The microscopic examination of the secretion in conjunctivitis.

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The microscopical examination of the secretion in conjunctivitis, with remarks on nomenclature and classification.

Although much has been written with regard to the bacteriology of the conjunctiva, both healthy and diseased, there seems to be but little movement in this country towards the practical application of our knowledge of the pathology of conjunctivitis.

Various reasons may be suggested for this apparent apathy. Conjunctivitis is perhaps not as formidable here as it would seem to be on the continent, so that it has not received the same attention.

It is only within recent years that the pathology of conjunctivitis has been largely investigated, and the connection between its pathology and its diagnosis, prognosis and treatment is only now beginning to be appreciated. Lastly the time, trouble and expense, not to mention the special training, required for complete bacteriological examination constitute an effective deterrent.

It is my present Object to urge regular bacteriological examination in conjunctivitis, and to endeavour to show that for practical purposes a complete examination is unnecessary, and that in the great majority of cases sufficient evidence on which to base sound prognosis and treatment may be obtained from simple microscopic

examination of a dried film of the secretion.

Within the last ten years great progress has been made in regard to the pathology of conjunctivitis owing to the work of Axenfeld in Germany, Monax in France, Weeks in America, Gasparrini in Italy and many others, mainly on the continent. In England, Sidney Stephenson (129) advocates the more exact diagnosis of conjunctivitis, but there have been few other workers at the subject in this country.

The work of these and other observers has demonstrated the close connection with — one might almost say dependance upon — bacteriology, of the various inflammations of the conjunctiva and has introduced a new element into their diagnosis.

In 1879 Neisser showed the microorganismal origin of cases of ophthalmia in newborn infants, and the bacterial character of diphtheritic conjunctivitis was established by Babes (14) in 1886, although this affection was clinically described as long ago as 1854 by Von Graefe. In 1886 Weeks (142) described the bacillus which now bears his name; his researches were closely followed by those of Koch and Cantulis and in 1894 the identity of the form of conjunctivitis due to this organism was fully established by Monax (147, 84) under the name of "conjonctivite aigue contagieuse."

In 1896 Monax (86) described the diplobacillus which has

been named after him and the affection to which it gives rise as conjunctivite subaiguë.

Many other organisms have been found in association with conjunctivitis although the above are by far the most important, and the endeavour to associate each special organism with a definite variety of the disease in causal relationship is still being carried on by many workers.

A great deal of evidence has been produced, which goes to show that affections apparently similar from a clinical point of view and not previously differentiated, are in reality produced by different microorganisms (Minne 82), while it is practically impossible to associate a fixed clinical picture with each special microbe, as both the virulence of the latter and the susceptivity and reaction of the individuals affected vary within wide limits (Uhthoff 133).

As yet, however, but little use has been made of this knowledge in ophthalmic practice and it seems pertinent to ask two questions:-

1. Is a bacteriological investigation of cases of conjunctivitis necessary or advantageous as a guide to diagnosis & treatment?
2. Is it feasible for the ordinary practitioner?

I wish to consider the subject from the point of view of the busy general practitioner, rather than that of the specialist. Conjunctivitis is very common in general practice either sporadically or in epidemics. General practitioners are

usually very busy and may say, "There is no necessity to spend time on bacteriological examinations, conjunctivitis may be treated quite well without them".

I shall endeavour to show that this is not the case, and that if accurate diagnosis is to be considered an essential preliminary to rational prognosis and treatment, then bacteriological examination is required.

In connection with diagnosis, it is convenient to have some form of classification, the terminology of which shall have a direct reference to the factor made use of in distinguishing the various forms included.

Under the system at present in vogue conjunctivitis is classified upon a clinical basis. The primary divisions of acute and chronic are further subdivided according to some prominent feature such as the nature of the secretion — catarrhal, purulent etc., or the state of the mucous membrane — phlyctenular, membranous, granular and so on. Such a classification would certainly be satisfactory did each of these terms denote a pathological, as well as a clinical, entity, and did each group include cases, really as well as apparently, similar in nature, that is, having essentially similar etiology, and treatment.

Recent research has shown that terms such as "catarrhal" or "purulent" conjunctivitis include in reality cases of the most diverse nature, with corresponding variations in prognosis and

treatment, and moreover such cases often cannot be clinically differentiated but only by bacteriological examination.

Maax and Beach (93) in 1896, speaking of acute conjunctivitis, said that its varieties were then only beginning to emerge from the chaos into which pathological anatomy had plunged them. The objective aspect of inflammation has ceased to be the only thing and etiological classification has been reached. Terms such as catarrhal, purulent or pseudomembranous are insufficient without an etiological qualification. For we know that the same infection can take on different clinical forms and an anatomical lesion is a deceitful criterion to be boldly cast away as a basis for classification. Gonococci, Weeks bacilli, streptococci or Loeffler's bacilli may determine equally a fibrinous or a pseudo membranous exudation (M.+B. 93).

Thus the trend of modern opinion is towards the recognition of the bacterial factor in the causation of conjunctivitis, and towards the expression of this recognition in the nomenclature and classification of the various forms. (Uhthoff 133).

Maax (84), Gonin (47) and Petit (104) condemn the old clinical classification as insufficient on account of the want of precision of terms, such as "purulent ophthalmia" and "catarrhal conjunctivitis" and consider it necessary to base a classification on the etiology and the evolution of the lesions as well as on the clinical appearances. Petit (104) points out that, in this connection, etiology should not be considered as synonymous with bacteriology.

Axenfeld and Fick (12), and Sidney Stephenson (129) express the hope that conjunctivitis may be classified etiologically in the future but, together with Schanz (117) and Uhthoff (133) hold that it is not possible in the present state of our knowledge.

Coppez (30) in 1896 discussed two alternative methods of classification, which recognised the bacteriological factor. The first is the old classification with the terms qualified by the names of the microbes present, the second the bacteriological classification, the various clinical forms being included under the heading of each microorganism. Coppez, with Uhthoff Axenfeld and Fick and Stephenson, favours the first method, considering that it separates all the forms and connects the clinical signs with the etiology, while the diagnosis is easy and the treatment can be at the same time symptomatic and prophylactic. The second form, he considers to have the advantage of exactly recognising the etiology of the affection, and of pointing out prophylaxis, and the treatment most definitely indicated as, for instance, serotherapy. His objections to it are, that some cases are not included at all, that mild and severe cases are classed together, and the difficulty of bacteriological examination which may take longer to complete than the patient to recover.

According to Menax and Petit (94) bacteriological classification is only possible in connection with gonococci, Weeks bacilli and diplobacilli, and the liability to confound etiology with bacteriology should be guarded against. A bacteriological

classification, including all forms, is premature and illusory, though as knowledge of pathology advances it will become more complete. (M. & P. 94).

The chief point here, in connection with the present subject, is that a bacteriological ~~ob~~ examination is equally necessary, whatever forme of classification is adopted, and I hope to show that it is only in exceptional cases that this will occupy a length of time sufficient to rob it of its advantages.

Gouin (47) has endeavoured to solve the problem by producing a classification, which is a compromise between the new and the old. He considers the information obtained by a knowledge of the bacterial factor more useful, although less accessible, than that obtained by other methods. He says (p. 189):- "Il est evidemment plus simple d'appliquer à une conjonctivite l'epithete de catarrhale ou de pseudomembraneuse que de decider si elle est provoquée par le bacille Weeks ou le bacille diphtheritique; mais le question est de savoir où sera la plus grande utilité; dans l'estimation facile et rapide de la forme clinique, ou dans l'appreciation plus delicate de la cause agissante. Une description clinique n'est point encore un diagnostic...."

Gouin defends his classification thus:- (p 192)

"L'essentiel n'est pas de trouver dès aujourd'hui une classification modèle capable de reunir en un système uniforme toutes les formes connues et à connaitre, mais de soustraire du tout-y-va de la conjonctivite catarrhale

"et de la classe aussi complexe des conjonctivites pseudomembraneuses les quelques types morbides mieux etudiés que des indications précieuses séparent des autres types moins connus. A ces derniers il faut donner les cadres très élastiques, qui permettent d'accueillir toutes les formes nouvelles jusqu'à ce qu'une étude plus approfondie permette de les classer à leur tour en connaissance de cause. Comprise de cette façon la classification etiologique restera incomplète ou plutôt inachevée, mais non pas étroite comme le lui reproche Coppez, sûrement moins étroite que celle où les types de catarrhal, de granulaire, et de pseudomembraneuse sont donnés comme immuables."

The terms trachoma, phlyctenular conjunctivitis and spring conjunctivitis are retained by Gouin, as they carry a deeper significance than that expressed in the name alone. The first indicates a clinical and pathological entity, not merely any conjunctivitis with granulations, any more than the second and last indicate either any conjunctivitis which occurs in the spring or any form which presents phlyctenulae.

In this classification conjunctivitis is divided into three main groups.

The first includes forms due to known microorganisms, the gonococcus, Weeks bacillus, diplobacillus of Morax and the diphtheria bacillus. These forms are mentioned as Gonococcal, Weeks, diplobacillary and diphtheritic conjunctivitis.

The second group contains firstly those forms whose specific cause is not known, or where the microbes present give

no special indications. That is to say, all other forms due to infection not included in the first group, forms due to pneumococci, streptococci, staphylococci and other microbes, but which cannot yet be considered as definite entities according to the particular organism present. In these neither prognosis nor treatment is fixed and definite. This arrangement is intended to be provisional so that any one of the included forms may be transferred to Group I when it is sufficiently well known to be made a distinct variety. Petit, for instance, considers that pneumococcal conjunctivitis is too well known to be classed along with staphylococcal. (Annales d'oculistique, Tome 122. p. 78.)

Trachoma and phlyctenular conjunctivitis are placed in the second group as forms whose specific cause is unknown. Should the latter turn out to be essentially nonmicrobic and due to the diathesis of the patient it would be transferred to Group III, which includes spring, catarrhal, traumatic and chronic conjunctivitis, forms not associated with the presence of specific microorganisms.

Mixed forms would be placed according to their most prominent features.

Finally Gouin remarks that etiological classification is possible for the great majority of cases and is greatly facilitated by microscopic examination of the secretion.

This classification seems to me to be superior to either of Coppez' two alternatives, and I have used it as a basis in this essay.

Much has been done recently to show the great diversity in actual nature of forms of conjunctivitis having the same outward appearance. Thus the researches of Bach and Neumann (15), Augières (4), Gouin (47) and Veasey (136) have shown that various affections are included under the name of catarrhal conjunctivitis: Gouin, Jessop (64) and Roscher (110) have done the same for membranous conjunctivitis; and Gouin, Groenouw (50) and Von Ammon (138) for ophthalmia neonatorum.

The necessity for due recognition of the various organisms is well illustrated by an analysis of these researches, which I have arranged in tabular form.

1. Catarrhal Conjunctivitis.

	Bach and Neumann.	Augières.	Gouin.	Veasey.
Cases examined.	110	26	310	64
Description.	Simple Catarrh.	Catarrh	Catarrh.	Acute catarrh.
Diplobacillus of Morax.	35	17	185	
Bacillus of Weeks.	1?	1?	10	3
Pneumococcus.	15		10	5
Staphylococcus.	57		83	8.
Streptococcus.			5	
Loeffler's bacillus.				
Various bacilli.			6	
Various cocci.		4		
No organisms.	2	4	11	

I have omitted the works of Pes (99) from this scheme as his heterodox views as to the identity of the Weeks bacillus prevent his results being compared with those of others.

In 76 cases of catarrhal conjunctivitis Pes found pure infections – i.e. with one organism only – in 47. Of these 4 were due to the diplococcus of Fraenkel, 17 to the bacillus of Loeffler, 2 to the diplobacillus of Morax, 2 to streptococci and 8, 7 and one were associated with the staphylococcus aureus albus and cereus albus respectively. The large number of cases due to the Loeffler bacillus originates in Pes' view that this organism and that of Weeks are identical, a view in which he is supported by Schanz (120) alone.

2. Membranous Conjunctivitis.

	Gonin (47)	Rosher (119)	Jessop. (64)
Description.	Pseudo-membranous.	Croupous.	Membranous.
No. of cases.	13	5	13.
B. of Loeffler.	7		8
B. of Weeks.	1		
Pneumococcus.	1	1	
Streptococcus.			2.
Staphylococcus.	4		3.
Gonococcus.		1	
Xerosis bacillus.		3	

3. Opthalmia of the Newborn.

	Gonin.	Groenouw.	Von Ammon.
No. of Cases.	38	100	100
Gonococcus.	22	41	56
Pneumococcus.	4	5	15
Bacillus of Weeks.	3		
Staphylococcus.	5	4	2
Streptococcus.		2	
Colon bacillus.		7	
Bact. pneumoniae			3
Pseudogonococcus.			2
Micrococcus luteus		1	
Undecided.	2	40	22.
No organisms	0		

Much more similar evidence exists but the above represent the chief recent researches and show that the recognition of the bacterial factor is necessary for correct diagnosis. Besides demonstrating the fact that the same clinical appearances may be produced by different microbes, these researches and others — to be referred to later — show that the same microbes often produce different clinical appearances.

I now turn to some further evidence in favour of bacteriological examination. Schanz (117) considers

that the modern practitioner is compelled ("gezwungen") to examine his cases bacteriologically. In cases where the clinical picture affords no definite diagnosis a coverglass preparation will often clear up the nature of the affection.

Morax (86) says that the pathological reactions known as conjunctivitis are caused by different microbes. The appearance and above all the clinical course of the affection is in intimate connection with the bacterial agent. Yet, beside the typical cases where a purely clinical diagnosis is possible there are many others in which bacteriological examination is necessary: the inflammations caused by the same agent may be very variable in anatomical form, intensity and complications. The factor governing the prognosis is above all the causal agent, and it is necessary to recognise this in each case. (Morax 86). (also Morax and Beach 93)

According to Sidney Stephenson mere inspection will not always suffice for diagnosis and bacteriological examination of the discharge is often necessary. By this means differential diagnosis of the greatest value may be established, which cannot be obtained by any other method of investigation, and sound and convincing evidence procured upon which to base prognosis and treatment. The diagnosis of ophthalmia, he says, "nowadays rests mainly upon the particular kind of microbe found in secretion from the inflamed eye." Again - "In short, ... a particular disease germ does not always give rise to a particular reaction. Hence the paramount importance of a bacteriological examination of the

"secretion for purposes, not only of prognosis and treatment but also of diagnosis." (Stephenson, 129).

