body as the simple reaction of two simple cell organs. He must squarely face the probability that the nucleus is itself a complex organism, as he must also admit that the cell body consists not of one protoplasm but of many protoplasms. Cytologists are laboriously endeavoring to ascertain in what measure the chromosomes are qualitatively different in respect to the processes of growth and differentiation. If such qualitative differences are definitely proved to exist, a new and great field will be opened in cellular physiology and pathology. Already attempts have been made to bring the facts of tumor formation and the like into relation with disturbances in the chromosome groups. I have stated that false combinations of chromosomes have been experimentally shown to lead to false forms of development. So far as I am aware, attempts to find a similar explanation of perverted growths in the body have thus far been without positive results, though some interesting suggestions in this direction have been offered. But it should not be forgotten that in nuclei which show little or no visible differentiation of the chromosomes profound changes might take place without giving visible sign of their presence. Such changes might be immediately induced by any one of many conceivable causes—by parasites, perverted forms of metabolism, the presence of specific forms of toxins and so on—and having once arisen might persist for an indefinite number of cell generations long after the initial exciting cause had passed away. It is still an open question whether the cell is able to regulate the character of the chromosome groups after disturbance, but on the whole such evidence as we have lies on the negative side of the question. Certainly there is nothing more surprising than the stubbornness with which abnormalities in the chromosome groups, when once they have arisen, are perpetuated generation after generation, so long as they do not lead to multipolar division. Such an abnormality, once arisen, even in a single epithelial cell, might therefore lead to an extensive pathologic growth of definite histologic character, in which we might seek in vain for a visible causative agent. I fear, however, that cytology is not yet in a position to bring much help to the pathologist, for we are still too ignorant of the mechanism of normal differentiation to have much to say about that of abnormal forms. It is my impression that this problem can not at present be successfully attacked in the case of the higher animals and that we must for a time be content to rely on the study of much lower ones, such as the insects, where for some unexplained reason the differentiation of the chromosomes is far more clearly shown.

In conclusion, I wish to repeat that, whether we are on the right track or not in these cytologic studies, they stand on a perfectly concrete, definite and intelligible basis and can be put to the test of observation and experiment. The facts of heredity have always stood among the most wonderful and apparently mysterious phenomena of organic nature. It is no wonder if they long seemed inexplicable and if some naturalists have regarded, perhaps still regard, the hope of discovering their mechanism in detail as chimerical. To-day, I believe, this attitude can only be taken by those who have not closely followed the remarkable lines of inquiry that I have endeavored to sketch.

Naming of Carbon Compounds.—Thiol: Thi + ol is a sulphur alcohol. These are compounds in which the oxygen of the alcohol group is replaced by sulphur, thus ethane thiol is $\text{CH}_3\text{CH}_2\text{SH}$.—*Pharm. Rev.*, September, 1906.

Original Articles

BACTERIOLOGY OF THE RESPIRATORY TRACT,

WITH ESPECIAL REFERENCE TO INFLUENZA BACILLI.*

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INTRODUCTION.

These studies were carried on with a view of determining the frequency of occurrence of influenza-like bacteria in the sputa and throats of persons afflicted with the various infectious diseases, and also of comparing such bacilli for the purpose of determining possible variations which might lead to a subdivision of the influenza group. In a previous paper¹ on the bacteriology of whooping cough I discussed the occurrence of these bacilli in this disease and also gave some data on their occurrence in other infections. Here I shall refer to some of these results and add to them further data on certain properties of these bacilli.

TECHNIC.

The technic used in examining the respiratory tract for bacteria was briefly as follows: In nearly all of the cases sputum was obtained in a sterile Petri dish, and as soon as possible brought to the laboratory and examined. In some cases it was impossible to obtain the sputum and throat swabs were used. The sputum, as a rule, was washed in several changes of sterile water or broth, and from this washed sputum smears were made, and also a small particle was shaken thoroughly in a tube of plain broth for plating. The washing was for the purpose of removing the ever-present saprophytes coming from the oral cavity as the sputum is expectorated. Inoculations were then made from the tube of plain broth into melted plain agar at a temperature of 40 to 42 C., to which about 5 drops of pigeon blood had been added, and this was plated in the usual manner. Pigeon blood was used because it was found that, as a rule, the influenza organisms grow better on this than on other bloods, a fact first noted by Pfeiffer.

