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GONOCOCCAL VERSUS CHLAMYDIAL NEONATAL CONJUNCTIVITIS: DIAGNOSIS AND SYSTEMIC TREATMENT

CONJUNTIVITE NEONATAL GONOCÓCICA VERSUS CLAMIDIAL: DIAGNÓSTICO E TRATAMENTO SISTÊMICO

CONJUNTIVITIS NEONATAL GONOCÓCICA FRENTE A CLAMIDIAL: DIAGNÓSTICO Y TRATAMIENTO SISTÉMICO

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ABSTRACT

Neonatal conjunctivitis caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis* requires pathogen-directed systemic treatment because ocular findings may accompany infection beyond the conjunctiva. Gonococcal disease can progress rapidly to corneal ulceration, perforation, and disseminated infection, whereas chlamydial disease can coexist with nasopharyngeal infection and subsequent pneumonia. This focused narrative review synthesizes PubMed-indexed guidance, clinical studies, and evidence reviews on distinguishing the two conditions, obtaining diagnostic specimens, and selecting systemic therapy. Presentation timing and discharge characteristics help prioritize the differential diagnosis but are insufficient to identify the organism reliably. Suspected gonococcal ophthalmia requires urgent ocular assessment, conjunctival Gram stain and culture with susceptibility testing, simultaneous chlamydial testing, and prompt systemic treatment. Recommended therapy for isolated gonococcal ophthalmia is ceftriaxone 25–50 mg/kg intravenously or intramuscularly once, up to 250 mg, with cefotaxime considered when ceftriaxone is unsuitable. Chlamydial ophthalmia is treated with oral erythromycin at 50 mg/kg/day in four divided doses for 14 days; short-course azithromycin is used in some protocols, although the neonatal comparative evidence remains limited. Both macrolides are associated with infantile hypertrophic pyloric stenosis, particularly after early exposure, requiring counseling and surveillance. Topical antibiotics alone are inadequate for either

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infection. Follow-up, evaluation for systemic involvement, and assessment and treatment of maternal infection and partners are essential. Ocular prophylaxis does not eliminate the need to investigate symptomatic infants, especially because it does not reliably prevent chlamydial infection.

Keywords: Ophthalmia Neonatorum. *Neisseria gonorrhoeae. Chlamydia trachomatis*. Systemic Antibiotics.

RESUMO
A conjuntivite neonatal causada por *Neisseria gonorrhoeae* ou *Chlamydia trachomatis* requer tratamento sistêmico direcionado ao patógeno, uma vez que a infecção pode envolver outras estruturas além da conjuntiva. A infecção gonocócica pode evoluir rapidamente para ulceração corneana, perfuração e infecção disseminada, enquanto a infecção por *Chlamydia* pode coexistir com infecção nasofaríngea e, consequentemente, pneumonia. Esta revisão narrativa sintetiza diretrizes, estudos clínicos e revisões de evidências — indexados na base PubMed — sobre a diferenciação entre essas duas condições, a coleta de amostras para diagnóstico e a escolha da terapia sistêmica. O momento do surgimento dos sintomas e as características da secreção ocular auxiliam na priorização do diagnóstico diferencial, mas não são suficientes para identificar o agente etiológico com segurança. A suspeita de oftalmia gonocócica exige avaliação ocular urgente, realização de coloração de Gram e cultura da secreção conjuntival (com teste de sensibilidade), testagem concomitante para *Chlamydia* e início imediato de tratamento sistêmico. A terapia recomendada para a oftalmia gonocócica isolada é a ceftriaxona, em dose única de 25–50 mg/kg (por via intravenosa ou intramuscular, até o limite de 250 mg); a cefotaxima pode ser considerada nos casos em que a ceftriaxona não seja adequada. A oftalmia por *Chlamydia* é tratada com eritromicina via oral, na dose de 50 mg/kg/dia, dividida em quatro tomadas diárias, por 14 dias; alguns protocolos utilizam azitromicina em esquema de curta duração, embora as evidências comparativas em neonatos ainda sejam limitadas. Ambos os macrolídeos estão associados ao risco de estenose hipertrófica do piloro em lactentes, especialmente após exposição precoce, o que demanda orientação aos responsáveis e monitoramento clínico. O uso isolado de antibióticos tópicos é inadequado para ambas as infecções. O acompanhamento, a investigação de possível acometimento sistêmico, bem como a avaliação e o tratamento da infecção materna e de seus parceiros, são fundamentais. A profilaxia ocular não elimina a necessidade de investigar lactentes sintomáticos, sobretudo porque ela não previne, de forma confiável, a infecção por *Chlamydia*.

