Chlamydial ocular infection

Chlamydial ocular infection is the commonest cause of ocular morbidity and blindness. It is divided into trachoma of eye to eye transmission, which is hyperendemic in rural populations of developing countries, and paratrachoma of genital to eye transmission which is endemic in urban populations of developed countries.

Chlamydiae are obligate intracellular bacteria which grow in the cytoplasm of epithelial cells, producing inclusion bodies which contain non-infectious reticulate bodies and infectious elementary bodies. There are two species; Chlamydia trachomatis which is a human pathogen, causing ocular, genital and systemic infections, and Chlam. psittaci, which is pathogenic for other mammals and birds, but occasionally causing ocular and systemic infections in man. Chlam. trachomatis is divided into various serotypes; TRIC (TR for trachoma and IC for inclusion conjunctivitis) agent serotypes A, B and C, (generally responsible for trachoma) and serotypes D, E, F, G, H, I, J and K generally responsible for genital and associated ocular and systemic infections and lymphogranuloma venereum (LGV) agent serotypes 1, 2 and 3.

Trachoma, a chronic follicular conjunctivitis, is hyperendemic in the rural communities of the Middle East, Africa, Asia, Southern and Central America. In some villages, the entire population is affected, some with active disease and others with complications. A total of 500 million people are affected. About 5 to 10 million of these are blind, and many more millions are in danger of becoming blind. Blindness caused by trachoma is totally preventible.

Trachoma affects both eyes. It presents in various clinical forms. In young babies, it appears as a moderate to severe papillary conjunctivitis without pannus or scarring, resembling neonatal chlamydial ophthalmia (TRIC ophthalmia neonatorum). In young children, trachoma appears in its classical form, as a chronic follicular conjunctivitis of the upper tarsal conjunctiva, associated with active pannus. In older children and young adults, follicular responses and conjunctival scarring may both be present. McCollan divided the clinical course of the disease into four stages. However, this classification is of limited value because it does not indicate the degree of severity of trachoma or the blinding complications. The new method of grading for the severity of trachomatous inflammatory and blinding complications, proposed by Dawson, Jones & Darougar (1975), is much more satisfactory.

The most important complications of trachoma are severe conjunctival scarring, entropion and trichiasis. These result in misdirected lashes which abrade the cornea, causing ulcers, leading to scarring and loss of vision. These complications generally occur in patients over 40 years old, although they occasionally occur in young mothers of children who have severe trachoma.

From the epidemiological viewpoint, trachoma can be divided into two categories; blinding and non-blinding disease (Dawson et al., 1975). Non-blinding trachoma is associated with a low prevalence of mild or moderate trachoma and the absence of trichiasis, entropion and corneal scars. This type of trachoma is endemic in areas with improving standards of living and hygiene. Blinding trachoma is characterized by a high prevalence of severe disease and blinding complications. It is generally associated with overcrowding, poor standards of living, lack of sanitation and sub-standard levels of hygiene and medical care. Under these conditions, babies contract trachoma at an early age (two to three months). Pre-school children have a high prevalence of severe disease, and a proportion of adults, particularly those living in large families with several young children, have active diseases. Children are the main reservoir of infection, harbouring high numbers of infectious particles and continuously shedding agent in their eye secretions (Darougar et al., 1979).

Chlamydial particles can be transmitted by flies, fingers, towels or bed clothes. It has been shown that flies rapidly transmit ocular discharges from one patient to another and carry viable chlamydial particles (Jones, 1975). We have found that under laboratory conditions, flies transmit chlamydial infection from one animal to another (Forsey & Darougar, 1981).

The distinction between blinding and non-blinding trachoma is of great importance. In organizing programmes for prevention of trachoma, it is essential to direct scarce resources of man-power, drugs and equipment to areas of blinding trachoma where they are most needed.

