THE TRACHOMA PROBLEM

Part of this paper was read on behalf of the Author at the April meeting of the International Organization for the Campaign against Trachoma, 1935

BY

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It is with considerable hesitation that I venture to make a somewhat hurried contribution to a topic which has already been overwritten, lest I add more dust to the fog in which it is enveloped.

My excuse is that this clinic in conjunction with the King Institute of Preventive Medicine close by, has worked at the trachoma problem on and off for the past 15 years without publishing more than a few official notes, inasmuch as our work did not differ in any important respect from some of the positive and negative investigations published in detail by others.

Recently, however, Dr. C. G. Pandit, the Officiating Director of the King Institute and his co-workers, co-operating in a new line of investigation with me and my staff have made at least one observation which may well give a fresh stimulus to the somewhat disorganised attack on the trachoma problem similar to, if feebler, than that with which Noguchi revived the interest of the ophthalmic world in this subject in 1927. At that time the hopes placed in the Halberstaedter Prowazek inclusions had become fainter just as today the B. granulosis has left unfulfilled the anticipation of its discoverer. Work centred on both, has, however, strengthened the investigation of the vital point. We trust that the Madras observations will at least act as a reinforcement.

Julianelle and Harrison pointed out in the Amer. Jl. of Ophthal. for November, 1934, that "a precursory study of the literature in trachoma reveals the confusion existing on the subject." They are not the first to remind the ophthalmological world of this fact, but we can hardly be reminded of it too often. Their desire to establish a sound background or foundation for the study of the problem by the confirmation of observations already recorded in the literature, is a basic necessity. They trace the present confusion primarily to "a general vagueness of the cause." Whilst this is no doubt true it is equally clear to many research workers that there is also a general vagueness as to what is meant by trachoma clinically; a fact which the authors referred to, fully acknowledge by making a statement of their cases selected for experimentation. It must be emphasized that in investigating trachoma the first
obstacle which presents itself to the experimental scientist is the difficulty which clinicians have in deciding what exactly they mean by trachoma. The longer one pursues this question the more difficult does the answer become, for experimental purposes. The research workers of the past 15 years are not peculiar with regard to legitimate doubts, although they might have been more meticulous in trying to answer, in view of the more exacting nature of experimental research as to the delimitation of the problem in hand, and the necessity for either building a research on old foundations truly laid or laying new foundations. What does the average ophthalmologist mean by trachoma? Are we entitled to think that there is any specific disease entity to which this name may be given? The answer is in the affirmative, but when we come to examine the question in the light of the evidence—written and verbal—of those whose experience entitles them to an opinion it is at once apparent that the gravest doubts have assailed the master observers of the past half-century as to the clinical limits within which any one of them would confine the ultimate entity.

To attempt a detailed chronological survey of the literature with a view to setting forth diverging views would be a monumental work and quite unnecessary for my purpose as the fact is fairly obvious without this. Analogy leads us to think that outside the limits which the individual observer adopts, be these wide or narrow, lie a congeries of what might be called trachomatoid affections. I do not refer to those conditions which stand out distinctly from trachoma when clinically well defined, such as spring catarrh and the follicular conjunctivitis of adenoid hyperplasia, but conditions, more especially in their earlier stages, which represent an inflammatory response of the lymphoid tissue of the conjunctiva to noxious influences, which some would definitely label trachoma, others, perhaps in genuine doubt, might call trachoma-like, or preferably trachomatoid. The difficulties in establishing personal criteria are great, and still greater if we attempt to find universal criteria. It was not from inexperience that Roemer spoke of "Trachoma?" or that Fuchs hesitated to dogmatize, although others of the latter's school have been bolder in this respect. Many and varied have been the attempts to define phenomena as pathognomonic. The presence of the cell inclusions of Halberstaedter and Prowazek held at one time by some to be proof positive are to-day placed by the work of Thygeson and others almost in the opposite camp. It would seem that if they indicate anything they suggest that the blennorrhoea of the new born, of Morax and swimming-bath conjunctivitis together constitute a condition *sui generis*. McKee sums up the position of the "H.P." inclusions in the January number of the *Amer. Jl. of Ophthal.*; he himself having independently arrived
at the same conclusions as Stewart, namely a bacterial origin of these bodies. Over 10 years ago I listened to divergent views on the significance of these bodies in the Freiburg clinic by Axenfeld on the one hand and von Szily on the other. They have passed through varying fortunes since then at the hands of Lindner and many others, but are not yet of certain diagnostic value. There may well be varieties of conjunctival cell inclusions some of which are bacterial in origin and some akin to the so-called true inclusions of the virus diseases. One has only to examine Negri bodies by the most recent refinements of staining—as demonstrated to me a few days ago by Col. Shortt, Director of the Pasteur Institute, Kasauli, to realise that the internal structure of cell inclusions has still many things to disclose to the microscopist. To take a different approach, certain writers have held and some still hold, that trachoma does not flare up at the start like an acute bacterial disease, others, more careful, say that it may do so. Morax has been quoted in support of a non-acute origin. It is hardly likely that he would hold such an opinion today in view of the evidence of the artificial production of trachoma in the human subject, or should he do so, it would merely separate as trachoma or trachomatoid, the affection which started gently or violently as the case might be. Some would have it that if trachoma does start acutely it is because of some bacterial concomitant. This is more difficult to disprove on the experimental human subject.