Palavras-chave: Oftalmia Neonatal. *Neisseria gonorrhoeae. Chlamydia trachomatis*. Antibióticos Sistêmicos.

RESUMEN
La conjuntivitis neonatal causada por *Neisseria gonorrhoeae* o *Chlamydia trachomatis* requiere un tratamiento sistémico dirigido al patógeno, ya que la infección puede manifestarse más allá de la conjuntiva. La infección gonocócica puede progresar rápidamente hacia la ulceración corneal, la perforación y la diseminación sistémica; por su parte, la infección por *Chlamydia* puede coexistir con una infección nasofaríngea y derivar en neumonía. Esta revisión narrativa sintetiza guías, estudios clínicos y revisiones de evidencia —indexados en PubMed— sobre cómo diferenciar ambas entidades, obtener muestras para el diagnóstico y seleccionar el tratamiento sistémico adecuado. El momento de aparición de los síntomas y las características de la secreción ayudan a orientar el

diagnóstico diferencial, pero no son suficientes para identificar el microorganismo con certeza. Ante la sospecha de oftalmia gonocócica, es necesario realizar una evaluación ocular urgente, tinción de Gram y cultivo de la secreción conjuntival (incluyendo pruebas de sensibilidad), pruebas simultáneas para *Chlamydia* e instaurar de inmediato un tratamiento sistémico. El tratamiento recomendado para la oftalmia gonocócica aislada consiste en una dosis única de ceftriaxona (25–50 mg/kg, por vía intravenosa o intramuscular, hasta un máximo de 250 mg); en caso de que la ceftriaxona no sea adecuada, puede utilizarse cefotaxima. La oftalmia por *Chlamydia* se trata con eritromicina oral a una dosis de 50 mg/kg/día, dividida en cuatro tomas diarias durante 14 días; algunos protocolos emplean azitromicina en ciclos cortos, aunque la evidencia comparativa en neonatos sigue siendo limitada. Ambos macrólidos se han asociado con la estenosis hipertrófica del píloro en lactantes —especialmente tras una exposición temprana—, lo que exige asesoramiento y vigilancia. El uso exclusivo de antibióticos tópicos es insuficiente para tratar cualquiera de estas infecciones. Es fundamental realizar un seguimiento, evaluar la posible afectación sistémica, y valorar y tratar tanto la infección materna como la de sus parejas sexuales. La profilaxis ocular no exime de la necesidad de investigar a los lactantes sintomáticos, sobre todo porque no previene de manera fiable la infección por *Chlamydia*.

Palabras clave: Oftalmia Neonatal. *Neisseria gonorrhoeae. Chlamydia trachomatis*. Antibióticos Sistémicos.

1 INTRODUCTION

Conjunctivitis during the first month of life has infectious and noninfectious causes, but sexually transmitted pathogens deserve specific attention because delayed recognition can threaten vision or systemic health. Neisseria gonorrhoeae and Chlamydia trachomatis are generally acquired through perinatal exposure to maternal infection. Their management differs from routine treatment of uncomplicated conjunctivitis in older children because topical treatment does not address the complete neonatal infection.[1,2]

Gonococcal ophthalmia can produce rapidly progressive purulent inflammation and corneal destruction. Chlamydial ophthalmia often develops less explosively, but infection can involve the nasopharynx and may be associated with pneumonia later in infancy. These distinctions determine urgency and treatment, while overlap in presentation requires laboratory investigation rather than diagnosis by appearance alone.[2,3]

Declining disease frequency in settings with effective prenatal screening can reduce clinicians' familiarity with these presentations. Prophylaxis given at birth may also create false reassurance, particularly when maternal infection was not detected or treatment was incomplete. A symptomatic neonate should therefore be evaluated on the current findings, irrespective of a documented prophylactic application.[1,4]

2 OBJECTIVE

This review compares the clinical recognition, laboratory diagnosis, and systemic treatment of gonococcal and chlamydial neonatal conjunctivitis. It evaluates the rationale for systemic therapy, the limitations of available antimicrobial evidence, and the relevance of macrolide-associated pyloric stenosis. It also addresses corneal assessment, extraocular infection, follow-up, and prevention through maternal care.

