Ocular Prophylaxis for Gonococcal Ophthalmia Neonatorum: Evidence Update for the U.S. Preventive Services Task Force Reaffirmation Recommendation Statement

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Introduction

In the absence of preventive measures, it is estimated that gonococcal ophthalmia neonatorum will develop in approximately 28% of infants born to women with gonorrheal disease in the United States (1). Although *Neisseria gonorrhoeae* causes ophthalmia neonatorum less frequently than *Chlamydia trachomatis* and nonsexually transmitted agents, identifying and treating the infection is especially important because gonococcal ophthalmia neonatorum can result in corneal scarring, ocular perforation, and blindness (2). Furthermore, the conjunctivae occasionally serve as a portal of entry for gonococcal septicemia, arthritis, or other forms of invasive disease (3). In 2007, there were 355,991 cases of gonorrhea reported in the United States, which is a rate of 118.9 cases per 100,000 persons (4). Despite the relatively stable rates of reported gonorrhea in the United States for the past 10 years, these rates are still far from the *Healthy People 2010* goal of 19 cases per 100,000 persons (5).

The diagnosis and treatment of gonococcal infections in pregnant women is the best method for preventing neonatal gonococcal disease. Newborns at increased risk for gonococcal ophthalmia neonatorum include those whose mothers lacked prenatal care or who have a maternal history of sexually transmitted infections or substance abuse, and newborns who do not receive ocular prophylaxis. Intracellular gram-negative diplococci identified in conjunctival exudates suggest gonococcal ophthalmia neonatorum and justifies presumptive treatment for gonorrhea after cultures have been obtained.

However, ocular prophylaxis is still warranted because not all women receive prenatal care, and therefore not all women are able to be diagnosed prenatally. Currently, prophylaxis for gonococcal ophthalmia neonatorum is recommended immediately after birth for all infants and is required by law in most states. Prophylactic regimens using 1.0% solution of silver nitrate, 1.0% tetracycline ophthalmic ointment, or 0.5% erythromycin ophthalmic ointment are considered equally effective. However, tetracycline ophthalmic ointment is no longer available in the United States. The advantages of using silver nitrate include its low cost, lack of allergic potential, and lack of bacterial resistance. However, silver nitrate is associated with a transient chemical conjunctivitis that may temporarily impair vision and affect the appearance of the infant, and is no longer manufactured in the United States (3). A 2.5% solution of povidone-iodine may be useful in preventing ophthalmia neonatorum (6), but a product for this purpose has not been approved for use in the United States at this time (7).

In 1996, the U.S. Preventive Services Task Force (USPSTF) recommended prophylactic ocular topical medication for the prevention of gonococcal ophthalmia neonatorum in all newborns (grade A recommendation), noting that there is good evidence that blindness due to gonococcal ophthalmia neonatorum has become rare in the United States since the implementation of providing universal preventive medication to infants (8). In 2005, as part of a broad review of gonococcal screening in adults, the USPSTF reviewed an updated literature search on the harms of ocular prophylaxis. At that time, the USPSTF reaffirmed its grade A recommendation.

In 2009, the USPSTF decided to update its recommendation statement on gonococcal ophthalmia neonatorum prophylaxis. Because the previous recommendation was based on well-established, evidence-based standards of practice in current medical practice, the USPSTF chose to conduct a reaffirmation update for this topic. The USPSTF performs reaffirmation updates for older recommendation statements that remain priorities of the USPSTF, are within the scope of the USPSTF, and for which there is a compelling reason for the USPSTF to have a current recommendation statement.

To assist the USPSTF in updating the recommendation on the prophylaxis of gonococcal ophthalmia neonatorum, staff at the Agency for Healthcare Research and Quality (AHRQ) performed a literature search and consulted with subject matter experts. The goal of this targeted review was to find new, high-quality evidence regarding the benefits and potential harms of prophylactic treatment of gonococcal ophthalmia neonatorum. The methodology of the literature search is described in Appendix 1.

Evidence of the Benefits of Gonococcal Ophthalmia Neonatorum Prophylaxis

Since the introduction of Credé's method in 1881, instilling one eye drop of 1% silver nitrate at birth to reduce ophthalmia neonatorum has been practiced worldwide. Advantages of the use of silver nitrate for prophylaxis include its low cost, lack of allergic potential, and absence of bacterial resistance to the compound. Disadvantages include development of chemical conjunctivitis with associated exudate in many neonates and treatment failure if the gonococcal infection occurs prior to birth.

