

Evaluation and Management of the Healthy Neonate with Conjunctivitis

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I have no financial
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Motivation

Call from Reading Hospital ER

- 3 week old neonate with conjunctivitis X 24 hours
 - Born at Reading Hospital
 - Full term
 - Maternal history negative for GC/Chlamydia in 3rd trimester
 - Received erythromycin eye prophylaxis at birth
 - Breastfed
 - Discharged home at 48 hours of age after uneventful birth stay
 - No other symptoms
 - PE unremarkable except for bilateral conjunctivitis and mucopurulent discharge.



Neonatal Conjunctivitis



All changes saved in Drive



Questions Responses Settings

Based on the history presented, the next best step in the evaluation and management of this infant is

Dropdown

1. Bacterial cultures alone
2. Bacterial cultures including GC, PCR for GC and Chlamydia
3. Gram stain of eye discharge
4. Gram stain and Giemsa stain of eye discharge
5. Add option

Required





5. Add option

Required

You suspect that the infection is caused by a gram negative bacteria. The best choice for empiric coverage is

- Polytrim (trimethoprim) ophthalmic drops
- erythromycin ophthalmic ointment
- oral azithromycin
- moxifloxacin ophthalmic solution

Vertical toolbar with icons for adding content (plus), text (Tt), image, video, and list.





Questions Responses Settings

moxifloxacin ophthalmic solution



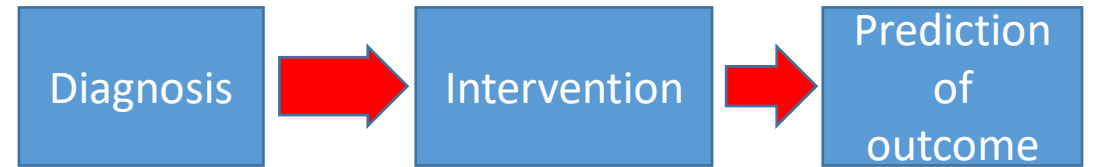
Two days after the initial evaluation, the neonate returns for follow up. On examination, there is minimal improvement and the cultures obtained at the initial evaluation yielded *Pseudomonas aeruginosa*. The best option at this point is

- Ciprofloxacin ophthalmic soltuion
- Admit to hospital
- Ciprofloxacin ophthalmic plus oral ciprofloxacin
- ceftriaxone IM plus moxifloxacin ophthalmic



The Medical Decision Making Process

- The 3 questions every parent has form the core of this process:
 - What's wrong with my child?
 - What are you going to do about it?
 - Are they going to get better?



- The medical decision making process is linear
 - Everything flows from the diagnosis
 - Once the diagnosis is known, appropriate therapy can be implemented
 - Outcomes of therapy can then predicted based on risk factors, etc.

Formulating a Clinical Assessment and Clinical Problem...The key to evidence based practice

- Clinical Assessment

- A simple declarative statement that summarizes what is known about the patient.
- Components
 - Define the Patient population and gender
 - Neonate (< 1mo)
 - Infant (1 mo – 1 year)
 - Toddler (1 year – 3 years)
 - Preschool (3 years – 5 years)
 - School aged (5- 12 years)
 - Adolescent (> 12 years)
 - Define the time course of the disease process
 - Acute – days
 - Subacute – weeks
 - Chronic – months
 - Identify the most salient feature of the illness that emerges from the history, physical and initial laboratory evaluation.
 - Identify a question of diagnosis, therapy or prognosis

