Update/Le point

Epidemiology and control of gonococcal ophthalmia neonatorum*

M. Laga,[1] A. Meheus,[2] & P. Piot[1]

From a public health point of view gonococcal ophthalmia neonatorum (GCON) is important as it can rapidly lead to blindness. The frequency of GCON is determined by the prevalence of maternal gonococcal infection. In most industrialized countries the prevalence of gonorrhoea in pregnant women is less than 1%; in developing countries the rates are between 3% and 15%, more than 50% being due to penicillinase-producing Neisseria gonorrhoeae *strains (PPNG). The rate of transmission from mother to newborn is between 30% and 50%.*

Strategies for the control of GCON include: (1) prevention of gonococcal infection in women of childbearing age, (2) detection and treatment of gonococcal infection in pregnant women, (3) eye prophylaxis in the newborn at birth, and (4) diagnosis and treatment of GCON. Eye prophylaxis by the instillation immediately after birth of either 1% silver nitrate eye drops or 1% tetracycline eye ointment is very effective. This reduces the GCON incidence by 80% to 95% and is highly cost-effective, particularly in high-risk settings.

Epidemiology

Disease manifestation

Ophthalmia neonatorum (ON) is defined as a purulent conjunctivitis in infants less than 30 days old, where the Gram stain of an eye smear shows at least one polymorphonuclear leukocyte per high-power field. Of the many causes, the two main ones are *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Although there are different patterns of disease, the manifestations produced by any one agent are not sufficiently distinctive to lead to an etiologic diagnosis from the clinical signs alone.

Gonococcal ophthalmia neonatorum (GCON) tends to appear earlier and to be more severe than the chlamydial infection. Differences in the incidence of ON, by etiology, obtained in Nairobi from a cross-sectional clinic-based study and a population-based cohort study are shown in Table 1; *C. trachomatis* was the most frequently identified cause when 1019 mother–infant pairs were followed up for 1 month, while *N. gonorrhoeae* accounted for the majority of cases seen at the sexually transmitted diseases (STD) clinic. GCON begins between 1 and 13 days from birth and is mostly bilateral and purulent, the conjunctivae and eyelids being oedemic and hyperaemic. If untreated, diffuse epithelial oedema of the cornea gives it a hazy greyish appearance. Coarse white opacities (infiltrations) appear near the border of the cornea and the sclera, and can enlarge and become ulcerated by the end of the second or third week. These ulcerations can lead to perforation of the eyeball with loss of vision. When new blood vessels invade the cornea, corneal scarring may occur. The initiation of effective treatment dramatically changes the course and outcome of the disease, usually with recognizable improvement within 24 hours.

It is difficult to estimate the risk of blindness associated with gonococcal ophthalmia. In 1880, over a hundred years ago, in Stuttgart the incidence of GCON varied from 1% to 14% and 20–79% of children in institutions for the blind had a history of GCON. After introduction of ocular prophylaxis at birth, GCON dropped dramatically and the percentage of institutionalized children whose blindness was caused by GCON steadily declined. At present, in many developing countries the incidence of GCON is still high although blindness in children is not reported to be highly prevalent; however, since blind children

* A résumé of this article in French appears on pages 476–477.

[1] Department of Microbiology, Institute of Tropical Medicine, Antwerp, Belgium.

[2] Programme of Sexually Transmitted Diseases, World Health Organization, 1211 Geneva 27, Switzerland. Requests for reprints should be sent to this author.

Reprint No. 5001

Bulletin of the World Health Organization, 67 (5): 471–478 (1989)

Table 1: **Comparison of the incidence and etiology of ophthalmia neonatorum (ON) in Nairobi from a cohort study and clinic-based survey**[a]

	Cohort study[b]		Cross-sectional study:[c]
	Incidence per 100 live births	Percentage of all ON ($n=181$)	percentage of all ON ($n=149$)
Gonococcal ophthalmia	2.8	12%	43%
Chlamydial ophthalmia	7.3	32%	13%
Gonococcal and chlamydial ophthalmia	0.8	3%	4%
Non-gonococcal, non-chlamydial ophthalmia	12.3	53%	40%
Total	23.2		

[a] Data from references *10* and *17*. 9, 10 and 17 ?
[b] Cohort of 1019 mothers and infants followed up for the first month of life.
[c] Survey of infants with ON presenting at the sexually transmitted diseases clinic in Nairobi.

have a higher mortality rate, the true extent of the problem would not be apparent in prevalence surveys. In a clinic-based study on 64 neonates with GCON, 16% proved to have corneal involvement (*10*). It is not yet clear which factors are responsible for a more fulminant course of disease; virulence of some strains or unusual susceptibility of the host, e.g., cases among premature babies, have been suggested.

