

A FURTHER STUDY OF THE BACTERIOLOGY OF SUPPURATION IN THE ACCESSORY SINUSES OF THE NOSE.

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INTRODUCTION.—In the *Edinburgh Medical Journal* for November 1905 we published the results of our investigation into the bacteriology of nasal sinus suppuration and drew certain conclusions from these observations. As some points seemed to require further elucidation, the work has been continued and fresh deductions drawn. In the present series of investigations we have examined the bacteriological condition of forty-three antral cavities which were the seat of suppuration and which were uncomplicated by associated suppuration in any of the other sinuses. We report further upon seventeen cases in which inflammation of the antrum was complicated by a similar condition of the ethmoid or frontal sinuses or of both. In addition, we have examined six frontal sinuses, one frontal mucocele, one orbital abscess, and one case in which the antral orifice was blocked and the cavity was full of mucoid secretion. One dental cyst has also been examined, making a total of seventy patients from whom specimens have been obtained. Eight of these patients have also furnished teeth which have been examined for the comparison of bacteria found in them with the bacteria found in coincident sinus suppurations. We report our observations under the following headings:—I. The bacteriology of sinus suppuration, including a comparison between recent and more chronic cases of uncomplicated antral suppuration, and the assignment of predominance to special micro-organisms in individual instances. II. The causation of foetor. III. The pathways of infection. IV. The bacteriology considered from a clinical standpoint; and V. The conclusions which we consider warranted by the facts.

I. BACTERIOLOGICAL TECHNIQUE.—The collection of the specimens for examination was undertaken by one of us (A. L. T.) and the bacteriological work was conducted by the other (C. J. L.). The specimens were obtained from patients in hospital and in private

practice, and comprised instances of both acute and chronic conditions. The specimens were, in most of the cases, obtained direct from the cavity or from washings, and not by posturing the patient. The pus was collected either in sterile tubes or on sterile swabs enclosed in sterile tubes. It was transmitted by post to the laboratory, so that its examination began on the day following the collection. On its arrival, culture media were inoculated and direct films were afterwards prepared on clean slides. The routine method consisted in the inoculation of blood-serum, agar, and broth, both for aerobic and for anaerobic cultivation, and, in addition, of glucose agar and glucose broth for anaerobic cultivation. In certain cases, such as those with influenzal history, an agar medium spread with blood or mixed with serum was utilised. The serum agar used in the previous investigation (*op. cit.*) was not so frequently employed; on the other hand, blood-serum and blood-agar were utilised more freely and proved quite good substitutes. The primary cultures having been made, the direct films were next stained and examined microscopically. One film was stained by the Ziehl-Neelsen method for the detection of tubercle bacilli. Another film was stained by Gram's method and examined for the presence of micro-organisms. There was generally no difficulty in finding several varieties of bacteria in the direct film, and in this way assistance was obtained as to the varieties to be looked for in the cultures and as to the organisms which showed numerical preponderance in the pus itself. Both aerobic and anaerobic cultures were made in every case, because in the former investigation (*op. cit.*) anaerobic culture was not invariably tried; it was hoped that in this series an estimate of the proportion of cases in which strict anaerobic organisms occur would be obtained. The inoculated media were incubated at blood heat (37° C.). The aerobic cultures were examined after one or two days' incubation, films were stained from all the cultures and compared with the direct films from the pus. If the tubes of blood-serum and agar did not furnish pure cultures of one or more organisms, the growth was plated out in order to separate the different varieties. The broth was always plated out, generally on agar on the second day. The plates were inoculated by spreading the culture over the medium with a platinum spreader. The plates were incubated at the same temperature (37° C.), and from them subcultures were made of the different organisms present. It was sometimes necessary to repeat the plating process more than once in order to obtain pure cultures. Further tests were then devoted to the identification

of the cultural characters of the various organisms, to questions of their pathogenicity and to the observation of fœtor production. Films were generally stained for preservation and many of these have been photographed. Reproductions of these photographs will be published in a future paper. The anaerobic cultures were subjected to a similar procedure, but in their case longer periods of incubation were given. The original cultures inoculated from the swab were placed in a jar from which the oxygen was absorbed by alkaline pyrogallate. The jar was corked and further sealed by wax. The cultures were allowed to grow for four or five days before the jar was opened, they were then examined and, if they showed any organisms other than those already noticed in the aerobic cultures, plate preparations were made. Glucose agar plates were spread and cultivated in an atmosphere of purified hydrogen gas in Bulloch's apparatus. To ensure that no air should be contained in the Petri dishes themselves, the covers were removed and the plates were inverted and inserted on the shelves of a plate-rack. When the apparatus was full of hydrogen the supply was cut off and any oxygen, in any remaining air that might be present in the chamber, was absorbed by passing in some caustic soda solution on to pyrogallic acid in a dish at the foot of the chamber. The whole apparatus was put into the incubator after being securely sealed and was kept at 37° C. for four or five days. The plates were then removed, any fœtor noted, and the colonies on the glucose agar were examined, subcultured, and tested as to their identity and pathogenicity; occasionally a repetition of the plating process was required and carried out, though it was attended with difficulty in that these organisms are apt to die out. For the most part anaerobic organisms flourished but feebly and their colonies were apt to be small and hard to find. Some of them did not live long enough to permit of full determination of their characters. We think that with some of these anaerobes symbiosis may be a factor in growth, and that some cultures have died in the endeavour to get the organisms to grow separately.

Investigation of Pathogenicity.—The pathogenicity of many of the cultures was tested by inoculation into animals. The animals chiefly used were guinea-pigs, but mice and rabbits also served for this purpose. The inoculations were generally subcutaneous but occasionally intra-peritoneal. The results of such experiments must be interpreted in the light of other known facts in each case. In some cases no organism was pathogenic for the guinea-

pig when thus tested, though more than one variety had been isolated from the pus. In other cases we have found two or more organisms actually pathogenic after isolation and subculture from the pus. It must be remembered that the process of isolation in pure culture and the subsequent preparation of a culture for inoculation may take several days, especially in the case of anaerobes, so that there is opportunity for some of these organisms to decline in virulence before the test is applied. For this reason some strains of organisms which might have been expected to show virulence on animals failed to do so. Immediate inoculation of the pus itself might have shown some organisms to be pathogenic which later in subculture from the pus produced little or no sign of pathogenicity. Positive results in cultural experiments are of great value, but they will not bear exaggerated interpretation. Chronic cases may show organisms pathogenic to animals, but it is not therefore certain that these organisms were responsible for the origin of the human condition. They may have gained access to the cavity after the inflammation has been started by other organisms. Where the duration of a case is measured by years it is certain that the flora of the cavity will vary during the illness, and a sample of pus at one time will not give exactly the same organisms as those obtained at another time. Amongst the secondary organisms there might well be some pathogenic to animals but not responsible for the origin of the complaint.

