This document is made available electronically by the Minnesota Legislative Reference Library as part of an ongoing digital archiving project. http://www.leg.state.mn.us/lrl/sonar/sonar.asp

STATE OF MINNESOTA
COUNTY OF HENNEPIN

BEFORE THE MINNESOTA
COMMISSIONER OF HEALTH

In the Matter of the Proposed
Amendments to MHD 326(o)

STATEMENT OF NEED
AND REASONABLENESS

This rule is necessary for the prevention of infant blindness due to gonococcal infection. The attached reports indicate that silver nitrate in a 1 percent solution prevents 98% of newborns at risk of infection from developing gonococcal ophthalmia neonatorum. This proposal will continue to insure this high level of prevention while facilitating the inclusion of newer and more effective antibiotics in the prophylactic regimens authorized by the Commissioner.

As a result of recent information linking another organism, chlamydia, to ophthalmia neonatorum,[1,2] the Centers for Disease Control and the American Academy of Pediatrics have revised their recommendations for prevention of ophthalmia neonatorum to include tetracycline and erythromycin ointments or drops.[3]

Gonorrhea remains the most common reportable communicable disease in Minnesota. In calendar year 1980, 3400 new infections were reported in Minnesota women. Of this total 91% occurred in women of childbearing age (under 35). According to the statement of the American Academy of Pediatrics Committee on Drugs, Committee on Fetus and Newborn, Committee of Infectious Diseases "The prevalence of largely asymptomatic genital gonococcal infections in pregnant women and the occurrence of gonococcal ophthalmia neonatorum (estimated at 28%) born to infected women indicate the need for continued prophylaxis for all newborn infants."[4] According to the Centers for Disease Control, "silver nitrate prophylaxis reduced the risk of infants developing gonococcal ophthalmia neonatorum to less than 2%".[5]

---

[1]Alexander ER: Chlamydia: The Organism and Neonatal Infection, Hospital Practice July, 1979, Attached hereto and made a part hereof in Attachment #1.

[2]Frommel GT, et al: Chlamydial infection of mothers and their infants., the Journal of Pediatrics, Vol. 95, No.1, July, 1979, Attached hereto and made a part hereof in Attachment #2.

[3]GONORRHEA Center for Disease Control Recommended Treatment Schedules 1979, Attached hereto and made a part hereof in Attachment #3.

[4]American Academy of Pediatrics, Committee on Drugs, Committee on Fetus and Newborn, Committee on Infectious Diseases: Prophylaxis and Treatment of Neonatal Gonococcal Infections, PEDIATRICS Vol.65, No.5, May,1980, Attached hereto and made a part hereof in Attachment #4.

[5]MMWR 27:107, 1978, Attached hereto and made a part hereof in Attachment #5.

The existing rule is too specific in requiring silver nitrate prophylaxis when the tetracycline or erythromycin regimens are recommended. In this proposal the Commissioner updates the recommended prophylactic treatment according to recommendations by the Centers for Disease Control and the American Academy of Pediatrics.

Paragraph (2) of the proposed rule is revised to reflect the reality that health professionals in addition to licensed physicians, nurses and midwives are involved in the delivery of newborn babies. The intent in this proposal is to be more inclusive and reflect the reality of modern practices.

Paragraph (3) of the proposed rule is revised to reflect the reality that health professionals in addition to licensed physicians, nurses and midwives provide care for newborn babies. The present rule requires only the "midwife to call a licensed physician when infection or inflammation is apparent". In reality nurses and other licensed health professionals are providing medical care for newborn babies and must also be responsible for notifying a licensed physician when these infections are observed in newborn infants under their care.

The basis for recommending deletion of all of paragraph (4) is that this requirement is unreasonable. Including "any and all persons", "any relative", etc. is so general that it would be difficult to identify any individual as a person in charge. Furthermore, requiring reporting of all cases of infection of eyes would needlessly overwhelm the state and local health officials. Such reports may include merely redness of the eyes, or a discharge from the eyes. Rigid compliance of the reporting requirements under this old rule would result in thousands of cases reported each year. There is no feasible action the State Health Department can take to prevent transmission to others of such infections. It is essential that a specific causative organism or agent be identified so that treatment and preventive measures can be taken.

With the exception of the portion of paragraph (5) requiring the keeping of records of cases the revision proposes the repeal of the remainder of this rule. The basis for this repeal being that it is unreasonable to make demands of institutions which might be budgetarily prohibitive. Prompt notification of a licensed physician, and assurance of treatment of cases as covered in other paragraphs adequately covers the intentions of the old rule.

Paragraph (6) and subparagraphs are repetitious. MHD 316 adequately covers reporting of communicable diseases. The proposed revision repeals MHD 316(o)(6) because it is unclear as to its meaning. If it refers to the reporting of gonorrhea, it is already addressed in MHD 326(n) and is therefore repetitious and unnecessary.

The Commissioner has chosed to initiate this revision under the provisions of Minn. Stat. §15.0412, Subd. 4(h) (Supp.1981). Under this provision, no public hearing will be required unless such is requested in writing by seven persons. Given the unclear mandate of the Legislature and the demonstrated need for revision of this rule, it is anticipated that this rule will be uncontroversial and that no hearing will be necessary.

Dated 12/24/81

STATE OF MINNESOTA
MINNESOTA DEPARTMENT OF HEALTH

David F. Brownell

David F. Brownell, Chief
Venereal Disease Control Program

Chlamydia: The Organism and Neonatal Infection

E. RUSSELL ALEXANDER *University of Washington, Seattle*

Once believed to be large viruses, the causative agents of trachoma, psittacosis, inclusion conjunctivitis, and venereally transmitted genital tract infections have been reclassified as bacteria and placed in their own order, Chlamydiales. These organisms also can cause eye and respiratory infections in infants born to mothers with genital tract infection. Diagnosis, therapy, and prevention of such infections are described.

Several recent studies indicate that a high percentage of infants born to mothers with genital tract chlamydial infections become infected at birth and subsequently develop inclusion conjunctivitis or respiratory tract infection, or both. Since chlamydiae are estimated to cause between 30% and 40% of nongonococcal urethritis and cervicitis in this country, and since an average of 8% of pregnant women carry chlamydiae in their cervices at parturition, the risk of neonatal infection constitutes a major public health problem.

The chlamydial organisms cause trachoma, psittacosis, and lymphogranuloma venereum, as well as venereally transmitted genital tract infections and inclusion conjunctivitis. Over the years they have been called by a number of different names, including Bedsonia, Miyagawanella, and TRIC agents, the latter an acronym for the subset that causes trachoma-inclusion conjunctivitis. Chlamydiae are notable for being on the borderline between viruses and bacteria. For many years they were classified as viruses. Now it is clear that they are in fact bacteria, but because of their peculiar life cycle they have been placed in their own order, which consists of one genus, Chlamydia, with two species, *Chlamydia psittaci* and *Chlamydia trachomatis*.

Although chlamydiae share with viruses the trait of being obligate intracellular parasites, by definition this is true only in the intracellular stage of their life cycle, which begins extracellularly. The extracellular form of the organism is the elementary body, and it alone is infectious. Attaching to a host cell, the elementary body induces active phagocytosis and is ingested in a vesicle that becomes the setting for the next stage of the cycle. (More than one elementary body may be phagocytosed by a single host cell.)

Chlamydiae have a cell wall and two nucleic acids but are incapable of synthesizing ATP to meet their energy needs. Once the elementary body has been phagocytosed – it has an intrinsic property that allows it to circumvent host cell defenses that would normally lyse the phagosome – it becomes reorganized into the initial body. Larger than the elementary body, the initial body diverts the host cell's synthetic functions for its own metabolic purposes and proceeds to divide by binary fission, producing daughter microcolonies of chlamydiae. About 18 to 24 hours after infection, the initial bodies become reorganized into elementary bodies that subsequently exit the now disrupted host cell, ready to infect new host cells. The full cycle takes about 40 hours. The sequence results in a slow, steady accumulation of chlamydial particles within infected cells – the intracellular inclusions that are the diagnostic hallmark of chlamydial infection.

Several features distinguish the two species of chlamydiae. The inclusions of *C. trachomatis* accumulate glycogen and thus stain with iodine, whereas the inclusions of *C. psittaci* do not. Another difference is their response to sulfonamides – *C. trachomatis* is sensitive, *C. psittaci* is not. In addition, *C. trachomatis* is primarily a human pathogen, while *C. psittaci* causes disease in humans only via zoonoses, such as psittacosis and ornithosis.

The *C. trachomatis* species can be further subdivided into strains causing lymphogranuloma venereum (three serotypes) and strains causing ocular-genital infections (12 serotypes). The two subgroups differ significantly in their biologic activity. The lymphogranuloma venereum strains are more invasive, being capable of spontaneous cell-to-cell serial transmission in tissue culture and in vivo invasion of many tissues in addition to epithelial cells. The ocu-

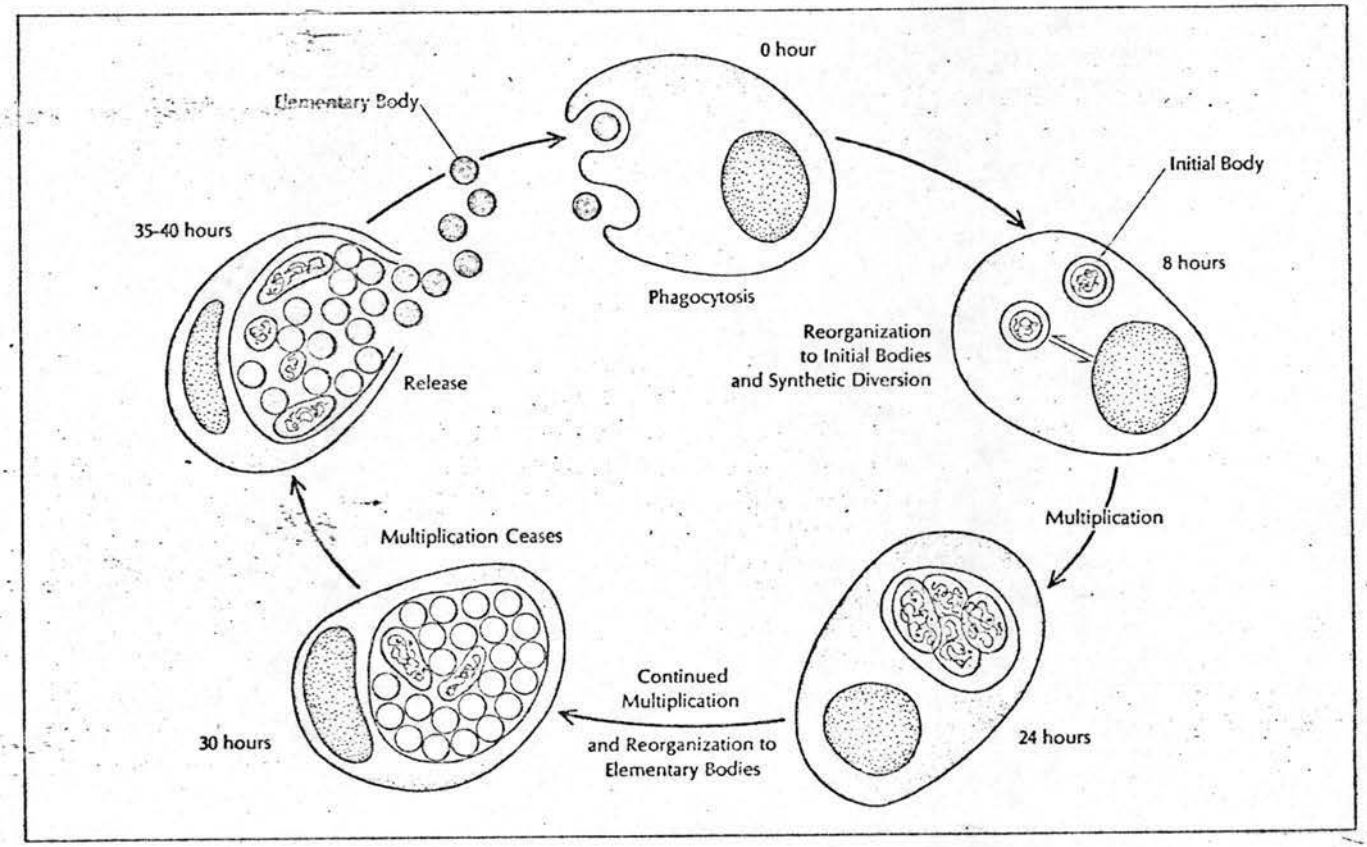
Dr. Alexander is Professor, Department of Epidemiology, School of Public Health and Community Medicine, University of Washington, Seattle.

lar-genital strains are not readily invasive in tissue culture and apparently grow in vivo only in columnar epithelial cells, which are found in the conjunctiva, respiratory tract, gastrointestinal tract, cervix, urethra, and rectal mucosa.

