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COMMUNICATIONS

A DISCUSSION ON THE AETIOLOGY OF TRACHOMA
WITH SPECIAL REFERENCE TO BACTERIUM
GRANULOSIS (NOGUCHI)

BY

ROWLAND P. WILSON

MEMORIAL OPHTHALMIC LABORATORY, CAIRO, EGYPT

General Considerations

THERE is probably no subject in the whole of ophthalmology which teems with greater difficulties or has given rise to wider diversity of opinion than the subject of trachoma.

Sociological, clinical and aetiological problems alike cry aloud for immediate solution. Opinions and theories without number have been forthcoming but the original problems not only remain but also have become more complicated than ever. Indeed, the difficulties have increased so enormously and the confusion has become so great that at last we are now having to return to the beginning to ask ourselves "What is trachoma?"

To-day, when we compare the definitions of trachoma as given by authorities on the subject, we find that no two agree on all points. This, however, should not confound seekers after truth nor mystify them because experts are not entirely in accord. It must be remembered and admitted that the essential features of trachoma may become modified to a greater or lesser extent according to the type of patient, his constitution, his social condition, his nationality, the locality in which he lives, the presence of mixed infection, the preponderance of one or more essential

features of the disease, the duration and treatment of the disease and other individual factors.

Trachoma in its various stages may present very varied clinical appearances but if we take the whole picture and progress of the disease into account and have regard to the factors which may modify the disease, there will, I believe, be far less confusion in our conception of what constitutes trachoma.

We find then as we survey modern views that even with regard to the clinical appearances of the disease there is very wide diversity of opinion. Some for instance would regard follicular conjunctivitis and trachoma as essentially the same disease the latter being an advanced stage of the former, while others consider inclusion blennorrhoea of adults as identical with trachoma.

If such be the case the problem of aetiology becomes a most complex one as it must certainly be very difficult to explain such varied appearances on the basis of the same inciting agent.

For the moment, however, we are not so much concerned with what constitutes trachoma as with the latest developments in regard to the aetiology of this disease.

Aetiology

Since the times of Koch¹ many attempts have been made to attach an aetiological importance to one micro-organism or another but of more recent years certain schools have sought to establish their firm conviction that trachoma is a non-specific disease. In 1926, Royer² suggested that trachoma might be a deficiency disease and quite a number have been inclined to think that fundamentally there is a vitamin deficiency. It is true that trachoma shows a selective affinity for the poor and underfed but it must not be forgotten that the conditions under which such people live are much more likely to be the cause of the prevalence of the disease than the food which they eat. In a recent ophthalmic survey of a typical country village the only patient over one year of age in whom we could find no trachoma was a marasmic child. Up to the present there has been no experimental or clinical evidence to confirm the above opinion.

Of more importance, however, is the conception that trachoma is a local manifestation of a constitutional derangement. Foremost in this school is Angelucci³ who insists on the relationship of "adenoidism" to trachoma. His view is that trachoma is not a distinct entity *per se* but an advanced stage of follicular conjunctivitis in which the cornea becomes involved. He says that trachoma finds in adenoid patients the best circumstances for the development of the severest cases but does not deny the fact that there may be an infectious element in the disease. One must

admit that there is much to be said for many of Angelucci's contentions, but to insist on an essential relationship between "adenoidism" and trachoma seems to be unjustified so far as trachoma in Egypt is concerned.

In the past, doubt has often arisen as to the infectivity of trachoma and even to-day there are strong supporters of opposite opinions. The balance, must, however, weigh in favour of trachoma being a transmissible disease. The occurrence of epidemics, its spread in institutions, and accidental and experimental infections would all tend to confirm this opinion. During the Great War hundreds of soldiers in the Russian and Austro-Hungarian Forces succeeded in infecting themselves with trachoma in order to avoid active military service, while the numerous investigators, notably Sattler⁴, Greeff, Frosch and Clausen⁵, Piringer, Addario⁶, Taboriski⁷ and others, have reported convincing records of the transmission of the disease from man to man. In regard to this contention, however, it remains a very difficult problem to explain the not uncommon condition of unioocular trachoma.