At the other extreme, nearly all observers are agreed that scar tissue at least is an essential part of untreated trachoma. Some would argue that an untreated trachomatoid ophthalmia (the name seems less objectionable than trachomatoid conjunctivitis), which does not go on to the formation of scar tissue cannot be trachoma. I can argue against this view by stating that in at least one case of a normal human volunteer inoculated with "trachoma" material, from which followed a trachomatoid condition, there was spontaneous recovery with so little scar tissue that the healed conjunctiva would have been passed as normal by the bulk of ophthalmic specialists not accustomed to use the corneal microscope for such work. This production of scar tissue is no doubt one of the outstanding features of trachoma and the trachomatoid affections, but it is an extremely variable feature and alone cannot be used by experimentalists as a criterion of trachoma. Like others interested in this subject I called on Noguchi in 1927 to see his chimpanzees. To me there did not appear any reason for adopting a view which subsequently gained ground that his animals could not have acquired trachoma because certain clinical features of the human disease were absent. One of the features mentioned was this scar tissue formation. One cannot argue that because the clinical appearances of a human disease transmitted to animals are
different from those in man (even in an apparently gross histopathological respect), it is not the same affection; at least no research worker accustomed to animal experiment would be convinced by such argument. Incidentally Fuchs considered Noguchi's chimpanzees showed the clinical equivalent of human trachoma. I do not wish to minimize the scar tissue feature but only to point out that even this, the sheet anchor of clinical trachoma, may lead us into difficulties. It has been brought home to me, as I presume it has to many other workers, that the handling of the lids frequently has a considerable influence on the formation and distribution of scar tissue. In following up experimental human cases with the corneal microscope one has only to observe the fissuring and tearing of the sub-epithelial and even the epithelial coats which result from a little extra tension on the everter, to get a new conception of the appalling traumatisms to which the trachomatoid ophthalmias are subjected by the average eye specialist. In the swollen congested earlier stages of the disease, the slightest extra tension causes rupture of the conical baskets of capillaries which form the vascular scaffolding of the papilliform sub-epithelial tissue proliferation. These capillary haemorrhages are so prominent that it is surprising that they have not been more stressed by workers like Wilson. Even the fine honeycomb markings determined by the deeper or basal vessels of the capillary papillae are sometimes greenish-brown, apparently owing to diapedesis or seepage of red cells and deposition of blood pigment. This naturally leads us to the attempts to find characteristic clinical beginnings such as Wilson's proto-trachomatous stage as determined by the slit-lamp, and the observations of Cuenod and Nataf on the early cicatricial changes. From a recent prominent English review one might well get the impression that Wilson considers his proto-trachomatous stage pathognomonic, although Wilson distinctly states that these changes cannot be regarded as diagnostic of trachoma. One gathers that Wilson hesitates to add another clinical stage to those introduced by MacCallan and probably most research workers will sympathize with this attitude. We have never been able to adopt the Egyptian clinical classification in this hospital, although MacCallan's typing has no doubt proved extremely useful to many. If we turn to histopathology for help we get little, although in this sphere there is greater uniformity of views. Recent workers have added nothing material to Mayou's Hunterian lecture of 30 years ago. The sub-epithelial plasma cell infiltration between the follicles is still the only definitely characteristic thing about the trachomatoid group. Histopathologically there does not appear to be any such thing as a "follicle" peculiar to what we visualise as trachoma. Kirkpatrick with his extensive experience in the pathological department of this school, and with access to a far
greater amount of material than Mayou, could not add anything definite. He handed on his scepticism of the average diagnosis of trachoma to me and I have found it easy to agree with him. No doubt Herbert's contribution to the clinical isolation of spring catarrh cases by finding a preponderant eosinophilia in conjunctival slides was a distinct advance although it is surprising how often it fails on the side of negative findings, not positive as one might expect in a country with over 80 per cent. of hookworm infections. The examination for an excess of lymphocytes, plasma cells, or eosinophiles in conjunctival smears is a disappointing clinical test in doubtful early trachomatoid affections.

