

control the action of the germs. As there is generally no need to deal with the drains, or to disinfect rooms or houses for these special cases, no upset of the domestic arrangements is necessary.

6. In the household where a patient is convalescing from typhoid fever the additional precautions of boiling all the milk or water used for drinking or in the preparation of food should be undertaken, and uncooked foods should be avoided.

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THE COMMON COLD: ITS PATHOLOGY AND TREATMENT,

WITH ESPECIAL REFERENCE TO VACCINE THERAPY.¹

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I.—INTRODUCTION.

In a recent publication on catarrhal fevers by Dr. R. Prosser White we find the following: "I venture to submit that our zeal and interest in a disease should be proportional not to its rarity but to its frequency; and to call trifling, a disease which incapacitates members of every class of society oftener and more commonly than any other, and has the reputation of initiating so diverse and numerous ailments, is a travesty of facts. This condition, the bane of the household and the scourge of the community is allowed to run riot, practically ignored by our leaders, our medical schools and our text-books." A feeling exactly in accord with that expressed by these very true words was the cause of my undertaking the present research into this common affection, which, again to quote Dr. Prosser White, "is a source of inconvenience, if not danger, to the strong, and is often followed by severest consequences in the old and the young, the feeble and the debilitated—which may be the active factor in overburdening an already embarrassed heart, setting up the final catarrh in the later stages of phthisis or multiplying the difficulties and distresses of the chronic invalid suffering from bronchitis and emphysema." The work conducted during two years' tenure of the Gull studentship has been completed in my private practice, with the result that I think I can fairly claim to have placed the bacteriology upon a sounder footing, indicated means whereby a differential diagnosis of the causal organism or organisms may be made in any given case from a consideration of the clinical features, and to have demonstrated the utility of vaccine therapy not only in shortening acute attacks and thereby preventing secondary complications, but also in curing chronic cases and in securing immunity, more or less complete, from further attacks, acute or chronic, in those who are especially susceptible to this very troublesome and common complaint.

II.—DEFINITION OF A COLD.

For the purposes of this research a cold may be defined as a local inflammation of any portion of the respiratory tract, from the mouth and external nasal meatus to the bifurcation of the bronchi, together with the sinuses annexed thereto; such as the frontal and ethmoidal sinuses, the maxillary antrum, and the Eustachian tube; inflammations due to the ordinary pyogenic cocci are, however, excluded. The conditions thus included are the so-called colds in the head, sore throats, and tracheal coughs. The word "fever" has been avoided, inasmuch as any rise of temperature is, more often than not, local and not general; indeed, the true body temperature, obtained either per rectum or by means of the urine, is more often than not subnormal. Colds are always acute at the onset but may go on to a chronic stage, persisting for even 20 years, punctuated at intervals by acute exacerbations. The acute cold exhibits the following stages. 1. Local anæmia of the mucous membrane. This probably precedes infection, so ought perhaps to be called a pre-catarrhal condition. This is succeeded by local hyperæmia,

the natural response of the body to the preceding anæmia. 2. After infection there is a period of incubation, during which the hyperæmia increases to a greater or less extent. Few opportunities of measuring this have presented themselves, but in one case it could be fixed at only two hours; the usual period, however, seems to be about 12 hours, but varies according as to whether the infection is a fresh one from without or due to a lighting up into activity of organisms already resident in these parts. During this period there may be dryness and tickling of the palate and fauces and a few sneezes may be given, soon to be followed by a general feeling of malaise and chilliness, which marks the completion of the incubation period and the onset of the third stage—viz., the period which may be called the "catarrhal plateau." This is characterised by greatly increased mucous secretion, the attempt of the body to rid itself of the invaders. If the fauces be involved there is a definite sore-throat, if the trachea a resultant cough. The feeling of general malaise continues, often accompanied by headache, constipation, and distaste for food; there may be some pyrexia; the secretion of sweat and urine is diminished and the latter may be loaded with urates. After from 18 to 48 hours the mucous secretion diminishes and the fourth or subacute stage is entered upon. The mucous discharges become thick and contain leucocytes and lymphoid cells which cause the discharges to become yellow in colour. This lasts for a period varying from two or three days to as many weeks, when it either ceases and cure is established, or it persists for months or even years and enters upon the fifth stage, which is that of true chronicity, marked by continuous excessive secretion of thick mucus and the feeling aptly described as "stuffiness of the nose." Such a chronic condition is punctuated at intervals by periods of exacerbation or by acute attacks due to a second organism.

III.—BACTERIOLOGY.

A.—Technique Employed.

Before any attempt can be made at the determination of the bacterial agents in the production of pathological conditions it is obviously necessary to determine what are the normal bacterial inhabitants of the part or parts. Accordingly healthy noses and throats were examined as well as catarrhal. The technique employed was as follows.

1. *For the trachea.*—The mouth having been thoroughly gargled several times with sterile water, by means of a violent cough some mucus was expectorated and received in sterilised water; a small compact piece was washed two or three times and then inoculated upon one or more of the following—agar, blood agar, nutrose ascitic agar or so-called "nasagar," blood serum. After 24 hours' incubation at 37° C. films were prepared as well as some from the original mucus, stained with methylene blue and by Gram's method, and examined microscopically. The organisms were then isolated when necessary.