There seems little doubt then that trachoma is a communicable disease, but the question remains as to whether it is due to a single specific infection or not. Williams⁸ (1912—1913) and others believe that it is a chronic inflammatory condition produced by ordinary pathogenic bacteria and the authors of the chapter on trachoma in the System of Bacteriology published by the General Medical Research Council of Great Britain suggest that "it would seem that trachoma does not supervene on a normal conjunctiva but that some form of inflammatory reaction is necessary before the condition appears." It ought to be possible to clear up the latter uncertainty from clinical experience but this is actually difficult as there exists in all cases of trachoma a stage during which it is impossible to state the diagnosis definitely because of the appearances being simply those of any ordinary simple chronic conjunctivitis. There exists, therefore, in true trachoma what one might call a "proto-trachomatous" stage which is indistinguishable from certain other forms of simple chronic conjunctivitis. From the experimental point of view we are also greatly handicapped in that no animal shows typical trachoma when inoculated with human trachoma.

To establish unquestionably the specificity of trachoma, one must first be able to isolate from all cases of active trachoma a specific micro-organism or virus, which on inoculation into the *human* conjunctiva will reproduce an unmistakable trachoma and from which the same organism or virus must be obtainable.

I have deliberately said *human* conjunctiva because of the immediately preceding statement. Numerous experiments have

been performed on monkeys and on the higher apes, but in no case have the typical lesions as seen in the human conjunctiva been induced. When human trachomatous materials are inoculated into the animal conjunctiva various clinical changes have been observed. It is perhaps not necessary that exactly similar lesions should be reproducible, but until now, no one has been able to establish what, in animals, is the exact equivalent of human trachoma. Indeed, interpretations of positive inoculations in animals are particularly open to criticism. I⁹ have previously reported my findings in relation to spontaneous follicular disease in monkeys and recent experience has impressed upon me more than ever the fact that we can never arrive at any determinate conclusions so long as we confine our experiments to animals. We have shown, as have other workers, that monkeys may suffer from a folliculosis of the conjunctiva either spontaneous or induced and that this condition may at times bear a slight similarity to human trachoma. Recently I inoculated and re-inoculated two *Macacus rhesus* monkeys with scrapings from human trachoma; the first inoculation was negative in both instances but after the second inoculation both monkeys developed a condition which was in every clinical respect absolutely indistinguishable from a typical natural folliculosis. It would, however, greatly help us if material from animals such as these two and from animals suffering from the spontaneous condition could be transferred to the human conjunctiva to note the result. Such experiments might greatly repay to scientific knowledge the sacrifice which suitable volunteers would be called upon to make.

If then trachoma owes its origin to a specific cause does it belong to that group of diseases to the cause for which a filterable virus has been attributed? On the one hand, Pfeiffer and Kuhnt¹⁰ in 1905 made repeated unsuccessful attempts to induce trachoma in human subjects with materials obtained by filtering emulsions of trachomatous tissues, and more recently Trapesontzewa¹¹ inoculated the eyes of blind volunteers and also her own eyes, but in all alike with negative results. The experiments in both instances, however, lacked an important control inasmuch as the original materials and the residues after filtration were not tested for infectivity. Hess and Roemer (1910), however, repeated the experiments of Pfeiffer and Kuhnt, but in addition tested the residues, and they obtained positive results in animals with the residues and negative with the filtrates. They therefore concluded that the virus is not filterable. Such experiments are, however, not entirely conclusive. On the other hand, Nicolle, Cuénod and Blaizot¹² as a result of their experiments on chimpanzees and magots concluded that the virus of trachoma is filterable. More recently, Cuénod and Nataf¹³ have suggested that the filterable factor of trachoma may possibly

live in symbiotic relationship with a non-filterable factor, the B. granulosis perhaps being the non-filterable factor.