The relationship between inclusion conjunctivitis in the infant and genital tract infection in the mother has been recognized since the beginning of this century, after a precedent was established with recognition of the cause-effect relationship between maternal gonorrhea and ophthalmia neonatorum. The characteristic inclusions of *C. trachomatis* were first described in conjunctival cells from patients with trachoma in 1907. Soon after, they were identified in conjunctival scrapings from infants with nongonococcal ophthalmia neonatorum and adults with conjunctivitis and in cells from the genital tracts of adults with urethritis or cervicitis. The relationship between parental genital infection and infant ocular infection was demonstrated cytologically before 1910. By 1911, the German ophthalmologist K. Lindner had enough evidence to suggest that almost 30% of nongonococcal urethritis was caused by the same agent that caused both infant and adult inclusion conjunctivitis. The organism, now known as *C. trachomatis*, was finally isolated in 1957 by F-F T'ang in mainland China, using embryonated hens' eggs. The use of penicillin and streptomycin was the usual method of preventing bacterial contamination in cell cultures at that time. Penicillin was not then being manufactured in China and was scarce. Perhaps this was fortunate since it turned out that *C. trachomatis* is sensitive to penicillin, and the required trick was to grow it in a medium containing streptomycin alone. Subsequently, during the 1960s, a number of investigators retraced the pattern of infection by isolating the organism from the conjunctivas of infants with inclusion conjunctivitis, from the genital tracts of men with urethritis and of women with cervicitis, and from both the eyes and genital tracts of adults with inclusion conjunctivitis.

In several prospective studies, the prevalence of chlamydial infection in pregnant women has been found to vary from 2% in Boston to 6% in San Francisco to between 8% and 13% in Seattle. The differences between population groups are probably not geographic but relate to demographic differences in the study groups, which, in turn, relate to past experience with chlamydial infection. Women with chlamydial genital tract infection generally tend to be young, to come from low socioeconomic groups, and to have a history of venereal disease.

Two years ago, we undertook a pilot study at University Hospital, Seattle,

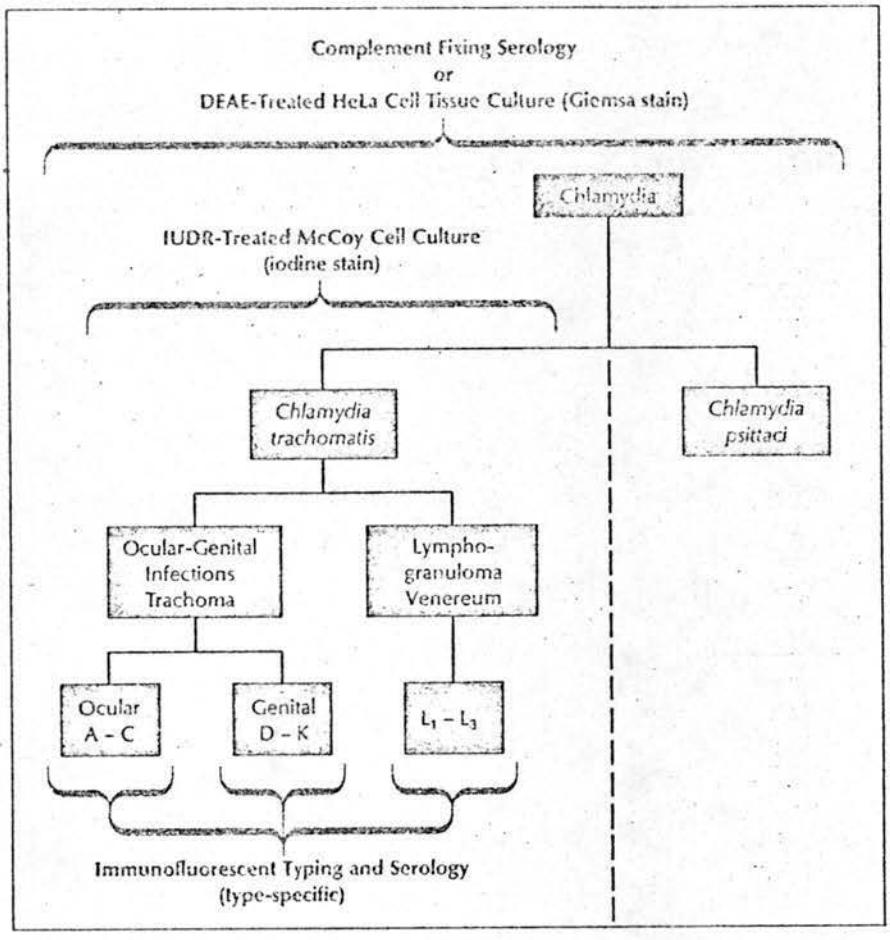


Life cycle of chlamydial organisms begins when small elementary bodies infect host cell by inducing active phagocytosis. During the next eight hours they reorganize into the larger reticulated initial bodies, which then divert the cell's synthetic functions to their own metabolic needs and begin to multiply by binary fission. About 24 hours after infection, the daughter organisms begin reorganizing into infective elementary bodies. At about 30 hours, multiplication ceases, and by 35 to 40 hours, the disrupted host cell dies, releasing new elementary bodies that can infect other host cells and thus continue the cycle.

to assess the risk of neonatal infection and disease in infants born to mothers with chlamydial genital infection. In the study, 142 unselected pregnant women attending a prenatal clinic at the hospital had cervical cultures done for evidence of chlamydial infection. The cultures of 18 women were positive at 36 to 40 weeks gestation, and eight of the 18 infants born to these women developed conjunctivitis. Follow-up studies at one year of age revealed that 12 of the same 18 infants had serum antibody to genital strains of *C. trachomatis*, including six who had had no history of neonatal conjunctivitis.

These findings indicated an infection rate of 13% in the obstetric clinic population and of 6% in the total group of infants. Both figures are considerably higher than any previously reported. A study at University Hospital 10 years ago found chlamydial infection in 1.3% of pregnant women attending the obstetric clinics. Other investigators have reported inclusion conjunctivitis in fewer than 1% of infants. The higher incidence detected in our study may reflect an increase in prevalence of the organism or in detection of less severe conjunctivitis, or both. In any case, the results not only confirm that inapparent infection of neonates occurs but that it may be relatively common. Recently, the results of another pilot study by Julius Schachter and associates at the University of California, San Francisco, showed that 10 of 25 infants born to mothers with chlamydial genital tract infection had laboratory-proved inclusion conjunctivitis. Thus, it appears that the risk of eye infection is between 33% and 50%. In other words, one third to one half of the babies born to infected women will develop inclusion conjunctivitis, while, on the basis of the Seattle findings, approximately two thirds will give evidence of having been infected. Installation of silver nitrate in the eyes of newborns as prophylaxis for ophthalmia neonatorum apparently does not affect *C. trachomatis*, since all of the infants in our study received it.

Inclusion conjunctivitis of the newborn usually develops between seven and 14 days following delivery. It should be differentiated from chemical conjunctivitis due to silver nitrate, which usually appears within the first four days, and from gonococcal ophthalmia neonatorum, which characteristically becomes severe in the first week of life.



Flow chart summarizes current knowledge of Chlamydia taxonomy and the various laboratory procedures used in identifying and differentiating the organisms. All Chlamydia can be demonstrated by complement fixation or by HeLa cell-tissue culture methods. To differentiate between C. trachomatis, *a primary human pathogen, and* C. psittaci, *largely an animal pathogen, the IUDR-treated McCoy cell culture method is used. For differentiation among strains causing ocular, genital, and lymphogranuloma venereum infections, immunofluorescent and serologic typing is necessary.*

Inclusion conjunctivitis produces congestion and edema and some discharge, which may become serosanguineous if the conjunctiva is acutely inflamed. Follicles are not seen on the conjunctiva of the infant as they are in trachoma and adult inclusion conjunctivitis. The infant conjunctiva apparently is not capable of producing a follicular reaction to any stimulus.

The diagnosis can be confirmed readily in most cases by taking a scraping of the upper or lower conjunctiva and staining with Giemsa stain, which reveals the characteristic inclusions. The definitive diagnosis is made by culturing the organism. T'ang's time-consuming egg-yolk culture method has been supplanted by cell culture. The cells most often used are McCoy cells, which are first treated by irradiation or by treatment with 5-iodo-2-deoxyuridine (IUDR), cycloheximide, or cytochalasin B. The effect of this treatment is not fully known but it appears to affect cell growth. Some laboratories use L cells or HeLa cells. Prior to incubation, the inoculum is centrifuged with the cell substrate to obtain cell infection. Hospital laboratories are not usually equipped for this procedure, although many large medical center laboratories are developing the capacity to culture the organism.

Clinical and Laboratory Data for Infants Born to Mothers with Genital Chlamydial Infection

Patient Number	Conjunctivitis (age in weeks at onset)*	Culture for Chlamydia	Typical Inclusions on Giemsa Stain	Fluorescent Antibody (FA) for Chlamydia Antigens on Smear	Tear Antibody (age in weeks at first positive test)	Serum Antibody at 1 Year of Age	Clinical Findings** at 1 Year of Age
1	●	●			● (30)	●	○
2	●	●			●	●	○
3	●	●			●	●	
4	●	●			●	●	○
5	●	●			●	●	○
6	●	●			●	●	○
7	●	●			● (12)	●	○
8	●	●	●	●	●	●	○
9	●	●			●	●	○
10	●	●			● (20)	●	●
11	● (1)	●	●	●	● (10)	●	○
12	● (5)	●	●	●	● (14)	●	○
13	● (6)	●	●	●	● (12)	●	○
14	● (6)	●			●	●	●
15	● (1)	●			●	●	○
16	● (1)	●	●	●	●	●	○
17	● (2)	●	●	●	●	●	●
	● (8)†	●	●	●			
18	● (2)	●	●	●	● (12)	●	●
	● (8)†	●	●	●			

● Negative ● Positive *Conjunctivitis: ● Mild ● Severe †Recurrence
**Clinical Findings: ○ Normal ○ Micropannus

Serologic identification of the organism is also possible, but that will probably remain a function of research laboratories until a radioimmunoassay or a similar method is developed.