As noted in the original recommendation of 1996, the efficacy of prophylactic agents other than silver nitrate was explored in a non-randomized clinical trial in Kenya (8). Isenberg and colleagues (6) compared the benefits of povidone-iodine prophylaxis with the well-established benefits of silver nitrate and erythromycin ophthalmic prophylaxis. Isenberg concluded that all three agents were equally effective in the prevention of gonococcal infection, but povidone-iodine prophylaxis resulted in significantly fewer cases of ophthalmia neonatorum overall and fewer cases of *C trachomatis* infections in infants as well.

A more recent, smaller randomized clinical trial by Ali and colleagues (9) in Iran explored the benefits of using 2.5% sterile betadine eye drops in 330 neonates. Although no cases of gonococcal ophthalmia were diagnosed in either group, there was a significant reduction in the total number of clinical conjunctivitis cases among newborns who received 2.5% betadine prophylactic therapy ($p=0.030$).

Evidence of the Harms of Gonococcal Ophthalmia Neonatorum Prophylaxis

No new studies of harms were identified.

Recommendations of Other Groups

The American Academy of Pediatrics recommends prophylaxis of newborn infants with a 0.5% erythromycin ophthalmic ointment or 1% tetracycline ophthalmic ointment (which is no longer available in the United States). Each is available in single-dose forms. Use of povidone-iodine in a 2.5% solution may also be useful, but a product for this purpose is not available in the United States. Prophylaxis should be provided to all infants shortly after birth. A monitoring system to ensure prophylaxis is provided to all infants and in a timely manner is recommended. Additionally, infants born to mothers with known clinical gonorrhea infection require intravenous or intramuscular antibiotics, as topical prophylaxis alone is inadequate for these infants (10).

The Centers for Disease Control and Prevention recommend a single application of either 0.5% erythromycin or 1% tetracycline ointment into both eyes as soon as possible after birth, with use of single-use tubes or ampoules preferable to multiple-use tubes. Establishment of a monitoring system to ensure that all infants receive prophylaxis is recommended (11).

In 2003, the World Health Organization recommended the application of either a 1% silver nitrate solution or 1% tetracycline ointment into the eyes of all infants at the time of birth. It also recommends additional treatment for those infants born to mothers with gonococcal infection (12).

In 1994, the Canadian Task Force on Preventive Health Care released guidelines for gonococcal ophthalmia neonatorum, recommending universal prophylactic use of 1% silver nitrate drops or 1% tetracycline or 0.5% erythromycin ointment within one hour of birth in single-dose ampules (13).

In January 2009, the Canadian Paediatric Society reaffirmed its 1983 published statement on ophthalmia neonatorum, recommending that all infants receive prophylaxis with silver nitrate, tetracycline, or erythromycin as soon as possible after birth to reduce the risk of gonococcal ophthalmia neonatorum (14).

Emerging Issues and Research Gaps

Povidone-iodine in a 2.5% solution may be an effective prophylactic regimen, but more studies are required, and a product for this purpose is currently not available in the United States. Furthermore, the efficacy of erythromycin or povidone-iodine prophylaxis of penicillinase-producing *N gonorrhoeae* is not known.

Conclusion

In summary, the USPSTF found no substantial new evidence regarding the benefits or harms of prophylaxis for the prevention of gonococcal ophthalmia neonatorum.

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Appendix 1. Literature Search Process for the Reaffirmation Evidence Update

AHRQ staff performed a targeted literature search for the benefits and harms of prophylaxis of gonococcal ophthalmia neonatorum. The literature search was limited to the period of January 1, 1995, to March 1, 2009.

The databases searched were PubMed and the Cochrane Library. A series of searches using combinations of MeSH terms and keywords were performed, and the results were limited to core journal articles. Results were supplemented with recommendations from subject matter experts and reference list reviews.

All articles were reviewed for predetermined inclusion/exclusion criteria by two team members at each stage of review (title, abstract, full article). A consensus process was used to resolve any reviews which resulted in differences of opinion.