WHOOPING COUGH.

In sixty-eight cases of whooping cough, influenza-like bacilli were isolated sixty-one times. In the remaining seven cases they were not found after several examinations. Usually they were found in the first examination, this being true in forty-eight of the sixty-eight cases. In two cases the organisms were found several days before the whoop occurred, but at this time the patients had a severe cough and expectorated much mucus. Examination in six cases during the early stages before the whoops began failed to reveal the organisms. Later when the spasms appeared the bacilli were found. They may remain in the throat for a considerable period of time even after the spasms disappear. During the paroxysms they are coughed into the surrounding air in large numbers, as may be shown by holding blood agar plates before the child while coughing. In some cases the bacilli are extremely numerous, and on the plates are in almost pure culture, while in other cases they are relatively few in the cultures. In those negative cases, where opportunity was offered, persistent search both by smear and culture failed to reveal the organism. In one of these cases the *Micrococcus*

* From the Memorial Institute for Infectious Diseases, Chicago.
1. Jour. of Infect. Dis., 1906, iii, 1.

catarrhalis was found in nearly pure culture; in several others streptococci were especially numerous.

It is sometimes true that in the early spasmodic stage the influenza-like bacilli can not be found, and later they may appear suddenly in large numbers. In two cases this fact was especially conspicuous. Both were in the third week of the disease and had very violent spasms of coughing with typical whoops. Several examinations of sputum at intervals of two or three days both by smear and culture failed to show any of the bacilli, but many streptococci. Suddenly the bacilli appeared in the sputum in large numbers and thus continued.

Smears made from the washed sputum and stained by Gram's method with counterstain of dilute carbol-fuchsin show, as a rule, a large number of the small non-Gram-staining influenza-like bacilli. This is not an absolutely reliable means of detecting them; one may become very suspicious of their presence by smear examination, but further confirmation should be made by means of culture.

Pneumococci were found in every specimen and were about in the same proportion as in normal throats. Under this term are included those colonies which appear in the plates with a greenish halo about them. Streptococci were found in nearly every specimen of sputum examined. In a number of cases this group of organisms was very abundant and even more numerous than those of the pneumococcus group. As a rule, they were few, not more than three or four colonies on a plate. Compared with the normal, this class of organisms was somewhat more prevalent. The *Micrococcus catarrhalis* was found in large numbers in some of the cases, and organisms belonging to the diphtheria group were found in eight instances. Several strains were given to Miss Hamilton, for identification, who found some of them to be true diphtheria bacilli and other strains to be pseudo forms; they were never found in large numbers. In one case a child had a typical case of whooping cough with no evidence of diphtheria. A swab obtained from the throat showed numerous influenza organisms, but no diphtheria bacilli in smear or blood agar plates. Five days later the patient appeared with a well-developed membrane showing on examination many typical diphtheria bacilli together with some influenza bacilli.

MEASLES.

Twenty-three cases of measles were examined, in nearly all of which sputum was obtained for this purpose. They were examined during the stage of eruption and had, as a rule, the cough so frequently present early in this disease. In thirteen of these cases the influenza bacilli were isolated; in four they were the predominating organism, being found in almost pure culture in washed sputum. In some of the other cases they were very few. Pneumococci were always present and about to the same extent as found in normal throats. Streptococci were numerous in a few cases, but, as a rule, much less so than pneumococci. The *Micrococcus catarrhalis* was found in ten cases; in two of these it was very abundant, being more numerous than any other organism present. Influenza bacilli were not present in these two cases. Typical diphtheria bacilli whose colonies possessed wide hemolytic zones were obtained in two cases; they were not numerous. Five of the cases were complicated with otitis media. In one of these cases only were influenza bacilli found in the discharge; they were present in very large numbers and in nearly pure cul-

ture, a few streptococcus colonies appearing with them. About ten days previous to this, examination of the sputum showed the presence of influenza bacilli in considerable numbers. Another examination of the ear discharge was made eleven days later. At this time the influenza bacilli were no longer present, but there was obtained, in almost pure culture, a diphtheria-like organism. In a second case a double otitis media developed, and in culture from the ear discharge were found numerous streptococci, a few diphtheria bacilli, a few staphylococci and also a few typical pneumococci which fermented inulin and gave a green colony on blood agar. From the other three cases of otitis media streptococci were obtained pure in one of them, and diphtheria bacilli mixed in the remaining two. One of the cases of measles during convalescence had a profuse nasal discharge. Cultures of this material showed pneumococci, streptococci, a few diphtheria bacilli and also influenza-like bacilli. About a week later there developed a pus infection of the upper lip extending into the left cheek. Both smears and cultures from the pus showed a pure growth of *Staphylococcus pyogenes aureus*.

