ON CERTAIN AFFECTIONS OF THE MUCOUS SURFACES AND THEIR RELATION TO DIPHTHERIA.

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The subject upon which I wish to read a short paper this evening is one of great interest, but also of great difficulty. In our study of diphtheria we meet with it in two aspects, firstly as an endemic disease, and secondly as an epidemic disease. The prevalence of endemic diphtheria, at least in many towns and districts, does not appear to vary with the season of the year, contrary to what occurs in the case of epidemic diphtheria, the incidence of which is most marked in the autumn and winter months. Some authorities have gone so far as to say that the prevalence of diphtheria in an endemic form is always quite unaffected by the season of the year, but I am not aware that statistics are available which would show this to be true in the case of the country at large.

When we come to investigate the cause of epidemics of diphtheria, we find conditions at work the influence of some of which is more or less doubtful, such, for instance, as the influence of fluctuations of the level of the ground or subsoil water, unusually damp seasons, diseases of domestic animals, emanations from sewers; and others about the influence of which there can be no doubt, for instance, the consumption of infected food such as milk, the prevalence of sore-throat, and the gathering together of children suffering from sore-throat, especially at schools. It is with this sore-throat, and affections which I believe are closely allied to it, that I have to deal this evening. The mere presence of isolated cases of diphtheria in a district, or the attendance of children suffering from, or recovering from, diphtheria at school—a condition which most undoubtedly frequently obtains—does not appear to be sufficient to originate epidemic diphtheria; but some other contemporaneous conditions are required for the

development of an epidemic of this disease. I need hardly refer here, also, to the frequency with which diphtheria does not spread by infection, even among persons who would be regarded as susceptible; and the frequency with which prolonged exposure to infection, such as is seen in nurses and medical men, fails to originate the disease.

Of late we have had a steadily increasing amount of evidence to show that the condition which is by far the most frequent accompaniment of epidemic diphtheria consists in the prevalence of sore-throat. The frequency with which extensive prevalence of sore-throat has preceded or accompanied epidemics of diphtheria has led, on the one hand, to the idea brought forward by Dr. Thorne Thorne in his Milroy Lectures, "that there is reason to believe that attacks of so-called sore-throat exhibit under favouring conditions a progressive development of the property of infectiveness, culminating in a definite specific type which is indistinguishable from true diphtheria"; and, on the other hand, to the idea that these forms of sore-throat, which are without the physical characters of diphtheria, are yet due to the poison or virus of diphtheria, and are capable of communicating the disease to healthy individuals.

This relation between the gathering together of children suffering from sore-throat and the outbreak of epidemic diphtheria, appears to be comparable to the outbreak of epidemic ophthalmia which sometimes appears to be determined by the aggregation of children suffering from the affection of the eyes known as "granular lids"; and its explanation is equally difficult. Unfortunately, we have very little information concerning the physical characters of the forms of sore-throat which precede or accompany epidemic diphtheria, and this is, I think, due chiefly to the fact that a comprehensive inquiry into any given epidemic has usually been commenced either after the outbreak had come to an end, or at any rate when it was on the wane; so that opportunity is not afforded of making a comprehensive clinical report on the features of this sore-throat. The gathering of reports from local medical men respecting these affections is also of little value, since, owing to the trivial character of the sore-throat attacks, no notes of cases are kept, and such evidence would consist almost entirely of recollections, and therefore such reports would not be trustworthy. The subject is also of importance on account of its bearing on the question, whether under the provisions of the Infectious Disease Notification Act such

cases of sore-throat should be notified as diphtheria or not, and also to determine, if possible, whether persons suffering from these forms of sore-throat should be isolated from their fellows or not.

Having for several years kept this subject of the nature of these affections of the throat and their relation to diphtheria in view, I have taken every opportunity of making observations which might throw any light upon the question. In the beginning of November 1890, my attention was first drawn to a peculiar form of sore-throat, accompanied and followed by great debility, which at that time became very prevalent in South London, and which was in some instances accompanied by affections of other mucous surfaces. Since that date I have met with similar affections, which in some instances appeared to have connection with epidemic diphtheria, in others not; and I propose to give a short account of my experiences.

