Clinical Ophthalmology

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EVIDENCE TO PRACTICE

Bacterial conjunctivitis

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Clinical question: What is the best treatment for bacterial conjunctivitis?

Results: Topical antibiotics expedite recovery from bacterial conjunctivitis. The choice of antibiotic usually does not affect outcome.

Implementation: Recognition of key distinguishing features of bacterial conjunctivitis

• Pitfalls that can be recognized in the history and physical examination
• Choice of antibiotic
• When to refer for specialist treatment.

Keywords: bacterial conjunctivitis, topical antibiotics

Bacterial conjunctivitis

Definition: Bacterial conjunctivitis is inflammation of the conjunctiva as a result of bacterial infection.

Etiology: Most commonly Staphylococcus species in adults, and Streptococcus pneumoniae and the Gram-negative organisms Haemophilus influenzae and Moraxella catarrhalis in children. Contact lens wearers are at particular risk for Gram-negative infections such as Pseudomonas aeruginosa. Neisseria gonorrhoeae is primarily a neonatal etiology.

Incidence: One recent study estimates an annual incidence rate of 135 per 10,000 in the US.1

Economics: The same study found the estimated total direct and indirect cost of treating bacterial conjunctivitis in the US to be $589 million annually. Accounting for a 20% variation in annual incidence rate and treatment cost resulted in an estimated cost range of $377 to $857 million per year.

Level of evidence used in this summary: Systematic reviews, meta-analyses, and randomized controlled trials from 1990 to 2010.

Search sources: Ovid MEDLINE, PubMed, Cochrane Library, NHS evidence, Clinical Evidence.

Outcomes: From the patient perspective, the main outcomes are:

1. Speed of symptomatic resolution
2. Convenience of treatment
3. Avoidance of complications.

Consumer summary: Bacterial conjunctivitis is inflammation of the conjunctiva caused by direct contact with infected secretions. The most common organisms are Staphylococcus species, S. pneumoniae, H. influenzae, and M. catarrhalis. It presents with conjunctival injection, mucopurulent discharge, and crusty eyelids. The diagnosis is usually clinical. The condition is often self-limiting, but there is good evidence that antibiotics improve remission rates. Most of
the current evidence suggests that the choice of topical antibiotics and the treatment regimen do not significantly affect the rate of recovery from infection. Failure to recognize and treat bacterial conjunctivitis may lead to complications, such as keratitis or anterior uveitis.

The evidence

Do any interventions make a difference to the resolution of bacterial conjunctivitis?

Systematic reviews: 2
Meta-analyses: 1
Randomized controlled trials: 10

The Cochrane systematic review,2 which includes a meta-analysis, concluded that “acute bacterial conjunctivitis is frequently a self-limiting condition, but the use of antibiotics is associated with significantly improved rates of clinical and microbiological remission”. The systematic review by Clinical Evidence3 concludes that topical antibiotics are “beneficial” in people with culture-positive nongonococcal bacterial conjunctivitis and “likely to be beneficial” when used empirically in people with suspected bacterial conjunctivitis within 1–2 days if symptoms do not resolve on their own. Oral antibiotics, ocular decongestants, warm compresses, and saline were found to be of “unknown effectiveness”.

Most randomized controlled trials (see Table 1) showed that topical antibiotics accelerate bacterial eradication and help resolve the signs and symptoms of bacterial conjunctivitis. However, in two trials,4,5 clinical recovery at seven days after presentation was found to be unaffected by the use of antibiotics, even though one of the two trials4 still found an improvement in microbial cure rate with antibiotics.

Which antibiotics are best for accelerating resolution of bacterial conjunctivitis?

Systematic reviews: 1
Meta-analyses: 0
Randomized controlled trials: 26

Table 2 lists the antibiotics studied, along with their microbial coverage, mechanism of action, and availability. The systematic review3 concluded that “there is no clear best choice for topical antibiotics – local microbiological resistance patterns, cost, dosing regimens, and other patient factors (such as allergies and compliance) are important considerations in addition to efficacy”. Results from randomized controlled trials (Table 3) are varied, but many found similar