Petit considers that the clinical study of a case should include a study of its etiology, as well as of its anatomy and relation to contagion. Microscopic examination in conjunctivitis may show the cause and clear up doubts as to diagnosis, prognosis and treatment. (Petit 104)

Corsini states that in conjunctivitis bacteriological research is the sole means of establishing a diagnosis with certainty.

"The bacteriological report is a sure means of classifying the affection; many cases of conjunctivitis which present all the clinical data necessary to place them in one class or another, when studied from the bacteriological standpoint, often represent attenuated cases of a conjunctivitis due to quite a different pathogenic agent, which, in a condition of greater virulence would have produced an exudation of a very grave and deleterious nature." (Corsini 33).

In commencing catarrhal cases, in epidemics, and in single acute cases bacteriological examination is necessary, while in simple forms it is very serviceable, according to Leufels & Fick (12) Max and Petit (94) find bacteriological examination especially useful in cases of mixed infection. It should be complementary to clinical examination, the diagnosis being based on the clinical appearance of the case, the surroundings of the patient and the history, especially of infection. In 14 cases out of 188 they found that the clinical diagnosis was reversed by bacteriological examination.

Pes (99) goes much farther in holding that neither microscopic examination nor culture is sufficient unless inoculation experiments to prove the virulence of the organisms found are proceeded to. This can only hold good in the case of diphtheria for organisms such as gonococci, Weeks bacilli and the diplobacillus of Xerax do not grow on ordinary media and the demonstration of their virulence would be difficult to effect in any case, while their mere detection affords the necessary indications for prognosis and treatment.

The practical necessity of bacteriological examination is, I think, undoubted. At the same time any tendency to base a diagnosis entirely upon this is to be avoided. It should rather, as Gouin suggests, take its place as a part of the clinical examination of the patient, having the same relation to the eye as the routine examinations of urine, blood, or sputum have to internal medicine.

It now remains to consider the feasibility of bacteriological examination and its suitability for daily, I might say for consulting room, use. I repeat here, that I do not wish to treat this question from the point of view of scientific research but rather from that of actual practice, the object being to obtain indications for prognosis and treatment in a rapid reliable and inexpensive way.

The question naturally arises here as to the nature of the bacteriological examination to be undertaken.

We have cultivation and direct microscopic examination to choose from. The method by cultivation is obviously not suited to our purpose, requiring as it does a considerable amount of time not to mention expense and labour.

A suitable method for practical requirements must be rapid, cheap and reliable. No busy practitioner will use even the most reliable method if it occupies too much time or causes expense out of proportion to its advantages.

The examination of a film of secretion by the microscope is the method which fulfills our conditions, as it requires only the simplest apparatus and very little special training, in contradistinction to what is necessary in order to work with cultures, and chiefly because it can be completed within five minutes.

There is a large body of evidence in favour of the value and reliability of microscopic examination. That of Schanz and Petit has been quoted already.

Sidney Stephenson says – "Happily in most of the cases of ophthalmia that fall under the notice of the practitioner, the making of cultures may be dispensed with. Indeed, bacteriological investigation may be reduced to its simplest form, namely, the staining of coverglass preparations from pus or membrane…"
(Stephenson. 129.)

Axenfeld and Tick (12) also write in support of this method, and Uhthoff (133) speaks strongly in favour of the advantage of microscopic examination in many cases.

Collomb quotes the following propositions as generally accepted by those versed in ocular bacteriology.

1. In health the conjunctival secretion is poor in bacteria. Coverglass examination is negative.
2. Many different non pathogenic organisms may occur accidentally in the conjunctiva, but the ordinary flora are the xerosis bacillus and the staphylococcus albus.
3. In pathological secretion only the pathogenic agent is seen. "This is Morax's (86) view but Collomb thinks the statement too absolute. Some saprophyte may develop sufficiently to be visible on a coverglass. (Collomb. 27)

Axenfeld and Tick agree with Morax and Beach (93), that as a rule, in the height of the inflammation, the causal bacteria are in such numbers as to eclipse the non causal or accidental organisms, though this may not be the case in diphtheria Morax and Petit (94, 104) lay stress upon the number and disposition of the bacteria seen by the microscope as being of great importance and a reliable basis for diagnosis.

Morax says that in acute conjunctivitis the microscopical examination of the secretion gives in all cases a certain diagnosis (M. 84), and that only the causal organism is seen in a coverglass preparation (M. 86); in any case important evidence in demonstrating the predominating species of

microbe is to be obtained in this way. (Morax 85).

According to Corsini, microscopical examination of conjunctival secretion is of great value in diagnosis and may be necessary to determine the exact character of a conjunctivitis. It is, however, not equally satisfactory or easy in all forms, though comparatively certain in the usual examples of catarrhal conjunctivitis.

Gouin (47) is strongly favour of this method. He says (p.96) that ophthalmologists are agreed, that, apart from the question of virulence, microscopic examination is of much greater practical value than culture or inoculation. Notwithstanding this, it is not able to, and ought not to, replace diagnosis made by the clinical signs, it merely strengthens the diagnosis.

Gouin tabulates the following points:-

1. It gives more information about the probable origin of the disease than the simple clinical examination.
2. It permits of the institution of a rational prophylaxis with more certain assurance.
3. It gives indications for treatment which the clinical form present can only slightly modify.
4. It authorises prognosis with more certainly than the anatomical appearance alone of the lesions.

Whenever it shows, better than cultures do, the ~~exact~~ relative numbers of the various organisms present, which gives it an advantage in cases of mixed infection as the bacilli

present may not all develop equally readily on the same medium.

Gouin states his results as conclusive in about 70% of the cases examined, negative-but none the less useful - in about 25% and equivocal in about 8%. At the same time he mentions that it might have been omitted, without damaging the diagnosis in about 55% of the cases. That is to say that in these cases the clinical diagnosis was confirmed, surely a confirmation not to be despised. On the other hand in as many as 22% of the cases it was indispensable for correct diagnosis.

In view of the support given by these authors I think the advantages of microscopic examination are evident, in confirming, amplifying and, it may be, correcting the clinical diagnosis.

Microscopic examination may give either a positive or a negative result. It is positive when numerous specific organisms are evident, typically arranged in relation to each other and to the cells, and giving definite staining reactions. It is negative when only a few organisms, whose relation to conjunctivitis is doubtful, or non at all are seen. In the former case attention is directed immediately to some special form of conjunctivitis, in the latter a number of special forms are excluded.

In this connection the classification of Nimax & Petit (94, 104) is of interest

Group I. Microbes which only occur in man, and not on all of his mucous membranes. They cause inflammation by their mere presence without any previous traumatism and are destroyed unless transported directly from one mucous membrane to another. This group includes the gonococcus, bacillus of Weeks and the diplobacillus of Morax.[1]

Group II. Microbes which occur normally on some of our mucous membranes and which, in certain badly ascertained conditions, can proliferate and cause inflammation. This group includes pneumococci and some varieties of streptococci.

Group III. Organisms which can only cause inflammation on ground prepared by previous infection; these are diphtheria bacilli and various streptococci & staphylococci.

It is only in reference to the members of the second and third groups that any difficulty can arise, as they may be confused with each other and with non-pathogenic organisms while their causal relation may be questioned. As mentioned above however the numbers of organisms seen are a clue to the causal relation in most cases.

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[1] The non-occurrence of the bacillus of Morax on the healthy conjunctiva is disputed by Rymowitch (112) who found it in 6 out of 100 cases examined, while Plaut and Zelewski (106) found it three times in the conjunctiva after excision of the tear sac but in the absence of disease. I have myself seen a bacillus, microscopically indistinguishable, in the normal conjunctiva.

Two microorganisms must however be mentioned which may proliferate in a conjunctiva, inflamed from some other cause, and thus form a prominent feature in a film, These are the xerosis bacillus and the staphylococcus albus, which according to Morax(84), Axenfeld and Fick (12), Collomb (27) Gonin (47) Rymowitch (112) and others are normal inhabitants of nearly every conjunctiva and often proliferate enormously, especially the former, in irritated conjunctivae.

I have not found any author who has mentioned difficulties in microscopic diagnosis due to these organisms, excepting in the case of diphtheria in which the resemblance of Loeffler's and the xerosis bacilli may cause confusion. This point is mentioned under diphtheritic conjunctivitis. In practice the eye soon gets very familiar with the appearance of the xerosis bacillus as it is seen so frequently.

It will now be convenient to consider the various forms of conjunctivitis seperately with special regard to the bearing of microscopical examination on their diagnosis prognosis and treatment.

For the sake of convenience I shall follow Gonin's arrangement.

The first group contains four forms, namely gonococcal, Weeks, diplobacillary and diphtheritic conjunctivitis. The first three are bacteriologically the best known (Morax & Petit 94) and it is here that

microscopical examination is most successful and reliable. From a bacteriological point of view they are also definite forms, the prognosis and treatment being governed almost entirely by the organisms present.

An analysis of the work of Gouin, Morax & Petit and Lundsgaard (79) will show the numerical importance of these forms in proportion to other forms of conjunctivitis.

	Gouin.	Morax & Petit.	Lundsgaard.	Total.
Total cases.	~~785~~	243	107	1135.
Gonococcal.	30	10	5	45.
Weeks.	19	94	3	116.
Diplobacillary.	185	63	38	286.
Other forms.	551	76	61	688.
Percentage.	29.8	68.7	43.0	~~40~~.

The proportion apparently differs according to the locality. Lundsgaard has for instance hardly found the Weeks bacillus in Copenhagen, while Gouin's percentage is reduced by the presence of a large number of traumatic cases and chronic non-microbic irritations of the conjunctiva in his collection. The general average is forty-seven percent.

1. Gonococcal Conjunctivitis.

This form of conjunctivitis is known in this country as "gonorrheal" and on the continent (Knapp, Groenouw etc) as "blennorrhagic" although Axenfeld and Fick prefer the term "gonorrheal". Gonin uses the term "conjonctivite gonorrhéique".

It is usually discussed as affecting infants as "ophthalmia neonatorum" and adults as "purulent ophthalmia". The name leucorrheic ophthalmia has also been used to designate specially a form affecting female children who are usually also suffering from vulvovaginitis at the same time. Knapp (84) states that this affection differs in no way from blennorrhagic conjunctivitis of adults and infants. There is also the "Conjonctivite blennorrhagique spontanée of Fournier (40), which Knapp (84) considers to be a manifestation of general gonococcal infection. The question, however, of metastatic gonorrheal conjunctivitis does not concern us here.

Petit (104), Greef (49) and Von Ammon (138) propose to get rid of all these names at one sweep and to designate the affection according to the presence or absence of gonococci, which is the basis of prognosis. Following these authors, and in view of the fact that Gonin, Groenouw (50), Von Ammon and others have shown that purulent ophthalmia at any age is not always associated with gonococci, and that these may give rise to a conjunctival secretion of a catarrhal nature I prefer the term "Gonococcal" although in opposition to Schanz (119) who considers that the present

state of our knowledge does not justify the separation of a gonococcal class.

Schanz (120) has also recently thrown doubts upon the pathogenicity of the gonococcus but it is unnecessary to do more than barely refer to the discussion between this author and Axenfeld on the subject. (Axenfeld 11).

A few years ago purulent ophthalmia in infants was thought to be always gonococcal, Roux (84) considered it so much so ~~that~~ as to render microscopic examination unnecessary in all cases.

Uhthoff (133) states that neither in infants nor in adults is purulent conjunctivitis due to gonococci only. Axenfeld and Tick (12) state the percentage of gonococcal cases as unknown and mention pneumococci, colon bacilli and staphylococci as causes of purulent conjunctivitis in the newborn. Stephenson (129) finds in the practice of seven observers (446 cases) 72.83 % of gonococcal cases and in his own practice (45 cases) 66 %. I have already given an analysis of the cases of Gouin, Groenouw and Von Ammon. The latter are interesting as being all purulent cases (Augeneiterungen) and therefore to be expected to be gonococcal, and yet his gonococcal cases are two per cent less than Gouin's, who included all forms of conjunctivitis, while 11 % above Groenouw's, who did the same.

Francisco's ($\frac{43}{100}$) percentage is rather higher as he found

gonococci in 30 out of 40 cases of ophthalmia neonatorum and the bacillus of Weeks in the remainder.

Recently the diplobacillus of Morax has been described as a cause of infantile ophthalmia both purulent and otherwise by Collomb (28) and Andrade (2), and Zur Nedden (145), and the influenza bacillus by Jundell (66) and Zur Nedden (144, 146).

Reynolds (109) divides ophthalmia neonatorum clinically into muco purulent and gonorrheal, and as the latter is also purulent he divides the three forms according to the causal microbes. He mentions four classes. (a) Micrococcus Pasteuri, (b) Pneumococcus or bacillus of Weeks, (c) Staphylococcus and (d) gonococcus.

In the adult we find the same conditions prevailing, namely, that a great variety of other bacteria besides gonococci may produce a reaction identical with what is generally accepted as the typical clinical picture of a gonococcal ophthalmia, and only to be distinguished clinically by its milder course and lesser tendency to affect the cornea in most cases.

Without going into great detail here I may mention Axenfeld (10) who considers the bacillus of Weeks, pneumococcus diplobacillus of Morax, pseudo gonococcus, colon bacillus and Loeffler's bacillus in cases where a membrane is present, as causes of purulent conjunctivitis and Carsini (33) who divides ocular blennorrhoea into four groups according

to the bacterial cause :- (1) Gonococcus, (2) Pneumococcus, (3) Diplococcus, (4) Bacterium Coli, bact. diphtheriae, the staphylococci and the meningococcus intracellularis. To these Suit (124) adds the influenza bacillus.