3 METHODS

Targeted PubMed searches through October 16, 2026, combined neonatal conjunctivitis with diagnosis, treatment, prophylaxis, systematic review, and macrolide-associated pyloric stenosis. Additional primary studies and evidence reviews were retrieved by title or identifier, and the neonatal sections of the CDC sexually transmitted infection guidance were checked directly. All bibliography entries were verified against PubMed metadata.

This focused narrative review prioritized neonatal treatment guidance, clinical efficacy studies, and evidence on adverse events and prophylaxis. It did not use a registered protocol, duplicate screening, formal risk-of-bias scoring, or a new meta-analysis. Historical treatment studies are discussed as supporting evidence and do not supersede current neonatal dosing or formulation recommendations.

4 RESULTS AND DISCUSSION

4.1 PRESENTATION AND THE LIMITS OF CLINICAL DISTINCTION

Gonococcal infection commonly becomes apparent two to five days after birth and may cause marked eyelid edema, chemosis, and copious purulent discharge. Chlamydial conjunctivitis more often begins around five to twelve days after birth, although timing varies and the intervals overlap. Age at presentation can guide suspicion but should not be used to exclude either pathogen.[2]

The severity and speed of progression deserve more weight than a rigid incubation schedule. A neonate with substantial purulence, conjunctival inflammation, or any corneal abnormality requires urgent assessment for gonococcal disease and other aggressive infections. Less dramatic inflammation remains compatible with chlamydial infection and does not remove the need to consider systemic treatment.[1,2]

The differential diagnosis includes other bacteria, nasolacrimal obstruction with discharge, chemical irritation, and herpes simplex infection. Vesicular lesions, corneal involvement, or systemic illness can change the immediate investigation and treatment priorities. A suspected sexually transmitted cause should not prevent investigation of alternative or concurrent infection when the clinical picture is atypical.[1]

4.2 INITIAL EXAMINATION AND SPECIMEN COLLECTION

The assessment should document eyelid swelling, conjunctival inflammation, the amount and character of discharge, and the condition of the cornea. Ophthalmic review is urgent if the cornea cannot be adequately assessed or if ulceration, opacity, or epithelial breakdown is suspected. Neonatal evaluation should also address feeding, temperature, respiratory status, and other signs suggesting infection beyond the eye.[1,2]

Conjunctival material should be collected before antibiotics when this can be achieved without delaying treatment of a sight-threatening presentation. For suspected gonorrhea, Gram stain provides rapid presumptive evidence, while culture allows organism confirmation

and antimicrobial susceptibility testing. The microbiology laboratory should be informed of the suspected pathogen so that appropriate collection, transport, and culture conditions are used.[2]

Intracellular gram-negative diplococci strongly support presumptive gonococcal treatment, but other Neisseria species and Moraxella can resemble gonococci on microscopy. A negative or nondiagnostic stain also cannot safely overrule a strongly suggestive presentation. Culture and susceptibility testing remain important, particularly when disease progresses or the response to treatment is unexpected.[2,5]

4.3 TESTING FOR CHLAMYDIAL INFECTION AND COINFECTION

Chlamydial specimens should include conjunctival epithelial cells obtained from the everted eyelid rather than discharge alone. Culture, direct fluorescent antibody testing, and validated nucleic acid amplification methods can be used according to local laboratory capability. In the United States, the CDC notes that conjunctival NAAT use requires laboratory validation because the specimen application is not FDA-cleared.[2]

Testing for chlamydia should accompany evaluation of gonococcal ophthalmia, and a chlamydial result should not automatically end the search for gonorrhea when the presentation remains concerning. A recent report documented neonatal gonococcal infection with chlamydial coinfection and resistance to a fluoroquinolone. A case report cannot establish prevalence, but it demonstrates that mixed infection and resistance can invalidate assumptions based on a single organism or prior topical exposure.[5]

Older diagnostic literature emphasized cell culture and the need to identify nasopharyngeal carriage in addition to ocular infection. Modern molecular testing improves practicality, but its interpretation still depends on the specimen and assay used. A positive ocular test establishes an important treatment target, while additional respiratory or systemic testing should follow the infant's clinical findings.[2,6]

4.4 SYSTEMIC THERAPY FOR GONOCOCCAL OPHTHALMIA

For isolated gonococcal ophthalmia, CDC guidance recommends ceftriaxone 25–50 mg/kg intravenously or intramuscularly as a single dose, with a maximum dose of 250 mg. This is a neonatal weight-based regimen and should not be replaced by an adult gonorrhea dose or by repeated topical antibiotic applications. Treatment should begin promptly after appropriate specimens are obtained when gonococcal infection is strongly suspected.[2]

