Gonococcal infection in the newborn

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INTRODUCTION — Perinatal acquisition of sexually transmitted diseases (STDs) can have serious consequences for the newborn [1]. Ophthalmia neonatorum (newborn conjunctivitis) was caused principally by Neisseria gonorrhoeae at one time in the United States and was the most common cause of blindness. Although this newborn infection has decreased in frequency throughout the world, the consequences of untreated disease remain grave. Gonococcal infection in the newborn is reviewed here. Neonatal infection with other sexually transmitted organisms is discussed separately. (See "Chlamydia trachomatis infections in the newborn" and "Congenital syphilis: Evaluation, management, and prevention" and "Hepatitis viruses and the newborn: Clinical manifestations and treatment" and "Diagnostic testing for HIV infection in infants and children younger than 18 months".)

EPIDEMIOLOGY — Gonococcal infections in pregnant women are estimated at less than 1 percent in developed countries and between 3 and 15 percent in developing regions; >50 percent of the infections in the latter countries are caused by penicillinase-producing strains (PPNG) [2]. Perinatal transmission is estimated to occur in 30 to 40 percent of cases. Coinfection with Chlamydia trachomatis is frequent and HIV transmission is heightened in the presence of gonorrhea [3-5]. (See "Epidemiology of Chlamydia trachomatis infections" and "Treatment of uncomplicated gonococcal infections", section on 'HIV counseling and testing'.)

In one series of neonatal gonococcal infections in Florida from 1984 through 1989, 68 cases were documented; 81 percent of these were gonococcal ophthalmia neonatorum [6]. A number of studies of the causes of ophthalmia neonatorum from different parts of the world have shown a decreasing frequency of N. gonorrhoeae as the etiology of the infection, as illustrated by the following:

- A study of 332 infants with conjunctivitis from Argentina established a pathogen in 50 percent of cases [7]. Haemophilus influenzae, Streptococcus pneumoniae, and Staphylococcus aureus were the most common organisms. No cases of gonococcal ophthalmia neonatorum were identified, and C. trachomatis accounted for 8 percent of infections.
- N. gonorrhoeae and C. trachomatis were responsible for <5 percent of cases of ophthalmia neonatorum in a series of 81 infants with this infection in United Arab Emirates; S. aureus was the most common pathogen [8].
- In a series of 163 cases of neonatal conjunctivitis from India, N. gonorrhoeae was recovered in only a single patient; staphylococci were again the most frequent isolates [9].

The overall epidemiology of N. gonococcal infection is discussed separately. (See "Epidemiology and pathogenesis of Neisseria gonorrhoeae infection", section on 'Epidemiology'.)

PATHOGENESIS — N. gonorrhoeae are gram-negative diplococci. The structure of the organism resembles other gram-negative bacteria with a cell envelope composed of an inner cytoplasmic membrane, a middle layer of peptidoglycan, and an outer membrane [10]. The outer membrane contains lipooligosaccharide, phospholipid, and a variety of proteins. Porin (formerly called protein I) accounts for 60 percent of the outer membrane protein content, allows for the passage of solutes, and forms the basis of a classification system [11]. Por 1A and Por 1B are the two major antigenic classes, and both are comprised of serovars upon which the serotyping system for gonococci is based [12]. Por A strains tend to be resistant to the bactericidal effect of serum and preferentially cause bacteremia [11,12].

Infection with N. gonorrhoeae encompasses four specific stages [13-15] (see "Epidemiology and pathogenesis of Neisseria gonorrhoeae infection"):

- Attachment to the mucosal cell surface
- Local penetration or invasion
- Local proliferation
- Local inflammatory response or dissemination

Initial attachment of gonococci to the surface of columnar epithelial cells is mediated by type IV pili, which are filamentous outer membrane appendages composed of multiple subunits, the most important of which is pilin or pilE, which forms the pilus fiber

[16]. Other outer membrane structures involved in gonococci attachment include PilC proteins and Opa (opacity related proteins, formerly labeled protein II).

Local invasion initially involves multiple adhesins that interact with a variety of host receptors. After attaching to mucosal cells, gonococci become engulfed in a process known as parasite-directed endocytosis. Gonococci are able to undergo intracellular replication, both within phagocytic vacuoles and within columnar epithelial cells. The organism has developed complex strategies to avoid host defense mechanisms, allowing dissemination to occur. Mucosal surfaces and subepithelial tissues are the primary sites of infection [10]. However, the organism may extend through lymphatics or, less often, the bloodstream, and cause systemic disease.

PERINATAL TRANSMISSION — Newborns typically acquire gonococcal infection during delivery. Perinatal transmission occurs in 30 to 40 percent of cases of maternal cervical infection in the United States [17]. Intrauterine infection also can occur after rupture of the membranes.