Of these organisms, with the clinical appearances they produce will be referred to in turn in order to avoid repetition: it will be preferable here to turn to the second point in favour of a bacteriological examination, namely the variations in the clinical aspect of the inflammation produced by gonococci.

The typical clinical picture of gonococcal ophthalmia needs no description here. It is a violent purulent inflammation associated with grave danger to the cornea. In view of the evidence of Groenouw and Von Ammon and others we must believe that there is an unbroken chain of intermediate forms from a simple catarrh to the typical purulent form all due to the gonococcus.

Darier (34) holds that there is no true purulent ophthalmia without gonococci, but that all forms of gonococcal inflammation are not equally severe.

According to Uhthoff (133) there may be a membrane in the early stage of gonococcal conjunctivitis and Roscher (110) and Lundsgaard (79) quote cases of membranous conjunctivitis due to gonococci.

Groenouw (50) states positively that there is no certain diagnosis from the clinical aspect.

It would appear then, that, however great the probability may be that a typical purulent ophthalmia is gonococcal, it need not necessarily be so while in the same way, the most unlikely case may in reality be associated with this organism. In the first case we are entrapped into giving a serious prognosis and adopting a wrong or unnecessary treatment, while in the second the source of infection is missed and prophylaxis neglected. Even though the individual affected with a mild form may not suffer severely himself, yet we have no assurance that other cases infected from this source may not be of the greatest severity.

Even in the less atypical forms, purely clinical diagnosis is not always of the easiest. Schneider (122) mentions as possible difficulties, diphtheria of the conjunctiva, acute trachoma, acute chalazium, lid erysipelas and purulent chorioiditis.

Kibbee (68) in urging the use of the microscope to diagnose gonococcal conjunctivitis mentions the treatment of atypical cases as simple catarrh, and asserts strongly that it is not possible to say that a case is not gonorrheal by the clinical signs only. He also brings forward evidence of the possible medico-legal value of a labelled and dated microscopic preparation of conjunctival secretion.

Knapp (71) in supporting Kibbe gives an illustration as amusing as it is instructive. Having a doubtful case, he

sent the patient to a distinguished dermatologist, from whom he returned with a letter to the effect that a great many diseases with very long names had successfully been excluded, that the affection was probably syphilitic, and that another interview in about four days time would be advisable to decide the matter. It occurred to Professor Knapp to examine the secretion microscopically with the result that an abundance of gonococci were observed.

Andrade's (2) case is a good illustration of the desirability of examining the secretion in ophthalmia neonatorum. An infant three days after birth developed a conjunctivitis with purulent secretion and oedema of the lids. On the strength of the clinical evidence alone protargol was prescribed and later on silver nitrate 2% solution. The inflammation, although modified, persisted obstinately and on microscopic examination the diplobacilli of Moax were found, even inspite of the constant treatment. The exhibition of Zinc now rapidly cured the condition which under other treatment had persisted for three months.

The appearance of gonococci in a microscopical preparation of pus is well known. They are described by Schanz (117) as "semel-förmig" or kidney shaped, 0·8 to 1·6μ in length. Kiefer (69) considers that they do not vary much in size in contradistinction to the very similar meningococcus intracellularis. Each member is a diplococcus,

formed of two of the kidney shaped cocci having their straight or concave sides in apposition.

The arrangement and disposition of the cocci is very characteristic: They lie in little groups in the protoplasm of the leucocytes, occasionally in the nuclei (Kiefer[69]) Unless these intracellular groups are seen the diagnosis is not certain (Schanz 117). A few may be seen free also, Corsini (83) says that it is only when the conjunctival secretion has been reduced by treatment, that they are found only inside the cells.

Most authors are agreed that the detection of gonococci by the microscope is both simple and reliable. Mnax (84, 88) holds that they are characteristic whether in a seropurulent, purulent, or pseudomembranous exudate, and that if the observer is familiar with Gram's method and searches inside the cells it is impossible to confound them with other cocci. Decolourisation with absolute alcohol should not be prolonged more than half a minute as the gonococcus is very easily decolourised. The coffee bean shape should not be too much insisted on as rounded or irregular forms are equally characteristic (Knax 88). Again Knax and Beach (93) say that for anyone accustomed to the use of the microscope the search for and recognition of gonococci is an elementary matter, and confusion is impossible when two preparations are made one with a single stain and the other by Gram's method.

According to Minne (82) the three special characters of the gonococcus, namely its shape, its reaction to Gram's method, and its presence inside the leucocytes if found together are sufficient to establish the diagnosis.

Groenouw (50) considers the appearance of gonococci in the leucocytes and in or on the epithelial cells and their reaction to Gram's method as characteristic. They may be distinguished from staphylococci and pneumococci by the greater numbers in the cell. After reviewing the question of possible confusion with cocci, which decolourise by Gram's method he decides that these are very rare if present at all on the conjunctiva and puts down Manthen's results to bad workmanship. He considers that diplococci which decolourise by Gram's method may on this ground alone, with the greatest probability, be considered to be gonococci. In his 100 cases the only cocci which decolourised were gonococci. Finally Groenouw holds that the coverglass method is superior to that of culture, which never demonstrates the presence of gonococci where the microscope has failed, and that the latter always gives a correct result.

Groenouw's authority is certainly deserving of all respect but in view of the statements of Krukenberg (7 & 9 ante) it seems possible that in rare cases mistakes might occur.

The only organisms likely to cause confusion are the meningococcus intracellularis and diplococci belonging to the staphylococci including the so-called pseudo-gonococci

which are gonococcus-like diplococci which decolourise by Gram's method.

With regard to the first two, Gram's method of staining is to be relied upon and its constant use is justly insisted upon by Morax (88), Axenfeld (10), Uhthoff (133), Stephenson (129) and every writer on the subject. According to Kiefer (69) and Fraenkel (42) the reaction of the meningococcus intracellularis to Gram's method is doubtful, but it seems to decolourise less easily than the gonococcus which looses its colour very rapidly (Morax 88). The greater number of the meningococci present and their variability in size are also points of difference. Fraenkel (42) and Haglund (54) describe cases of conjunctivitis clinically resembling gonorrhoea. Coverglass examination showed groups of diplococci of 15 or 20, often intracellular and very closely resembling gonococci. They stained by Gram. Diplococci which belong to the staphylococci are easily distinguished according to Groenouw (50) as they stain by Gram's method and have not the typical arrangement, the intracellular groups consisting of only three or four members whereas gonococci fill the cells completely.

Uhthoff (133) also supports the reliability of Gram's method in regard to the pseudogonococci of many authors.

There would however appear to be more difficulty in connection with the pseudogonococcus of Krukenberg.

Krukenberg (72) considers that as a rule there is no difficulty in diagnosing gonococcal ophthalmia.

Differential diagnosis is important on account of the difference in prognosis and treatment. A coverglass preparation usually suffices. He goes on to describe a diplococcus, morphologically identical with the gonococcus and which decolourises by Gram's method. Such cocci were found in 3 out of 40 cases in which there was no sign of catarrh beyond slight injection.

Krukenberg concludes that such cocci are not very rare on the human conjunctiva, and that although microscopical examination as a practical means of detecting the gonococcus loses nothing in value, yet in future outbreaks or slight cases apparently showing gonococci should not be considered to be gonococcal until the organism has been further investigated by culture.

In practice such an investigation is not likely to be made as, although a busy practitioner might make a culture from a specially virulent case, he is not likely do do so from a mild case.

Morax (90) considers Krukenberg's coccus to be a variety of gonococcus, while Haglund (54) suggests that it may be a form of diplococcus intracellularis meningitidis.

I have myself seen diplococci resembling gonococci very closely but with certain differences. The groups are very frequently extracellular and do not contain more than eight or nine members, very rarely more. They are more heaped together than gonococci which usually lie just barely touching one another, evenly distributed. I have not seen the typical

appearance of a cell completely filled by diplococci, with anything else than gonococci.

That all staphylococci do not hold the stain equally tenaciously in the presence of alcohol, I am convinced, as I have more than one preparation showing groups of cocci, one group being stained and the other decolourised. I have not noticed a group with some members decolourised and others stained. I incline to think that with ~~more~~ less prolonged decolourisation all would have retained the stain. More observation on this point would be interesting.

Besides their shape I consider the characteristics of gonococci in secretion to be the following (1) Rapid decolourisation by Gram's method. (2) Position in purulent secretion practically all intracellular. (3) The characteristic appearance, here and there, of a cell quite filled with evenly distributed cocci which barely touch one another. (4) Absence of the slightest tendency towards the grape-bunch or cannon-ball-heap arrangement.

Any gonococcus-like diplococci which I have seen, whether staining by Gram or not, have not presented the last three characteristics.

For practical purposes Krukenberg's pseudogonococcus may be neglected and the conclusion is legitimate that, as Grenouw and the great majority of observers assert, the detection of gonococci by the microscope is reliable.

With regard to a negative result in a suspicious case Stephenson (129) points out the necessity of making several

examinations before deciding on the absence of gonococci. He also mentions that other organisms such as Xerosis bacilli and ordinary pyogenic cocci may occasionally be present. Groenouw found the bacillus coli occasionally and the bacterium pneumoniae once, in association with gonococci. Goiri found the bacillus of Weeks in one case.

As a rule however, as Petit (104) says, no other organisms are to be seen. Uhthoff (84) states that the more intense the inflammation the more likely are the gonococci to be in pure culture.

When gonococci are detected in a case of conjunctivitis the prognosis at once becomes more serious. Von Ammon's (138) non-gonococcal cases had one third less ulcers than the gonococcal ones. Groenouw's (50) cases show that it is the presence of the gonococcus rather than the severity of the inflammation that is to be taken as an indication of danger to the cornea. In none of his 100 cases, which were not gonococcal, did ulceration occur while the fact of a gonococcal case being catarrhal proved to be no indication of security.

The numbers of gonococci present seem to have very little relation to the severity of the case. When in moderate numbers the case may be severe or light, if in very great or very small numbers the case is more likely – but not certain – to be severe or light respectively.

The detection of other organisms, such as those mentioned above, does not appear to modify the diagnosis prognosis or

treatment. It is interesting to note however, that the worst case of corneal ulceration in Groenouw's paper showed few gonococci but numerous pneumococci.

By making further examination during the progress of the case the results of the treatment may be appreciated better than by mere clinical observation, which may easily sanction the cessation of treatment while gonococci are still present in the secretion and thus leave the case free to spread infection.

Morax (88) says that the termination of the affection is marked by the complete disappearance of the gonococci.

Naturally the discovery of the absence of gonococci in a purulent case of ophthalmia neonatorum improves the prognosis, although I cannot agree with Greef that it contra indicates the necessity for any treatment beyond constant washing with weak lotions. The indications for treatment in non-gonococcal infantile ophthalmia depend upon the clinical features of the case and on the nature of the causal agent, in the same way as in gonococcal cases.

Weeks Conjunctivitis.

The second of the bacteriologically well known forms of conjunctivitis is that known by the awkward name of Weeks conjunctivitis. First described by Weeks (142) as "acute conjunctival catarrh" this name was retained by Morax (147) in 1892 but changed by him in 1896 (84) to "acute contagious conjunctivitis" because the character of the secretion was found to vary from catarrhal to purulent and on account of the markedly contagious character of the affection.

Gouin prefers the term "Weeks conjunctivitis" as being simpler and more direct, other forms being both acute and contagious. In this country there is apparently no generally accepted name and it is known by any of the above titles, and also as acute ~~purulent~~ mucopurulent conjunctivitis. (Stephenson 129) This term is open to the same objection as the term acute catarrhal conjunctivitis as it associates the affection with a particular form of secretion.

"Weeks conjunctivitis" is certainly better than any of the other names but better still, I venture to suggest would be the term "microbacillary conjunctivitis". This is simple and less awkward than Weeks conjunctivitis, while no less definitely directing attention to the most important point, namely, the presence of the bacillus of Weeks which, to my mind, has every claim to the name of microbacillus that the organism named after von Heran has to that of diplobacillus.

Not only is the bacillus of Weeks the smallest bacillus, which

occurs on the conjunctiva but it occurs nowhere else, and also ranks amongst the smallest of all bacilli, while its appearance, arrangement and staining reactions further characterise it. In view of these points I consider the term "microbacillary conjunctivitis" as superior to any of the others mentioned above.

Although the identity of the Weeks bacillus is generally accepted by the authors I have quoted, it should be mentioned that Pes (99) and Schanz (120) consider it to be a variety of the diphtheria bacillus, while Smit (124), Jundell (66) and Rymowitsch (111) hold that it may be identical with the influenza bacillus. Axenfeld (11) and Bietti (20) disagree with Schanz, while Morax (66) opposes Jundell.

As regards the practical importance of this form of conjunctivitis the evidence is somewhat conflicting, which is what might be expected in the case of an extremely infectious disease often appearing in epidemic form. Carsini (33) found the Weeks bacillus in 20 per cent of cases resembling acute catarrhal conjunctivitis; Morax (147) in every case; Veasey (136) found it only occasionally in Philadelphia; Gonin in only 10 out of 310 cases of catarrhal conjunctivitis; Morax and Petit (94) in 94 out of 243 cases of all kinds; Bach and Neumann (15) and Lundsgaard (79) appear to have found it practically not at all. In Edinburgh and Leith it is quite common, especially in Leith.

The clinical features have been repeatedly described. I need only refer to the accounts of Weeks (142) in 1886, of Morax in 1892 (147), and 1894 (84), of Morax and Beard (93) in

1896, by Weichselbaum and Muller (143) and Wenax and Petit (99) in 1898, and Petit (104), Stephenson (129) and Hoffmann (61) in 1900.