| Author | Number of patients randomized | Interventions | Outcome measures | Results |
|--------|-----------------------------|---------------|-----------------|---------|
| Abelson et al4 | 279 | One group received azithromycin | Clinical resolution and bacterial eradication | Higher rate of microbial and clinical cure with antibiotic. |
| Everitt et al5 | 307 | Two groups received chloramphenicol | Symptomatic relief | Antibiotic decreased the duration of symptoms. |
| Hwang et al6 | 249 | One group received levofloxacin | Clinical resolution and bacterial eradication | Higher rate of microbial and clinical cure with antibiotic. |
| Karpecki et al7 | 269 | One group received ciprofloxacin | Clinical resolution and bacterial eradication | Higher rate of microbial and clinical cure with antibiotic. |
| Leibowitz8 | 177 | One group received ciprofloxacin | Culture results | Higher rate of microbial cure with antibiotic. |
| Lichtenstein and Rinehart9 | 167 | One group received levofloxacin | Clinical resolution and bacterial eradication | Higher rate of microbial and clinical cure with antibiotics. |
| Miller et al10 | 284 | One group received norfloxacin | Bacterial eradication and clinical resolution | Higher rate of microbial and clinical cure with antibiotic. |
| Rietveld et al11 | 181 | One group received fusidic acid | Clinical resolution and bacterial eradication | No difference in clinical recovery rate but higher rate of microbial eradication with antibiotic. |
| Rose et al12 | 326 | One group received chloramphenicol | Clinical cure by day 7 | No significant difference between antibiotic and placebo |
| Tepedino et al13 | 957 | One group received ciprofloxacin | Clinical resolution and bacterial eradication | Higher rate of microbial and clinical cure with antibiotic. |
### Table 2 Topical antibiotics used to treat bacterial conjunctivitis

| Antibiotic            | Class               | Coverage          | Mechanism       | Availability                                      |
|-----------------------|---------------------|-------------------|-----------------|--------------------------------------------------|
| Azithromycin          | Macrolide           | Broad-spectrum    | Bacteriostatic  | Azasite® 1% (Inspire Pharmaceuticals Inc)        |
| Besifloxacin          | Fluoroquinolone     | Broad-spectrum    | Bactericidal    | Besivance® 0.6% (Bausch and Lomb)               |
| Chloramphenicol       | Chloramphenicol     | Broad-spectrum    | Bacteriostatic  | Topical drops not marketed in US                 |
| Ciprofloxacin         | Fluoroquinolone     | Broad-spectrum    | Bactericidal    | Ciloxan® 0.3% (Alcon Laboratories Inc) Ointment or drops |
| Fusidic acid          | Protein synthesis inhibitor | Primarily Gram-positive | Bacteriostatic | Not available in US Fucithalmic® 1% (Leo Pharma) in Canada and UK |
| Gatifloxacin          | Fluoroquinolone     | Broad-spectrum    | Bactericidal    | Zymar 0.3% (Allergan Inc)                        |
| Gentamicin            | Aminoglycoside      | Primarily Gram-negative Bactericidal | Generic 0.3% drops |
| Levofloxacin          | Fluoroquinolone     | Broad-spectrum    | Bactericidal    | Iquix® 1.5% (Vistakon Pharmaceuticals)           |
| Lomefloxacin          | Fluoroquinolone     | Broad-spectrum    | Bactericidal    | Not available in US                              |
| Moxifloxacin          | Fluoroquinolone     | Broad-spectrum    | Bactericidal    | Vigamox® 0.5% (Alcon Laboratories Inc)           |
| Neomycin-polymyxin    | Aminoglycoside, polymyxin and gramicidin | Broad-spectrum | Bactericidal    | Neosporin® (King Pharmaceuticals Inc)            |
| Netilmicin            | Aminoglycoside      | Primarily Gram-negative Bactericidal | Not available in US |
| Norfloxacin           | Fluoroquinolone     | Broad-spectrum    | Bactericidal    | Chibroxin 0.3% (Merck and Co Inc) Not available in US |
| Ofloxacin             | Fluoroquinolone     | Broad-spectrum    | Bactericidal    | Generic 0.3% eye drops                           |
| Providone-iodine      | Fluoroquinolone     | Broad-spectrum    | Bactericidal    | Betadine 5% (Alcon Laboratories Inc)             |
| Rifamycin             | Rifamycin           | Broad-spectrum    | Bactericidal    | Not available in US                              |
| Tobramycin            | Aminoglycoside      | Primarily Gram-negative Bactericidal | Tobrex® 0.3% (Alcon Laboratories Inc) ointment or drops |