These results show the large number of varieties of bacteria that may be found in such cases. Streptococci seem to be the most frequent invaders, but the lesions can not be attributed to any one specific organism. The tissues appear to be so non-resistant that any variety that may happen to be present in the upper respiratory passages may find therein a suitable place for growth.

VARICELLA.

Eleven cases of varicella in young children were examined. Some of them were in the early stages, others later in the disease. Practically all had a slight cough. Influenza-like organisms were isolated in seven of the eleven cases; in two they were very numerous. Streptococci, few in number, were found in eight, diphtheria bacilli in one, and *Micrococcus catarrhalis* in all. These latter organisms were very numerous in two cases in which influenza bacilli were absent. The greenish pneumococcus colonies were found in all cases and about to the same extent as in normal throats.

MENINGITIS.

Opportunity was afforded to examine three cases of epidemic meningitis in children. In the nose in one case was found an influenza-like bacillus. Meningococci were isolated in two of the three cases from the nasal mucosa where they occurred in large numbers. All of them showed some nasal symptoms. One of these cases developed a double otitis media. Streptococci and diphtheria bacilli were isolated in culture, but no meningococci. This case, early in the disease, had a purulent conjunctivitis from which a typical meningococcus was isolated. The conjunctivitis completely disappeared in a few days on boric acid irrigation, leaving no serious result. Another case of interest may be mentioned here: A child 8 years old came into the hospital with the diagnosis of meningitis. She was in coma; the temperature ranged from 102 to 104 F.; marked rigidity was present not only of the muscles of the neck and back, but also of the limbs and especially of the jaw. Spinal puncture was made with negative results. Swabs from the nose showed nearly pure culture of diphtheria bacilli and a few were obtained from a throat swab. Antitoxin was administered. In thirty-six hours the temperature was normal, and the child made a rapid recovery. During convalescence otitis media developed, and in the discharge were isolated numerous diphtheria bacilli and

streptococci. This case illustrates the importance of nose and throat examination in infections generally.

INFLUENZA BACILLI IN OTHER INFECTIONS.

In order to show the prevalence of influenza bacilli, some data will be given on the occurrence of influenza bacilli in adults in other infections. In twelve cases of bronchitis they were found in the sputum five times; in seventeen cases of typical clinical influenza the bacilli were only found three times. In twenty normal throats of adults they were found twice, but not in large numbers.

From the above data we conclude the organisms of the influenza type are very commonly found in the throat in various infectious diseases. In whooping cough they are found in nearly every case some time during the course; often as soon as the whoop begins or slightly before and again not until some time after the spasms occur. In measles they occur very commonly and early in the disease, that is, within the first three or four days. There also generally appears to be an increase in the number of streptococci in both these diseases over that in the normal. Otitis media complicating infectious diseases is due to a variety of organisms, of which the influenza bacilli may be one, but organisms of the streptococcus and diphtheria group are more frequently responsible. Some of the latter organisms are true diphtheria, others appear to be pseudo forms (Hamilton).

The *Micrococcus catarrhalis* is an organism whose significance is rather difficult to interpret. It is a non-Gram-staining diplococcus, practically indistinguishable from the meningococcus in its morphology, but differs essentially in cultural and other properties. It is not uncommon to find organisms of this kind in the normal throat and nose, but, while sometimes quite abundant, they are seldom the predominating organism. In whooping cough they are commonly found in the sputum, though it must be said it is very rare to find them as the predominating organism. In measles and varicella they are even more common and occasionally are found in large numbers and to the exclusion largely of other organisms. It appears probable that they are increased in all infections of the respiratory passages, but it is difficult to say just how much they have to do in producing the symptoms. That they may play a part in some cases can hardly be questioned, and in support of this a few cases will be cited in which this organism occurred in almost pure culture.