From these descriptions it appears that the typical condition is a more or less acute catarrhal or muco-purulent conjunctivitis of slight or moderate intensity. The ocular conjunctiva is injected, as well as the palpebral, and may show little haemorrhages. There is some swelling and a pink tinge of the lids. In children corneal complications are rare and slight when they do occur, in adults they are relatively more common and more serious.

The usual type is both frequently and widely departed from. The Koch's bacillus may produce an inflammatory reaction simulating, to a greater or less degree, almost every other form of conjunctivitis, thus rendering clinical diagnosis impossible. Accurate diagnosis is important, not because micro-bacillary conjunctivitis is a dangerous affection which must not be allowed to escape detection but because in an atypical form it might be mistaken for a more serious disease, and the prognosis and treatment modified accordingly, or its intensely infectious character might be overlooked and prophylactic measures neglected.

The following points will illustrate and explain these views. The affection may be chronic, (Wenax & Beach 93) and in this case may be associated with papillary hypertrophy of the conjunctiva (Hoffmann 61) or granulations (Wenax 92).

A clinical picture resembling phlyctenular conjunctivitis may be

be produced (Monax, Markus 80, Petit 94 + others), resembling gonococcal conjunctivitis even to causing corneal ulcers, (Monax 147, 93,) A membrane may be present leading to confusion with the milder forms of diphtheritic conjunctivitis (Hoffman, Uhthoff etc) It may cause the development of follicles (Sromakowski 51) and according to Axenfeld and Fick (12), Petit (104) and Veasey (136) is clinically indistinguishable from pneumococcal conjunctivitis. The clinical appearances described by Markus (80) in an epidemic of mucobacillary conjunctivitis in Bielefeld present so wide a departure from the type as to merit separate consideration. Markus observed in all 150 cases. All the fresh cases presented phlyctenulae on the corneal margin. Some cases presented the appearance of acute trachoma with swelling of the follicles. Many became chronic, the bacilli being present in great numbers after five or six months, and liable to sub-acute relapses, although acute commencement was the rule.

In five adults phlyctenulae were present. In these the clinical picture differed somewhat from that in the children, there being more severe pericorneal injection. Atropin — never necessary in children — was required and only dilated the pupil partly. In the adults one eye escaped in three cases, never in the children.

In 60 cases examined by the microscope the Weeks bacillus was found in a pure state. Its presence was established in all the fresh and nearly all the chronic cases.

This would tend to show that this affection may, ~~under~~ in circumstances of some special nature, assume a form, much

more virulent or more troublesome than it does usually.

According to Knox and Beach the phlyctenulae caused by the Koch bacillus differ from those of ordinary phlyctenular conjunctivitis in being little serous exudations lifting up the conjunctiva, whereas the latter are accumulations of leucocytes. This distinction is however not always easy to make by mere observation especially in young children with marked photophobia.

It is obvious then, that purely clinical diagnosis although reliable in many typical cases, may often be misleading.

Knox and Petit (94) found that the majority of cases were diagnosable without the aid of the microscope, but that in mild or complicated cases errors were common. It is just these mild cases which ought not to be allowed to escape detection, for, as the same authors say (p. 173) "la bénignité d'un cas n'implique nullement la bénignité des cas aux quels il donnera naissance". Here also, as in gonococcal conjunctivitis, the affection is much more severe in adults than in children. Knox (84) and Petit (104) state that corneal lesions occur practically only in adults. Thus a mild case of microbacillary catarrh in a child, overlooked and treated as if of no importance, may be the origin of permanent damage to sight in one of its parents.

Relapses are also not uncommon, especially if more than one member of a family are affected, rendering it necessary to treat all infected members simultaneously.

These facts indicate the advantage of a microscopical examination which is strongly recommended by Knox and Beach

who consider microscopical diagnosis as both necessary and certain, and that it is unnecessary to make cultures for this purpose.

Gouin (47) considers the clinical symptoms too irregular for diagnosis, which presents no difficulty if the microscope is used, and according to Petit (104) the use of the microscope is indispensable as it is in the early stages that a diagnosis is required, though by waiting for the evolution of the affection it may be differentiated from true diphtheritic or blennorrhagic conjunctivitis. Cosini (33) stands alone in finding the Koch's bacillus in cultures in cases in which it had been missed by the microscope.

Stephenson (129) considers the presence of this bacillus as the "central fact of ordinary mucopurulent Ophthalmia" and says that it may always be seen in coverglass preparations of the discharge. A preparation of the secretion from a case of micrococcal conjunctivitis shows the following features, according to Monax and others.

Numerous leucocytes are seen, usually of the polymorphonuclear variety. Both free and in the cells lie numbers of a small thin short bacillus measuring from 0.75 to 1.0μ in length. They do not stain as deeply as other organisms such as staphylococci or xerosis bacilli. Petit describes them as staining more deeply than the protoplasm of the cells and less deeply than the nuclei, when a simple stain is used, and suggests staining the preparation for a longer time so as to overstain the other organisms. I do not think that this is necessary, while it is certainly

inconvenient. The poles often stain somewhat more deeply than the centre and the bacilli decolourise by Gram's method. Sometimes two or three are seen end to end forming a short chain. There are always organisms in the leucocytes and their number varies. There may be only one or two or the protoplasm of the cell may be crammed with them. Weichselbaum and Müller note the presence of masses of the bacilli closely packed together. I have observed this feature: the masses seem to consist of a pure culture of the bacillus and occupy an area in the field about equal to the size of a large squamous epithelial cell.

As a rule no other organisms are seen or only a very few. Others are present, and may be demonstrated by culture but are not often seen in coverglass specimens, and according to Lenox and Petit never in a way to cause confusion.

The size, appearance, arrangement and staining reactions of the Wahs bacillus are characteristic. Morphologically it has been compared by Lenox and Beach to the bacillus of mouse septicaemia and to the tubercle bacillus, confusion with either of which needs hardly be apprehended.

Stephenson warns against confusion with the colon bacillus and Friedlanders pneumonia bacillus, both of which occur in the eye and react negatively to Gram.

Rymowitsch (111) and Jundell (66) consider that it is morphologically indistinguishable from the influenza bacillus, which also decolourises by Gram's method.

No confusion in my opinion can arise with any of the above,

if the observer be at all familiar with the appearance of the organism. The colon bacillus is much larger, does not present the same numbers or grouping, stains more deeply and is only rarely met with on the conjunctiva. The same applies to the pneumo-bacillus of Friedlander. According to Zur Nedden (146) a glance is sufficient to distinguish between the influenza bacillus and the Weeks bacillus, and he goes so far as to suggest that Jundell never could have seen a Weeks bacillus.

I venture to corroborate Zur Nedden's opinion, unless either or both of these bacilli vary very widely in form and arrangement, of which there is no evidence.

The numbers and position of the bacilli present vary with the stage and intensity of the affection. According to Morax (84) in the first few days they are in small numbers and mostly inside the phagocytes. By the third or fourth day they are very numerous. In intense cases they may be inside every cell. Stephenson (129) mentions the relation of the numbers of the bacillus to the severity of the case as a marked peculiarity of the Weeks bacillus and says that a mere inspection of a microscopical preparation of the discharge will afford information as to the intensity of the affection. In some mild chronic cases I have also seen very numerous free bacilli. After treatment they become scarce and mostly intracellular.

Although, as mentioned above, the Weeks bacilli are usually in a practically pure state, yet mixed infections occasionally occur. Gouin mentions a case of combined gonococcal

and microbacillary infection, and Zur Nedden (145) and Stephenson (129) cases presenting both the bacillus of Weeks and the diplobacillus of Morax. The latter author observes that if cases of trachoma become affected by Weeks bacilli an acutely infectious form of trachoma is set up and its spread greatly facilitated. Morax and Beach (93) consider the recognition of the Weeks bacillus as important in order that parents may be warned and the children excluded from school, and also as necessary to a correct prognosis, in purulent cases for example.

According to Petit (104), if the bacillus of Weeks is found, the case can be mastered in a few days, and if no corneal trouble is present when seen, none will arise after the adoption of proper treatment.

Thus the discovery of the Weeks bacillus in a case of conjunctivitis, however severe and grave it may appear modifies the prognosis greatly for the better, while in a case of mild catarrh its presence indicates the institution of prophylactic treatment and the use of some more active germicide than the boric lotion which is the usual application for such cases.

Diplobacillary Conjunctivitis.

This form of conjunctivitis like the last mentioned has enjoyed several names before the present one.

First described by Morax (86) in 1896 under the name of "conjonctivite subaigue", Axenfeld (7) and Peters (101) called it chronic diplobacillary conjunctivitis; in 1899 Collomb (27) and Bietti (9) dropped the term "chronic" and it is now known as diplobacillary conjunctivitis.

This history emphasises the fact that here also, clinical has had to give way to bacteriological terminology.

The identity and pathogenicity of the special organism has been proved by Morax (86) and Axenfeld (7) and though disputed at first, as for instance by Chauvel (25), are now thoroughly established.

Diplobacillary conjunctivitis is very common, whether epidemic or sporadic, and constitutes a large proportion of the catarrhal cases. Bach and Neuman (15) give 32 % of these cases as diplobacillary, Augières (4) 65 per cent, Gonin (47) 60 per cent. Even in regard to conjunctivitis in general its proportion seems to be considerable; it constituted 26 per cent of Morax & Petit's (94) cases, 24 per cent of Gonin's, 35 per cent of Lundsgaard's (79) and a large number of Collomb's (27), who however omits to state the exact number. In Edinburgh and Leith it is very common.

The course and clinical picture have been frequently described by Morax (86), Axenfeld (7), Peters (101), Bietti (9), Collomb (28), Stephenson (129), Zur Nedden (145) and others.

it may be seen,
From these authors, that, as in other forms of conjunctivitis of microbial origin, there is a typical symptomatology for the majority of cases, but the deviations from this are so frequent and so wide as to destroy the reliability of a purely clinical diagnosis.

Persons of both sexes and all ages and professions are liable to attack, and at all times of year, though country people adult ages, and hot dry periods seem to be factors of greater prevalence. In a typical case the clinical characters are well marked. The onset is often very insidious, and if one eye is affected first the other follows suit within two or three days. There is a little itching especially at the commissures, slight secretion, mostly at night, so that the lids adhere in the morning. This secretion accumulates in little greyish yellow balls in the internal angles, while a few flakes of fibrinous pus lie in the inferior conjunctival cul de sac. Special characters are held to be the frequent association with blepharitis, and the special injection, tenderness and not infrequent excoriation of the palpebral commissures, on account of which Axenfeld (8) uses the term "Angular blepharo-conjunctivitis". The ocular conjunctiva remains unaffected or nearly so.

So much for the type. Axenfeld, Gourin, and Zenkedden (145) have pointed out, as I have also been able to observe, that some or all of these symptoms may be present in the absence of the diplobacilli of Morax.

The most important variation is the acute purulent form

resembling acute gonococcal or microbacillary conjunctivitis. which is mentioned by Axenfeld, Hoffmann (60), Zur Nedden and Collomb. Andrade's (2) case of purulent ophthalmia in an infant due to diplobacilli has already been mentioned.

Corneal lesions are rare and not severe according to Axenfeld, Hoffmann and Peters. Bietti, Zur Nedden & Collomb also note cases, which appear to occur in the proportion of about 3 or 4 per cent. According to Pehl (104) an ulcer may be present with such a slight conjunctivitis, that the former may be alone observed and the latter missed.

The affection may be mistaken for phlyctenular conjunctivitis according to Axenfeld (8) There is some difference of opinion as to whether the phlyctenulae occur merely as a coincidence or as an effect of the diplobacilli. Collomb (29) and Axenfeld (8) consider that the diathesis of the patient is responsible for this complication, while Zur Nedden (145) holds that in some cases the direct action of the organisms is the cause.

Follicular conjunctivitis may also be simulated and here similar views are held. Gossin believes the follicles to constitute an "épiphénomène fréquent", and not a mere coincidence, which is the opinion of Axenfeld, Zur Nedden and Peters.

On the other hand the diplobacilli may be present without producing their characteristic lesions. According to Zur Nedden there is often no blepharitis: Collomb found this symptom in only seven per cent of his cases.

It is similar with the characteristic of angularity on which Bietti (19) lays stress, remarking that although all cases of angular conjunctivitis are not diplobacillary, yet unless both commissures are affected, the disease is not of this nature. He failed to find the bacilli in cases in which the inner canthi alone were affected.

Collomb found angular conjunctivitis in only 28% of his cases and Bach and Neumann in 54 per cent of theirs. My own experience is that either, both, or neither of the commissures need be affected.

Thus we are again compelled to resort to bacteriological examination for definite information, and of all forms of conjunctivitis this is the one most amenable to microscopic diagnosis.

The following description of a coverglass preparation is according to Kuhnax (86 etc) and Axenfeld (7 etc).

The secretion is more fibrinous and the leucocytes less numerous than in the other forms. The bacilli are large with rounded ends, which may appear thickened, and are arranged in couples, end to end. Each is 2-3 μ long and 1 to 1·5 μ broad, a couple measuring about five or 6 μ in length. They lie mostly free, a few may be seen inside phagocytes, and they show a marked tendency to aggregate into masses on the epithelial cells. The number present varies but is usually very great.

The bacilli stain readily and deeply with ordinary aniline dyes, occasionally the poles appear more strongly coloured than the

centre. They decolourise by Gram's method.

My own preparations confirm these points. The noticeable features are the fibrinous rather than leucocytic nature of the secretion in which numbers of epithelial cells are present. Very few bacilli are seen inside phagocytes. One can often detect their presence with a low power. (105 diameters)

The evidence in favour of the use of the microscope is practically unanimous. Morax[86,87] holds that in all doubtful cases diagnosis is easily established by the microscope, as the organisms are very easily recognised, and their number leaves no room for doubt. Axenfeld (788) found that reliance on clinical symptoms led to error and considers microscopical examination decisive:— "Es ist dieser Deckglasbefund bereits äusserst charakteristisch". Morax and Petit (94) state definitely that they have never seen any organism in conjunctival secretion which could be confounded with the diplobacillus.