A. *Suppuration of the Antrum of Highmore, the other sinuses not being involved.*—Under this heading there were forty-three specimens examined from forty-three cavities. The organisms found in the pus were of numerous varieties, the most common forms being the cocci, either pneumococci, staphylococci, or streptococci. It is characteristic, however, of antral pus to contain numerous varieties of organisms, and indeed it is seldom that specimens of the pus from different patients agree entirely in their bacterial flora. Streptococci were found in thirty-three, and staphylococci in thirty-four, of the forty-three cavities. These cocci, however, were not all of the pyogenic type, and their characters will be further discussed in a later paper. The pneumococcus was present in thirteen of the forty-three cavities. The numerical proportion of these three groups of organisms differs considerably from that noted in the previous paper (*op. cit.*), the pneumococcus being found much less frequently in the present series. The percentage of cases showing streptococci is much the same in the two series, and the same may be said in regard to the staphylococci. It is

common to find in antral pus diphtheroid bacilli and occasionally the bacillus of diphtheria itself. The members of this group which are most frequently met with are the bacillus of Hoffmann, the bacillus xerosis, the bacillus coryzæ segmentosus, bacillus septus and others, to which the generic title of pseudodiphtheria bacilli may be given. Examples of these types were present in sixteen of the forty-three cavities. The coliform bacilli occur in certain cases, and in this group we include not only *Bac. coli*, typical and atypical, but the bacillus of Friedländer and other organisms with similar general characters. This group was represented in nine of the cases. Another set of bacteria, which we may term the putrefactive group, are recognised in antral pus with considerable frequency. Of these organisms the bacilli named proteus, fluorescens, cloacæ, fæcalis and aureus, are the most common forms. Examples of these were present in ten of the forty-three cavities. The mesenteric group of bacilli is represented in seventeen of the cases. Its members consist of four varieties—ruber, vulgatus and fuscus, and also that termed niger, for which another name is *Bac. gangrenæ pulpæ*. These organisms show minor differences, but grade into each other so that it is sometimes difficult to assign a particular strain to its proper variety. The varieties ruber and vulgatus appear to be of less significance than the varieties fuscus and niger. The two latter are much more offensive in culture, and in some cases account for the presence of fœtor. Moreover, the niger variety is frequently, and the fuscus variety occasionally, pathogenic to guinea-pigs, while we have never found the other two kinds pathogenic. The organisms isolated from antral pus, and identified by their cultural characters as bacillus mesentericus, may differ from their type in regard to Gram's stain. Typically these organisms retain the stain and are Gram-positive, but certain strains we have met with in antral pus lose the stain rather easily and may even appear Gram-negative. Since the cultural characters are distinctly those of the bacillus mesentericus the variation in staining does not appear to be a sufficient reason to doubt their identity. Anaerobic organisms of various kinds, both bacilli and cocci, were present in nineteen cavities, while organisms of buccal and dental habitat were found in twelve cavities. Prominent anaerobic organisms were the bacillus perfringens, the bacillus ramosus and bacillus serpens, whilst amongst those associated with the mouth were bacillus buccalis maximus, bacillus necrodentalis and bacillus gangrenæ pulpæ besides the salivary streptococci.

There is a group of Gram-negative diplococci, of which *micrococcus catarrhalis* may be taken as a type, and representatives of this group were found in eleven cavities. It is not considered necessary to detail here the differences between the various cocci which make up this group. Other organisms were occasionally met with, such as the bacillus tuberculosis, the bacillus influenzae, the micrococcus tetragenus, the bacillus mucosus and bacillus rhinitis atrophicans.

While this is a somewhat extensive list, it does not purport to form a complete catalogue of the bacterial flora of antral suppuration. It does, however, give a fair impression of the groups of organisms which are most likely to be seen in cultures from such pus.

Comparison of Organisms in recent and more Chronic Cases of Uncomplicated Antral Suppuration.—The forty-three cases are divided into two groups, the recent comprising eight cases, and the more chronic or long-standing, thirty-five cases. The qualification for inclusion in the group of recent cases is that the discharge had not persisted for longer than three weeks. Our analysis of the bacteriology shows that, as in the previous investigation, the streptococci were more frequently associated with chronic purulent conditions than with recent infection. Of eight recent cases five, or 62 per cent., showed streptococci, but of thirty-five chronic cases there were twenty-eight, or 80 per cent., showing streptococci: staphylococci were present in 75 per cent. of recent cases and 80 per cent. of the chronic cases, but these figures include all kinds of staphylococci. Pyogenic staphylococci were present in four of the eight recent cases and in fifteen of the thirty-five chronic cases. Pneumococci were rather more common in recent than in long-standing cases, being present in three, or 37·5 per cent., of the recent as compared with ten, or 28·5 per cent., of the chronic cases. We note a marked difference in the prevalence of anaerobic bacteria in the two groups. Of the eight recent cases only one showed a bacillus which we had reason to think was a strict anaerobe, and in this case it was not possible to exclude the causative agency of more common aerobic organisms. In the thirty-five chronic cases anaerobic organisms were found in eleven instances, a notable contrast to the recent cases. The coliform bacilli were not observed in any of the recent cases, but were present in 25 per cent. of the chronic cases. The diphtheroid bacilli were found more frequently in chronic cases, though not entirely absent from the recent ones. Bacilli known to occur with

frequency in tooth troubles were recognised only in the long-standing cases. No recent case showed such organisms, but twelve of the thirty-five chronic cases showed one or other organism of this kind.

The Organism or Organisms regarded as Predominant in the Uncomplicated Antral Cases.—An attempt has been made to assign the cause in each case to one or more of the organisms present. We have taken into account (1) the pathogenicity of the organisms as ascertained by experiment upon animals; (2) the numerical preponderance of the different kinds of organisms in the films and in the cultures made directly from the pus; (3) the comparisons of the organisms found in the antral pus with those found in the teeth or in the nose of a patient suspected of dental or nasal infection respectively; and (4) the occurrence, comparatively rare, but illuminating when present, of only one species of organism in the pus films and cultures.