Inclusion conjunctivitis of the newborn, if untreated, usually lasts for one to two weeks, and whether or not it is treated, recurrence once or twice over the next two to three months is common. The treatment usually recommended is topical sulfacetamide, but orally administered erythromycin may be preferable. Controlled trials of erythromycin have not been completed, but use of the antibiotic appears to result in fewer relapses.

In general, inclusion conjunctivitis of the newborn is a benign, self-limited disease, but there is some evidence that this is not always the case. C.H. Mordhorst in Denmark has found, from long-term follow-up of families with chlamydial ocular-genital infections, that scarring, pannus formation and other characteristics usually associated with trachoma do occur in some patients, presumably as a result of reexposure.

The difference between trachoma in the Middle East, Asia, or Africa, where it is hyperendemic, and the entity of inclusion conjunctivitis in the United States and other developed nations is difficult to define other than on the basis of severity and sequelae. Clearly the two diseases are different in these two respects. The monkey model developed by S-P Wang and J.T. Grayston at the University of Washington has provided some explanation of these differences. When monkeys are inoculated on the conjunctiva with any of the ocular-genital *C. trachomatis* organisms, an acute follicular conjunctivitis develops that has the characteristics of trachoma. The disease is the same whether the organism was isolated from a case of inclusion conjunctivitis or nongonococcal urethritis in Seattle or from a case of trachoma in Egypt. In fact, if any difference is worth noting, it is that isolates from genital sources produce more severe disease in the monkey than isolates from trachoma.

In the monkey model, initial infection is self-limited. Pannus, which involves neovascularization across the limbus of the cornea and is a diagnostic sign of trachoma, develops in the monkey only after reinfection or on initial infection of a monkey previously sensitized by killed antigen. In other words, pannus formation denotes prior sensitization with the antigen. Other characteristics of trachoma that eventually lead to blindness, such as conjunctival scarring and deformation, entropion, and trichiasis, also develop in the monkey model after reinfection. It is highly probable that in countries where trachoma is not endemic, such as the United States, inclusion conjunctivitis represents a pri-

mary chlamydial infection. Although rare, more severe ocular infections that are clinically indistinguishable from trachoma occur in this country; on the basis of present evidence they probably represent reinfection. One other factor that affects severity is the presence of other bacterial eye infections. In fact, the distinguishing feature between trachoma-hyperendemic countries with or without blindness is the presence or absence of bacterial conjunctivitis in these respective populations.

Within the last two years, another risk to the newborn of maternal chlamydial infection has been documented. In 1977, Marc O. Beem and associates at the University of Chicago described a distinct pneumonia syndrome in infants who had previously had inclusion conjunctivitis. They showed that the pneumonia was related to *C. trachomatis* infection by isolating the organism from the nasopharynx and tracheal secretions of infants with the syndrome and by demonstrating that the infants developed specific antibody to *C. trachomatis*.

Several features distinguish pneumonia due to *C. trachomatis*. It develops between about four and 18 weeks of age and produces an afebrile illness with symptoms of congestion, wheezing, and a distinctive staccato cough. The paroxysms of staccato cough are not unlike those of pertussis, but they lack the inspiratory whoop that characterizes that disease. The clinical findings include diffuse crepitant rales on auscultation of the chest; hyperinflation of the lungs is seen on x-ray. Other characteristics of *C. trachomatis* pneumonia are an increase in eosinophils in peripheral blood (greater than 400 eosinophils per cubic mm) and elevated serum immunoglobins. We find that an IgG $\geq$500 mg/100 ml or an IgM $\geq$110 is characteristic of *C. trachomatis* pneumonia.

The diagnostic tests used for *C. trachomatis* pneumonia include recovery of the organism from the nasopharynx or tracheal secretions and various serologic techniques. The organism is quite distinctly localized to the posterior nasopharynx, and it is infrequently recovered from the oropharynx. Thus, the most appropriate methods for recovery are either a posterior nasopharyngeal swab or aspiration of nasopharyngeal secretions with a feeding tube attached to a syringe. Antibodies against *C. trachomatis* can be demonstrated in the serum. Local antibody can be demonstrated either in the nasopharyngeal secretions or in the tears, but this information adds little to the significance of the serum antibody test results.

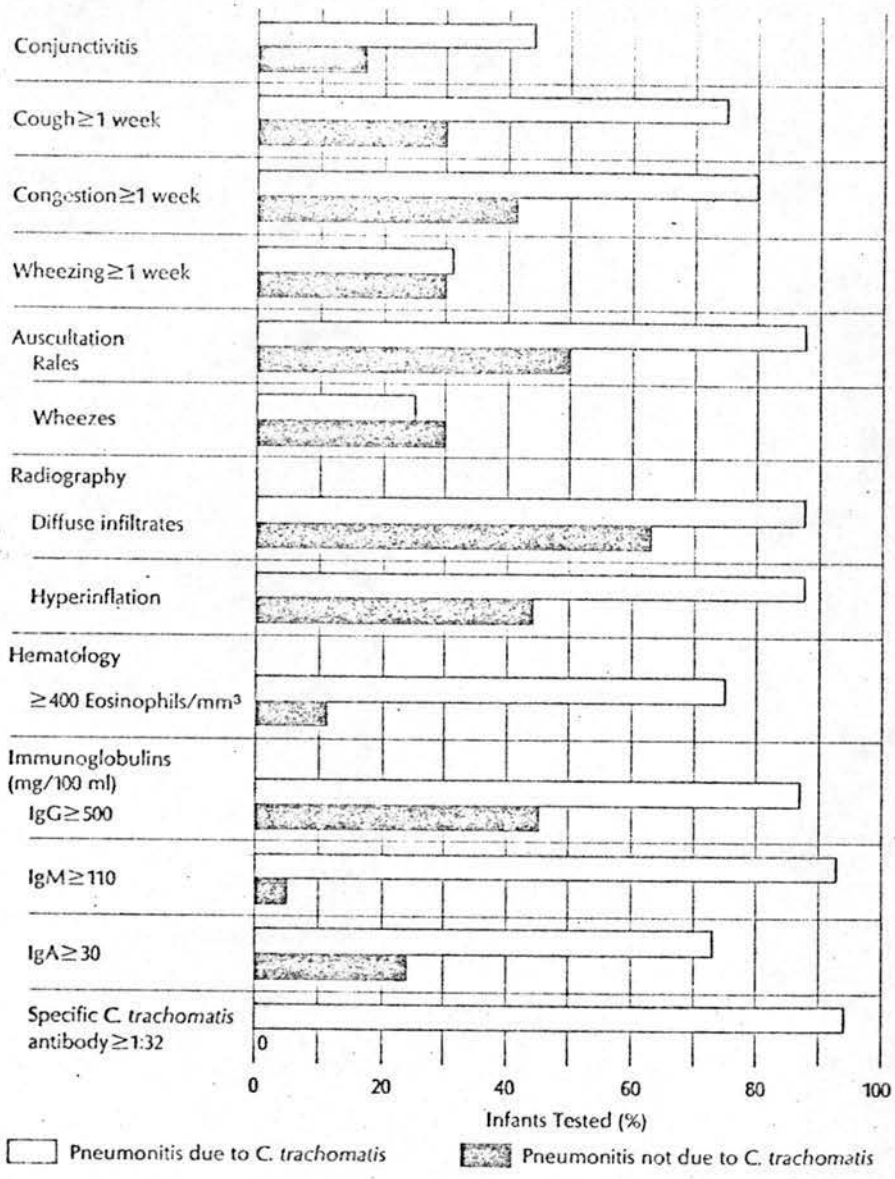
The evidence that *C. trachomatis* is the causative agent of the pneumonia syndrome is based on recovery of the agent from nasopharyngeal and tracheal secretions of infants with typical symptoms and, in three instances, from lung biopsy material. On the other hand, *C. trachomatis* has rarely been isolated from lung biopsy material, and inclusions have rarely been seen in such material. Consequently, some investigators have suggested that the syndrome is due to hypersensitivity rather than infection, and others have suggested that viruses, which are quite often found in association with *C. trachomatis*, are involved in the infection that produces the pneumonia.

The viruses associated with *C. trachomatis* in infants with pneumonia include cytomegalovirus, respiratory syncytial virus, rhinovirus, adenovirus, and enterovirus. However, available evidence indicates that *C. trachomatis* is the central etiologic agent in the disease. Beem and associates have noted that symptoms and clinical and laboratory findings are the same in infants from whom *C. trachomatis* alone is isolated and in those from whom both *C. trachomatis* and viruses are isolated. Furthermore, they found that the clinical course and the response to treatment were similar, regardless of whether *C. trachomatis* was isolated alone or in combination with viruses. In addition, our experimental results support the view that the pneumonia is due to *C. trachomatis*. We were able to induce the pneumonitis in infant baboons by inoculation with *C. trachomatis* and then recovered the organism from the lungs. Since *C. trachomatis* pneumonia is a chronic illness, which in many cases produces only mild to moderate symptoms, and respiratory viral infections are common in infants, it would not be too surprising to find frequent coinfection with these agents. The relationship between *C. trachomatis* pneumonitis and cytomegalovirus infection remains to be explored, but it should be noted that both are venereally transmitted agents that appear together in other epidemiologic settings. It should also be noted that the *C. trachomatis* serotypes recovered from infants with pneumonitis are the same as those recovered from genital sources.

Examination of lung biopsy material has revealed slight but intense infiltration of mononuclear cells in small airways, often causing blockage that presumably results in the hyperinflation typical of the disease. Although there is some observable damage to bronchial and pulmonary epithelium, it is not marked.

Controlled clinical trials of treatment of *C. trachomatis* pneumonia have been started only recently, therefore the preferable therapy remains to be demonstrated. In vitro tests with a variety of antibiotics have shown that tetracyclines and erythromycin are the most effective agents against the organism. Since tetracyclines should not be used in infants and children be-

Hyperinflation of the lungs is a consistent finding in chest x-rays of infants with proven chlamydial pneumonitis.



Clinical and laboratory findings in infants with afebrile pneumonitis (16 with proven chlamydial infection, 27 without evidence of chlamydial infection) are graphed. Findings characteristic of chlamydial pneumonitis were a staccato cough, lung hyperinflation and increased eosinophils and serum immunoglobulins.

cause of their effect on growing teeth, erythromycin is probably the drug of choice. Sulfisoxazole is somewhat less effective but can be used. Prolonged follow-up seems advisable in view of the well-known tendency of chlamydial infections to recur, even in treated patients. In this regard, our preliminary observations of the antibody response in treated infants are of interest. Administration of systemic antibiotics, even relatively ineffective ones, such as penicillin, had a depressing effect on antibody titers when compared with infants not given systemic antibiotics, or given topical ocular antibiotics only. Whether or not early systemic antibiotic treatment affects the immune response is not known. Beem found that systemic treatment with either sulfisoxazole or erythromycin produced clinical improvement of respiratory symptoms within one week and rapidly terminated shedding of *C. trachomatis*.

The risk of *C. trachomatis* pneumonia in babies born to infected mothers has not been determined. The early results of a number of prospective studies suggest that it is at least 5% and perhaps as high as 25%.