2. *For the throat.*—Swabs were taken from the hyperæmic areas, soft palate, posterior pharyngeal wall, fauces or tonsils, and treated as in the case of the tracheal mucus.

3. *For the nose.*—In order to avoid contamination with the organisms infecting the vibrissæ and vestibule the following procedures were adopted: (a) A piece of sterilised glass tubing about three inches long and of ample bore so as to admit the passage of a platinum loop was inserted up the nostril; along this tube a sterile loop was pushed and the protruded end rubbed over the surface of the nasal mucosa; it was then withdrawn through the glass tubing and a smear made upon agar, blood agar, blood serum, or nasagar, two or three such smears being usually made upon different media. (b) As an alternative method a sterilised nasal speculum was used to separate the nasal orifice and by means of a sterile swab cultures taken as high up the septum and turbinates as it was possible to get. (c) Experiment, however, showed that these precautions were hardly necessary in the case of nasal catarrh where organisms are always plentiful and that certain advantages were to be obtained by using the following procedure. The orifice of the nose having been well washed with warm soap and water and dried upon sterile lint, one nostril was closed and the nasal secretion forcibly expelled from the other upon sterilised cotton-wool. Ample material is thus obtained to inseminate numerous tubes and plates and to prepare films. In several cases cultures were made by two of these methods and identical results obtained.

¹ A thesis accepted for the M.D. degree (Branch II.), University of London.

In from 18 to 24 hours smears were made from the cultures and stained by Gram's method and with carbol methylene blue and with carbol fuchsin. Subcultures were then made upon agar and nasgar plates and the organisms which preponderated in numbers isolated.

B.—Results Obtained.

1. *Trachea*.—Inasmuch as no appreciable amount of mucus can be secured from the trachea in health the only results obtained have been from catarrhal cases. In every one of the cases a coccus was isolated which did not stain by Gram's method. The various cultural reactions in broth, on agar, gelatine, and nutrose ascitic agar (nasgar), as well as the microscopical appearances, indicated that this was an organism indistinguishable from the micrococcus catarrhalis. Cocci staining by Gram's method as well as various bacilli both staining and failing to stain by Gram's method were occasionally found, but were not constant like the micrococcus catarrhalis. It is therefore possible that this latter organism may be the common cause of tracheitis and by downward extension possibly, too, of bronchitis. It must, however, be noted that Gram cocci are present in 78 per cent. of normal throats and in 68 per cent. of catarrhal throats. The micrococcus paratetrigenus described by Roger in 1897, and also found by Bezançon and de Jong² in many cases during an epidemic of bronchial catarrhs in Paris in 1904-05, and by Benham³ in 11 out of 14 cases investigated in Brighton during 1907-08, was not met with.

2. *Throats*.—The bacteriological findings from 23 cases of as healthy throats as could be obtained and from 180 cases of non-diphtheritic inflammatory throats are given in Table I. The results were both disappointing and confusing. As is seen in the table, there were as many diphtheroids, Gram cocci and Friedländer's bacilli, in the one class as in the other. In neither was the micrococcus paratetrigenus ever seen in films or cultures.

TABLE I.

	Healthy.	Inflammatory.
Diphtheroids...	39 per cent.	38 per cent.
Bacillus septus ...	35 „ } 39 per cent.	29 „ } 38 per cent.
Hoffmann's bacillus ...	4 „ }	9 „ }
Gram cocci ...	78 „	68 „
+ Gram cocci ...	70 „	83 „
+ Gram bacilli ...	40 „	40 „
Bacillus of Friedländer ...	4 „	3.3 „

Two points may, however, be noticed. First, the question of virulence and pathogenicity could not be determined; and secondly, my figures for diphtheroids in normal throats is very much higher than that found by most authorities—viz., about 8 per cent. Whether the small number of cases examined (23), the class of patient (medical students and out-patients at hospital), or the time of the year (January and February) is responsible for this great divergence I am unable to say. In a series of 20 cases of slight sore throat accompanied by cold in the head or tracheal cough either diphtheroids, or Gram cocci, or both, were present in every instance, and I can only express the belief that these organisms are concerned in the production of sore throats. Dr. M. H. Gordon by the accidental absorption through a pipette of an emulsion of micrococcus catarrhalis has established the fact of this organism being capable of doing so.

3. *Noses*.—The difficulty of securing reliable bacteriological examinations of normal nasal cavities is great in London as so few people fail to give a history of recent colds; in the case of 20 as normal noses as were obtainable the following were the results of the alternative method mentioned under 3 (b). None were absolutely sterile but five only yielded air organisms such as sarcina lutea and aurantiaca, 10 gave only +Gram-staining cocci, six of these being staphylococcus albus, two staphylococcus aureus, and two staphylococci albus and aureus. From the remaining five cases in addition to Gram-staining cocci, the bacillus septus was obtained in one, and cocci failing to retain the stain by Gram's method and belonging to the pseudo-catarrhalis group in the other four. Air organisms were also present in most of these 15 cases. Of published observations elsewhere may be mentioned those of Hasslauer,⁴ who

examined 111 cavities and found staphylococcus pyogenes albus in 25 per cent., pneumococcus in 20 per cent., streptococcus pyogenes in 17 per cent., and diphtheroids in 13 per cent., more than one and not more than three or four different organisms being present. Von Besser⁵ examined 81 cases and found staphylococcus pyogenes aureus in 17.5 per cent., pneumococcus in 17.5 per cent., streptococcus pyogenes in 8.7 per cent., and Friedländer's bacillus in 2.5 per cent. Lewis and Turner⁶ examined 26 specimens from 16 persons; only three of these were sterile, in 13 only one organism was present, in nine two organisms only, and in one three organisms. On investigating the pathogenicity of the organisms which they isolated these last observers found that the organisms derived from nine healthy noses were non-pathogenic to animals, and in two cases they were pathogenic, and the conclusion was arrived at that not only are the organisms present only in small numbers but that their virulence and vitality alike are low.