- Clinical Problem

- A searchable question based on the clinical assessment

- Clinical Assessment

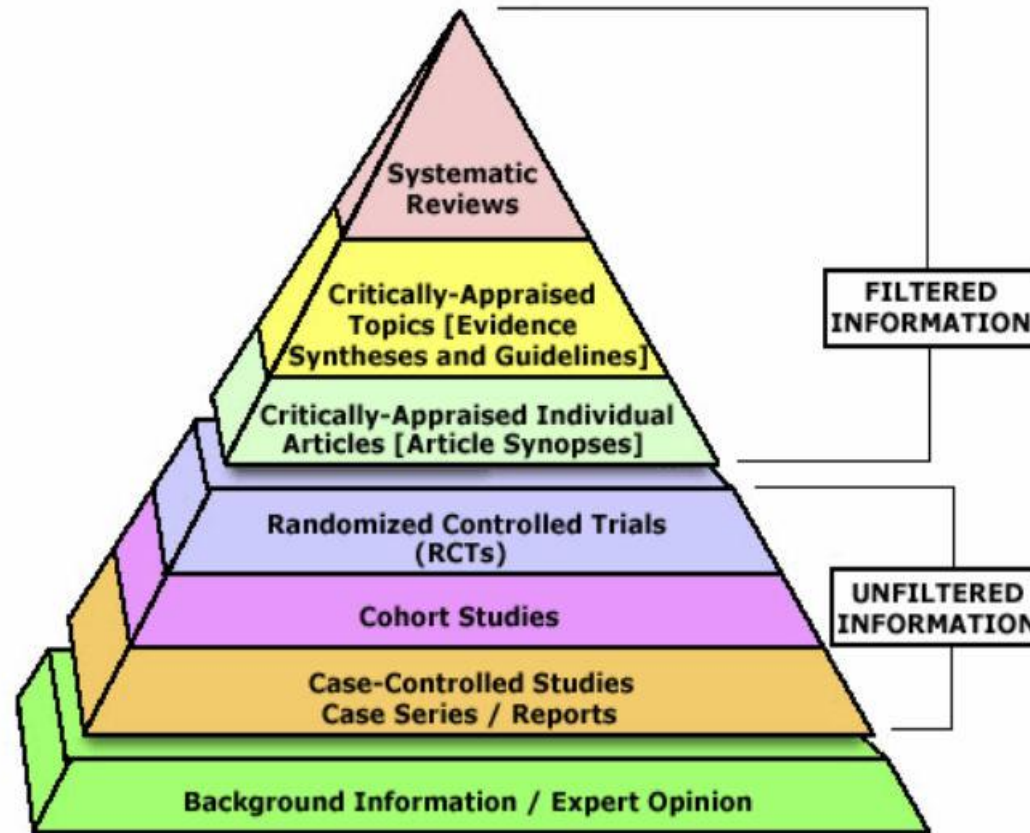
- This is a 3 week old neonate with a benign prenatal, neonatal and perinatal history presenting with the acute onset of conjunctivitis

- Clinical Problem

- What are the etiologies (diagnosis) of neonatal conjunctivitis?

Evidence Based Approach

Hierarchy of Evidence



Evidence on Neonatal Conjunctivitis

- Cohort Studies
 - Incidence and Clinical Characteristics of Infantile Conjunctivitis in a Western Population. *Am J Ophthalmol.* 2022;241:145-148. doi:10.1016/j.ajo.2022.04.008
 - 576 neonates in Minnesota
 - Cultures from 20%
 - Chlamydia in 3
 - Ophthalmia neonatorum in a tertiary referral children's hospital: A retrospective study. *Eur J Ophthalmol.* 2022;32(1):587-591. doi:10.1177/1120672121994734
 - 54 Irish neonates 2013-2018
- Expert Opinion
 - Ophthalmia neonatorum treatment and prophylaxis: IPOSC global study. *Graefes Arch Clin Exp Ophthalmol.* 2016;254(3):577-582. doi:10.1007/s00417-016-3274-5
 - Survey of 291 ophthalmologists
- Limited evidence
 - No guidelines, RCTs, multiple large cohort studies
 - Only 2 small cohort studies with limited bacteriologic data
 - One opinion survey
- Opportunity for research

Variability in the Evaluation and
Management of Healthy Neonates with
Uncomplicated Conjunctivitis
J Pediatr Ophthalm Strab, in press

I wish to thank my colleagues and co-authors who worked diligently on this project:

Camden Nelson – LKSOM Student (3rd year)

Bailee Deshler – LKSOM Student (4th year)

Brittany Bernstein, MD – Ophthalmology resident (3rd year)

Background

- *Ophthalmia neonatorum (ON)*
 - purulent eye discharge
 - edema
 - Conjunctivitis AND/OR
 - erythema of the eyelids
 - within the first four weeks of life
- *N. gonorrhoeae*
 - 1881-Associated with ON 1881
 - 1891 - Gonorrhoea accounted for 65-75% of cases of ON
 - 1983 –Gonorrhoea accounted for less than 0.1% of cases of ON
 - Prophylaxis
 - Antenatal maternal screening
- *C. trachomatis*
 - 1909 – described as inclusion conjunctivitis
 - 1957 – associated with *C. trachomatis*
 - 1980s-1990s – accounted for ~ 50% of ON cases