Recent Cases.—Of the eight recent cases two were pneumococcal; one of these showed a pure culture of the pneumococcus, and in the other the cultures were practically pure also, the only other organism present being a yeast. Three cases were undoubtedly influenzal in origin, for in them the bacillus influenzae was present in the films, and in two of the cases it was isolated in the cultures. It is possible that other cases also had an influenzal origin, but at the time the specimens were submitted the bacillus of influenza had died out or was not present in the swab. Pyogenic cocci were present in the remaining three recent cases, and in two of these the micrococcus catarrhalis was also present. In the recent cases evidence of dental infection was absent.

Chronic Cases.—None of the thirty-five chronic cases yielded a pure culture of only one organism, so that in the chronic cases predominance had to be assigned on other evidence than pure culture. In fifteen of them we think that it was possible to assign the cause of the suppuration to one organism, viz. to bacillus coli in six cases, to the pneumococcus in four, to streptococci in two, to the bacillus influenzae in one, to staphylococcus aureus in one, and to the tubercle bacillus in one. In the other twenty cases there occurred combinations which were more difficult to elucidate. Combinations of streptococci and staphylococci, of streptococci and pneumococci, or of all three kinds of cocci, were met with, and it is then not easy to differentiate the causative organisms. To the conjoint action of streptococci and staphylococci we assigned three cases, and to the conjoint action of

streptococci and pneumococci one case. Twelve cases, all clinically dental in origin, showed organisms common in decaying teeth, and we regarded these cases as due to such organisms, though in many of the specimens streptococci or other organisms were also present. Two other cases, classified also as dental infections, were bacteriologically attributable to anaerobic organisms, but these particular anaerobic bacilli we have not as yet demonstrated in cultures from teeth. Of the two remaining cases, both showing Gram-negative diplococci combined with non-pathogenic organisms, one had originated in an attack of influenza, but the pus at the time of examination showed no influenza bacilli. Without evidence of pathogenicity, it was difficult to assign these two cases to a special organism, but we think that the Gram-negative diplococci may have had some causal relation to the condition. The Gram-negative diplococcus in one of these cases was the ordinary micrococcus catarrhalis known to be associated with coryza, and in the other it was a similar organism with slight cultural differences from the recognised type of micrococcus catarrhalis.

So far, we have considered the predominance of special organisms in particular cases, making allowance for various considerations. Looking at the series of uncomplicated cases as a whole, we observe that out of eight recent cases two were probably due to organisms whose virulence was not capable of proof by experiment on the animals available, since these organisms did not produce in the animals any symptoms. Of the other six recent cases, five yielded virulent organisms, their virulence being demonstrated by experiment. The sixth case yielded a pure culture of the pneumococcus, and its failure to prove actively pathogenic may have been due to some experimental error. We may consider that in practically all recent cases the organisms are virulent.

Out of thirty-five chronic cases, twenty were proved by experiment to contain virulent organisms. This is a much smaller proportion than in the acute cases, but it is probable that the proportion will vary in different series of chronic cases according to the varieties of bacteria which happen to be present. Cultures of coliform bacilli and of staphylococci are more easily proved virulent than is the case with cultures of pneumococci, streptococci and anaerobic bacilli.

B. *Suppuration of the Antrum of Highmore complicated by a similar condition of one or more of the other sinuses.*—We

have examined seventeen specimens of the pus from seventeen antral cavities, complicated in ten cases with ethmoidal suppuration, in two cases with frontal suppuration, in four cases with both ethmoid and frontal suppuration, and in one case with ethmoidal and sphenoidal infection. As usual in these suppurations, cocci were present in all cases. Thirteen cavities showed streptococci of various kinds. Ten cavities showed staphylococci, but of these only five were pyogenic staphylococci, in the remaining five cases the staphylococci were of different varieties. Pneumococci were present in five cavities. Other organisms found were coliform and diphtheroid bacilli, Gram-negative diplococci like *micrococcus catarrhalis*, the bacillus of Friedländer, bacillus rhinitis atrophicans, bacillus pyogenes foetidus, and anaerobic and dental organisms. None of these cavities contained pus which was mono-organismal; all yielded impure cultures. The predominant organisms vary greatly, and in most of the cases there were several organisms implicated. Three only of the seventeen cases may possibly have been dental. If we contrast this percentage of possible dental cases with that found in chronic uncomplicated antra, the difference is striking. Where more than one sinus is affected, the pathway of infection is probably through the nasal chamber. There is more likelihood of the other sinuses infecting the antrum than of the antrum infecting the higher sinuses. In the complicated cases the coliform bacilli were frequently present, being found in eight cases, and probably playing a predominant part in six of them. The other two cases showed, in addition, a streptococcus, which was probably causal. One case associated with atrophic rhinitis showed the diphtheria bacillus, and the pyogenic cocci accounted for the rest.

The pathogenicity results in this series of seventeen complicated cases showed that virulent organisms were obtained in fourteen. The large proportion of positive results in cases which were chronic in duration is due to the number of these cases which yielded coliform organisms, such as do not easily lose their virulence to guinea-pigs. The streptococci and the coliform organisms were more prominent than the staphylococci and the pneumococci in this series.

C. *Suppuration in the Frontal Sinus alone.*—Examination was made of two frontal cavities, of which one was recent and one was old-standing. The recent case showed the pneumococcus and streptococcus pyogenes, the latter being found pathogenic. The chronic case was staphylococcal, but showed also the bacillus of

Hoffmann and bacillus mesentericus. Pus from the frontal sinus presents, as a rule, fewer varieties of bacteria than pus from the antrum. It is more easy to assign predominance to one organism, and it appears that cocci of one kind or another are generally responsible.

D. *Complicated Frontal Sinus Suppuration.*—Four chronic cases of this description were examined, in all of which the antrum was affected, while in one the ethmoid sinus was also involved. In one case the streptococcus pyogenes, in the second the pneumococcus, and in the third a staphylococcus, was the causal organism. The fourth case presented a different picture; in it the antrum had been the seat of a dental infection, and the pus from the frontal sinus showed a considerable variety of organisms. There was reason to believe that in this case the antrum had infected the frontal sinus, because the pus from both showed the presence of cocci, and of an anaerobic bacillus, the bacillus ramosus of Veillon and Zuber. This organism is not common in uncomplicated frontal sinus suppuration. The bacillus mucosus was also present in this case.