According to Carsini (33) confusion can only occur between the diplobacillus and the pneumobacillus of Friedlander and the ozoena bacillus. Morax's bacillus has no capsule and has a strictly bacillary shape. Moreover, according to Axenfeld Ozoena bacilli do not occur in conjunctivitis. A closer resemblance exists in the case of the diplobacillus liquefaciens of Petit (103) which has the same appearance though smaller and reacts similarly to stains. Its grouping and arrangement are, however, quite different and it occurs only in corneal ulcers.

It is hardly necessary to add more details of evidence as to the reliability of the microscope in this affection, Gouin, Collomb, Petit, Zur Nedden, Peters (101), Uhthoff (33) and Bietti all unite in its favour.

Beyond the diagnosis there is little information to be obtained from microscopic examination. According to Peters (101) there is no relation between the number of bacilli seen and the intensity of the case. Unax (87) holds exactly the contrary view, namely that the numbers present vary as the intensity of the case. According to Zur Nedden (145) a good deal depends upon the part from which secretion for examination is obtained if this is taken from the inner angle, whither all foreign bodies from the conjunctival surface are swept, great numbers of bacilli will be found even in mild cases but if secretion is taken from the cul de sac in all cases, a different result is obtained.

Axenfeld (7) points out that the causal bacilli quite eclipse any accidental organisms, which may be present. As the case becomes more chronic, these accidental microbes become more numerous and the diplobacilli less.

Usually the diplobacilli are seen in pure culture, especially if the secretion from the cul-de-sac is examined. Secretion from the caruncle often shows other organisms such as xerosis bacilli and staphylococci, whose presence has no influence on the case.

Cases of true mixed infection have been observed. Combined

diplo- and micro-bacillary has been mentioned already. Bach and Neumann (16) in 35 cases had one with pneumococci and one with Friedlander's pneumobacillus, besides others in which staphylococci, streptococci and xerosis bacilli were present.

Collomb and Van Redden believe that staphylococci are, to a greater or less extent, concerned in the production of the acute variety of diplobacillary conjunctivitis.

The prognosis in diplobacillary conjunctivitis is good. The detection of the diplobacilli indicates the exhibition of zinc preparations and attention to prophylaxis. Careful search should be made for unnoticed sources of infection in the patient's family and to ensure success, all should be treated at the same time.

Diphtheritic Conjunctivitis.

Although Béclard in 1821 was the first to describe diphtheritic conjunctivitis, it was Von Graefe, who in 1854 really established it as a clinical entity. The distinctive feature of this affection was the presence of a membrane, deep or interstitial in relation to the conjunctiva, to which it was adherent.

At the same time another membranous affection of the conjunctiva was recognised under the name of "ophthalmia crouposa", or croupous conjunctivitis. This affection was milder in character, the membrane being of a superficial nature, easily separated from the conjunctival surface.

These two diseases were, as Roseher (110) mentions, considered to be essentially different, and so described.

Recent observers, amongst whom may be mentioned Coppez (31) Uhthoff (133), Stephenson (129 & 130), Haab (52), Baumgarten (17) Gouin (47) and Vossius (139) have shown that variation in the nature of the membrane, or even its presence or absence, is quite compatible with diphtheria, in the sense of the affection caused by Loeffler's bacillus, and that there is no distinction beyond that of degree between a superficial or croupous exudation and an interstitial or so called diphtheritic infiltration on the conjunctiva.

Corsini (33), who quotes Sondille as his main authority, shows that since 1891, when Gallemaerts was the first to find Loeffler's bacillus in croupous conjunctivitis, there

has been no lack of evidence to show that all grades of conjunctivitis, from the simple catarrhal through the croupous to the diphtheritic form may be caused by Loeffler's bacillus, while membranous cases of the gravest nature have occurred in which this bacillus could not be found.

Uhthoff (133) supports these views and Stephenson (130) describes 43 cases, in which the diphtheria bacillus was found, which present every gradation between a mild inflammation and severe complicated membranous ophthalmia.

Baumgarten (17) considers, that as far as the anatomical structure of the membrane is concerned, there is no essential difference between croupous and diphtheritic inflammation. Coppez (31) holds interstitial and superficial pseudomembranous conjunctivitis to be bacteriologically identical and clinically joined by numerous intermediate forms.

According to Rossius (139) the diphtheria bacillus may cause a purulent, croupous or deep membranous conjunctivitis, the clinical picture being determined by the virulence of the bacillus and the response of the individual.

Haab (52) discusses a case of croupous conjunctivitis due to diphtheria bacilli and Steffens (127) gives a case of gangrene of the eyelid, with absolutely no sign of diphtheria which was apparently caused by the same organisms.

There is much more evidence of the same kind but

enough has been given to show that the diphtheria bacillus is capable of producing the most widely separated clinical conditions.

In the same way typical membranous conjunctivitis both deep and superficial may be caused by a variety of organisms. Uhthoff (133) mentions besides the bacillus of Loeffler, streptococci, staphylococci and pneumococci; of these, according to Roscher (110) Loeffler's bacilli are the most common and streptococci the most dangerous.

I have already given an analysis of some cases of membranous conjunctivitis by Gouin, Roscher and Jessop (64) showing, that it may be caused by various organisms including the Weeks bacillus, gonococcus and xerosis bacillus as well as those already mentioned. Similar evidence is given by Coppez (29), Axenfeld and Tick (12), Lor (78), Epe (37), Schanz (117), Stephenson (129), Petit (104) Kimpel (70), Schlesinger (121), Vossius (139), Myles Standish (126), Cassini (33) and others, whose observations add the meningococcus of Weichselbaum, the colon bacillus and the pneumobacillus of Fraenkel to the list of possible causes of membranous opthalmia, although as Axenfeld (13) has shown Loeffler's bacillus is by far the most common.

As might be expected, on account of this complicated pathology, the nomenclature and classification of diphtheritic or membranous conjunctivitis has recently been the subject of a good deal of discussion

Jocqs (65), Jessop, and Stephenson, suggest that terms such as croupous and pseudomembranous should be dropped and all such forms united into one class of "membranous conjunctivitis".

Van den Shaeten (135) holds a similar view but prefers the term "pseudomembranous". Jessop and Stephenson then divide the membranous forms into diphtheritic and non diphtheritic, the presence of Loeffler's bacillus in the former being the differentiating factor.

Van den Bergh (134) and Gonin (47) use the term diphtheritic to include all forms of conjunctivitis caused by Loeffler's bacillus, whether membranous or not, and the latter aptly expresses his point of view by using the phrase "conjonctivite loefflerienne" (p.94.).

Stephenson, however, himself points out that there may be no membrane in conjunctivitis due to Loeffler's bacilli, although Jessop (64) says, "I have yet to learn that a conjunctivitis can be set up by the diphtheria virus without the production of a membrane."

If ~~this~~ Stephenson's view is correct, then the expression "membranous conjunctivitis" does not include all forms due to diphtheria, and it would be better to adopt Gonin's terminology and consider as diphtheritic only such forms as are caused by Loeffler's bacillus without reference to the clinical appearance.

The presence of a membrane, then, is very little beyond

evidence of the possibility of diphtheria, and its absence, although strongly presumptive, does not absolutely exclude diphtheria.

Other signs may often be of assistance in diagnosis. Jessop lays stress on the presence of enlarged glands, albuminuria and fever, in the true diphtherial cases, while Stephenson mentions the puromucous stringy secretion and the usual unilateral infection; in his cases albuminuria was present in only 11 per cent.

Other writers prefer to direct their attention to the presence of Loeffler's bacillus and its detection.

Petit (104) considers that the history of a previous throat affection, the general condition of the eye and the presence of a false membrane on the conjunctiva are to be considered merely as presumptive evidence.

Stephenson (129) remarks (p.44.)- "Although it cannot be too often repeated that the only scientific way of diagnosing the condition is by discovering ~~the~~ diphtheria bacilli, yet in marked cases the objective clinical signs are quite enough." This, however may not always be the case as the observations of Koppen (29) and Lor (78) show, who describe cases exactly simulating severe diphtheria but caused by strepto- and gono-coccei respectively.

The existence of a membrane is nevertheless an indication of the necessity of a bacteriological examination according to Stephenson[128-129], Henax + Beach[93], Vossius[139] and others

Even though the diagnosis of diphtheria could be made clinically no indication would be given of the presence of mixed infection, with streptococci, a point mentioned by Roscher (110) Cosmi (33) and others as important for prognosis.

Minne (82), after reviewing the question, concludes in favour of the necessity of bacteriological observation in order to obtain promptly the necessary indications for treatment.

As regards relative frequency, membranous or diphtheritic conjunctivitis seems to be comparatively scarce. Stephenson's 43 cases represented 1·25 of the cases seen at the Ophthalmic hospital during the same time. Gouin's figures show in 785 cases of conjunctivitis 1·65 % of membranous and 0·9 % of diphtheritic nature. In Edinburgh and Leith both forms seem to be uncommon.

Diphtheritic infection however, on account of its infectious nature and the danger to the cornea, gains in importance what it loses through its comparative rarity and accurate diagnosis is of the greatest importance.

The microscope, though very serviceable, especially when the method by exclusion is practised, is not quite as reliable here as in other forms of conjunctivitis, both because diphtheria bacilli are more apt to be missed on account of small numbers than Weeks's diplobacilli, and on account of their resemblance to a common, non-pathogenic organism the xerosis bacillus.

On this account the preparation of specimens for the

detection of Loeffler's bacillus is a little more troublesome than in the case of an organism like the diplobacillus of Morax for instance.

A particle of discharge or a shred of false membrane is smeared over several coverglasses which are stained (1) with Thionin blue or Pick and Jacobsohn's stain, (2) with Gram's method and (3) with Neisser's stain.

Stephenson[129] describes the appearance of the organisms as follows:- "They are rods of irregular size and confused grouping, often clubbed at one or both ends and of curiously uneven contour. They are usually a little curved. When treated with certain samples of methylene blue or thionin blue, polychromatic effects may be observed, that is to say, small points lying in the protoplasm may be coloured differently from the rest of the organism. The Klebs-Loeffler bacillus stains with Gram's plan. When treated by Neisser's method it appears as a rod stained brown which shows within its substance two or three small oval granules of a dark dirty-blue colour; the coloured particles are seldom seen except towards one or other end of the bacillus. Neisser's method often affords a rapid method of diagnosis. My experience leads me to attach great practical value to its systematic employment in cases of suspected diphtheria."

Although in 1900 (see 129) Stephenson considered that for certain diagnosis the making of cultures was often necessary, on account of the resemblance between Loefflers and the

xerosis bacillus, which he styled a "pitfall for the unwary", in 1902 (130) he calls the latter organism "that bugaboo of ophthalmic bacteriology", and holds that by Neisser's stain the two may be differentiated "in the clearest way." He bestows the strongest praise on Neisser's method as enabling a diagnosis to be made during consultation. The fact that the xerosis bacillus retains the stain much more tenaciously than the Loeffler bacillus, when treated by alcohol in Gram's method, is also mentioned as a point of distinction. Finally he says, "In short in moderately experienced hands, there should, in my opinion, be no confusion between the organisms named." More than one examination should be made, as failure to find it does not prove its absence.

Even before the publication of Neisser's method Uhthoff (88) supported the use of the microscope in the diagnosis of conjunctival diphtheria. According to him, from a practical point of view microscopic examination is superior to cultivation, as the latter method brings into evidence bacilli which would not have been seen by the microscope, and which resemble diphtheria bacilli in culture, requiring inoculation experiments for differentiation. The delay of from four to eight days, necessitated by this procedure, entirely destroys the value of the examination. The microscope, however gives an immediate decision and it is to this, rather than to the results of cultivation, that one should turn

for indications for serotherapy. The bacilli, although never very numerous are easily recognised by their irregular aspect and tendency to swelling at one end. Gram's method should be used and the bacilli cannot be confounded with any other conjunctival organism.

In Neisser's (96) original method the double staining is performed upon a young culture of the suspicious organism.

As it is my object to examine the value of immediate microscopic examination this method cannot receive further consideration. I will only mention that Fraenkel (41) Uhthoff (133), Heinersdorff (56 etc), Coppez (31), and Bronstein (23) are in favour of it, the latter very strongly, while it is discredited by Gauss (148) And Schanz (114 etc), who indeed doubts any method, which proposes to diagnose diphtheria within 24 hours.

Neisser himself warns against reliance upon his method in connection with coverglass preparations from fresh material although stating that it may be successful in a few "happy" cases. Stephenson, as already pointed out, extolls its virtue when used in this way. Bronstein (23), whose paper refers to diphtheria of the pharynx, is a most decided supporter of the direct method. In 136 out of 172 cases he diagnosed diphtheria by the microscope. Cultures were made at the same time, and in no case did these fail to show Loeffler's bacilli when doublestained organisms had been observed microscopically. Even in the presence of numerous other

organisms the suspicious bacilli were clearly recognisable.

Not having seen any diphtheritic conjunctivitis in Edinburgh or Leith, where it seems to be rare, I cannot say much myself upon this subject, but, considering the evidence of Stephenson and Bronstein, it seems to me that too much reliance should not be placed on laboratory experiments, such as the work of Gauss (148), in connection with what is really a clinical observation. What is wanted, is an extensive series of coverglass examinations of conjunctival secretion, from all kinds of conjunctivitis, stained by Neisser's method, in order to show how other organisms met with in the conjunctiva, and especially the one known as the xerosis bacillus, react to this method of staining. Such an investigation would be of more practical value in this connection than the work of Gauss, as I see no reason why it should be assumed that bacilli in the conjunctiva and bacilli in test-tubes should react in the same way to stains; indeed Moran has shown that the Weeks bacillus ceases to stain altogether if grown on artificial media for a few generations. Inoculation experiments would be required to test the virulence of any double-staining organisms found, and cultures in order to ascertain the proportion of cases in which double-staining was obtained in this way and not by the direct method.

