

# Ocular Prophylaxis for Gonococcal Ophthalmia Neonatorum

## US Preventive Services Task Force Reaffirmation Recommendation Statement

US Preventive Services Task Force

**IMPORTANCE** In the United States, the rate of gonococcal ophthalmia neonatorum was an estimated 0.4 cases per 100 000 live births per year from 2013 to 2017. Gonococcal ophthalmia neonatorum can cause corneal scarring, ocular perforation, and blindness as early as 24 hours after birth. In the absence of ocular prophylaxis, transmission rates of gonococcal infection from mother to newborn are 30% to 50%.

**OBJECTIVE** To reaffirm the US Preventive Services Task Force (USPSTF) 2011 recommendation on ocular prophylaxis for gonococcal ophthalmia neonatorum.

**EVIDENCE REVIEW** The USPSTF commissioned a reaffirmation evidence update to identify new and substantial evidence sufficient enough to change its prior recommendation.

**FINDINGS** Using a reaffirmation process, the USPSTF found no new data that would change its previous conclusion that topical ocular prophylaxis is effective in preventing gonococcal ophthalmia neonatorum and related ocular conditions. The USPSTF found no new data that would change its previous conclusion that there is convincing evidence that topical ocular prophylaxis of all newborns is not associated with serious harms. Therefore, the USPSTF reaffirms its previous conclusion that there is convincing evidence that topical ocular prophylaxis for all newborns provides substantial benefit.

**CONCLUSIONS AND RECOMMENDATION** The USPSTF recommends prophylactic ocular topical medication for all newborns to prevent gonococcal ophthalmia neonatorum. (A recommendation)

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The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

### Summary of Recommendation and Evidence

The USPSTF recommends prophylactic ocular topical medication for all newborns to prevent gonococcal ophthalmia neonatorum (A recommendation) (Figure 1).

### Rationale

#### Importance

In the United States, the rate of gonococcal ophthalmia neonatorum was an estimated 0.4 cases per 100 000 live births per year from 2013 to 2017.<sup>1-4</sup> Gonococcal ophthalmia neonatorum can cause corneal scarring, ocular perforation, and blindness as early as 24 hours after birth.<sup>5-7</sup> In the absence of ocular prophylaxis, transmission rates of gonococcal infection from mother to newborn are 30% to 50%.<sup>8</sup>

#### Reaffirmation

In 2011, the USPSTF reviewed the evidence on prophylactic ocular topical medication for all newborns to prevent gonococcal ophthalmia neonatorum and issued an A recommendation.<sup>5</sup> The USPSTF has decided to use a reaffirmation deliberation process to update this recommendation. The USPSTF uses the reaffirmation process for well-established, evidence-based standards of practice in current primary care practice for which only a very high level of evidence would justify a change in the grade of the recommendation.<sup>9</sup> In its deliberation of the evidence, the USPSTF considers whether

Figure 1. USPSTF Grades and Levels of Evidence

What the USPSTF Grades Mean and Suggestions for Practice		
Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the Clinical Considerations section of the USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit	
Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as the number, size, or quality of individual studies. inconsistency of findings across individual studies. limited generalizability of findings to routine primary care practice. lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of the limited number or size of studies. important flaws in study design or methods. inconsistency of findings across individual studies. gaps in the chain of evidence. findings not generalizable to routine primary care practice. lack of information on important health outcomes. More information may allow estimation of effects on health outcomes.
The USPSTF defines certainty as “likelihood that the USPSTF assessment of the net benefit of a preventive service is correct.” The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.	

USPSTF indicates US Preventive Services Task Force.

the new evidence is of sufficient strength and quality to change its previous conclusions about the evidence.

**Benefits of Preventive Medication**

The USPSTF found convincing evidence that ocular prophylaxis of newborns with 0.5% erythromycin ophthalmic ointment can prevent gonococcal ophthalmia neonatorum.

**Harms of Preventive Medication**

The USPSTF found convincing evidence that ocular prophylaxis of newborns with 0.5% erythromycin ophthalmic ointment is not associated with serious harms.

**USPSTF Assessment**

Using a reaffirmation process,<sup>9</sup> the USPSTF concludes with high certainty that the net benefit of topical ocular prophylaxis of all newborns to prevent gonococcal ophthalmia neonatorum is substantial.

**Clinical Considerations**

**Patient Population Under Consideration**

This recommendation applies to all newborns regardless of gestational age (Figure 2).