As to the pathogenicity of the organisms in the six frontal sinus cases, the acute case yielded a virulent culture of streptococcus pyogenes. Of the five chronic cases, complicated and uncomplicated, two showed virulent organisms. In both cases these were staphylococci, but, in one case probably infected from the antrum, there was in addition a pathogenic bacillus.

E. *Special Cases.*—None of the four special cases (mucocoeles, cyst, &c.), yielded common pyogenic organisms. All four were mono-organismal, and no two were alike in their bacterial flora. We propose to reserve for a later paper the detailed description of these organisms.

So far attention has been directed to the varieties of organisms met with, to the contrast between recent and chronic cases, and to the predominant organisms present. The causation of fœtor in antral suppuration will next be discussed.

II. THE CAUSATION OF FÆTOR.—Maxillary sinus suppuration is frequently fœtid. More especially is this so in old-standing cases, though fœtor may be present in cases of recent origin. It is not always a simple matter to ascertain the cause of the fœtor, nor can we assume that fœtor is invariably due to the presence of a particular micro-organism; doubtless it is so in certain cases. We are able to adduce this from our cultural investigations owing to the identity of the odour from the pus with that of artificial

cultures of an organism isolated from the pus. In other cases the origin of fœtor is more complex. It may be due to more than one organism; for when two or three organisms have been isolated from the same case it has sometimes happened that each impure culture produced an odour more or less offensive, and any one of them might account for the fœtor. We believe that in some cases the cause of the fœtor is the interaction of several organisms, each of which in pure culture may be non-offensive. Such a condition was found in one case where several aerobic organisms gave no smell in pure culture, but a composite inoculation of them all into a single broth culture gave a plainly fœtid odour after forty-eight hours' aerobic incubation at 37° C. The organism or organisms causing fœtor may in some cases be aerobic and in other cases be strictly anaerobic types. The fœtor caused by anaerobic microbes is particularly objectionable, but even that produced by combinations of aerobic organisms can be very offensive. The fœtor may be positively fœcal, and in such cases it is usual to find organisms of the type of *Bac. coli* in the pus. The odour may then be due to the production of indol or other similar chemical products of the growth of the organism. No doubt there are many other offensive substances, the chemical nature of which we do not know, produced in sinus suppurations. We think there may be a further element in fœtor which is difficult to estimate, and that is the inefficiency of the aeration of the sinuses, more especially of the antrum. It is conceivable that aerobic organisms, which in pure culture on artificial media and with ample supply of air give no smell, may give rise to odour when growing in the human body under conditions of deprivation in the matter of oxygen. Proof of such a conception is not so easy to obtain, but it would not be wise to overlook this possibility in the case of the antrum. An analogous condition occurred in the laboratory when a bacillus, which in one of the cases was apparently the sole cause of fœtor, had an offensive smell in aerobic culture, but the fœtor was very distinctly worse in the anaerobic cultures of the same organism. The treatment of fœtid sinuses with oxygen was suggested with this fact in view, but the results were not sufficiently definite to encourage its regular use. On the whole, the most fœtid cases were those in which obligate anaerobes were present, but the estimate of the intensity of fœtor will vary somewhat with the individual observer. To some surgeons and patients one fœtor and to others another fœtor may appear more horribly offensive.

We shall consider first the fœtor of uncomplicated antral suppuration. It has been suggested that in antral suppuration fœtor is the result of the presence of anaerobic organisms. Undoubtedly it is so in certain cases, but by no means in all. We found fœtor present in antral cases in which no anaerobes could be recognised as well as in those cases of distinctly anaerobic origin. Fœtor may occur comparatively early in the history of an antral suppuration, because in the eight cases classified as recent—in none of which the discharge had persisted for more than three weeks—two were already fœtid. In one it was due to the *Bac. fluorescens putidus*, and in the other to a bacillus which could not be identified, but which was numerous in films, absent in aerobic culture, and scanty in anaerobic culture. It was possibly of the nature of *Bac. serpens*. Of the thirty-five chronic cases twenty-seven were stated to be fœtid. The chief organisms concerned in the production of fœtor in this group were the coliform and mesenteric bacteria and certain putrefactive organisms. They were responsible, either alone or conjointly, for the fœtor in the majority of the cases. In two cases, however, the odour was probably due to the interaction of microbes which in pure culture gave no smell. The organisms responsible for the fœtor in the dental and anaerobic cases were the *Bac. gangrenæ pulpæ*, *Bac. necrodentalis*, *Bac. perfringens*, *Bac. ramosus*, *Bac. serpens*, and *Bac. thetoides*. The coliform organisms included *Bac. coli*, typical and atypical, *Bac. pyogenes fœtidus*, &c. The mesenteric bacilli were the varieties formerly mentioned, especially *fuscus* and *niger*. The putrefactive bacteria included *proteus vulgaris*, *proteus cloacinus*, *Bac. fluorescens putidus*, *Bac. proteus fluorescens*, *Bac. aureus*, *spirillum rugula* and other spirilla. The study of fœtor as revealed in the seventeen complicated antra is particularly helpful. Five cases were mentioned as fœtid, and of these only the two which were undoubtedly of dental origin owed their fœtor to anaerobes. Two cases were due to *Bac. coli*, and the fifth case to the combination of aerobes. Of the remaining twelve cases five showed aerobic organisms which caused offensive odour in cultures, viz. *Bac. coli*, *Proteus*, *Bac. pyogenes fœtidus*, *Bac. mesentericus*, and *Bac. fluorescens*. One other case yielded offensive anaerobes, and was the third of these cases ascribed to a dental origin. The conclusion is forced upon one that fœtor does not appertain only to those cases in which the mouth is the source of infection, but is equally an attribute of nasal infections.

Frontal suppuration may or may not be foetid. Two of the six cases examined were foetid. One was an uncomplicated case, and the foetor was due to *Bac. mesentericus fuscus*. The other was complicated with antral inflammation of dental origin, and the foetor was due to the anaerobic bacillus ramosus.

III. THE PATHWAYS OF INFECTION.—From what has already been stated, it is clear that we regard infection of the antrum as due both to nasal and buccal infection; it may be well, however, to allocate the cases in this respect. Of the sixty cases uncomplicated and complicated, we regard forty-two as due to nasal and eighteen to dental infection.

INFECTION OF THE ANTRUM.

