

## Severe endemic trachoma in Tunisia

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Since trachoma responds to some antibiotics and sulphonamides that have been available for a generation, it has been assumed that it would by now have undergone the same precipitous decline in prevalence as syphilis and tuberculosis. The areas in which this happy expectation has been borne out, however, are only those that have enjoyed economic development (Assaad, Maxwell-Lyons, and Sundaresan, 1969; Blagojevic, Savic, and Litricin, 1973). For example, we found only 30 cases of active disease among 2800 school-children recently surveyed for trachoma in Tunis. In contrast, the examination of children of the same age in a southern Tunisian oasis uncovered active trachoma in 85 per cent (Dawson, Daghfous, Messadi, Hoshiwara, Vastine, Yoneda, and Schachter, 1974).

This continuing high prevalence in economically undeveloped areas poses an especially grave public health problem which is disguised by the simple statement of overall prevalence rates. Because of widespread general improvement in public health programmes there has been an enormous increase in the number of people aged under 15 years, and it is this age group, burgeoning in rural areas affected by trachoma, that harbours the seeds of a future dramatic increase in blindness. This is preventable blindness, however, since active infectious trachoma responds to sulphonamides, the tetracyclines, and erythromycin. For this cogent reason the disease should now be vigorously attacked in undeveloped rural areas, where it continues to be both endemic and severe.

The study reported here was undertaken to quantify the prevalence of trachoma and its sight-threatening sequelae in two rural populations—one just beginning to develop economically, the other still with a traditional rural economy. The pattern of trachoma and its visually disabling lesions in these communities is probably characteristic of its pattern in endemic areas the world

over. Information on the intensity and disabling complications of the disease in such communities is essential if the success of treatment is to be judged with any accuracy and if programmes are to be developed that yield the best results within the limitations of the available economic and human resources.

### Population and methods

Two oasis villages in southern Tunisia were selected. One of them (Chott Sidi Abdel Sellem) was near a large town in which the pace of economic development had been accelerating for the five years before this study was undertaken. The second village (El Golaâ) was a pre-Saharan oasis whose economy was based on traditional agriculture—the cultivation of dates and vegetables on irrigated land. The climatic and certain demographic features of the two villages are summarized in Table I. Many of the men from both villages worked in other parts of Tunisia or in Europe and usually remitted part of their earnings to their families. Most of the houses were constructed of earth and

**Table I** *Climate, population, and income in two Tunisian villages, Chott and El Golaâ*

	<i>Chott</i>	<i>El Golaâ</i>
Temperature		
January		
Maximum	24°C (75°F)	24°C (75°F)
Minimum	12°C (54°F)	-3°C (27°F)
July		
Maximum	41°C (105°F)	44°C (111°F)
Minimum	24°C (75°F)	21°C (70°F)
Rainfall		
December 1970	77 mm (3 in)	32.5 mm (1.3 in)
Population		
Total	1962	1880
Percentage aged < 14 years	49.6 per cent	52.2 per cent
Annual income/person	\$120	\$109

located outside the shady, cultivated part of the oasis. Artesian drinking water was obtained from public fountains, often some distance from the houses. Above-ground latrines were located near most houses and in the fields.

In both villages the relatively high mortality rate from infectious diseases in infancy and childhood had been dropping steadily, and children under 15 years of age constituted about one-half of the resident population. In each village there was a 'dispensaire' who distributed medications for common conditions. The consumption of tetracyclines (usually for gastroenteritis) and penicillin (usually for fevers and respiratory diseases) is shown in Table II. A physician visited Chott twice a week and El Golaâ once a week. Chott was near a town (Gabès) with a well-equipped regional hospital and readily accessible facilities, whereas El Golaâ was 28 km from a small satellite hospital with one physician and small staff who cared for a population of some 36 000.

Among young children in both villages (as in other communities in the region) an acute mucopurulent conjunctivitis began each year in May, reached an epidemic peak in October, and subsided with the onset of cooler weather (Huet, 1958; Vastine, Dawson, Daghfous, Messadi, Hoshiwara, Yoneda, and Nataf, 1974a). During the epidemic flies (for the most part *Musca* sp) were numerous. They clustered on the children's eyes and particularly on those with purulent conjunctivitis. This pattern of seasonal epidemics of purulent conjunctivitis has been well described in trachomatous areas of North Africa and the Middle East (Huet, 1958; Maxwell-Lyons and Amies, 1949).

