

This section looks back to some ground-breaking contributions to public health, reproducing them in their original form and adding a commentary on their significance from a modern-day perspective. To complement the theme of this month's *Bulletin*, Ulrich C. Schaller and Volker Krauss review the 1881 paper by Carl S.F. Credé on the use of silver nitrate for the treatment of neonatal inflammatory eye disease. A translation follows of the original paper from *Archiv für Gynaekologie*.

## Is Credé's prophylaxis for ophthalmia neonatorum still valid?

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Ophthalmia neonatorum (ON), or neonatal conjunctivitis, has been a major health problem in many parts of the world for centuries. At the end of the 19th century in Europe, for example, the prevalence of ON among live births in maternity hospitals exceeded 10%, producing corneal damage in 20% and blindness in approximately 3% of affected infants (1–3). Up to 50% of children in blind schools were there because of ON (1, 2). Credé noticed that ON was transmitted from mother to infant by contagion during delivery, mostly caused by *Neisseria gonorrhoeae*, and introduced the simple technique of cleaning the eyes of newborn infants with a 2% aqueous solution of silver nitrate. This intervention alone reduced the number of cases of ON in Credé's maternity hospital in Leipzig from 30–35 per year to only one in the second half of 1880 (4), and led ultimately to a dramatic reduction in the prevalence of ON in Europe and around the world.

Today, blindness from ON is rare. In industrialized countries this is because of a lower prevalence of sexually transmitted disease (STD) in pregnant women and prophylaxis at birth (1, 2). The prevalence of ophthalmia due to gonococcal infection is reported as 0.04 per 1000 live births in Belgium and the Netherlands and 0.3 per 1000 live births in the USA (1). However, the spectrum of infectious agents has changed since Credé's time. Nowadays *Chlamydia trachomatis* is the most frequent sexually transmitted pathogen in industrialized countries (1, 2, 5, 7): prevalence ranges from 5 to 60 per 1000 live births in the USA, 4 per 1000 in the United Kingdom, and 40 per 1000 in Belgium (1). Our own data have shown a

chlamydial infection in 34.4% of 15 neonates with ON: *N. gonorrhoeae* could not be isolated, and other pathogens found were *Staphylococcus* spp., *Streptococcus* sp., *Haemophilus influenzae* and Enterobacteriaceae (7).

The prevalence of ON varies considerably around the world. In a study from Kenya in which 1000 mothers and children were examined, 28.5% of mothers were infected with *C. trachomatis* and 9.5% with *N. gonorrhoeae*. Neonates with clinical signs of conjunctivitis had chlamydia in 28.7% of cases and gonorrhoea in 20.2%. This was in contrast to infants seen at an STD clinic, where *N. gonorrhoeae* was the predominant cause of conjunctivitis (1, 2). Worldwide, 1000–4000 newborn babies become blind every year because of ON. In the United Arab Emirates, 81.5% of children with ON showed bacterial or fungal infection, but only 5% of all cases were caused by *C. trachomatis* or *N. gonorrhoeae* (6).

ON can be infectious or chemical in origin. The two agents of major health importance are *N. gonorrhoeae* and *C. trachomatis* (1, 2, 5–8). Other causes of ON include *Escherichia coli* and *Haemophilus* and *Enterococcus* spp. Herpes simplex virus may cause neonatal keratoconjunctivitis but this is rare, and usually occurs in the setting of a more generalized herpes simplex virus infection. In some patients the cause of ON remains unknown.

The risk of blindness due to ON depends on the availability of medical care, which is still a problem in rural areas of developing countries and in urban slums. As a public health measure it is important to prevent STDs and their consequences in pregnant women and the neonates. The choice of different intervention strategies will depend on the prevalence of the causative STD agents in the population and on financial, laboratory and diagnostic resources. Therefore the "gold standard" in most parts of the world is still the method that was introduced by Credé, though the recommended concentration was later reduced to 1% silver nitrate solution to lessen irritation (1, 2). The

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preventive measure was very effective, and within a few years the prevalence of gonococcal ophthalmia declined from 10% to 0.3% of births.