	Nasal.	Dental or Buccal.	Total.
Uncomplicated cases	28	15	43
Complicated cases	14	3	17
	42	18	60

It will be seen that by far the larger proportion of buccal infections occur in those cases where the antrum is alone involved. The antrum may more easily be infected from the other sinuses than itself infect them. If the antrum commonly infected the other sinuses we would expect less disproportion between the nasal and buccal infections in complicated cases. Further, we might expect to find anaerobic and dental organisms in pus from the other sinuses. This we rarely find to be the case. The pus from the higher sinuses generally yields aerobic organisms. In only one case of frontal suppuration did we find any anaerobic bacilli, and in that case there was reason to believe that the frontal condition was consecutive to abscess of the antrum.

We have tried to show that pus from the antrum may contain the same organisms that are present in decayed or suppurating teeth from the same patient. In four cases in this series we have found in the antral pus, and in teeth extracted at the time of operation, the same organisms. The organisms associated with dental trouble, which in two of the cases we have isolated from antral pus, were the *Bac. necrodentalis* and the *Bac. gangrenæ pulpæ*. In a third instance these were accompanied in both the

teeth and the sinus by the anaerobic bacillus ramosus. This is the first time, so far as we are aware, that this bacillus has been isolated from a tooth, though we have found it in other cases of sinus suppuration. It was originally described by Veillon and Zuber in pus from appendicitis, and it was found in the antrum by Stanculeanu and Baup. The nomenclature is rather unfortunate, as the same designation has been given to an entirely different organism which must not be confounded with this strict anaerobe. The name is fairly descriptive of the appearance of the organism in film preparations. We hope to publish a photograph of it along with others in a later paper. The fourth case did not yield the same bacilli in both the tooth and the specimen of pus from the antrum. Mouth organisms, however, were present in the latter, and the same pyogenic streptococcus was obtained both from the tooth and from the antrum.

In some cases, where we examined both a tooth and pus from the antrum, we failed to find evidence of tooth infection, and in the majority of these cases the clinical history pointed rather to a nasal infection.

IV. THE BACTERIOLOGY OF UNCOMPLICATED ANTRAL SUPPURATION CONSIDERED FROM A CLINICAL STANDPOINT.—Our attention has been directed mainly to considering how far the bacteriology of uncomplicated antral suppuration will assist us in determining the best line of treatment to be adopted in any given case. Notwithstanding the fact that suppuration in the maxillary sinus is of fairly frequent occurrence, and that it has for so many years received the attention both of the general surgeon and the specialist, we are still unable to say definitely in every case what operative procedure should be carried out. Two methods of treatment have been recognised in connection with antral suppuration; first, irrigation of the sinus for the purpose of restoring the lining membrane to a healthy condition, which may be termed the conservative method; this is performed either through an opening in the alveolar process, or through the outer wall of the inferior meatus of the nose. The second, which may be called the radical procedure, consists in opening the antrum through the canine fossa and curetting the diseased lining membrane in whole or in part; the operation is completed by establishing a large opening in the naso-antral wall, and closing the wound in the buccal mucous membrane. In this way the sinus is partially obliterated. It has been argued by some that the latter procedure should be adopted in every case in which the discharge from the antrum has persisted

for more than a comparatively short period, so that the mucous membrane of the cavity can be carefully inspected through the large opening in the facial wall, and either left untouched or removed according to the appearances which it may present.

No one with any experience of chronic antral suppuration will deny the uniform success which follows the radical treatment of the sinus; nevertheless, all will admit that a certain proportion of the cases, sometimes, indeed, cases of very considerable chronicity, will readily cure after a short course of lavage through a nasal or even an alveolar opening. The difficult question has always been to decide which of these cases may rightly be selected for the simpler line of treatment. It is with this object in view that we have carefully considered the bacteriology of the discharge. We have always advised against a routine practice of opening through the canine fossa, notwithstanding that it is the only route by which the interior of the antrum can be properly inspected. As a rule, in the latter operation chloroform anæsthesia is necessary. In spite of the advances which have been made in operating under local anæsthesia, we still think that the radical operation upon the antrum is better carried out, alike for patient and surgeon, under a general anæsthetic. Again, the division of the sensory nerves to the gums, upper lip, and teeth causes a good deal of discomfort to the patient for a considerable length of time; and, further, he is probably obliged to absent himself for at least a week from his work. Moreover, in the present state of our knowledge, it is not always possible to determine by inspection whether the lining membrane of the antrum should be left untouched or removed. The simpler operation, on the other hand, now almost invariably practised through the nasal cavity, can be effectively done under local anæsthesia alone, or with the addition of a single administration of chloride of ethyl; the patient does not suffer from the post-operative discomfort which is experienced after the more extensive dissection which the other operation entails, and he can return to his work in one or two days.

It seems reasonable, therefore, and it is undoubtedly more scientific, to attempt to formulate some working basis whereby we may conclude before operation whether conservative treatment will effect a cure or whether the patient should only be offered the more radical procedure. Whether this is possible from the facts before us, we must now proceed to investigate. For the last two or three years we have devoted considerable attention to this question, studying mainly the bacteriology and cytology of the dis-

charge, its duration, and the pathway of infection of the antrum. Clinical experience shows that the duration of the discharge from the sinus prior to treatment cannot be taken by itself as the determining factor in treatment. While it is true that the majority or, indeed, all cases of recent origin readily cure by lavage, the converse cannot be said of cases with a protracted history. Lavage through a nasal opening has been followed by cure in the course of a few weeks in cases which have discharged for five, six, or twelve years or more, while it has failed to do so in others of much shorter duration, such as eight months, one and three years. Some other factor or factors must therefore be considered. For this purpose, however, we have preferred to adopt a clinical classification based upon the duration of the discharge, and have divided the forty-three cases of uncomplicated antral suppuration examined bacteriologically into two main groups, the recent and the chronic.

The Recent Cases.—In this group we have eight cases in which the discharge had persisted from two days to three weeks. The pneumococcus was present in three, being found in pure culture in two of them, while in the third it was in combination with the streptococcus pyogenes and a form of staphylococcus. A streptococcus was present in five, and a staphylococcus in six of the eight cases. In addition to the three main types of organisms, we found the bacillus influenzae in two, the micrococcus catarrhalis in two, and a diphtheroid bacillus in three. A marked feature in these cases was the absence of the *Bac. coli* and anaerobic organisms. In one case a bacillus was recognised in large numbers in the pus, but it could not be obtained in pure culture or fully identified. It was a Gram-negative bacillus, which was absent in aerobic cultures, but present with cocci in anaerobic broth culture. It probably accounted for the fœtor noted in the case, but there is no evidence as to its part in the production of the disease. All the cases were of nasal infection, and were treated by nasal lavage, the majority by a few intra-nasal punctures and irrigation, two by the establishment of a permanent opening. All were cured in a very short period of time.