A young man entered the hospital with marked bronchitis and laryngitis, accompanied with almost complete loss of voice. He expectorated considerable mucus, and this material washed in sterile water gave an almost pure culture of *Micrococcus catarrhalis*; smears of the sputum showed the same organism. This condition turned out to be the initial bronchitis of typhoid fever. Butler reported, before the Chicago Medical Society, an epidemic occurring in young infants at the Maternity Department of the Presbyterian Hospital of Chicago, characterized by the occurrence of fever and laryngeal and bronchial symptoms. Of these cases one patient died and came to autopsy. There was a broncho-pneumonia present and a large amount of purulent mucus in the trachea and bronchi. In both smears and cultures of this material the predominating organism by far was a typical *Micrococcus catarrhalis*. In this case, however, there were also a few pneumococci and their presence makes it difficult to interpret the significance of the former organism. Many of the micrococci were inside the

leucocytes, showing that they are readily susceptible to phagocytosis. Examination of the blood and other body fluids for bacteria gave negative results.

In a third case the patient had, following an ordinary cold, a persistent choking cough which continued for a number of weeks. The cough was very distressing, especially at night, and caused the patient to lose sleep. Otherwise she was well. A small amount of thick mucus was expectorated, and this chiefly in the morning on rising. Examination of this sputum washed in sterile water gave an almost pure culture of *Micrococcus catarrhalis*. The same result was obtained at two different examinations at an interval of about ten days.

M. Kirchner,² in 1890, observed this coccus in patients with influenza and associated it with the etiology of the disease. R. Pfeiffer cultivated this germ from the sputum in a variety of infections of the respiratory tract and gave it its present name. Ghon and H. Pfeiffer² found it eighty-one times in 140 cases of respiratory affections; they considered it usually saprophytic, but capable of producing at times acute or subacute lesions. It has been found by many others, especially in the respiratory tract in various infections of children, and has been associated with the cause of pertussis by Ritter and Buttermilch.

From the above data and the reports of others it appears that the *Micrococcus catarrhalis*, though frequently present as a saprophyte in the normal respiratory passages, is often associated with various kinds of inflammatory conditions in this region, especially in children. It can not be considered a specific organism for any particular characteristic group of symptoms, but appears to act as a common invader secondary to a variety of specific diseases. The possibility of its being a primary invader at times and under certain conditions seems reasonable.

The occurrence of the influenza bacilli in so few of the cases of clinical influenza or grippe is worthy of some comment. These cases were all diagnosed clinically as acute influenza and were typical in their symptomatology. The sputum was obtained early in the disease, and in almost every case the plates were characterized by the relatively large number of streptococcus colonies present. In those cases in which the influenza bacilli were found they were not present in especially large numbers. It is undoubtedly true that most of the cases reported as clinical influenza, at least in recent years, are not influenza infections at all, but are infections with other organisms, principally streptococci and pneumococci and perhaps also the *Micrococcus catarrhalis*. It appears to be true that a number of organisms can produce practically an identical clinical picture, and this has come to be known as influenza or grippe since the great epidemic of 1889-90. By many, such cases are assumed, without a bacteriologic examination, to be infections with the influenza bacillus, whereas in reality, as the above data, as well as many recent reports in the literature indicate, the cause is usually due to other organisms, the most common of which is undoubtedly the streptococcus.

The significance of the influenza bacilli found so frequently in the throat in infections of various kinds deserves some comment. These bacilli have a low degree of virulence for animals. If very large quantities are injected into the peritoneal cavities of guinea-pigs the animal dies in twelve to twenty-four hours and the

2. Ztschr. f. Hyg., 1890, ix, 528.

bacilli may be recovered from the blood. Attempts to exalt their virulence have not been very satisfactory.

Finding them occasionally in normal throats indicates the possibility that they may exist as harmless saprophytes or as organisms with a potential pathogenic function awaiting an opportunity favorable for development. That they are not always harmless saprophytes is shown by the fact that bacilli isolated from whooping cough and transplanted in the normal mucosa of the human throat will multiply abundantly and produce definite reaction. In one such experiment made by the writer on a young man whooping cough did not develop, but a slight fever lasting for a few days and some throat symptoms occurred, accompanied with the expectoration of a large amount of thick tenacious mucus in which the bacilli existed in large numbers in almost pure culture. We are, therefore, justified in attributing to them pathogenic properties for man, even though they may not be a specific primary cause of disease.