Gonococcal infections

Prevalence in pregnant women. Data on the prevalence of gonorrhoea among women receiving antenatal care give an estimate of the potential complications in puerperal women and neonates. Table 2 summarizes the prevalence of gonorrhoea in pregnant women from surveys in different countries. The reported prevalence from the USA shows wide geographical variations ranging from 0.6% to 7.6% in the different populations studied. Generally, much higher prevalence rates were observed in populations in the USA than in other industrialized countries where they are usually below 1%. In most African countries the prevalence rates among antenatal clinic patients range from 3% to as high as 22%. The few published results from other

Table 2: **Prevalence of gonococcal infections among pregnant women worldwide**

Place	No. tested	Gonococcal cervical infection (%)	Year/reference
Africa:			
Cameroon: Yaoundé	296	14	1984/*11*
Rural area		22	
Gabon: Masuku[a]	530	5.5	1984/*29*
Gambia: Bakau		6.7	1984/*19*
Ghana: Accra	148	3.4	1985/*3*
Kenya: Nairobi	3751	6.5	1986/*17*
South Africa: Bloemfontein	1200	11.7	1986/*28*
Zambia: Lusaka	—	11.2	1986/*14*
Asia:			
Malaysia: Kuala Lumpur	744	0.54	1981/*12*
Europe:			
Norway: Trondheim	686	0.3	1986/*24*
United Kingdom: Cardiff	625	0.16	1975/*25*
Glasgow	1000	0.2	
Newcastle	311	0	
USA:			
Minnesota	6464	2.7	1978/*8*
San Francisco	6854	0.6	1987/*26*
Seattle	543	2	1986/*13*
New York	1082	2.6	1985/*20*

[a] Formerly called Franceville.

continents suggest that some but not all countries have a prevalence rate similar to that in Africa.

Since the mid-1970s, worldwide dissemination of penicillinase-producing *N. gonorrhoeae* (PPNG) strains and of strains with chromosomally-mediated penicillin and tetracycline resistance increased progressively. The proportion of gonococcal infection due to PPNG strains is summarized in Table 3, which shows the need for new approaches to gonorrhoea therapy.

Transmission rate from mother to baby. The neonate acquires GCON during delivery through the infected birth canal. Occasionally the disease has been transmitted to infants delivered by Caesarian section after prolonged rupture of the membranes (*27*)

The transmission rate from mother to child in the absence of ocular prophylaxis has been estimated in two prospective studies in Africa (Table 4). In Kenya (Nairobi) GCON developed in 28 out of 67 babies whose mothers had *N. gonorrhoeae* infections, a transmission rate of 42% (seven babies were lost for follow-up), while in Cameroon, 30% of exposed babies (12/40) developed GCON; the incidence rates are therefore 3.6 and 4 per 100 live births, respectively. These incidence rates are very high, compared with those from Western countries (average, 0.06%). Asymptomatic carriage of *N. gonorrhoeae* in the eyes with minimum inflammation has been described (*23*). In the above-mentioned studies from Africa no children were identified with an asymptomatic gonococcal infection in the eyes.

The study from Kenya demonstrated that the transmission rates of PPNG and non-PPNG strains were similar. When the mother is infected with both *N. gonorrhoeae* and *C. trachomatis* at the same time, the gonococcal transmission rate to the newborn is significantly higher (68% instead of 31%, $P<0.01$) (*17*). This study also showed that postpartum endometritis in the mother was a significant risk factor for GCON which may be explained by differences in pathogenicity of the strains, by both conditions arising from maternal chorioamnionitis, or by factors protecting the mothers against postpartum upper genital tract infection which might also protect the newborns against ocular infection.