The bacteriology of the mucosa in 42 cases of colds investigated in London during the years 1905, 1906, 1907, 1908.—The results which I have obtained in 42 cases of colds are given in tabular form in Table II.; only the presence of organisms which may be regarded as possibly causal is indicated. A few cocci staining by Gram's method and occasional non-pathogenic air organisms were also found in the cultures, but once identified as such were then disregarded. It will be seen that only one of the four organisms was present in the great majority of the cases. In Nos. 2 and 6 (Table III.) a very few of the second organisms were present, while in Nos. 11, 13, and 21 two organisms were found in about equal numbers; these last three cases were of a specially severe type.

TABLE II.

Bacillus of Friedländer alone	In 8 cases = 19 per cent.
„ influenza „	„ 1 case = 2.4 „
„ septus „	„ 11 cases = 26.2 „
Micrococcus catarrhalis „	„ 12 „ = 28.6 „
Bacillus of Friedländer + bacillus septus ...	„ 3 „ = 7.1 „
Bacillus of Friedländer + micrococcus catarrhalis ...	„ 2 „ = 4.7 „
Bacillus septus + micrococcus catarrhalis ...	„ 4 „ = 9.7 „
No definite organism isolated ...	„ 1 case = 2.4 „
Total number of cases	42

Too much importance must not be attached to the percentage figures given, although the results are obtained from observations spread over nearly four years. The bacillus of Friedländer is, I think, thereby made out to be a more frequent cause of colds than it really is, while the figures for bacillus septus and micrococcus catarrhalis are too low. By studying, say, 50 cases in any given epidemic results totally at variance with these might be obtained and a percentage value of even 100 obtained for either the bacillus septus or micrococcus catarrhalis. It is due to this fact that the claims of these organisms have been unduly pressed at various times by different observers. The rarity of the bacillus influenzae and the total absence of the micrococcus paratetrigenus are alike striking in the above series; this is probably due entirely to the fact that London was not affected by epidemics due to either of the above micro-organisms during these years.

C. Justification of the View that Colds are Due to the Organisms Indicated.

It may well be asked what grounds there are for regarding these several organisms as even being capable of producing colds, and still more especially of having produced the particular attacks here indicated, inasmuch as it has been shown that the micrococcus catarrhalis and closely allied forms are frequently resident in the healthy tract, that the bacillus of Friedländer is present in between 2 and 4 per cent. of healthy noses, and that diphtheroids infect from 8 to 12 per cent. of noses and throats presenting no pathological features. To this it may be replied that from a certain percentage of normal throats pneumococci or the Klebs-Löffler bacillus may be similarly isolated and may even

² Bulletin de la Société Médicale des Hôpitaux de Paris, March 2nd and 16th, 1905.

³ Proceedings of the Brighton and Sussex Medico-Chirurgical Society, 1903, p. 84.

⁴ Centralblatt für Bakteriologie und Parasitologie, Jena, 1902, Band xxxiii., p. 47.

⁵ Beiträge zur Pathologischen Anatomie und Allgemeinen Pathologie, Jena, 1889, Band vi., S. 33.

⁶ Edinburgh Medical Journal, November, 1905, p. 393.

possess pathogenic properties, and yet these cases have neither pneumonia on the one hand nor diphtheria on the other. The important factors are, *inter alia*, first, one of pathogenicity of the organism, and, secondly, of susceptibility of the individual. These questions I have the more

TABLE III.—Summary of the Bacteriology of the Cases.

No. of case.	Nature of case.	Bacillus of Friedländer.	Bacillus Influenzae.	Bacillus septus.	Micrococcus catarrhalis.
1	Chronic 12 years.	+	—	—	—
2	Acute 2 days.	—	—	Few.	+
3	„ 1 day.	+	—	—	—
4	Acute upon chronic of 4 months.	+	—	—	—
5	Acute 1 day upon subacute of 2 weeks.	+	—	—	—
6	Acute 5 days.	+	—	Few.	—
7	„ 12 hours.	—	+	—	—
8	„ 12 „	—	—	+	—
9	„ 3 „	—	—	+	—
10	Subacute 12 days.	—	—	—	+
11	Acute 2 days.	—	—	+	+
12	„ 1 day.	—	—	—	+
13	„ 2 days.	+	—	+	—
14	„ 1 day.	—	—	+	—
15	Subacute 14 days.	—	—	+	—
16	Chronic 17 years.	+	—	—	—
17	Acute 2 days.	—	—	+	—
18	„ 3 days.	—	—	—	+
19	„ 1 day.	+	—	—	—
20	„ 1 „	+	—	—	—
21	„ 1 „	+	—	+	—
22	„ 2 hours.	+	—	—	—
23	„ 2 „	—	—	—	+
24	„ 2 days.	—	—	+	—
25	„ 1 day.	—	—	+	+
26	„ 4 days.	—	—	+	—
27	Acute on subacute of 14 days.	—	—	—	+
28	Acute 1 day.	—	—	—	+
29	„ 2 days.	+	—	—	+
30	„ „	—	—	+	—
31	Acute two days upon chronic of 20 years.	+	—	—	+
32	Acute 1 day.	—	—	+	—
33	„ 3 days.	—	—	+	+
34	Chronic tracheal catarrh of 20 years.	—	—	—	+
35	Acute outburst in No. 34.	—	—	—	+
36	Acute 1 day.	—	—	—	+
37	„ 3 days.	?	—	—	—
38	„ 2 „	—	—	+	—
39	„ 3 „	—	—	—	+
40	„ 3 „	—	—	—	+
41	„ 1 day.	—	—	—	+
42	Chronic 10 years, with acute outbursts.	—	—	+	+

