PFEIFFER'S BACILLUS AND INFLUENZA.

A Serological Study.

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The literature which has grown up in the very short time since the pandemic of influenza in 1918 is already so voluminous that it cannot be abstracted and analyzed in a brief space. Moreover, such an analysis, at the present time, would not be profitable. The methods employed by different bacteriologists in cultivating the influenza bacillus of Pfeiffer have been so diverse that comparison of results is valueless. There is, at present, hardly any difference of opinion that, with an adequate bacteriological technique, Pfeiffer's bacillus is found to be very commonly present in the respiratory tract of persons suffering from influenza and its attendant pneumonia. Moreover, the bacillus is also widespread in the upper respiratory mucous membranes of persons who have not had influenza, and even of persons who have not, so far as is known, been exposed to the epidemic disease.

We may accept the wide prevalence of the so called influenza bacillus as established and admitted and then proceed to the next and more important, because essential, question of the relationship of the bacillus to the symptom-complex influenza. Except in epidemic periods this symptom-complex is not so definite as to enable a sure and prompt diagnosis of influenza to be made; hence the cultivation of the Pfeiffer bacillus in interepidemic periods, from the upper respiratory tract, is not significant, necessarily, of clinical influenza. Possibly, indeed, there is no pathogenic microorganism, except the omnipresent pyogenic cocci, so frequently present in those parts as the Pfeiffer bacillus.

But even though the etiological rôle of the Pfeiffer bacillus in influenza has come to be seriously questioned, the part it plays in the

pathological complex characterizing this severe disease may still call for definition. Fortunately, in respect to this point there are other means available than mere presence in cultures to determine pathogenic action. The study on which this paper is based was begun early in the epidemic. In the meantime other publications bearing on the same topic have appeared. But it would seem that the subject is one on which additional evidence and more varied tests are desirable; hence the presentation of our results.

Culture Media.

Rabbit blood agar was the routine medium used in searching for Pfeiffer's bacillus during life and at autopsy, until Avery's oleate agar[1] became available. For serological work a medium made in the following way proved most suitable. Fresh rabbit blood was boiled for 2 minutes in a water bath, then centrifuged. The resulting clear, pale pink or yellow fluid was found by spectroscopic examination to contain hemoglobin. Two or three drops were added to 5 cc. of melted agar (pH 7.5) and slanted, while 0.5 cc. was added to a tube containing 20 cc. of broth (pH 7.8). Thus a solid medium and a fluid medium were obtained in which Pfeiffer's bacilli grew abundantly, and washing to get rid of blood or serum was not necessary. The bacilli live only 5 to 6 days on this medium, however. To keep stock cultures, blood broth, in which the bacilli remain viable for 6 weeks or more, proved by far the most suitable medium, while for isolation of the organisms the oleate agar was best.

Serological Reactions.

It was clear that for serological study sera from convalescent patients as well as monovalent immune sera experimentally produced were needed. Rabbits weighing 1,600 gm. proved to be best suited for the purpose of immunization. By means of intravenous injections of live Pfeiffer bacilli, in increasing doses, administered every 3rd day, antisera were produced with ten strains, seven isolated during the epidemic and three obtained several years ago.

[1] Avery, O. T., *J. Am. Med. Assn.*, 1918, lxxi, 2050.

Agglutination.—It was difficult to get even suspensions of Pfeiffer's bacillus suitable for agglutination tests. Blood broth cultures were not sufficiently profuse, and cultures grown on solid medium clumped spontaneously whether washed or not. Centrifuging had the effect of making the bacilli stick together in small clumps which could not be broken up. Finally, bacilli grown on the boiled-blood-centrifugate-agar were suspended in distilled water, while the serum dilutions were made in normal salt solution. The mixtures were kept at 55°C. for 2 hours, then at room temperature over night. At the end of 2 hours no agglutination had taken place; consequently the 18 to 20 hour reading was the only one that could be noted. The controls obtained by this method were fair for most strains, but unsatisfactory for others. Three strains clumped so much spontaneously that they could not be used for agglutination tests. The strains of Pfeiffer's bacillus varied in the degree of their agglutination reactions, as well as in the kind; four were inagglutinable in every serum tested, one agglutinated only in its homologous monovalent rabbit serum in dilutions of 1: 100, while three other strains clumped in 1: 50 dilutions in that serum. The presence of higher agglutinin content for heterologous than for homologous strains was noted for three sera made with strains of Pfeiffer's bacilli isolated from epidemic cases.