Conjunctival infection is the commonest clinical form of *N. gonorrhoeae* infection in the newborn, but the mucous membranes of the vagina, the pharynx, the rectum and the ear canal may also be colonized. Isolation rates of *N. gonorrhoeae* from the pharynx in neonates with gonococcal ON range from 7% to 15% (*10, 17*). The transmission rate of *N. gonorrhoeae* from the maternal cervix to extraocular sites has never been determined in the absence of GCON and the natural history of extra-ocular gonococcal infection is unclear. The possibility of extra-ocular colonization of *N. gonorrhoeae* in infants with gonococcal ON has therapeutic implications and GCON should therefore always be treated systemically.

Table 3: **Percentage of gonococcal infection due to penicillinase-producing *N. gonorrhoeae* (PPNG) in various countries**

Country	PPNG strains (%)	Year/Reference
Belgium	6	1986/*15*
Netherlands	11	1986/*7*
United Kingdom	2	1985/*1*
USA	0.5	1982/*6*
Kenya	55	1986/*17*
Zambia	41	1986/*14*
Rwanda (Kigali)	51.9	1984/*4*
Tanzania (Dar es Salaam)	19.2	1984/*21*

Strategies for control

Four different strategies are available for controlling GCON in neonates.

(1) Primary prevention

Pregnant and non-pregnant women (or their partners) who are at risk can protect themselves from acquiring gonococcal infections through behavioural modification and/or the use of barrier contraceptives. Primary prevention has not generally been successful in the

Table 4: **Prevalence of maternal gonococcal infections and transmission rate from mother to child in the absence of ocular prophylaxis**

Place and reference	Prevalence (%)	No. of neonates presenting with GCON	Transmission rate (%)	Incidence per 100 live births
Kenya (Nairobi) (*17*)	7 (67/1019)[a]	28	42[b]	3.6
Cameroon (Yaoundé) (*11*)	14 (40/296)	12	30	4

[a] Figures in parentheses indicate the No. of women infected/No. of women screened.
[b] This figure is a minimal estimate since 7 out of 67 newborns were lost for follow-up; the real transmission rate ranges between 42% and 52%.

control of STD in the past, but the increase in incurable viral infections that are transmitted sexually, such as AIDS, may renew interest in primary prevention of STD.

Data demonstrating a reduction in the prevalence of gonococcal infections in women as a result of behavioural change and condom use are not yet available.

(2) Screening/case-finding and treatment of gonococcal infections during pregnancy

There are two basic approaches for early detection and/or treatment depending on the availability of laboratory services and resources: (*a*) identification of the infection through laboratory confirmation (mass screening or selective screening), and (*b*) mass treatment (indiscriminate or selective) without laboratory confirmation.

• ***Mass screening.*** Unfortunately countries with the highest prevalence of infection, and thus the greatest need for detection programmes are in general those that are the least able to afford and perform screening. Routine screening for gonococcal infections in pregnancy has been abandoned in many European countries (because of very low prevalences), but is still practised in the USA. It has not yet been introduced in most developing countries because of lack of diagnostic facilities. The minimum prevalence necessary for a cost-effective screening programme has not been defined, but considering the preventable maternal and neonatal complications, it would probably be low (about 1%). Another complication is that women at high risk for gonococcal infections often do not attend antenatal care.

The best way for laboratory diagnosis of gonorrhoea is by culture, but a cheaper alternative is direct microscopic examination of a Gram stain of the cervical discharge. The latter is not a very valid test, the positive predictive value in cases where the prevalence of gonococcal infections in women is 5%, 15%, and 25% being 29%, 47% and 63%, respectively. Thus the use of Gram-stain screening is only advocated in areas with a high prevalence of gonococcal infections in women (> 15%).

• ***Selective screening.*** The cost-effectiveness of screening programmes can be increased by concentrating on high-risk groups. These groups can be defined by epidemiologic risk profiling, presence of symptoms, or presence of clinical signs of cervicitis.

In a series of 1000 pregnant women in Nairobi, being single and residing in certain areas were risk factors for gonococcal infection (*17*).

• ***Mass treatment.*** Mass treatment would be indicated only if it was shown to be more cost-effective than early detection programmes, or if detection is impossible. Since in many areas the prevalences of gonococcal infections in pregnant women exceed 5% (see Table 2), indiscriminate mass treatment could be the most effective strategy if all maternal and perinatal complications resulting from maternal gonococcal infections are taken into account.