At the present time the only clinical entities definitely associated with natally acquired chlamydial infection are inclusion conjunctivitis and pneumonia, but it is reasonable to expect that a relationship with other diseases will be found. For instance, Beem and associates found middle-ear abnormalities in more than half of 41 infants with *C. trachomatis*-positive pneumonia. The abnormalities consisted of an opaque, pearly-white color, diffuse-light reflex, poorly distinguishable short process, and, in some cases, bulging of the tympanic membrane. Myringotomies done on one or both ears of 11 of these infants consistently yielded gelatinous middle-ear secretions, and *C. trachomatis* was isolated from ear aspirates of three infants. The finding suggests that *C. trachomatis* may contribute to otitis media in infancy. Such a possibility and its potential long-term effects need to be evaluated.

Similarly, it is unlikely that pneumonia is the only respiratory consequence of nasopharyngeal infection with *C. trachomatis* in infancy. Our experience, as well as that of other investigators, suggests that by one year of age, children who have had *C. trachomatis* infections in infancy have an excess in both frequency and severity of respiratory infections. The extent and characteristics of both upper and lower respiratory tract infections without pneumonia have not been defined.

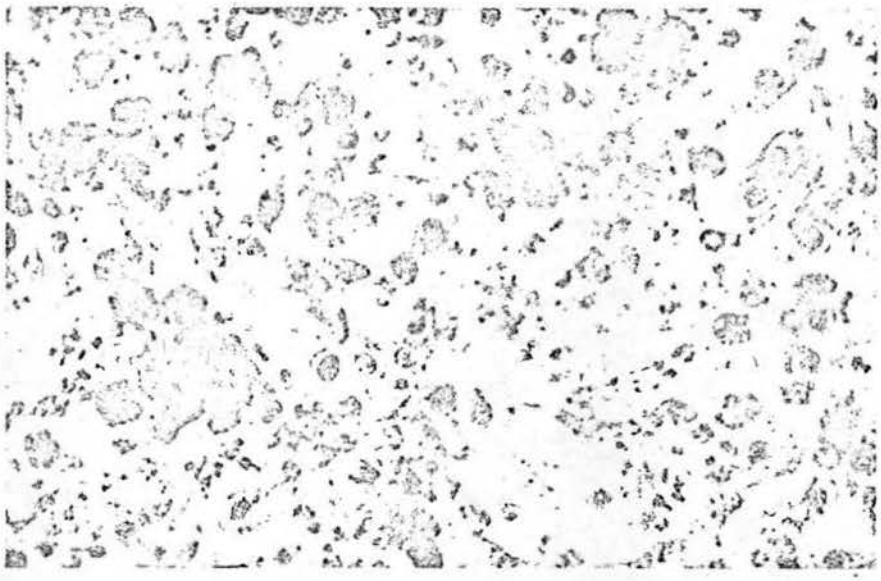
It is also likely that *C. trachomatis* will be found to contribute to respiratory infections at older ages. The results of serologic studies done by Grayston and Wang indicate that *C. trachomatis* infection in infancy has a continuing effect on respiratory infections at older ages.

Our finding that 13 of 14 infants with *C. trachomatis* pneumonitis had positive tear antibody tests suggests a high incidence of inapparent and apparent conjunctivitis prior to the development of pneumonitis. Half of these infants had histories of conjunctivitis, which suggests that nasopharyngitis and pneumonitis may occur by direct extension down the respiratory tract from an ocular focus. It is also likely that a heavy intrapartum

dose of *C. trachomatis* could infect both conjunctiva and nasopharynx concurrently, and even the lower respiratory tract by aspiration.

The possibility of preventing inclusion conjunctivitis of the newborn is currently under investigation. The basis for the present approach is the success of mandatory silver nitrate prophylaxis in preventing ophthalmia neonatorum. Several studies are in progress to test the effectiveness of erythromycin ointment as a substitute for silver nitrate in the prevention of both gonococcal and chlamydial infections of the eyes in newborns. If the results are definitive, erythromycin may become the recommended agent for neonatal ocular prophylaxis in the future. However, it is unlikely that topical ocular erythromycin will prevent nasopharyngeal infection of the newborn or its apparent sequela, respiratory disease.

The most effective preventive of natally acquired chlamydial infections would be detection and treatment of pregnant women prior to delivery. Unfortunately, no simple, routinely applicable method is available for such a course of action. Diagnostic tests for identifying *C. trachomatis* genital infections are not universally available. While the typical chlamydial inclusions are readily apparent in conjunctival smears, they are infrequently found in cervical smears. For diagnosis of both male and female genital infection, the organism must be recovered on a swab and then isolated in tissue culture. Furthermore, chlamydial infection in women is not usually accompanied by any manifest disease of the cervix, although one clinical entity, a hypertrophic papillary cervicitis, has been described in association with *C. trachomatis* genital infections in women. Another problem arises from the observation that some women who are found to be *C. trachomatis*-positive early in preganancy spontaneously revert to negative before delivery. And, vice versa, some women who are negative on first examination become positive later in pregnancy. These cases may represent a flare-up of latent cervical infection related to the immunologic changes that occur in pregnancy. In fact, the majority of women with proven chlamydial cervical infection during pregnancy spontaneously revert to negative postpartum. In addition, when the sexual partners of pregnant women with chlamydial cervical infection have been studied, the great majority have been found to have chlamydial urethral infection. Although most of these cases have been asymptomatic, there is usually a history of past urethritis.



Iodine stain reveals typical chlamydial inclusion bodies in McCoy cell culture. To obtain growth of the organism, cells were pretreated with 5-iodo-2-deoxyuridine.

Until we have a better understanding of the natural history of *C. trachomatis* infections in pregnancy, it would seem more important to identify women as infected or not in the last trimester in order to define those at risk of infecting their infants.

Regardless of whether the diagnosis is made in early or late pregnancy, another problem arises, and that is what antibiotic to use in treatment of the mother. Again, although there are no recommendations in this area at the present time in the United States, the common practice in the United Kingdom is to treat infected pregnant women with erythromycin. Sexual partners should be treated at the same time to prevent maternal reinfection. (The diagnosis and treatment of genital chlamydial infections will be discussed in more detail in a subsequent article.) □

Selected Reading

Harrison HR, English MG, Lee CK, Alexander ER: *Chlamydia trachomatis* infant pneumonitis. Comparison with matched controls and other infant pneumonitis. N Engl J Med 298:702, 1978

Tipple MA, Beem MO, Saxon EM: Clinical characteristics of the afebrile pneumonia associated with *Chlamydia trachomatis* infection in infants less than six months of age. Pediatrics 63:192, 1979

Beem MO, Saxon E, Tipple MA: Treatment of chlamydial pneumonia of infancy. Pediatrics 63:198, 1979

Chandler JW et al: Ophthalmia neonatorum associated with maternal chlamydial infections. Trans Am Acad Ophthalmol Otolaryyngol 83:302, 1977

Wentworth BB, Alexander ER: Isolation of *Chlamydia trachomatis* by use of 5-iodo-2-deoxyuridine-treated cells. Appl Microbiol 27:912, 1974

Chiang WT, Alexander ER, Wei PY, Fresh JW: Genital infection with TRIC agents in Taiwan. Am J Obstet Gynecol 100:422, 1968

Schachter J: Chlamydial infections (third of three parts). N Engl J Med 298:540, 1978

Attachment #2
00-3522

Reprinted by the
U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
from THE JOURNAL OF PEDIATRICS, Vol. 95, No. 1, July 1979

Chlamydial infection of mothers and their infants

In 340 women, cultured prospectively during their pregnancies, the rate of infection with Chlamydia trachomatis *was 8.8%. The women with positive cultures tended to be younger and more often single and black than their counterparts with negative cultures. There were no statistically significant clinical differences between the two groups. Eighteen children born to* Chlamydia *culture-positive women and 16 born to negative women were followed for nine months to examine the potential effects of maternal infection on infant growth, development, and illness. Eleven of 18 study patients had culture or tear antibody evidence of* Chlamydia *infection, as opposed to one of the control subjects (P = 0.00093). Eight of these 11 had clinical conjunctivitis, and two of the eight developed pneumonia. Growth retardation and developmental abnormalities were not detected in either group. It is concluded that maternal carriage of* C. trachomatis *is associated with a high incidence of clinical illness in the offspring.*

George T. Frommell, M.D., Richard Rothenberg, M.D.,*
San-pin Wang, M.D., and Kenneth McIntosh, M.D., with the technical assistance of Cynthia Wintersgill, B.A., Jane Allaman, B.S., and Inara Orr, R.N., *Denver, Colo., Atlanta, Ga., and Seattle, Wash.*

CHLAMYDIAL INFECTIONS are regularly associated with certain nonspecific genital syndromes in both men and women.[1] These syndromes may well be the most common sexually transmitted diseases in the United States (Center for Disease Control, Venereal Disease Control Division, Atlanta, Georgia: unpublished data), but clinical manifestations are usually not severe, and long-term sequelae are not well documented. The recent description of a protracted pneumonia associated with *Chlamydia trachomatis* in infants[2-5] has shed new light on the importance and potential public health impact of genital carriage of *Chlamydia.* There is at present little information concerning the risk associated with chlamydial infection in pregnant women and their offspring.[6] In this study we cultured a large group of mothers prospectively during their pregnancies. Infants born to *Chlamydia* culture-positive and *Chlamydia* culture-negative women were followed to trace the development of disease and disability.

From the Department of Pediatrics (Infectious Disease), University of Colorado Medical Center, the Colorado State Health Department, the United States Public Health Service, Center for Disease Control, Venereal Disease Control Division, and the Department of Pathobiology, School of Public Health, University of Washington.

Supported in part from a contract (CDC 21-74-527 from the Venereal Disease Control Division of the Center for Disease Control) from the United States Public Health Service, and Grant 5-R01-EY-00219 from the National Eye Institute.

**Reprint address: Technical Information Service, Center for Disease Control, Atlanta, GA 30333.*

MATERIALS AND METHODS

Maternal population. Between October 3, 1975, and March 5, 1977, 340 women attending the Obstetrics Clinic of the Colorado General Hospital, at low risk for the complications of pregnancy and at less than 32 weeks' gestation on first visit, were enrolled in the study. Participation was voluntary and written informed consent was obtained.