A careful comparison was made of the influenza-like bacilli from the various groups of diseases in which organisms of this type were isolated. This included whooping cough, measles, epidemic meningitis, varicella, clinical influenza, bronchitis, normal throats, and also strains isolated from conjunctivitis, scarlet fever, and tonsillitis. Morphologically and culturally no differences are found which would serve to subdivide them into groups. The organisms from these various diseases agree very closely. Strains from the same disease differ from each other slightly. Some tend to form threads very readily and are slightly larger than other strains, but this was found in all the diseases where a number of strains were isolated. Altogether about one hundred different strains have been tested. Without exception all require hemoglobin media. They are non-Gram-staining, short bacilli and stain more deeply at the ends with methylene blue. In the throat they never form threads, but in culture nearly always a few may be found, and in some strains this tendency is very marked, especially in the older cultures. We may say, then, that these bacilli agree very well with the influenza bacillus as described by Pfeiffer, and the forms showing a tendency to form threads correspond to his pseudo-influenza bacilli which he found in broncho-pneumonia and other conditions. That there is no essential difference between them seems to have been definitely determined by a number of writers, and the result given in this paper also indicate such to be true.

AGGLUTINATION OF INFLUENZA-LIKE BACILLI.

In order to show possible differences in the strains of influenza-like bacilli, rabbits were immunized against organisms isolated from whooping cough, measles, clinical influenza, scarlet fever, varicella, tonsillitis and conjunctivitis. The animals were first injected subcutaneously with the living germ and later intraperitoneally with gradually increasing doses. Finally they were injected twice with two agar slants of the living germs intravenously. The animals gradually lost weight, but otherwise showed little effects from the injections. At first they were injected once a week and later twice a week, this being continued for from eight to twelve weeks. The agglutination tests were made by the microscopic method and controlled with the microscope. This is the method of Cantani, Wollstein and others. There was some difficulty at first in getting homogeneous suspensions of the bacilli, but by using young cultures,

preferably from twelve to eighteen hours old, thoroughly agitating them in normal salt solution and then centrifuging out the clumps that may remain a satisfactory suspension was obtained for agglutination purposes. The serum was diluted with normal salt solution and the dilutions 1/10, 1/20, 1/50, 1/100, 1/200, 1/500, 1/1000, and occasionally higher were used. The serum of normal rabbits causes some clumping in all strains at a dilution of 1/10. Occasionally some strains were clumped at 1/20, but never any higher. In the immune animals agglutinins are present at the end of six weeks or earlier. In from eight to twelve weeks they are abundant. The sera in all the animals agglutinated the homologous organism at a much higher dilution than any strain isolated either from the same disease or from another disease. This was true, without exception, in every test made. All the sera agglutinated the homologous organisms in dilutions of 1/500, some at a dilution of 1/1000, and in one instance the serum from an animal immune to an organism from tonsillitis at a dilution of 1/5000. The agglutination of the other organisms varied considerably, but in most instances showed some increase above that obtained with normal serum. As a rule, this varied from 1/50 to 1/100 and occasionally rose to 1/200. Organisms from the same disease as the organism used to immunize, but from a different patient, did not appear to be agglutinated at higher dilutions than organisms isolated from other diseases. Table 1 is given as a fairly typical illustration of the agglutination of these bacilli. Tables showing the agglutination by sera immune against these bacilli from other sources show the same facts as this table and are consequently omitted. In every case, as in the table given, the agglutination of the homologous organism takes place with far higher dilutions of the serum than that of any other strain. It appears, therefore, from these results that common agglutinins are developed for all these strains of influenza-like bacilli about to the same extent and on this basis no subdivision of these bacilli into groups can be made.

TABLE 1.—AGGLUTINATION OF INFLUENZA-LIKE BACILLI BY RABBIT SERUM IMMUNIZED AGAINST A BACILLUS ISOLATED FROM PERTUSSIS.