The district to which my first observations were more particularly confined was that extending on the south side of the river Thames from Battersea to Bermondsey. At that time, as physician to a dispensary, I was in the habit of seeing large numbers of people at their own homes; and also out-patients at the dispensary, and at a hospital the patients at which were drawn almost entirely from the same district. Since November 1890, I have noticed a continued prevalence of this sore-throat each year, and the period of prevalence has been almost entirely that extending from the beginning of November in one year to the end of May in the following year. I have had the opportunity of admitting several children suffering from this form of sore-throat into a hospital, in order the better to observe the course of the temperature and other characters of the affection. I have preserved notes of over thirty cases, and should estimate that at least 150 persons suffering from this affection have been under my care up to the present time.

In its clinical features this sore-throat is characterised in its early stages by a marked flushing of the face of the affected person. The face has also a swollen and puffy appearance, due to actual swelling of the subcutaneous tissue, especially that in the neighbourhood of the eyelids. There is also a general puffy swelling of the tissues of the neck behind the angles of the jaw in most cases; and in all instances marked enlargement of the glands of both sides of the neck in this situation, together with tenderness on pressure.

This swelling of the glands of the neck is one of the most marked features of the affection, and persists for a considerable time, in some instances at least for weeks after all other symptoms have disappeared. At the time when the patient presents the flushed appearance of the face, on examination of the throat there is found more or less swelling of the soft palate and fauces, with an increased secretion of mucus, which, especially in young children, is often present in large quantity on the back of the pharynx. Swelling of the tonsils is present also in some instances, but not invariably, and never to a marked degree. The most characteristic feature in the throat consists in the presence of bright red patches of injection; these patches are sharply defined, and most commonly present on the soft palate and fauces, in some instances extending all along the margin of the soft palate; they are much less commonly found on the surface of the tonsils. In the centre of these bright red patches of injection a white film or pellicle is found in the earliest stage of the affection, but this pellicle rapidly disappears, especially if any gargle is used for the throat; and in twenty-four to forty-eight hours it has generally completely disappeared. If the affection is watched from the first onset, it is seen that it begins with the formation of a white pellicle of this description surrounded by a bright red ring of injection, and from which as a centre the injected patch enlarges progressively for several days. This pellicle or film can be pulled off only with difficulty, because it has no defined edge, and is scarcely appreciably raised above the surrounding surface. On removal of this pellicle or film a red, slightly raw surface is left, which does not bleed. The film, on microscopical examination, is found to consist entirely of sodden, swollen, and opaque epithelial cells, and has none of the characters of diphtheritic membrane. When the white pellicle has disappeared, the red surfaces are seen to be studded with enlarged projecting mucous follicles, giving them a velvety appearance. At this stage of the affection the appearances closely resemble the red injected surfaces which remain for some time in the throat after the disappearance of the membrane in cases of undoubted diphtheria.

This affection of the throat is followed by prolonged anæmia and debility. The temperature is at first raised to 102 deg. or 103 deg., but becomes normal in the course of two or three days, and has no regular course. The pulse is quickened during the early stages of the affection,

and subsequently becomes feeble and irregular. No paralytic sequelæ have been observed in any instance, although the patients were under observation for from four to six weeks; but it must be mentioned that in three instances the patellæ reflexes were absent from the commencement of the illness, and continued absent as long as the patients were under observation, which was in one instance for a period of six weeks. Owing to the plantar reflexes being absent from the very commencement of the illness, and the absence of any further paralytic symptoms in these three instances, I am of opinion that these were not cases of slight diphtheritic paralysis, but were instances of persons in whom these reflexes were normally absent. No suppuration of the glands of the neck or other sequelæ were observed, nor did any case terminate fatally.

I have now to describe some affections of the mouth, nostrils, and vulva, which have also come under my observation, sometimes in association with the form of sore-throat above described in the same individual, sometimes without such association, or in members of a family some of whom were suffering from sore-throat.