fully investigated in the case of the bacillus of Friedländer and the inference of its causal relationship seems amply justified. As regards pathogenicity, each strain on isolation was introduced into a rabbit, rat, and guinea-pig. In all but two cases where the animals were made extremely ill but survived for three days, when they were killed by chloroform, the animals died, usually within 24 hours. In every case the typical capsulated diplo-bacilli were recovered from the heart blood and peritoneal fluid; post mortem the animals presented areas of pneumonic lung, enlarged spleens, and, where the inoculation had been intraperitoneal, peritonitis, especially over the liver and spleen. The virulence was of a high degree.

Secondly, Case 1 was proved to have the organism continually present in large numbers in the nasal mucosa. During several exacerbations these were discharged from the nose in large numbers; within a very short time workers in the same room, whose nasal cavities had just been proved to be practically sterile and who were free from colds, developed severe attacks, during which the bacillus of Friedländer was found to be abundantly present in their nasal mucus. Further, Case 1 was finally cured both of the chronic and acute attacks by injection of a vaccine prepared from his organism and repeated cultivations have since failed to find the bacillus of Friedländer present. Again, in the instance of Case 4, a chronic one of four months' standing, the disappearance of symptoms and organism was simultaneous.

Thirdly, an emulsion of Friedländer's bacillus was spilt in the laboratory where three individuals were working; within a few hours each developed a mild catarrhal attack during which the bacillus was found in the nasal mucus.

Fourthly, reference to the opsonic charts (1 and 2) appended of Cases 1 and 16 shows that the index to Friedländer's bacillus was abnormally high during the chronic stages and that it was influenced by an exacerbation of the infection just as one would expect it to be were the acute attack due to the given organism.

Fifthly, the percentage of cases in which this organism was found was very much in excess of that found in healthy noses by von Besser, 2·5, and by Lewis and Logan Turner, 4.

The claims of the bacillus influenzae to be regarded as a cause of nasal catarrh are too well known to require discussion, whilst those of the micrococcus catarrhalis have been well demonstrated by Dunn and Gordon⁷ in the case of an epidemic in Hertfordshire which closely simulated influenza, by Pfeiffer, by Lord, and by Bezançon and de Jong in Paris.⁸ By accidentally sucking up some emulsion of this organism which he had prepared Gordon⁹ records the onset after 24 hours of a cold which gradually extended down the trachea. From the nasal discharge he recovered the organism at the close of the attack. In Cases 2, 10, 12, 18, 23, 27, 28, 35, 36, 39, 40, and 44 this organism was obtained in practically pure culture from the nasal mucus. The patient in Case 2 was one of a household of eight who had been attacked one after the other by severe colds. Cases 27, 25, and 28 present this interesting feature—they were "contacts." Case 27 had had a subacute attack for about 14 days and developed an acute cold without sore throat. 24 hours later patient No. 25 had a severe cold beginning with a sore throat. No. 28 then came into contact with No. 25 and followed suit without a sore throat. All three patients yielded abundant growth of the micrococcus catarrhalis; from No. 25 alone was the bacillus septus in addition isolated.

As regards the capacity of the micrococcus catarrhalis to produce nasal catarrh there is then little doubt, but whether it is the direct causal agent in all catarrhal cases in which it alone is isolated is not so certain. A coccus at all events very closely allied to it is, as I have shown, an extremely common inhabitant in normal throats, perhaps even to the extent of from 70 to 80 per cent.

The claims of the bacillus septus are much more difficult to decide. It is true that Cautley¹⁰ found it in seven out of eight cases of cold which he investigated, or in 88 per cent., Prosser White¹¹ in 17 out of 21, or in 81 per cent., and Benham in 25 out of 27, or in 91 per cent. My results were in 11 out of 42 cases, or 26·2 per cent., by itself, and in three others along with Friedländer's bacillus and in two with the micrococcus catarrhalis. It is true that the percentage of healthy noses which nurture this organism is between 8 and 12 per cent. and the contrast seems almost convincing. It must, however, be noted that these observers were not aware that Friedländer's bacillus could produce a cold and accordingly omitted to consider its etiological claims. In five out of his 27 cases Benham found —Gram bacilli and one of these was proved to be the bacillus of Friedländer and the others may have been; in two others the bacillus influenzae seems to have been present, and in yet 13 other