The Chronic Cases.—The second group consists of thirty-four cases classified clinically as chronic, in which the discharge had persisted from five months to twelve years. In the section on bacteriology the total numbered thirty-five, but as one of the patients declined treatment, the case cannot be considered in connection with therapeutic measures. As six of the group were

treated at the outset by the radical operation they may be dismissed, thus leaving a total of twenty-eight for consideration. The following subdivision based upon the duration of the discharge will simplify the study of the chronic cases:—(a) Four cases in which the discharge had existed five (two cases), six, and eight months; (b) eight cases in which the affection had been complained of for more than one and less than two years; (c) five cases with discharge for two years; (d) two cases with discharge for three years; (e) three discharging for five years; (f) one for six years; (g) one for eight years; (h) one for twelve years; (i) three for several years without any definite period of time being stated.

(a) A study of the four cases in which the discharge had persisted five, six, and eight months demonstrated that the streptococcus pyogenes was present in two, combined in one with the staphylococcus pyogenes aureus and Bac. coli, in the other with the Bac. necrodentalis and Bac. mesentericus fuscus. The staphylococcus cereus albus occurred along with the Bac. cloacæ in one, and the streptococcus anginosus occurred in the fourth case, combined with the bacillus aureus and a diphtheroid bacillus. The two cases in which the streptococcus pyogenes was absent were cured. Of the two associated with the streptococcus pyogenes one was cured by the nasal operation, the other failed to cure by alveolar lavage.

In three of the four, both bacteriologically and clinically, the infection was nasal; two were treated by the nasal and one by the alveolar opening, and all were cured. The fourth, of eight months' duration, was of dental origin, containing the Bac. necrodentalis; it was treated by lavage through an alveolar opening without success, but was readily cured two years later by a radical operation.

We have thus twelve cases discharging for less than one year, eight of very recent origin—two days to three weeks—and four in which the discharge had existed for a few months, five to eight. Eleven were of nasal infection, ten being treated by the nasal and one by the alveolar route, and all were cured. The twelfth, in which the discharge had persisted for eight months, was of dental origin; it was treated through the alveolus, and was not cured. The streptococcus pyogenes was present in six of the cured cases and also in the unsuccessful case. We must regard the comparatively short duration of the discharge in these cases as an important factor in determining the success of the treatment by lavage.

(b) A study of the eight cases in which the discharge had been

present between one and two years demonstrates the presence of the pneumococcus and the streptococcus pyogenes in seven, the two organisms being associated together in six of them. Staphylococci also occurred in five of the same six cases. Dental and anaerobic organisms were found in six of the cases, such as *Bac. necrodentalis*, *Bac. gangrenæ pulpæ*, *Bac. plexiformis*, *Bac. perfringens*, and *Bac. serpens*. Six of the cases, therefore, were of dental and two of nasal infection. Three cases which contained the streptococcus pyogenes were cured, two by the nasal and one by the alveolar operation; the remaining four, which contained the same organism, were uncured, one being treated by nasal and three by alveolar lavage. The eighth case in the group contained the pneumococcus and a Gram-negative diplococcus, and was cured by a nasal operation. In summing up we find that the two cases of nasal infection were cured by the nasal operation, while of the six cases of dental infection, two were cured, one by nasal and one by alveolar lavage, the remaining four being uncured, one by nasal and three by alveolar lavage.

(c) In five cases in which the discharge had persisted for two years, the pneumococcus was present in two; in one case associated with a staphylococcus, and in the other in pure culture. Both cases were of nasal infection and were cured by nasal lavage. The remaining three contained the streptococcus pyogenes in association with a staphylococcus; in two of them the *Bac. coli* was also present. One was of dental and two of nasal origin; all were treated by alveolar lavage and were uncured. It is interesting to note in this group that the two cases without the streptococcus pyogenes and treated by the nasal route were cured, while the three with the streptococcus and treated by the alveolar route were uncured. How far was the success or failure in treatment due to the method of procedure adopted, or to the absence or presence of the streptococcus pyogenes?

(d, e, f) Six cases occurred with the discharge persisting for three (two cases), five (three cases), and six (one case) years, and it will simplify the description to study them together. In this group the pneumococcus was not found. The streptococcus pyogenes and a variety of staphylococcus occurred in all the six cases. Anaerobic organisms were present in five. Five of the cases were probably of dental infection, four showing bacteriological evidence of such. Three of the cases containing the streptococcus were cured, all of dental origin, two being treated by nasal and one by alveolar lavage. The remaining three cases containing the strepto-

coccus were uncured, two of dental and one of nasal origin, two being treated by nasal and one by alveolar lavage. In this group there are no discriminating facts, cases with similar organisms, route of infection and method of treatment being alike cured and uncured.

(*g, h, i*) Five cases of eight, twelve, and several years' duration complete the list of chronic uncomplicated antral suppuration. A staphylococcus was found in four cases, combined with the streptococcus pyogenes in two. Diphtheroid bacilli occurred in all, the Bac. coli in two, and the tubercle bacillus in one. In all, the pathway of infection was nasal. The three cases in which there was no streptococcus pyogenes were cured, two by nasal and one by alveolar lavage. The two cases containing the streptococcus pyogenes were uncured by alveolar lavage. We must again ask the question, how far success and failure in treatment were due to the method of procedure or to the presence or absence of the streptococcus pyogenes?

Placing on one side the eight recent cases of nasal infection, cured by nasal irrigation, we must now proceed to summarise the twenty-eight chronic cases in relation to the points dealt with above, namely, the duration of the discharge, the variety of organism, the route of infection and the kind of operation performed. Of the twenty-eight cases, fifteen were cured, thirteen were uncured.