Demographic data and information relating to current sexual activity were obtained from each patient. A cervical culture for *Chlamydia* was taken at the initial obstetric evaluation, at 32 weeks' gestation, at parturition, and at the postpartum visit. More frequent cultures were usually obtained from women found to be *Chlamydia* culture positive. Serum was also obtained at each visit and frozen at −20°C. In addition, cervical and urine cultures for *Herpesvirus hominis* and cytomegalovirus were obtained at each visit. All women underwent cervical culture for *Neisseria gonorrhoeae* on the first two visits; appropriate treatment and epidemiologic follow-up were offered to all

Table. Clinical and laboratory results in *Chlamydia* culture-positive study group

Mothers			*Infants*					
Evidence of C. trachomatis *infection*			*Evidence of* C. trachomatis *infection*					
Patient No.	*By culture of cervix (wk gestation)*	*By serum antibody (type)*	*By culture*		*By tear antibody*		*Conjunctivitis*	*Comments*
			Site‡	*Age (wk)*	*Type*	*Age (wk)*		
1	16	ED	–	–	Neg		No	
2	31	F†	–	–	GF	5, 17, 24, 46	No	Bilateral micropannus at 1 yr
3	13	GF	–	–	Neg		No	
4	32, 38, 39*	GF	–	–	GF	39	No	
5	35	ED	R	5	ED	24, 43	Yes	Mother positive 6 wk postpartum
6	22, 28	ED	NP	7	ED	Birth, 7, 26	Yes	Infant developed pneumonia at 4 wk of age
7	24, 33, 35, 37	Ed	–	–	Neg		No	Infant developed recurrent wheezing at 6 wk
8	32, 36, 38*	GF	NP	11, 27	GF	13, 27	Yes	Infant developed pneumonia at 6 wk of age; mother positive 6 wk postpartum
9	32	H	–	–	Neg		No	
10	22, 31, 40*	ED	NP	13	ED	13	No	Bilateral micropannus at 1 yr
11	30, 35	GF	–	–	Neg		No	
12	23	I	–	–	Neg		No	
13	19	ED	–	–	Neg		No	
14	34	ED	–	–	ED	18	Yes	
15	32, 37	D†	NP	2	ED	9, 13	Yes	Bilateral micropannus and small anterior stromal opacity, o.s. at 1 yr
16	35	ED	R	3	ED	9, 17, 26, 46	Yes	Mother positive 6 wk postpartum
17	17, 24	ED	C NP	3, 5, 17 17	ED	17, 33, 40	Yes	
18	22, 30, 36, 41*	ED	NP, R	12	ED	12	Yes	

*Day of delivery.
†Isolate was typed and confirmed the antibody type in serum.
‡R = Rectal, NP = nasopharynx, C = conjunctiva, – = not done.

women with positive cultures. A total of 775 chlamydial cultures were obtained during pregnancy or at delivery from the 340 women.

Infant population. Infants born to 18 of the 30 Chlamydia culture-positive women were followed from birth to 9 months of age, along with a control population of infants born to mothers who remained *Chlamydia* culture-negative throughout pregnancy; 12 of the culture-positive women either were lost to follow-up or refused further participation. Control infants were, as often as possible, those born at the next delivery of a *Chlamydia* culture-negative mother following each Chlamydia culture-positive delivery; when this was not possible, the infant born at the closest subsequent delivery of a negative mother was then accepted. Eighteen mothers and their 19 infants (including one set of twins) were originally enrolled in the control group. Eight of these 18 mothers had serum antibody detected in an initial screening test, indicative of previous *Chlamydia* infection. All eight were further examined for IgM antibody; three had anti-*Chlamydia* IgM which was thought to be suggestive of recent (although not necessarily current) infection. They were omitted from the analysis. Careful cultural, serologic, and clinical follow-up of the infants of these three mothers revealed no evidence of chlamydial infection in any.

A separate informed written consent was signed by both parents for inclusion of the child in the study. All infants followed were delivered vaginally, and silver nitrate ophthalmic prophylaxis was employed in all instances. At birth and at two to three weeks of age, the conjunctiva, nasopharynx, umbilicus, genitals, and rectum were cultured for *Chlamydia*. At six weeks, three months, and nine months the conjunctiva, nasopharynx, genitals, and occasionally the rectum were cultured. Infants in the infected group were each cultured an average of 5.4 times, and those in the control group an average of 5.6 times.

Tear secretions for antibody determination were obtained at the time of follow-up cultures, starting usually at two to three weeks of age. Cord blood IgM determina-

tions were performed in most instances. Height, weight, and head circumference were determined routinely, as was psychomotor development through use of the Denver Prescreening Developmental Questionnaire.[7] Infants were examined and evaluated by one of us (G. T. F.) at each follow-up visit. All infants were observed for eye disease (conjunctivitis with exudate of any type) and pneumonia as well as other clinical illness. Children with evidence of chlamydial eye disease during the study period were re-examined at one year of age.

Compliance with the protocol was excellent among control patients and somewhat less good in the infected group, who, perhaps because of their sociodemographic characteristics (see below), tended to miss appointments and move without leaving forwarding addresses. Because of this difficulty, cultures were often not taken during acute illness, conjunctivitis in particular.

Chlamydia cultures. Infant nasopharyngeal specimens were obtained using a sterile 8-French suction catheter inserted through the nares to the posterior pharynx. Secretions were aspirated and placed in transport media. All other specimens were obtained using sterile cotton-tipped applicators. Specimens were frozen at −70°C until processed. Chlamydiae were isolated according to the method of Wentworth and Alexander,[8] using McCoy cells treated with IUdR.

Tear antibodies and serologic studies. Tear secretions were collected from the study and control infants by means of a 5 × 20 mm strip of filter paper applied along the lower lid margin of each eye with sterile forceps. After complete saturation, the filter paper strips were placed in vials containing 0.2 ml of phosphate-buffered saline, yielding an approximate tear dilution of 1:10. Serum antibody was measured in mothers in the study and control groups. Both tear and serum antibody were determined by the microimmunofluorescence method, using CJ, A, H, I, K, B, ED, and GF antigens and a conjugate containing antihuman IgM, IgA, and IgG combined (Hyland Laboratories, Los Angeles, Calif.). Titers of 1:8 for serum and 1:10 for tears (the lowest tested) were considered positive. Some positive sera were further analyzed using separate anti-IgM and IgG conjugates.[9] In two study mothers in whom the predominant antibody type in the serum was in doubt, the cervical isolates were examined in order to determine the precise infection serotype (Table). Cord blood IgM determinations were made by radial immunodiffusion (TRI-Partigen IgM Standard Kit, Behring Diagnostics).

Other cultures. *Herpesvirus hominis* and cytomegalovirus were recovered in human embryonic lung fibroblasts and identified by routine virologic procedures. *Neisseria gonorrhoeae* was isolated on Thayer-Martin medium and identified by routine bacteriologic methods.

Statistical analysis. The Fisher exact test and the critical ratio for difference of proportions were used for statistical analysis.[10]

RESULTS

Maternal population. Cultures obtained during pregnancy from 30 of the 340 women (8.8%) enrolled in the study grew *Chlamydia*. *Chlamydia* culture-positive women differed significantly from those who were *Chlamydia* culture-negative with regard to certain sociodemographic characteristics. They tended to be younger (53% in the 15 to 19 year age range vs. 27%, $P \leq 0.01$) and more frequently black (27% vs 9%, $P \leq 0.01$), or unmarried (33% vs. 14%, $P < 0.01$). More of the *Chlamydia* culture-positive women lived at home with their parents, perhaps as a correlate of age. The father of the child was usually the current sex partner in both groups, but among married *Chlamydia* culture-positive women, the husband was less likely to be the father of the child. There was no difference between the two groups with regard to income or enrollment on welfare.

The positive and negative groups were similar in clinical characteristics. There were no significant differences in previous obstetric history, complications of labor and delivery, condition at initial evaluation of the newborn child (Apgar score, birth weight, and estimated gestational age), and postpartum complications. Previous infection with *Chlamydia* in the maternal population can be judged by the prevalence of anti-*Chlamydial* IgG in culture-negative mothers. Of 18 women examined, eight had IgG antibody to one of the serotypes tested.

Ten of the 340 women (2 *Chlamydia* culture-positive and 8 culture-negative) were culture positive for *Herpesvirus hominis* and three (all *Chlamydia* culture negative) carried cytomegalovirus. Six patients had gonorrhea (2 *Chlamydia* culture-positive and 4 culture-negative).

Infant population. Eighteen infants (7 male and 11 female), delivered vaginally to women harboring *C. trachomatis* during gestation, were enrolled for follow-up study. Sixteen infants (9 male and 7 female) born to *Chlamydia* culture-negative women served as control subjects. There were no significant differences between the two groups with regard to gestational age, birth weight, length, head circumference, growth patterns, and psychomotor development during the study period.

Eleven infants (61%) in the study group developed evidence of infection with *C. trachomatis*. Eight of the 11 were culture positive from at least one site and all 11 developed tear antibody to *Chlamydia*. In 6 of these 11,

early tear samples were available and antibody was shown to be absent before infection. Eight infants developed conjunctivitis, with onset at one to nine weeks of age. Seven of these eight were culture positive (two from the conjunctiva itself and the remainder from other sites), and the eighth had only tear antibody. Of the three clinically normal infants with tear antibody, one was culture positive as well. In all instances, the infant tear antibody type was the same at that in maternal serum. Breast-feeding was weakly but not significantly associated with development of clinical conjunctivitis. In the study group, six of nine breast-fed infants developed conjunctivitis as against two of nine bottle-fed infants ($0.01 > P > 0.05$ by the Fisher exact test).

In contrast, only a single infant of a control mother developed evidence of *Chlamydia* infection ($P = 0.00093$ by the Fisher exact test). This child's mother had IgG (but no IgM) antibody to the GF serotype group of *Chlamydia*, but was never culture positive during pregnancy. The infant had purulent conjunctivitis at two weeks of age which was not cultured but which responded to sulfonamide therapy. Cultures taken at birth and 10, 23, and 35 weeks of age were negative. At 5 months of age antibody to the GF serotypes was found in her tears.

Two of the infants in the study group with conjunctivitis subsequently developed a chronic pneumonitis (onset at ages 4 and 6 weeks). Both were afebrile and had a dry, nonproductive cough, interstitial infiltrates on chest roentgenogram, and positive nasopharyngeal cultures. Other bacterial and viral cultures obtained from these infants were negative. One child required hospitalization and was treated with ampicillin and kanamycin parenterally for three days. The other was treated with erythromycin as an outpatient. Both recovered completely in four to six weeks.

One further child in the study group, without evidence of chlamydial infection, developed recurrent wheezing at 6 weeks of age. He was admitted at 3 months of age, when both viral and chlamydial cultures were negative, and discharged with a diagnosis of "asthma."

As shown in the Table, the nasopharynx was the most common positive culture site (seven of the eight infants). Three infants had positive rectal cultures and, as noted, two had positive conjunctival cultures as well. No cultures taken during the nursery stay grew *Chlamydia*. Initial isolations occurred between 2 and 13 weeks of age, in five of eight infants before 9 weeks of age. Shedding of the organism continued as late as 27 weeks in one instance. Tear antibody tended to become positive later than cultures, in 9 of 11 infants at or after 9 weeks of age. In one instance antibody was present at birth. Cord IgM levels were measured in 16 of the 18 study patients and in 13 of the 16 control subjects; all were within normal limits.

All 11 infants with evidence of Chlamydia infection had follow-up ophthalmologic examinations at one year of age. No active eye disease was found, but three of the infants had a mild bilateral micropannus. Two of three had not had previous clinical conjunctivitis or positive cultures, but did have tear antibody as evidence of infection. The third had, in addition, a small anterior stromal opacity in the eye from which a previous positive culture had been obtained. In no instance were these changes thought to be a hindrance to vision.

DISCUSSION

Recent reports suggest that *C. trachomatis* may be an important pediatric pathogen in a nontrachomatous area such as the United States. Schachter et al[2] first reported a child with conjunctivitis and pneumonitis. Subsequently, Beem and Saxon[3] reported 12 cases of pneumonia in infants characterized by dry hacking cough, chronic pulmonary infiltrates, and an afebrile course. All of these children had positive nasopharyngeal cultures. Frommell et al[4] strengthened the association by obtaining a lung biopsy positive for *C. trachomatis* from another such patient. Chandler et al[5] cultured 142 women during the last month of gestation, of whom 18 were *Chlamydia* positive (12.7%). Eight infants born to these 18 women developed clinical conjunctivitis, although none developed pneumonia. Finally, a recent survey by Harrison et al[1] found chlamydial infection in 9 of 30 consecutive infants under 6 months of age hospitalized with pneumonia, and in only one of 28 matched control subjects. The clinical aspects of this characteristic subacute pulmonary disease were confirmed.