⁷ Brit. Med. Jour., August 26th, 1905.
⁸ Bulletin de la Société Médicale des Hôpitaux de Paris, March 2nd and 16th, 1905.
⁹ Brit. Med. Jour., June 2nd, 1906, p. 1318.
¹⁰ Local Government Board Reports, 1894-95.
¹¹ Catarrhal Fevers.

instances—Gram cocci which may have been micrococcus catarrhalis were seen, and in two cases isolated and proved to be the micrococcus catarrhalis, so that Benham's deductions may be entirely misleading, as may also be those of the other observers above referred to. A consideration of the occurrence in catarrhal affections of the eye and urethra of its close ally, bacillus xerosis, still further weakens its claims. Pathologists no longer regard this as a pathogenic organism, yet in the healthy eye and healthy urethra it is not commonly present, whereas in catarrhal conditions set up by the Koch-Weeks and Morax-Axenfeld bacilli and by the gonococcus it is practically omnipresent (in between

together. Further, in the instance of Case 17, a medical man and close observer, suffering from an acute attack, to which he was very subject and which always continued subacute for several weeks, I isolated this organism and made a vaccine for the patient. Upon the sixth day when he felt very ill I injected him with 275,000,000 dead organisms. On the next day he was better, and on the following day he was quite well, while his index rose from 0·9 to 1·7. Again, a friend who travels much by rail and always catches cold and sore throat on these occasions, upon several of which I isolated the bacillus septus, was about to undertake a long train journey; he welcomed the suggestion of an inoculation and

TABLE IV.—*Table of Symptoms, with Bacteriological Findings.*

No. of case.	Headache.	Malaise.	Sore throat.	Tonsillitis.	Cough.	Nasal discharge.	Muscle pains.	Temperature above 100° F.	Eustachian tube involved.	Sneezing.	Tracheitis and bronchitis.	Acute.	Subacute.	Chronic.	Bacillus septus.	Bacillus influenza.	Bacillus Friedländer.	Micrococcus catarrhalis.
1	—	++	—	+	—	+++	—	—	—	+	—	—	—	+	—	—	+	—
2	++	++	—	—	—	++	+	—	—	+	—	+	—	—	—	—	—	—
3	—	+	—	—	—	++	—	—	+	+	—	+	—	—	—	—	—	+
4	—	+	—	—	—	+	—	—	—	+	—	—	+	—	—	—	+	—
5	—	++	—	—	—	++	—	—	—	+	—	—	+	—	—	—	+	—
6	—	++	+	—	—	++	—	+	—	—	—	+	—	—	+	—	+	—
7	—	++	—	—	+	++	—	+	—	—	—	+	—	—	—	+	+	—
8	—	—	+	—	—	+	—	—	—	+	—	+	—	—	+	—	—	—
9	—	—	+	—	—	+	—	—	—	—	—	—	—	—	—	—	—	—
10	—	—	—	—	+	+	—	—	—	—	+	—	+	—	—	—	—	+
11	—	+	+	—	+	+	—	—	—	—	—	+	—	—	+	—	—	+
12	—	+	+	+	+	++	—	—	—	—	—	+	—	—	—	—	—	+
13	+	++	+	+	—	+++	+	—	—	—	+	+	—	—	+	—	—	+
14	—	—	—	—	+	++	—	—	—	+	—	+	—	—	+	—	+	—
15	—	—	—	+	—	—	—	—	—	—	—	+	—	—	+	—	—	+
16	—	—	—	—	—	+	—	—	+	—	—	+	—	—	+	—	—	—
17	—	+	+	—	—	+	—	—	+	—	+	—	—	+	—	—	+	—
18	++	—	+	+	—	+	—	—	—	—	—	+	—	—	+	—	—	—
19	—	+	—	—	—	+	—	+	—	—	+	+	—	—	—	—	—	+
20	—	+	—	—	—	+++	—	—	—	—	—	+	—	—	—	—	+	—
21	—	++	++	—	—	++	—	—	+	+	—	+	—	—	—	—	+	—
22	—	+	—	—	—	++	++	+	—	—	—	+	—	—	+	—	+	—
23	—	+	—	—	—	++	—	—	—	+	—	+	—	—	—	—	+	—
24	+	+	+	—	++	++	—	—	—	—	+	+	+	—	—	—	—	+
25	—	—	+	—	—	+	+	—	—	—	—	+	—	—	+	—	—	—
26	—	—	+	—	+	+	—	—	—	—	+	+	—	—	+	—	—	+
27	—	+	—	—	—	+	—	—	—	—	—	+	—	—	+	—	—	—
28	—	—	—	—	+	+	—	—	—	—	—	—	+	—	—	—	—	+
29	+	++	—	—	+	++	—	—	—	—	—	+	—	—	—	—	—	+
30	—	—	+	—	++	+++	++	—	+	—	+	+	—	—	—	—	+	+
31	+	+	—	—	—	+	—	—	—	—	—	+	—	—	+	—	—	—
32	+	+	+	—	++	++	—	—	+	—	—	—	—	+	+	—	+	—
33	—	—	+	+	+	++	—	—	—	+	+	—	+	—	+	—	—	+
34	—	—	—	—	+	—	—	—	—	—	+	+	—	—	—	—	—	+
35	—	—	+	—	—	+	—	—	—	—	—	—	—	+	—	—	—	+
36	—	+	—	—	++	+	—	—	—	—	—	+	—	—	—	—	—	+
37	+	+	—	—	—	++	—	—	—	—	+	+	—	—	—	—	?	—
38	—	—	+	—	—	+	—	—	—	—	—	+	—	—	+	—	—	—
39	—	+	—	—	+	++	—	—	—	—	—	+	—	—	—	—	—	+
40	—	—	—	—	++	++	—	—	—	—	—	+	—	—	—	—	—	+
41	—	++	—	—	++	+	—	—	—	+	+	+	—	—	—	—	—	+
42	—	—	+	—	—	++	—	—	+	—	—	—	—	+	+	—	—	+