Duration of the Discharge.—In estimating the influence that the duration of the discharge has upon the result of irrigation treatment, we are merely emphasising a well-known clinical fact when we repeat that some cases of long-continued discharge are cured by lavage, while others of much shorter duration fail to be so. Thus if we divide the twenty-eight chronic cases into two groups, one in which the discharge varied from five months' to two years' duration, we find that of seventeen cases nine were cured and eight were uncured, giving 52 per cent. of cures. Whereas in the second group, in which the discharge had persisted from three to twelve years there were eleven cases, of which six were cured and five were uncured, giving 54 per cent. of cures. Therefore a proportionately similar number of the more chronic cases were cured. In chronic cases the duration of the discharge is not a factor that can be taken by itself in deciding whether lavage or radical treatment is to be adopted.

Pathway of Infection.—Of the twenty-eight cases, fifteen were regarded as of nasal, and thirteen of dental infection. Of the

fifteen nasal cases, ten were cured, *i.e.* 66 per cent.; five were uncured. Of the thirteen dental cases, five were cured, *i.e.* 33 per cent.; eight were uncured. In this series much better results were obtained in the nasal than in the dental infections.

Operative Procedure.—Fourteen cases were treated by intra-nasal and fourteen by alveolar lavage; of the former, eleven or 78 per cent. were cured, three were uncured; of the latter, four or 28 per cent. were cured, and ten were uncured. The difference in the result of the two methods is striking. It is now generally admitted that opening the antrum through the alveolus is not a satisfactory procedure, and we have not practised this method during the last two years.

Variety of Organisms.—We have elsewhere indicated that, as the result of observations already published (*Brit. Med. Journ.*, October 1908), we were inclined to the view that when the pus in the discharge from a case of chronic antral suppuration contained the streptococcus pyogenes, the result of treatment by lavage was less satisfactory than when that organism was absent. We have therefore examined the twenty-eight cases in the series in this connection. In eight of them the streptococcus pyogenes was not found; all were cured by lavage. In the remaining twenty cases the streptococcus pyogenes was present associated with other forms of bacteria. Of these, seven were cured and thirteen were uncured. We do not wish to lay too much stress upon the above facts, but they appear to us to be of some significance. Their significance, however, may be to some extent discounted when we consider the operative procedure adopted in the various cases. We have already noted the superiority of intra-nasal irrigation. Of the eight cases without the streptococcus, seven were cured by nasal and one by alveolar lavage. Of the seven cases with the streptococcus which were cured, five were treated by nasal and two by alveolar lavage. Of the thirteen cases with the streptococcus which were uncured, three were treated by nasal and ten by alveolar irrigation. Of the twenty streptococcal cases, therefore, eight were treated by nasal operation, and five, or 62 per cent., were cured; while twelve were treated by alveolar operation and only two, or 16 per cent., were cured. It seems only fair to admit that the alveolar method of procedure may have unfavourably influenced the result in the streptococcal cases.

Cytology of Antral Discharge.—We have sought to throw additional light upon the selection of the line of treatment by a study of the cell elements in the discharge from the affected

cavity, having been stimulated to do so by the work of Dr. William Milligan in connection with suppuration in the middle ear cleft. The work has been carried out by Dr. John M. Darling, and his results have been published in the *Edinburgh Medical Journal*, December 1909. As a number of the cases which he examined belong to the series which form the text of this paper, his conclusions are of special interest. Epithelium, polymorphonuclear pus cells, and lymphocytes are the types of cells recognised. The mucous membrane of the diseased antrum has been examined in a number of cases by Dr. J. S. Fraser. It is obvious from a histological examination of the lining membrane that the inflammatory process shows more advanced changes in one part of the cavity than in another. Consequently the cells found in the discharge cannot give us more than an approximate idea of the degree of the changes which have taken place in the mucosa. Thus, polymorphonuclear cells and columnar epithelium thrown off from one part of the mucous membrane may predominate in the films examined in a case in which at the same time advanced changes have taken place in another part of the mucosa. Presumably when degenerated columnar cells, polymorphonuclear leucocytes in abundance, and lymphocytes in small amount are present in the discharge, the inflammatory process is probably not deep-seated. The presence of large numbers of lymphocytes, on the other hand, indicates the existence of more advanced granulomatous changes. Dr. Fraser, however, was able to demonstrate in the mucosa a marked lymphocytic infiltration in cases in which the cytological examination of the fluid washed out of the antrum showed the cellular elements to consist almost entirely of polymorphs (*Journ. of Laryngology*, London, September 1909).

Dr. Darling concluded from his observations that the presence or absence of relatively large numbers of lymphocytes in the discharge did not depend upon the chronicity of the suppurative disease; in other words, as we have already shown, the duration of the discharge is not itself a factor from which we are to determine that the case is chronic and cannot be successfully treated by lavage. He has further shown, however, that cases in which the discharge shows relatively small numbers of lymphocytes have a better prospect of cure by lavage than those in which an excess of lymphocytes occurs. When the ratio of lymphocytes to polymorphonuclear leucocytes is greater than one to six or eight he considers that the lymphocytes in the fluid are in excess. He further found that, independent of the period of duration of the

discharge, cases in which there was an excess of lymphocytes associated with the streptococcus pyogenes were seldom cured by lavage.

We are therefore justified in concluding, as a result of our bacteriological and cytological observations, associated with our results in the treatment of antral suppuration by lavage, that a knowledge of the organisms and of the kind of cells in the discharge is of undoubted assistance in determining the operative procedure to be adopted. Further, that if lavage is to be carried out, it should be by the intranasal and not by the alveolar opening.

The question naturally arises as to whether an explanation can be given of the tendency of the streptococcal cases to resist treatment by lavage. Two possible explanations have presented themselves to us, namely the pathogenicity of the organism and the possibility that the streptococcus pyogenes finds its way more readily than other organisms into the deeper parts of the mucous membrane, where it comes no longer under the influence of antiseptic irrigation. With regard to the first point, the pathogenicity of the organism, we have already pointed out in the section on bacteriology that it is extremely difficult to say in chronic cases that any one organism is mainly responsible for the pathological condition, because the bacterial contents of the pus vary during the course of the illness, and a condition started by one organism may be maintained by others. Hence the organism of most potent pathogenicity at the time of the examination may not be the same as that which originally started the complaint. Our experiments do not show that the virulence of the streptococcus pyogenes at the time of the examination provides any explanation of the incurability of these cases. The proof of its pathogenicity was sometimes provided by experiment, while in other cases the streptococcus had lost its virulence. Again, we have not sufficient grounds for saying that other pathogenic organisms alone or in combination will explain the incurability of the cases. Thus, the *Bac. coli*, pathogenic by itself or in combination, was present in six of the cases, two being cured by lavage and four uncured. The pneumococcus was pathogenic in three, of which two were cured and one was uncured; a staphylococcus in three, one being cured and two being uncured. Dental and anaerobic organisms were pathogenic in ten, of which three were cured and seven uncured. We are unable to say also whether the explanation of the failure of lavage is to be found in the condition of the

patient's blood. It is possible that it may be due to a deficiency in the individual's protective substances to deal with the streptococcus or other organisms even with the assistance of lavage. The treatment of a series of cases with a specially prepared streptococcus vaccine should be able to decide this point. Such a method of investigation would in our opinion be more reliable than numerous observations of the opsonic index—another method which naturally suggests itself.