Why does trachoma cause blinding lesions under certain conditions? Primary experimental infection of human volunteers and
animals with trachoma agent produces a moderate to severe but self-limiting follicular conjunctivitis with no pannus or scarring. But when such patients or animals are re-infected, they develop pannus, scarring and lid deformities (Jones, 1960; Tarizzo, Nataf & Nabli, 1967; Wang & Grayston, 1967). The observations suggest that re-infection may play an important role in the development of complications. Studies of guinea pigs infected with guinea pig inclusion conjunctivitis agent (Chlam. psittaci) indicate that delayed-type hypersensitivity to Chlamydia may play an important role in the development of scarring, pannus and lid deformities. Primary infection produces an acute conjunctivitis lasting for four to six weeks, with many chlamydial inclusions, but does not produce pannus or scarring (Monnickendam et al., 1980a). When animals are re-infected they develop a delayed-type hypersensitivity to the agent. Multiple re-infection causes chronic disease which continues for months leading to scarring, pannus and lid deformities (Monnickendam et al., 1980b). These studies suggest that the various clinical forms of trachoma which are found in babies, children and adults may reflect changes in the immunological status of the host as a result of multiple re-infection.

Paratrachoma of genital to eye transmission comprises neonatal chlamydial ophthalmia (NCO) or TRIC ophthalmia neonatorum, and adult chlamydial ophthalmia (ACO) or inclusion conjunctivitis. These infections are generally associated with chlamydial urethritis (non-gonococcal urethritis) or chlamydial cervicitis (non-gonococcal genital infection) which are probably the commonest sexually transmitted diseases. Paratrachoma is becoming more common because of the increasing incidence of chlamydial genital infection.

NCO is an acute papillary conjunctivitis, which is acquired through the infected cervix of the mother. The incidence of NCO is dependent on the prevalence and activity of infection in the cervix of mothers. Nearly 50% of babies born to mothers with isolation positive chlamydial cervicitis may develop the infection (Alexander et al., 1977). The incubation period of NCO is usually about five to seven days, but it can vary between one to 40 days. One or both eyes may be infected. NCO is associated with profuse watering and muco-purulent discharge, swelling of the lids, hyperaemia, oedema and papillary responses in the conjunctiva. The cornea usually remains normal (Freedman et al., 1966). In untreated babies, the infection may become chronic and continue for several months or years. In such cases follicles, pannus and scarring may develop. Mild and sub-clinical forms of NCO have also been reported. Babies with NCO may develop rhinitis, pharyngitis, pneumonia (Beem & Saxon, 1977; Dunlop et al., 1980) and genital infections (Dunlop et al., 1966).

ACO usually occurs in young adults (15 to 40 years old) and is associated with chlamydial genital infection. Chlam. trachomatis can be isolated from the cervix of most women and from the urethra of about half of the men with ACO. Transmission is from the genital tract to the eye probably by fingers or towels. Patients with ACO are generally sexually active, often have multiple sexual consorts and a history of other sexually transmitted diseases.

ACO is a chronic follicular conjunctivitis of acute onset. The incubation period is about one week and the infection is unilateral in about 70% of cases. It is associated with watering, discharge, foreign body sensation, photophobia and redness. The infection may present as inclusion conjunctivitis (IC), TRIC punctate keratoconjunctivitis (TPK) or occasionally as trachoma (TR). IC is the commonest form, and is associated with papillary responses, which are more severe in the upper tarsal conjunctiva, and follicles, which are more numerous and larger in the lower lid conjunctiva and in the fornices. The cornea occasionally develops mild to moderate fine punctate keratitis. TPK is similar to IC, with coarse sub-epithelial punctate keratitis in addition. The keratitis presents as large, discrete opacities in the superficial stromal area of the cornea which are very similar to the sub-epithelial opacities associated with ocular adenovirus infection. Occasionally, patients with ACO develop pannus and scarring similar to trachoma (Jones, 1964). This occurs only in patients who develop chronic infection following multiple recurrences, or re-infections.

Chlamydial agents other than Chlam. trachomatis serotypes A to K can also cause ocular infection. LGV agents and psittacosis agent cause an acute but transient papillary conjunctivitis. Feline keratoconjunctivitis (FKC) agent, a member of Chlam. psittaci, causes a chronic follicular conjunctivitis (Schachter, Ostler & Meyer, 1969) similar to paratrachoma. The reservoir of infection is
domestic cats with conjunctivitis. In London, we have isolated this agent from the eyes of patients with follicular conjunctivitis and from the eyes of their domestic cats. In recent years, we have isolated a few strains of *Chlam. psittaci* from the eyes of patients with moderate to severe follicular conjunctivitis. These isolates are serotypically different from other strains of *Chlam. psittaci* known to be pathogenic for man (Darougar et al., in preparation).