95 and 99 per cent. of all cases). My figures—in 9 out of 20, or 45 per cent.—moreover show that it may be a very common inhabitant of the non-catarrhal throat. Distinct evidence of the pathogenicity of the bacillus septus is therefore very necessary and is so far entirely lacking, despite several attempts at demonstration. Despite these facts certain considerations induce me to think that it is a factor in the production of colds. In 11 out of my 42 cases this organism was present in almost pure culture—at least, despite the use of such culture media as blood agar, blood serum, and nutrose ascitic agar I could find no other organism recognised as the possible cause of a cold. The cold and organism disappeared

was given 275,000,000 dead organisms. Despite a long and very cold all-night journey, for the first time for years he developed neither sore throat nor nasal catarrh, nor during the succeeding 12 months has he developed a cold at all. Close attention to the clinical symptoms in my cases has revealed the fact that the bacillus of Friedländer rarely, if ever, produces a sore throat. In Cases 6, 13, and 21, in which both the bacillus of Friedländer and the bacillus septus were found a sore throat was a prominent feature, and out of the 11 cases in which the bacillus septus alone was found, ten had pronounced sore throats as the earliest symptom. It would therefore appear that the chief rôle of the

bacillus septus is the production of the sore throat. The fact that in my 220 cases of sore throats the percentage in which this organism was found was only 27 against a percentage of 45 for normal throats would seem to negative this view; but I think that chance, the time of year, or some other factor decreed that my figures for healthy throats should be much too high, for other observers have found the percentage to be between 8 and 12 per cent. To sum up, I believe that the *bacillus septus* is the true etiological factor in the production of a certain percentage of colds, but that through neglect to use appropriate media and to observe the occurrence of the other possible organisms certain observers have obtained much too high a figure and have been thereby led to the belief that it is *the* cause of the common cold.

As regards the *micrococcus paratetrigenus*, which was not present in any of my cases, ample evidence of pathogenicity is forthcoming. Thus, Bezançon¹² found it in the blood of a patient dying from endocarditis, in a case of fatal pulmonary gangrene, and in the cerebro-spinal fluid of a patient in whom paraplegia followed upon pulmonary infection due to this organism. Not only did he find it in a state of practical purity in the sputum of cases of bronchitis and broncho-pneumonia but also in all those of angina with pultaceous exudate during the winter of 1904-05. Benham¹³ records similar results at Brighton during 1907-08.

Three other important considerations there are which strongly substantiate the view that these organisms stand in a directly causal relationship to the common cold. First, that during any given epidemic a diagnosis of the organism present can almost infallibly be made, as is shown later, from consideration of the symptoms, each organism producing its own type of cold; secondly, that during any given epidemic of colds the same organism is recoverable from practically every case in pure culture; and thirdly, that subsequent immunity can be secured by injections at suitable intervals of vaccines of these organisms.

If the results given in Table IV. be compared with those obtained by Benham¹⁴ it will be seen that the symptoms caused by the *micrococcus catarrhalis* and the *micrococcus paratetrigenus* closely resemble each other.

IV.—DIFFERENTIAL DIAGNOSIS OF THE SEVERAL VARIETIES OF COLD.

Each organism produces a more or less distinct type of cold. If only one organism be present the differential diagnosis is, as a rule, easy, but when two occur together, as in six of my cases, the difficulty is greater. Division of colds into acute, subacute, and chronic facilitates the consideration—by subacute I mean lasting from two to three months, with an occasional slight exacerbation; by chronic those that persist over six months, even to 20 years. Examination of Table IV. will show that the following scheme may be drawn up:—

—	Bacillus of Friedländer.	Bacillus influenzae.	Bacillus septus.	Micrococcus catarrhalis.
Acute	+	+	+	+
Subacute	+	No.	Rarely.	+
Chronic... ..	+	—	—	+

Thus we see that the only three cases of truly chronic nasal catarrh which were fully investigated were all due to the *bacillus* of Friedländer.

While the *micrococcus catarrhalis* is probably largely responsible for chronic tracheitis—though secondary infection by staphylococci, streptococci, and more or less avirulent pneumococci also probably plays an important part—it would not appear to cause a chronic nasal catarrh, unless perhaps in cases where the infection extends to the accessory sinuses, and especially the Eustachian tube as in Case 42.