Our study is in agreement with these results and demonstrates the high rate of *Chlamydia* infection (61%) and clinical disease (44%) in infants born to *Chlamydia* culture-positive mothers. These results are of particular interest since women initially at high risk for complications of pregnancy were excluded. The social and demographic differences between *Chlamydia* culture-positive and culture-negative mothers are in agreement with those of Chandler et al[5] and may reflect increased sexual activity at an earlier age. There is no apparent association, however, between culture positivity and the clinical course of pregnancy and delivery. Similarly, maternal carriage of *Chlamydia* does not appear to affect the growth and development of the child, but seems to play a significant role in the appearance of *Chlamydia*-associated illness.

Only two infants in our study were found to shed *Chlamydia* from the conjunctivia, despite the presence of conjunctivitis in eight. In some other studies, *Chlamydia* have been cultured with apparent ease from the conjunctivae[3, 11] whereas in Chandler's study,[6] which was similar to the present survey in being prospective, only three of eight infants with conjunctivitis and born to a culture-positive mother yielded *Chlamydia*. Our low isolation rate was probably due to at least two features of the study: timing of cultures in relation to disease was often poor, owing in part to problems with follow-up of the infected group; and cultures were frozen before tissue inoculation. On the other hand, studies in monkeys[12] suggest that tear antibody develops only when infection of that eye has occurred. Moreover, early tear samples in the majority of our infected infant population showed no antibody; for this reason, it is unlikely, except in the possible instance of the infant positive at birth, that we were measuring maternal, passively acquired tear IgG. The data in our study are thus consistent with an etiologic relationship between conjunctivitis and *Chlamydia* infection.

The absence of elevated IgM in cord blood suggests that intrauterine infection did not take place. In most infants, the timing of the appearance of culture positivity and tear antibody is consistent with infection during passage through the birth canal. On the other hand, the association with breast-feeding (suggesting more intimate handling of the child by the mother) raises the possibility of postpartum transmission. In either event, *Chlamydial* carriage by the mother would appear to be associated with a high incidence of clinical illness in the child.

We are indebted to Dr. Watson Bowes, and the staff of the Obstetrics Clinic, Colorado General Hospital, for their support, and to Dr. S. Lance Forstat, for performing the ophthalmologic examinations.

REFERENCES

1. Schachter J, Causse G, and Tarizzo ML: Chlamydiae as agents of sexually transmitted diseases, Bull WHO 54:245, 1976.
2. Schachter J, Lum L, Gooding CA, et al: Pneumonitis following inclusion blennorrhea, J PEDIATR 87:779, 1975.
3. Beem MO, and Saxon EM: Respiratory tract colonization and a distinctive pneumonia syndrome in infants infected with Chlamydia trachomatis, N Engl J Med 296:306, 1977.
4. Frommell GT, Bruhn FW, and Schwartzman JE: Isolation of Chlamydia trachomatis from infant lung tissue, N Engl J Med 290:1150, 1977.
5. Harrison HR, English MG, Lee CK, and Alexander ER: Chlamydia trachomatis infant pneumonitis: Comparison with matched controls and other infant pneumonitis, N Engl J Med 298:702, 1978.
6. Chandler JW, Alexander ER, Pheiffer AT, et al: Ophthalmia neonatorum associated with maternal Chlamydia infections, Trans Acad Ophthalmol Otol 83:302, 1977.
7. Frankenberg WJ, et al: The Denver prescreening developmental questionnaire (PDQ), Pediatrics 57:744, 1976.
8. Wentworth BB, and Alexander ER: Isolation of Chlamydia trachomatis by use of 5-iodo-2-deoxyuridine-treated cells, Appl Microbiol 27:912, 1974.
9. Wang SP, Grayston JT, Kuo CC, Alexander ER, and Holmes KK: Serodiagnosis of Chlamydia trachomatis infection with the micro immunofluorescence test, *in* Hobson D, and Holmes KK, editors: Nongonococcal urethritis and related infections, Washington, D.C., 1977, Amer Soc Microbiology, pp 237-248.
10. Snedecor GW, and Cochran WG: Statistical methods, Ed 7, Ames, Iowa, 1972, Iowa State University Press.
11. Darougar S, Jones BR, Kinnison JR, Vaughan-Jackson JD, and Dunlop EMC: Chlamydial infection: Advances in the diagnostic isolation of Chlamydia, including TRIC agent, from the eye, genital tract, and rectum, Br J Vener Dis 48:416, 1972.
12. Wang SP, and Grayston JT: Local and systemic antibody response to trachoma eye infection in monkeys, *in* Nichols RL, editor: Trachoma and related disorders caused by chlamydial agents, Amsterdam, 1971, Excerpta Medica, pp 217-232.

GONORRHEA

Center for Disease Control Recommended Treatment Schedules* 1979

*These recommendations were established after deliberation with these therapy consultants: HC Neu, MD, College of Physicians and Surgeons, Columbia University; EH Braff, MD, San Francisco Dept of Public Health; G Cunningham, MD, Southwestern Medical School, Dallas; KK Holmes, MD, PhD, USPHS Hospital, Seattle; F Judson, MD, Dept of Health and Hospitals, Denver; W McCormack, MD, State Laboratory Institute, Boston; EM Mears, Jr, MD, New England Medical Center, Boston; JD Nelson, MD, Southwestern Medical School, Dallas; M Nelson, MD, Orange County, Calif.; SM Sgroi, MD, Suffield, Conn.; F Sparling, MD, School of Medicine, The University of North Carolina, Chapel Hill; Lt. Col. EC Tramont, Walter Reed Army Medical Center, Washington, D.C.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES / PUBLIC HEALTH SERVICE / CENTER FOR DISEASE CONTROL

GONORRHEA • CDC Recommended Treatment

Uncomplicated Gonococcal Infections in Men and Women

DRUG REGIMENS OF CHOICE

Aqueous procaine penicillin G (APPG): 4.8 million units injected intramuscularly at 2 sites, with 1.0 g of probenecid by mouth; **OR**

Tetracycline hydrochloride†: 0.5 g by mouth 4 times a day for 5 days (total dosage 10.0 g). Other tetracyclines are not more effective than tetracycline hydrochloride. All tetracyclines are ineffective as a single-dose therapy; **OR**

Ampicillin or amoxicillin: Ampicillin, 3.5 g, or amoxicillin, 3.0 g, either with 1 g probenecid by mouth. Evidence shows that these regimens are slightly less effective than the other recommended regimens.

Patients who are allergic to the penicillins or probenecid should be treated with oral tetracycline as above. Patients who cannot tolerate tetracycline may be treated with spectinomycin hydrochloride, 2.0 g, in 1 intramuscular injection.

SPECIAL CONSIDERATIONS

Single-dose treatment is preferred in patients who are unlikely to complete the multiple-dose tetracycline regimen. The APPG regimen is preferred in men with anorectal infection.

Pharyngeal infection is difficult to treat. High failure rates have been reported with ampicillin and spectinomycin.

Tetracycline treatment results in fewer cases of postgonococcal urethritis in men. It may eliminate coexisting chlamydial infections in men and women.

Patients with incubating syphilis (seronegative, without clinical signs of syphilis) are likely to be cured by all the above regimens except spectinomycin. All patients should have a serologic test for syphilis at the time of diagnosis.

Patients with gonorrhea who also have syphilis or are established contacts of syphilis patients should be given additional treatment appropriate to the stage of syphilis.

TREATMENT OF SEXUAL PARTNERS

Men and women exposed to gonorrhea should be examined, cultured, and treated at once with one of the regimens above.

FOLLOW-UP

Follow-up cultures should be obtained from the infected site(s) 3-7 days after completion of treatment. Cultures should be obtained from the anal canal of all women who have been treated for gonorrhea.

TREATMENT FAILURES

The patient who fails therapy with penicillin, ampicillin, amoxicillin, or tetracycline should be treated with 2.0 g of spectinomycin intramuscularly.

Most recurrent infections after treatment with the recommended schedules are due to *reinfection* and indicate a need for improved contact tracing and patient education. Since infection by penicillinase (β-lactamase)-producing *Neisseria gonorrhoeae* is a cause of treatment failure, posttreatment isolates should be tested for penicillinase production.

NOT RECOMMENDED

Although long-acting forms of penicillin (such as benzathine penicillin G) are effective in syphilotherapy, they have NO place in the treatment of gonorrhea. Oral penicillin preparations such as penicillin V are not recommended for the treatment of gonococcal infection.

Penicillinase-Producing *Neisseria Gonorrhoeae* (PPNG)

Patients with uncomplicated PPNG infections and their sexual contacts should receive spectinomycin, 2.0 g, intramuscularly in a single injection. Because gonococci are very rarely resistant to spectinomycin and reinfection is the most common cause of treatment failure, patients with positive cultures after spectinomycin therapy should be re-treated with the same dose.

A PPNG isolate that is resistant to spectinomycin may be treated with cefoxitin, 2.0 g, in a single intramuscular injection, with probenecid, 1.0 g, by mouth.

†Food and some dairy products interfere with absorption. Oral forms of tetracycline should be given 1 hour before or 2 hours after meals.

Treatment in Pregnancy

All pregnant women should have endocervical cultures for gonococci as an integral part of the prenatal care at the time of the first visit. A second culture late in the third trimester should be obtained from women at high risk of gonococcal infection.

Drug regimens of choice are APPG, ampicillin, or amoxicillin, each with probenecid as described above.

Women who are allergic to penicillin or probenecid should be treated with spectinomycin.

Refer to the sections on acute salpingitis and disseminated gonococcal infections for the treatment of these conditions during pregnancy. Tetracycline should not be used in pregnant women because of potential toxic effects for mother and fetus.

Acute Salpingitis (Pelvic Inflammatory Disease)

There are no reliable clinical criteria to distinguish gonococcal from nongonococcal salpingitis. Endocervical cultures for *N. gonorrhoeae* are essential. Therapy should be initiated immediately.

HOSPITALIZATION

In the following situations, hospitalization should be strongly considered: uncertain diagnosis, in which surgical emergencies such as appendicitis and ectopic pregnancy must be excluded; suspicion of pelvic abscess; severe illness; pregnancy; inability of patient to follow or tolerate an outpatient regimen; or failure of patient to respond to outpatient therapy.

ANTIMICROBIAL AGENTS

Outpatients: *Tetracycline**: 0.5 g, taken orally 4 times a day for 10 days. This regimen should not be used for pregnant patients; **OR**

APPG: 4.8 million units intramuscularly, ampicillin, 3.5 g, or amoxicillin, 3.0 g, each with probenecid, 1.0 g. Either regimen is followed by ampicillin, 0.5 g, or amoxicillin, 0.5 g, orally 4 times a day for 10 days.

Hospitalized patients: *Aqueous crystalline penicillin G*: 20 million units given intravenously each day until improvement occurs, followed by ampicillin, 0.5 g, orally 4 times a day to complete 10 days of therapy; **OR**

*Tetracycline**: 0.25 g, given intravenously 4 times a day until improvement occurs, followed by 0.5 g orally 4 times a day to complete 10 days of therapy. This regimen should not be used for pregnant women. The dosage may have to be adjusted if renal function is depressed.