Association with prematurity — Untreated maternal gonococcal disease appears to increase the risk of preterm delivery [18]. Reported rates of prematurity range from 13 to 67 percent, although most studies include relatively few patients and provide little information on associated conditions or concurrent infections [19-24].

In one study, the rate of preterm delivery was 22 percent of 222 patients [19]. In another series from South Africa, untreated gonococcal infection was associated with an attributable risk of prematurity of 72 percent, although the number of such infected patients was small [21]. In another report of 166 cases and 175 controls who were evaluated for STDs, the attributable risk of gonococcal infection for preterm birth was 14 percent [18]. The association with prematurity appeared to be specific for gonococcal infection and not other STDs.

OPHTHALMIA NEONATORUM — The eye is the most frequent site of gonococcal infection in the newborn. As noted above, gonococcal infection is a rare, although serious, cause of ophthalmia neonatorum in developed countries due in large measure to the use of routine prophylaxis. Although also decreasing in frequency in developing countries, it still causes blindness [25].

Clinical features — Infection typically causes a purulent conjunctivitis, with profuse exudate and swelling of the eyelids (picture 1). Without treatment, the infection can extend from the superficial epithelial layers into the subconjunctival connective tissue and the cornea, leading to ulceration, scarring, and visual impairment.

The infection usually becomes manifest two to five days after birth. However, factors including ophthalmic prophylaxis, inoculum size, or variations in virulence may result in a more indolent course and delay in onset.

Diagnosis — Newborns who develop conjunctivitis after the first day of age or appear to have severe or persistent chemical conjunctivitis should be evaluated. A Gram stain of the conjunctival exudate should be examined for the presence of typical gram-negative intracellular kidney bean-shaped diplococci.

Culture of the exudate should be performed using selective media (eg, modified Thayer-Martin medium) that inhibit normal flora and nonpathogenic Neisseria organisms. If organisms are detected on Gram stain, anal and oropharyngeal cultures also should be obtained as other Neisseria species cannot be distinguished from N. gonorrhoeae.

Newborns with conjunctivitis should be evaluated for C. trachomatis. Coinfection with this organism is common with gonococcal disease. (See "Chlamydia trachomatis infections in the newborn".)

The infant's mother and her sexual partner(s) should be evaluated and treated for gonococcal infection (see "Treatment of uncomplicated gonococcal infections"). She also should be evaluated for other STDs including HIV infection.

Treatment

Infants with ophthalmic disease — Infants with gonococcal ophthalmic disease should be hospitalized and observed for response to therapy and for disseminated disease. Presumptive treatment should be started after obtaining cultures in infants with organisms seen on Gram stain or in those with negative Gram stain, but who are considered to be at high risk (eg, mother with no prenatal care, history of STDs, or substance abuse).

Treatment consists of a single dose of ceftriaxone (25 to 50 mg/kg, not to exceed 125 mg, intravenously or intramuscularly) [4]. A single dose of cefotaxime (100 mg/kg, intravenously or intramuscularly) is an alternative option and is preferred for neonates with hyperbilirubinemia and those receiving calcium-containing intravenous (IV) solutions (eg, parenteral nutrition) [26].

Topical antibiotic therapy alone is inadequate and is not necessary when systemic treatment is provided. The eyes should be irrigated frequently with saline until the discharge clears.

Asymptomatic infants of untreated mothers — Asymptomatic infants whose mothers have untreated gonococcal infection are at high risk for acquiring infection. These infants also should receive systemic treatment with a single dose of ceftriaxone (25 to 50 mg/kg, up to a total dose of 125 mg, administered intravenously or intramuscularly) or cefotaxime (100 mg/kg, administered intravenously or intramuscularly) and should be evaluated for chlamydial infection [4].

Prevention — The most effective measure to prevent both gonococcal and chlamydial infections is to diagnosis and treat these infections in pregnant women. In addition, prophylactic antibiotic eye therapy reduces the risk of gonococcal conjunctivitis; however, it is not effective in preventing C. trachomatis conjunctivitis.

Maternal screening — The Centers for Disease Control and Prevention (CDC) recommends screening for gonorrhea in women who are at increased risk for infection (eg, those with previous gonorrheal infection or other STDs, with new or multiple sex partners, with inconsistent condom use, who engage in commercial sex work and drug use, and who live in communities with a high prevalence of disease) [4]. A large study in Uganda found that treating pregnant women presumptively for STDs in areas where these infections are prevalent is effective in reducing the incidence of STDs in the newborn; ophthalmia neonatorum was reduced by 37 percent [27].

Neonatal prophylaxis — The risk of contracting gonococcal conjunctivitis is markedly reduced by effective prophylaxis [2]. Prophylaxis can be administered up to one hour after birth to facilitate infant-family attachment. The following are regimens recommended by the American Academy of Pediatrics [3] and the CDC.

- Erythromycin (0.5 percent) ophthalmic ointment
- Tetracycline (1 percent) ophthalmic ointment; tetracycline ophthalmic ointment is not available in the United States.

