

THE MORPHOLOGY OF THE INFLUENZA BACILLUS*

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Pfeiffer¹ described a "true influenza" bacillus and a "pseudo-influenza bacillus." He was unable to distinguish these organisms in direct smears of exudates, where they both appeared as small bacilli with rounded ends. Culturally they were identical. He based his distinction on the fact that smears from cultures of the true influenza bacillus showed small bacilli with few longer forms, while smears made from cultures of the pseudo-influenza bacillus showed long, threadlike organisms. The pseudo-influenza bacillus was isolated by Pfeiffer from three cases of bronchopneumonia.

In bacteriologic examinations of the sputum, blood and lungs during the present epidemic of influenza, both forms of the influenza bacillus have been encountered. In some cases aerobic plates of the sputum have yielded practically pure cultures of the small gram-negative bacillus contaminated only by rare colonies of staphylococcus. Sputum from other cases has yielded equally pure cultures of the long, threadlike organism designated by Pfeiffer as pseudo-influenza bacillus.

This long, threadlike form appeared in the blood culture of a patient whose sputum contained the same type of organism. Aerobic plate cultures of the pneumonic area in a lung showed a pure culture of an organism which at the end of twenty-four hours' growth appeared in smears as a very small, gram-negative bacillus, and at the end of forty-eight hours, as long, wavy or curled, gram-negative threads which would ordinarily be classed as a leptothrix. In every case direct smears of the sputum showed only the small, bacillary form.

These findings suggested that however unlike the two forms appeared in smears made from cultures, there was a possibility that they were the same organism.

In order to determine if the reaction of the medium influenced the morphology of the organism, medium was prepared by adding human blood to a series of tubes containing agar which, after sterilization, titrated 1.5, 1.0, 0.4, 0.2 acid, neutral, 0.2, and 0.7 alkaline expressed in percentages of normal sodium hydroxid with phenolphthalein as an indicator. Seven sets of these tubes were inoculated with different strains of organisms. Four of the strains used were small bacilli, such as Pfeiffer termed true influenza. Three were the threadlike forms which he considered pseudo-influenza bacilli. Smears were made from the tubes at the end of twenty-four and forty-eight hours.

The three strains that resembled leptothrix in the original cultures still showed the long threads in the more acid medium, but on the 0.2 acid and neutral tubes they grew as small bacilli which could not be distinguished from true influenza bacilli. The four strains that grew in the original cultures as small bacilli showed transitions from the longer, sometimes threadlike forms on the more acid medium to the small bacillary forms on the slightly acid and neutral tubes.

Kato² reported a gram-negative leptothrix which he believed to be the cause of pleuropneumonia. In a bacteriologic study of the pneumonia occurring at Camp Pike last winter, Dick³ found leptothrix organisms predominating on plates of the sputum in 6 per cent. of the cases. He described them as "very minute colonies, barely visible to the naked eye, but extremely numerous. There was no effect on blood. The organisms were gram-negative and varied in length from organisms resembling influenza bacilli, to long, slightly wavy organisms extending half way across the field. It was not possible to cultivate these organisms beyond one or two subcultures, and their importance is undetermined."

Where there is such variation in morphology in different cultures of the same strain, it does not seem justifiable to classify influenza bacilli as true and pseudo on the basis of morphology alone. In attempting to isolate influenza bacilli, it is important to recognize the leptothrix-like form as well as the small bacillary form.

