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Second Report

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EXPERT COMMITTEE ON TRACHOMA

Second Session

Geneva, 7-14 September 1955

Members :

Professor G. B. Bietti, Director, Ophthalmological Clinic, University of Parma, Italy

Sir Stewart Duke-Elder, Director of Research, Institute of Ophthalmology, University of London, England

Professor Ida Mann, Ophthalmic Consultant to the Government of Western Australia, Public Health Department, Perth, Australia (*Rapporteur*)

Dr Y. Nakamura, Professor of Ophthalmology, Nippon Medical College ; Executive Director, Japan Ophthalmological Society, Tokyo, Japan

Dr R. Nataf, Conseiller du Ministère de la Santé publique pour les maladies oculaires endémo-épidémiques et la recherche scientifique ; Chef de Service du Centre ophtalmologique et antitrachomateux, Tunis, Tunisia (*Chairman*)

Dr G. Sicault, Directeur de la Santé publique et de la Famille, Rabat, Morocco

Dr V. Tabone, Ophthalmic Surgeon, Central Hospital, Valetta ; Consultant Ophthalmologist, Victoria Hospital, Gozo, Malta

Dr R. M. Taylor, Head, Department of Virology, United States Naval Medical Research Unit No. 3, Cairo, Egypt

Dr P. Thygeson, Clinical Professor of Ophthalmology, School of Medicine, University of California Medical Center, San Francisco, Calif., USA (*Vice-Chairman*)

Secretariat :

Dr M. Giaquinto, Section of Endemo-Epidemic Diseases, WHO (*Secretary*)

Dr M.-J. Freyche, Section of Epidemiological Information and Morbidity Statistics, WHO

Dr F. Maxwell Lyons, Health Officer for Communicable Eye Diseases, Regional Office for Europe, WHO

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EXPERT COMMITTEE ON TRACHOMA

Second Report *

The Expert Committee on Trachoma held its second session in Geneva from 7 to 14 September 1955.

The session was opened by Dr P. Dorolle, Deputy Director-General of the World Health Organization. The Committee elected Dr R. Nataf Chairman, Professor P. Thygeson Vice-Chairman, and Professor Ida Mann Rapporteur.

The proposed agenda was discussed and adopted.

1. Etiology of Trachoma and Laboratory Research

1.1 Etiology

The Committee recognizes that the cause of trachoma is an agent of the psittacosis-lymphogranuloma (Chlamydozoaceae) group of atypical viruses, at present designated as *Chlamydozoon trachomatis*, and that it is seen typically in conjunctival scrapings, in colony form in epithelial cells as Halberstaedter-Prowazek (HP) inclusion bodies [1] and free in the exudate, especially during the early stages or acute manifestations of the disease, as elementary and initial bodies. The Committee does not consider that any satisfactory proof has been produced of the existence of submicroscopic forms of the virus or of the presence of the virus in subepithelial tissues, but it agrees that further exploration of contrary claims is indicated.

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* The Executive Board, at its seventeenth session, adopted the following resolution :

The Executive Board

1. NOTES the second report of the Expert Committee on Trachoma ;
2. THANKS the members of the Committee for their work ;
3. AUTHORIZES the publication of the report ; and, furthermore,
4. REQUESTS the Director-General to prepare from time to time for the Executive Board documentation on the latest developments in the research and control activities in trachoma, with particular reference to the possible development of resistance to antibiotics or other therapeutic agents.

(Resolution EB17.R14, *Off. Rec. Wld Hlth Org.*, 1956, **68**, 5)

[1] In view of past confusion of trachoma inclusion bodies with non-specific cytoplasmic material including pigment granules, extruded nuclear substance, various cell granules, etc., the term " HP inclusion body " should be reserved for scientific purposes to indicate a cytoplasmic epithelial-cell inclusion body containing (1) a carbohydrate matrix and (2) elementary and/or initial bodies.

1.2 Present state of laboratory research

The Committee has surveyed the present state of laboratory research in trachoma and recognizes that slow but definite advances have been made, particularly in the definition and classification of the etiological agent, in the pathology of the disease, and in the microscopic diagnosis.