The mechanism of filtration, however, is not a simple one, for as Rivers¹⁴ has shown there are numerous "factors which serve to influence the results of all filtration experiments." It is possible that one or more of such factors may explain the radically opposite opinions which are at present held on the filterability of the trachoma virus.

Intimately associated with this particular phase of the trachoma problem is the problem of "cell-inclusions" which may often be found in epithelial scrapings of trachomatous conjunctivae.

When Prowazek and Halberstaedter¹⁵ first observed these peculiar bodies in the epithelial cells it was thought that the active virus of trachoma had been found. It was soon discovered, however, that similar bodies were to be found in other diseases of a totally different kind. The difficulty was further complicated by the fact that Stargardt and Heymann¹⁶ found identical bodies in blennorrhoea of the new-born and in the cervical and urethral mucosa respectively of the parents of children with ophthalmia neonatorum. Hertzog¹⁷ was led to the conclusion that trachoma is due to a strain of gonococcus which lives as an intra-epithelial parasite, but Lindner¹⁸ also found them in the urethra in non-gonorrhoeal cases. It is important to state here the theory propounded by Lindner, who believes that the viruses of trachoma and inclusion blennorrhoea were originally the same, but the former by repeated passage from one conjunctiva to another has acquired the property of producing trachoma while the latter lives in the genital tract and produces, when transferred to the conjunctiva of the new-born, an inclusion blennorrhoea.

Inclusion bodies have now been found in a large number of diseases both ophthalmic and otherwise, but Lindner, Aust¹⁹, Taboriski²⁰ and others still insist on the parasitic nature of these bodies in trachoma.

The view that the inclusion bodies of Halberstaedter and Prowazek represent living parasites is, however, not supported by certain recent investigators. Bengston²¹, for instance, was able to induce in guinea-pigs forms corresponding in appearance to the so-called "elementary bodies" of Prowazek and the "initial bodies" of Lindner by inoculating the conjunctiva with certain Gram-negative rod-shaped organisms isolated from the conjunctivae of patients suffering from trachoma, and it is her belief that the "elementary bodies" and the "initial bodies" represent modifications of the organism originally introduced, the modifications being brought about by the action of lytic substances in the conjunctival fluids and tissues.

Gifford and Lazar²² have further reported the production of

typical inclusion bodies in the conjunctiva of rabbits and guinea-pigs by inducing an artificial conjunctivitis with *Bacillus pseudotuberculosis* rodentium, nicotine and croton oil. They, therefore, feel that if inclusions can be produced by chemical irritants, they cannot be degenerated bacteria and conclude that they are of no importance in the aetiology and diagnosis of trachoma. Others again, von Szily²³, Solovieff²⁴ have considered the inclusions as probably only products of nuclear degeneration.

It is probable, however, that many erroneous observations have been published in regard to inclusion bodies and, as Rivers¹⁴ emphasizes, "opinions regarding inclusions should only be made by men trained in the normal and pathological tissues." Many controversial points have been raised in regard to the character and significance of inclusion bodies and although the belief in their aetiological relationship to trachoma had up till recently fallen largely into disrepute, one must not in the light of the most recent research put the subject on one side as being of no importance. To quote Rivers¹⁴ again "Under properly controlled conditions the presence of inclusions, accepted as significant, will undoubtedly in the majority of instances be indicative of the presence of a virus in the immediate vicinity."

I have summarized the position with regard to "cell inclusions" and filterable viruses in rather more detail because the subject is at present assuming increasing importance.

And now finally I must deal with the recent researches of Noguchi on the aetiology of trachoma and note especially the work which has been done since his original monograph was published.