Subacute colds appear to be due to either the *bacillus* of Friedländer or to the *micrococcus catarrhalis* or *micrococcus paratetrigenus*. The two latter fall into this category from their great tendency to invade the trachea and bronchi. Neither the *bacillus* of Friedländer nor the *bacillus septus*,

so far as I am aware, induces catarrh of the trachea; the former probably does in those cases of pneumonia for which it is responsible, but after all these are not common. I have never recovered the *bacillus septus* from tracheal mucus. The persistent hacking tracheal or “winter” cough is thus probably due either to the *micrococcus catarrhalis* or *micrococcus paratetrigenus*. Not only does the *bacillus* of Friedländer fail to affect the trachea, but it also does not cause a painful throat, differing in this both from the *bacillus septus* and the *micrococcus catarrhalis*. It confines its attention to the nose and accessory sinuses and the post-nasal space.

The differential diagnosis of the acute forms of cold is not very difficult. The mode of onset and the condition of the throat are very helpful. If the first symptoms affect the fauces and pharynx either the *micrococcus catarrhalis* or the *bacillus septus* is certainly present; if the larynx and trachea become speedily involved the former of these or *micrococcus paratetrigenus* is indicated; to hear a patient coughing is quite sufficient to enable a diagnosis of *micrococcus catarrhalis* or *micrococcus paratetrigenus* to be made. The severity of the constitutional symptoms also varies: those of the *bacillus septus* are but slight, those of the *micrococcus paratetrigenus* are moderate unless the epidemic assume a broncho-pneumonic type, while the lassitude and mental depression in the cases of the three others, and especially of influenza, may be extreme. The temperature is high as a rule (from 100° to 104° F.) only in the case of influenza and is often accompanied by a relatively slow pulse. Other systems, such as the circulatory, nervous, or digestive, also frequently become involved. Nasal catarrh, as a rule, is slight and much yellowish-green lumpy mucus may be expectorated swarming with the bacilli. In the cases due to Friedländer’s *bacillus* the temperature rarely rises above 99·5°, and the pulse is not slow, nor do other systems become involved. The flow of nasal mucus is always extreme; in one case it was found to be between 15 and 20 cubic centimetres per hour.

Value of differential diagnosis in prognosis.—The *bacillus* of Friedländer being probably the only cause of a chronic nasal catarrh and the risk of involvement of the Eustachian tube, middle ear, and accessory sinuses being considerable, the prognosis in the case of this organism should be very guarded and much greater care should be taken by the patient. As will be mentioned later, the risks of chronicity can be considerably reduced by the administration of an autogenous vaccine.

In the case of the *bacillus septus* even sub-chronicity is rare and complications of any sort are very little to be dreaded; this is the type of cold which gets well of itself with very little attention and a good prognosis can therefore be given.

The case of the *micrococcus catarrhalis* stands upon a different footing and the prognosis must be much more guarded. Extension to the Eustachian tube and middle ear is not altogether infrequent, while downward extension to the trachea and bronchi is habitual.¹⁵ A persistence of the cough is therefore to be anticipated and possible bronchial complications are to be feared. I doubt if these latter ever occur with the *bacillus septus* and probably but rarely with the *bacillus* of Friedländer. The nervous, digestive, and circulatory systems are also liable to be affected.

These remarks about the *micrococcus catarrhalis* probably hold with additional force in the case of the *bacillus influenzae*, but of this I cannot speak from experience, having only encountered one mild case during the past four years.

In the case of the *micrococcus paratetrigenus* the chief danger would appear to be bronchitis and broncho-pneumonia, as in Bezançon and de Jong’s cases.

V.—CAUSATION OF COLDS.

It may be granted that the essential factor is the occurrence of infection; infection alone, however, is insufficient unless the dose of organisms be sufficiently large and their virulence sufficiently great. As we have seen, from 8 to 12 per cent. of healthy noses contain diphtheroids and from 2·5 to 4·0 per cent. Friedländer’s *bacillus*; similarly a considerable percentage of throats harbour pneumococci and

¹² Précis de Microbiologie Clinique, p. 143.
¹³ Proceedings of the Brighton and Sussex Medico-Chirurgical Society, 1908.
¹⁴ Loc. cit.

¹⁵ Barker described before the Surgical Section of the Royal Society of Medicine on March 10th last a case of meningitis secondary to otitis media, which in turn must have been secondary to a nasal catarrh. The *micrococcus catarrhalis* was obtained in pure culture from the middle ear and meninges.

Klebs-Löffler bacilli, yet develop neither pneumonia on the one hand nor diphtheria on the other.

Age.—Colds are the more dangerous to the very young and the very old, but age seems to have no influence whatever upon the incidence of an attack.

Conditions of life.—Those who live much in the open air certainly seem less liable to colds than those who live in cities, but poverty and wealth seem to have but little bearing. Colds are no respecters of persons; if anything the rich are more liable than the poor, or, at all events, they make more of their colds. With a view to ascertain the influence of fatigue and lack of food, upon one day in winter I did without food all day, took excessive exercise, returning home covered with perspiration. Quickly stripping I then stood hot and exhausted at an open window for ten minutes till thoroughly chilled. Although the bacillus of Friedländer was then in my nose, as I had proved the day before, no cold developed. A fortnight later, warmly clad and well fed, I caught an unsought-for cold.