Source of Organism.	Dilutions.							Salt Solution Control.
	1/10	1/20	1/50	1/100	1/200	1/500	1/1000	
Pertussis (homologous organism)	+++	+++	+++	++	++	++	+	0
Pertussis (not homologous)	+++	+++	+	+	0	0	0	0
Measles	+++	+++	+++	++	+	0	0	0
Conjunctivitis	+++	+++	++	++	0	0	0	0
Tonsillitis	++	++	+	+	0	0	0	0
Laryngitis	+++	+++	++	+	0	0	0	0
Varicella	+++	+++	+++	++	0	0	0	0
Influenza	++	+++	++	++	+	0	0	0

During the past season so few cases of pertussis in which these bacilli are common were available for examination that studies on the agglutinative property of the sera of patients for these influenza-like bacilli have hardly begun. This subject will be largely reserved for consideration at some future time and only a few statements made here. Normal human serum produces clumping of the strains of bacilli given in Table 1 at dilutions of 1/10 and slightly at 1/20. Practically no difference appears between the strains in this respect. In four cases of pertussis the sera clumped the bacilli from pertussis cases in slightly higher dilutions than those isolated from other sources. These dilutions

varied from 1/100 to 1/200. In one case of "grippe" in which the patient's throat showed these bacilli were very numerous, the serum fourteen days after the onset did not agglutinate the homologous strain or strains from other sources.

PHAGOCYTOSIS OF INFLUENZA BACILLI.

Within the last few years a large amount of study has been given to phagocytosis of bacteria and through animal and test-tube experiments considerable light has been thrown on the mechanism of this process. It has been shown by Wright and others that bacteria, as a rule, are taken up by leucocytes only when serum is present. Leucocytes washed several times in salt solution are no longer capable of ingesting organisms, but if serum is added to these corpuscles they promptly regain this property. The serum, therefore, is the important factor in determining phagocytosis, and the particular substance in the serum which causes it has been called "opsonin." A study of the influenza bacillus with reference to phagocytosis was made and the results will be briefly indicated.

Pfeiffer noted the occasional occurrence of these bacilli inside the leucocytes in the sputum in influenza bacilli more particularly in the latter part of the attack. In the sputum in other infections such as pertussis in which similar bacilli are found, it is only occasionally that they are encountered inside the pus cells. When the bacilli in moderate quantities are injected into the peritoneal cavity of animals they are taken up in large numbers by the numerous invading polynuclear leucocytes, but if very large amounts of bacilli are injected the exudate contains few leucocytes and the animal dies in 12 to 20 hours. The few leucocytes, however, which may be present under these conditions readily take up the bacilli.

In the test-tube, strains isolated from measles, whooping cough, tonsillitis, pharyngitis, varicella, influenza, and conjunctivitis were all found to be readily taken up by human leucocytes in defibrinated blood in the course of twenty minutes or less. If washed, leucocytes are used the bacilli are also taken up, but not so rapidly as when serum is added to them. When thick suspensions of bacilli are used in from twenty to thirty minutes the leucocytes in both cases are crowded with them. If dilute suspensions are used in twenty minutes a distinct difference in phagocytic activity between the washed and unwashed leucocytes in favor of the latter is seen, but after from four to eight hours this difference disappears, the leucocytes now being usually so filled with the bacilli that their number can not be accurately determined by count.

This phagocytosis in salt solution, which may be referred to as spontaneous phagocytosis, appears at present at least somewhat exceptional, for nearly all bacteria so far tested seem to require the presence of serum for phagocytosis. However, it has been observed by Miss Tunnicliff in this laboratory that abundant phagocytosis of the *Bacillus fusiformis* occurs in salt solutions without the presence of serum, and it is also known that carmine particles are readily taken up by leucocytes in the absence of serum. Wright observed spontaneous phagocytosis of tubercle bacilli in certain concentrations of salt solution. The greatest spontaneous phagocytosis occurred in a .6 per cent. solution; this progressively decreased and practically disappeared in a 1.3 per cent. solution. Varying concentrations of salt, at least within the above limits, have no effect on phagocytosis of influ-

enza bacilli. This is shown in Table 2. In this experiment a thin suspension of bacilli was used, otherwise phagocytosis would have been so rapid that the bacilli could not be counted in the 20-minute and 2-hour intervals.