These affections consist in the presence of white patches on the mucous membrane of the lips, nostrils, or vulva. These patches present a fairly well-defined margin; they are very slightly raised above the surrounding surface, and are surrounded by a bright ring of injection. A bright red injected surface remains after their disappearance, which occurs spontaneously in the course of two or three days. If these patches are pulled off they leave a raw surface, which bleeds readily. In the case of the nostrils and lips, the patches very often extend for some distance on to the neighbouring skin, and are accompanied by a slight enlargement of the corresponding lymphatic glands. When present in the nostrils, they can often be seen to extend backwards for some distance into the nares, and are accompanied by a thin ichorous discharge from the nose. On microscopical examination, the white patches are found to consist of sodden, swollen epithelium only, with a few blood corpuscles adhering to the surface by which they were attached to the mucous membrane. These patches were never present on the interior of the buccal mucous membrane, but in two instances were noted upon the tongue. In some instances this affection is present in one of the above-mentioned situations only, in others in two or more of these situations at the same time. Their mutual association with one another, and with the form of

sore-throat above described, together with the identical microscopical characters of the white pellicle, and the bacteriological evidence, which will be referred to later, all appear to show that these affections are identical with the affection noted in the throat, and are due to one common cause.

We come now to study the question of the nature of these affections. Are they a modified form of diphtheria or not, and if not, do they stand in any direct relation to diphtheria? The evidence for and against these views is in the first place epidemiological, and concerns their relationship when present in the form of epidemics; secondly clinical, thirdly pathological, and fourthly bacteriological.

With regard to the study of these affections from the epidemiological point of view, I have sometimes found them associated with epidemic diphtheria, sometimes not. I must, in the first place, say that I have not been able to trace any connection between these affections and diphtheria in London, apart from their seasonal prevalence, which coincides more or less with the seasonal prevalence of diphtheria in London. I have never been able to find any evidence of the presence of true diphtheria in families the members of which were suffering from these affections in London; but I need hardly refer to the extreme difficulty of carrying on any investigation of this kind in London, owing to the complexity of the factors at work.

However, in the year 1893, I was fortunate enough to have two excellent opportunities for investigating the subject. In the autumn of 1893 I was engaged in investigating an epidemic of diphtheria which was in progress in a town of between 9,000 and 10,000 inhabitants, in which at the time I commenced the inquiry it had already caused 28 deaths, and which also had invaded certain of the surrounding villages. On inquiry, I found in the case of the town, that the evidence pointing to the public elementary schools as the chief means of spread of diphtheria was almost irresistible. Out of 51 invaded households, in 44 instances, or 86 per cent., the first individual, and often the only person to be affected, was a child attending a public elementary school. I found that there was a great prevalence of sore-throat among children in the town, which had preceded and accompanied the outbreak of diphtheria. On examining into the clinical character of this form of sore-throat, then present in the town, I found it to be identical with that already described as prevalent in South

London, and that in some instances it was accompanied by affections of the lips and nose, exactly similar to those before mentioned; with the addition in many instances of nasal catarrh, in which no accompanying film or pellicle could be seen at the time of examination. On inquiry, I found that the affections which had preceded the outbreak of diphtheria had exactly resembled those which were then present among the children in the town. I had the opportunity of examining the children in all the public elementary schools of the town, and found that these affections were prevalent among the children actually at school at the time, but were almost entirely confined to the younger children. Children suffering from the before-described form of sore-throat were found in all the schools; and in all except one, children presenting white patches at the margins of the mouth or nostrils were found also. To show, for example, the extreme prevalence of these affections, I may say that among 144 children in one schoolroom I found 20 suffering from the above-described form of sore-throat; and in the same school, several children presented white patches in the neighbourhood of the mouth or nose, similar in their character to those already described. On inquiry at the houses in the town, I found several instances where children were suffering from these affections who were below the school age, and where no member of the family went to school, and among which no attack of diphtheria had occurred. I also found that the younger children at a public institution presented these affections to a marked extent, although no attack of diphtheria had occurred in the institution. Now, on inquiring into the surroundings of these children in this institution, I found that none of them went to school in the town, but all attended a country school some distance away, and never mixed with the town children. On visiting this country school, I found the children attending there at the time were entirely free from these affections, and also that no attack of diphtheria had occurred among them or in the village.