Bacterium granulosis (Noguchi)

In May, 1926, Noguchi, at the invitation of Dr. F. I. Proctor, made a bacteriological study of five cases of trachoma taken from an Indian School in New Mexico. These five cases were minutely studied, using various cultural methods, and every kind of micro-organism which was isolated from the materials was tested on monkeys. A great variety of bacteria was found and all with the exception of one small Gram-negative bacillus, which he found in four of the five cases, failed to produce any changes in the conjunctiva of the experimental animals. The bacillus, to which he gave the name *Bacterium granulosis* was, however, pathogenic for monkeys and apes and produced in them a granular conjunctivitis closely resembling trachoma in man. Here it is of extreme interest to note that when Lindner later examined the original cases from whom the tissues had been taken, it was precisely the patient from whom Noguchi had been unable to isolate *B. granulosis* that Lindner declared to be free from trachoma.

Noguchi further succeeded in transferring to chimpanzees, baboons, and *Macacus rhesus* monkeys through four direct successive tissue passages the experimental granular conjunctivitis which he had first induced with pure cultures of *B. granulosis*; likewise he was able to isolate the same bacillus from the lesions induced in the animals.

He also noted that when lesions were induced in one eye the infection spread spontaneously to the other eye. Pannus was, however, never seen but it is reported that scar formation was observed.

Since the publication of Noguchi's work there has been a tremendous revival of interest in the problem of trachoma and several workers have published confirmatory reports on Noguchi's findings. In America, Finnoff and Thygeson²⁶ have isolated nine strains (from two Indians, two Japanese and six whites); Kendall²⁷ one strain (from a white); Tilden and Tyler²⁸ six strains (all from Indians); Olitsky²⁹ three strains (all from whites) and all strains conform exactly to Noguchi's original strains.

In other parts of the world, reports of positive findings of *B. granulosis* have come from Addario³⁰ in Sicily, Stepanowa and Azarowa³¹ in Ukraine, Weiss³² of St. Louis (strain isolated in Tunis), Lumbroso³³ in Tunis, Bietti³⁴ in Italy and Lindner and Rieger³⁵ in Vienna, but there is some doubt as to whether these strains isolated in the Old World are exactly identical with *B. granulosis* or not. Until now there is no report of any of the above strains having been checked by the Rockefeller Institute, New York. Stepanowa, Azarowa and Lumbroso reported positive results from inoculations of their strains into monkeys. Bietti isolated two strains from 16 patients but reports that when these were tried on monkeys' eyes and on his own eyes the results were negative. With regard to Lindner and Rieger they report that their two strains were isolated from cases of folliculosis (although Finnoff and Thygeson have failed to find *B. granulosis* in non-trachomatous diseases of the eye) but it would appear from the description of these strains that they correspond very closely if not exactly with *B. granulosis*. Animal inoculations with the two strains proved negative and so Lindner inoculated his own conjunctiva. Three weeks later a folliculosis appeared without inflammation and after 2½ months the lesions had almost completely disappeared.

Amongst those who have failed to find *B. granulosis* in trachomatous patients may be mentioned, Bengston³⁶ of the United States Public Health Service, Morax³⁷ and Brückner³⁸, while yet others have been unable to produce any lesions in *Macacus rhesus* monkeys with cultures of the organism received from the Rockefeller Institute, New York.

From this it will be seen that the confirmatory evidence from countries other than America is not wholly reassuring. There are numerous difficulties associated with the isolation of *B. granulosis* and it is easy to isolate from the conjunctiva minute Gram-negative organisms, some of which bear a very striking similarity to Noguchi's bacillus with which they may be quite easily confused. One has therefore to be very critical in the interpretation of one's results.

Recent Results of Cultivation Experiments

In 1928 I³⁹ reported to the Ophthalmological Society of Egypt that an organism which appeared to correspond very closely with *B. granulosis* had been isolated from cases of Egyptian trachoma but further experimental work showed that it was probably only one of the small Gram-negative motile rods which may occasionally be isolated from the conjunctiva. The strain was lost before the true nature of the organism could be determined. Throughout the past year renewed attempts were made to isolate *B. granulosis* from further cases but without success. Dr. A. F. Abbassi who has also made repeated attempts to isolate the bacillus likewise failed.

