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RECONSIDERATION OF TRACHOMA I AND IV AND CRITERIA OF CURE

by

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The recent advances in Trachomatology have necessitated a reconsideration of the various aspects of trachoma, whether from the aetiological, pathological, therapeutic or prevention and eradication points of view. Even a standard definition for trachoma was felt necessary and was formulated by the Expert Committee on Trachoma in its second meeting, 1955(1).

Such a standardization in all aspects of trachoma will be rendered more imperative as the question of trachoma is tackled on an international basis, which we all hope to achieve through the fruitful efforts of the WHO.

Up to the present time, the clinical description of trachoma changes is based on MacCallan's classification of the stages of trachoma. This classification was described and adopted nearly half a century ago, at the time when the nature of trachomatous infection was very obscure. Allowance was made in this classification for concomitant diseases like bacterial infection or vernal catarrh, as they affect the development or the sequence of development of the three prominent features of trachoma, namely: the follicles, the papillae and the scarring. The four stages in MacCallan's classification sounded like chronological steps reflecting the clinical picture of trachoma.

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After half a century of brilliant advances in trachomatology, it will be only natural that MacCallan's classification will be needing reconsideration. The WHO Expert Committee on Trachoma recommended in its first report (1952) an elaborate modification of MacCallan's classification. This modification is nearly a shorthand description of any given case. It is a most accurate method of recording clinical findings on examination, and the results of treatment. This modification, therefore, gives no modified classification of stages, but only a description of each case per se. The original MacCallan's classification was therefore not actually modified, although the need for doing so was expressed at various times and in different countries. References 2-10, tabulated below, express definitely this view. Some authors, e.g. Nataf(2) actually suggested a new classification.

On dividing any pathological process into stages, I think, to be accurate, this should be done on the following lines:

1. A stage covering the onset
2. A stage of progress towards maximum
3. A stage of regression till cure

To define the first stage, all methods of diagnosis will be needed to verify the true nature of the disease. For the second stage the specific clinical signs and pathological changes will govern the picture. For the third stage all criteria of cure will be needed to verify its peak of complete healing.

Studying MacCallan's classification in these lines, we find that its four stages are all really only manifestation of what changes we expect in the second stage mentioned above. MacCallan's Tr.I is no more the stage of onset as it is well known, while Tr.IV stands ambiguous and meaningless. In this, I will quote MacCallan's own description of this stage in his article published in Rev. Int. du Trach. 1951, p.191: "This Tr.IV is the final stage of trachoma. The conjunctiva is smooth. The eyelids may appear normal or there may be cicatricial deformity. Theoretically Tr.IV is the final stage of trachoma, a cure having been affected either naturally or as the result of treatment..... Incomplete cicatrization is, however, the rule - such cases belong to stage III".

Even MacCallan himself finds difficulty in differentiating between the third and fourth stage of his classification.

Such a confusion in the conception of this stage Tr.IV has actually amounted to the extent of some authors (e.g. Kimura[11]) publishing a study of measures of prevention of Tr.IV and its age incidence, in the same way as other active stages of MacCallan's classifications were being discussed.

Considering Tr.IV as a stage of the disease and not as a sign only, has in the past resulted in an unwarranted confusion in making statistics on the actual incidence of trachoma or on the trachoma-index in any country. This fact is well illustrated in the Circular on Trachoma, distributed by the Regional Committee for the Eastern Mediterranean (seventh session) [12], where statistics on the trachoma-index made by the WHO experts in the various countries of the Region were quoted. Their deduction in the incidence of trachoma was cautiously approached as far as the Tr.IV stage was concerned. Some of these experts had to give two figures as to the incidence of trachoma in the country; a figure including the Tr.IV stage and another excluding it, and therefore including only the so-called active or infective trachoma.

I suggest, therefore, that Tr.IV should not be considered a stage of trachoma and that all cicatricial stages of trachoma so far as the term is used, should end at Tr.III. The condition of the conjunctiva and cornea which indicates a previous and healed attack of trachoma should, for statistical and recording purposes, be considered alone as an entity and designed for example, by such term as (Ex-trachoma). It is well known now that this condition of Tr.IV or as suggested "Ex-tr." need not be consecutive to other stages. Spontaneous cure of early stage of trachoma is common. Quoting Maxwell-Lyons[13] "There is growing weight of evidence that trachoma is showing an increasing tendency to spontaneous cure in adolescence with less scar formation and consequently with less risk of late disabling complications". This was also Delon's observation[14] in his report on CED pilot project in Egypt, where he states that in children after 12 years of age trachoma forms are in most cases cicatrized and that healing is generally spontaneous.

Apart from Egypt, there are many statements from authorities on trachoma that the spontaneous cure is a frequent occurrence.

Such important statement has been made repeatedly by various observers in various countries. Professor Mitsui[16] in his report on a visit to North Africa discussed this point as follows:

"Ferrand and Rheinhards emphasized the fact that a clinical cure of trachoma (e.g. full cicatrization) appeared a long period of time after the chemotherapy (e.g. the viral and bacteriological cure). I have experienced the same thing in Japan and reported in WHO Trachoma, 16, 12 Sep. 1951 . This fact also coincided with our view that in chronic stages of trachome, an essential cure resulted prior to a clinical cure. Ferrand, Rheinhards and myself considered that after disappearance of the virus by antibiotic treatment, it took a certain period of time until trachomatous inflammations disappeared and this was because of the chronically proliferative character of inflammation in the chronic stages".

