



CHAPTER

16

*Prophylaxis
for Gonococcal
and Chlamydial
Ophthalmia
Neonatorum*

By Richard B. Goldbloom

Prophylaxis for Gonococcal and Chlamydial Ophthalmia Neonatorum

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The term ophthalmia neonatorum applies in this chapter to acute conjunctivitis in the newborn from any cause. In 1979, the Canadian Task Force on the Periodic Health Examination concluded that there was good evidence to support prophylaxis with routine instillation of 1% silver nitrate solution into each eye at birth. Several important developments have occurred over the subsequent years: 1) Other antibiotics, notably tetracycline and erythromycin, have been evaluated as alternative agents for the prevention of gonococcal and chlamydial ophthalmia neonatorum; 2) The importance of Chlamydia trachomatis as a cause of neonatal conjunctivitis has been recognized; and 3) Concern has been expressed regarding the transient chemical conjunctivitis that may occur following instillation of the silver nitrate solution and the possibility that this complication will interfere with parent-infant attachment ("bonding"). The evidence does not demonstrate the superiority of any one prophylactic agent and in 1992¹ the Task Force recommended the use of 1% silver nitrate solution, 1% tetracycline ointment or 0.5% erythromycin ointment, primarily to prevent gonococcal ophthalmia.

Separate chapters were prepared on screening for gonorrhea (Chapter 59) and Chlamydial infection (Chapter 60).

Burden of Suffering

In the absence of preventive measures it is estimated that gonococcal ophthalmia neonatorum will develop in approximately 28% of infants born to women with gonorrhea. Gonococcal conjunctivitis is usually severe, and *N. gonorrhoeae* can penetrate the intact corneal epithelium and cause microbial keratitis, ulceration and perforation. Maternal gonococcal infection is particularly common in developing countries, where penicillin-resistant gonococci account for up to 60% of the strains isolated. Infection in such women is often asymptomatic. Since 1981 the rate of reported gonorrhea in Canada (about 230 per 100,000) has been steadily decreasing; in 1989 there were 19,110 cases (73 cases per 100,000); 8,421 of the cases involved women aged 15 to 59 years. The number of reported cases of penicillinase-producing *Neisseria gonorrhoeae* (PPNG) infection increased from 591 in 1988 to 1,046 in 1989; 92% were reported in Ontario and Quebec.

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At a community health centre, 7.1% of women having routine gynecologic examinations tested positive for *C. trachomatis* infection

In 1989 the Laboratory Centre for Disease Control, Ottawa, received reports of 55,186 cases of chlamydial infection across Canada (excluding British Columbia and the Yukon Territory). In 1989-90 women aged 15 to 39 years accounted for 34,802 of the cases of genital chlamydial infection (excluding British Columbia and the Northwest Territories). Although chlamydial infection became nationally notifiable in 1990, reporting practices may vary between provinces and territories. More than 4 million cases of chlamydial infection occur each year in the U.S., and 155,000 infants are born to women with cervical infection. At a community health centre in Montreal, 7.1% of women presenting for a routine gynecologic examination were found to have *C. trachomatis* infection. Chlamydial infection can cause pseudomembranous or membranous conjunctivitis in the newborn that may result in conjunctival scarring and corneal infiltrates. The recorded risk of conjunctivitis in infants born to women with *C. trachomatis* infection has varied from 18% to 50%.

In descending order of frequency, the infectious causes of ophthalmia neonatorum are *C. trachomatis*, *Staphylococcus*, *N. gonorrhoeae*, *Streptococcus*, *Hemophilus* and, rarely, herpes simplex virus, molluscum contagiosum virus and papilloma virus.

Maneuver

Instillation of 1% silver nitrate solution or antibiotic ointment (0.5% erythromycin or 1% tetracycline) into the conjunctival sac of the newborn soon after birth.

Effectiveness of Prevention

Gonococcal Ophthalmia

The establishment of legal requirements for silver nitrate prophylaxis was followed by a dramatic reduction in the incidence of blindness due to gonococcal ophthalmia neonatorum.^{<2,3>} Other agents have been evaluated in controlled trials of varying design.

In a prospective controlled clinical trial Lund and associates^{<4>} compared the effectiveness of 1% silver nitrate solution and 0.5% erythromycin ointment in the obstetric units of three hospitals in Capetown, South Africa. In the 13 months before the trial began, when ocular prophylaxis was not practised, the incidence of gonococcal ophthalmia neonatorum in the study area was 273 per 100,000 live births. Twenty-eight cases of gonococcal ophthalmia neonatorum were diagnosed among 24,575 births during the 13-month pretrial period, as compared with only five cases among 23,883 births during the 12 months after the prophylaxis was introduced ($p < 0.001$). Four of the five infected infants had inadvertently not received prophylaxis. During

the same two periods the incidence rates of gonococcal ophthalmia neonatorum in three midwife obstetric units that did not practise ocular prophylaxis were unchanged (39 cases in the pretrial period vs. 38 in the trial period).

