You are asked to see a 1,700-g, 12-day-old male infant who has severe purulent conjunctivitis. The infant was born at 33 weeks' gestational age to a mother whose prenatal blood testing was negative for syphilis and gonorrhea and who had a negative history for herpes simplex infection. The infant received eye prophylaxis at birth with 1% silver nitrate, had minimal respiratory symptoms, and was receiving increasing amounts of enteral feedings. At 10 days of age, he developed vomiting, diarrhea, and erythema of the left eye. On physical examination, the conjunctiva and upper and lower lids of the left eye are edematous, and there is copious yellow drainage. The lid margins show crusting and denudation of the skin, with papulovesicular lesions. A group of 0.5 x 0.5 cm vesicles is present on the central forehead. Bacterial culture of the exudate is negative at 24 hours, and Gram stain is negative for organisms. Treatment with a topical ophthalmic antibiotic ointment begun 24 hours earlier has resulted in no clinical improvement. The only other findings of note on the physical examination are prematurity and mild jaundice.

Of the following, the MOST likely cause of this infant's ophthalmia is

- [ ] chemical conjunctivitis
- [ ] Chlamydia trachomatis
- [ ] herpes simplex
- [ ] Neisseria gonorrhoeae
- [ ] Staphylococcus aureus

You selected 5, the correct answer is 3.

The clinical features described for the infant in the vignette are consistent with the diagnosis of ophthalmia neonatorum, specifically keratoconjunctivitis from herpes simplex virus (HSV) infection. Ophthalmia neonatorum or neonatal conjunctivitis is defined as purulent conjunctivitis developing in the first 28 days after birth and is the most common ocular disease in newborns. Neonatal conjunctivitis may be caused by a variety of pyogenic organisms, but sexually transmitted organisms are frequent in the neonatal period. In developed countries where screening for prevention of gonorrhea is conducted during pregnancy, Chlamydia is by far the most common organism responsible for ophthalmia. Noninfectious causes of ophthalmia include chemical irritation, primarily from silver nitrate prophylaxis. Ophthalmia neonatorum occurred in up to 15% of infants born during the 19th century, and Credé was the first to report prevention by using silver nitrate drops for prophylaxis, which reduced the incidence of ophthalmia from 10% to 0.3% of infants. This infection rate and the resultant blindness were reduced further with the introduction of sulfonamide and penicillin antibiotics in the 1900s. By 1950, new entrants to schools for the blind attributable to ophthalmia neonatorum had decreased to only 1%.

There are three clinical presentations of neonatal HSV infections: disseminated (involving multiple organs with or without central nervous system involvement); encephalitis with or without skin, eye, or mouth involvement; and infection localized to the skin, eyes, and mouth. Epidemiologically, approximately 40% of neonatal HSV infections are localized to the skin, eyes, and mouth and are referred to as mucocutaneous keratoconjunctivitis. Ocular infection may be the only manifestation of neonatal HSV infection. Both HSV I and II are implicated. More than 90% of affected infants have vesicles that appear in clusters, as described for the infant in
the vignette, with the typical onset of presentation occurring at 10 to 11 days after birth, presumably following perinatal acquisition. Vesicles often erupt on the body part that presented during labor and delivery. Some 80% of HSV eye infections are unilateral, and vesicles often occur on the eyelid in primary infection, but not in reactivated disease. Although bulbar conjunctival ulceration is unusual, when present, it is virtually pathognomonic for primary HSV I infection. Keratitis can occur in as many as 50% of primary cases and is characterized by mild epithelial irregularities that have the characteristic dendritic pattern of epithelial disease seen in reactivation.

Outcome data from the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group documented minimal mortality from isolated mucocutaneous HSV infection. However, one third of affected infants developed neurologic sequelae, especially if they had three or more recurrences of vesicles within 6 months of the initial infection. Infection involving the eye may result in chorioretinitis, microphthalmia, retinal dysplasia, and cataracts. Diagnosis is made by positive viral culture of the vesicular fluid or conjunctival swab specimens. Positive findings on polymerase chain reaction assay for viral DNA from sample sites also are diagnostic. Therapy is systemic acyclovir plus topical ophthalmic antiviral drugs as an adjunct to parenteral therapy. The administration of oral prophylactic acyclovir after initial therapy has been reported anecdotally to prevent recurrent disease, particularly within the first 6 postnatal months. Studies to evaluate the effectiveness of a prophylactic antiviral regimen are ongoing.

In the United States, chemical irritation following eye prophylaxis with silver nitrate or antibiotic drops may occur in up to 90% of treated infants. Chemical conjunctivitis usually is noted within hours after instillation of the offending drops and resolves by 48 hours in most cases. Irritation typically is bilateral. Examination of the exudate shows epithelial desquamation and polymorphonuclear leukocytes. The culture is negative or may show normal flora. Although treated with silver nitrate, the infant in the vignette does not have the clinical presentation for chemical conjunctivitis.