NOTES ON THE PRESENT EPIDEMIC OF RESPIRATORY DISEASE*

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From September 20 to October 31, we saw both in our services at the Michael Reese Hospital and in private practice approximately 500 cases of epidemic respiratory disease. The various forms of onset will easily fall into three groups: the first characterized by symptoms of a more or less severe coryza, the second by varying degrees of prostration, backache, headache, chilly sensations and elevated temperature, and the third by a feeling of indefinite discomfort, with no fever, but in a few hours a definite rise of temperature. Careful examination at the beginning of the disease, in all cases, usually revealed few signs, except for a slight reddening of the anterior pillars of the pharynx, and in many instances an intense congestion of the conjunctivae. Many patients who were coughing violently showed no signs of bronchial involvement, the cough probably being due to an intense congestion of the trachea. However, in a large percentage of our cases, careful examination at the onset showed a more or less circumscribed area, sometimes no larger than the bell of a stethoscope, which would manifest râles or dulness or changes in the breath sounds. It is our opinion that all these cases should be considered pneumonia, as a large percentage of this type does not show the drop to normal in three or four days.

DANGER OF PULMONARY SIGNS

One of the most important lessons learned from the epidemic is the potential danger residing in these small pulmonary signs, even when the temperature is normal. In several of our cases, a very slight pulmonary condition, after careless exposure to cold, developed into severe pneumonia. The development of pneumonic symptoms in these patients occurred either (1) after a complete defervescence, following on the footsteps

* From the laboratory of St. Luke's Hospital.
1. Pfeiffer: Ztschr. f. Hyg., 1893, **13**, 356.

2. Kato: Mitt. a. d. Med. Fakt. d. k. Univ. zu Tokyo, 1915, **13**, 441.
3. Dick, G. F.: A Bacteriologic Study of the Pneumonia Occurring at Camp Pike, Ark., THE JOURNAL A. M. A., May 23, 1918, p. 1529.

of a more or less severe febrile period, lasting from one to two days; (2) after a drop in temperature, but not to normal, or (3) without a reduction, but instead with an elevation of the temperature on the third or fourth day. In any one of these three forms, the physical signs of bronchopneumonia would be present at the beginning of this phase of the disease, or would appear within a day or two. It is our opinion that the persistence or appearance of a rise in temperature on the third day indicates bronchopneumonia.

The appearance of the patient early in the disease does not betray his condition. Aside from the conjunctivitis and mild pharyngitis, already mentioned, the patient does not appear ill. Later, however, with the advance in the pneumonic process and an increase in the toxemia, cyanosis, sometimes with more or less edema of the face, becomes prominent. Stupor, restlessness and delirium may appear. At times, the uncanny combination of absence of the radial pulse, profuse perspiration and cyanosis, with the patient in full possession of his mental faculties, indicates only too clearly the fatal termination. The low pulse rate, which has been so characteristic of the disease, is a definite sign. Patients seen early with a pulse rate above 100 always evoke a suspicion of some other disease, although occasionally an increased pulse rate may have been caused by too large doses of acetylsalicylic acid. Late in the disease, with an increase in the severity of the condition, a rapid pulse rate is present. One rather striking feature was the inverted type of temperature. Many of our patients would be normal except at 4 or 8 a. m. The combination of the slow pulse, with this inverted type of temperature, sometimes made the diagnosis of influenza, when otherwise the diagnosis would have been difficult to establish.

Perhaps the most common site of the pneumonic disturbance was in the left lower lung, posteriorly, although no portion of the lung was particularly exempt, and no particular site had any special prognostic value. The type of pulmonary pathologic condition varied clinically from the small patch, which ordinarily would be considered merely a bronchitis, to a large massive pneumonia, with general edema of both lungs, and expectoration of bright red blood.

RESPIRATORY RATE

The respiratory rate early was as a rule slow, even though the temperature and pulse rate were increased. The appearance of an increased respiratory rate, from 40 to 50, indicated not only an increase in pulmonary involvement, but what seemed of more significance, an increase in toxemia. At times a definite air hunger, suggestive of a severe acidosis, made its appearance. From our experience, we have come to look on an increased respiratory rate, even though the temperature and pulse did not become elevated, as of more unfavorable significance than almost any other sign. On the contrary, when the temperature was high and the respiratory rate low, the condition was not considered unfavorable.