A histological examination of the mucous membrane of the antrum has also been made in several cases by Mr. Henry Wade, with a view to investigating the changes produced in it by the chronic suppurative process, especially in connection with the organisms found in the discharge. The material was obtained partly from cases which had been unsuccessfully treated by irrigation and which afterwards underwent the radical operation, and partly from cases which were at the outset radically treated. Examination of these specimens, however, has not produced proof either of the deeper penetration of the streptococcus pyogenes into the tissue or of greater destructive changes. It was unfortunately impossible to say whether the cocci found in the mucosa belonged to the streptococcal or staphylococcal variety. We have had the opportunity of examining the diseased mucous membrane from one case in which a staphylococcus was present in the discharge. In this case the discharge had persisted for three years; no streptococcus had been found on culture, the chief organisms being the staphylococcus cereus albus, a Gram-negative diplococcus and bacillus flavus. The surface epithelium was much denuded, being entirely absent over considerable areas. Some of the mucous glands were empty and collapsed, while others showed considerable destructive changes. A few of these formed large retention cysts, with structureless contents. Lymphocyte cells adjacent to the denuded epithelial areas were abundant, but there was nowhere any evidence of an abscess in the tissues. This case was treated by the radical operation without any previous course of lavage. Several cases were examined in which both the streptococcus pyogenes and a variety of staphylococcus were associated in the discharge. In two there were a number of microscopic abscesses in the submucous tissue crowded with cocci. In another, in which there were in addition dental organisms, a suppurating retention cyst was found. In another case in which the streptococcus and staphylococci were obtained on culture, microscopic abscesses were also found in the sections;

in none of these, however, could the cocci be defined in the tissues as of the streptococcal form. While these facts are in themselves interesting, we do not think that they furnish sufficient proof of the greater virulence of the streptococcus pyogenes. Although lavage in chronic cases appears to be more successful when this organism is not present and less so when it is, no satisfactory explanation of this clinical fact is derived from our study of the bacteriology of the suppuration, or from the pathological appearances of the lining mucous membrane. It is possible that direct inoculation of the pus might prove the streptococcus to be virulent; in our experiments the isolation of the organism caused delay which might well be and probably was accompanied by loss of virulence.

V. CONCLUSIONS.—We advance the following conclusions from the facts disclosed in our investigations:—

1. That sinus suppuration is not caused by any one particular micro-organism.
2. That while bacilli may cause suppuration, we think that pyogenic cocci of various kinds are more often responsible.
3. That four main types of cocci are commonly met with in sinus suppuration, viz. pneumococci, streptococci, staphylococci, and diplococci of the type of micrococcus catarrhalis.
4. That the following groups of bacilli are frequently present in sinus suppuration—(a) *Bac. coli* and its allies; (b) putrefactive bacteria such as proteus and its allies; (c) dental organisms such as *Bac. gangrenæ pulpæ* and *Bac. necrodentalis*; (d) an obligate anaerobic group, of which prominent members are *Bac. perfringens* and *Bac. ramosus*; (e) a diphtheroid group; and (f) *Bac. influenzae*.
5. That the pus in a considerable number of chronic uncomplicated antral cases contains organisms of dental and buccal habitat, and that in some of these cases it is possible to isolate identical organisms from the pus and from diseased teeth extracted at the time of the operation upon the sinus.
6. That clinical and bacteriological investigations agree in showing that nasal infection of the antrum is more common than dental infection and that probably about one third of the cases of antral suppuration are due to dental infection.
7. That while in bilateral sinus suppuration the pus from the two antra may contain the same bacteria, this is not invariably the case; we have isolated from one antrum a virulent diphtheria bacillus, which was absent from the other.
8. That in recent cases of sinus suppuration the streptococci

were found virulent in 60 per cent., and in the cases of chronic suppuration only 30 per cent. have been proved virulent.

9. That foetus is the result of the growth of certain organisms, sometimes of those responsible for the suppuration and sometimes of those concerned in the decomposition of the products of inflammation. That both aerobic and anaerobic organisms are capable of causing foetus.

10. That foetus may be present in antral suppuration of very recent origin as well as in chronic cases, and that antral cases of nasal infection as well as those of dental infection may be foetid.

11. That recent cases of maxillary sinus suppuration (duration in this series two days to three weeks) readily cure by lavage.

12. That when lavage is practised whether in recent or chronic cases, it should be carried out through the nasal cavity: the alveolar opening should be abandoned.

13. That a certain proportion of chronic cases of antral suppuration are cured by lavage, but we cannot determine from the history of the case, the duration of the discharge, or the path of infection which cases may be so treated successfully.

14. That some assistance in the choice of lavage may be obtained by a preliminary microscopical examination of the cell elements in the discharge and from a bacteriological investigation of the pus.

15. That the value of cytological examination, however, is minimised by the fact that the inflammatory process causes more advanced changes in one part of the lining mucous membrane of the antrum than in another.

16. That in those cases in which the discharge shows a relatively small number of lymphocytes, the prospect of cure by lavage is greater than when an excess of lymphocytes occurs. (J. M. Darling.)

17. That chronic cases in which no streptococcus pyogenes is found in the pus, more readily respond to lavage than those in which the same organism is present.

18. That when in chronic cases there is an excess of lymphocytes in association with the streptococcus pyogenes, treatment by lavage should not be attempted.

19. That neither inoculation experiments nor histological examination of the lining membrane of the antrum explains the apparently greater resistance of the streptococcus pyogenes to treatment by lavage.

20. That failure in treatment by lavage may possibly be due to

a deficiency in the patient's protective substances to deal with the streptococcus, and that a specially prepared streptococcic vaccine might be appropriately tried in these cases.

21. That we have no evidence that any special combination of organisms is responsible for the failure of treatment by lavage.
