

MUTERMILCH (J.) Compliments of L. Webster Fox M. D.
1304 Walnut St. Phila., Pa.

TRACHOMA

—BY—

JULES MUTERMILCH, M. D.,

Translated for the Ophthalmic Record by

L. WEBSTER FOX, M. D.,

PHILADELPHIA, PA.



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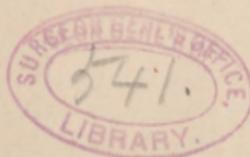
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In the January Number (1893) of *Annales D'Oculistique*, Dr. Mutermilch has written an exhaustive article on the pathology of trachoma. As the editor of the *Record* has arranged for the publication of an article* by the famous ophthalmic surgeon on "The Pathological Anatomy of Chronic Inflammation of the Conjunctiva", I feel that this paper will be an acceptable continuation of the other. Dr. Mutermilch says oculists are far from being agreed on the significance of the term trachoma which serves to determine various forms of conjunctivitis which differ greatly to the naked eye. To some, the presence of a follicle, there need be but one, suffices to prove the diagnosis of trachoma; in others this affection begins when the follicles are developed on the retrotarsal fold. (Adamuck); to others again it is the one characteristic which alone permits of the diagnosis of trachoma. As to the etiology of this affection there is a marked disagreement among authorities, who divide themselves into two classes. The one (Dualists) consider trachoma as an essential disease developing under the influence

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of a specific parasite and having nothing to do with follicular conjunctivitis (Sæmisch.) The other (Unatarists) consider trachoma to be only a consecutive condition of follicular conjunctivitis. There are also a number of ophthalmic surgeons who see trachoma is every chronic inflammation of the conjunctiva, making no distinction between chronic blennorrhœa, chronic contagious conjunctivitis, etc., etc.

In the chaos of these divers opinions one may find some points on which all ophthalmic surgeons are agreed; these are, the chronic character of the disease in question; its infectious origin; the facility with which it is communicated, often taking an endemic character; and, finally, the gravity of the affection, for it frequently provokes very serious complications in the cornea.

If we compare the clinical observations with those given anatomically, we arrive at conclusions essentially contrary to the ideas formerly admitted by the authorities on the subject of trachoma; we easily see that no definition of trachoma is satisfactory and that the contagious character of the disease, as generally accepted, is false, owing to there being no basis of real facts.

Histological research made in many different cases of chronic conjunctivitis has shown me from an anatomical standpoint that there are different forms of chronic inflammation. In all conjunctival inflammations, so dissimilar to the naked eye, from the simplest to the most exaggerated, I constantly find the same anatomical alterations, not differing in the least degree. The clinical observations are not in discord with the anatomical pictures, but, on the contrary, confirm in a very evident manner the gradual change of one form of the disease to the other. Those students who consider Trachoma as an independent affection and distinct from follicular conjunctivitis, base their opinion on the following fact: Follicular conjunctivitis generally heals without leaving any mark or cicatrice and provokes no complications in the cornea.

As a general rule the classifications based on the aspect, and the different size of the follicules, their localization, and other points have no foundation, and are the cause of the confusion

existing on the subject of trachoma. The follicule, I am convinced, is nothing but the result of the lymphoid infiltration exaggerated in the sub-epithelium tissue (adenoid.) As the abundant migration of the lymphoid elements of the vessels is provoked by the divers agents, and as this phenomenon is observed in the various morbid processes, the follicule may accompany all the inflammatory affections of the conjunctiva, some being the origin and intensity of it. Already the elevation of the hyperæmia of the conjunctiva may give impulse to the production of follicules, especially in badly nourished individuals. After the instillation of atropia or eserine into the conjunctival sac, we may see numerous follicules produced: Dust, smoke, irritating vapors, which may have acted for some-time on the conjunctiva often produce the active development of the follicules. Individuals who have errors of refraction, especially when not corrected by glasses, are subject to ocular hyperæmia, by reason of the constant effort of accommodation and in these persons are often observed in the conjunctiva these follicules more or less abundant, following the general condition of the organization. Consequently one need not be surprised to find the conjunctiva filled with follicules after the minimum alterations of the epithelium, and to see these productions disappear only after the improvement of hygienic conditions. Thus then, that which certain ophthalmic surgeons name follicular conjunctivitis is often not even an inflammation. One ought to speak of this singular state of the conjunctiva by the name of folliculosis employed originally by Adamuck. (It is necessary to remark that this author has given a marked significance to this expression.) If then in folliculosis the alterations of the conjunctiva do not progress, and if this condition is not transformed into typical trachoma (granular ophthalmia of the authors), it is not because the folliculosis and trachoma present two distinct forms produced by two different parasites, but for the simple reason that the folliculosis is not an inflammatory process. The production of follicules explains itself easily as we already know in all normal cases pre-eminently inflammatory, for there exists many favorable conditions to their development.