The country district surrounding the town included nine villages, at which there were public elementary schools. Diphtheria occurred in epidemic form in two only of these villages. I had the opportunity of examining the children in the schools of all the nine villages, and found that, with one exception, the children attending school in those villages in which epidemic diphtheria had been absent were free from any affections similar to those already described. The children in the schools in those villages in which epi-

demic diphtheria was present were, however, suffering from these affections to a large extent, and they were present to a limited extent among the children at school in a village in which diphtheria was not known to be present.

In the spring of the year 1893 I was concerned in the investigation of an outbreak of diphtheria which occurred in three small wards in a children's hospital, which were all on the same floor, and directly continuous with one another, so that they formed practically one ward. With the exception of one case, the outbreak, which caused eight deaths, was entirely limited to these wards. On investigating the condition of the children in the wards of the hospital, I found that in these three wards in which diphtheria had occurred many children were suffering from affections of the throat and nose identical with those before described, but the children in the other wards of the hospital were entirely free from these affections. There was, however, no evidence that these affections had preceded the outbreak of diphtheria, but that they were contemporaneous with it there was no doubt.

In 1891, whilst in charge of a lying-in hospital, I observed a limited outbreak of an affection, consisting in the development of small, yellowish white patches surrounded by an inflamed area on the vulva of lying-in women after delivery. The affection was altogether trivial; in some instances a slight elevation of temperature was the only additional symptom, and no diphtheria nor sore-throat preceded or accompanied it, nor did any paralytic symptoms follow; in short, all the indications of diphtheria were absent. In the same year, Messrs. Ehrhart and Favre published, in the *Nouvelles Archives d'Obstétrique et de Gynécologie*, under the heading of "Clinical and Bacteriological Researches on an Epidemic of Benign Puerperal Diphtheria at the Paris Maternité", an account of an outbreak at the Paris Maternité, which appears to have been of a similar nature, and was entirely devoid of any semblance to diphtheria, except in so far as a greyish-yellow irregular membranous exudation appeared on the vulva in 33 lying-in women in less than three weeks, and in one infant only a patch of membrane appeared in one eye. The affection was altogether trivial, and had no tendency to a fatal termination, nor was it known to be followed by any paralysis. No account is given of the microscopical examination of the membrane, but extensive cultivation and inoculation experiments were made, as the result of which it was found that a great number of micro-

cocci were present in the membrane, and also a bacillus which had some resemblance to the bacillus diphtheriæ, but which could not be permanently cultivated. It appears to me, therefore, and it is practically admitted by the authors, that the diphtheritic nature of this outbreak was not proved.

Lastly, I must add that I have, in several instances, seen these affections of the throat, mouth, or nose precede by a few days the onset of undoubted diphtheria.

On reviewing the foregoing observations, it will be seen that these affections have sometimes accompanied epidemic diphtheria, and at other times they have prevailed apart from diphtheria altogether. In the case of the town before referred to, it is to be noted that these affections preceded epidemic diphtheria, that they existed in the public institution, and among families no members of which were attending school, and among which diphtheria had not occurred, but that the connecting link between these affections and diphtheria appeared to be attendance at public elementary schools, at which schools I may state that there was abundant opportunity for the spread of contagion of diphtheria through the medium of children returning to school convalescent from diphtheria, or in clothes which had been worn whilst suffering from diphtheria; or by children attending school from households members of which were at the time suffering from diphtheria.

Clinically it will have been seen from the foregoing account that the affections above described have some resemblance to diphtheria, inasmuch as a white pellicle or film is present, accompanied by glandular enlargement and heightened temperature. The fleeting character of this pellicular formation, its entire disappearance occurring in the course of two or three days at the most, and the absence of any paralytic sequelæ, are features which distinguish these affections from diphtheria. In no instance have I seen any indication of extension to the respiratory tract, or albuminuria, or any tendency to a fatal termination.

From the pathological point of view these affections are distinguished from diphtheria by the characters of the film or pellicle which is present on the mucous membrane of the throat, lips, nose, or vulva, which has none of the characters of the fibrinous exudation composing the false membrane of diphtheria, but consists entirely of swollen and opaque epithelium cells. With regard to the pathological changes in the cervical glands, and the possibility of changes in other organs of the body, I have, of course, no information, owing to the non-fatality of the affections.

