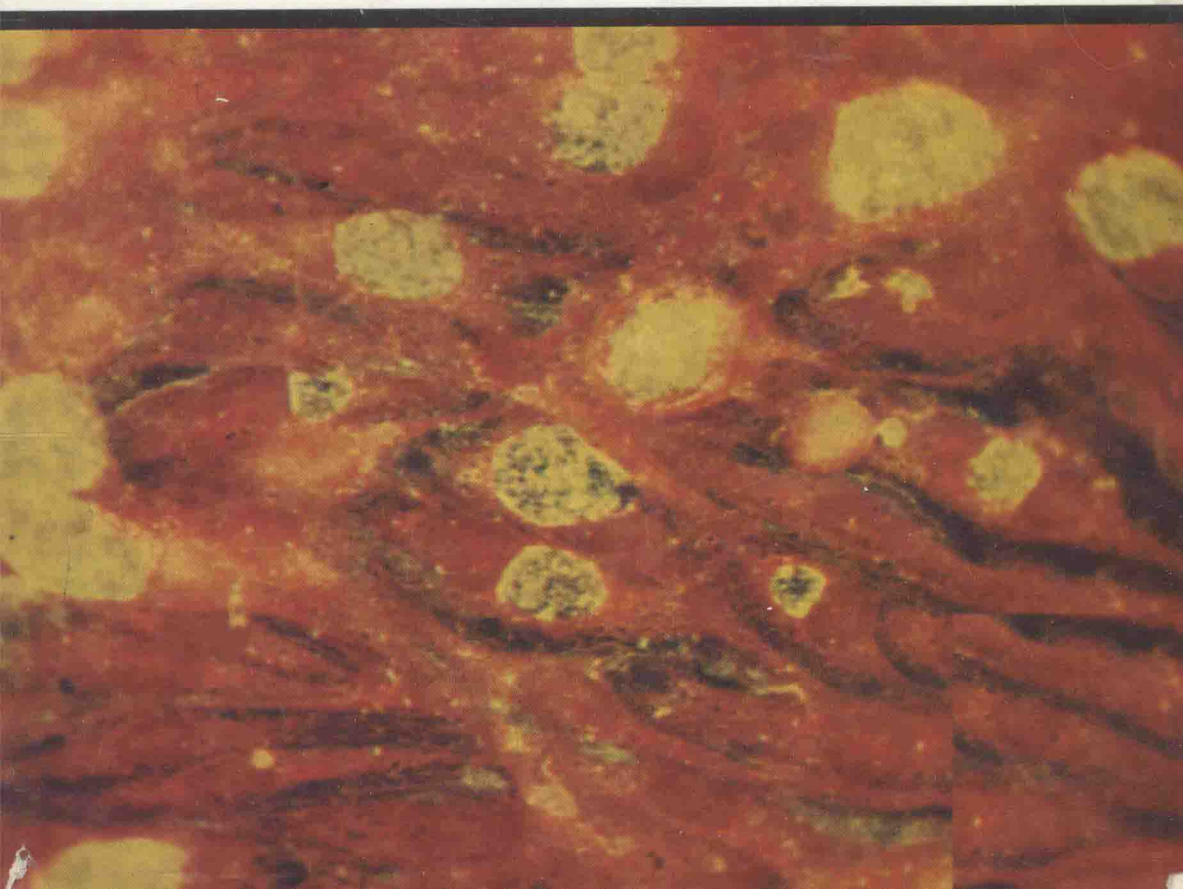
TRACHOMA AND RELATED DISORDERS

ROGER L.NICHOLS

EXCERPTA MEDICA



Trachoma and related disorders

caused by chlamydial agents

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Foreword

It is my privilege to welcome you to this conference. The first conference concerned with the biology of the trachoma agent was convened by the New York Academy of Sciences in 1961. A second conference was sponsored by the Proctor Foundation for Research in Ophthalmology and by the Harvard School of Public Health in 1966. These proved successful in the stimulation of research and the exchange of information. We hope that this 1970 colloquium will be no less effective in these regards.

It has been less than a decade and a half since the trachoma agent was isolated by Dr. T'ang. A respectable body of scientific knowledge has accumulated during this short time. We know now that trachoma is one of a complex spectrum of related agents. Scientists working with the causative agents of diseases caused by related organisms have done much to further our insight into trachoma, and we regret that limitations of time and budget have not permitted more of these researchers to contribute data to this conference. All of us, I am sure, are sorry that Dr. Phillips Thygeson, who organized and managed the second conference on trachoma, was unable to participate in these deliberations. We salute him and the other trachomatologists who could not join us.