Inflammation of the conjunctiva may last for a longer or

shorter period, according to the species of the microbe, the hygienic condition of the patient, and the general state of his organization.

Every ophthalmic surgeon has had occasion to notice frequently conjunctivitis characterized by the presence of abundance of follicles, cured comparatively quickly without any traces or complications of the cornea; these inflammatory forms which have been wrongly included in the same class with the folliculosis, often terminate favorably, not because of the quantity of the follicles nor when they have developed in the conjunctival cul-de-sac, and not on the tarsus, and finally are not of the same nature as the microbes which have given place to them. Agents are at work here of a totally different nature, to find which we must inquire into the hygienic condition of the patient, and, what is more important perhaps, into the general state of his organization. Ophthalmic surgeons, who have had the opportunity of observing the endemics of trachoma in schools, prisons, garrisons, endemics striking one locality, report very interesting facts which give us a new light on this vexed question of the origin of trachoma, from a clinical standpoint at least. They maintain that all the milder forms of follicular conjunctivitis are trachoma. Nuel and Leplat, ardent followers of Saemisch, have watched an endemic of trachoma in Luxembourg, and declare that their convictions have been shaken, for they have seen the successive change of one morbid form to the other. Wallerstein, who has also had to do with an endemic of follicular conjunctivitis, explains in a categorical manner, that this inflammation transforms itself often into serious typical trachoma. The inverse observations are very interesting and very characteristic; the serious forms of trachoma, self-propagating by contagion, provoke slight conjunctivitis.

I have observed for several years, a family, of which the father was sometime ago attacked by a malignant form of trachoma. Four years since two sons were attacked by this disease; the children complained of a slight suppuration, watering and ptosis, especially when they worked in the evening. I found the conjunctiva hyperæmic, slightly flecked, and containing follicles. After some weeks of treatment (the follicles

were squeezed out) the boys were completely cured. In this case, I have no doubt at all that the follicular conjunctivitis of the children came from the father's disease, who, having no idea of the contagiousness of his attack, often slept with one or other of them.

Gerkin, who has recently published statistics of a very serious epidemic of trachoma, it having attacked the inhabitants of a large town of Kasan, reports very interesting details, which prove that among the patients, the youngest were nearly all exclusively attacked by the lighter forms of follicular conjunctivitis.

Joelson describing an epidemic of follicular conjunctivitis in a school, tells us that those who had been longest in the establishment suffered principally from trachomatous conjunctivitis; he observed also, the change of the slight inflammations to the serious ones, and advises us not to be optimistic when one has to do with a mild conjunctivitis.

Schilling observed a similar endemic in Wartenberg, and remarks that parents and the elder children were attacked by trachoma; the children attending school, and those from one to six years old only presented a simple catarrh or disseminated follicles; this author considers follicular catarrh and trachoma to be different phases of one and the same process. We see then that the clinical signs alone do not allow us to pronounce on the nature of a follicular conjunctivitis. Will it terminate in a favorable manner, or indeed, is it the first step of true trachoma? If trachoma and follicular conjunctivitis are two different diseases, then each one must according to the infectious character be provoked by a special microbe. Nevertheless, in spite of the numerous bacteriological researches, which have been made during the last ten years to discover the special microbe of trachoma, none have been given, as far as we know, any positive result. We shall not be accused of exaggeration, when we say that there have been as many microbes found, as there have been investigators. The numerous inoculations made on animals have furnished no better results. The verified inoculations executed by others experimentally bring negative results. The accepted micro-cocci of Michel has not justified

the faith placed in it, for Schmidt-Rimpler declares never to have found it in cases of trachoma.

For those who are interested in this question the observations of Staderini are the most remarkable. This author declares that the diplo-cocci found by him have always given a negative result when inoculated in animals, healthy, well nourished and well cared for. On the contrary those inoculated animals, which were in a bad state of hygiene gave the best results. Would not the inoculation of other microbes be positive in these cases?