Although the two above-mentioned strategies are complex, expensive and operationally very difficult, they offer benefits besides lowering the incidence of GCON, such as reducing other complications (postpartum endometritis) related to *N. gonorrhoeae*. Rates of reinfection should be examined in order to assess the need for repeated mass treatment or inclusion of sex partners. Selected treatment regimens should be evaluated for efficacy, development of resistance (in areas with high proportions of PPNG), side-effects, and cost.

(3) Ocular prophylaxis at birth

The transmission of *N. gonorrhoeae* from the maternal cervix to the newborn's eyes can be interrupted by the use of eye drops or ointment immediately after birth.

Three different regimens have been recommended: silver nitrate, 1% eye drops; tetracycline, 1% eye ointment; and erythromycin, 0.5% eye ointment. Only the first two have been evaluated prospectively in areas with a high proportion of multiresistant gonococcal strains, including penicillinase-producing *N. gonorrhoeae*. The results from Kenya demonstrated equal efficacy of silver nitrate drops and tetracycline ointment in the prevention of GCON, the attack rate among exposed newborns given silver nitrate and tetracycline being 7% and 3%, respectively (Table 5). These findings are consistent with risk estimates of transmission from mother to child when prophylaxis was given (*2, 27*).

In the other studies (all retrospective) on the efficacy of the three regimens in preventing GCON, the prevalence of gonococcal infections in the mother was often unknown and the expected rate of GCON was too low to discern any protective effect.

Among the many explanations for the failure of ocular prophylaxis to prevent neonatal ophthalmia are acquisition of infection *in utero* following prolonged rupture of membranes, failure to instil the agent directly into the conjunctival sac, flushing of the eye after administration of silver nitrate (to prevent chemical conjunctivitis), postpartum acquisition of GCON either by autoinoculation or from other infected persons, and the failure to differentiate chlamydial conjunctivitis from GCON.

Silver nitrate is cheap, but is toxic if overconcent-

Table 5: **Attack rates of GCON among exposed newborns receiving silver nitrate, tetracycline, and no prophylaxis[a]**

	Silver nitrate	Tetracycline	No prophylaxis[b]
Attack rates of GCON (%)[c]	7.0 (5/71)[d]	3.0 (2/66)	46.6 (28/60)
Efficacy compared to no prophylaxis	83%	93%	

[a] Includes only exposed infants seen at follow-up visits; data from reference *18*.
[b] Infants from a historical cohort.
[c] The difference between the silver nitrate and tetracycline groups was 4.0% (95% confidence interval: −3.4 to 11.4).
[d] Figures in parentheses are the No. of newborns with gonococcal ophthalmia/No. of newborns exposed to *N. gonorrhoeae*.

rated (through bad preservation). Single-dose ampoules are much more expensive and less easily available. Tetracycline is nontoxic and may remain longer in the eye because it is an ointment; multidose preparations (which did not cause complications in the Nairobi trial) are cheap and widely available in developing countries. Erythromycin ointment is expensive and not available in many poor countries.

It has been shown that a delay in prophylaxis of more than 4 hours after birth is associated with a 4–5-fold increase in risk of GCON (*22*). Prophylaxis should therefore be given as soon after birth as practical, preferably within one hour, for both hospital and home births. Traditional birth attendants' kits should include a single-dose dispensing system for eye prophylaxis. There is no doubt that such prophylaxis is operationally the most feasible strategy and the most cost-effective approach of the four. In areas with a high prevalence of gonococcal infections in pregnant women prophylaxis at birth should be reinforced or (re)introduced immediately as an initial step in the reduction of neonatal morbidity related to STD in pregnancy.

(4) Diagnosis and treatment of GCON

Early diagnosis and appropriate treatment of gonococcal ophthalmia is important since the infection can rapidly lead to blindness. The presence of a high proportion of penicillin-resistant strains requires a more expensive and less available treatment regimen in many areas of the world.

Some countries with a low prevalence of gonococcal infections (e.g., Netherlands) have adopted the strategy of diagnosis and treatment of GCON in the newborns. The presence of neonatal infection is the indicator for an infection in the parents, and screening during pregnancy is not performed. In very low prevalence areas, with good coverage of health services, this strategy may be the most cost-effective, but has never been evaluated systematically. Unfortunately, in most countries where gonococcal infections are highly prevalent, the diagnostic facilities and appropriate treatment regimens are not available, and control programmes should therefore focus on ocular prophylaxis.