Our repeated observations in Egypt, fully support these views, and we have suffered a good amount of confusion and misunderstanding on reporting on the index of trachoma in a given community or section of population, especially in studies of results of mass campaign, various evaluations, or specifications in case findings. The MacCallan's Tr.III and Tr.IV stages have become, in the light of recent advances in the trachoma field, most uncertain. This has also resulted in an unfortunate confusion as far as the interpretation of therapeutic results is concerned so much so that a multiplicity of trachoma virus strains has been suggested as a theory to explain the discrepancy in therapeutic results.

The MacCallan's classification of the stages of trachoma has overshadowed the principal fact that trachoma is principally an epithelial infection resulting in a keratoconjunctivitis, as a rule with simultaneous involvement of the corneal and conjunctival epithelium. All reports on the presence of the virus in subepithelial tissue, have produced no satisfactory proof to this effect, and therefore the conjunctival and corneal epithelial viral infection should govern the incidence, course and cure of the disease which we designate as trachoma. The histopathological changes of the conjunctival tissue, on which MacCallan's classification is based, are no more than pathological reactions (inflammatory or degenerative) which are not due to direct virus infection of the mesoderm, but according to reliable reports, are due to a soluble

toxin of the trachoma virus, such as occurs in other members of the chlamydozoaceae. Of course such histopathological changes are also influenced in many cases by other accompanying conditions of the conjunctiva, such as mechanical irritation, allergic state, or bacterial infection whether acute or chronic. Taking the true nature of trachoma into consideration, it was natural that all recent investigations and reports consider both the clinical diagnosis and criterion of cure should be based on epithelial examinations, whether in stained scrapings or biomicroscopically. Next to this sure method of observation, came the cytological studies of epithelial scrapings, conjunctival exudation or secretion, and material from ruptured follicles. The significance of epithelial and cytological methods of diagnosis in trachoma is well and fully reported upon by eminent workers in various countries, and their significance is established whether for diagnosing the presence of trachoma or its absence or disappearance.

In MacCallan's stages, the one designated as Tr.I will be according to the above considerations just as subject to confusion as the Tr.IV stage. MacCallan's consideration of the Tr.I as the first stage of trachoma infection in Egypt, has misled many observers, until Wilson coined the term Pre-trachoma which describes the incipient stage of trachoma infection. This Tr.I is only the first stage in the histopathological reaction of the mesodermal tissue in the viral infection of the conjunctiva. It is a well known fact now that the appearance of follicles in the conjunctiva is not the earliest sign of trachoma, but only a proof of its establishment. The presence of these follicles is no peculiarity of a definite succession of any stage in trachoma. Only when the cellular reaction is mild that these follicles are seen clinically, whether as Tr.I or Tr.IIA. In cases with intense cellular activity due to one reason or other, such as bacterial infection, the conjunctival mesoderm reacts in a papillary hepertrophy, with the clinical manifestations of papillary trachoma, e.g. Tr.IIB. Histologically in such cases, follicles, though buried, are always present. When the inflammatory reaction subsides, either spontaneously or as a result of treatment, these follicles may become visible clinically. Therefore trachomatous follicles may be so masked in either the papillary or the cicatricial stage of the

disease as to be grossly unrecognizable (Thygeson, 17). The first stage of trachoma should only be nominated so when based on epithelial examination, either in the conjunctival or corneal part. Conjunctival epithelium can be examined microscopically through stained scrapings and more recently through the admirable technique of fluorescent microscopy. In the cornea the biomicroscope is necessary to show the early punctate erosions, stainable with fluorescin, which are distributed principally over the upper half of the cornea. These are earliest manifestations of trachoma infection and are followed by subepithelial infiltration and of course extension of limbal capillary loops. Diagnosing early trachoma viral infection through study of either conjunctival or corneal epithelium, is only natural since we are dealing with an epithelial infection. It is a process very parallel to that followed by the virologist to determine the growth of the cellular changes produced by the virus in the cells of the culture used, e.g. HeLa cells.

In countries where bacterial secondary infection is predominant, the epithelial diagnosis of early trachoma may not be so helpful as the cytological study of conjunctival scrapings and smears from discharge. This is actually the case in Egypt. In India, Agarwal[18] says: "One can also surmise that in countries where trachoma is very common, there probably exists a pre-trachomatous stage (e.g. a stage before the so-called Tr.I) wherein there is no clinical manifestations of trachoma but a change in cytology of conjunctival smears has already begun".