Methods

- Dataset

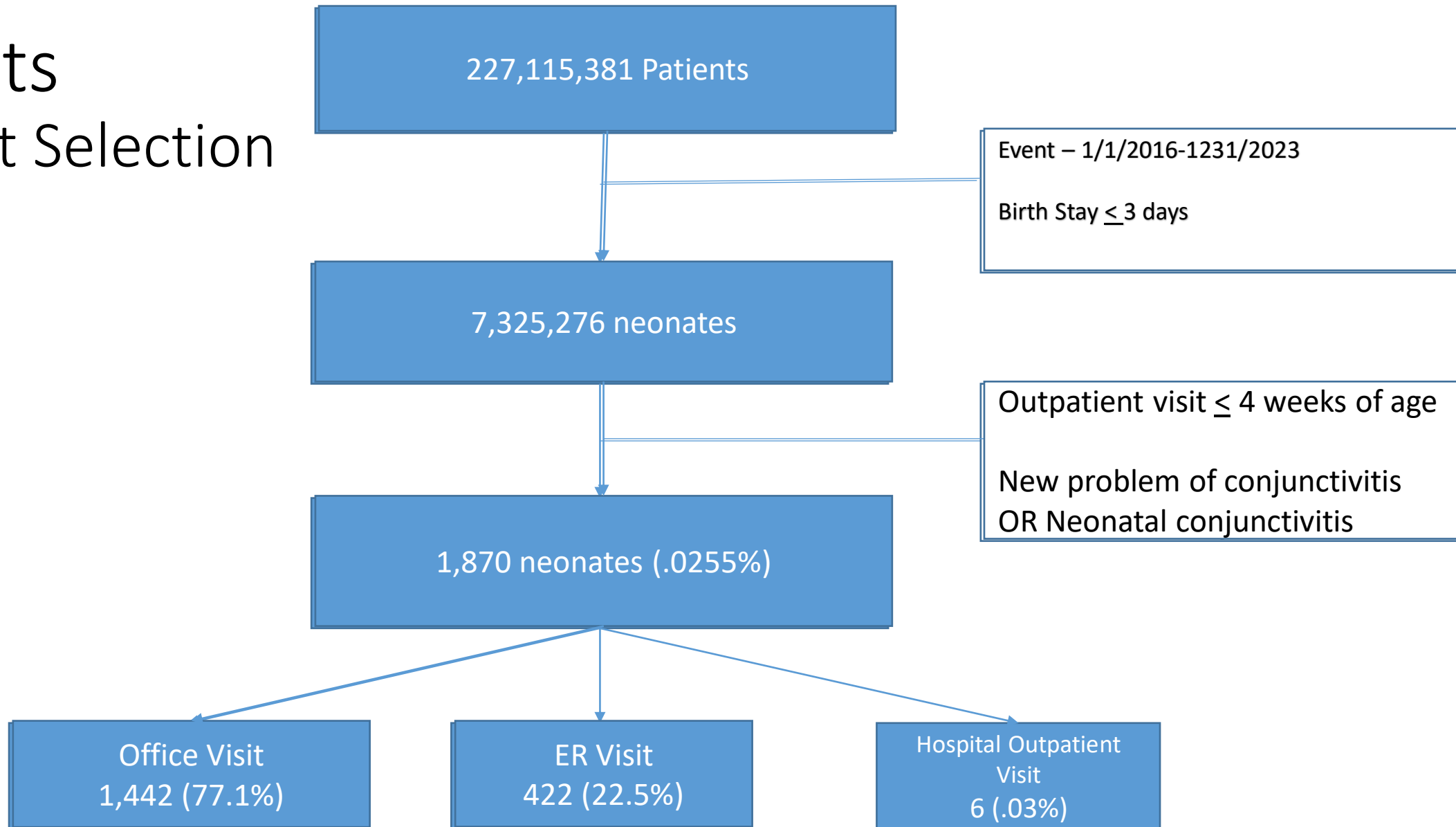
- Cosmos
 - Deidentified, relational database
 - 227,115,381 patients with Epic records from the US and Lebanon
 - Data entered remotely and verified centrally
- Selection Criteria
 - Newborns discharged between 1/1/2016 and 12/31/2022
 - Newborn stay ≤ 3 days
 - Age ≤ 4 weeks of age
 - Sentinel Event
 - Outpatient visit
 - Physician's office
 - ER
 - Hospital outpatient
 - New problem of conjunctivitis
 - Conjunctivitis(ICD 10; H10.*) OR
 - Neonatal conjunctivitis (SNOMED)