One normal rabbit serum was encountered which agglutinated the Pfeiffer bacillus in a dilution of 1: 20.

The serum of five normal human adults did not agglutinate Pfeiffer's bacillus in any dilution, while two other normal sera reacted in dilutions not exceeding 1: 10. Sera from eleven patients were tested during the 2nd week of illness. Five had had a mild bronchopneumonia attending the influenza attack, and the serum from two of these agglutinated Pfeiffer's bacilli in dilutions of 1: 100, while the other three sera did not contain agglutinins for these bacilli in dilutions higher than 1: 40. Sera from six cases of simple influenza without pneumonia contained no agglutinins for Pfeiffer's bacillus in two instances, and reacted in dilutions of 1: 40 in four others.

Agglutination reactions with the bacillus of Pfeiffer were not satisfactory because of the tendency to spontaneous clumping of the organisms. The wide variations in the results recorded in the litera-

ture may depend partly on this difficulty. Fleming[2] studied twenty-one influenza patients and found the agglutinin content of their sera low; only six agglutinated Pfeiffer's bacillus in dilutions higher than 1:32, and of these only one reacted above 1:128, giving a positive reaction in a dilution of 1:1,000. He also found that strains differed in their ability to agglutinate.

Adults who had been inoculated with vaccine made from several strains of Pfeiffer's bacilli developed agglutinins in their blood within 6 to 10 days, but only rarely were these present in dilutions higher than 1:100.

Complement Deviation.—Antigens were made in two ways: (*a*) Cultures grown in blood broth were centrifuged to throw out the blood cells, and the supernatant fluid was pipetted off, heated to 55°C. for 45 minutes, and tested. Against this antigen controls with sterile broth were always done in parallel series.

(*b*) Cultures in boiled-blood-coagulate-broth were centrifuged for 30 minutes and the precipitate was washed twice in salt solution, then resuspended in fresh salt solution and tested. The use of tricresol was discarded because it tended to make the antigens anticomplementary. A standard of turbidity for the suspended washed bacilli was evolved which approximated 10 cc. of salt solution to the precipitate from 25 cc. of broth culture. However, this amount had to be adjusted to the individual growth.

Tests with cultures of varying ages showed that the maximum strength of antigen was obtained in 3 days. The strains of Pfeiffer's bacilli varied in their antigenic power. In seven instances the antigen was strong, in eight, weak; while seven other strains failed to yield an active antigenic product. Whenever possible, sera were tested against antigen made from (*a*) a meningeal strain isolated during the epidemic, and (*b*) another meningeal strain isolated 2 years ago; (*c*) three respiratory epidemic strains; (*d*) a sporadic respiratory strain; (*e*) a strain isolated from a healthy carrier. Blood from forty-four persons was tested.[3] Of these, fourteen were patients convalescent 6 to 23 days after the onset of an attack of influenza, nineteen

[2] Fleming, A., *Lancet*, 1919, i, 138.

[3] I am indebted to Dr. Walter W. Palmer for his courtesy in allowing me to obtain blood from several patients in the wards of the Presbyterian Hospital.

had recovered from influenza 1 to 4 months previously, four were healthy carriers who had never been ill with influenza, and four were healthy controls. One fatal case of influenzal meningitis was studied, and also two patients who had suffered from diseases other than influenza—lobar pneumonia in one instance, laryngitis and pharyngitis in the other.

Sera from four normal adults were tested as controls. They had not been ill during the past fall and winter, had not suffered from colds, had not been vaccinated against influenza, and carried no Pfeiffer's bacilli in their sputum. No complement-binding reaction was obtained with any antigen in any of these four sera.

Sera from convalescent patients were examined at the end of the 1st week and reexamined in three cases at the end of the 2nd week after onset. Dilutions of 1: 5, 1: 10, and 1: 20 were used and showed a diminishing strength of reaction. The results are shown in Table I. All the sera gave a fixation reaction on the 6th or 7th day, and all but two reacted with antigens made from more than one strain of Pfeiffer's bacillus. The three sera which were obtainable a second time reacted more strongly at the end of the 2nd week than on the 6th day. Five were mild cases without any signs of broncho-pneumonia, while seven were complicated by pneumonia. It is to be noted that the sera of patients who suffered from pneumonia complicating influenza had stronger complement-binding power than did the sera of uncomplicated cases. No convalescent case failed to show fixation antibodies at the end of a week, though these were sometimes small in amount and limited in kind. No differentiation of strains was possible from these results.