In a prospective clinical trial,⁵ the efficacy of prophylaxis with silver nitrate drops, tetracycline ointment and erythromycin ointment were compared among 12,431 infants born during the study period. Treatment was changed monthly. Gonococcal ophthalmia neonatorum occurred in one infant in the silver nitrate group, three in the tetracycline group and four in the erythromycin group; these differences were not statistically significant. Seven mothers of these eight infants had received no prenatal care, and five were drug abusers. The respective risks of gonococcal ophthalmia neonatorum after prophylactic treatment were 0.03%, 0.07% and 0.1%.

Laga and colleagues² compared the efficacy of 1% silver nitrate drops and 1% tetracycline ointment in a controlled trial involving 2,732 newborns in Kenya. The prevalence rate of intrapartum gonococcal infection was 6.4%; the frequency of multiresistant strains was high. The drugs were alternated every week for 15 months and were administered within 30 minutes after birth. To evaluate the protective efficacy of the two regimens mother-infant transmission rates were compared with those observed in a cohort study at the same hospital before prophylaxis was given at birth. After the silver nitrate and tetracycline prophylaxis the prevalence rates of gonococcal ophthalmia neonatorum were 0.4% and 0.1% respectively (difference not statistically significant). Attack rates in newborns exposed to *N. gonorrhoeae* at birth were 7.0% among those who received the silver nitrate and 3.0% among those who received the tetracycline (95% confidence interval: 3.4% to 11.4%). Thus, compared with the rates among the historical controls, the incidence of gonococcal ophthalmia neonatorum was 83% lower among infants treated with silver nitrate and 93% lower among those treated with tetracycline. Two factors may have contributed to the higher attack rates in the silver nitrate group. First, three of the five cases of infection occurred during the first week of the study, before nurses were fully familiar with the technique for applying the silver nitrate drops. Second, a substantial number of patients were lost to follow-up: 31% by day 7 and 57% by day 28.

In summary, the available evidence indicates that 1% silver nitrate solution, 1% tetracycline ointment and 0.5% erythromycin ointment have comparable efficacy in preventing gonococcal infection. On the basis of cost estimates and the attack rates reported in the Kenyan trial, tetracycline is more cost-effective than silver nitrate. Unfortunately, the only costs considered were those of the antibiotics used in prophylaxis and treatment. Given this limitation as well as the differences in 1) the price and availability of antibiotics or silver nitrate



1% silver nitrate solution, 1% tetracycline ointment and 0.5% erythromycin ointment have comparable efficacy in preventing gonococcal infection

ampoules; and 2) the prevalence of gonococcal infection and PPNG strains, these results cannot be generalized to Canada.

Chlamydial Ophthalmia Neonatorum

The evidence supporting the efficacy of any of the currently available agents (silver nitrate, erythromycin or tetracycline) in preventing chlamydial ophthalmia neonatorum is conflicting and inconclusive.<2,5-7>

Chemical Conjunctivitis Due to Prophylaxis

Randomized clinical trials have shown that the use of silver nitrate in the delivery room decreases eye openness and inhibits visual responses within the first hour after birth. A comparison of times and places indicated that the use of single-dose wax ampoules reduced the accidental instillation of high concentrations of silver nitrate solution (as a result of evaporation of water). However, in a large case series, silver nitrate instillation (by ampoule, with or without rinsing) within the first hour after birth caused conjunctivitis in 90% of infants between 3 to 6 hours of age; the ocular reaction subsided within 24 hours in most cases. Topically applied antibiotics resulted in chemical conjunctivitis in less than 10% of cases and compared with silver nitrate have been associated with a 2.5 to 12-fold reduction in the incidence of such ocular reactions. This finding is consistent with the results of controlled trials, but its clinical significance has not been determined. The possibility that chemical conjunctivitis after silver nitrate prophylaxis might impair parent-infant bonding, by interfering with eye contact, was one of the main reasons for introducing a topical antibiotic ointment. This led to widespread abandonment of silver nitrate prophylaxis in the 1980s in favour of the more expensive antibiotic ointments.

In a randomized clinical trial Butterfield, Emde and Svejda<8> compared the effect on bonding of silver nitrate prophylaxis given immediately after birth and 1 hour after birth. Although mothers in the first group noted diminished eye openness it did not alter their baby-focused attention or prevent their pleasure and excitement in the initial encounter. For fathers the increased eye openness associated with delayed prophylaxis appeared to encourage more affectionate attention. These observations suggested that there might be some merit in delaying silver nitrate prophylaxis for a short time after birth but did not indicate any significant effect on ultimate parent-infant attachment.