In accepting the infectious theory of trachoma, we should be much embarrassed had we to explain many facts presented to us daily, for our observation. Many persons who are intimately connected with trachomatous subjects for many years are not affected by the disease. The conjunctiva of their eyes remains perfectly healthy; thus we see that the husband is not affected by the wife, the children by the parents and vice versa. In my hospital practice during the last seven years, I have not seen the contagion spread between those having healthy conjunctiva, and the trachomatous; not for lack of opportunity, for the patients were all confined in one small room, badly ventilated, no precautions taken whatever, and no suspicion of the possibility of infection. The nurses who have been in service for many years have never been attacked by conjunctivitis, although they daily finger the dressings of the trachomatous, and frequently neglect to disinfect their own hands. Similar facts cannot have escaped the notice of all ophthalmic surgeons, and several who believe in the contagious character of trachoma attribute a very important part to a particular disposition of the organism (Venneman) (Raehlman) and to the scrofulous character of the patient. (Truc.) (Malgat.) The majority of the authorities assign bad hygienic conditions and poverty as the chief reason of the propagation of trachoma, and, on the contrary, the well-to-do should be the best anti-trachomatous subjects. Thus then the association of bacteriological research with clinical facts, which frequently gives the lie to the contagious character of trachoma, permits us to conclude that the microbe of trachoma is not yet discovered, for the simple reason that it does not exist.

For the rest, the even course of trachoma proves already that its origin cannot be due to the action of the less predominating microbes. This affection lasts sometimes for ten years, and this in individuals who are not in the most unfavorable conditions for the arrest of the inflammation.

Exacerbations separated by intervals more or less long, repeat themselves *ad-infinitum* and break out, so to speak, on the least provocation. The slightest excess (an evening passed at the theatre, a few hours reading, the return to customary work) suffices to cause a return of the inflammation which seemed to have quite disappeared. I have often seen patients leave the hospital in very good condition and return the day after with a serious exacerbation.

If we would place the question in a still more critical fashion, we could not rest content with the etiology of trachoma as it is generally accepted, and we must search for reasons more in accord with known facts; and, indeed, the facility with which each fresh exacerbation is caused, in a very serious form sometimes, the insignificant cause which provokes it, all that we know of the same tissue, and its anatomical structure, has made us submit the very important transformations which have weakened the resistance of its elements to the unfavorable actions of exterior agents. The supporters of the infectious theory of trachoma are disposed to attribute the sudden exacerbations to the action of the microbes; this is how they understand the proceeding of the latter:—At the moment when the inflammatory manifestations disappear, the diseased tissue does not become free from the microbes which have provoked them; these microbes continue to live, although inactive, during the entire phase of the apparent cure. Under the influence of certain exterior irritations their vital energy temporarily appeased, awakens; they multiply rapidly and re-commence the destructive process in the tissue which serves them as their abode. I do not accept this theory. It is difficult to admit that the microbes remain inactive even for a short time in a tissue which offers them such an excellent ground for culture. These armistices appear to us less acceptable when they last, as they often do, for a year or more, between the trachomatous exacerbations. It

is not easy, on the other hand, to admit that each fresh attack is produced by a new infection: they are often produced under conditions which completely exclude the possibility of a re-infection. The exterior agents, such as smoke, dust, etc., which can only cause a simple hyperæmia or at most a slight catarrh in a well conditioned patient, produce in the trachomatous, apparently cured, a serious exacerbation, and no ophthalmic surgeon is surprised. If we allow then, as the chief sign and characteristic of trachoma, the very slight powers of resistance in the tissue where the morbid process takes place, we can then more easily explain to ourselves why trachoma does not constitute an independent disease, why it produces other chronic inflammations, slightly conjunctival, why this affection develops itself without the predominant intervention of the least of the microbes, why finally, it lasts during a long period of years. In order to understand what are the properties of the tissue which determine its greater or less resistance to exterior agents, we ought first to study the physiological character of the epithelial cells which fight the battle for existence in the normal conditions; and then we should examine the alterations of the disease and arrest the progress of it. The normal epithelium of the conjunctiva presents, as we know it, the character of the mucous epithelium and rests on an adenoidous tissue, moist and spongy. Above all there exists in the organism a constant relation between the epithelium and the sub-epithelial tissue. The mucous epithelium constituting a secreting, independent organ, demands by reason of its function, an abundant flow of nutritive secretion which it pours into the sub-epithelial tissue, richly vascularized.