Since optimal therapy for hospitalized patients has not been established, other antibiotics in addition to penicillin are frequently used.

SPECIAL CONSIDERATIONS

Failure of the patient to improve on the recommended regimens does not indicate the need for stepwise additional antibiotics, but requires clinical reassessment.

The intrauterine device is a risk factor for the development of pelvic inflammatory disease. The effect of removing an intrauterine device on the response of acute salpingitis to antimicrobial therapy and on the risk of recurrent salpingitis is unknown.

Adequate treatment of women with acute salpingitis must include examination and appropriate treatment of their sex partners because of their high prevalence of nonsymptomatic urethral infection. Failure to treat sex partners is a major cause of recurrent gonococcal salpingitis.

Follow-up of patients with acute salpingitis is essential during and after treatment. All patients should be recultured for *N. gonorrhoeae* after treatment.

Note: Physicians are cautioned to use no less than the recommended dosages of antibiotics.

Acute Epididymitis

Acute epididymitis can be caused by *N. gonorrhoeae, Chlamydia*, or other organisms. If gonococci are demonstrated by Gram stain or culture of urethral secretions, treatment should be APPG, 4.8 million units, ampicillin, 3.5 g, or amoxicillin, 3.0 g, each with probenecid, 1.0 g. Either regimen is followed by ampicillin, 0.5 g, or amoxicillin, 0.5 g, orally 4 times a day for 10 days; OR

Tetracycline*: 0.5 g, orally 4 times a day for 10 days.

If gonococci are not demonstrated, the above tetracycline regimen should be used.

Disseminated Gonococcal Infection

TREATMENT SCHEDULES

There are several, equally effective treatment schedules in the arthritis-dermatitis syndrome. These include the following.

Ampicillin/amoxicillin: ampicillin, 3.5 g, or amoxicillin, 3.0 g, orally, each with probenecid, 1.0 g, followed by ampicillin 0.5 g, or amoxicillin, 0.5 g, 4 times a day orally for 7 days; OR

Tetracycline*: 0.5 g, orally 4 times a day for 7 days. Tetracycline should not be used for complicated gonococcal infection in pregnant women; OR

Spectinomycin: 2.0 g, intramuscularly twice a day for 3 days (treatment of choice for disseminated infections caused by PPNG); OR

Erythromycin: 0.5 g, orally 4 times a day for 7 days; OR

Aqueous crystalline penicillin G: 10 million units intravenously per day until improvement occurs followed by ampicillin, 0.5 g, 4 times a day, to complete 7 days of antibiotic treatment.

SPECIAL CONSIDERATIONS

Hospitalization is indicated in patients who may be unreliable, have uncertain diagnosis, or have purulent joint effusions or other complications.

Open drainage of joints other than the hip is not indicated. Intra-articular injection of antibiotics is unnecessary.

MENINGITIS AND ENDOCARDITIS

Meningitis and endocarditis caused by the gonococcus require high-dose intravenous penicillin therapy. In penicillin-allergic patients with endocarditis, desensitization and administration of penicillin are indicated. Chloramphenicol may be used in penicillin-allergic patients with meningitis.

Gonococcal Infections in Pediatric Patients

With gonococcal infections in children beyond the newborn period, the possibility of sexual abuse must be considered. Genital, anal, and pharyngeal cultures should be obtained from all patients before antibiotic treatment. Appropriate cultures should be obtained from individuals who have had contact with the child.

*Food and some dairy products interfere with absorption. Oral forms of tetracycline should be given 1 hour before or 2 hours after meals.

Prevention of Gonococcal Ophthalmia

When required by state legislation or indicated by local epidemiologic considerations, effective and acceptable regimens for prophylaxis of neonatal gonococcal ophthalmia include ophthalmic ointment or drops containing tetracycline or erythromycin OR a 1% silver nitrate solution.

SPECIAL CONSIDERATIONS

Bacitracin is not recommended. The value of irrigation after application of silver nitrate is unknown.

Management of Infants Born to Mothers with Gonococcal Infection

The infant born to a mother with gonorrhea is at high risk of infection and requires treatment with a single intravenous or intramuscular injection of aqueous crystalline penicillin G, 50,000 units to full-term infants or 20,000 units to low-birth-weight infants. Topical prophylaxis for neonatal ophthalmia is not adequate treatment. Clinical illness requires additional treatment.

Neonatal Disease

GONOCOCCAL OPHTHALMIA

Patients should be hospitalized and isolated for 24 hours after initiation of treatment. Untreated gonococcal ophthalmia is highly contagious. Aqueous crystalline penicillin G, 50,000 units/kg/day, in 2 doses intravenously should be administered for 7 days. Saline irrigation of the eyes should be performed as needed. Topical antibiotic preparations alone are not sufficient or required when appropriate systemic antibiotic therapy is given.

COMPLICATED INFECTION

Patients with arthritis and septicemia should be hospitalized and treated with aqueous crystalline penicillin G, 75,000 to 100,000 units/kg/day, intravenously in 2 or 3 divided doses for 7 days. Meningitis should be treated with aqueous crystalline penicillin G, 100,000 units/kg/day, divided into 3 or 4 intravenous doses, and continued for at least 10 days.

Childhood Disease

Children who weigh 100 lbs. (45 kg) or more should receive adult regimens. Children who weigh less than 100 lbs. should be treated as follows.

UNCOMPLICATED DISEASE

Uncomplicated vulvovaginitis, urethritis, proctitis, or pharyngitis can be treated at 1 visit with amoxicillin, 50 mg/kg, orally with probenecid, 25 mg/kg (maximum 1.0 g), OR with aqueous procaine penicillin G, 100,000 units/kg, intramuscularly plus probenecid, 25 mg/kg (maximum 1.0 g).

SPECIAL CONSIDERATIONS

Topical and/or systemic estrogen therapy are of no benefit in vulvovaginitis. Long-acting penicillins, such as benzathine penicillin G, are not effective. All patients should have follow-up cultures, and the source of infection should be identified, examined, and treated.

GONOCOCCAL OPHTHALMIA

Ophthalmia in children is treated as in neonates, but the dose of penicillin is increased to 100,000 units/kg/day intravenously.

COMPLICATED INFECTIONS

Patients with peritonitis or arthritis require hospitalization and treatment with aqueous crystalline penicillin G, 100,000 units/kg/day, intravenously for 7 days. Aqueous crystalline penicillin G, 250,000 units/kg/day, intravenously in 6 divided doses for at least 10 days, is recommended for meningitis.

ALLERGY TO PENICILLINS

Children who are allergic to penicillins should be treated with spectinomycin, 40 mg/kg, intramuscularly. Children older than 8 years may be treated with tetracycline, 40 mg/kg/day, orally in 4 divided doses for 5 days. For treatment of complicated disease, the alternative regimens recommended for adults may be used in appropriate pediatric dosages.

AMERICAN ACADEMY OF PEDIATRICS

Committee on Drugs
Committee on Fetus and Newborn
Committee on Infectious Diseases

Prophylaxis and Treatment of Neonatal Gonococcal Infections

The Center for Disease Control (CDC), after consultation with a panel of experts, has revised its recommendations for prevention of gonococcal ophthalmia neonatorum. These recommendations now state, "ophthalmic ointment or drops containing tetracycline or erythromycin or a 1% silver nitrate solution" are effective and acceptable.[1-3] This is a change from previous recommendations which highlighted silver nitrate as the primary agent for prophylaxis.[4] The American Academy of Pediatrics' committees support these recommendations.

The prevalence of largely asymptomatic genital gonococcal infection in pregnant women and the occurrence of gonococcal ophthalmia in untreated infants (estimated at 28%)[5] born to infected women indicate the need for continued prophylaxis for all newborn infants.

Some clinicians have argued that silver nitrate prophylaxis immediately after delivery may, in theory, impair maternal-infant bonding by reducing eye contact.[6,7] Although it is well-known that silver nitrate, with or without subsequent flushing, results in a high frequency of chemical conjunctivitis,[8,9] other agents, particularly ointments, may also impair vision temporarily and affect the appearance of the infant.

In view of the available information about the prophylaxis of gonococcal ophthalmia neonatorum and treatment of infected infants, the American Academy of Pediatrics makes the following recommendations:

1. A 1% silver nitrate solution in single-dose ampules or single-use tubes of an ophthalmic ointment containing 1% tetracycline or 0.5% erythromycin are effective and acceptable regimens for prophylaxis of gonococcal ophthalmia neonatorum.

2. None of the agents used for prophylaxis should be flushed from the eye following instillation. Critical studies have not evaluated the efficacy of silver nitrate prophylaxis with and without flushing, but anecdotal reports suggest that flushing may reduce the efficacy of prophylaxis. In addition, flushing probably does not reduce the incidence of chemical conjunctivitis.[5]

3. Prophylaxis should be given shortly after birth. No studies have evaluated the effect of delaying prophylaxis on its efficacy. Some authors suggest prophylaxis may be administered more effectively in the nursery than in the delivery room.[10] Although definitive data are not available, delaying prophylaxis for up to one hour after birth probably will not affect efficacy and should facilitate initial maternal-infant attachment. *Hospitals in which prophylaxis is delayed should establish a check system to ensure that all infants are treated.*

4. Infants born by cesarean section should also receive prophylaxis against gonococcal ophthalmia. Although gonococcal infection is usually transmitted during passage through the birth canal, ascending infection also occurs. However, the precise risk of gonococcal infection in untreated infants born by cesarean section has not been determined.

5. Most infants born to mothers with clinically apparent gonorrhea are prevented from developing gonococcal ophthalmia with current modes of prophylaxis. However, an occasional case of gonorrheal ophthalmia may occur in such infants.[5,11-13]

Therefore, intravenous or intramuscular aqueous crystalline penicillin G should be administered to these infants. A single dose of 50,000 units for term or 20,000 units for low-birth-weight infants is rec-

PEDIATRICS (ISSN 0031 4005). Copyright © 1980 by the American Academy of Pediatrics.

ommended. Topical prophylaxis alone is inadequate for these infants.

6. Infants with clinical evidence of ophthalmia or complicated (disseminated) gonococcal infection should be hospitalized under isolation and treated appropriately. Because gonococcal ophthalmia is highly contagious, infected infants must be managed with either wound and skin precautions[14] or secretion precautions[15] for 24 hours after initiation of treatment with aqueous crystalline penicillin G, 50,000 units/kg body weight daily in two doses intravenously for seven days. The eyes should be irrigated with saline. Topical antibiotics are superfluous when appropriate systemic antibiotic therapy is given. Ophthalmologic consultation is suggested. Infants with extraocular gonococcal infections such as arthritis or septicemia, should be treated with aqueous crystalline penicillin G, 75,000 to 100,000 units/kg body weight daily in two to three doses intravenously for seven days. Infants with gonococcal meningitis should also be treated with aqueous crystalline penicillin G, 100,000 units/kg body weight daily in three to four doses intravenously for at least ten days. Note: The emergence of strains of *Neisseria gonorrhoeae* resistant to penicillin must be recognized. Attempts should be made to isolate the organism from the mother and the child so antibiotic sensitivity can be determined. If other forms of antimicrobial therapy become necessary because of a poor clinical response to penicillin, these sensitivities would be available as a therapeutic guide.