A complete census of each village was made by a public health nurse familiar with trachoma control programmes and himself an inhabitant of the region. In addition to a record of the age, sex, family interrelationships, and primary occupation of each member of the family the census included information on each house about the type of construction, the water supply, the number of rooms, and the method of disposing of excreta.

#### CLINICAL EXAMINATION

We made all clinical observations with the standard biomicroscope (slit-lamp) and recorded the following signs (suggested for the 'short' examination by the Fourth Scientific Group on Trachoma (World Health

Organization, 1966a)): trichiasis and/or entropion, lymphoid follicles on the upper tarsal conjunctiva, mature tarsal follicles, papillary hypertrophy on the upper tarsal plate, conjunctival scarring, superficial corneal vascularization (vascular pannus), corneal infiltration, corneal scarring, trachoma stage according to the MacCallan classification, and mucopurulent conjunctivitis.

Since the definition and scoring of lymphoid follicles on the upper tarsal conjunctiva given by the WHO (World Health Organization, 1966a) can be interpreted in different ways by different observers we used a modified definition for this sign, which is described elsewhere (Dawson, Elashoff, Hanna, and Wood, 1968). Two other departures from established WHO practice were the tabulation of trichiasis and/or entropion as a separate sign, and the measurement of the person's visual acuity at the time of the first examination.

We recorded the clinical findings for each patient on a standard form at the time of examination and later transferred the data to Holerith-type punch cards for processing.

#### STRATIFICATION OF CASES BY CLINICAL INTENSITY

Since the MacCallan classification of trachoma does not adequately describe the intensity of the clinical disease a simple stratification of cases was devised. From the recorded clinical scores of lymphoid follicles (F) and papillary hypertrophy (P) on the upper tarsal conjunctiva the intensity of the conjunctival inflammatory disease was classified as severe, moderate, mild, or inactive, as follows

	Follicles	Papillary hypertrophy
Severe	1, 2, 3	3
Moderate	3	2
Mild	3 or 2	1 1, 2
Insignificant or inactive	0, 1	1, 2

#### SCHEDULE OF EXAMINATIONS OF POPULATION SAMPLED

Starting in the autumn of 1969 and continuing through the winter and spring of 1970 one of us (MM) examined the entire population of both villages. A subsample of some 20 to 25 families was selected in each village, a total of 220 residents of Chott and 180 of El Golaâ. Only families in which there was a preschool-age child with active trachoma were selected. The sample was thus deliberately biased in favour of families with active trachoma and children. The families in these two subsamples were re-examined once or twice a year by two examiners working independently.

#### LABORATORY STUDIES

To detect the infective load of trachoma agent we took conjunctival scrapings from the children under 15 in the subsample at the initial and all subsequent examinations and stained them with either Giemsa or fluorescent antibody, as described elsewhere (Dawson and others, 1974). Material for bacterial culture was also taken from the eyes of this group (Vastine, Dawson, Hoshiwara,

**Table II** *Antibiotic consumption and medical care in Chott and El Golaâ (1970)*

	Chott	El Golaâ
Tetracyclines, doses* (250-mg or 100-mg tablets or 20-mg solution)	1023	404
Penicillin, doses* (1 000 000 or 500 000 units)	961	725
Medical care		
No. visits to clinics/year	1371	951
Nearest hospital (km)	2	28

\*Doses per 1000 persons per annum

Yoneda, Daghfous, and Messadi, 1974b). In addition, some of the laboratory studies of conjunctival scrapings from children participating in treatment trials in a village two kilometres from El Golaâ are reported here (Dawson and others, 1974; Dawson, Hoshiwara, Daghfous, Messadi, Vastine, and Schachter, 1975).

**Results**

**VISUAL DISABILITY**

From our measurements of central visual acuity an unusually high rate of visual impairment was apparent in individuals over the age of 30 (up to 14 per cent in El Golaâ) (Table III). Although most of this visual loss could be attributed to corneal scarring, a few persons were blind from other causes such as untreated glaucoma. In the industrialized countries of western Europe or the United States the percentage of 'legally blind' in the total population ranges from 0.05 to 0.2 per cent (World Health Organization, 1966b).