Into the question of the identity of the xerosis bacillus and that of Loeffler, asserted by Schanz (116), Peters (100) and Peo (99) and disputed by Copper (31) and Axenfeld (9) it is not necessary to

enter here.

Bietti (20) believes in the pathogenicity of the xerosis bacillus Corsini (33) and Peters (100) believe that cultivation and inoculation are necessary to differentiate the two, while Sproneck (125) requires the inoculation to be controlled by antidiphtheritic serum.

Although Pes (99) believes the bacillus of Weeks and that of Loeffler to be identical, this cannot affect microscopical examination by which these organisms are clearly differentiated.

Pes (98) holds that in suspected diphtheritic conjunctivitis, microscopic examination is of more value in eliminating other forms, caused by organisms readily recognised such as gonococci, pneumococci or Weeks bacilli, than in demonstrating the presence of Loeffler's bacilli. Knapp (98.) reviewing Pes' work, remarks that although the number of diphtheria bacilli seen in a preparation may not be great, sufficient facility to enable a probable diagnosis to be made, may be attained with practice, while in connection with mixed infection and the presence of other organisms the microscope gives more reliable information.

Petit (104) also considers microscopical examination of the greatest importance, and especially valuable in excluding other forms of conjunctivitis. If there is doubt it will be more often correct to decide against diphtheria, but not unless abundance of typical organisms is seen. The presence of a

number of bacteria, morphologically resembling Loeffler's bacilli is to be considered as presumptive evidence of true diphtheria. More than one examination should be made, using Gram's method, and if no bacteria are seen no conclusion at all is derivable. Gonin (47) holds that in diphtheria too much reliance should not be placed on microscopical examination, yet the presence of bacilli resembling those of Loeffler in a membrane justifies a diagnosis of diphtheria and indicates specific treatment. Sprosick (125) says that true diphtheria bacilli occur on the conjunctiva in numbers only in true diphtheritic infection, in other cases only seldom and then isolated specimens. The cultural and morphological resemblance between the true and the pseudo-diphtheria bacilli is very close.

Minne (82), while supporting the use of Neisser's stain, does not consider the microscope very reliable in diphtheria. A cover-glass preparation, he remarks, will convince the observer of his difficulties. According to Corsini (33) the microscopical diagnosis of diphtheritic conjunctivitis requires special care and some patience.

Besides the bare diagnosis of the diphtheritic or non-diphtheritic nature of the case, some further information may be obtained by the microscope.

Corsini (33), quoting Sondilli, says that long thin straight bacilli few in number are found in the mildest form of croupous conjunctivitis, in conditions of medium gravity

the bacilli are shorter, larger and bent, and in the severe form they are curved, twisted, numerous and associated with many streptococci. The gravity of the case depends upon poly-microbic association and Horiulence of the bacilli.

According to Morax and Beach (93) the bacilli often occur in pure culture but frequently strepto- and staphylococci are seen. In Stephenson's cases the diphtheria bacilli were pure 6 times out of 43, in 38 there were various staphylococci and in seven streptococci besides a few other organisms. He could trace no correspondence between the various forms of the bacillus and the nature of the case, nor between the associated organisms and the severity.

Other authors, however, agree with Corsini that the presence of streptococci makes the prognosis more serious as the efficacy of serotherapy is less assured. Gouin's two most serious cases, one of which lost both eyes, were associated with streptococci. He thinks the prognosis, although good in the croupous cases, should be guarded in general. According to Uhthoff (133), the presence of streptococci need not necessarily indicate a severe case, yet, on the whole, cases of pure diphtherial infection are more favourable.

Petit (104) refering more particularly to existing corneal lesions, considers that the prognosis is subordinated to secondary streptococcal infection of the cornea, and that in the presence of this it is doubtful and good in its absence.

Despaquet (35) treated ten cases with serum, and found that

the membranes persisted in the mixed cases for fifteen days and in the others for eight only.

Mathieu (81) concludes that serum, although good in the purely diphtherial cases, is of less value in the mixed forms. Serum should be injected before waiting for a bacteriological examination, if the clinical signs point towards diphtheria.

Jessop (64) lays stress on the importance of diagnosis in diphtherial cases in connection with treatment and isolation. It is obvious that rapid diagnosis is of the greatest value to the general practitioner who has to ask himself whether serum is to be used and whether the case is to be notified.

Petit (104) holds that if diphtheria cannot be eliminated by the discovery of other specific organisms by the microscope, then the case should be treated as one of diphtheria. The presence of gonococci or Weeks bacilli would, in his opinion, exclude diphtheria. In any case the withholding of serum is to be considered less risky than its possibly unnecessary administration, a view supported also by Schlesinger (121)

According to Roscher (110) Pes and Malfi advise the use of serum in all cases of croupous ophthalmia without waiting for a bacteriological examination

Lagrange (75) upholds the use of the microscope as giving an immediate and exact decision. Bad results from serotherapy are due to waiting too long, and serum should be used if the clinical signs indicate it.

Haab (52) and Uhthoff (133) recommend serotherapy in

doubtful cases.

The necessity for recognising streptococcal cases of membranous ophthalmia is urged by Morax (131) as antidiphtheritic serum has no action in such cases. Coppez and Funck (32) after investigating the statistics of cases of membranous ophthalmia treated by antidiphtheritic serum conclude that it has no action in the streptococcal cases.

Morax and Beach (93) consider that serum is only of use where Loeffler's bacilli are found.

Rimpel (70) gives a case due to diplococci and Coppez (29) one due to streptococci, in which the use of antidiphtheritic serum was unsuccessful. Schlesinger (121) and Morax (89) quote similar cases and suggest the use of Marmorek's anti-streptococcic serum in these cases.

Vossius (139) seems to be alone in the opinion that anti-diphtheritic serum is also useful in non-diphtheritic cases.

On the other hand, the prognosis in a severe case of membranous ophthalmia is improved by the discovery of an organism such as the bacillus of Weeks and the treatment correspondingly modified.

The evidence I think points to that the conclusion that in suspected diphtheritic conjunctivitis microscopic examination is of the greatest importance, and often reliable in itself by positively demonstrating Loeffler's bacillus, or otherwise by adding one more link to the chain of evidence required for diagnosis and prognosis.

The second group in Gonin's arrangement includes all the remaining forms of conjunctivitis due to bacterial infection. For clinical purposes he distinguishes those associated with inflammation of the tear ducts or lacrymal sac, from which the infection reaches the conjunctiva, from those in which this is absent and infection is from without. As far as concerns microscopical examination it is unnecessary to observe this distinction.

Excluding the four microorganisms already discussed a variety of others are found in conjunctivitis, including pneumococci, streptococci, staphylococci, the influenza and colon bacilli, Friedlander's pneumonia bacillus, the ozoena bacillus, the meningococcus intracellularis, the organisms of tubercle, leprosy and glanders and various forms of mycosis.

Some of these are mere curiosities, others as the pneumococcus are of more importance.

The value of microscopic examination in these cases is greater as a means of excluding members of the first group, than in establishing a definite diagnosis in respect of any one organism.

Positive evidence may, however, usually easily be obtained in regard to the more important forms, especially in epidemics.

Pneumococcal Conjunctivitis.

Applying the same rule here as in other forms of conjunctivitis, by the term pneumococcal conjunctivitis is understood that form, which is due to pneumococci, whatever its clinical aspect may be.

In this country pneumococcal conjunctivitis has not the same claim to consideration as it has in America where it is very common. Gifford (45) and Veasey (136) found the pneumococcus to be the most common cause of acute catarrhal conjunctivitis in Philadelphia and Omaha.

Henax and Petit, Lundsgaard, Gonin, Pes and Bach and Neumann had very few pneumococcal cases. In Edinburgh and Leith it does not appear to be common.

Epidemics may occur as mentioned by Axenfeld (6) and Stephenson (129).

The clinical characters of pneumococcal conjunctivitis have been described by Henax (84), Axenfeld (6), Uhthoff (133) Gifford (45) Junius (67) and many others, according to whom the character of the inflammation is that of a mild acute catarrh. There is slight rose-coloured oedema of the lids at first, diffuse redness with a little swelling of the conjunctiva, on which a superficial grey membrane frequently forms. The ocular conjunctiva is also injected and may present small haemorrhages. The secretion is fairly free, and is watery with little flakes of pus floating in it.

The same conditions prevail here as in the forms of conjunctivitis already discussed: other microbes, notably the Weeks bacillus produce an identical clinical picture, while pneumococci themselves produce practically any clinical forms. Axenfeld and Fick (12) quote Guasparini's view that pneumococcal is clinically indistinguishable from Weeks conjunctivitis. Veasey (130) and Gifford (45) corroborate this view and urge the advantages of bacteriological examination as a means of distinction.

A comparison of the two clinical pictures will show that they are practically identical. Pneumococcal conjunctivitis has been said to affect children only, to be monocular and noncontagious (Morax 84), but Axenfeld (6) and Gifford (45) have disproved these points and clearly shown the very close resemblance to the microbacillary form. Membrane formation occurs more frequently in association with pneumococci, phlyctenulae occur frequently in both (Axenfeld 5).

Methorst (133) states that catarrhal, phlyctenular, granular and membranous forms may occur, and although the clinical diagnosis may often be correct, it is not sufficient. Axenfeld and Fick (12) and Gifford (45) mention the occurrence of an acute form resembling gonococcal ophthalmia.

Roscher (110) gives a case of membranous conjunctivitis with corneal ulcer, simulating a severe diphtheritic infection

but due to pneumococci alone, and Truginele (44) a similar case complicated with an abscess in the eyelid.

In adults a chronic form may occur (Minne 82, Axenfeld 12). Axenfeld (68) Gifford (45) Uhrax and Petit (94) and Whithoff (133) all urge the necessity of bacteriological examination and consider the microscope efficient in the great majority of cases, although Gifford thinks that unless serum cultures are made the organism may sometimes escape detection. To this it might be replied that this method might err in the opposite direction and detect pneumococci more often than they are the real pathogenic agents, as the pneumococcus has been frequently found on the healthy conjunctiva.

According to Morax (88), Stephenson (129), Halle (55) and Minne (82) the microscopical examination presents few difficulties numerous lancet shaped diplococci, with their broader ends apposed, are seen free in the cells. They may be only in pairs or in short chains of from four to six members. Capsules apparently may or may not be seen. Gifford (45) and Uhrax (88) consider the capsules distinctive. Axenfeld (6) saw none while Gouin (47) states that they are always indistinct and sometimes absent. In some of my preparations the capsules are obvious in others not.

Gifford (45) and Schanz (145) say that the lancet shape is not always present, and that phagocytes may be seen crammed with the organisms as occurs with the bacillus of Koch's.

The only possible causes of confusion mentioned are the gonococcus, from which it is of course easily distinguished by Gram's method, and the diplococci of Wilbrand, Saenger and Stöhrlin mentioned by Axenfeld, which however are very different in shape and size.

Gourin (47) thinks that badly stained pneumococci may be mistaken for Weeks bacilli; Gram's method of course avoids this error. Groenouw (50) mentions sequented xerosis bacilli, resembling short chains of pneumococci, as another possible element of confusion. The former are distinguishable by their clublike form, general appearance and arrangement and the fact that they are rarely intracellular.

The pneumococci are usually in pure culture. Halle (55) detected no other organisms either by the microscope or by culture. A few xerosis bacilli or staphylococci may be seen but not in a way to confuse the diagnosis.

Mixed infection seems to be more uncommon than in other forms of conjunctivitis: Groenouw mentions a case with gonococci, and one of my preparations shows numerous diplobacilli of Morax and pneumococci together.

Although this affection is generally benign, severe cases leading to destruction of the eyes have been described by Hertel (59) in children whose condition had been reduced by measles.

Axenfeld (6) urges the importance of differential diagnosis on account of the good prognosis in pneumococcal

conjunctivitis. The affection lasts only a few days and heals without treatment, so that it is unnecessary to adopt vigorous measures. At the same time prophylaxis must be considered as adults are apt to suffer more severely, and the affection is often very infectious.

Streptococcal Conjunctivitis

This is a comparatively rare form of conjunctivitis. Gouin had only 6 cases of streptococcal infection in a total of 785 cases of conjunctivitis. Uhnax and Petit (94) and Lundsgaard (79) do not mention it, Pes (99) and Groenouw (50) each mention two cases.

Axenfeld and Fick (12), Uhnax (88) Ohlthoff (133) and others mention two clinical forms, the catarrhal and the membranous, the latter occurring more frequently.

Uhnax and Beach (93) mention the membranous form as especially seen in children during the declining period of measles and scarlet fever and sometimes independently. It may evolve rapidly and seriously damage the cornea, being even more dangerous in this respect than diphtheritic conjunctivitis with which it has long been confused.

As already pointed out there is no clinical distinction between true diphtheritic and streptococcal membranous

conjunctivitis and it is unnecessary to repeat the evidence here. In connection with treatment, however, the differential diagnosis is very important.

Morax (89) mentions two cases reported by Aubineau. The clinical picture was that of diphtheria, and antidiphtheritic serum was injected but without avail, even after a week. Bacteriological examination having shown only streptococci and staphylococci, Marmoret's serum was used, with immediate beneficial effect visible within 24 hours. Lagrange (76), Minne (82) and Schlesinger (121) also recommend this treatment.

The catarrhal form was described by Parinaud (97) in 1892 and afterwards by Morax (84) in 1894, as conjonctivite lacrymale à streptocoques. The clinical picture is that of conjunctivitis combined with serous otitis and usually accompanied by acute inflammation of the mucous lining of the tear sac. There is intense injection of the conjunctiva which may be darkred or violet, it is both circumcorneal and general and affects the subconjunctival vessels. The secretion is fluid with flakes of pus. As a rule only adults are affected.

This characteristic combination is not always present. Gonin (47) besides two such cases, had two associated with otyes, one with ciliary blepharitis and one, in an infant, resembling purulent ophthalmia and which resulted in the loss of an eye.