One patient had been inoculated 5 weeks before she became ill with influenza with a vaccine of Pfeiffer's bacillus only. Her serum gave a reaction with but one antigen of five used. The influenzal attack had been a mild one, and apparently the inoculation did not increase the complement-binding power of her serum in the presence of Pfeiffer bacillus antigen.

An infant with Pfeiffer bacillus (influenzal) meningitis, who died on the 7th day of illness, gave a strongly positive reaction on the 6th day, with two antigens, one made from a meningeal strain of Pfeiffer's bacillus isolated 2 years before, and the other made from a strain

TABLE I.

Complement Fixation with Blood of Convalescent Patients.

Individual No.	Vaccine.	Day of illness.	Serum dilution.	Antigens.							
				M	D	325	R	W	T	I	280
1	1 mo. before.	9th	1: 5	0	+++	0		0			0
			1:10	0	+++	0		0			0
			1:20	0	+	0		0			0
2	0	9th	1: 5	+++	+++	+++		+++			0
			1:10	+++	+++	++		++			0
			1:20	+	++	+		0			0
3	0	7th	1: 5	0	+	++	++	++	++	++	++
			1:10	0	+	++	+	+	++	+	0
			1:20	0	0	+	0	0	0	0	0
	0	13th	1: 5	+	+++	+++	+++	+++	+++	+++	++
			1:10	0	+++	+++	+	++	++	+	0
			1:20	0	++	++	+	+	0	0	0
4	0	6th	1: 5	0	+	0	0	0		0	0
			1:10	0	+	0	0	0		0	0
			1:20	0	0	0	0	0		0	0
	0	12th	1: 5	0	+++	0	0	0		0	0
			1:10	0	+++	0	0	0		0	0
			1:20	0	++	0	0	0		0	0
5	0	6th	1: 5	+	++	0		0		0	0
			1:10	0	+	0		0		0	0
			1:20	0	0	0		0		0	0

W is a strain of Pfeiffer's bacillus isolated from a case of influenzal meningitis during the epidemic; T a strain isolated from a case of influenzal meningitis 2 years ago; M and D strains isolated from the lungs of influenzal pneumonia cases during the epidemic; 325 and R strains isolated from the sputum of influenzal pneumonia cases during the epidemic; I a strain isolated from the lungs of an influenzal pneumonia case 3 years ago; and 280 a strain isolated from the throat of a healthy adult carrier.

0 indicates complete hemolysis, no fixation of complement; + + + no hemolysis, complete fixation of complement; + + and + varying degrees of fixation of complement.

TABLE I—*Concluded.*

Individual No.	Vaccine.	Day of illness.	Serum dilution.	Antigens.							
				M	D	325	R	W	T	I	280
5	0	12th	1: 5	++	+++	0		0		0	0
			1:10	0	+++	0		0		0	0
			1:20	0	+	0		0		0	0
6	0	7th	1: 5	0	+++	++	+++	+++			
			1:10	0	+++	++	+++	+			
			1:20	0	++	0	+	+			
7	0	8th	1: 5	0	+++	+++	+++	+++			
			1:10	0	+++	++	+++	+			
			1:20	0	+++	0	+	0			
8	0	14th	1: 5	0	+++	+++	0	+++			
			1:10	0	+++	+	0	+			
			1:20	0	+	0	0	+			
9	0	6th	1: 5			+++			++		
			1:10			+++			++		
			1:20			+			+		
10	0	9th	1: 5	+	+++	++	++	+++	+++	++	++
			1:10	0	+++	++	+	+++	+	+	+
			1:20	0	+	0	0	++	0	0	0
11	0	7th	1: 5		+++					+	
			1:10		+					+	
			1:20		0					0	
12	0	14th	1: 5	++	+++				++	++	
			1:10	++	+++				+	+	
			1:20	0	+++				0	+	
13	0	13th	1: 5		+++					++	
			1:10		+++					+	
			1:20		++					+	
14	0	23rd	1: 5	+++	+++	+++	++		++	++	++
			1:10	++	+++	+++	+		++	++	+
			1:20	+	+	++	+		++	++	+