Thanks to this adenoidous tissue, the regeneration of the epithelial elements works very rapidly and it is this easy reproduction which causes the resistance of the normal conjunctival epithelium to the pernicious agents. In slight chronic conjunctivitis, catarrhal, produced by the constant irritation of the conjunctiva, be it by smoke, dust, irritant fumes, etc. (in manufactories, badly ventilated laboratories,) may be finally under the influence of certain microbes, of a less malignant nature, the young epithelial cells situated directly on the adenoidous

tissue, not content merely to repair the losses of the superficial range but augment their reproductive energy to such a point that the epithelial strata is notably thickened. It is probable that the thin film of mucous producing epithelium recovering all the surface of the conjunctiva protects to a certain point the superficial layer. If we examine under the microscope the conjunctiva which has undergone trachoma with all its multiple exacerbations we shall see that its epithelium is changed in type, has taken the epidermoidous character and rests upon the compact conjunctival tissue, and has no resemblance, from an anatomical point, to the old adenoidous tissue.

We say then that the inflammatory process is extinguished, but that merely means that the anatomical equilibrium between the epithelium and its base is attacked again, and that the tissue has become as resistant as it was before the disease. What is it that now constitutes this resistance of the conjunctiva. Why have these same insignificant causes which formerly sufficed to provoke a very serious inflammation become now perfectly inoffensive in the same individual? It is not difficult to answer these questions. The epithelial elements with which we have at present to do, regenerate much less energetically than the mucous elements, but in the place of the superficial layers formed by the degenerate elements, almost cartilaginous, present an excellent barrier to the passage of micro-organisms in the depth of the tissue and resist but weakly the exterior agents. In this phase of trachoma we have to do with a kind of epithelium very similar to the external integument: If the resistance of the normal conjunctival epithelium is due to the vitality of its anatomical elements, that is to say, to the capacity of its very rapid reproduction, if the reason is purely physiological, after the termination of trachoma, this resistance is become passive, it becomes so by reasons of a purely mechanical nature.

The mucous epithelium has now pursued a long and steady course, having changed its type to the epidermoidal. It will be easy for us to understand how and why it has worked this transformation if we recall the close connection existing between the epithelium and the sub-epithelial tissue, if we connect the clinical progress of the disease to the anatomical picture of its

successive phases. Each inflammatory attack of the epithelium provokes in the adenoidous tissue a cellular infiltration, which sometimes attains considerable dimensions. This infiltration as we know it, often forms more or less abundant follicles.

If the conjunctiva has been attacked at all, be it ever so mildly, traces are not always to be found, because one part of the lymphoidous cells eliminated through the conjunctival sac, and one part is taken up by the lymphatic vessels and so returned to the general circulation, and those, finally, which have suffered necrosis are absorbed, such as the follicles; the adenoidous tissue and the epithelium now return to *statu-quo ante*. This is what takes place after each acute catarrhal attack of the conjunctiva and after the contagious conjunctivitis. Suppose now that the individual who has had an acute conjunctivitis is attacked for the second or third time, etc., or when the inflammatory process is stopped for some time, thanks to the bad condition of hygiene, the inflammatory infiltration and the quantity of follicles increase more and more; it is evident that the resorption will demand more time and the lymphatic elements degenerate, the follicles and blood vessels, which have developed during the inflammation and disappeared after its termination, are replaced by the conjunctival tissue of a new formation. Greater accumulation of the lymphoidous elements in the adenoidous tissue has been prolonged, the follicles are more abundant, the conjunctival fasciculus is produced anew in the sub-epithelial tissue. There must naturally now result an important transformation of the adenoidous tissue which will lose a large part of the nutritive secretion. This modification of the sub epithelial tissue must forcibly influence the epithelial elements; these, receiving less of the nutritive secretions cannot form the normal type, and assume a different aspect.

The less pronounced modification of sub-epithelial tissues are not without a marked effect on the epithelial cells which do not lose, after the extinction of the inflammatory process, their capacity of rapid reproduction, nor their secreting properties.

It will not be the same when the conjunctival fasciculi develop themselves in large quantities and attach themselves to

the adenoidous tissue; in these conditions the regenerated epithelium presents a very original appearance.

The cells situated in the deepest structures present divers, figures, oval or fusi-form, often triangular, at right angles towards the sub-epithelial tissue. Among the superficial elements we find a flattened form in which it is often difficult to demonstrate the presence of the nucleus. We have then an intermediate form between the old mucous epithelium and the future epidermoidal; this epithelium has lost in part the resistance of the mucous epithelium by reason of the important modification undergone by the adenoidous tissue; it is no longer able to reproduce rapidly; on the other hand the superficial cells do not sufficiently protect it from behind for they have not obtained the character of the corneal cellules. From the moment that the conjunctival epithelium has undergone this essential modification, the conjunctiva passes to this second characteristic phase, which has been differentiated as an independent disease called trachoma, or, as certain authorities term it, granular ophthalmia.