As regards the clinical appearances of the conjunctiva alone, in early or even more marked cases where yet the cornea is not obviously affected, there is, and has been for years, such divergence of opinion that it becomes ridiculous to use a term which denotes a disease entity to embrace the conceptions of various authorities. About 14 years ago, I visited Swanley to try to get an idea of what Treacher Collins regarded as definite early trachoma. I find on looking up my notes the opinion which I did not then dare to express verbally: "I feel sure some of these cases would become normal if left untreated." We have sometimes been able to put cases with a similar diagnosis from well-known European and Asiatic clinics to this test and have not been disappointed. Our present practice is to treat all trachomatoid cases, if without corneal complications (and sometimes even those with distinct corneal changes), by lavage, till we feel that they must be treated as trachoma. Some months ago when discussing trachoma with F. F. Tang in the Lester Institute, Shanghai, where he had isolated a number of strains of B. granulosis from trachoma cases, I asked to see a case. It did not seem to me that the only case available for demonstration at the time could be regarded clinically as trachoma for experimental purposes. I hope I made this statement on the spot, if not, he, as an experimental scientist rather than a clinician, will forgive me for making it now.

From a statistical aspect the confusion which exists in the minds of ophthalmic specialists over the clinical appearances of the disease called trachoma is of importance. Last year the International Association for the Prevention of Blindness and the International Organisation Against Trachoma forwarded its 1934 report. In a section, on British India, occurred the following statement: —

"Dans un regiment de cavalerie en garnison dans la Province de la Frontière Norde-Ouest, 97% des Sikhs, 93% des soldats du Punjab et des Pathans, et 50% des Dogras étaient atteints de trachome.

Dans un bataillon d'infanterie en garnison dans la Province de la Frontière du Nord 73%, des Sikhs 48% des soldats du Punjab et des Pathans, et 39% des Dogras étaient atteints de trachome."
The British Journal of Ophthalmology

The statement seemed to me to require confirmation or elucidation, not only in the interests of trachoma research, but also in the interests of the Army in India. I visited the Public Health Commissioner with the Government of India, Simla, who placed the responsibility for the part of his report—from which the figures are supposed to have come—with the Director of Medical Services in India. The D.D.H.P., Army Headquarters, India, did not understand how these figures were arrived at and questions their correctness, so, in order to clear the matter up, I have placed the latter in direct communication with the author of the above quotation. I give this as an instance of the elasticity or breadth of the present methods of clinical diagnosis. There would certainly appear to be room for doubt as to whether the figures are correct if we accept the sense in which many well-known ophthamical specialists use the word trachoma. If we use the word trachoma in as loose a sense as that employed by those who primarily furnished the figures on which this international report was based, it may well do as much harm to the cause of the prevention of blindness as the Association intends to do good. Once the average practitioner in a country like India gets hold of the idea that any case of trachomatoid ophthalmia—or as he calls it, “granular lids”—is trachoma, he treats it as trachoma, quite likely by one of the more appalling methods advocated by ophthalmologists for severe or obstinate cases. This definitely ensures a larger number of serious ophthalmias in India than would otherwise be the case. For years I have been trying to teach both students and post-graduates to avoid diagnosing “granular lids” in eye cases about which they are uncertain and thus condemning their patients to the more crude treatments recommended for trachoma.