However, *C. trachomatis* has become more frequent than *N. gonorrhoeae* in many parts of the world, and Credé's prophylaxis has therefore become a controversial issue because of its ineffectiveness against the former pathogen. In addition, silver nitrate was criticized as being a cause of chemical conjunctivitis (1, 2, 5, 8). For these reasons, prophylaxis with silver nitrate has been abandoned in several countries (e.g. USA) and replaced by prophylaxis with 0.5% erythromycin or 1% tetracycline ointment, which is presumed to be more effective in preventing chlamydial ophthalmia. A problem with antibiotics is the high incidence of multidrug-resistant gonococcal strains, including penicillinase strains and strains with relatively high minimum inhibitory concentrations for tetracycline (1, 5).

Some countries (e.g. Denmark, Sweden, and the United Kingdom) discontinued general prophylaxis for ON altogether, arguing that no substance is 100% safe for the purpose. In these countries the risk of contracting a sight-threatening infection with *N. gonorrhoeae* is extremely low (5). However, in Denmark there were 8 cases of ON caused by *N. gonorrhoeae* within 3 years of discontinuing a general use of Credé's prophylaxis in 1985. Also, in Florida, there was an increase of incidence of gonococcal ophthalmia within 5 years of discontinuing Credé's prophylaxis (55 cases in 1984–89). In Sweden, an increase of the prevalence of infections with *N. gonorrhoeae* was noticed (5). In many industrialized countries only vague data on the incidence of ON are available, and the condition still represents a serious health problem worldwide, mainly in Africa, with a risk of blindness. The prevalence of *N. gonorrhoeae* among antenatal outpatients in Africa ranges from 4% to 15%. Data from developing and industrialized countries alike would argue for a general enforcement of prophylaxis for ON (1, 2).

Preventing infection of the neonate by treating infection in pregnant women (1, 5) can only be carried out in places where medical care is well organized, so that pregnant women at risk can easily be screened for STDs and treated accordingly. However, screening for chlamydial infection in

pregnant women is not easily implemented, and re-infection often occurs. In developing countries a general screening would be too costly.

Recently, povidone-iodine has been shown to be effective in preventing ON (5, 8). Treatment results were comparable with those obtained with silver nitrate and erythromycin for gonococcal ON and superior in the prophylaxis of chlamydial ON. In addition, povidone-iodine offers added antiviral activity against both human immunodeficiency virus and herpes simplex virus, produces no chemical conjunctivitis or antibiotic resistance, and is cheap. In the developing world a 5-ml container of povidone-iodine costs US\$ 0.10, whereas tetracycline ointment costs US\$ 0.31, erythromycin ointment US\$ 0.74 and one dose of silver nitrate US\$ 7.30. Clearly, povidone-iodine may be an ideal antiseptic for widespread prevention of ON, especially in developing countries. At a recent meeting of the Ophthalmic Society of Austria, povidone-iodine was considered to be the substance of choice for the prophylaxis of newborns against ON (5).

Credé's prophylaxis represented a tremendous step forward in the prevention of inflammatory eye disease in newborns in the late 19th century. But his original prophylaxis is mainly effective against gonococcal ophthalmia whereas chlamydial ON is now more widespread, and silver nitrate may cause chemical conjunctivitis. In industrialized countries ON is no longer a public health problem and different strategies for prevention are available, so some countries have chosen to stop prophylaxis at birth and to opt instead for early treatment. But growing populations, urbanization and increasing promiscuity cause a rising incidence of ON in developing countries.

Routine prophylaxis with topical antibiotics carries the risk of resistance, especially in patients with ON due to gonococcal infection. Povidone-iodine as a topical anti-infective appears to be an effective and cheap alternative. Further epidemiological research and monitoring on the incidence of ON and the prevalence of the various agents in different parts of the world are needed, so that prevention and treatment can be adjusted accordingly and experience with new options can be analysed for wide use. ■

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