From November 1930 to January 1931, we were very glad to have working with us in the Memorial Ophthalmic Laboratory, Giza, Dr. Phillips Thygeson of Denver, Colorado, who in company with Dr. F. I. Proctor had made a special visit to investigate Egyptian trachoma. During the two months of work, 16 cases of definite active trachoma showing all the typical signs of the disease were very carefully investigated. The same cases were independently studied by Dr. Thygeson, Dr. Abbassi and myself, but not one of us succeeded in isolating a single strain of *B. granulosis*.

The micro-organisms common in most conjunctival sacs were found, *e.g.*, xerosis bacilli, diphtheroids, and staphylococci in every case, sarcinoids, a few strains of streptococci and pneumococci, Koch-Weeks and Morax-Axenfeld bacilli and numerous strains of other Gram-negative bacilli. A few small and large Gram-positive rods were also encountered. It was the experience of each of us to find amongst the Gram-negative bacilli, to which special attention was paid, some very small forms which morphologically were indistinguishable from *B. granulosis* and were also actively motile. In certain respects the cultural characters of some were also very similar to those of *B. granulosis* and were only finally rejected on failing to agglutinate with rabbit immune serum.

Afterwards, through the kindness of Dr. Thygeson, who left with

me some of the strains of suspicious Gram-negative bacilli which he himself had isolated, I was able to pool all the various strains into several groups and to inoculate *Macacus rhesus* monkeys therewith. Neither the strains isolated by myself nor by Dr. Thygeson gave rise to positive results in any of the monkeys even after three heavy inoculations on successive days.

Therefore, although I believe we have followed closely the technique recommended by Noguchi, our results have been entirely negative.

Recent Results of Transmission Experiments with Bacterium granulosis and Infected Monkey Tissue

(1) *Transmission experiments with B. granulosis*:—On several occasions, different strains of Bacterium granulosis have been very kindly sent to me by Dr. Simon Flexner, Director of the Rockefeller Institute and by Dr. Olitsky of the same Institute and these strains have always conformed to the morphological, staining, cultural and biological reactions described by Noguchi.

Up till the end of 1929, one *Cercopithecus aethiops*, three *Macacus sinicus* and two *Macacus rhesus* monkeys had been inoculated with the above strains, but the results after 4 to 5 months observation were entirely negative. Another *Macacus rhesus* monkey which died 16 days after sub-conjunctival inoculation showed no abnormal lesions.

A new batch of *Macacus rhesus* monkeys was received from India early in 1930 and two separate attempts to induce granular lesions in three of them with fresh strains received from America failed to produce more than a slight temporary reaction. After each separate attempt the monkeys were observed for a period of 3 to 4 months.

Later in the year (working in conjunction with Dr. Phillips Thygeson) these three monkeys were again subjected to re-inoculation, two with fresh strains sent by Dr. Flexner and one with a strain brought to Egypt by Dr. Thygeson, but again the animals proved refractory. Other four monkeys (*Macacus rhesus*) were inoculated and re-inoculated several times by Dr. Thygeson with strains which he had brought from America but again with no reaction whatsoever.

Thus after trying several different strains of *B. granulosis* we utterly failed to induce positive granular lesions in 13 monkeys.

(2) *Transmission experiments with infected monkey tissue*:—Were it not for the fact that Dr. Thygeson brought to Egypt two monkeys in which he had induced granular lesions in America we should have been unable to carry out tissue experiments. These monkeys on arrival did not show very marked lesions but

a small piece of the infected conjunctiva was transferred from one of them to a *Macacus rhesus* monkey. After 11 days the inoculated eye was a little congested but it was re-inoculated with fresh tissue. By the 28th day from the first inoculation, an unquestionably positive result had ensued with marked follicle formation and thickening of the conjunctiva which, however, always presented a glistening surface.

On the 38th day, when re-examined the uninoculated eye still appearing healthy, secretion from the infected eye was transferred to the sound eye; six days later this eye showed definite signs of involvement, and marked lesions quickly developed.