**ACTIVE AND HEALED TRACHOMA**

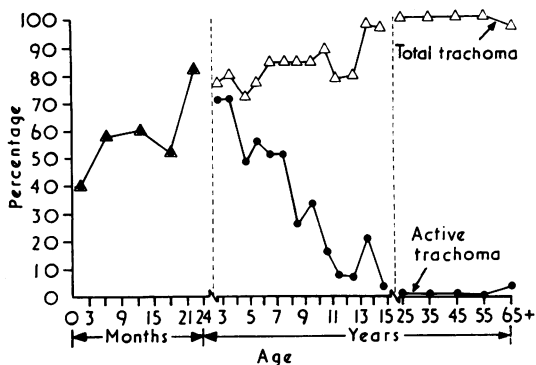
In the classification of trachoma patients 'active' trachoma corresponds to MacCallan stages I, II, and III or with intensity gradings of severe, moderate, and mild (Dawson and others, 1974; World Health Organization, 1962). All patients with 'active' trachoma show signs of inflammation, particularly lymphoid follicles on the upper tarsal conjunctiva, and all patients with 'inactive' or 'healed' trachoma show conjunctival scarring, characteristic corneal vascularization, or both. In surveys individuals without any of these signs are classified as 'trachoma negative' or stage 0.

The prevalence of trachoma in the two Tunisian villages showed that about half of the children in Chott were infected before age 2 and that the prevalence of active disease declined steadily to age 15 (Fig. 1). While all persons over 15 years of age in Chott had had trachoma in the past, only about 80 per cent of those from 2 to 15 years had been affected, and in children under age 2 the prevalence of trachoma, both active and healed, was even lower.

**Table III** Visual acuity in Chott and El Golaâ

Age	Chott		El Golaâ	
	No. tested	Percentage with visual loss*	No. tested	Percentage with visual loss*
6-9	225	—	271	0.4
10-14	252	0.5	282	1.5
15-29	318	0.3	278	1.5
≥30	511	7.0	662	14.0

\*Visual acuity 20/400 (10/200) or less

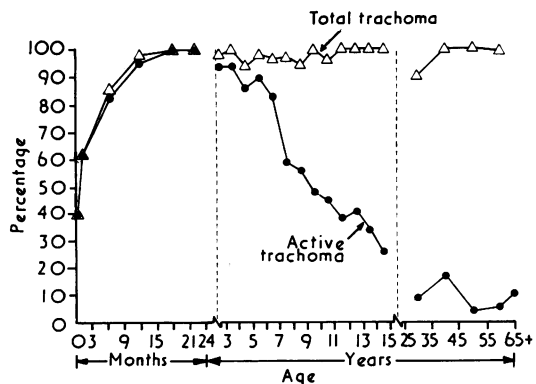


**FIG. 1** Trachoma prevalence in Chott. Active trachoma includes only inflammatory, infectious disease. Total trachoma includes all active and healed cases

In contrast, half the children in El Golaâ had active disease by the age of 3 months and all were infected by the age of 2 years (Fig. 2). The percentage of active disease then declined up to age 15 but was still 5-10 per cent in the adult population.

**INTENSITY AND PREVALENCE OF CHLAMYDIA**

Severe and moderate cases of chlamydia were most prevalent in children under age 5 but had virtually disappeared by age 10 in Chott and by age 15 in El Golaâ (Figs 3 and 4). Thus the bulk of active, infectious cases occurred in the population under 15 years of age. The disproportionately large number of residents under the age of 15 was owing to recently reduced rates of infant mortality and to the emigration of adult men seeking employment elsewhere. The prevalence of trachoma agent paralleled the clinical intensity of the disease. Trachoma agent was detectable in 56 per cent of severe cases, in 20 per cent of moderate cases, and in 4 per cent of mild cases (Table IV). The



**FIG. 2** Trachoma prevalence in El Golaâ. Active and total trachoma defined as in Fig. 1

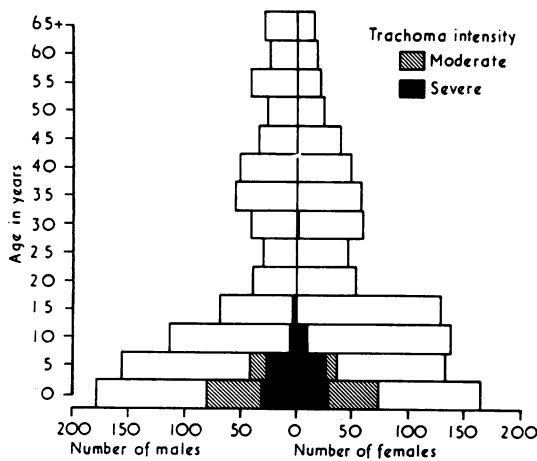


FIG. 3 Total numbers of males and females in each 5-year age cohort in Chott and the number of severe and moderate cases of active trachoma in each cohort