TABLE 2.—SHOWING EFFECT OF VARYING CONCENTRATIONS OF NaCl ON PHAGOCYTOSIS OF INFLUENZA BACILLI BY NORMAL HUMAN CORPUSCLES WASHED FOUR TIMES.

Concentration of NaCl Solution.	Phagocytosis.		
	20 minutes.	2 hours.	6 hours.
.6 per cent.	.5	3.1	20+
.7 per cent.	.3	2.4	20+
.8 per cent.	.9	4.8	20+
.85 per cent.	.3	4.0	20+
.9 per cent.	.4	8.5	20+
1.0 per cent.	.1	0.9	20+
1.1 per cent.	.15	1.2	20+
1.2 per cent.	.1	8.0	20+
1.3 per cent.	.2	3.8	20+
1.4 per cent.	.3	3.9	20+

Spontaneous phagocytosis can not be satisfactorily explained by insufficient washing of the corpuscles. In some of the experiments these corpuscles were washed seven times, and each time there was added many times as much salt solution as there were corpuscles present. This amount of dilution and washing is quite sufficient to completely inhibit phagocytosis of staphylococci and meningococci. In several of the experiments staphylococci and meningococci were used as controls, and in no instance were they taken up even after eight hours.³ Again spontaneous phagocytosis can not be explained by long-continued cultivation on artificial media. Eleven strains isolated from various sources without exception showed spontaneous phagocytosis, though some had been isolated from the throat lesions only a few days, while others had been under cultivation for five months. The possibility of explaining the large numbers of bacilli in the leucocytes after a few hours by growth having occurred inside the leucocyte from an occasional ingested bacillus was ruled out by using bacilli killed by heating to 46 C. for thirty minutes. That the bacilli do not become sensitized by growing on blood media which they require was shown by using washed corpuscles in the media and also by heating the blood to 95 C. for one hour before adding it to the media. Lastly, spontaneous phagocytosis is not the mere adhesion of the bacilli to the surface of the leucocyte, for its appearance is identical with that of phagocytosis occurring in serum, and mere adhesion of bacteria to a leucocyte is manifested by a marginal arrangement of the organisms. We are justified, therefore, I think, in considering the influenza bacillus an organism which does not require the presence of serum and which may be classed with such inert bodies as carmine particles. Opsonins, therefore, do not appear to be the only factor which control the ingestion of bodies by leucocytes. The fact should be borne in mind, however, that in the presence of serum this process of phagocytosis is accelerated.

It has been shown for a number of organisms that phagocytosis is more active in immune serum than in normal serum, and this has been explained by the increased opsonic content of the former. Experiments to determine this point were made, using the sera of rabbits immunized against various strains of influenza or-

3. In the staphylococcus suspension the leucocytes are disintegrated to such an extent in the course of a few hours by the leucocidin formed by these organisms that phagocytosis can not be determined.

ganisms. The results with six sera on eight different strains of bacilli show some variation, but it was found that frequently phagocytosis in the immune serum exceeded that in normal serum and in some cases it was marked. There was little, if any, difference between the phagocytosis of the homologous organism and other strains from the same or from some other disease.

Some factors enter into the determination, however, which make it very difficult, if not impossible, with present methods, to obtain an accurate estimation of a possible opsonic increase in the immune serum. As disturbing elements may be mentioned spontaneous phagocytosis which can not be eliminated from the determinations. Another factor to be considered is the agglutination of these bacteria by immune sera. Bacteria in clumps naturally are taken up in larger numbers than in homogeneous suspension, and consequently increase in phagocytosis in agglutinating serum does not necessarily mean increase of opsonin. These facts, together with the fact that these bacilli are extremely small, staining poorly, as a rule, and would be difficult to accurately count even under the most favorable conditions, render opsonic determination for these organisms with the present methods at least very untrustworthy.

SUMMARY AND CONCLUSIONS.

1. Influenza-like bacilli are very commonly found in the upper respiratory tract in various infectious diseases and especially in whooping cough. Occasionally they occur in normal throats.

2. Various organisms occur in the discharge in otitis media, the streptococci being the most common; occasionally influenza bacilli are found.