JOHN C. SNYDER

Contents

I

MOLECULAR BIOLOGY, CHEMISTRY AND METABOLISM OF TRACHOMA

1. Evolution of *Chlamydia**

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A discussion of the evolution of *Chlamydia* implies that we know a great deal about a large number of these organisms. Although there are still important gaps in our knowledge, the agent of meningopneumonitis (MN, *C. psittaci*) has been studied systematically in several laboratories. The information that we have on its structure, chemical composition, developmental cycle, enzymatic activity in an extracellular as well as in an intracellular environment, and on its interaction with the host cell is far greater than what we know of rickettsiae, non-cultivable mycobacteria, and most of the cultivable pathogens. In fact, we may consider the MN agent as the *Escherichia coli* of host-dependent bacteria. Excellent fundamental work has been done with a number of other established strains of *C. psittaci* and *C. trachomatis*. The least information is available on isolates that have not yet been adapted to yield large harvests in eggs and cell cultures. These are our primary concern and a discussion of evolution must be based on the assumption that knowledge painstakingly obtained with established strains applies to them. As our work progresses, this assumption must be continuously challenged.

The size of the genome

Sarov and Becker (1969) isolated the deoxyribonucleic acid (DNA) of the TE-55 strain of *C. trachomatis* by a procedure which minimized shearing and yielded a large number of cyclic forms. Electron microscopic measurements and density gradient determinations indicated that an unsheared molecule of DNA contains about 11×10^5 nucleotide pairs. A comparison of this value with those obtained by others with chlamydiae and other bacteria and with viruses is illustrated in Table I. Kingsbury (1969) obtained somewhat lower values for two strains of *Chlamydia*, but his method was entirely different. It was based on the finding by Britten and Kohne (1968) that the rate of reassociation between single strands of

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TABLE I

Size of bacterial and viral chromosomes

Organism	10^5 nucleotide pairs	Method [a]	Reference
Escherichia coli [b]	45	AR	Cairns (1963)
Neisseria catarrhalis	23	RK	Kingsbury (1969)
N. meningitidis	17	RK	Kingsbury (1969)
Rickettsia rickettsi	15	RK	Kingsbury (1969)
Chlamydia psittaci (MN)	8.5	RK	Kingsbury (1969)
C. trachomatis (MRC-1/G)	6	RK	Kingsbury (1969)
C. trachomatis (TE-55)	11	EM, DG	Sarov and Becker (1969)
Mycoplasma hominis	8.5	EM	Bode and Morowitz (1967)
Vaccinia virus	2.5	EM, DG	Sarov and Becker (1967) Becker and Sarov (1968)
Coliphage T2 [b]	1.4	AR	Cairns (1961)
Polyoma virus	0.05	EM	Weil and Vinograd (1963)

[a] AR = autoradiography; RK = reassociation kinetics; EM = electron microscopy; DG = density gradient.
[b] Reference chromosomes.

bacterial DNA fragments is inversely proportional to the size of the genome. Among the bacteria studied, the spread in size of the DNA is about 8-fold, but there is no overlap with the larger viruses. The spread among double-stranded DNA viruses is at least 50-fold. The DNA of chlamydiae are among the smaller bacterial DNA, but not necessarily the smallest. The experiments of Bode and Morowitz (1967) are entirely comparable to those of Sarov and Becker (1969) and it is apparent that the genome of the agent of trachoma is at least as large as that of *Mycoplasma hominis*, which, of course, is capable of multiplication without the support of host cells. Thus, chlamydiae have sufficient DNA to account for a multitude of functions. Their inability to grow independently of host cells can best be attributed to adaptation to an intracellular environment, rather than to extensive deletions in their genomes.

Functions reflecting adaptation to intracellular environment

Cell wall. Tamura, Manire, and their associates (Tamura and Manire, 1967; Tamura *et al.*, 1967; Manire and Tamura, 1967; Matsumoto and Manire, 1970) isolated reticulate bodies of the MN agent, relatively uncontaminated with dense particles (elementary bodies) and were able to carry out a series of studies on each form. Both types of cells were shown to have trilaminar cell walls, but those of the reticulate bodies lacked rigidity and were more easily disrupted by sonic treatment and trypsin. Tribby (1970) recently obtained good evidence that the cell walls of both forms contain peptidoglycans, but the reticulate bodies are less rigid because the peptidoglycans are not cross-linked by peptide bridges. This finding in part unravels the mystery of the developmental cycle. In a suitable