From this monkey, tissue was transferred to one of the *Macacus rhesus* monkeys which had resisted three separate attempts to induce lesions with cultures of *B. granulosis* and in 10 days it was clear that the early stages of a positive result were well established. When examined on the 16th day there were well-marked lesions in both eyes, the infection having spread spontaneously to the uninoculated eye.

Infection of Monkeys by Contact

From the time that this last monkey was inoculated with tissue it was caged with two other monkeys which had also resisted three separate attempts to induce lesions with pure cultures of *B. granulosis*, and after one month one of them had developed early lesions, first in the eye which had never been inoculated and then a week later in the other eye. After $2\frac{1}{2}$ months both eyes showed severe lesions. The other monkey, however, remained normal (*i.e.*, after $2\frac{1}{2}$ months.)

It is therefore clearly demonstrated that one can always obtain positive results in monkeys by tissue transfer, that infection may also be conveyed to monkeys by swabbing a healthy eye with secretions from an infected eye, and that infection may occur as a result of co-habitation. These experiments wholly confirm similar experiments by Tyler and Olitsky.

Transmission Experiments with Human Trachomatous Materials

In December, 1928, at the International Congress of Tropical Medicine and Hygiene held in Cairo, I reported among other cases the results of inoculating two *Cercopithecus aethiops* monkeys with human trachomatous materials. Both of these monkeys developed marked lesions which, however, later subsided into a condition which was indistinguishable from folliculosis in monkeys. (See coloured plates in the above report).

As the above experiments were performed on *Macacus rhesus* monkeys it was therefore desirable to compare in the same species the lesions produced by monkey tissues with those produced by human trachomatous tissue.

Two *Macacus rhesus* monkeys were accordingly heavily inoculated twice with tissues from cases of trachoma in their most infective stages. Both animals developed lesions in the inoculated eyes only but the appearances were typically those of and absolutely indistinguishable from a mild case of spontaneous folliculosis.

Transmission Experiments to the Human Conjunctiva

It is obvious from the preceding experiments and on account of the possible fallacies in interpretation which may arise out of the fact that monkeys are susceptible to spontaneous and induced follicular lesions of simple character (folliculosis), that animal experiments are of limited value. During the past year several investigators (Weiss⁴⁰, Howard⁴¹ and myself) working with recognized strains of *B. granulosis*, have made inoculations into the healthy conjunctivae of blind volunteers. Both Weiss and Howard have had negative results and one case of perfectly healed trachoma inoculated by myself also failed to develop lesions. In three other volunteers I have also had negative results. One of these was a patient suffering from an incurable disease who died three weeks after inoculation, but up to the time of death there were no signs of any pathological changes. The other two volunteers both proved entirely refractory to the first attempt to induce lesions, but a second attempt was made seven months later with a mixture of the most virulent strains with which Dr. Thygeson was able to supply me but which, however, had previously failed to produce the disease in monkeys. One patient (a man aged 38 years, free from trachoma but suffering from a mild catarrhal conjunctivitis from which no pathogenic organisms could be cultured), developed 18 days later an acute angry-looking conjunctivitis in the inoculated eye and later a similar condition in the uninoculated eye, but of less severity. The palpebral conjunctivae, upper and lower, became deeply congested and granular in appearance, the globe also showed slight circumcorneal congestion, but there was very little discharge. The inflammation lasted about a week and the eyes gradually returned to their previous condition leaving no trace of the *B. granulosis* infection. Secretion taken from this patient's eye during the height of the inflammation, when inoculated into a monkey, failed to produce any pathological lesions. After three months the patient still remained well.

The other patient, a girl aged 16 years, in whom it was difficult

to say if she had ever had trachoma or not, developed only very mild conjunctival congestion one month after inoculation and this quickly disappeared entirely.