- Data collected

- Linked to sentinel event or birth history
- Demographic base
- Medical history and examination from sentinel event
- Billed procedure database
- Medications database
- Diagnosis[All] database

Results

Patient Selection



Results

Demographics and Clinical Presentation

- N = 1870
- Gender
 - Female = 805 (56%)
- Country of care
 - American = 1805 (96.5%)
- Race
 - White – 1048 (56%)
 - African American – 413 (22.1%)
 - Asian - 68 (3.6%)
 - Native American – 19 (1%)
 - Not Identified – 253 (13%)
- Gestational Age
 - Full Term – 1685 (90.1%)
 - 33-37 weeks – 185 (9.9%)
- Chief Complaint
 - Fever – 1047 (56.0%)
 - Cough – 1078 (57.6%)
 - Nasal congestion – 754 (40.3%)
 - Eye discharge – 411 (22.0%)
 - Fussiness – 276 (14.8%)
 - Feeding issues – 49 (2.65%)
- Vital signs at Initial Examination
 - RR > 60 – 155 (8.3%)
 - O₂Sat < 92% - 75 (4%)
 - T > 38°C – 51 (2.7%)

Results

Laboratory Testing at Sentinel Visit

- No testing for majority of patients
- Conjunctival cultures – 399 (21.3%)
 - Presumed positivity rate (based on bills for sensitivity testing of isolates) – 205/399 (51.3%)
- Giemsa and/or Gram's staining of conjunctival exudate – 338 (13.1%)
- Aerobic blood cultures – 309 – 16.5%
- NAAT for HSV – 125 (6.7%)
- NAAT for *C. trachomatis* – 149 (8.0%)
- Viral cultures – 19 (1.0%)
- Cultures for *C. trachomatis* – 136 (7.3%)

Diagnoses in addition to neonatal conjunctivitis or conjunctivitis (ICD-10 H10.*) recorded at the sentinel visit in 1870 healthy neonates.

Additional Diagnoses*	N	%
Unspecified acute conjunctivitis (H10.9)	691	37.0%
Other mucopurulent (H10.021,.022,.023, .0290)	142	7.6%
Other bacteria (B96.*)	86	4.6%
Congenital stenosis lacrimal duct (Q10.5)	51	2.7%
Streptococcus/Staphylococcus (B95.*)	46	2.5%
Gonococcal conjunctivitis (A54.31)	29	1.6%
Viral conjunctivitis (B30.*)	22	1.2%
Chlamydial infection (A74.*, P23.1, A56)	11	0.6%
Herpesviral conjunctivitis (B00.*)	0	0.0%
Pseudomonas (B96.5)	0	0.0%

*ICD 10 codes in parentheses

Results

Antibiotic Usage

	no. of patients	Percentage
Antibiotics by class*	1752	93.7%
Macrolides (1416)	1148	61.4%
Aminoglycosides (1676)	227	12.1%
Cephalosporins (772)	106	5.7%
Penicillins (1429)	99	5.3%
Antiviral (1608)	16	0.9%
Sulfonamides (151)	11	0.6%
Quinolone (595)	NR	NR
Vancomycin (136)	NR	NR

*number of generic and trademarked agents are shown in parentheses.