The Committee recognizes the importance of the now numerous claims for temporary cultivation of *C. trachomatis* in tissue culture and in the yolk sac and chorioallantois of the developing chick embryo, but is not convinced that, at the time of writing, cultivation in series or in quantity has been accomplished.

The Committee considers trachoma to be a keratoconjunctivitis, as a rule with simultaneous involvement of the cornea and conjunctiva, but would welcome further exploration, from the laboratory aspect, of the development of the virus in corneal tissues during the evolution of the disease.

The Committee has noted with gratification the recent laboratory progress made in the recognition and definition of viruses causing those non-trachomatous follicular conjunctivitides sometimes confused with trachoma (see section 2.4, page 7).

1.3 Recommendations for further laboratory research

A great surge forward of knowledge in the diagnosis, epidemiology, control, and even treatment of a communicable disease has commonly followed the successful propagation of its causative agent in vitro or in some convenient laboratory animal. This may prove to be true for trachoma. It is recommended, therefore, that every effort be made to cultivate the virus of trachoma by some workable and generally applicable method, and that it be established without doubt that the virus being cultivated is the real cause of trachoma.

It is suggested that the most promising way to achieve this end is through the intimate collaboration of virologists and ophthalmologists—the virologists to apply the methods most suitable for virus cultivation and the ophthalmologists to verify that the agent cultivated is capable of producing lesions characteristic of trachoma.

In view of the importance of establishing that the virus under cultivation is the cause of trachoma, it is proposed that the following procedure be adopted: (1) demonstration of HP inclusion bodies (as defined in footnote 1 on page 3) in serial cultures; (2) production, in monkeys or apes, of experimental trachoma capable of transmission in series; (3) demonstration of serological relationship of the cultured virus to trachoma. In all cases the final proof should be the production of typical

trachoma in human volunteers after sufficient passages in culture to eliminate the dilution factor.

Although the Committee deplores the necessity for human inoculation (not at present a dangerous procedure in view of effective chemotherapy), it insists that this criterion be fulfilled, as at the present time experimental trachoma cannot be diagnosed with certainty in hosts other than man. The Committee stresses that the disease produced by experimental inoculation in man should be rigidly differentiated from all forms of non-trachomatous follicular conjunctivitis and that such differentiation should be made by two or more competent observers and should be documented by the results of microscopic examinations of scrapings and biopsies and by photography of the upper tarsal and upper limbal areas.

The Committee further recommends :

(1) that in order to facilitate transport of the virus for experimental purposes first priority be given to studies designed to test the survival of trachoma virus (*a*) in the frozen state, (*b*) after freeze-drying, and (*c*) after suspension in glycerol ;

(2) that special clinical and pathological research be directed to the subject of experimental trachoma in monkeys and apes, to differentiate it from non-trachomatous follicular disease in these animals and to establish criteria for its diagnosis ;

(3) that further work be carried out to determine the reliability of cytologic diagnosis of active trachoma by the examination of (*a*) epithelial scrapings and expressed follicular material, and (*b*) biopsy specimens ;

(4) that further work be carried out on serological reactions in trachoma ; (It is recognized that major studies must await the culture in quantity of trachoma virus, but it is recommended that in the meantime further exploration of the serological relationships of trachoma virus to other members of the Chlamydozoaceae group be carried out. Refined methods of serology with suitable trachoma antigen should be explored, including the haemagglutination-inhibition test, the test for antitoxins, and the fluorescent antibody technique and its modification.)

(5) that further work be done on the possibility of the existence of a toxin produced by the trachoma virus ;

(6) that further testing of the tissue specificity of *C. trachomatis* be carried out to determine whether cells of mesodermic origin are ever parasitized in vivo or in vitro ;

(7) that further exploration of the provocative effect of cortisone and other steroids, caustics, bacterial toxins, etc., be continued, to determine their value both as a test of cure and as a possible means of increasing susceptibility to chemotherapy ;

(8) that extensive in vitro testing of various therapeutic agents be carried out as soon as culture in series of trachoma virus becomes possible;

(9) that the development of a vaccine should be attempted as soon as culture virus becomes available;

(10) that the role of insect (arthropod) vectors, particularly flies, in the transmission of trachoma be subjected to laboratory investigation.