### Table 3 Randomized controlled trials comparing different topical antibiotics

| Author                  | Number of randomized patients | Interventions                                      | Outcome measures                                      | Results                                                                 |
|-------------------------|-------------------------------|---------------------------------------------------|-------------------------------------------------------|------------------------------------------------------------------------|
| Adenis at al\(^14\)     | 131                           | 0.3% ciprofloxacin versus 0.3% norfloxacin        | Clinical resolution and bacterial eradication         | No difference between the two antibiotics                               |
| Adenis et al\(^15\)     | 41                            | 0.3% ciprofloxacin versus 1% rifamycin             | Clinical resolution and bacterial eradication         | Higher clinical cure rate with ciprofloxacin on day 7 (but below statistical significance: \( P = 0.061 \)), no difference in microbial cure |
| Bloom et al\(^16\)      | 464                           | Ciprofloxacin versus tobramycin                    | Clinical resolution and bacterial eradication         | No difference between the two antibiotics                               |
| Bremond-Gignac et al\(^17\) | 150                          | 1.5% azithromycin versus 0.3% tobramycin           | Clinical resolution and bacterial eradication         | Greater bacteriologic cure with azithromycin on day 3, no difference in clinical or bacteriologic cure on day 9 |
| Chisari et al\(^18\)    | 190                           | Ciprofloxacin versus norfloxacin                   | Clinical resolution and bacterial eradication         | No difference between the two antibiotics                               |
| Cochereau et al\(^19\)  | 1043                          | 1.5% azithromycin for 3 days versus 0.3% tobramycin for 7 days | Clinical resolution and bacterial eradication         | Higher rate of clinical cure with azithromycin on day 3, no difference in clinical or bacteriologic cure on day 9 |
| Denis et al\(^20\)      | 1043                          | 1.5% azithromycin for 3 days versus 0.3% tobramycin for 7 days | Microbiological resolution                           | No difference between the two groups                                    |
| Gallenga et al\(^21\)   | 99                            | 0.3% lomefloxacin BID versus 0.3% tobramycin QID   | Clinical resolution and bacterial eradication         | No difference between the two groups                                    |

(Continued)
| Author | Number of randomized patients | Interventions | Outcome measures | Results |
|--------|-----------------------------|---------------|------------------|---------|
| Granet et al<sup>22</sup> | 84 eyes of 56 patients | Polymyxin/trimethoprim QID versus 0.5% moxifloxacin TID | Relief of signs and symptoms | Faster clinical resolution with moxifloxacin |
| Gwon<sup>23</sup> | 345 | 0.3% ofloxacin versus 0.3% tobramycin | Clinical resolution and bacterial eradication | Similar efficacy between the two treatments, more rapid symptom relief with ofloxacin |
| Isenberg et al<sup>24</sup> | 459 total, 124 culture-positive for bacteria | 1.25% povidone-iodine versus neomycin-polymyxin B-gramicidin | Clinical resolution | No difference between povidone-iodine and antibiotic |
| Jackson et al<sup>25</sup> | 484 | 1% fusidic acid versus 0.3% tobramycin | Clinical resolution, bacterial eradication, compliance, subjective “convenience” of treatment | No difference between clinical or microbial resolution, higher compliance and convenience with fusidic acid among younger patients |
| Kernt et al<sup>26</sup> | 276 | Enhanced-viscosity 0.3% tobramycin BiD versus 0.3% tobramycin QID | Clinical resolution | No difference between the two groups |
| Lichtenstein et al<sup>11</sup> | 167 | 0.5% levofloxacin versus 0.3% ofloxacin (versus placebo) | Clinical resolution and bacterial eradication | Higher microbial eradication rate with levofloxacin in 2–11-year-old children; no difference between the two antibiotics in other age groups |
| Malminiemi et al<sup>27</sup> | 45 | 0.3% lomefloxacin versus 1% fusidic acid | Clinical resolution and bacterial eradication | No difference in clinical recovery but higher rate of bacterial eradication with lomefloxacin after 3–5 days |
| McDonald et al<sup>28</sup> | 1161 | 0.6% besifloxacin versus 0.3% moxifloxacin | Clinical resolution and bacterial eradication | No difference between the two groups; higher rate of eye irritation with moxifloxacin |
| Milazzo et al<sup>29</sup> | 45 | 0.3% netilmicin versus 0.3% tobramycin | Clinical resolution and bacterial eradication | No difference in clinical resolution, better microbiologic outcome with netilmicin |
| Miller et al<sup>30</sup> | 246 | Norfloxacin versus chloramphenicol | Clinical resolution and bacterial eradication | No difference between the two groups |
| Normann et al<sup>31</sup> | 456 newborns | 1% fusidic acid versus 0.5% chloramphenicol | Clinical resolution and compliance | No difference in efficacy but better compliance with fusidic acid |
| Papa et al<sup>32</sup> | 209 | Netilmicin versus gentamicin | Clinical resolution and bacterial eradication | Greater efficacy rate with netilmicin |
| Power et al<sup>33</sup> | ? | 0.3% ciprofloxacin versus 0.5% chloramphenicol | Clinical resolution and bacterial eradication | No difference between the two groups |
| Protzko et al<sup>34</sup> | 743 | 1% azithromycin in DuraSite versus 0.3% tobramycin | Safety, clinical resolution and bacterial eradication | Similar safety and efficacy between the two groups |
| Robert et al<sup>35</sup> | 1043 | 1.5% azithromycin versus 0.3% tobramycin | Clinical resolution | No difference between the two groups |
| Schwab et al<sup>36</sup> | 423 | 0.5% levofloxacin versus 0.3% ofloxacin | Clinical resolution and bacterial eradication | More rapid microbial resolution with levofloxacin, similar clinical resolution |
| Tabbara et al<sup>37</sup> | 40 | 0.3% lomefloxacin versus 0.3% ofloxacin | Clinical resolution | No difference between the two groups |
| Zhang et al<sup>38</sup> | 132 | 0.3% levofloxacin versus 0.3% ofloxacin | Clinical resolution and bacterial eradication | No difference between the two groups |

