for adults aged 18 years and over

²Consider oral antibiotics first-line, where appropriate.

³Check any previous urine culture and susceptibility results and antibiotic prescribing for this indication and choose antibiotics accordingly.

⁴Review treatment after 14 days and either stop the antibiotic or continue for a further 14 days if needed.

⁵Only use where there is bacteriological evidence of sensitivity and good reasons to prefer this antibiotic (<u>BNF, April 2018</u>).

⁵Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total of 14 days then review.

See the evidence and committee discussion on choice of antibiotic.

Summary of the evidence

Self-care

 No systematic reviews, randomised controlled trials (RCTs) or observational studies of the efficacy of non-antimicrobial treatments for acute prostatitis were identified. However, paracetamol (with or without a weak opioid, such as codeine) and non-steroidal anti-inflammatory drugs (NSAIDs) have well-established efficacy and safety profiles for managing pain; and maintaining full hydration is important in people with acute prostatitis.

Committee discussion on self-care

- Based on experience, the committee agreed that it was reasonable to consider paracetamol (with or without a weak opioid, such as codeine) for managing pain in adults with acute prostatitis. These medicines have a well-established efficacy and safety profile for managing pain.
- If preferred and suitable, a NSAID could be considered. However, NSAIDs can interact with quinolones, potentially increasing the risk of seizures, and this should be taken into account when selecting antibiotics and pain relief.
- Based on experience, the committee agreed that people should be advised about the adequate intake of fluids because maintaining full hydration is important in people with urinary tract infections, including acute prostatitis.

Antibiotics

- Acute prostatitis is a bacterial infection needing prompt treatment with antibiotics.
- Gram-negative bacteria are the most common causative pathogens in acute prostatitis, most commonly *Escherichia coli*, *Proteus species*, *Klebsiella species* and *Pseudomonas species*.
- Complications of acute prostatitis include acute urinary retention secondary to prostatic oedema, chronic prostatitis, prostatic abscess, bacteraemia, epididymitis and pyelonephritis.

Efficacy of antibiotics

 No systematic reviews, RCTs or observational studies of the efficacy of antibiotics for treating acute prostatitis were identified.

Safety of antibiotics

 Quinolones can interact with NSAIDs, potentially increasing the risk of seizures (<u>BNF, April 2018</u>).

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- Allergic reactions to penicillins occur in 1 to 10% of people and anaphylactic reactions occur in less than 0.05%. People with a history of atopic allergy (for example, asthma, eczema and hay fever) are at a higher risk of anaphylactic reactions to penicillins. People with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics (<u>BNF, April 2018</u>). See the NICE guideline on <u>drug allergy: diagnosis and management</u> for more information.
- Aminoglycoside doses are based on weight and renal function and whenever possible treatment should not exceed 7 days (<u>BNF, April 2018</u>).
- There are restrictions on the use of co-trimoxazole in the UK. It should only be used in urinary tract infections where there is bacteriological evidence of sensitivity and good reasons to prefer this antibiotic (<u>BNF, April 2018</u>).
- See the <u>summaries of product characteristics</u> and <u>BNF</u> for information on contraindications, cautions and adverse effects of individual medicines.

Committee discussion on antibiotics

- The committee agreed that acute prostatitis is a bacterial infection needing prompt treatment with antibiotics, but no evidence was identified to support this.
- The committee was aware of several guidelines, which reflect current practice, that make recommendations based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns.
- Based on experience, the committee agreed that adults with acute prostatitis should be offered an antibiotic. Urine should be sent for culture to confirm susceptibility of the bacteria and inform treatment choice.
- The committee agreed that when results of urine cultures are available, if the results suggest the bacteria are not susceptible to the antibiotic given, the antibiotic should be changed. In line with good antimicrobial stewardship, narrow spectrum antibiotics should be used wherever possible, and antibiotics switched from intravenous to oral where applicable.

 The committee agreed that if symptoms do not start to improve within 48 hours of taking an antibiotic, people should be referred to hospital because of concerns around complications, such as such as acute urinary retention or prostatic abscess, and treatment failure because of resistant bacteria.

Choice of antibiotic

- Many antibiotics penetrate the prostate gland poorly, but quinolones reach therapeutic levels in the prostate. Where quinolone resistance is a concern, other antibiotics that can reach therapeutic prostate levels include thirdgeneration cephalosporins (such as ceftriaxone), carbapenems (such as aztreonam, imipenem or ertapenem), some aminoglycosides, piperacillin, minocycline, doxycycline, erythromycin, clindamycin and trimethoprim (Lipsky et al. 2010). In acute prostatitis, where there is intense inflammation of the prostate gland, antibiotic penetration can be better than in chronic prostatitis (National guidelines for the management of prostatitis, BASHH, 2001).
- Several guidelines make recommendations on antibiotic choice based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns. These include:
 - European Association of Urology guidelines on urological infections (2017)
 - <u>RCGP/BASHH Sexually transmitted infections in primary care guidelines</u> (2013)
 - BASHH national guidelines for the management of prostatitis (2001).

Committee discussion on choice of antibiotic

 No evidence was identified to guide the choice of antibiotics for treating acute prostatitis. The committee was aware of several guidelines, which reflect current practice, that make recommendations based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns.