The bacteriological evidence that I am able to bring forward has been directed almost entirely to ascertaining whether these affections were diphtheria or no, and has been so far entirely of a negative character. Cover-glass preparations of the film or pellicle removed from the throat or other parts, and of the secretions of the throat in the vicinity of the red patches, have shown the presence of large numbers of micro-organisms, chiefly cocci. These cocci were present either singly or in pairs, or in the form of dense colonies embedded in a structureless material. The affection was found not to be due to the presence of the "thrush" fungus, or to any other form of fungus. No organisms resembling the bacillus diphtheriæ were ever found present in sufficient numbers to justify the opinion that the affection was diphtheria. Cultivation experiments entirely failed to produce any organism resembling the bacillus diphtheriæ, but a micro-coccus growing in orange-yellow colonies was always obtained, sometimes in pure culture. With regard to the pathogenic properties of this micro-coccus, I have not made any investigations. It is well known that many observers have stated that they were unable to obtain an organism having the characters of the bacillus diphtheriæ from cases of diphtheria, but they have obtained a micro-coccus.

At this point I may be permitted to refer to one of the latest reports from one of these observers who have failed to find the bacillus diphtheriæ; this report is by Dr. Albert Wilson, and is contained in the *Transactions of the Pathological Society of London for* 1891. As the result of extensive cultivation and inoculation experiments made during an outbreak of diphtheria, he failed to obtain any specific organism from the true diphtheritic membrane; but from a thin grey exudation, which in the epidemic preceded the formation of membrane, he obtained a micro-coccus growing as small orange-coloured patches on gelatine at a temperature of 60° F. With this micro-coccus he claims to have produced true diphtheria in pigeons, both by inoculation of scratches on the mucous membrane of the throat and by hypodermic injection. He especially says that the micro-coccus is found only in a milky-grey transparent exudation forming on the swollen mucous membrane of the throat, which in a few cases he has watched to precede the formation of diphtheritic membrane; and he states that "I attach the highest importance to this early exudation as being the only true hunting-ground for the organism of diphtheria". It appears to me to be

extremely probable that Dr. Wilson was here dealing with an epidemic of diphtheria which was accompanied by affections of the throat such as I have described, and that his bacteriological conclusions were really made upon the examination of the film or pellicle which I have before drawn attention to as preceding the invasion of diphtheria in some instances, and which may exist in the form of an affection entirely separate from diphtheria.

To summarise these foregoing observations, it would appear that the clinical, pathological, and bacteriological evidence which I have been able to bring forward tends to show that these affections are not diphtheria, nor a mild or modified form of diphtheria. The evidence derived from their study from an epidemiological point of view indicates that these affections may prevail apart from diphtheria, and under circumstances in which their origin by infection from diphtheria is negatived. On the other hand, it appears that in outbreaks of epidemic diphtheria these affections may, and do, sometimes accompany and precede the epidemic, and it appears probable that the prevalence of these affections has a large share in determining the outbreak of diphtheria in an epidemic form in some instances. The way in which these affections act is probably by creating a lesion of the mucous surfaces by which the virus of diphtheria obtains entry; or, on the other hand, it is probable that there may be a condition of commensualism in these two affections, and that epidemic diphtheria may be likened to a lichen in the vegetable kingdom, which consists of a fungus parasitic upon an alga, the alga being represented by the thin film or pellicle existing in these affections, and upon which the more powerful and predominating virus of diphtheria becomes, like the fungus, grafted, and flourishes. If this is the case, the contradictory conclusions of bacteriologists who have investigated diphtheria may be perhaps explained.

I do not think that the evidence which I have brought forward this evening is by any means conclusive. The subject is one of the greatest complexity, and I have only touched upon the fringe of it; still, the object of my paper will be served if it succeeds in directing attention to the importance of a comprehensive study of the features of the sore-throat and allied affections which accompany epidemic diphtheria, and if it elicits the experience of others, who have had larger opportunities than myself, concerning the nature of these affections.