TRACHOMA

(Note on some interesting features which appeared in connection with a combined research by various members of the Government Ophthalmic Hospital and the King Institute of Preventive Medicine, Madras, 1935-6)

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In the *Brit. Jl. of Ophthal.* of June, 1935, I discussed in a general way some of the practical difficulties in connection with investigations into the aetiology of trachoma. In the same article an experimental advance was claimed in this connection, namely, the appearance of growths on the chorio-allantoic membrane of the chick when inoculated with unfiltered trachoma material. The possible value of the observation was hopefully alluded to, but those of us engaged in the research fully realised that it might prove sterile for various reasons apparent to any one familiar with experimental bacteriological work. Dr. C. G. Pandit conducted the laboratory aspect of the research and the detail of the combined work was published in the *Indian Journal of Medical Research* (Pandit, Wright, Sanjiva Rao, Satyanathan, October, 1935).

Briefly, our results indicated that material derived from the washed conjunctivae of persons suffering from clinical trachoma, when implanted on the chorio-allantoic membrane of the chick in the unfiltered condition produced growths which could be sub-passaged and were sterile to ordinary laboratory media. A suspension of such growths did not reproduce the disease on the normal human conjunctiva. Trachoma material such as that used for the egg inoculations when implanted on the normal human conjunctiva reproduced trachoma seven times out of seven. The average incubation period was five days. The onset of the condition was sometimes acute, sometimes quiet and almost non-inflammatory. The conjunctival changes were always trachomatoid in nature. The limbal vascularisation was not constant. Sometimes the marginal capillary changes were no more than might be observed in keratitis due to various causes. There was a tendency to spontaneous recovery in most cases. They were dealt with by lavage with a minimum of trauma. Certain experiments suggested that heating the trachoma material to 120° F. for two minutes was detrimental to the infective agent.

In continuing the work in 1935-36 we planned to investigate the effect of filtering the trachoma material through collodion membranes prior to implantation on the chick. Before this could be

commenced Lt.-Col. H. E. Shortt, I.M.S., who assumed the Directorship of the King Institute of Preventive Medicine, Guindy, kindly offered his criticism and co-operation and shortly afterwards took up the direction of the laboratory aspect of the research. During the year the clinical investigation was concerned largely with testing the infectivity of filtered trachoma material. The laboratory aspect of the work was side-tracked since controls revealed that a variety of agents other than known viruses and unfiltered trachoma material produced similar chorio-allantoic growths with varying histopathological changes. Under the circumstances Col. Shortt found it necessary to institute an enquiry into the classification of the chorio-allantoic changes according to the nature of the irritant used and the histopathological effect produced.

At first sight this seemed to be the end of our original idea, that possibly a trachoma virus was responsible for the chorio-allantoic growths produced in 1934. It may be so, but until the whole question of the effect of different agents (organismal, chemical, mechanical, known virus, etc.), on the chorio-allantoic membrane of the chick is worked out, nothing further can be said as to the significance of the effects of inoculations with unfiltered,—but apparently bacteriologically sterile—trachoma material. This also applies to the fact that our most recent egg inoculations with trachoma material filtered through collodion membrane 1.8μ a.p.d. gave growths which were successfully sub-passaged, when ground and filtered through similar membranes. The investigation into the chorio-allantoic reactions to irritants was pursued during 1936 in Col. Shortt's absence by Dr. C. G. Pandit, who agrees with me that a few words about this aspect of the work are permissible pending detailed publication.

It appeared that many such growths were what one might call epitheliomatoid in character in so far as the chorio-allantoic epiblast (?) is concerned showing marked proliferation, cell nest formation, etc. That whereas chemical and mechanical irritants produced growth-like tissue changes, these were not sub-passable, whereas pure virus growths and certain organismal growths were, even in the latter case when the material used for sub-passage was ground and filtered through membranes a.p.d. 1.1μ . This suggestion of mutation naturally stimulated renewed interest in our trachoma growths. The essential details of the laboratory and clinical work for 1935-36 will be published in due course in the *Indian Journal of Medical Research* under the rules of the Indian Research Fund Association which made a grant towards the investigation. Meantime it may be stated here in a general way that the clinical research work of 1935-36 appeared to support several aspects of the trachoma problem to which I have