recovered from the lung in a fatal case of bronchopneumonia occurring during the epidemic. With antigen of a strain of Pfeiffer's bacillus from a healthy carrier, isolated during the course of the epidemic, and with that of a respiratory strain isolated from a sporadic case 4 years ago, no reactions were obtained. It is to be regretted that it was not possible to obtain a larger quantity of serum from this baby, so that it might have been tested with antigen made from its homologous strain of Pfeiffer's bacillus. The results obtained with this serum confirm the point previously shown;[4] namely, that meningeal strains of Pfeiffer's bacillus are virulent and yield a strong antigen, and that while respiratory strains are more apt to be nonvirulent and yield a weak antigen, virulent respiratory strains may be encountered which yield a strong antigen.

Complement fixation tests with Pfeiffer bacillus antigen made with the blood of nineteen individuals who had entirely recovered from influenza, which had attacked them 1 to 4 months previously, gave irregular results. At the end of a month one serum gave only an incomplete reaction with two antigens, and after 6 and 7 weeks only low complement-binding content was found in two other sera. 2 months after the illness no reaction was obtained with one serum, while three others gave strong reactions even in dilutions of 1: 20, and a fourth reacted well in a dilution of 1: 5, but not higher. After 3 months one serum gave complete reactions only in dilutions of 1: 5, while another was positive in dilutions of 1: 10. 4 months after influenza two sera were entirely devoid of complement-binding body content.

1 month after the influenzal illness a man who had been inoculated with three doses of vaccine made with three strains of Pfeiffer's bacillus, 4 months before the attack began, gave very strong reactions in dilutions of 1: 10. 2 months after the attack of influenza the sera of two subjects inoculated with Pfeiffer bacillus vaccine 3 months before the illness reacted as strongly as did two unvaccinated patients, while one reacted much less well. In comparing the serum of inoculated and of non-inoculated individuals, it becomes evident that the administration of a vaccine, made from several strains of Pfeiffer's

[4] Wollstein, M., *J. Exp. Med.*, 1915, xxii, 445.

bacillus, did not have any apparent influence on the degree of the complement-binding reaction with the antigens of Pfeiffer's bacillus when an interval of 3 or 4 months had elapsed between the inoculation and the influenzal illness. The patient whose serum was poor in this fixing antibody 1 month after the attack is apparently the exception, when viewed in the light of Table I.

Sera from four carriers were tested. All denied any respiratory illness in the previous 6 months. One had been inoculated with vaccine made from Pfeiffer's bacilli only. Two of the four carriers gave no reaction with several antigens. The inoculated individual and one person who had not been vaccinated reacted strongly. One of the carriers whose serum was negative to this test received Pfeiffer bacillus vaccine, and 1 week after the third dose had been injected his serum contained complement-binding bodies for three of six antigens against which it was tested.

To sum up, complement-binding antibodies were absent from the blood of four normal individuals who had not had influenza, and who were not carriers of Pfeiffer's bacillus. In the blood of influenza patients the fixing antibodies were present at the end of the 1st week, increasing in strength during the 2nd week, and were, as a rule, demonstrable at the end of 3 or 4 weeks. At the end of the 2nd month after an attack of influenza these antibodies were strongly present except in one case. At the end of the 3rd month complement fixation was still demonstrable in patients' serum, but in 4 months it had entirely disappeared. A complicating pneumonia increased the complement-binding power of the serum.

Monovalent immune rabbit sera were made with ten strains of Pfeiffer's bacillus and all bound complement in the presence of antigens made both from homologous and from heterologous strains. Normal rabbits were used as controls and their sera gave negative results.

Precipitins.—With the same antigen as that used for the complement fixation test, precipitins were demonstrable in every convalescent patient's serum tested, while they were absent from the serum of normal persons. Antigens made from homologous strains of Pfeiffer's bacillus gave no stronger precipitin reactions than did those made from heterologous strains. The earliest precipitin reaction noted was on the 6th day of the illness, and the latest, 3 months after the attack.

Poisonous Filtrates.

According to Parker[5] filtrates of Pfeiffer bacillus cultures grown in heated blood broth for 6 to 20 hours are poisonous for rabbits when inoculated intravenously. Tests were made with twenty-five strains of the bacilli. The filtrates from seven strains killed rabbits weighing 1,300 to 1,600 gm. within 1 to 2½ hours when inoculated intravenously in doses of 2 or 3 cc. Much larger doses (5 cc.) were required to kill the animals with filtrates of other strains. Death was sometimes, though rarely, delayed until 12 to 15 hours after the injection of the poison.