7. Gonococcal infections in pregnant women, even though they are asymptomatic, may be associated with fetal wastage, early and prolonged rupture of membranes, premature labor, and delivery of low-birth-weight infants.[11,16] They also may result in sepsis or scalp abscess if intrauterine fetal monitoring is used.[12,13] Failure to treat an infected woman before or at the time of delivery may result in transmission of gonococcal infection postnatally to infants who escape infection at delivery.

COMMITTEE ON DRUGS
Sydney Segal, MD, Chairman
Walter B. Anyan, Jr, MD
Reba M. Hill, MD
Ralph E. Kauffman, MD
Howard Mofenson, MD
Albert W. Pruitt, MD
Henry R. Shinefield, MD
Harvey S. Singer, MD
Miles M. Weinberger, MD

COMMITTEE ON FETUS AND NEWBORN
Alfred W. Brann, MD, Chairman
Robert T. Hall, MD
Rita G. Harper, MD
George A. Little, MD
M. Jeffrey Maisels, MD
George H. McCracken, MD
Ronald Poland, MD
Philip Sunshine, MD
John A. Whittinghill, MD

COMMITTEE ON INFECTIOUS DISEASES
Edward A. Mortimer, Jr, MD, Chairman
Vincent A. Fulginiti, MD
Philip A. Brunell, MD
Ernesto Calderon, MD
James D. Cherry, MD
Walton L. Ector, MD
Anne A. Gershon, MD
Samuel P. Gotoff, MD
Walter T. Hughes, Jr, MD
Georges Peter, MD

REFERENCES

1. Center for Disease Control: Gonorrhea. CDC recommended treatment schedules. *Morbidity Mortality Weekly Rep* 28: 13, 1979
2. Center for Disease Control: Gonorrhea, CDC recommended treatment schedules. *Ann Intern Med* 90:809, 1979
3. Center for Disease Control: Gonorrhea, CDC recommended treatment schedules. *J Infect Dis* 139:496, 1979
4. Center for Disease Control: Silver nitrate prophylaxis for gonococcal ophthalmia neonatorum. *Morbidity Mortality Weekly Rep* 27:107, 1978
5. Davidson HH, Hill J, Eastman JJ: Penicillin in the prophylaxis of ophthalmia neonatorum. *JAMA* 145:1052, 1951
6. Butterfield PM, Emde RN, Platt BB: Effects of silver nitrate on initial visual behavior. *Am J Dis Child* 132:426, 1978
7. Klaus MH, Jerauld R, Kreger NC, et al: Maternal attachment: Importance of the first postpartum days. *N Engl J Med* 286:460, 1972
8. Nishida H, Risemberg HM: Silver nitrate ophthalmic solution and chemical conjunctivitis. *Pediatrics* 56:368, 1975
9. Yasunaga S, Kean EH: Effect of three ophthalmic solutions on chemical conjunctivitis in the neonate. *Am J Dis Child* 131:159, 1977
10. Pierog S, Nigam S, Marasigan DC, et al: Gonococcal ophthalmia neonatorum. *Am J Obstet Gynecol* 122:589, 1975
11. Handsfield HH, Hodson WA, Holmes KK: Neonatal gonococcal infection. *JAMA* 225:697, 1973
12. Thadepalli H, Rambhatla K, Maidman JE, et al: Gonococcal sepsis secondary to fetal monitoring. *Am J Obstet Gynecol* 126:510, 1976
13. Plavidal FJ, Werch A: Gonococcal fetal scalp abscess: A case report. *Am J Obstet Gynecol* 127:437, 1977
14. *Infection Control in the Hospital*, ed 4. Chicago, American Hospital Association, 1979, pp 88–99
15. *Isolation Techniques for Use in Hospitals*, ed 2. DHEW Publication No (CDC) 78-8314. Center for Disease Control 1978
16. Amstey MS, Steadman KT: Asymptomatic gonorrhea in pregnancy. *J Am Vener Dis Assoc* 3:14, 1976

LIBRARY
MINNESOTA DEPARTMENT OF HEALTH
717 Delaware Street S. E.
Minneapolis, Minnesota 55440
APR 7 1978

Attachment #5

CENTER FOR DISEASE CONTROL

MMWR

MORBIDITY AND MORTALITY WEEKLY REPORT

March 31, 1978 / Vol. 27 / No. 13

Current Trends

Silver Nitrate Prophylaxis for Gonococcal Ophthalmia Neonatorum

The National Society for the Prevention of Blindness and the American Academy of Pediatrics have stated in recent years that infants' eyes should *not* be irrigated after instillation of 1% silver nitrate ($AgNO_3$) (*1,2*). The package insert from the drug manufacturer also states that irrigation (usually done with normal saline or distilled water) is not recommended.

Maine's Department of Human Services--noting that many hospitals are irrigating infant's eyes, apparently to minimize the chemical conjunctivitis caused by $AgNO_3$—conducted a survey in March 1977 to determine how widespread this practice is. The nursery or delivery suite supervisor was contacted by telephone in all Maine hospitals that deliver babies. Of 44 hospitals 23 (52%) still used irrigation; 11/44 (25%) specified that they had no definite policy on this matter. Thus, 10/44 (23%) of hospitals were acting according to present recommendations. The survey also revealed that a few hospitals routinely used penicillin ophthalmic solutions instead of $AgNO_3$, although the latter is required by Maine law. After the survey a letter was circulated to hospitals to correct the practices.

Reported by K Hill, MD, Waterville; E Johnson, WS Nersesian, MD, Acting State Epidemiologist, Maine Dept of Human Services; Clinical Research Sect, Venereal Disease Control Div, Bur of State Services, CDC.

Editorial Note: The chemical conjunctivitis caused by $AgNO_3$ drops is self-limiting, usually resolving within 24-48 hours. It is less severe if the drops are stored in individual wax ampules. This procedure minimizes evaporation, which would increase the concentration of the solution.

CDC's gonorrhea treatment recommendations include the use of $AgNO_3$ without saline rinse for all newborn infants (*3*). $AgNO_3$ prophylaxis appears to be more effective in preventing gonococcal ophthalmia neonatorum (GC-ON) than saline eye washings or no prophylaxis (*4-7*). $AgNO_3$ prophylaxis is not 100% effective, however, as shown in 1 study of 46 cases of gonococcal ophthalmia which occurred in spite of some form of $AgNO_3$ prophylaxis (*8*). Nevertheless, according to that study the risk of GC-ON developing in an infant born to an infected mother was less than 2% when $AgNO_3$ was used.

The occurrence of GC-ON in spite of the use of $AgNO_3$ may be caused by several factors: (1) improper application, (2) washing with water or saline, (3) silver cation precipitation by saline to form silver chloride crystals, (4) infection of the eyes before delivery because of premature rupture of the membranes in an infected woman, and (5) failure to treat an infected mother with subsequent transmission to her infant after the delivery.

Well-designed studies are needed to investigate other preparations which may be useful as prophylaxis against GC-ON. Other possibly effective agents have either not been adequately studied (tetracycline and erythromycin), are less effective (bacitracin), or have serious adverse effects, such as sensitization (penicillin). The possibility of infection with a penicillinase-producing gonococcus also exists.

In addition to proper instillation of $AgNO_3$ without rinsing, other measures are essential in preventing GC-ON, including: (1) prenatal screening of pregnant women at their initial visits and before delivery, (2) appropriate evaluation of all neonatal conjunctival discharges with Gram stain and culture, and (3) continuing education for obstetric and pediatric personnel who will be required to diagnose and manage this complication.

References

1. National Society for the Prevention of Blindness: Control of ophthalmia neonatorum: A position statement. Sight Sav Rev 43:11-13, 1973
2. American Academy of Pediatrics: The Report of the Committee on Infectious Diseases. Evanston, Illinois, American Academy of Pediatrics, 1977, p 107
3. MMWR 23:341, 1974
4. Mann I: Clinical observations on prophylaxis of ophthalmia neonatorum. Br J Ophthalmol 38:734, 1954
5. Greenberg M, Vanden JE: Ophthalmia neonatorum: Evaluation of different methods of prophylaxis in New York City. Am J Public Health 51:836, 1961
6. Pearson HE: Failure of silver nitrate prophylaxis for gonococcal ophthalmia neonatorum. Am J Obstet Gynecol 73:804, 1957
7. Mellin GW, Kent MP: Ophthalmia neonatorum. Is prophylaxis necessary? Pediatrics 22:1006, 1958
8. Armstrong JH, Zacarias F, Rein MF: Ophthalmia neonatorum: A chart review. Pediatrics 57:884, 1976

Plague Vaccine – Continued

Chen TH, Meyer KF: An evaluation of *Pasteurella pestis* fraction-1-specific antibody for the confirmation of plague infections. Bull WHO 34:911-918, 1966

Marshall JD Jr, Bartelloni PJ, Cavanaugh DC, et al: Plague immunization. II. Relation of adverse clinical reactions to multiple immunizations with killed virus. J Infect Dis 129(Suppl):S19-S25, 1974

Marshall JD Jr, Cavanaugh DC, Bartelloni PJ, et al: Plague immunization. III. Serologic response to multiple inoculations of vaccine. J Infect Dis 129(Suppl):S26-S29, 1974

Published in MMWR 17:171, 1968; reprinted 18(43 Suppl):14, 1969; revised 21(25 Suppl): 19-20, 1972.

Current Trends

Clarification: Silver Nitrate Prophylaxis for Gonococcal Ophthalmia Neonatorum

Following the publication of an article in the MMWR entitled, "Silver Nitrate Prophylaxis for Gonococcal Ophthalmia Neonatorum," several inquiries have been directed to CDC regarding a statement in the editorial note (*1*). The sentence (in the second column, second paragraph), which concerned the need for investigation of prophylactic preparations against gonococcal ophthalmia neonatorum, read: "Other possibly effective agents have either not been adequately studied (tetracycline and erythromycin), are less effective (bacitracin), or have serious adverse effects, such as sensitization (penicillin)." It should be changed to read: "Other agents for topical eye prophylaxis have either been less adequately studied (tetracycline and erythromycin), are less effective (bacitracin), or may cause sensitization (penicillin or neomycin)."

No proven cases of penicillin anaphylaxis in newborns from either topical or systemic administration of the drug have been reported to CDC. Sensitization of newborns by penicillin or neomycin eye prophylaxis is a distinct but unproven possibility.

Reported by the Venereal Disease Control Div, Bur of State Services, CDC.

Reference

1. MMWR 27:107, 1978

Erratum, Vol. 27, No. 25

p214 In the article, "Malaria in Participants of a Natural History Safari to Kenya, Africa," the 10th line of the first paragraph of the editorial note indicated that the weekly dose of chloroquine used for malaria prophylaxis is 550 mg. The correct figure is 500 mg.

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE / CENTER FOR DISEASE CONTROL
ATLANTA, GEORGIA 30333 OFFICIAL BUSINESS

Postage and Fees Paid
U.S. Department of HEW
HEW 396

Director, Center for Disease Control
William H. Foege, M.D.
Director, Bureau of Epidemiology
Philip S. Brachman, M.D.
Editor
Michael B. Gregg, M.D.
Managing Editor
Anne D. Mather, M.A.
Chief, MMWR Statistical Activity
Dennis J. Bregman, M.S.

Library 421S
Minnesota Dept. of Health
717 Delaware St. SE
Minneapolis, MN 55440

HEW Publication No. (CDC) 78-8017 Redistribution using indicia is illegal.