Figure 2. Clinical Summary: Ocular Prophylaxis for Gonococcal Ophthalmia Neonatorum

Population	Newborns
Recommendation	Provide prophylactic ocular topical medication to prevent gonococcal ophthalmia neonatorum. Grade: A
Preventive Medication	Erythromycin ophthalmic ointment is the only drug approved by the US Food and Drug Administration for the prophylaxis of gonococcal ophthalmia neonatorum. Ocular prophylaxis of newborns is mandated in most states and is considered standard neonatal care.
Relevant USPSTF Recommendations	The USPSTF recommends screening for gonorrhea in all sexually active women 24 years and younger and in older women at increased risk for infection, as well as pregnant women.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to <https://www.uspreventiveservicestaskforce.org>.



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### Preventive Medication

Erythromycin ophthalmic ointment is considered effective in preventing gonococcal ophthalmia neonatorum.<sup>10</sup> Other medications, such as tetracycline ophthalmic ointment and silver nitrate, have been evaluated for the prevention of gonococcal ophthalmia neonatorum but are no longer available in the United States.<sup>3</sup> Gentamicin was used during a period of erythromycin shortage, although its use was associated with ocular reactions (chemical conjunctivitis).<sup>11</sup> Povidone-iodine has been proposed for prophylaxis, but there are limited data on its benefits and harms.<sup>3</sup> Currently, erythromycin is the only drug approved by the US Food and Drug Administration for the prophylaxis of gonococcal ophthalmia neonatorum.<sup>11</sup> Ocular prophylaxis of newborns is mandated in most states<sup>6</sup> and is considered standard neonatal care.<sup>11</sup>

### Additional Approaches to Prevention

The rates of gonococcal ophthalmia neonatorum are related to gonococcal infection rates in women of reproductive age.<sup>3</sup> Accordingly, screening for and treatment of gonococcal infection in pregnant women is an important strategy for reducing the sexual transmission of gonorrhea and subsequent vertical transmission leading to gonococcal ophthalmia neonatorum. While screening and treatment programs have reduced the rates of gonorrhea in pregnant women, there are large disparities in access to prenatal care in the United States.<sup>1,12</sup> Risk-based prophylaxis has also been proposed as an alternative strategy for preventing gonococcal ophthalmia neonatorum. Currently, there are no risk-based tools for screening pregnant women and no studies examining the use of risk-based vs universal prophylaxis. Therefore, ocular prophylaxis remains an important tool in the prevention of gonococcal ophthalmia neonatorum.

### Useful Resources

The USPSTF recommends screening for gonorrhea in all sexually active women 24 years and younger and in older women at in-

creased risk for infection, as well as pregnant women.<sup>13</sup> The Centers for Disease Control and Prevention provides clinical guidance for ocular prophylaxis and treatment of gonococcal ophthalmia neonatorum.<sup>10</sup>

## Other Considerations

### Research Needs and Gaps

The only available drug approved by the US Food and Drug Administration for the prevention of gonococcal ophthalmia neonatorum is 0.5% erythromycin ophthalmic ointment. It is currently unknown whether *Neisseria gonorrhoeae* has developed resistance to erythromycin ointment in the United States. However, given increased antimicrobial resistance noted in other countries, further research is needed to find safe and effective alternatives to erythromycin. Another area for research is whether risk-based prophylaxis of newborns, based on maternal risk factors, is as effective as universal prophylaxis.

## Discussion

### Burden of Disease

Ophthalmia neonatorum is conjunctivitis occurring in infants during the first month of life. Gonococcal ophthalmia neonatorum occurs when gonococcal infection is transmitted to newborns during delivery by women infected with *N gonorrhoeae*.<sup>10</sup> The rates of gonococcal conjunctivitis in infants are directly related to the rates of gonorrhea among women of reproductive age.<sup>3</sup> In the United States, adolescents and young adult women have the highest rates of gonorrhea, with rates peaking at age 19 years (872.2 cases per 100 000 women); among women aged 20 to 24 years, there were 648.8 cases per 100 000 women in 2017.<sup>1</sup> Estimated rates of gonorrhea among pregnant women in the US primary care

setting are not available. Although gonococcal infection rates have declined since national screening programs were implemented in the 1970s, reported gonorrhea cases have increased recently, from 105.3 cases to 171.9 cases per 100 000 population from 2013 to 2017, respectively.<sup>1</sup> An estimated 6.2% of births in the United States occur among women receiving little to no prenatal care, although rates as high as 20% have been documented in certain populations based on location and race/ethnicity.<sup>12</sup>

Data based on infant age (younger than 1 year) and specimen source (conjunctiva or eye) indicate there were an estimated 42 infections ( $\leq 0.4$  cases) per 100 000 live births per year from 2013 to 2017.<sup>1</sup> However, limitations in reporting suggest this is an underestimate.<sup>14</sup> Using a broader definition that includes cases with unknown, other, or missing specimen sources, the prevalence of gonococcal ophthalmia neonatorum during that period could possibly be higher.<sup>3</sup>