The effects of intravenous injection of a potent filtrate from an early culture of Pfeiffer's bacillus were quite uniform. The animals gradually became more and more quiet, so that in 30 to 45 minutes they sat in a hunched up position with no movement but that of very rapid respiration. Intestinal peristalsis was increased until at the end of 60 to 90 minutes the animals were passing fluid feces. Gradually the head leaned, then fell to one side, and the animal slowly fell over. After one or two attempts to rise, all muscular efforts ceased, and it lay on its side, breathing very rapidly and irregularly, with the head becoming more and more retracted. Death was often preceded by general convulsions. Non-lethal doses caused the symptoms of muscular weakness, irregular respiration, retraction of the head, and diarrhea; but the rabbit did not fall over on its side or go into a convulsion, and recovery gradually took place so that the animal was well within 3 or 4 hours, though more quiet than before the injection. The leucocytes fell within 1 hour after inoculation, and a difference of 5,000 to 12,000 from the initial count was noted. The recovered animals showed a rise within 4 to 5 hours, and on the following day the leucocytes were always as high or higher than before the injection of the filtrate.

Postmortem examination showed constant changes in the lungs. These organs were deep pink in color, mottled with dark red or brown areas of hemorrhage, often most marked in one or both lower lobes. Punctate subpleural hemorrhages were numerous and general. The lungs were edematous; frothy fluid exuded from the cut surface and

[5] Parker, J. T., *J. Am. Med. Assn.*, 1919, lxxii, 476.

from the trachea and bronchi. The mucosa lining the larynx, trachea, and large bronchi was dark red or purple in color from an intense congestion, while bright red points of capillary hemorrhages were numerous.

The intestinal contents were fluid. The kidneys and liver were congested. In female rabbits the Fallopian tubes were always bluish red in color and on section showed an intense congestion of all the coats. The blood vessels in the cerebrospinal meninges were filled with blood. No gross hemorrhages were apparent in the nervous system. The suprarenals were pale pink in color.

Microscopic examination of the brain showed minute areas of perivascular diapedesis in sections of the medulla. The lungs showed a congestion of all the vessels so exquisite as to constitute a natural injection. A comparative absence of leucocytes was striking; both within the lumen of the vessels and in the alveoli they were few in number. The connective tissue septa were edematous. Many alveoli contained red blood cells, and the epithelium lining the walls was intact; other alveoli contained granular, coagulated serum in which air bubbles were apparent.

In the female the Fallopian tubes showed an intense congestion of the blood vessels in the mucosa, while some muscle fibers had undergone hyaline degeneration.

Control experiments were made by injecting normal incubated broth intravenously into rabbits. No symptoms followed, and at autopsy no lesions were found. A filtrate of typhoid bacillus culture was also injected as control. The animals died after 15 to 18 hours, and at autopsy showed a hypostatic congestion of the lungs and some discoloration due in large part to the fact that they had been dead several hours before they were examined. The edema and punctate hemorrhages were lacking.

The sera of rabbits inoculated with increasing doses of filtrates of young cultures of Pfeiffer's bacilli occasionally protected other rabbits against one fatal dose of homologous and heterologous filtrates, but no serum protected against more than one lethal dose of poison. Normal rabbit serum protected almost as many animals as did the sera of the inoculated rabbits. The nature of the poison remains in doubt, but it is evidently not a toxin, since there is no definite incu-

bation period between its inoculation and the appearance of symptoms, and a protective serum does not result from its repeated injection into rabbits.

Protection Experiments.

Attempts to protect mice against lethal doses of Pfeiffer's bacilli by means of rabbit sera made with poisonous filtrates proved unsatisfactory. The sera never reached a high potency because the rabbits became emaciated and died when the injected poison was a strong one, and they reacted but slightly to a weak one. Consequently the results of protection experiments on mice with such a serum were irregular and misleading. A strong antibacterial serum was more readily obtained and protected a greater number of mice against a lethal dose of Pfeiffer's bacilli, whether the serum was given 24 hours before the bacilli were injected, or after 15 minutes contact with the dose of culture (Table II).

TABLE II.

Protection Experiments with Mice.