2. Definition, Diagnosis, and Differential Diagnosis of Trachoma and Non-Trachomatous Follicular Conjunctivitis

The definition and the criteria of diagnosis (clinical and laboratory) of trachoma are laid down by the Committee as follows:

2.1 Definition of trachoma

Trachoma is a specific communicable keratoconjunctivitis, usually of chronic evolution, caused by an agent at present classified as *Chlamydozoon trachomatis*, characterized by the formation of follicles, papillary hyperplasia, and pannus,[1] and typically leading to scar formation.

2.2 Clinical diagnosis

In making the clinical diagnosis of trachoma, two at least of the following should be present:

(1) follicles (conjunctival or limbal);

(2) epithelial keratitis most marked in the upper part of the cornea;

(3) pannus in the upper part of the cornea;

(4) typical scars.

2.3 Acute versus insidious onset

The Committee considers that trachoma may arise as an acute disease even in the absence of secondary bacterial or viral infection; but this acute onset is rare. Most cases of uncomplicated trachoma are of insidious onset. The term "chronic" should not be used in this connexion.

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[1] Trachomatous pannus is the invasion of the upper part of the cornea by the disease, in the form of cellular infiltration and neovascularization. Residual vessels remaining after the regression of the infiltration constitute inactive pannus.

2.4 Differential diagnosis

The following forms of non-trachomatous follicular conjunctivitis are recognized by the Committee :

Acute follicular conjunctivitis

1. Inclusion conjunctivitis
2. Acute follicular conjunctivitis, Béal type
3. Epidemic keratoconjunctivitis
4. Acute herpetic keratoconjunctivitis
5. Newcastle disease conjunctivitis
6. Pharyngoconjunctival fever

Chronic follicular conjunctivitis (Axenfeld type)

Toxic follicular conjunctivitis

1. Molluscum contagiosum conjunctivitis
2. Eserine conjunctivitis and conjunctivitis due to other miotics
3. Conjunctivitis due to other animal or vegetable products

Folliculosis

The differential diagnosis of these various types of follicular conjunctivitis is given in tabular form in the Annex (page 19).

3. Regional Differences in the Epidemiology and Clinical Aspects of Trachoma

3.1 General

It is agreed that differences occur in the clinical and epidemiological picture of trachoma as found in different regions. The principal differences reported are related to :

(1) age of onset ;
(2) clinical evolution ;
(3) frequency of spontaneous cure ;
(4) frequency of disabling sequelae ;
(5) response to treatment.

The following factors are admitted to be involved in determining the incidence and type of trachoma found:

(*a*) presence of associated bacterial infections;

(*b*) racial susceptibility;

(*c*) presence of conditions of poverty, dirt, overcrowding, and ignorance; these undoubtedly predispose to the spread of trachoma throughout a population, once the causative agent has been introduced;

(*d*) mode of transmission, including social habits and presence of possible arthropod vectors which may be able to contribute to the spread of the disease and especially to that of the associated conjunctivitis;

(*e*) geological and certain climatological factors of the different areas, which particularly favour the formation and dissemination of irritant dust; dust may produce minor injuries which allow of the entry of the causative organism;

(*f*) nomadic habits; nomadic persons seem in general to suffer from a less severe form of trachoma than the stationary population.

It is agreed that the following factors do not directly and appreciably affect the development of trachoma:

Diet. Trachoma occurs equally in vegetarian populations, in meat eaters, in persons living on a mixed diet, in well-nourished persons, and in persons showing a certain amount of protein, calorie, and vitamin deficiencies.

Temperature and altitude. Trachoma can occur in tropical, subtropical, temperate, and cold zones, at sea level and at high altitudes.

The Committee recognizes that in the present state of our knowledge it is impossible to say whether or not different strains of the causative agent exist which could be in part responsible for differences in the chemical and epidemiological picture.

3.2 Age of onset

It is agreed that the more heavily infected a population, the earlier the age of onset.

3.3 Clinical evolution

The clinical differences observed may be due in part to variations of the virulence of the causative agent, but are certainly related to the severity and the frequency of associated conjunctivitis. This factor may indeed dominate the whole epidemiological picture.