Prophylaxis for gonococcal conjunctivitis is discussed separately. (See "Overview of the routine management of the healthy newborn infant", section on 'Eye care'.)

OTHER LOCALIZED INFECTION — In addition to conjunctivitis, localized infection of other mucosal surfaces can occur. The pharynx, vagina, urethra, and anus can be affected [10]. Scalp abscesses may result from infection introduced by a fetal monitoring electrode [28]. Neonates with a scalp abscess or in whom sepsis is suspected should be treated for disseminated infection. (See 'Treatment' below.)

Diagnostic evaluation consists of cultures from the affected site, blood, and cerebrospinal fluid (CSF) to make certain that infection has not spread. With the exception of scalp abscess, which is treated in the same manner as disseminated disease, localized infection should be treated with a single dose of ceftriaxone (25 to 50 mg/kg, not to exceed 125 mg, administered intravenously or intramuscularly) or cefotaxime (100 mg/kg, administered intravenously or intramuscularly).

DISSEMINATED INFECTION AND SCALP ABSCESS — Disseminated disease may present as sepsis, arthritis, or meningitis. Septic arthritis is the most common manifestation of disseminated disease [29-31]. Gonococcal bacteremia and/or meningitis are rare in the newborn, but can be a complication of ophthalmia neonatorum [17,32].

Clinical features — Gonococcal arthritis typically presents at 2 to 21 days of age. The infant may appear only mildly to moderately ill, and the temperature may be normal or slightly elevated [31]. Multiple joints usually are affected. The infant typically refuses to move the painful, affected limb.

Diagnosis — Cultures should be obtained of blood and CSF. Fluid should be aspirated from an affected joint and Gram stain and culture obtained. Specimens obtained from the conjunctiva, vagina, oropharynx, and rectum are useful for identifying the primary site(s) of infection. A positive Gram stain of exudate, CSF, or joint aspirate provides a presumptive basis for initiating treatment [4].

Treatment — Infants with arthritis, septicemia, and/or abscess should be treated for seven days with ceftriaxone (25 to 50 mg/kg per dose every 24 hours, intravenously or intramuscularly) [3,4]. Cefotaxime (25 mg/kg per dose every 12 hours, intravenously or intramuscularly) is preferred in infants with hyperbilirubinemia and those receiving calcium-containing intravenous fluids (eg, parenteral nutrition) [3,26]. If meningitis is documented, the duration should be extended to 10 to 14 days [3].

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword (s) of interest.)

- Basics topics (see "Patient education: Newborn conjunctivitis (The Basics)")

SUMMARY AND RECOMMENDATIONS

- Newborns acquire gonococcal infection during delivery. The perinatal transmission rate is about 30 to 40 percent in women with cervical infection. (See 'Perinatal transmission' above.)

- In the newborn, the eye is the most frequent site of gonococcal infection and is typically characterized by a purulent conjunctivitis with profuse exudate and swelling of the eyelids. Without treatment, the infection can extend from the superficial epithelial layers into the subconjunctival connective tissue and the cornea, leading to ulceration, scarring, and visual impairment. The diagnosis is confirmed by culture of the exudate. (See 'Ophthalmia neonatorum' above.)
- Empirical antibiotic therapy of a single dose of ceftriaxone (25 to 50 mg/kg, not to exceed 125 mg, intravenously or intramuscularly) is administered in any infant with suspected gonococcal ophthalmia neonatorum. Infants with confirmed gonococcal disease should also be evaluated for coinfection with Chlamydia trachomatis. (See 'Ophthalmia neonatorum' above.)
- The incidence of gonococcal ophthalmia neonatorum has decreased with the use of routine antibiotic prophylaxis and maternal screening for sexually transmitted disease. (See 'Prevention' above.)
- Other localized gonococcal infections include infections of other mucosal surfaces, which are treated with a single dose of ceftriaxone (25 to 50 mg/kg, not to exceed 125 mg, administered intravenously or intramuscularly) or cefotaxime (100 mg/kg, administered intravenously or intramuscularly). (See 'Other localized infection' above.)
- In newborns, systemic gonococcal infection (eg, septic arthritis, sepsis, and/or meningitis) is rare and is usually a complication of localized infection. Infants with arthritis, septicemia, and/or scalp abscess should be treated for seven days with ceftriaxone (50 mg/kg per dose every 24 hours, intravenously or intramuscularly) or cefotaxime (50 mg/kg per dose every 12 hours, intravenously or intramuscularly). Cefotaxime is recommended for infants with hyperbilirubinemia and those receiving calcium-containing intravenous fluids. In patients with meningitis, the duration of therapy is extended to a minimum of 10 days. (See 'Other localized infection' above and 'Disseminated infection and scalp abscess' above.)

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GRAPHICS

Gonococcal ophthalmia neonatorum

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Graphic 66751 Version 1.0

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