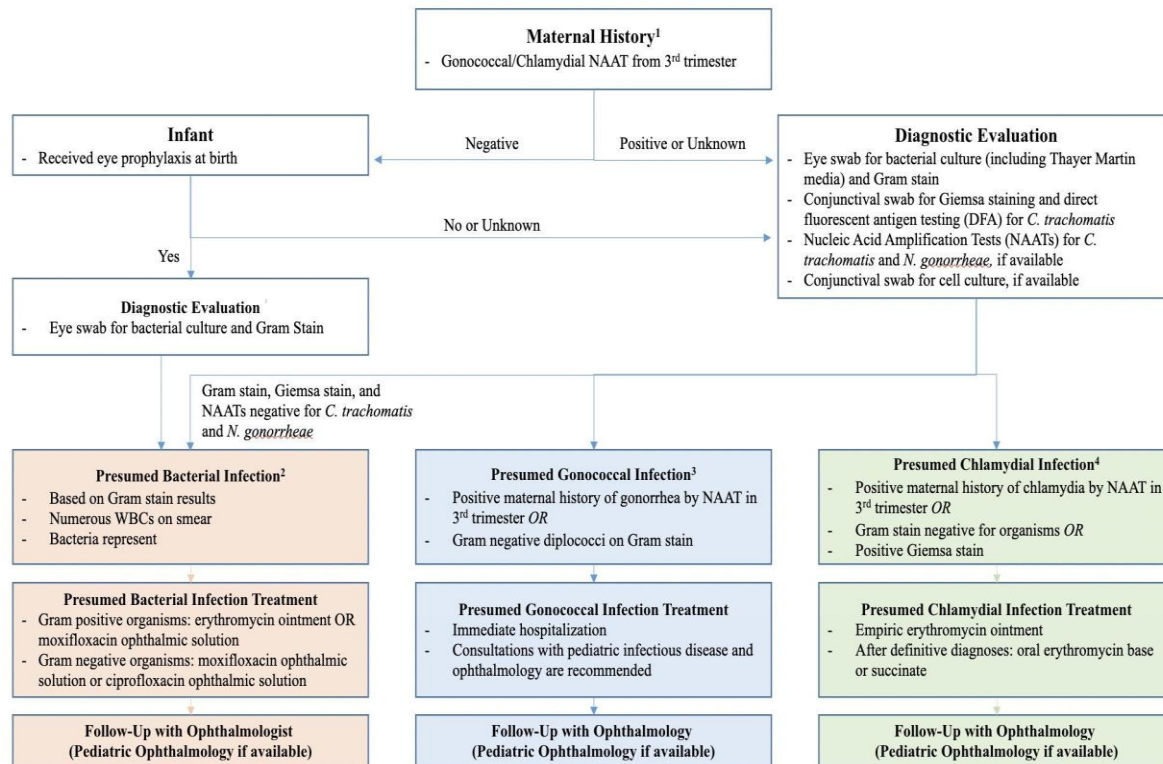
NR = Cosmos does not report values less than 10.

<i>Ophthalmic Antibiotics</i>	1486	79.5%
Macrolides	1067	57.1%
Polymyxin	231	12.4%
Polymyxin B sulfate/Trimethoprim	207	11.1%
Gentamicin sulfate	152	8.1%
Tobramycin	43	2.3%
Sulfonamides (151)	11	0.6%
 <i>Oral Antibiotics</i>	 214	 11.4%
Macrolides	154	8.2%
Penicillins	39	2.1%
Cephalosporins	40	2.1%
 <i>Antibiotics, intravenous</i>	 144	 7.7%
Penicillins	60	3.2%
Cephalosporins	55	2.9%
Aminoglycosides	40	2.1%
Macrolides	NR	NR

Summary

- Evaluation and management of the healthy neonate with conjunctivitis is variable.
 - 21.3% of neonates were cultured but over 50% of the cultures appeared to be positive
 - 94% received topical antibiotics
 - 8.2% received oral macrolides while the incidence of *C trachomatis* was less than 1%.
 - 7.7% of infants received intravenous antibiotics but only 2.7% were febrile over 38°C.
- Guidelines from the AAP, PIDS and/or AAPO are required to standardize the approach

A framework for the evaluation management of the healthy neonate with conjunctivitis



- ¹ Infants born to mothers with evidence of herpes genitalis at birth or with physical findings suggestive of neonatal herpes should be managed according to AAP guidelines³⁶
- ² Empiric topical therapy is based on Gram stain results. At the present time, only erythromycin, moxifloxacin, and ciprofloxacin are approved for the use in infants less than 4 weeks old. For infections due to Gram positive organisms:
 - **Erythromycin ointment** 0.5% - apply 1 cm ribbon 6X/day X 10 days OR **Moxifloxacin** ophthalmic solution 0.5% - 1 drop in affected eye tid X 7 days.³⁵
- For gram negative or mixed infections:
 - **Moxifloxacin** ophthalmic solution 0.5% - 1 drop in affected eye tid X 7 days³⁵ OR **Ciprofloxacin** hydrochloride .3% - 1-2 drops every 2 hours X 2 days followed by 1-2 drops every 4 hours X 5 days.³⁴
- Definitive therapy is based on the results of bacterial culture and sensitivity testing. Topical therapy is typically adequate and should be limited to agents approved for the use in neonates.
- Infants with *C. trachomatis*, *N. gonorrhoeae* or *Ps. aeruginosa* should be managed with guidance from an infectious diseases physician.
- Infants with fever, cough or other associated symptoms should be managed in accordance with AAP, PIDS and/or IDSA guidelines.