The epithelium deteriorating easily under the hurtful influence of the agents to which it is momentarily exposed provokes certain reflex alterations in the adenoidous tissue (sanguinary hyperæmia, sanguinary infiltration) ulceration of the cornea (pannus) and it is thus that it presents the typical picture of trachomatous exacerbations. After each of these exacerbations the adenoidous tissue becomes richer in conjunctival fibres. The regenerated epithelium approaches more and more to the epidermoidal epithelium, its superficial cells receive less and less of the nutritive secretions, they diminish gradually and at last we obtain on the surface of the conjunctiva another type of epithelium namely, the epidermoidal. Thus terminates trachoma.

We see then that the cure is effected only when the tissue has made its resistance perfect. Anatomically it is completely changed, but each exacerbation in the progress of this affection brings us to the desired end. As the modifications of the adenoidous tissue are always the same whatever may be the form of the cellular infiltration, diffused, or under the form of follicules, we may unhesitatingly conclude that each inflammation of the conjunctiva, it matters not of what origin, may pass as typical

trachoma. So indeed may chronic catarrhal conjunctivitis, follicular conjunctivitis pass as chronic blennorrhoea. The epidemic propagation of trachoma still remains to be explained and the circumstances which contribute to this disease have been classed among the infectious ones. The first question finds its answer in what we have just been saying, if an acute inflammation attacks individuals, remaining in close contact and in the same hygienic conditions (garrisons, schools, prisons, etc.) if this inflammation is conveyed to all the patients by the vitiated air of the common habitation (Joelson's case) it is not to be wondered at that these people are later infected by trachoma. As to the possibility of being infected by typical trachoma from intercourse with the trachomatous, I consider that as a scientific prejudice. A healthy man will only take a trachomatous disease as a very slight inflammation. On the normal conjunctiva one constantly finds an enormous quantity of all sorts of microorganisms. They are simply the result of our sojourn in an atmosphere full of different pathogenic germs, for example in the hospitals, and from the bad habit we all have of rubbing our eyes with non-disinfected fingers. The microbes on perfectly healthy eyes multiply rapidly and give rise to all the phenomena of conjunctival inflammation, but on the pathological conjunctiva of the trachomatous, the number of the germs and the many varieties are considerably greater. Petresco read before the Ophthalmological Society of Paris (1888) his researches on this point and speaks of microbes *staphylococcus albus*, *aureus*, *citreus* and even the *strepto-coccus*. It is not surprising to find the secretion of a trachomatous eye provoke a catarrhal or a very serious affection in a healthy eye, a similar result may be produced by inoculating a healthy eye from pus taken from a suppurating wound. It is true that the benign inflammation produced in this manner may give rise to true trachoma, but the origin of the infection has not the importance of a veritable etiological starting point, it being only an accidental agent.

The pathological processes develop and progress in the same manner in the same tissue, it matters not where it is situated in the organism, for the cause is the same in all cases. We must now wait for the careful examination of chronic urethritis, giv-

ing analogous results to those which we have obtained from studying trachoma. The position of the oculist is so much the more advantageous in that it allows him to follow step by step the inflammatory process, to study successively the anatomical pictures, and, which is very important, its very close connection with the clinical progress. On the contrary, a similar study of chronic blennorrhagia of the urethra is impossible, and it is, it seems to me the only reason why there is not a single work on this question from which we can obtain analogous results to mine.

In recent literature concerning chronic blennorrhagical urethritis we find some facts which justify my supposition.

Baraban, in 1890, published a very interesting paper on the modification of the urethral epithelium in a man attacked by chronic blennorrhagia. He observed the change of the cylindrical epithelium to a stratified flat epithelium, and attributes it to the prolonged irritation of the cellules by the gonococci and to a fault of nutrition which lasts even when the last parasite has disappeared from the tissue. In his treatise on the anatomy of chronic blennorrhagia in man, Singer considers equally the passage of cylindrical epithelium into pavement epithelium and affirms categorically that this transformation is in relation with the alteration of the sub-epithelial tissue.

I am convinced that these writers have not obtained results absolutely identical with mine for the simple reason that their microscopical researches have not been made parallel with clinical observations.