Proposed interventions

Cultural acceptability, political feasibility and psychosocial effects

A major objection to the use of silver nitrate therapy has been the high incidence of chemical conjunctivitis. Some developing countries even abandoned ocular prophylaxis because of this. The problem can be overcome by using tetracycline ointment instead of silver nitrate drops, which is at least as effective and has no side-effects.

Instilling drops or ointment in the eyes of a newborn may decrease visual alertness of the infant during the first hours of life. These problems are of concern to those who believe this may impair maternal–infant bonding by reducing eye contact (*5*). However, any potential impairment of maternal–infant bonding does not outweigh the increased risk of GCON from delaying the instillation of ocular prophylaxis.

Cost-effectiveness and feasibility

The strategy of detection and treatment of gonococcal infections in pregnancy has the advantage of not only reducing GCON but also other maternal complications. It is, however, a very expensive (if the goal is to reduce GCON) and operationally complicated strategy, and it is currently not feasible in most areas of the developing countries.

The cost of the use of ocular prophylaxis has been compared with the cost of early diagnosis and treatment of GCON in a group of 1000 women, with a prevalence of gonococcal infection of 10% (Table 6). The cost for 1000 prophylactic regimens is US$100 for silver nitrate 1% drops (single-dose wax ampoules) and $50 for tetracycline 1% ointment (multidose tubes for 10 babies, $0.50 per tube). It is estimated that despite ocular prophylaxis, 7% and 3% of the babies in the silver nitrate and tetracycline group, respec-

Table 6: **Estimate of costs for the control of GCON among 1000 pregnant women with prevalences of gonococcal infection of 10% and 1%**

	Silver nitrate	Tetracycline	No prophylaxis
Cost of 1 dose	US$ 0.10 (single-dose ampoule)	$0.05 (multidose tubes)	
Cost for 1000 neonates	$100	$50	
Attack rates of GCON among newborns[a]	7%	3%	47%
10% prevalence:			
Cost of treatment of GCON (single dose, $5)[b]	$35	$15	$235
Total cost	$135	$65	$235
Cost per adverse outcome averted[c]	$2.90	$1.40	$5
1% prevalence:			
Cost of treatment of GCON (single dose, $5)[b]	$3.50	$1.50	$23.50
Total cost	$103.50	$51.50	$23.50
Cost per adverse outcome averted[c]	$22	$11	$5

[a] Rates based on Nairobi clinical trial (*17, 18*); see Table 5.
[b] Optimal treatment for GCON is ceftriaxone 125 mg, IM single dose (*16*).
[c] Adverse outcome includes only GCON here.

tively, will develop GCON, compared to 47% of those who receive no prophylaxis.

The price of one treatment regimen for GCON varies from $5 (ceftriaxone 125 mg, intramuscular single dose) to $2 (kanamycin 75 mg + topical tetracycline) (*16*). The assumption is that each case of GCON would be brought to the health care facilities and receive appropriate treatment.

The total cost of the three programmes (silver nitrate, tetracycline, and no prophylaxis) for a group of 1000 women (with a 10% prevalence of GCON) is $135, $65 and $235, respectively, resulting in a cost per adverse outcome averted of $2.90, $1.40 and $5 (see Table 6). Indirect costs of visual impairment due to late or inadequate treatment are not taken into account.

It is clear that the strategy of ocular prophylaxis is more cost-effective than early diagnosis and treatment. It is furthermore more convincing on humanitarian grounds, especially in areas where availability of efficacious drugs are scarce.

In low-prevalence areas of maternal gonococcal infection (<1%), the price of ocular prophylaxis is higher than the price of treatment of actual cases with GCON (see Table 6). However, the potential risk of blindness (if not adequately treated) warrants further use of ocular prophylaxis in all countries where the coverage of health care is not optimal.