Groenouw (50) mentions a purulent and an ordinary catarrhal case. Corsini (33) also notes a streptococcal case of purulent ophthalmia.

Knapp (88) mentions a form, simulating severe purulent ophthalmia, occurring in children and tending towards corneal complications.

Clinical diagnosis is not always likely to be successful and microscopic examination is required to definitely ascertain the nature of the case.

According to Parinaud (97), Knapp (88) and Kinnie (82) the streptococci may easily be recognised by the microscope. Their arrangement in chains and reaction to Gram's method suffice to distinguish them. The chains are composed of from two to 8 or 10 members. Schanz (117) notes the occasional presence of a specially large individual in such a chain. The average size is about 1·0μ in diameter, somewhat larger than average staphylococci. According to Knapp (88) they are less numerous in the lacrymal than in the membranous form.

Parinaud (97) found that these cases react much better to perchloride of mercury than to silver nitrate, a practical point in favour of exact diagnosis. The discovery of streptococci is also a warning of possible iritis.

In other respects the prognosis and treatment are governed more by the condition of the iris and lacrymal sac than by the microscopical finding.

Staphylo-coccal conjunctivitis.

The relation of staphylococci to conjunctivitis is not yet thoroughly understood. Uhthoff (133) doubts whether there is a form due directly to staphylococci. As Axenfeld and Fick mention, the difficulty here is that these organisms in greater or less numbers are an almost constant accompaniment of most forms of conjunctivitis especially if chronic.

According to Gonin (47) and Groenouw (50) cases of conjunctivitis may be considered as staphylococcal in which these organisms are present in relatively the greatest abundance, in the absence of other known pathogenic microbes such as gonococci or diplobacilli. Gonin admits that the presence of staphylococci does not necessarily mean that they are the cause of the affection, and he includes as "conjonctivites avec staphylocoques" only cases in which large numbers of staphylococci formed the main feature of the microscopical appearance.

The practically constant presence of the non-pathogenic staphylococcus albus is also a source of confusion, especially in connection with microscopic diagnosis, as it of course cannot be distinguished in this way.

According to Groenouw (50) the clinical appearances produced by this organism are (1) phlyctenular conjunctivitis or a similar affection, (2) purulent or catarrhal & (3) membranous conjunctivitis.

Stephenson (129) mentions staphylococcal conjunctivitis as a "pus infection of the conjunctiva", resembling clinically Weeks conjunctivitis, and having a tendency to phlyctenulae around the cornea and slight membranous exudation. It is frequently associated with impetigo or eczematous dermatitis of the eyelids or face.

Cosini (33) had ten cases, in which only staphylococci were present, but hesitates to ascribe a pathogenic action to these.

Pes (99) attributed 19 cases of catarrhal conjunctivitis out of 47 to staphylococci.

Jessop (64) and Minax and Petit (94) quote cases of membranous conjunctivitis due to staphylococci.

Such cases cannot be clinically recognised as staphylococcal and yet this is necessary in connection with prognosis and treatment, as the prophylactic and other measures required in microbacillary and diphtheritic conjunctivitis are not required in the staphylococcal form which heals easily.

According to Schanz (117) Winne (82), Groenouw (50) & others staphylococci are easily recognised by their shape and grouping and positive reaction to Gram's method. They are round, about 0.7μ in diameter, sometimes they vary in size; they tend to lie in irregular or grapebunch like clusters. Short chains of three or four members may occur and do not indicate streptococci. They may be distinguished

from pneumococci by the absence of the capsule and lance-point shape and by the occurrence of other forms mixed up with the diplococcus forms.

From gonococci they are distinguished by their positive reaction to Gram's method, and by their shape, grouping and more frequent extracellular and less frequent intracellular position. When they do occur inside the cells only a few pairs are seen as a rule, never the characteristic crowd of gonococci inside a leucocyte. Sometimes however the resemblance is close, in these cases Gram's method with short decolourisation is essential.

Staphylococci are much more commonly seen in connection with other organisms than alone, and it is in the latter case only that their presence is to be regarded as causal. Their influence on prognosis and treatment, when seen along with organisms such as diplobacilli or diphtheria bacilli, is discussed with these forms.

The value of the diagnosis of staphylococcal conjunctivitis is practically entirely negative, that is to say the prognosis is improved and the treatment simplified by the exclusion of more dangerous or more infectious forms.

Tubercular Conjunctivitis.

Primary tuberculosis of the conjunctiva is so rare that it may be discussed very shortly.

Eyre (38) in 25 000 consecutive ophthalmic cases found only eight of tubercular conjunctivitis.

Other observers give the proportion as considerably less.

The clinical appearances seem to vary greatly, Eyre gives the following five varieties:-

(1). With small miliary ulcers.

(2) With subconjunctival nodules.

(3) With hypertrophied papillae and granulation tissue.

(4) Cretaceous excrescences of a jelly-like consistency.

(5) With pedunculated tumours - true conjunctival polypus.

Other variations may occur, Levy (77) gives a case of conjunctivitis diagnosed clinically as diphtheria and isolated, but which turned out to be tubercular. Wagner (140) mentions the simulation of trachoma, a point carefully gone into by Heinersdorff (58), who gives an illustrative case. His conclusion is that clinical diagnosis is insufficient.

Birsch-Hirschfeld and Hausmann (21) describe 3 cases two of which resembled trachoma. They consider that in former times many cases of tubercular infection have been treated as trachoma.

Gourfein (48) notes a case of glanders clinically resembling tubercular conjunctivitis.

According to Eyre (38) it is often extremely difficult to satisfactorily settle the diagnosis without the aid of the microscope

or even the inoculation of an animal with a fragment of the diseased tissue. Brosalino (22) says that the latter is the most certain method, an opinion one must certainly subscribe to, adding the rider that it is also the most tedious and troublesome.

Vieusse (137) believes microscopical examination to be unnecessary, and Armaignac (3) holds that clinical diagnosis is as a rule valid but may be supported and confirmed by bacteriological examination.

The search for indications of tuberculosis by the microscope is more troublesome than the previous examinations for other bacilli. The most rapid method is to smear a coverglass with scrapings from the floor of an ulcer or a nodule and to stain this by Ziehl's method. If there is time and apparatus sections may be prepared from a portion of the tissue.

The form and appearance of tubercle bacilli is well known. According to Mirone (82) they appear as thin rods 1.5 to 4.0 μ long, straight or slightly curved. Eyre (38) describes them, as seen in sections, as lying scattered in the tissues without relation to the giant cells, singly or in groups of 3 or four, rarely in groups of from ten to thirty. They are more easily found in cases belonging to groups (1), (2), and (6) than the others. In his 8 cases tubercle bacilli were seen in four and giant cells in five. In sections tuberculous structure with giant cells may be seen without the bacilli.

Cherry[26] and Haemers (53) give cases in which the bacilli were seen by the microscope. In Fischer's (39), Heinersdorff's (58) and Levy's (77) and one of Busch-Hirschfeld and Hausmann's[(21)] cases, giant cells and tubercular cellular growth were seen but no bacilli. Armaignac (3), Busch-Hirschfeld and Hausmann (21), Pagel (107) and Holz (62) report the success of the coverglass method of examination in demonstrating the bacilli either in debris from a nodule or scrapings from an ulcer.

The discovery of tubercle bacilli makes the prognosis very serious, as although some cases recover, others end in general tuberculosis. Busch-Hirschfeld and Hausmann (21) call attention to the modification in treatment indicated by the establishment of the tubercular nature of a case previously considered to be trachomatous.

I think it will be reasonable to allow to microscopical examination the same value here as it has in the case of the sputum from a case of suspected phthisis, that is to consider it as a procedure giving strong support and confirmation to clinical diagnosis.

Other forms of conjunctivitis due to infection.

Conjunctivitis due to the influenza bacillus has recently been described by Zur Nedden (144, 146), Smit (124) and Jundell (66) who have investigated about thirty cases.

Zur Nedden (144) describes a case of typical purulent conjunctivitis in a child ten days old, which was supposed to be gonorrhoeal. Microscopical examination, however, showed no gonococci, but enormous numbers of a small plump bacillus or cocco-bacillus, mostly extracellular in position and decolourised by Gram's method. Cultivation identified them with Pfeiffer's influenza bacillus. The same organism was subsequently found in two ~~cases~~ simultaneous cases in one family, and this year Zur Nedden (146) gives an account of ten cases, nine of which occurred in children under one year.

The clinical picture varies from a mild catarrh to a purulent conjunctivitis. The majority of the cases were severe, a very mild form occurring only once, in a man of thirty years.

Zur Nedden's conclusion is that the influenza bacillus causes a mild to moderately severe conjunctivitis affecting the palpebral conjunctiva and fornices. The clinical appearance is not characteristic. Infants are predisposed to this form and the younger they are the more severe the inflammation.

Smit (124) mentions a purulent case in a young adult, resembling gonococcal conjunctivitis, in which the influenza bacillus was found, and subsequently four more influenzal cases

Jundell (66) observed an epidemic of influenza affecting 102 children in an hospital. In nine cases of conjunctivitis he found the influenza bacillus. Six cases were very mild, two moderate and one was purulent.

From the variability of the clinical appearances it is evident that clinical diagnosis cannot be relied upon. Although Jundell says the bacilli are not always well seen in cover-glass preparations, according to Zur Nedden their appearance is characteristic and this method is reliable.

The bacilli are very small, short and ovoid and decolourise by Gram's method. They differ from the Weeks bacilli in being thicker in proportion to their length than these are, and in being rarely intracellular. Although Smit (124) supports Rymowitsch (111) and Jundell (66) in the view that the Weeks bacillus and the influenza bacillus are the same, Zur Nedden says that the first glance excludes the former. In one of my preparations from a case of chronic catarrhal conjunctivitis which the patient described as the "remains of influenza", there is a bacillus corresponding in shape and arrangement to that described and figured by Zur Nedden (144). It is certainly quite distinct morphologically from the Weeks bacillus.

Zur Nedden found staphylococci and pneumococci occasionally in addition, and in one case, in which a membrane was present, streptococci to whose agency he ascribed this formation. In my case numerous Gram staining organisms corresponding to xerosis bacilli were present.

According to Zur Nedden the prognosis is good as the affection is generally benign, and if well treated heals in a short time without complications. He believes however that the eye may be primarily affected and that therefore this form of conjunctivitis is not to be regarded as a harmless condition, as it may be the precursor of general influenzal infection.

Therefore the affection requires recognition and energetic treatment with a 2% silver nitrate solution.

The remaining microorganisms are the colon bacillus mentioned by Bietti (18), Groenouw (50) and others, the pneumonia bacillus of Friedlander (Eyre 37. etc), the meningococcus intracellularis (Fraenkel 42, Haglund 54) the ozena bacillus (Lenox 88 etc), the bacillus of glanders (Gourfein 48, Strzeminski 131), the leprosy bacillus and cereal forms of mycosis, cases of conjunctivitis due to which are given by several authors.

The relation of most of these microorganisms to the present subject has already been discussed. From a practical point of view the distinctive identification of these organisms is of no particular advantage once the more important bacteria have been excluded as, except in the case of glanders and leprosy, the prognosis and treatment vary according to the clinical appearances rather than the pathogenic agents. The two exceptions are so rare

that they can hardly be said to influence the general question under consideration.

The remaining forms of conjunctivitis in Group II of Gonin's classification are phlyctenular conjunctivitis and trachoma.

The much discussed etiology of the former has no connection with the present subject. After searching the literature I have been unable to find any evidence that the very common affection generally known as phlyctenular conjunctivitis, which occurs so frequently in strumous or scrofulous children, can be distinguished from other forms of conjunctivitis by any positive character in the secretion.

On the other hand, there is abundant evidence which has already been given, that this affection is to be distinguished from others, clinically similar, such as diplobacillary, microbacillary, or pneumococcal conjunctivitis, by the absence of any specific microorganism, when the secretion is microscopically examined.

The practical outcome is, that if such an examination give an indefinite or negative result the usual tonic treatment is indicated, if however a specific organism is found the treatment must be modified in the direction of exterminating it by suitable measures.

I mean, that as some cases of strumous or phlyctenular

conjunctivitis are associated with Weeks bacilli or diplobacilli and some are not, it is insufficient to base a treatment on the general and local condition of the patient as clinically observed, in ignorance of the presence or absence of such organisms.

The possibility of a combination of affections must of course be kept in mind.

In some cases, especially in the epidemic of micro-bacillary conjunctivitis discussed by Markus (80) the organisms present seem to have caused the phlyctenulae, in others these may be, as Axenfeld (8) believes, purely the individual response to any irritant, depending more on the diathesis of the sufferer than the nature of the exciting cause. Thus one case of phlyctenular conjunctivitis may be infectious and another not, one may require Zinc treatment and another merely boracic lotion and a tonic, and in the absence of microscopic examination these points may be missed.

As regards follicular conjunctivitis and trachoma a similar state of affairs prevails, with this difference that, especially for the latter, from time to time specific organisms have been described, which were each in turn asserted to be causally related to the affection.

Sisson (123) after reviewing the work done on trachoma

finds that the question of a causal organism is still in statu quo; not so Syudacker (132), who, after minutely describing a small diplococcus which he had isolated from cases of trachoma, and with which he had produced a similar affection in the human subject, says (P215)- "In the early stages of trachoma, and frequently even after the lapse of some time, it is often impossible by means of the methods now employed to state with certainty whether the case before us is one of that disease or not. Can a diagnosis be made with absolute positiveness?

Unquestionably yes. If one can find within the secretions or in the contents of the expressed follicles, an organism such as I have described, he may with absolute certainty call the disease trachoma."...