- Based on experience, the committee agreed that treating acute prostatitis requires high doses of quinolones, second or third-generation cephalosporins or broad-spectrum penicillins (possibly combined with an aminoglycoside), with intravenous or oral use based on the severity of symptoms and the ability to take oral medicines. These antibiotics reach therapeutic levels in the prostate, and are in line with current guidelines and practice.
- Based on experience and resistance data, the committee agreed that the choice of first and second-line oral antibiotics for managing acute prostatitis are:
 - first-line: ciprofloxacin or ofloxacin (quinolones), or trimethoprim (for adults unable to take a quinolone; trimethoprim generally has a lower risk of resistance in men, and can reach therapeutic prostate levels)
 - second-line: levofloxacin (a quinolone) or co-trimoxazole
- The committee agreed that second-line oral antibiotics should be reserved for use after discussion with a specialist. This is to preserve the use of the broader spectrum quinolone, levofloxacin, for people with a more severe infection, and because of restrictions on the use of cotrimoxazole in the UK.
- The committee agreed that the choice of **intravenous antibiotics** for managing acute prostatitis in people who are severely unwell or unable to take oral antibiotics (with combined use if sepsis is a concern) are:
 - ciprofloxacin or levofloxacin (quinolones)
 - cefuroxime or ceftriaxone (second or third generation cephalosporins)
 - piperacillin with tazobactam (a broad-spectrum penicillin)
 - gentamicin or amikacin (aminoglycosides).
- This choice allows intravenous antibiotics to be selected based on the severity of illness and likely pathogens, antibiotic susceptibilities from culture results when available, and local resistance patterns.

Antibiotic course length

- Several guidelines make recommendations on antibiotic course length based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns. These include:
 - European Association of Urology guidelines on urological infections (2017)
 - <u>RCGP/BASHH Sexually transmitted infections in primary care guidelines</u> (2013)
 - BASHH national guidelines for the management of prostatitis (2001).
- In line with the Department of Health guidance (<u>Start smart then focus</u>), the NICE guideline on <u>antimicrobial stewardship</u>, recommends considering a review of intravenous antibiotic prescriptions at 48 to 72 hours, documenting response to treatment and any available culture and susceptibility results to determine if the antibiotic should be continued or switched to a narrower spectrum or an oral antibiotic.

Committee discussion on antibiotic course length

- No evidence was identified to guide antibiotic course length for treating acute prostatitis. The committee was aware of several guidelines that make recommendations based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns.
- Based on experience, the committee agreed that treating acute prostatitis requires oral antibiotics for between 2 and 4 weeks, with initial intravenous antibiotics if adults are unable to take oral antibiotics or are severely unwell. This is in line with current guidelines and practice.
- However, in line with good antimicrobial stewardship, 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. Firstline antibiotics for acute prostatitis are quinolones, which are broadspectrum antibiotics. These antibiotics, in particular, should be used for the shortest effective time because they can create a selective advantage for bacteria resistant to these 'last-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* infection in community settings.

- Use of intravenous antibiotics should be reviewed by 48 hours (taking into account the persons response to treatment and susceptibility results from urine culture) and switched to oral treatment where possible.
- The committee agreed that a minimum of a 14-day course of all the recommended antibiotics was required for acute prostatitis. At 14 days, treatment should be reviewed, and either stopped or continued for a further 14 days as needed. From experience, the committee discussed that whether to continue treatment or not would be based on the person's history or risk of developing chronic prostatitis, their current symptoms and any recent examination, urine or blood test results. Continued symptoms, such as fever or lower urinary tract symptoms (dysuria, frequency, urgency, or acute urinary retention) require ongoing treatment.

Antibiotic prophylaxis for preventing infective complications, including acute prostatitis, after biopsy

 One double blind RCT from Iran (<u>Dadashpour et al. 2016</u>) and 4 observational studies from Taiwan, Turkey or Korea (<u>Lee et al. 2015</u>, <u>Chiang et al. 2007</u>, <u>Ryu et al. 2016</u> and <u>Bulut et al. 2015</u>) compared the effectiveness of various short-term antibiotic regimens in preventing complications, including acute prostatitis, after prostate biopsy. All the observational studies were retrospective analyses of medical records, often with non-concurrent controls. The prophylactic antibiotics varied, but most studies used a quinolone. The definition of post-biopsy complications, including acute prostatitis, varied between clinical symptoms (fever more than 38°C or more than 39°C, chills, dysuria, frequent urination and pelvic pain), abnormal digital rectal examination or urinalysis.

Committee discussion on preventing acute prostatitis and other complications after prostate biopsy

- The committee reviewed the available evidence and agreed that it was limited by its design (mostly observational studies) and its relevance to UK practice (studies were undertaken in Iran, Taiwan, Turkey and Korea where the choice of antibiotics may be very different).
- The committee agreed that the limitations with the evidence base, and the wide range of antibiotics included at varying dosage regimens, makes interpretation of study findings difficult.
- The committee agreed that the available evidence on antibiotic prophylaxis was insufficient to make recommendations and local microbiologists should be consulted.

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 <u>medicines adherence</u>).

Resource implications

 Recommended antibiotics are all available as generic formulations, see <u>Drug Tariff</u> for costs.