Résumé

Epidémiologie et prévention de l'ophtalmie du nouveau-né

Les étiologies les plus importantes de l'ophtalmie du nouveau-né sont *N. gonorrhoeae* et *C. trachomatis*. Du point de vue de la santé publique, l'ophtalmie gonococcique (OGNN) est prioritaire puisque cette affection peut mener rapidement à la cécité chez le nouveau-né. La fréquence de l'OGNN dépend de la prévalence de l'infection gonococcique chez les femmes enceintes. Dans la plupart des pays industrialisés, cette prévalence est inférieure à 1%. Dans les pays en développement, elle est souvent comprise entre 3% et 15%, et plus de la moitié des infections sont dues à des souches de *N. gonorrhoeae* productrices des pénicillinase (NGPP). Cela signifie que la pénicilline n'est plus efficace pour traiter l'OGNN et que si des antibiotiques efficaces, qui sont plus coûteux, ne sont pas disponibles, le risque de cécité est considérable pour le nouveau-né. Celui-ci est infecté à l'accouchement pendant le passage dans la filière génitale. Le taux de transmission du gonocoque du col utérin aux yeux du nouveau-né est de 30 à 50%.

Les stratégies de lutte contre l'OGNN sont: 1) prévention de la gonococcie chez les femmes en âge de procréer, 2) dépistage et traitement de la gonococcie chez la femme enceinte, 3) prophylaxie oculaire chez le nouveau-né immédiatement après la naissance, et 4) diagnostic et traitement de l'OGNN.

La femme peut se protéger de la gonococcie et des autres maladies sexuellement transmissibles (MST) par un comportement sexuel adapté et l'utilisation du préservatif par le partenaire.

Le dépistage de la gonococcie chez la femme enceinte suivi d'un traitement adéquat prévient aussi bien les complications chez la femme que chez le nouveau-né (OGNN). Mais la prévalence de la gonococcie étant basse dans la plupart des pays industrialisés, cette stratégie a un rapport coût/efficacité trop faible. Un dépistage sélectif, c'est-à-dire dans des sous-groupes de femmes enceintes à risque élevé de

gonococcie, peut être envisagé. Dans les pays en développement, le facteur limitant pour le dépistage est le manque d'infrastructures de laboratoire. Le test recommandé est la culture du gonocoque, peu réalisable en dehors de quelques centres de référence dans ces pays. Dans des conditions de haute prévalence de la gonococcie chez la femme enceinte, un traitement systématique pourrait éventuellement être envisagé.

L'instauration d'une prophylaxie oculaire immédiatement après la naissance est très efficace. Par l'utilisation soit de collyre de nitrate d'argent à 1%, soit de pommade ophtalmique de tétracycline à 1%, l'incidence de l'OGNN diminue de 80 à 95% et cette stratégie a un rapport coût/efficacité élevé, particulièrement lorsque la prévalence de la gonococcie chez la femme enceinte est élevée.

Le diagnostic et le traitement adéquat comme stratégie principale de lutte contre l'OGNN ne sont acceptables que dans les pays à faible prévalence de gonococcie chez la femme enceinte et où la couverture et la qualité des services de santé sont optimales. Il est donc clair que la prophylaxie oculaire reste la stratégie de choix dans tous les pays et régions où la couverture sanitaire laisse encore à désirer.