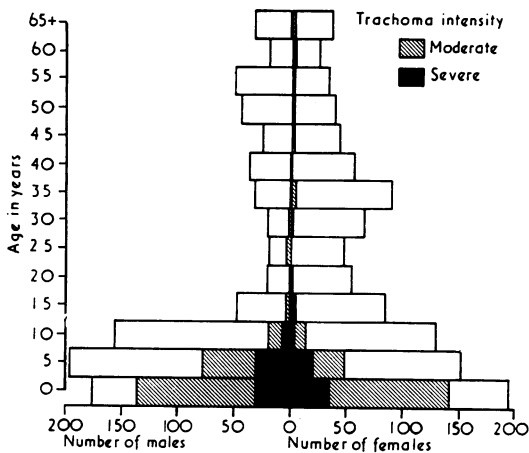


FIG. 4 Total number of males and females in each 5-year cohort in El Galaâ and the number of severe and moderate cases of active trachoma in each cohort

severe and moderate cases were therefore more likely to serve as sources of infection for other members of the community.

In a series of chemotherapy trials carried out in a village near El Golaâ chemotherapy only temporarily suppressed the inflammatory disease in 6- to 9-year-olds (Dawson and others, 1974; Dawson and others, 1975). In treated patients, however, there was a four to tenfold decrease in the prevalence of chlamydia-positive smears in the various intensity groups (Table IV). Thus antibiotic treatment may reduce the transmission of the agent more than would be expected from its clinical efficacy.

DISABLING LESIONS

Active trachomatous inflammation of the conjunctiva may progress to irreversible conjunctival and corneal scarring that threatens blindness and to corneal scarring that actually causes visual loss (Fig. 5). Conjunctival cicatrization first manifests itself as linear scars (Fig. 6), but in severe cases the lid margins become distorted and abrade the eyeball and cornea either with individual cilia (trichiasis) or by the whole inturned lid margin (entropion) (Fig. 7). The cornea, which in agricultural communities is already often exposed to minor trauma and foreign bodies, may thus be subjected to constant abrasion by the inturning eyelashes. Diffuse scarring of the conjunctiva also reduces the aqueous and mucous components of the tears and in this way produces a relatively 'dry eye'. Without an adequate protective tear film minor corneal abrasions may easily become infected and lead to corneal ulceration, scarring, and loss of vision (Fig. 7).

In this study trichiasis or entropion, or both, and the severest grade of conjunctival scarring were considered to be *potentially* disabling, and severe central corneal scarring (grade 3) was considered to be *actually* disabling. Severe corneal scarring rarely occurred in the absence of trichiasis/entropion or severe conjunctival scarring. The presence of potentially or actually disabling lesions increased sharply at 20 years of age in both villages (Fig. 8). In Chott there was a slight increase in potential disability at age 45 and an increase in actual disability at age 40. In El Golaâ potentially disabling lesions appeared in some 5- to 10-year-olds, increased in incidence up to age 30, and affected 35 per cent to 45 per cent of the population after age 30. Severe corneal scarring occurred early in El Golaâ, affecting a significant proportion of persons by age 25 and increasing dramatically

Table IV Trachoma intensity and prevalence of agent before and after chemotherapy

Intensity	Giemsa and/or FA positive			
	Before treatment		After treatment†	
	No. positive/No. tested	Percent positive	No. positive/No. tested	Percent positive
Severe	53/94	56	10/49	20*
Moderate	44/220	20	11/237	4.6*
Mild/inactive	2/47	4	1/120	1

\*Prevalence of agent and intensity of disease significantly lower in antibiotic-treated groups (P < 0.01)

†With topical tetracycline or rifampicin

over age 50, although the overall rate of potential and actual disability did not change (Fig. 8).

Although the incidence of disabling lesions increased to age 35 in both villages, acute inflammatory disease almost disappeared by age 15 (Figs 3 and 4). Since scarring is undoubtedly a direct result of the inflammatory process this apparent 10- to 20-year lag was probably attributable to a low but persistent rate of inflammatory disease in adult life, leading to an accumulation of disabling lesions, or to a shrinking of conjunctival scars produced in childhood, with resultant occurrences of trichiasis or entropion years after the healing of the inflammatory disease.