- Maternal Neonatal history
 - Negative for GC/Chlamydia
 - Eye prophylaxis received
- Most likely bacterial infection
- Gram stain of eye discharge

The screenshot shows a Google Forms editor interface for a form titled "Neonatal Conjunctivitis". The form is currently in "Questions" mode. The question text is: "Based on the history presented, the next best step in the evaluation and management of this infant is". The question type is set to "Dropdown". There are five options listed:

1. Bacterial cultures alone
2. Bacterial cultures including GC, PCR for GC and Chlamydia
3. Gram stain of eye discharge
4. Gram stain and Giemsa stain of eye discharge
5. Add option

At the bottom of the question editor, there are icons for copy, delete, and a "Required" toggle switch which is currently turned off. The browser's address bar shows the URL: docs.google.com/forms/d/1L1WLWJ4zMpcAYKfwAq0MwqW7YFAHfQu2otn52ZLHYs/edit. The Windows taskbar at the bottom shows the time as 10:09 AM on 9/10/2024.

- Topical trimethoprim and erythromycin have limited gram negative activity
- Oral macrolides are associated with pyloric stenosis in this age group
- Moxifloxacin is approved for this age group and has broad gram negative activity

The screenshot shows a Google Forms editor interface. The browser tabs at the top include "Google Forms: Online Form Cre..." and "Neonatal Conjunctivitis - Goog...". The URL is ".google.com/forms/d/1L1WLIWJ4zMpcAYKfWaq0MwqW7YFAHFQu2otn52ZLHYs/edit". The form title is "njunctivitis". The "Questions" tab is active, showing a question titled "5. Add option". The question text is "You suspect that the infection is caused by a gram negative bacteria. The best choice for empiric coverage is". The question type is "Multiple choice", and the "Required" toggle is turned on. The options are:

- Polytrim (trimethoprim) ophthalmic drops
- erythromycin ophthalmic ointment
- oral azithromycin
- moxifloxacin ophthalmic solution

The Windows taskbar at the bottom shows various application icons and the S&P 500 index at +0.30.

SHAH, SAMIR S. BA; GALLAGHER, PATRICK G. MD. Complications of conjunctivitis caused by *Pseudomonas aeruginosa* in a newborn intensive care unit. The Pediatric Infectious Disease Journal 17(2):p 97-102, February 1998.

- Described 18 premature infants with pseudomonas conjunctivitis
- Systemic complications in 7
 - bacteremia (5)
 - meningitis (3)
 - brain abscess (1)
 - pneumonia (1)
 - suppurative otitis media (1)
- Based on these risks, AAP guidelines recommend admission to hospital for evaluation and systemic therapy.

The screenshot shows a Google Forms editor interface. The browser tabs at the top include 'Google Forms: Online Form Cre...' and 'Neonatal Conjunctivitis - Goog...'. The URL is 'https://www.google.com/forms/d/1L1WLIWJ4zMpcAYKFwAq0MwqW7YFAHfQu2otn52ZLHYs/edit'. The form title is 'nconjunctivitis'. The 'Questions' tab is selected, showing a multiple-choice question. The question text is: 'Two days after the initial evaluation, the neonate returns for follow up. On examination, there is minimal improvement and the cultures obtained at the initial evaluation yielded *Pseudomonas aeruginosa*. The best option at this point is'. The options are: 'moxifloxacin ophthalmic solution', 'Ciprofloxacin ophthalmic soltuion', 'Admit to hospital', 'Ciprofloxacin ophthalmic plus oral ciprofloxacin', and 'ceftriaxone IM plus moxifloxacin ophthalmic'. The 'Responses' and 'Settings' tabs are also visible. The Windows taskbar at the bottom shows various application icons and the S&P 500 index at +0.30.