Ceftriaxone requires particular caution in neonates with hyperbilirubinemia, especially premature infants, and neonatal contraindications and intravenous calcium exposure must be checked. Cefotaxime 100 mg/kg intravenously or intramuscularly once is an alternative for neonates unable to receive ceftriaxone because of simultaneous intravenous calcium administration. Choice in other contraindication scenarios should be made with neonatal and infectious-disease specialists rather than by using an unvalidated substitute.[2]

A single-dose ocular regimen is appropriate only when the presentation is isolated ophthalmia. Neonates should be assessed for sepsis, arthritis, meningitis, or other evidence of dissemination, with blood, cerebrospinal fluid, or joint sampling as clinically indicated. Disseminated infection requires a different systemic treatment course and specialist management, so the one-dose recommendation must not be generalized to a systemically ill infant.[2]

The biological rationale for systemic treatment is reinforced by the potential for gonococci to invade the cornea and disseminate. Topical therapy alone cannot provide reliable treatment of these risks, even if discharge temporarily improves. Local cleansing or irrigation may assist examination and removal of secretions, but it does not replace systemic antibiotics or urgent management of corneal complications.[1,2]

4.5 SYSTEMIC THERAPY FOR CHLAMYDIAL OPHTHALMIA

CDC guidance recommends erythromycin base or ethylsuccinate at a total oral dose of 50 mg/kg/day, divided into four daily doses for 14 days. The distinction between the total daily dose and the dose given at each administration is essential to avoid a fourfold error. The prescribed formulation, concentration, and infant's current weight should be checked, with clear instructions for completing the course.[2]

Systemic therapy addresses both conjunctival infection and extraocular carriage, which explains why topical antibiotics alone are inadequate. In an older randomized study, oral erythromycin eradicated chlamydial infection in 14 of 15 treated infants, whereas persistent conjunctival infection occurred in eight of 14 after topical sulfacetamide. The small historical study supports the treatment principle, while its erythromycin formulation should not be copied in place of current guidance.[3,7]

A systematic review identified 12 studies involving 292 neonates and pooled seven studies using erythromycin 50 mg/kg/day for 14 days. Estimated clinical cure was 96% and microbiological cure 97%, with gastrointestinal adverse effects reported in approximately

14%. The certainty was low to very low because the studies were small and at risk of bias, so these estimates do not eliminate the need to confirm clinical response.[8]

Azithromycin offers a shorter course, commonly 20 mg/kg orally once daily for three days in protocols that select it for neonatal chlamydial infection. The same review reported microbiological cure of 86% with the three-day course and 60% after a single dose, both based on very small samples with wide confidence intervals. CDC guidance acknowledges limited neonatal azithromycin data, and regimen selection should therefore follow the applicable neonatal protocol with planned follow-up rather than assume equivalence to erythromycin.[2,8]

4.6 TREATMENT FAILURE AND RESPIRATORY INVOLVEMENT

The CDC cites an approximate erythromycin effectiveness of 80% for ophthalmia and notes that a second course may be required. This estimate differs from the higher pooled cure proportions in selected treatment studies because evidence sources, definitions, and follow-up vary. Persistent symptoms should prompt review of adherence, dosing, the microbiological diagnosis, and alternative causes rather than automatic reassurance that a standard course must have eradicated infection.[2,8]

Infants with chlamydial ophthalmia should be assessed for concurrent or subsequent respiratory disease. Chlamydial pneumonia typically presents later, often at one to three months, and may include a repetitive staccato cough and tachypnea without prominent fever. New respiratory symptoms require clinical evaluation and should not be dismissed because the conjunctivitis has improved.[2,3]

4.7 MACROLIDES AND INFANTILE HYPERTROPHIC PYLORIC STENOSIS

Both erythromycin and azithromycin have been associated with infantile hypertrophic pyloric stenosis after exposure early in life. A large retrospective cohort found the association strongest during the first two weeks, with increased risk persisting through six weeks. For azithromycin exposure in the first 14 days, the adjusted odds ratio was 8.26, with a wide confidence interval of 2.62–26.0; the corresponding erythromycin estimate was 13.3.[9]