The accumulation of corneal scars in still older adults may reflect cumulative corneal damage from trichiasis/entropion, foreign bodies, and bacterial infections, probably worsened in advancing age by loss of tears and trachomatous scarring.



FIG. 7 Trichiasis and resultant corneal scarring in adult with healed trachoma



FIG. 5 Conjunctiva of everted upper eyelid with severe intensity trachoma in 6-year-old child. One linear scar can be seen but papillary infiltration obscures blood vessels and follicles

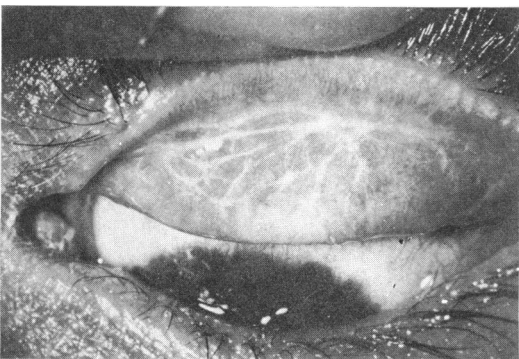


FIG. 6 Same eye as Fig. 5 after three weeks' treatment with topical tetracycline. Inflammation has subsided revealing scarring severe enough to threaten visual acuity

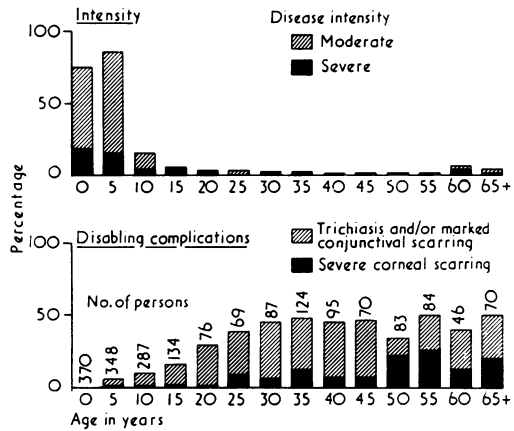


FIG. 8 Prevalence in El Golaâ of severe and moderate trachoma and of visually disabling or potentially disabling lesions in the better eye of each individual. Bulk of active disease occurs before age 15 but prevalence of disabling complications increases to age 25. Increase in severe corneal scarring appears at age 50

CHANGES IN INTENSITY AND DISABLING LESIONS, 1969-72

Since most of the inflammatory disease was in children under 10 years of age the distribution of trachoma intensity in this age group was evaluated in population subsamples (Fig. 9). In both villages there were initially more active cases in the subsamples than in the entire population, a result of selecting for the subsamples only families with a trachomatous preschool child. When children under 10 in these same families were re-examined in 1972 the situation in El Golaâ had remained virtually unchanged. Despite the subsample bias towards disease activity the overall intensity of the disease had decreased dramatically in Chott. During this period the construction of an electric

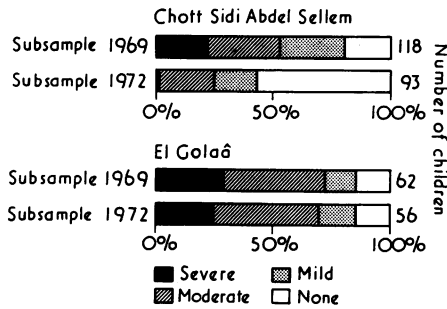


FIG. 9 Active trachoma in a selected subsample of children under 10 years of age in each village in 1969 and 1972

generating plant and chemical fertilizer plant immediately adjacent to Chott had led to a marked economic improvement in the village.

Conjunctival inflammation tended to mask the conjunctival scarring (Figs 5 and 6). Thus an apparent increase in scarring in Chott, or example, may have been due in part to the 'unmasking effect' of the decrease in inflammation. There was no suggestion that scarring in itself was necessary for healing.

#### BACTERIAL PATHOGENS

In both villages seasonal epidemics of purulent conjunctivitis started in early summer and reached a peak in late October. As reported elsewhere (Vastine and others, 1974a, 1974b), the epidemic disease, which was always more severe and widespread in El Golaâ, was associated with *Haemophilus* sp., pneumococci, *Moraxella* sp., and *Staphylococcus aureus* but not with *Streptococcus viridans* or diphtheroids. Such seasonal epidemics of purulent conjunctivitis are commonly associated with endemic trachoma, and in some regions with *Neisseria* infection as well (Maxwell-Lyons and Amies, 1949). In Tunisia we have found *Neisseria* sp. in only a few cases, however, despite special efforts to recover them on special bacteriological media (Vastine and others, 1974a, 1974b). From other studies we have learned that the ocular bacterial pathogens are eliminated by 10 or 12 days' antibiotic treatment, but that the 'non-pathogens' persist (Vastine and others, 1974a; Dawson and others, 1975).