If we consider clinical opinion on the value of the vascular invasion and infiltration of the cornea which eventually give rise to pannus as one of the criteria of trachoma, it appears that there is not so much room for divergence. A typically situated “pannus trachomatous” as it is called, when well established, with facets, rounded follicular infiltrations, or Herbert’s pits, together with the conjunctival plasma cell hyperplasia, follicle formation, and scar tissue formation, gives a picture which most ophthalmologists would regard as affording satisfactory clinical criteria of trachoma. When we try, however, to establish certain of the early stages of the corneal invasion as pathognomonic it is more difficult and again we have serious differences of opinion. Wilson, for instance, has suggested that a certain type of behaviour of the extreme capillary fringe—the terminal marginal corneal loops of Graves—indicates trachoma when taken in conjunction with suggestive conjunctival appearances. I must contest this view. I have seen the appearances he describes in otherwise
suspicious cases which did not progress to typical trachoma when left untreated, in inflammatory cases of a non-trachomatoid nature, and finally so slightly marked in the induced human disease as to be indefinite. Herbert's lacunae and pits are regarded by many as characteristic. Unfortunately, there is some confusion amongst recent workers about what he actually described as may be gathered from the explanation of their origin by Meyerhof. I do not know if Herbert would agree today that the pitting he described was equivalent to the "ocelles" of Bonnet, but he originally made a point of dissociating his lacunae and pittings from a follicular genesis, so that those writers who see in these appearances the subsidence of small follicles are not observing what was originally described. If one regards the response to treatment as helpful in establishing a diagnosis there is much to be said in support, provided it is remembered that the ordinary response of the conjunctival membranes to the majority of noxious influences is that which one would expect of a lymphoid tissue.

One is tempted to think of an analogous problem and how its solution was aided to a great extent by treatment. I refer to what was formerly known as "dysentery"—now more aptly called "the dysenteries" or "dysenteric group of affections." It is still possible to find another dysentery although, thanks to a great extent to workers in this country, the number of distinct entities within the group is already considerable. In the early stages of the response of the mucous membrane of the large bowel there was formerly little to help the pathologist; it was more exact methods of bacteriology and parasitology and effects of treatment which cleared the air.

The treatment of trachoma has been so futile that in bad cases we are satisfied with destroying the conjunctiva and allowing scar tissue to replace it. The idea that this is the ultimate goal of treatment has steadily gained ground with the profession in general until it has been adopted on a large scale in the treatment of early trachomatoid affections, and in fact in every conceivable conjunctival affection with which early trachoma might be confounded. It is unnecessary to point out the folly of applying standard methods of trachoma treatment to a conjunctiva which, if left alone or washed with a non-irritant, would return to normal. In fact if one goes round the world, as I have done, observing the methods employed in the various dispensaries (and ophthalmic clinics) in the treatment of the trachomatoid and other affections of the conjunctiva, one is left with the impression that if some of the patients have not got trachoma when they first come to the clinic—and who is to say in the early stages whether they have or not—they will certainly be fortunate in not having either trachoma or its equivalent by the time they leave after a course
of treatment. Empirical treatment, then, can do a great deal of harm, but it may also help us in eliminating certain cases which we might otherwise regard as definitely trachomatoid. Expectant treatment by mild harmless methods, whilst the eyes are under careful observation, is wise in the hands of expert and inexpert alike. I am hardly alone in having observed peculiar cases of the disappearance of what might be regarded as typical classical trachoma. For example, a typically trachomatous conjunctiva returned to normal limits after an attack of generalized dermatitis exfoliativa due to arsenic. It may be said that this was of course syphilitic conjunctivitis; this is the most likely explanation, but the clinical condition deceived a number of experienced ophthalmologists. There is no need to multiply instances of other empirical cures; all workers of experience have no doubt observed them. The point I wish to make is, that if mild harmless drug treatment and lavage causes permanent disappearance of early trachomatoid signs, or relieves them so that the condition is recurrent but non-progressive, the affection is not trachoma although it may be trachomatoid, and the correct label should be used. The words "granular lids" in this connection should be abolished from the literature and from the hospital and dispensary nomenclature of countries actively interested in the prevention of blindness. Numerous empirical experimental methods of treatment have been tried, sometimes on a small scale, at other times more extensively, and these need concise tabulation for the information of workers interested in this possible line of attack on trachoma. One might prolong a discussion on the difficulties and confusions which confront the investigator in this great problem. I shall only refer to one more, that of using animals to aid our diagnosis. Already one of the fallacies in this connection has been alluded to; we must not necessarily expect trachoma to adopt the same behaviour in animals, even the Simians, as it does in man. Within the past few years a great deal has been done to clear up questions of Simian experiment, e.g., the extent to which natural monkey conjunctivitis may be confused with experimentally produced lesions. The same may be said of the attempt to determine—by means of large scale experiments—the typical results of transferring material from trachomatoid and other ophthalmias to different species of Simians (Olitsky, Thygeson and others). This is certainly a move in the right direction. I might perhaps mention that it is important to be quite certain of the species used. I have noticed in one laboratory a confusion between rhesus and sinecus. So far no clear case has been made out for the retransference of any experimentally produced trachomatoid affection to man. At least one recent writer has suggested that experimental work in human volunteers is more likely to produce fruitful results.
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This would appear to be so, and it seems desirable that such work, e.g., that of Piringer and other observers should be accurately and fully tabulated. At the beginning of this paper it was suggested that the investigation of the trachoma problem was disorganised. This is the impression one gets from a perusal of the literature. In view of the fact that there is such widespread interest in the problem and that the recent literature indicates a more concentrated effort, it may not be out of place to suggest that an attempt be made to abstract the international literature and present it under the different headings of investigation in an orderly and abbreviated form available to future investigators in any of the different fields, for easy reference. Such a work might well form part of the programme of an international association such as the International Organisation against Trachoma or of a journal such as the Revue du Trachome.