**Chlamydia trachomatis** is an obligate intracellular bacterial parasite. Of the three species, *C psittaci*, *C pneumoniae*, and *C trachomatis*, only the last is a genital pathogen associated with neonatal infection. Approximately 4% to 5% of sexually active women are colonized with *Chlamydia*. After delivery to an infected mother, 53% of infants born vaginally and 19% of infants delivered by cesarean section are colonized. Conjunctivitis develops in 25% to 50% and pneumonia in 5% to 20% of exposed infants. *C trachomatis* conjunctivitis, also known as inclusion blennorrhea, usually is acquired during passage through the birth canal. The incidence is reflective of the prevalence of *Chlamydia* in the community. *Chlamydia* conjunctivitis often starts as a watery discharge, progressing rapidly to purulent exudate with marked swelling of the eyelids. Although it may occur as early as 24 hours after birth, conjunctivitis generally develops in the second postnatal week. Inflammation may be mild or severe, with primary involvement of the tarsal conjunctiva. The exudate is a mixed polymorphonuclear and mononuclear leukocytic infiltrate. The follicular nature of the infection is absent in neonates due to their lack of lymphoid tissue, but pseudomembranes may be evident. The inclusion bodies that are diagnostic of *Chlamydia* are located within the epithelial cells of the conjunctival surface. Therefore, smears prepared from only the exudate are not adequate. Gently obtained scrapings of the conjunctiva, which can harvest epithelial cells, are required for diagnosis. Giemsa staining of the scrapings show Leber cells and inclusion-bearing epithelial cells. Culture remains the gold standard, but it is not widely available. Alternatively, nucleic acid amplification tests (NAAT) on scrapings have been used successfully to establish the diagnosis. Fourteen days of oral erythromycin is the therapy of choice. Trials of topical antibiotic therapy have resulted in failure rates as high as 50%. If left untreated, inflammation gradually resolves. However, some infants maintain a persistent conjunctivitis, with neovascularization of the cornea that results in scarring. Coinfection with other sexually transmitted organisms, such as *Neisseria gonorrhoeae*, must be considered and investigated simultaneously. The efficacy of oral erythromycin is approximately
80%; occasionally, a second course of therapy may be required. To date, the best prevention strategy is to screen and treat pregnant women who harbor the infection. For women who have untreated Chlamydia infection at the time of delivery, the American Academy of Pediatrics recommends close expectant management of infants unless follow-up cannot be ensured. Prophylactic erythromycin treatment for all infants of untreated mothers currently is not recommended due to an increased risk of pyloric stenosis.

 Conjunctivitis due to N gonorrhoeae is virtually indistinguishable from that caused by Chlamydia. It produces an acute purulent conjunctivitis that appears 2 to 5 days after birth. Presentation at up to 19 days of age has been reported. Infants typically develop severe edema of the eyelids, chemosis, and progressive profuse and purulent conjunctival exudate. Progressive disease causes corneal ulceration and may cause perforation and loss of vision or loss of the globe. The infection can spread systemically and result in death. For this reason, gonococcal infection must be excluded in every case of conjunctivitis in infants. Diagnosis is confirmed by culture of the exudate. Gram stain shows the presence of gram-negative diplococci and polymorphonuclear leukocytes. Approximately 32% of N gonorrhoeae strains have shown some resistance to penicillin, tetracycline, or both. For this reason, ceftriaxone is considered the therapy of choice. Infants also should receive frequent topical irrigation with saline until the discharge is eliminated. Topical antibiotic therapy alone is inadequate and unnecessary if systemic antibiotics are administered. If appropriate therapy is initiated before corneal involvement develops, spread of infection is rare, but the possibility should be investigated. Prophylactic eye drops administered immediately after birth with 1% silver nitrate, tetracycline, or erythromycin ointment is recommended by the American Academy of Pediatrics. None of these topical agents is effective in eradicating Chlamydia.

One of the most common sites for staphylococcal infection is the conjunctiva. Purulent staphylococcal conjunctivitis cannot be distinguished clinically from that caused by other organisms. It responds well to topical antibiotic therapy, usually resulting in no residual damage. Infection caused by Staphylococcus or other organisms, except those mentioned previously, more commonly reflect infection acquired during the neonatal period. Seventeen percent of cases of neonatal conjunctivitis were found to be due to S aureus in a prospective controlled trial. Other bacterial organisms encountered included Haemophilus influenzae, Streptococcus pneumoniae, Pseudomonas aeruginosa, and group B Streptococcus. Culture and Gram stain of the exudate establish the diagnosis. Caution must be used in interpreting results, however, because the exudate may reflect normal bacterial inhabitants of the skin and mucous membranes.

Any infant who has conjunctival discharge should be evaluated carefully to determine the cause by performing three tests: Gram stain of the exudate, bacterial culture of the exudate, and Giemsa stain and Chlamydia culture or NAAT of scrapings made from lower palpebral conjunctiva after the exudate has been removed.

References:


Content Specification(s):

2516. Understand the causes and differential diagnosis of neonatal ophthalmia
2517. Understand the clinical and laboratory features of neonatal ophthalmia
2519. Understand the treatment and complications of neonatal ophthalmia
2531. Understand the causes and differential diagnosis of infections of the skin and mucous membranes
2567. Understand the epidemiology and prevention of neonatal *Neisseria gonorrhoeae* infections
2568. Understand the pathogenesis, clinical manifestations, and diagnosis of neonatal *Neisseria*
2572. Understand the treatment and complications of neonatal *Neisseria gonorrhoeae* infections
2577. Understand the clinical manifestation and diagnostic criteria of neonatal infection with *Staphylococcus aureus* and *Staphylococcus epidermidis*
2609. Understand the epidemiology, pathogenesis, and prevention of neonatal infection with *Chlamydia*
2612. Understand the clinical manifestations and diagnostic criteria of neonatal infection with *Chlamydia*
2614. Understand the treatment and complications of neonatal infection with *Chlamydia*
2633. Understand the clinical manifestations of perinatal infections with herpes I, herpes II, cytomegalovirus, Epstein-Barr virus, and varicella-zoster
2635. Understand the treatment of perinatal infections with herpes I, herpes II,
cytomegalovirus, Epstein-Barr virus, and varicella-zoster
2636. Understand the complications of perinatal infections with herpes I, herpes II, cytomegalovirus, Epstein-Barr virus, and varicella-zoster