3. The *Micrococcus catarrhalis* is a common inhabitant of the respiratory mucosa in infectious conditions and in some cases exist in nearly pure culture. It does not appear to produce specific lesions.

4. The influenza-like bacillus from whooping cough is pathogenic for man; its specificity is doubtful. Present data permit us to consider these bacilli as secondary invaders in all the diseases in which they are found. A primary invasion at times should be considered a possibility.

5. Influenza-like bacilli are readily taken up in the test-tube by unwashed leucocytes and to a less extent by washed leucocytes. This spontaneous phagocytosis is not affected by varying the concentration of the salt solution between 0.6 per cent. and 1.4 per cent.

6. Injection of these bacilli into animals causes the production of specific agglutinins and probably also an increase in opsonins in the serum. Because of the occurrence of spontaneous phagocytosis and agglutination in such sera the determination of the opsonic index for these bacilli is rendered unreliable.

THE CURE OF HYSTERICAL PARALYSIS BY RE-EDUCATION OF KINESTHETIC CENTERS.

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The sudden disappearance of hysterical paralysis, through religious excitement, hypnotic suggestion or great faith in the assertion of a particular physician, has been made so familiar to the profession that many, no doubt, think of it as the normal and eminently desirable mode of recovery. I have had a moderate share of such cases, sometimes being able, within the clinic hour, to make a patient with hysterical hemiplegia or paraplegia throw away his crutches and run about the room. These spectacular cures are intensely interesting and valuable from the purely scientific as well as from the practical standpoint, and they are within the reach of any physician who is sure of his diagnosis and able to pick out the favorable case.

Nevertheless, the method that aims at such sudden cures is not the one to be generally chosen. It will succeed in only a few of the cases and it stakes too much on the immediate effect of predictions, which, by promptly failing of verification, may prevent future success. Moreover, prompt success may have its disadvantages. Immediate relief from paralysis, which is only one symptom of the hysterical state, may prevent the patient from receiving that enlightenment and discipline which are essential to anything more than a superficial and transient improvement.

As a basis for a better method we must have an explanation of hysterical paralysis that will unite all favorable influences into a consistent plan of treatment. This was impossible a generation ago, but modern neurology can at least furnish a working hypothesis.

Probably the most constant accompaniment of hysterical paralysis is the anesthesia of the paralyzed parts, especially the absence of those sensations normally caused by motion. The patient can not feel the motions of the paralyzed limb nor can he think of them, except, perhaps, in visual images. Now this absence of kinesthetic sensations and kinesthetic ideas is not merely a complication. It must necessarily cause paralysis, because every voluntary motion must be preceded by the idea of the motion, and its continued execution must be controlled by an orderly series of sensations aroused by the movements already made.

These sensations and ideas of motion are a function of the sensory convolutions back of the Rolandic fissure. In normal volition these convolutions are first excited (by association impulses from other cortical centers) and then, directly or indirectly, by association impulses, they arouse the corresponding motor centers in the precentral convolution. In sending out these association impulses the kinesthetic centers are subject to facilitation and inhibition through the influence of other cortical centers. All that we know of the mental factors in hysteria favors the view that in hysterical paralysis the kinesthetic center is overwhelmed by a preponderance of inhibitory impulses, incidental to the perverted ideas and emotions. It can not act with sufficient vigor to awaken the idea of what is to be done or to send the necessary association impulses to the motor centers, so the limb remains motionless, although the motor centers, connecting tracts and muscles are in perfect order. This is in striking contrast to cases of organic paralysis caused by lesion below the cortex; in such cases the

Extraction of Set of False Teeth from the Esophagus.—Chiari has recently reported (*Wien. klin. Wochschr.*, xx, 147, 1907) the successful extraction of a set of 5 false teeth on a plate, 4.5 by 2.5 cm., which had been swallowed during sleep. The patient was a man of 38, who awakened suddenly with suffocation and retching, which soon subsided, but he could not eat solid food. He had no pain nor fever, and several physicians diagnosed cancer of the esophagus. After a month, radioscapy revealed the foreign body and it was readily inspected through an esophagus tube after cocaineization. A smaller tube was then introduced and the foreign body was drawn out readily, not through the tube, but with it. He has found inspection usually possible in such cases, as conditions that favored swallowing the body also favor inspection.