PubMed search strategy:

Limited to:

English
Human
Infant
Publication date from 01/01/1995 to 03/01/2009

For benefits:

MeSH terms: "conjunctivitis," "screening," "chlamydia infections," "gonorrhea"

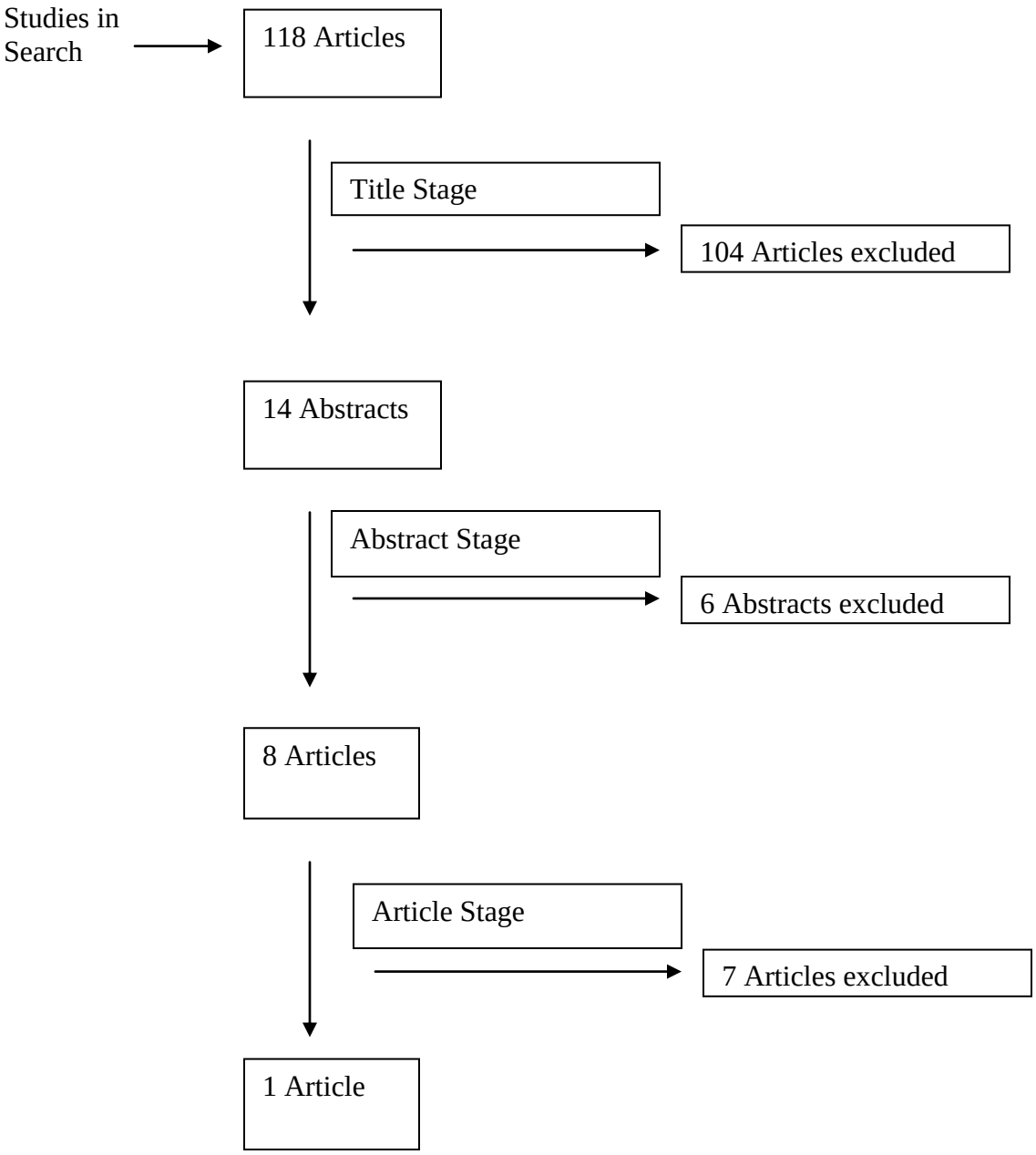
Limited to: randomized controlled trials, meta-analysis, systematic reviews

For harms:

MeSH terms: "drug toxicity," "drug hypersensitivity," "silver nitrate," "tetracycline," "erythromycin," "povidone-iodine"

Other terms: "harms," "adverse effects"

Results of the application of inclusion/exclusion criteria:



Appendix 2. Literature Search Exclusion Criteria

Reason Code*	Description
1. Population (6)	Study does not include defined population
2. Study Design (8)	Study does not meet design inclusion criteria (e.g., case report)
3. Not Condition (89)	Study is not on gonococcal ophthalmia neonatorum
4. Not U.S. (0)	Study is in a population not generalizable to the United States
5. Not Newborn (3)	Study subjects are not newborns
6. No Outcomes (6)	Study does not include information on appropriate benefits/harms
7. Not English (0)	Study is in a language other than English
8. Too Old (0)	Study was published outside of search dates or newer update is available
9. Other (0)	Number of study subjects is less than 100

*Number of excluded studies in parentheses.