In so far as our local researches are concerned I have adopted the working plan of regarding as trachoma donors only such cases as show marked conjunctival appearances including follicles, capillary haemorrhages and some evidence of cicatricial changes well within the limits acceptable to the bulk of ophthalmic specialists, together with pannus and its concomitants of a similar acceptability. The absence of "H.P." bodies or the B. granulosis is not regarded as a contraindication, nor is the presence of any bacterial inhabitant. An excess of eosinophiles in the conjunctiva is regarded as a contraindication to selection. For practical clinical purposes, cases falling outside these limits are regarded as trachomatoid, unless some definite indication places them under suspicion in another group such as that of follicular conjunctivitis, spring catarrh, etc.

It was originally intended to withhold publication of that part of our work which has recently centred around attempts to isolate a virus from trachomatoid ophthalmia until we proved it of definite value or otherwise, but circumstances connected with the exigencies of Government service demand that some of the results, however immature, should now be recorded in the organ devoted to official Indian research, viz., The Indian Journal of Medical Research. It may be briefly stated here without infringing Government regulations that a virus has been isolated on the allantoid membrane of the chick from cases which showed such clinical stigmata of trachoma as to leave little doubt of their general acceptability, but up to date attempts to reproduce the disease by implantation on the normal human conjunctiva either in the case of the original growth or that of the sub-passages has not been successful. This virus is filterable (by ordinary methods of filtration), and the filtrates reproduce similar lesions on the allantoid membrane. With regard to filtration it is well-known that vaccinia virus is filterable
with difficulty unless filtration is carried out with serum or broth. This renders doubtful some filtration experiments carried out by methods prior to this technique. With this in view we have not carried out transmission experiments with filtered human trachomatoid material on normal humans or allantoid membrane, as we think that in such filtration experiments Gradacol membranes (Elford) should be used. These were not available at the start of our experiments.

This paper is not intended to be a scientific criticism of matters referred to, nor does it pretend to touch upon the many important phases of the trachoma problem, nor yet to make even a passing reference to the work of some who have done more in this field than others whose labours have been referred to; it is nothing more than a superficially discursive and almost unpremeditated statement such as might have been delivered at the annual meeting of the International Association for the Prevention of Blindness and the International Organisation against Trachoma had I been able to attend.

CAMPAIGN AGAINST TRACHOMA*  
(Presidential Address)

BY

PROFESSOR DR. EMILE DE GRÓSZ

According to § 2 of the statutes of the International Organization against Trachoma, initiated on the occasion of the XIII Ophthalmological Congress by van der Hoeve and Marx, and formed at Geneva in 1930, one of the aims of this Organization is "to hold conferences directed to the strengthening of the scientific bases of the anti-trachoma campaign, to settle questions of aetiology, diagnosis, therapeutics, spread and prophylaxis, and to occupy itself generally with the scientific and social effects of trachoma as well as to prepare bills and legislative measures for the same."

The session held at Madrid in 1933, on the occasion of the XIV Ophthalmological Congress was in the service of this aim. Here MacCallan, Angelucci, Morax, Pittaluga and Thygeson presented very valuable referata on the aetiology of trachoma. The session held in Paris in 1934 together with the International Association for the Prevention of Blindness initiated by its esteemed president de Lapersonne, served the same cause. At this session the referendaries MacCallan, Issa Hamdi el Mazni bey,
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