Untreated gonococcal ophthalmia neonatorum can result in severe and lasting conditions, including corneal scarring, ocular perforation, and blindness.<sup>7</sup> There are no contemporary estimates of blindness related to gonococcal ophthalmia neonatorum in the United States. Historical estimates from 19th-century Europe show that gonococcal ophthalmia neonatorum was a major cause of childhood blindness, resulting in corneal damage in 20% of infected infants and blindness in 3%.<sup>15,16</sup> An observational study from Nairobi, Kenya, in the 1980s reported that 16% of a series of 64 infants with gonococcal ophthalmia neonatorum had corneal involvement.<sup>17</sup>

### Scope of Review

To reaffirm its 2011 recommendation on ocular prophylaxis for gonococcal ophthalmia neonatorum,<sup>5</sup> the USPSTF commissioned a targeted evidence review.<sup>3,4</sup> The aim of this review was to identify substantial new evidence that was sufficient to change the prior recommendation.

### Benefits of Preventive Medication

Previous USPSTF reviews found convincing evidence that topical ocular prophylaxis can prevent gonococcal ophthalmia neonatorum. The USPSTF found no new data that would change its previous conclusion that topical ocular prophylaxis is effective in preventing gonococcal ophthalmia neonatorum and related ocular conditions.

### Potential Harms of Preventive Medication

The USPSTF found no new data that would change its previous conclusion that there is convincing evidence that topical ocular prophylaxis of all newborns is not associated with serious harms. Possible harms include the potential for antimicrobial resistance to treatment medication.

### Estimate of Magnitude of Net Benefit

The USPSTF considered the evidence using a reaffirmation process and found that topical ocular prophylaxis is effective in preventing gonococcal ophthalmia neonatorum and related ocular conditions, with small associated harms and substantial benefit. Therefore, the USPSTF reaffirms its previous conclusion that there is convincing evidence that topical ocular prophylaxis for all newborns provides substantial benefit.

### Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from September 11 to October 9, 2018. Several comments questioned the continued need for universal prophylaxis given the relative low rate of disease. The USPSTF reaffirmed its recommendation based on several factors, including the rapid course and serious adverse effects of infection, increasing rates of gonococcal infection, and the large number of persons who do not receive screening for gonococcal infection during pregnancy in the United States. Comments also supported risk-based prophylaxis as an alternative strategy for prevention. However, there are no tools for assessing the risk of infection in newborns and no studies examining the use of risk-based vs universal prophylaxis. The USPSTF revised the recommendation to clarify this point. In addition, a number of comments promoted the use of iodine solutions (povidone-iodine) as an alternative to erythromycin ophthalmic ointment. The evidence review found limited studies on the use of iodine solutions and notes that they are not approved for use in the United States as ocular prophylaxis for gonococcal ophthalmia neonatorum. The USPSTF added language to address this concern.

### Reaffirmation of Previous USPSTF Recommendation

This recommendation is a reaffirmation of the USPSTF 2011 recommendation statement.<sup>5</sup> In 1996<sup>18</sup> and 2005,<sup>19</sup> the USPSTF reviewed the evidence on ocular prophylaxis for gonococcal ophthalmia neonatorum and found that the benefits of screening substantially outweigh the harms. For the current recommendation, the USPSTF commissioned a targeted review to look for substantial new evidence on the benefits and harms of ocular prophylaxis and determined that the net benefit of ocular prophylaxis continues to be well established. The USPSTF found no new substantial evidence that could change its recommendation and therefore reaffirms its recommendation to provide prophylactic ocular topical medication for all newborns to prevent gonococcal ophthalmia neonatorum.

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## Recommendations of Others

The Centers for Disease Control and Prevention, American Academy of Pediatrics, American College of Obstetricians and Gynecologists, and the World Health Organization all recommend universal topical ocular prophylaxis to prevent gonococcal ophthalmia neonatorum.<sup>1,20,21</sup> The Canadian Pediatric Society recommends against universal prophylaxis. Several European countries, including Denmark, Norway, Sweden, and the United Kingdom, no longer require universal prophylaxis, instead opting for a prevention strategy of increased screening and treatment of pregnant women.<sup>22</sup> In 2017, the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists recommended screening all pregnant women at risk for gonorrhea or who live in a high-prevalence area at the first prenatal visit; women with gonococcal infection should be retested in 3 to 6 months, preferably in the third trimester. In addition, if the result of the first test is negative but the woman is at high risk for gonorrhea, retesting at the beginning of the third trimester is recommended.<sup>20</sup>

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