#### LIVING STANDARDS AND INTENSITY AND GRAVITY OF TRACHOMA

It has been known that the poorer the community the more severe is the trachoma. The environmental influences that bring this about have not been clearly identified, although lack of water, which so

often characterizes desert populations, is often incriminated. In the hope of identifying the most important factors we compared the intensity and complications of trachoma in El Golaâ (the most severely affected village) with crowding, type of housing, water supply, and the presence of children under 5 years of age.

In children up to age 9 and in adults over 30 there was a suggestive association (probability between 5 and 10 per cent) of trachoma and crowding (three or more persons per room). In people over 15 years of age the type of housing (single family dwelling, multiple family dwelling or tent) was significantly associated (probability less than 5 per cent) with the presence of potentially disabling lesions. The presence of children under age 5 in the household had a suggestive association with intensity in 10- to 14-year-olds (who often tend their younger siblings) and a significant association with complications in 15- to 29-year-olds. The water supply (public fountain or spring) had a suggestive association with disease intensity only in children under age 5, but it also had a suggestive association with complications in 6- to 14-year-olds and a significant association in adults over 30.

Thus no single factor was clearly associated with disease intensity, although crowding and the water supply could have played some role. The high correlation of the disabling lesions of trachoma with poor housing and an inadequate water supply suggests that the most severely affected individuals are probably the poorest members of the community.

#### CONTROL MEASURES

The major efforts currently under way for the control of trachoma consist of, first, a mass antibiotic therapy programme among schoolchildren in the first and third school years. In endemic areas, like Chott and El Golaâ, two applications of chlortetracycline ointment are made daily for five consecutive days each month from January to June. Secondly, a three-day conjunctivitis control programme ('anti-Mrad') each October when an effort is made to treat all the children in the country with chlortetracycline ointment.

In a series of controlled therapeutic trials reported elsewhere (Dawson and others, 1974; Vastine and others, 1974a) treatment was given to primary schoolchildren and the clinical and microbiological findings were evaluated. When compared with treatment with boric acid ointment, topical applications of tetracycline, chlortetracycline, erythromycin, and rifampicin all resulted in a suppression of clinical intensity and detectable trachoma agent. Within four months of completing treatment however, there were no clinical differences in

antibiotic- and boric-acid-treated children. On the other hand, the prevalence of detectable trachoma agent was less than would have been expected in disease of such intensity (Table IV). Thus, while the effect of treatment on the clinical course of the individual case was apparently transitory, antibiotic therapy reduced the prevalence of demonstrable agent and thus probably the transmission of the disease in the community.

### Discussion

In these studies the intensity of trachoma in any one individual tended to remain relatively stable. The degree of intensity might be expressed as a stochastic process determined not only by microbial pathogens but also by environmental and host factors (Fig. 10). The pathogens include both the chlamydia and the ocular bacterial pathogens. Although we could not identify with certainty the environmental features of importance, the presence of young children in the household, crowding, and the unavailability of water for household use appeared to play a role. The overall economic level of the community was apparently also important. The single most important host factor was age, almost all of the active disease occurring in children under the age of 10 years.

The disabling complications of trachoma are the result of scarring brought about by active inflammation. In this study it appeared that only patients with disease of severe or moderate intensity for considerable lengths of time developed the severe scarring that leads to visual loss.

In a population with severe endemic trachoma the risk of acquiring the disease and of developing its disabling complications are presented schematically in Fig. 11. In El Golaâ 75 per cent of the children developed trachoma of severe or moderate intensity between birth and 9 years of age. Of these, two-thirds (or 50 per cent of the total number of adults) developed potentially disabling lesions, and in one-half of these (or 25 per cent of the total) severe corneal scarring and visual loss supervened. The pattern of active inflammatory trachoma and visual disability in these two Tunisian villages is probably typical of other undeveloped areas where the disease is still endemic. With economic development the prevalence of active trachoma of severe and moderate intensity declines (as in Chott) and few if any cases develop potentially blinding lesions. In the absence of economic improvement, however, the children with severe or moderate disease develop sufficient scarring by age 15 to make blindness an inevitable consequence for at least some of them.