In the last decade, laboratory diagnostic methods for chlamydia infections have improved considerably. Cytological tests for the direct demonstration of chlamydial inclusions, using immunofluorescent, Giemsa or iodine staining techniques provide a rapid diagnostic test with only moderate sensitivity (Darougar et al., 1971). Of these methods, immunofluorescence is the most sensitive. In recent years, several cell culture systems have been developed for isolation of Chlamydia. These are based on the chemical or physical treatment of cells, and centrifugation of specimens onto cell monolayers. Commonly used systems are HeLa 229 cells treated with diethylaminoethyl-dextran (Kuo et al., 1972), or McCoy cells treated with ionizing radiation (Gordon et al., 1969), 5-iodo-2-deoxyuridine (Wentworth & Alexander, 1974) or cycloheximide (Ripa & Mardh, 1977). These systems are equally sensitive for chlamydial isolation. Using irradiated McCoy cells, we have isolated *Clam. trachomatis* from up to 90% of patients with NCO and ACO, and from up to 73% of patients with severe trachoma (Darougar et al., 1977).

The micro-IF test provides a sensitive test for the detection of different immunoglobulin classes of type-specific chlamydial antibodies in blood and local discharges. A modified micro-IF test (Treharne, Darougar & Jones, 1977) using four pools of antigens of *Chlam. trachomatis* and *Chlam. psittaci* has been used extensively for sero-epidemiological surveys of chlamydial infections. This test can also be used for a presumptive diagnosis of ocular (Darougar et al., 1978) or genital (Treharne et al., 1978) infections based on the presence of IgM in the blood or the presence of IgG or IgA in local discharges. Finger-prick blood samples or local discharges are collected on small cellulose sponges which can be sent to the laboratory without cold storage.

*Clam. trachomatis* is sensitive to a number of antimicrobial drugs. Antibiotic sensitivity tests in cell cultures have shown that tetracyclines, rifampicin and macrolides are the most potent antichlamydial drugs. The sulphonamides are active against *Chlam. trachomatis* but not against *Chlam. psittaci* (Ridgway, Owen & Oriel, 1976; Treharne et al., 1977).

Trachoma and paratrichoma both respond well to topical or systemic treatment with antichlamydial drugs. Topical treatment with tetracyclines, erythromycin or rifampicin eye ointments three times daily for five weeks, cures up to 90% of patients. Systemic treatment with tetracyclines or erythromycin 15 mg/kg of body weight daily or doxycycline 1-5 mg/kg daily or sulphametapyrazine 30 mg/kg once a month for a period of two weeks is equally effective.

In areas of blinding trachoma, large scale identification of patients and implementation of eradication treatment is impractical. Intermittent topical therapy of the total population, or of the population at risk, with tetracycline eye ointment twice daily for five to seven days each month, or systemic treatment with doxycycline 5 mg/kg of body weight once a month, or sulphametapyrazine 30 mg/kg once a month for a period of four to six months during the high transmission season is recommended. Studies in southern Iran have shown that topical or systemic intermittent treatment reduces the severity of trachoma, and the shedding of chlamydial particles in eye discharges, which considerably reduces the rate of transmission of trachoma (Darougar et al., 1980). In these communities, the reduction in the rate of infection and re-infection, supplemented by promotion of health education and rising standards of hygiene and medical care, can convert trachoma into a non-blinding disease.

In babies with NCO, systemic treatment with erythromycin, with or without additional topical treatment is preferable because of a high failure rate of the topical treatment. Parents of these babies should be investigated and treated accordingly. In patients with ACO, systemic treatment with tetracyclines, macrolides or sulphonamides is strongly recommended because of the associated chlamydial genital infection. It is important to investigate and treat the sexual consorts of these patients.

S. DAROUGAR
Sub-department of Virology.
Institute of Ophthalmology.
Judd Street.
London WC1H 9QS
References