Opsonic index.—Reference to the chart of Case 1 will show that a high opsonic index is no protection against an acute attack, for such supervened when the index stood at 1.56, at 1.36, and again at 1.5. Anything which will, however, cause a sudden lowering of index will probably predispose to an attack. As I will show presently, the tissue plasma has a higher index than that of the blood. It seems probable, then, that local reduction in the index of the tissue plasma of the nasal mucosa is an important adjuvant to infection. How this can be brought about I know not, but can only suggest that local vaso-motor disturbance may play an important part, for one of the earliest symptoms of approaching catarrh is great congestion of the nasal mucosa. This is purely reflex, for it can often be removed by setting up another reflex, as by hanging the head out of an open window, sponging the skin of the body with cold water, or if the affection be unilateral by merely inclining the head to the opposite side. This view is in accord with the universal experience that the onset of a cold may often be determined by a cold draught of air striking the back of the head for a very few minutes. To this question of vaso-motor disturbance reference will again be made under the question of cure. That infection is accompanied, or more probably preceded, by a fall in the opsonic index and recovery by a rise is well shown by the following observations upon Case 1. About six weeks after treatment with a vaccine and cure of the long-standing chronic nasal catarrh a specimen of blood was taken. About 12 hours later all the symptoms of an oncoming acute cold began to develop and a second specimen was taken. Next day the cold had completely aborted and a third sample of blood was obtained. The indices of the three were then found to be as follows: before the onset of the cold, 2.6; at the onset, 2.0; and when the cold had aborted, 5.8. The cause of the spontaneous and speedy recovery was thus very evident.

The influence of the daily processes of life, such as the morning bath, meals, exercise, and rest, upon the opsonic index was also studied. With this end in view specimens of blood were taken at the following times and their indices were determined: (1) immediately on rising; (2) a quarter of an hour after the morning bath; (3) two hours after breakfast; (4) at 4 P.M.; (5) at midnight, i.e., after completion of digestion of dinner and after an evening walk; and (6) at 3 A.M., i.e., after three hours' repose. The results obtained, being the numbers of organisms taken up by 100 polymorphonuclear leucocytes, are set out in the following table:—

TABLE V.

Date.	1	2	3	4	5	6
15/5/06	380	402	435	—	—	—
15/5/06	317	351	380	—	—	—
29/5/06	680	736	733	810	861	—
1/6/06	165	150	134	—	—	—
6/6/06	534	571	—	—	626	536
12/6/06	375	413	—	—	427	—

From this we see that there is a steady gradual rise throughout the day, a maximum seemingly being attained

after digestion of the main meal of the day has been completed and after a full day's exercise has been taken. During the night the index steadily falls and from the determination of 6/6/06 would seem to reach a minimum by 3 or 4 A.M.

Experiments into the causation of this diurnal variation.—Assuming it, then, to be a fact that the opsonic index of the blood to various organisms rises during the day and falls during the night, the question arises as to the causation of this. The digestion of a meal is said to result in a tidal increase and decrease of the alkalinity of the blood, owing to the secretion of hydrochloric acid during digestion in the stomach and of alkalies during digestion in the duodenum. Exercise is said to result in decrease in the alkalinity of the blood owing to the formation of acids by the muscle metabolism. Observations were made to see whether an alteration either in the way of increase or decrease in the alkalinity of the serum had any influence upon the opsonic index. The normal alkalinity of the blood is between N/25 and N/30, say N/28. To one volume of blood serum were accordingly added (1) one volume of distilled water giving an alkalinity of N/56, (2) one volume of N/28 caustic soda giving an alkalinity of N/28, and (3) one volume of N/56 hydrochloric acid = N/112. These diluted sera were then used as if they were normal sera and comparison was made of their opsonic power, with the result (counts are numbers of organisms in 50 cells):—

TABLE VI.

Date.	Serum.	Alkalinity.		
		N/28	N/56	N/112
		Index.	Index.	Index.
8/6/06	1	71 = 1	47 = 0.66	66 = 0.93
—	2	36 = 1	68 = 1.89	53 = 1.75
12/6/06	1	675 = 1	641 = 0.95	462 = 0.68
16/6/06	1	134 = 1	174 = 1.30	200 = 1.49
—	2	176 = 1	169 = 0.96	190 = 1.14
—	3	139 = 1	189 = 1.35	138 = 1.00
		6.00	7.11	6.99

It will be seen that no constant effect was produced; it would, however, appear that a reduction in the alkalinity of the blood serum has a slight effect in raising the opsonic index. This is in accord with the findings of Hektoen and Ruediger¹⁶ that sodium bicarbonate among chemical bodies is a non-specific anti-opsonin. Lactic acid, again, is another such body; it may therefore be assumed that the accumulation of lactic acid in the body, as occurs during excessive muscular fatigue, will also conduce to infection. So well equipped is the human body with means to cope with disturbances in any of its functions that it is obvious that only when these disturbances are unusually great will the protective mechanism be broken down and predisposition to infection be established.

(To be continued.)

A CASE OF LICHEN PLANO-PILARIS IN WHICH THE SPINOUS ELEMENT PREDOMINATED.

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At the end of April, 1908, a married woman, aged 30 years, consulted me at St. John's Hospital for Skin Diseases, Leicester-square, concerning an eruption which she first noticed about six weeks previously. She had two children, five and two years old respectively. The patient considered herself to be a healthy woman, but had recently felt unusually fatigued and nervous.

Family history.—The patient's mother had died from consumption at the age of 34 years. There was nothing further

¹⁶ Journal of the American Medical Association, May, 1906.