Since the number of children surviving to adulthood is now much greater than in the past

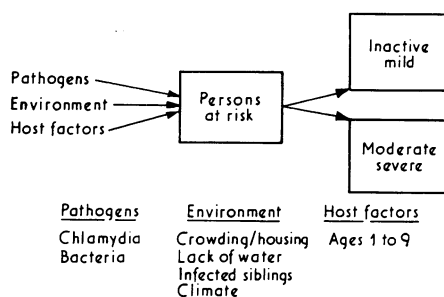


FIG. 10 Factors influencing intensity of trachoma in childhood. Intensity in each child tends to remain stable

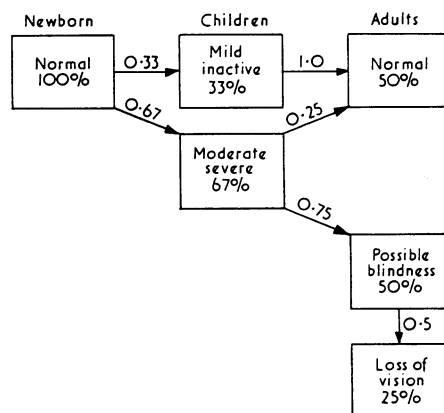


FIG. 11 Flow diagram showing the sequence of events leading to blindness from trachoma in El Golaâ. Percentages in each box indicate proportion of children with active disease and of adults with complications. Numbers over arrows indicate probability of individuals in one category passing to next category indicated by arrow

the need for medical services for the correctable problems (for example, surgery for trichiasis) will grow correspondingly, and any success in controlling childhood trachoma now will ease the demand for medical care and rehabilitation of the blind only 10–20 years from now. As time goes on, the visually disabled in endemic communities will add immeasurably to the medical, economic, and social burden of affected countries, and for this reason these communities should be the focus of public health programmes for trachoma control. Since the resources for trachoma control in affected countries are limited control efforts should be concentrated in the regions where the disease is most widespread and has the highest prevalence of severe or moderate cases.

Although the present forms of local chemotherapy produce only limited clinical results they seem to

have some generally beneficial effects. Systemic chemotherapy on a mass scale (as practised elsewhere) might be more effective but would carry unacceptable risks (drug reactions, increase in incidence of drug-resistant intestinal pathogens) in a population that could not be followed adequately (Hoshiwara, Ostler, Hanna, Cignetti, Coleman, and Jawetz, 1973). While newer methods of drug delivery to the eye such as the Ocuser device (Richardson, 1975) may result in a dramatic breakthrough in treating the active disease, the administrative framework of the control programme should also be improved so that preschool children could be treated and the efficacy of the control measures could be assessed regularly.

Economic development seems to offer the ultimate solution to preventing blindness from trachoma. While the many young adults who emigrate from endemic regions present little risk of infecting others in urban settings the uncontrolled inflammatory disease among children in affected villages will continue to produce scarring and eventual visual loss. Blindness from trachoma can be prevented only by controlling the disease in these severely affected rural areas. Even with the improved methods of antibiotic delivery now available much would be gained by concentrating resources on heavily affected communities and by utilizing medical assistants to the greatest possible extent.

### Summary

In two villages in southern Tunisia where trachoma was endemic 7 per cent and 14 per cent of adults respectively had visual acuity of 20/400 or less. In both villages active trachoma affected most children

under the age of two, reached a peak in two- to five-year-olds, then declined to age 15. The chronic inflammatory disease in childhood appeared to produce irreversible scarring of the eyelids, and loss of vision occurred in adult life due to corneal scarring caused by inturned eye lashes and loss of tears (dry-eye syndrome). Economic development in one village was associated with a decline in active, infectious disease. In the second village, whose traditional economy was unchanged, there was the same prevalence of active disease over a three-year period.

Unless economic development or public health control programmes reduce the prevalence of severe and moderate trachoma children now affected will develop the same blinding lesions as their parents. With the increasing numbers of children who survive there will probably be a dramatic increase in the numbers of the blind from trachoma in 10 to 20 years. Since active inflammatory trachoma in childhood responds to tetracyclines, erythromycin, and sulphonamides the disease should be attacked in those undeveloped rural areas where it continues to lead to blindness.

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