As monkey tissue transfers have always proved so successful I inoculated the last patient on two separate occasions (with an interval of one month) with tissue removed from a monkey showing well-marked lesions induced by a previous tissue transfer but on both occasions the results were completely negative.

Addario³⁰, however, has reported the production of a genuine trachoma in the human conjunctiva by infection with *B. granulosis*, but no one has yet confirmed his result.

In America, Dr. Richards and another person volunteered to submit to inoculation. In the former a severe granular conjunctivitis which closely simulated trachoma ensued, but cure was complete in a very short time with treatment. An acute conjunctivitis also resulted in the second volunteer, but the condition cleared up of its own accord after a few days.

Interpretation of Animal and Human Experiments

The question which now remains to be solved is "What is the relationship of *B. granulosis* to human trachoma?" Attempts have chiefly been made to solve this by using the *Macacus rhesus* and the higher apes as the experimental animal.

If the form of granular conjunctivitis which has been produced by Noguchi, Tilden, Tyler, Olitsky⁴², Finnoff, Thygeson and others is genuine trachoma then it is certain that there is a most intimate relationship between *B. granulosis* and human trachoma. But is it genuine trachoma? We are not sure what genuine trachoma looks like in monkeys and therefore it is impossible to answer this question conclusively.

I have seen a large number of cases of spontaneous folliculosis in monkeys. I have seen an identical picture induced from perfectly simple measures and I have also seen precisely the same picture induced after inoculation with human trachomatous tissues. If we were to argue on this basis alone we might be justified in saying that monkeys may suffer experimentally and spontaneously from genuine trachoma but the clinical course of the animal disease never follows that of the human disease.

The lesions which are induced by tissue transfers from one infected monkey to another, in certain respects resemble the human disease, but the tarsus is seldom involved, pannus has never been observed, the conjunctiva although thickened and raised by sub-epithelial follicles always remains smooth and glistening, the lesions are very localized and have only very rarely led to definite scar formation, indeed the clinical picture is just one of a severe

folliculosis. It is also of interest to note here Lindner's opinion⁴³ on the monkeys which he saw at the Rockefeller Institute. He says: "There is no doubt in my mind whatsoever that Noguchi's experimentally produced conditions have nothing in common with trachoma. It can scarcely be doubted that Noguchi has discovered not the cause of trachoma but one of the causes of folliculosis of the conjunctiva."

When the late Prof. Ernst Fuchs, however, was visiting America in 1930, he examined some of Noguchi's monkeys and in his opinion they were suffering from "undoubted trachoma."

But we believe that this problem will never be settled except as a result of human experiments. There have been several negative results up to date, while in others a simple acute reaction lasting only a short time and leading to none of the sequelae of trachoma has been the only result. Negative results following transfer of monkey tissue to the human eye are also of considerable importance. It is quite possible, however, that B. granulosus may be only pathogenic for the human conjunctiva under certain conditions.

The finding of B. granulosus has been the means of creating fresh and world-wide interest in the subject of trachoma. For the moment the evidence in favour of its being the cause of this serious disease is not convincing, but when we understand the conditions better it may yet prove to be the key that will serve to open the way not only to an accurate knowledge of the disease but also to a discovery of therapeutic measures which will enable us to rid and protect nations from its ravages.

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THE OCULAR COMPLICATIONS OF ACNE ROSACEA

BY

J. H. DOGGART

MOORFIELDS RESEARCH SCHOLAR

I.—Abstract of the Literature

Aetiology of Acne Rosacea.—The majority of sufferers from acne rosacea are women between the ages of 30 and 60 years. In many standard text-books the women are said to be five or more times as numerous as the men, but in Triebenstein's series of 274 patients, and in Rulison's 135, one-third were males. Triebenstein has seen the disease in infants less than three years old, but it is certainly unusual for anyone to be affected before the age of 20. The causation is not definitely known, although many writers on this subject have agreed in suspecting tea, alcohol, and dysmenorrhoea. Recent researches by Ryle and Barber showed that the average amount of gastric hydrochloric acid secreted by acne