Indeed the extensive studies of Thygeson, have proved that the diagnosis of the early stages of trachoma can be made consistently and reliably by means of epithelial conjunctival scrapings and in later stages by expressed follicular material. This has proved to be of great value both in the recognition of early or atypical cases and in the determination of the cessation of the trachoma infection. This is why it is universally felt that studies and records of trachoma should be freed of the yoke of the MacCallan's classification and particularly the Tr.I and Tr.IV stages. As by Nataf[19], the trachomatous picture needs an up-to-date reclassification to meet on one hand the clinical and scientific needs, and on the other hand administrative or quarantine purposes. In the latter purpose, it is most important to take into consideration the infectivity of the case rather than the clinical stages, which in MacCallan's

classification gives no indication whatsoever as to this purpose. For example, in the second report of the Expert Committee[1], p.12, is stated: "In cases where papillary hyperplasia exists without other signs of active trachoma, either conjunctival or corneal, the trachoma may be considered as clinically cured". In MacCallan's classification this picture is nominated Tr.IIB, which stands on the peak of the trachomatous histopathological changes. On the other hand, many reliable observers do not consider cicatrization in trachoma, however advanced, as an indication that the trachoma process has passed its first infective stage. Thygeson[18] and Nataf[20] state that the recurrence of inclusion bodies in old cicatricial cases of trachoma (acute reactivation of trachoma), has been seen by all trachomatologists. In all such cases observed by them inclusion bodies have been readily demonstrable. Such cases came in MacCallan's classification under Tr.III or Tr.IV.

There have been repeated attempts to conciliate the stage of MacCallan's classification with all recent advances in trachomatology. The attempt of the First Expert Committee on Trachoma in 1952 was mentioned above, but was not widely followed. Other attempts were made, but the difficulty is that the stages of MacCallan, as mentioned above, gave only the clinical picture, (especially that of Tr.I and Tr.IV) that bears no close relation to the stage of viral infection. Much more so with Tr.IV which should not bear the title of trachoma, if it is admitted to be the totally healed Ex.-tr. case. I suggest that MacCallan's stages should be modified to give the following conception:

Tr.I - The epithelial viral infection of the conjunctiva and cornea with all its preliminary reaction changes.

Tr.II - The next stage in which subepithelial inflammatory reaction and infiltration predominate, in the form of all types of follicles, papillae or pannus.

Tr.III - Is the declining stage of cicatrization, which when fully cicatrized and declared healed by the recognized criteria of cure will cease to be a case of trachoma.

Almost the same suggestion was made and followed by A. Fuchs[20] in his work in China with the UNRRA and the WHO, during the years 1946-1947. For statistical and recording purposes, especially in CED campaigns

and evaluations in mass treatments, the above-mentioned stage of Tr.III can be considered as non-infective and non-active stage, e.g. a stage of resolution, in which the inflammatory cellular reaction might take a long time to disappear, after the clearance of the virus invasion. I would like to emphasize the fact that I am only referring to the stage of the trachoma infection, especially when dealing with the disease in general. Any detailed description of an individual case will of course include reference to pathological changes seen, whether follicular, papillary, pannus or ulcer.

In other words when we speak of the trachomatous infection as such, we refer to its stage, but when we describe a given case of conjunctival or corneal trachoma we mention the pathological findings present as signs of this particular case.

It may be of interest to note here the present classification of trachoma adopted in China as reported at the First Afro-Asian Ophthalmological Congress by Chou Chang-Hu[21]. He said: "In view of the difficulty experienced, we have put forth a new classification of trachoma, which met with the unanimous approval of the Tenth Annual Conference of the Chinese Medical Association held in Peking in 1956. This new classification divides trachoma into three stages as follows:

Tr.I - Stage of active pathologic changes inclusive of follicles and papillary hypertrophy.

Tr.II - Stage of appearance of cicatrization

Tr.III - Stage of cicatrization being complete"

He adds: "with this classification formally adopted, the trachoma record in the whole country may be unified and mutual understanding swiftly promoted".

It is also of interest to note the Soviet school of trachoma classification as reported by T. Eroshevsky[22]: "In contrast to the other schools, the Soviet school divides trachoma into four stages: the first trachoma stage is the progressing stage characterized by the ever increasing development of inflammatory phenomena, infiltration of the conjunctiva, the appearance of follicles and progress towards pronounced trachoma. The second stage is the stage of regression, the stage of

reverse course. Here we observe various types of degeneration and the beginning of the scarring process. The third stage covers all the scarring processes of subsiding trachoma. There is a fourth stage of trachoma which, properly speaking, cannot be considered as such, e.g. the complete scarring of the conjunctiva and the absence of any sign of inflammatory infiltration.

CONCLUSION

The presently adopted MacCallan's classification of the stages of trachoma does not fulfil its purposes because:

1. It does not represent the real span of trachoma infection. Its first stage Tr.I is not the earliest stage and its last stage Tr.IV is no trachoma at all but cicatrized conjunctiva or cornea.

2. Its various stages do not bear any chronological succession, follicle, papilla and scarring being all possible findings in one case.

3. MacCallan's stages can only be considered as an excellent description of the various clinical manifestations or signs of conjunctival trachoma.

4. It is suggested that any classification of the stages of trachoma shall deal with the stage of the viral infection itself whether at onset, progress and regress. The clinical description of the lesion will be considered only when dealing or describing individual cases.

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