Prenatal Maternal Screening

The availability of effective ocular prophylaxis for gonococcal ophthalmia neonatorum does not diminish the importance of prenatal



For chlamydial ophthalmia, prenatal screening currently appears to offer better prospects for prevention than topical ocular prophylaxis

screening for and appropriate treatment of maternal gonorrheal and chlamydial infection (see Chapters 59 and 60). Indeed, several Western countries depend on universal prenatal care and contact tracing rather than on ocular prophylaxis to prevent gonorrheal ophthalmia. In the case of chlamydial ophthalmia, prenatal screening currently appears to offer better prospects for prevention than topical ocular prophylaxis in the newborn.

The ideal prophylactic agent would be both nontoxic and highly effective in preventing gonococcal, chlamydial and nongonococcal, nonchlamydial ophthalmia neonatorum. Since gonococcal ophthalmia poses the greatest threat to a child's vision it is generally believed that the principal goal of ocular prophylaxis should be the prevention of gonococcal infection.

Recommendations of Others

The American Academy of Pediatrics and the U.S. Centers for Disease Control (CDC) recommend administering ointment or drops containing tetracycline or erythromycin, or 1% silver nitrate solution, to the eyes of all infants shortly after birth. The CDC and the American College of Obstetricians and Gynecologists recommend obtaining endocervical cultures for *N. gonorrhoeae* in all pregnant women during their first prenatal visit; a second culture is recommended late in the third trimester for women at high risk of acquiring sexually transmitted diseases.

The U.S. Preventive Services Task Force has recommended that endocervical culture for gonorrhea be performed at the first prenatal visit in all pregnant women in high-risk categories.<9> Further, an ophthalmic antibiotic (erythromycin 0.5% or tetracycline 1% ophthalmic ointment) should be applied topically to the eyes of all newborns immediately after birth.

Conclusions and Recommendations

Prenatal screening for gonorrheal and chlamydial infections, particularly among high-risk women, should play a major role in the prevention of ophthalmia neonatorum.

There is good evidence to support the use of universal ocular prophylaxis for gonococcal ophthalmia, at least in the absence of universal prenatal screening for gonorrhea. Prophylaxis should be administered as soon as possible (within 1 hour) after birth; 1% silver nitrate solution, 1% tetracycline ointment and 0.5% erythromycin ointment are approximately comparable in efficacy.

The occurrence of transient chemical conjunctivitis in some infants after silver nitrate prophylaxis is a minor disadvantage. The risk can be reduced to some degree through the use of single-dose

ampoules. Alternatively, tetracycline or erythromycin ointment can be used. Additional considerations in choosing a prophylactic agent are individual preference, cost and the theoretic possibility that chemical conjunctivitis due to silver nitrate prophylaxis might adversely affect parent-infant bonding.

There is poor evidence to support the use of neonatal ocular prophylaxis with any agent for chlamydial ophthalmia neonatorum.

Unanswered Questions (Research Agenda)

The ideal form of topical prophylaxis would be equally effective in preventing both gonococcal and chlamydial ophthalmia, free of side effects such as chemical conjunctivitis and no more expensive than silver nitrate. The search for agents that fulfil these criteria is a worthwhile objective for future research.

Evidence

The literature was identified with a MEDLINE search up to September 1991, using the following MESH heading: ophthalmia neonatorum.

This review was initiated in March 1990 and recommendations were finalized by the Task Force in September 1990. A report with a full reference list was published in November 1992 (see reference #1 below).

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Prophylaxis for Gonococcal and Chlamydial Ophthalmia Neonatorum

MANEUVER	EFFECTIVENESS	LEVEL OF EVIDENCE <REF>	RECOMMENDATION
Universal ocular prophylaxis within 1 hr after birth with 1% silver nitrate solution, 1% tetracycline ointment or 0.5% erythromycin ointment (single-dose ampoules recommended for all agents)	Gonococcal infection: Dramatic reduction in incidence of gonococcal ophthalmia and blindness.	Comparison of times and places<2-5> (II-3)	Good evidence to recommend ocular prophylaxis in newborns (A)
	Prophylactic agents have comparable efficacy.	Controlled trials<2,5> (II-1)	
	Chlamydial infection: Prophylactic agents have comparable efficacy, but evidence for efficacy of any agent is inconclusive.	Randomized controlled trials<2,5,7> (I)	
	Immediate as opposed to delayed silver nitrate prophylaxis does not significantly affect parent-infant bonding.	Randomized controlled trial<8> (I)	