previously drawn attention. In contrast to the 1934 findings it was noted that material from typical cases of trachoma does not always infect the normal human conjunctiva. This may be due to a number of causes, *e.g.*, because the material is non-infective, the dose is insufficient, etc. In certain cases there was no conjunctival response to known infective material possibly because the individual was resistant, the dose insufficient, etc. As yet there is not sufficient evidence to explain these observations. Such findings opened up new fallacies in connection with the clinical side of the research and made the control work very difficult. It is significant, but as yet of doubtful interpretation, that filtered trachoma material (1.8μ a.p.d. collodion membrane), failed to infect the normal human conjunctiva in nine cases out of nine attempts. It is inevitable that in a research of this type the course of the investigation should be deflected to meet those difficulties as they become unmasked, the non-recognition of which would lead to fallacious conclusions. The deflection of the laboratory investigation has been stated above.

On the clinical side the fallacies which arose because certain cases of clinical trachoma (trachomatoid affections), do not transmit the disease—(whereas similar donors infect the same recipient)—may be partially got over by pooling the material collected from a number of apparently typical trachoma donors. I say partially, because it introduces a new fallacy, namely, dilution of a possible virus, which must be catered for by a concentration method. The fact that certain persons are apparently not susceptible to trachoma material known to be infective to others, raises a more serious problem, which demands separate investigation as regards individual and racial, acquired and natural aspects.

In this connection it may be noted that part of our experimental work published last year suggested that the serum of old healed trachoma cases had acquired certain properties of immunity. The tendency for the experimental disease is to recover spontaneously, provided the conjunctiva is not traumatised by unnecessary manipulations and the application of irritants, has its counterpart in routine out-patient work. The frequency with which one observes a uniformly scarred and healed conjunctival membrane, with a grey haze and occluded vessels in the upper part of the cornea, in perfectly quiet useful eyes, with a history of previous symptoms indicative of kerato-conjunctivitis which was not treated, is sufficiently significant. This is not meant to imply that the difference between the severe forms of trachoma, so familiar to all who deal with the disease, and the milder spontaneously healing forms, are determined by misdirected treatment; for experimental clinical work definitely shows that in certain cases the disease bursts forth in a fulminating manner and in others it starts

insidiously, and individuals vary in their response to the same infection. The difficulty of obtaining recipients makes controlled clinical investigation most tedious, but even a few definite data such as our clinical research has yielded make it worth the prolonged periods of observation demanded.

Apparently it is premature to assume and speak of the virus of trachoma, when filtration appears to protect the human conjunctiva from infection, even though chorio-allantoic growths resulting from filtered trachoma material may be sub-passaged when ground and filtered. The possibility of an agent with filterable and unfilterable stages must at least be considered. One must be very guarded about suggesting aetiological hypotheses on insufficient proof in such a problem, when, even the clinical criteria of the condition under investigation are not agreed upon amongst authorities. This fact deprives the figures collected and published in connection with trachoma of any real statistical value. It must be rare to find clinically an absolutely uncomplicated early trachoma and very difficult to make a positive diagnosis of such a condition. Mixed infections, environment and so on alter the clinical picture in the later stages. Even if we assume that certain apparently unmixed affections of the conjunctiva and cornea represent the disease "trachoma" *sui generis*, it is obvious that its aetiological agent is just as likely to fall into sub-groups as say some of the known pathogenic organisms, with presumably the production of a varying clinical picture. Should the agent be a virus this is perhaps more likely to be a feature. There has been a vast amount of new work on the trachoma problem in the past few years and in spite of a useful general advance some unjustifiable conclusions have been reached on insufficient evidence. It is essential that the research worker should guard against the acceptance of observations—his own or those of others—which favour a preconceived conclusion, as evidence, without confirmation. Morphological observations constitute poor evidence especially when dealing with such things as free elementary bodies. One ought to be less likely to fall into error when cultural and transmission methods are favoured, but as indicated above the difficulty in avoiding fallacies when trying to obtain evidence concerning the aetiological agent or agents in trachoma or the trachomatoid infections is enormous.