Recent writers, Addario (1) Dudzinski (36), Gromaborski (61) Menax (91) and others have failed to confirm Syudacker's results. Uhthoff (133) quotes Cazalis' view that trachoma stands in the same relation to conjunctivitis as phlyctenular, being the expression of a particular diathesis rather than the result of a particular irritant. Uhthoff regards the various diplococci described as indicating merely a mixed infection with gonorrhoea, as Zur Nedden (146) regards Mueller's bacillus as merely the influenza bacillus in cases of trachoma.

According to Menax (91,92,) superadded infection by pathogenic organisms is often present and it is necessary to appreciate the part they play. This may be done by microscopic

examination of the secretion. In diagnosing a case, which presents appearances similar to those of trachoma two sorts of granulations must be born in mind, those which constitute a hypertrophy induced by the chronic action of Weeks bacilli or gonococci and the true trachoma granulations, which are independent of microorganisms. The two forms can be differentiated clinically and the former last only a few months. Although Wecker (141) holds that the diagnosis of trachoma rests rather upon clinical features than upon the absence of pathogenic organisms, Uhthoff thinks the diagnosis should be reserved until this has been demonstrated.

Stephenson (129) points out that acute trachoma may be associated with the pneumococcus, bacillus of Weeks and the diplobacillus of Morax. Should a community containing sufferers from trachoma become infected with Weeks conjunctivitis, an intensely infectious form of trachoma is set up by which the disease is often spread. (Stephenson 129) Deutschmann (36) found the Weeks bacillus in acute cases, and also the diplobacillus of Morax.

Gromakowski (51), who agrees with the views of Cazalis mentioned above, found the Weeks bacillus in 8 out of 11 cases of acute superficial follicular conjunctivitis, and in 15 out of 42 cases of deep follicular conjunctivitis. In chronic cases he found only staphylococci and pus organisms.

Peters (102) finds that the diplobacillus of Morax flourishes

on the trachomatous conjunctiva, without producing any clinical alteration beyond slight secretion. The Weeks bacillus causes obstinate swelling of the conjunctiva associated with papillary growths in the neighbourhood of the tarsal border. Peters holds that in many cases of acute and subacute trachoma with secretion the Weeks bacillus influences the duration of the affection on account of these obstinate swellings.

It is obvious that the detection of these organisms in cases of trachoma has a practical value, for, in order to produce the most favourable conditions for recovery, they must first be removed from the conjunctiva by appropriate means, after which the case remains a pure and uncomplicated trachoma.

The point suggested by Stephenson (129), that an individual suffering from trachoma with Weeks bacilli is far more dangerous to his fellows than one suffering from either separately is also of practical interest.

Thus in trachoma the use of the microscope may assist the diagnosis and indicate special points in the treatment

Gowin classifies all remaining forms of conjunctivitis in a third group as spring, catarrhal, traumatic and chronic conjunctivitis. These forms all yield negative results to microscopic examination, which need only be undertaken in order to exclude the presence of any of the organisms already mentioned.

Spring and traumatic conjunctivitis are characterised by their history and appearance, but it will often be advisable to exclude the possibility of the superaddition of bacterial infection. The same applies with even more force to the catarrhal and chronic forms which only include cases, in which the absence of specific organisms, such as the diplobacillus of Morax, has been shown.

Appendix.

Microscopical Technique.

The method of making films is so well known that it is only necessary to mention here a few details, attention to which facilitates success, without lengthening the process. According to Menax and Beach (93) it is necessary to obtain a flake of secretion and to examine at the beginning or at the height of the inflammation, or else the causal microbe may be missed and only accidental or non-pathogenic organisms seen.

My experience leads me to agree with them for the most part, for unless cells are obtained upon the slide it is very hard to find any organisms. Occasionally however, in cases with very little watery secretion, I have found a considerable number of diplobacilli of Menax on the slide with only a few or no cells, when it was impossible to obtain a flake of pus.

With regard to the second provision, I have found many cases only applying for advice after the acute stage has passed off. Possibly if all cases came early the number of positive diagnoses made microscopically might be much increased and the number of negative or indefinite results reduced. It is of course in the incipient or acute stage that the organisms are most easily found.

The secretion if possible should be taken from the

deeper part of the conjunctival sac rather than from the inner canthus. In the former position the pathogenic agent is more likely to be obtained in a pure state, in the latter greater numbers may be found as the secretion is to some extent concentrated there but also numbers of accidental organisms will be found as all foreign bodies from the conjunctiva are accumulated at this spot.

It is better to gently smear the secretion over a coverslip or slide with a platinum wire, endeavouring to make as thin and even a layer as possible, than to squeeze it out between two coverglasses which distorts the cells and alters the natural relations of the organisms to each other and to the cells. For the same reason it is not advisable to add a drop of water to the secretion, so as not to alter the apparent relative proportions of organisms to cells n fibrinous matter.

The proper amount of secretion to take is the least quantity which will make a thin film.

The film is dried over any smokeless flame. Holding it in the fingers ensures that it will not be overheated. It is unnecessary to fix the film either by corrosive sublimate or by passing it through the flame. After staining, the coverslip may be mounted on a slide in canada balsalm, or if the preparation be made on a slide and, it is not wished to keep it, a drop of cedar oil

may be applied and the coverglass dispensed with.

In ordinary work, especially where not very much is being done every day, as in general practice, I can recommend no stain so much as Thionin blue.

It should be applied for from ten to thirty seconds. If time is a consideration a modified Pick and Jacobsohn's stain may be used. (See P. & J. 105).

I have found the following a good formula:-

Water 20 c.c.

Ziehl's Carbol fuchsin. 50–60 drops.

Saturated alcoholic solution of methylene blue 30–40 drops.

Stain in this mixture for one second, not longer, wash rapidly and dry immediately in filter paper. The cell bodies are stained pink and the nuclei blue and the organisms blue or dark red. Gonococci are beautifully picked out by this stain. The original Pick and Jacobsohn's (105) stain, colours the cells and nuclei too weakly to show the proper relations of the organisms to them, besides requiring 8–10 seconds to operate.

If there is any doubt about the organisms seen, or if gonococci or diphtheria bacilli are being looked for it is necessary to stain a second preparation by Gram's method. Axenfeld (90) and Groenouw (50) give very similar formulae. I have found Axenfeld's plan answer very well and the preparation is complete within five minutes. His solutions are as follows:-

1) Methyl violet 5% 8 8, Aniline oil 2, absolute alcohol 10. Mix fresh every fifteen days.
2) Iodine 1, potassium iodide 3, water 150.
3) Absolute alcohol.
4) Saturated aqueous solution of safranin.

After staining in (1) for 45 seconds, wash well, and dry the preparation in filter paper. Then apply the iodine solution for 25 seconds and dry, without washing. Decolourise for one minute in absolute alcohol, wash and counterstain with safranin for 15 seconds. This method produces very pretty contrasts. It is necessary to have a film very thin and very even if it is to be decolourised in one minute by absolute alcohol. It is further necessary to observe a time limit for decolourisation otherwise the method loses its value. In dealing with gonococci, Marx (84) considers that decolourisation should not be prolonged for more than half a minute, as otherwise various staphylococci may also decolourise. My own experience leads me to believe that some staphylococci decolourise more quickly than others, and that clove oil applied for a minute does not decolourise the xerosis bacillus.

If diphtheria is suspected Gram's method and Neisser's stain should be used as Stephenson recommends. It is unnecessary for me to give the formula for this stain here. Bronstein (23) recommends that in staining direct-

preparations longer time should be given than that allowed by Neisser and distilled water should be used for washing as the CO_2 in ordinary water spoils the colouring.

For tubercle bacilli Ziehl's method is the one to use, which also hardly requires description here.

Conducted in this way microscopical examination can hardly be said to be a laborious process. The preparation may be examined within less than five minutes, and in my opinion, the results repay the trouble.

My own work has consisted in the microscopic examination of the secretion in 105 cases of conjunctivitis in Edinburgh and Leith.

I have divided the results obtained by the microscope into positive, that is, giving information about the nature of the case by demonstrating a characteristic organism, and negative in which no indications for prognosis and treatment were obtained in this way, beyond the knowledge of the exclusion of other forms.

The negative cases include all in which the microbes seen were too few in number to allow all their characteristics to be observed; such as their grouping and relation to the cells. No case has been classed as positive in which only one or two organisms were seen.

Clinically the cases were mostly catarrhal, of varying degrees of intensity. Unfortunately there were no severe acute cases, which would have made the series more interesting.

In 53 cases characteristic organisms whose connection with conjunctivitis is understood were seen. These are therefore classed as positive results.

Of the remainder 35 showed either very few or no bacteria, 11 showed large numbers of the xerosis bacillus, and 6 crowds of staphylococci. As the presence of these organisms carries with it no special indications these cases are classed as negative.

	Simple Catarrh.			Strumous + phlyctenular.	Purulent.	Membranous.	Totals.
	Acute.	Subacute.	Chronic.				
Diplobacillus of Morax.	0	12	9	5			26
Bacillus of Weeks.	12	4	2	3			21
Pneumococcus.	1	1		1		1	4
Gonococcus.					1		1
Influenza bacillus.			1				1
Xerosis bacillus	1	5	4			1	11
Staphylococcus	2		2	2			6
Indefinite.	4	5	4	4			17
No bacteria.	4	5	3	6			18
	24	32	25.	21	1	2	

105

In the catarrhal cases it will be observed that there are no acute cases associated with the diplobacillus of Morax, while both subacute and chronic microbacillary cases occured.

In connection with diagnosis, nineteen cases presented clinical features resembling microbacillary conjunctivitis. On examination the bacillus of Weeks was found in eleven, that of Morax in one, xerosis bacillus in three, few organisms in two and none in two.

In eight cases in which the bacillus of Weeks was found there was no clinical indication of its presence.
In thirteen cases diagnosed as diplobacillary, the bacillus of Morax was found in ten, while one was indefinite and two showed no organisms. In exactly the same number of cases the same organism occurred without clinically betraying its presence.
Forty-nine cases gave no clinical signs sufficient to make any definite diagnosis. Of these eight were microbacillary, nine diplobacillary, two pneumococcal, one showed the influenza bacillus, seven xerosis bacilli, eleven were indefinite and showed no organisms.

Sixteen cases presented phlyctenulae. Of these three were associated with the bacillus of Weeks, two with that of Morax, two with the xerosis bacillus, while four were indefinite and five showed no organisms.

Five cases presented the features of what is commonly called Rheumatic conjunctivitis. In these there was a subacute or chronic inflammation, without much secretion, & considerable photophobia. Usually the complaint dated from an attack of measles. In these the diplobacillus of Morax occurred three times, the pneumococcus once and the other showed no organisms.

Two cases were associated with a thin grey adherent

follicle. One showed pneumococci and the other (which had been under treatment for some time before being examined) Xerosis bacilli only.

In six cases there was associated blepharitis so that they might have been called blepharo-conjunctivitis. Three of these only were diplobacillary, so that, in these cases at any rate, this feature is not particularly associated with the diplobacillus.

Two cases only occurred in infants under three months. Both had been attacked on the third day after birth. One was gonococcal and the other showed enormous numbers of the diplobacillus of Morax.

From the literature and from these cases I have drawn the following conclusions.

1. The evidence is against the possibility of a complete bacteriological classification of conjunctivitis in the present state of our knowledge.
2. For practical purposes such a classification is not necessary.
3. The recognition in a practical way of the bacterial factor in conjunctivitis is absolutely essential for rational diagnosis prognosis and treatment.
4. Although in many cases a certain amount of information may clinically be obtained on this point, yet bacteriological examination is in all cases of great service and quite essential in most.

5. The microscope affords a simple, rapid and — for practical purposes — reliable method of bacteriologically examining a case.

6. I in no way wish to suggest as a general principle that the morphological appearance of an microorganism is sufficient to distinguish it, yet I consider that, in the conjunctiva, which has to a certain extent its own pathological flora, the microscopic appearance of the inflammatory exudation is in many cases sufficiently characteristic to afford indications for diagnosis prognosis and treatment, otherwise unobtainable, or obtainable only after delay.

7. Microscopic examination is a necessary part, of, but not the whole of diagnosis. Its function is to support and confirm, it may be to amplify or correct, clinical diagnosis but not to supplant it.

I have to thank Dr Berry, Dr Mackay and Dr. Lyon for their kindness in allowing me to use their cases.

Description of Preparations.

No. A.1. From a case in a boy of 10 years, with phlyctenulae. The bacilli of Weeks are seen inside the phagocytes. M. blue

B.8. From a child of 14 months. Acute catarrhal conjunctivitis. Face cozemators. The bacilli of Weeks are in great numbers, scattered and in masses on the epithelial cells. Stained Thionin blue.

C.27. From a woman of 66 with typical clinical signs of diplobacillary conjunctivitis. Few leucocytes and large numbers of epithelial cells in the secretion. M. blue.

D.128. From an infant three months old which had had sore eyes since the third day after birth. Fibrinous secretion with large numbers of diplobacilli. Stained Pick & Jacobsohn modified.

~~E.133.~~ Also stained by Gram, showing numerous diplococci.

E.133. From an infant 4 weeks old. Slight purulent secretion. Stained Pick & Jacobsohn modified and Gram.

F. 67(1). Mucopurulent conjunctivitis of two years duration in spite of treatment in a woman of 36, dating from an attack of influenza. The bacilli are quite unlike those of Weeks. The xerosis bacilli are characteristically arranged. Stained P. & J. mod. and Gram.

G. 113. Conjunctivitis, violent at first, in a woman of 74. Now subacute. Numbers of pneumococci with and without evident capsules. stained P. & J. mod. & Gram.

H. 83. Mucopurulent conjunctivitis of two weeks duration associated with keratitis in a girl of 14. There

are diplococci present which sometimes very closely resemble gonococci but there are very few leucocytes and the cocci are free and scattered. Stained P. & J. (original formula) and Gram.

I. 87. Catarrhal conjunctivitis of two to three weeks duration in a girl of 13. Numerous staphylococci and diplococci, some decolourise by Gram, others do not. The resemblance to gonococci is only very superficial. Possibly in this case the decolourisation might have been absent if the manipulation had been more rapid.

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