**Abbreviations:** BiD, twice daily; TID, three times daily; QID, four times daily.
clinical and microbiologic efficacy among the topical antibiotics used. Some studies found faster bacterial eradication and/or clinical recovery with fluoroquinolones, azithromycin, or netilmicin compared with the more traditional antibiotics, such as tobramycin or polymyxin B/trimethoprim or gentamicin. Some studies found differences in patient compliance with different antibiotics. Microbiologic resistance patterns can also vary and would affect efficacy rates.

### Which treatment regimen works best for bacterial conjunctivitis?

| Author            | Number of randomized patients | Interventions                          | Outcome measures                  | Results                      |
|-------------------|------------------------------|----------------------------------------|-----------------------------------|------------------------------|
| Friedlaender39    | 50                           | 0.3% ofloxacin BID versus QID          | Clinical resolution and bacterial eradication | No difference between the two groups |
| Szaflik et al40   | 120                          | 0.5% levofloxacin TID × 5 days versus “standard regimen” (Q2H × 2 days, then Q4H × 3 days) | Clinical resolution and bacterial eradication | No difference between the two groups |
| Wald et al41      | 80                           | Oral cefixime + topical placebo versus topical polymyxin-bacitracin + oral placebo | Clinical resolution and bacterial eradication | No difference between the two groups |
| Yee et al42       | 104                          | 0.3% gatifloxacin BID versus QID       | Clinical resolution, bacterial eradication and safety | No difference between the two groups |

**Abbreviations:** Q2H, two hourly; Q4H, four hourly; BID, twice daily; TID, three times daily; QID, four times daily.

A few randomized controlled trials (Table 4) have focused on the effect of the treatment regimen, such as dosing, frequency, length of treatment, and route of administration, on efficacy rates. None have found a significant change in cure rate in association with the treatment regimen used.

### Conclusions

Bacterial conjunctivitis often resolves on its own, but the current evidence suggests that topical antibiotics help accelerate recovery from this self-limiting disease. Topical antibiotics used for treatment of bacterial conjunctivitis have similar efficacy rates. The treatment regimen does not affect recovery from bacterial conjunctivitis. Patients may prefer a simpler regimen.

### The practice

#### Potential pitfalls

- Contact lens wearers are predisposed to Gram-negative infections, carrying a higher risk of complications, such as bacterial keratitis. Pseudomonas and Acanthamoeba infections in contact lens wearers can lead to serious, sight-threatening complications if not recognized and treated appropriately. The contact lens storage case may be the nidus of the infection.
- If there is an associated keratitis or anterior uveitis, referral to a specialist may be recommended.
- Beware of combination topical antibiotic agents that contain steroids. These should be used with extreme caution and monitored by a specialist.

#### Management

Bacterial conjunctivitis can be managed by nonspecialists.

#### Assessment

- Redness, foreign body sensation and purulent/ mucopurulent discharge are common complaints; there may be itching, chemosis, or conjunctival papillae.
- Ask about contact lens wear.
- Assess for corneal involvement and intraocular involvement.
- Conjunctival swabs can be done for Gram stain, culture, and sensitivity to clarify diagnosis, particularly in more severe or refractory cases.
- Moderate to severe eye pain, photophobia, or change in visual acuity should raise suspicion for more serious causes.

#### Treatment

- Uncomplicated cases can be treated with a topical antibiotic such as tobramycin, trimethoprim/polymyxin B, a fluoroquinolone or chloramphenicol four times daily for 5–7 days to accelerate recovery.
- Patients should be seen every 2–3 days until signs and symptoms are resolved.
• Failure to respond to topical antibiotics may warrant referral to a specialist.

Indications for specialist referral
• Change in visual acuity
• Evidence of keratitis and/or anterior uveitis on slit-lamp examination
• Moderate-to-severe eye pain
• Failure to improve or worsening of symptoms in spite of treatment.

Further reading
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Disclosure
The authors report no conflicts of interest in this work.

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