No. of animals.	Serum (rabbit).	Method of administration.	Survived.
			per cent
53	Antitoxic (?).	24 hrs. before bacilli.	3.8
34	" (?).	After 15 min. contact with bacilli.	23.0
16	Antibacterial.	" 15 " " " "	25.0
20	"	24 hrs. before bacilli.	40.0
10	Normal.	24 " " "	1.0
10	"	After 15 min. contact with bacilli.	2.0

Human sera from six recovered patients were entirely lacking in protective effect when tested on mice inoculated with lethal doses of Pfeiffer's bacillus, although all these sera contained complement-binding bodies.

DISCUSSION.

As regards the serological reactions of Pfeiffer's bacillus with the sera of recovered patients, as well as with monovalent immune rabbit sera, the results with agglutination were irregular and not satisfactory.

As far as they showed positive results the epidemic and the sporadic strains reacted similarly.

At the Department of Health of the City of New York, Park and his coworkers[6] found Pfeiffer's bacillus present in 80 to 100 per cent of influenza patients. The bacilli isolated from different cases, however, did not produce identical immune bodies in inoculated animals as measured by the agglutinin absorption test, and Park concludes from these studies that there were many strains of Pfeiffer's bacillus, and not one epidemic strain, present during the pandemic.

Complement fixation reactions with human sera showed that normal controls did not contain complement-binding bodies for the Pfeiffer bacillus, but that the blood of recovered patients gave a positive reaction with more or less regularity in dilutions varying from 1:5 to 1:20. The binding could almost always be obtained with antigens made from more than one strain of the bacillus. On the other hand, with the sera of two patients in whose sputum Pfeiffer's bacilli were not found, and who suffered from lobar pneumonia and laryngitis respectively, no fixation was obtained. It would seem, then, that the reaction is due to something more than the presence of an increased amount of non-specific protein after a febrile attack.

With some immune rabbit sera binding was obtained in dilutions of 1:100. Normal human and rabbit serum controls did not bind.

Rapoport[7] examined a much larger series of cases than I was able to do. He studied influenzal pneumonia patients and controls. His results showed complement fixation bodies in 54.5 per cent of 295 convalescent influenzal pneumonia patients and in only 9.67 per cent of 300 controls. My results confirm his and show that patients who are convalescent from influenza without pneumonia also may have complement fixation bodies in their serum for a limited period of time and to a less marked degree.

Kolmer, Trist, and Yagle[8] demonstrated complement fixation in the serum of convalescent influenza patients with antigens made from Pfeiffer's bacillus, hemolytic streptococci, and *Micrococcus catarrhalis* but not with staphylococcus and pseudodiphtheria bacillus antigens.

[6] Park, W. H., *J. Am. Med. Assn.*, 1919, lxxiii, 318.

[7] Rapoport, F. H., *J. Am. Med. Assn.*, 1919, lxxii, 633.

[8] Kolmer, J. A., Trist, M. E., and Yagle, E., *J. Infect. Dis.*, 1919, xxiv, 583.

45 to 50 per cent of the sera reacted with Pfeiffer's bacillus, and only 38 per cent bound complement when streptococcus or *catarrhalis* antigens were employed. All the sera were tested in a dilution of 1:10. Consequently no light is thrown on the specificity of the reactions.

Precipitins were also found constantly in the sera of recovered patients and of immunized rabbits. The reaction for them was strongly marked both with heterologous and with homologous strains of Pfeiffer's bacillus.

CONCLUSIONS.

It has been shown that the sera of patients convalescent from influenza yield reactions for agglutinins, precipitins, and complement-binding bodies with antigens of Pfeiffer's bacillus. These reactions appear constantly at the end of the 1st week, increase in intensity during the 2nd week, and remain demonstrable for a period of 2 to 4 months. They were most complete in the sera of patients suffering from postinfluenzal pneumonia. It has also been demonstrated that the strains of Pfeiffer's bacillus isolated during the epidemic were morphologically and biologically similar to the strains isolated from influenza cases in other years, and antigenically they differed from them only quantitatively. The patients' serological reactions indicate the parasitic nature of the bacillus, but are not sufficiently stable and clean-cut to signify that Pfeiffer's bacillus is the specific inciting agent of epidemic influenza. They do, however, indicate that the bacillus of Pfeiffer is at least a very common secondary invader in influenza, and that its presence influences the course of the pathological process.