References

1. **Adler, M.W.** Epidemiology and treatment of penicillinase-producing *Neisseria gonorrhoeae*. In: Oriel, D.J. & Harris, J.R.W., ed. *Recent advances in sexually transmitted diseases*. Edinburgh, Churchill Livingstone, 1985, pp. 23–38.
2. **Armstrong, J.H. et al.** Ophthalmia neonatorum: a chart review. *Pediatrics*, **57**: 884–892 (1976).
3. **Bentsi, C. et al.** Genital infections with *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in Ghanaian women. *Genitourinary medicine*, **61**: 48–50 (1985).
4. **Bogaerts, J. et al.** *In vitro* antimicrobial sensitivity of *N. gonorrhoeae* from Rwanda. *Genitourinary medicine*, **62**: 217–220 (1986).
5. **Butterfield, P.M. et al.** Effects of silver nitrate on initial visual behavior. *American journal of diseases of children*, **132**: 426 (1978).
6. **Centers for Disease Control.** Global distribution of penicillinase-producing *Neisseria gonorrhoeae* (PPNG). *Morbidity & mortality weekly report*, **32**: 1–3 (1982).
7. **Committee on Health Care.** [*Guidelines on sexually transmitted diseases*.] The Hague, 1986 (in Dutch).
8. **Edwards, L.E. et al.** Gonorrhea in pregnancy. *American journal of obstetrics and gynecology*, **132**: 637–641 (1978).
9. **Fransen, L. et al.** Parents of infants with ophthalmia neonatorum: a high-risk group for sexually transmitted diseases. *Sexually transmitted diseases*, **12**: 150–154 (1985).
10. **Fransen, L. et al.** Ophthalmia neonatorum in Nairobi, Kenya: the roles of *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. *Journal of infectious diseases*, **153**: 862–869 (1986).
11. **Galega, F.P. et al.** Gonococcal ophthalmia neonatorum: the case for prophylaxis in tropical Africa. *Bulletin of the World Health Organization*, **62**: 95–98 (1984).
12. **Goh, T.H. et al.** Screening for gonorrhoea in a prenatal clinic in southeast Asia. *Sexually transmitted diseases*, **8**: 67–69 (1981).
13. **Gravett, M.G. et al.** Independent association of bacterial vaginosis and *Chlamydia trachomatis* infection with adverse pregnancy outcome. *Journal of the American Medical Association*, **256**: 1899–1903 (1986).
14. **Hira, S.K.** Sexually transmitted diseases—a menace to mothers and children. *World health forum*, **7**: 243–247 (1986).
15. **Institute for Hygiene and Epidemiology.** [*Surveillance of infectious diseases through a network of microbiology laboratories*.] Report No. 54, 1986 (in Dutch).
16. **Laga, M. et al.** Single-dose therapy of gonococcal ophthalmia neonatorum with ceftriaxone. *New England journal of medicine*, **315**: 1382–1385 (1986).
17. **Laga, M. et al.** Epidemiology of ophthalmia neonatorum in Kenya. *Lancet*, **2**: 1145–1148 (1986).
18. **Laga, M. et al.** Prophylaxis of gonococcal and chlamydial ophthalmia neonatorum. A comparison of silver nitrate and tetracycline. *New England journal of medicine*, **318**: 653–657 (1988).
19. **Mabey, D.C.W. et al.** Sexually-transmitted diseases among randomly selected attenders at an antenatal clinic in the Gambia. *British journal of venereal diseases*, **60**: 331–336 (1984).
20. **McMillan, J.A. et al.** Efficacy of maternal screening and therapy in the prevention of chlamydia infection of the newborn. *Infection*, **13**: 263–266 (1985).
21. **Maselle, W.B. et al.** Penicillinase-producing *N. gonorrhoeae* in Dar es Salaam, Tanzania. *African journal of sexually transmitted diseases*, **1**: 71–75 (1984).
22. **Muhe, L. & Tafari, N.** Is there a critical time for prophylaxis against neonatal gonococcal ophthalmia? *Genitourinary medicine*, **62**: 356–357 (1986).
23. **Podgore, J.K. & Holmes, K.K.** Ocular gonococcal infection with minimal or no inflammatory response. *Journal of the American Medical Association*, **246**: 242–243 (1981).
24. **Skjeldestad, F.E. & Delen, A.** The prevalence of *Chlamydia trachomatis* in the cervix of puerperal women, and its consequences for the outcome of pregnancy. *Scandinavian journal of primary health care*, **4**: 209–212 (1986).
25. **Sparks, R.A. et al.** Antenatal screening for candidiasis, trichomoniasis and gonorrhoea. *British journal of venereal diseases*, **51**: 110–115 (1975).
26. **Sweet, R.L. et al.** *Chlamydia trachomatis* infection and pregnancy outcome. *American journal of obstetrics and gynecology*, **156**: 824–833 (1987).
27. **Thompson, T.R. et al.** Gonococcal ophthalmia neonatorum: relationship of time of infection to relevant control measures. *Journal of the American Medical Association*, **228**: 186–188 (1974).
28. **Welgemoed, N.C. et al.** Prevalence of *Neisseria gonorrhoeae* infection in patients attending an antenatal clinic. *South African medical journal*, **69**: 32–34 (1986).
29. **Yvert, F. et al.** Les infections gonococciques au Gabon, Haut-Ogooué. *Pathologie biologie*, **32**: 80–81 (1984).