These observational estimates describe relative association rather than the probability that an individual treated infant will develop obstruction. They do not justify withholding indicated therapy for confirmed or strongly suspected chlamydial infection. They support

careful selection of the regimen, avoidance of unnecessary exposure, and counseling about progressive vomiting, feeding difficulty, and the need for reassessment.[9,10]

A meta-analysis found a significant association between direct postnatal macrolide exposure and pyloric stenosis, while evidence about prenatal or breastmilk exposure was less conclusive. This distinction prevents extending neonatal direct-exposure findings to every form of maternal antibiotic treatment. Follow-up should remain attentive to feeding and vomiting even when a shorter macrolide course is selected.[10]

4.8 PROPHYLAXIS AND MATERNAL MANAGEMENT

Ocular prophylaxis and treatment of established infection are separate interventions. Erythromycin ointment given at birth does not reliably prevent chlamydial conjunctivitis or nasopharyngeal infection, so prior prophylaxis does not exclude disease. Comparative studies and a subsequent review found no significant protective advantage of erythromycin or tetracycline over silver nitrate for neonatal chlamydial outcomes.[11,12]

A Cochrane review of 30 trials involving 79,198 neonates found that prophylaxis probably reduced conjunctivitis of any cause, but organism-specific evidence was less certain. No included trial reported the review's primary serious visual outcomes, and comparisons did not establish a consistently superior intervention. These evidence limitations should be distinguished from current public-health recommendations, including the CDC recommendation for routine erythromycin prophylaxis in the United States.[2,13]

Recent expert discussion has questioned universal prophylaxis in settings with effective prenatal screening, but this remains a policy question rather than a reason to neglect current local requirements. Maternal screening, treatment, and communication of results to the neonatal team are central to prevention. Mothers of infected infants and their partners require evaluation and treatment under the appropriate sexually transmitted infection pathway.[2,4]

Table 1

Evidence supporting diagnosis, treatment, and prevention

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Workowski et al. (2021) [2]	CDC STI guidance; neonatal gonococcal and chlamydial infection.	Systemic treatment required; evaluate extraocular disease and maternal infection.	Use neonatal weight-based regimens; topical therapy alone is inadequate.
Heggie et al. (1985) [7]	Historical randomized comparison; chlamydial conjunctivitis treated orally or topically.	Oral eradication 14/15; persistent conjunctival infection after topical therapy 8/14.	Supports systemic treatment; historical formulation is not a current prescribing template.
Zikic et al. (2018) [8]	Systematic review; 12 treatment studies, 292 neonates.	Pooled erythromycin clinical/microbiological cure 96%/97%; limited azithromycin data.	Evidence low to very low certainty; follow-up and adherence remain necessary.
Eberly et al. (2015) [9]	Large retrospective cohort of infant macrolide exposure.	Early exposure associated with IHPS, strongest during the first two weeks.	Counsel and monitor; observational association is not an individual absolute risk.
Smith-Norowitz et al. (2021) [12]	Review of prospective comparative neonatal chlamydial prophylaxis evidence.	No demonstrated reduction with antibiotic ointments versus silver nitrate.	Birth prophylaxis does not exclude chlamydial ocular or extraocular infection.
Kapoor et al. (2020) [13]	Cochrane review; 30 prophylaxis trials, 79,198 neonates.	Reduced all-cause conjunctivitis; organism-specific evidence less certain.	No trial data on serious visual outcomes; prevention is distinct from treatment.

CDC, Centers for Disease Control and Prevention; IHPS, infantile hypertrophic pyloric stenosis; STI, sexually transmitted infection. Historical treatment studies do not supersede current neonatal recommendations.

5 LIMITATIONS OF THE EVIDENCE

The neonatal therapeutic evidence is much smaller than the literature for adult genital infection. Historical trials use different formulations, diagnostic methods, and cure definitions, while contemporary resistance reports often consist of individual cases. This focused narrative synthesis did not exhaustively retrieve all studies or perform a new quantitative comparison, and current neonatal guidance takes precedence over historical regimens.[5,8]

6 CONCLUSION

Gonococcal and chlamydial neonatal conjunctivitis both require systemic treatment, but gonococcal disease demands particular urgency because of rapid corneal injury and

possible dissemination. Laboratory investigation should identify the organism, assess potential coinfection, and preserve susceptibility information when gonorrhea is suspected. Correct neonatal dosing, assessment for extraocular disease, surveillance for treatment failure and macrolide-associated pyloric stenosis, and maternal and partner care are essential to effective management.[2,8,9]

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