COUGH AND EXPECTORATION

Cough was a prominent and troublesome symptom in the majority of cases. Generally unproductive at the onset, later it became painful and accompanied by nummular expectoration and abdominal pain, probably muscular, from the strain of coughing. Where bloody expectoration occurred, the cough was not so frequently accompanied by pain.

PLEURITIC PAIN

Actual pleuritic pain, either thoracic or referred abdominal, occurred in a small percentage of cases. In these cases a pleuritic friction rub could be heard. Fluid in the chest, either serofibrinous, bloody or purulent, occurred, more frequently later in the epidemic than at the beginning. The removal of the fluid except in cases of empyema even in small amounts, by exploratory thoracentesis, seems to be followed by definitely favorable changes in the course. Involvement of the accessory sinuses of the nose is probably very common, and a routine examination ought to be established to rule this out. Ear infections, which were so common in the epidemic of 1891, were comparatively rare at the beginning of the epidemic, but apparently are becoming more prominent as late sequelae.

BLOOD PRESSURE

There was a normal or slightly diminished systolic blood pressure in those patients in whom the disease ran a moderate course. The diastolic pressure, however, was considerably lower than was to be expected. A systolic pressure of 100, with a diastolic pressure of 40, was a not uncommon occurrence. When the diastolic pressure was high or comparatively high, some cause was to be found, as a nephritis. One patient whose systolic pressure was 120, diastolic 85, with Cheyne-Stokes breathing during her pneumonic phase, had a systolic pressure of 180, and diastolic of 115 on recovery from the pneumonia. In no case, except when an organic heart lesion had previously existed, was there found a dilated right heart indicative of cardiac failure.

MENSTRUATION

In the women practically all menstruated between the first and third day of the disease, and many of these patients had considerable menstrual difficulty in the period following the disease. It is too early yet to speak definitely on this subject. Many women had considerable difficulty in urination at the beginning of the disease. Anuria of from twelve to twenty hours was not uncommon, so that catheterization had to be resorted to on account of a large urinary bladder tumor. Albumin and casts were found frequently in the later stages of the disease. Intense headache, rigidity of the neck and back, with spinal fluid under high pressure, suggested meningitis. However, cytologic and chemical study of the spinal fluid yielded negative results. The patient made an uneventful recovery.

Although one hears considerable of gastro-intestinal influenza, the large majority of the patients do not have gastro-intestinal symptoms, except when they are severely ill, when nausea, vomiting, and complete anorexia may set in. Many patients, however, complained of intense abdominal pain, which was apparently due to a muscular disturbance from the violent coughing. In the later stages of the epidemic, and likewise perhaps two or three weeks before the epidemic reached Chicago, we saw a number of cases of acute gastroenteritis which may or may not have been associated with the epidemic. In many instances, the clinical picture was similar except for the location of the disease.

BACTERIOLOGIC FINDINGS

The accompanying table (1) shows clearly the incidence of positive bacterial findings. Positive blood

cultures were without prognostic significance. A leukopenia was the rule, except when an empyema developed. In these cases, a leukocytosis from 10,000 to 18,000 obtained.

We had a number of cases complicating other diseases, and strangely enough these patients were apparently no worse off than others. We had three cases complicated by bronchial asthma, one with a massive pneumonia, and another in which the patient was not so severely ill; all made uneventful recoveries. At least one case, and perhaps more, occurred on top of an old pulmonary tuberculosis. Several patients had organic heart disease, and none of these died. Two cases complicated chronic nephritis; one patient made uneventful recovery and one died.

PERCENTAGE OF TIMES BACTERIA WERE PRESENT IN EXAMINATIONS *

| | Number of Exam- inations | B. Influenzae | Streptococci | | | Pneumococcus | M. Catarrhalis | Friedlander's Bacillus | Diphtheroids | Staphylococcus |
|---------------------------|-----------------------------|---------------|------------------------|--|------------------------------|--------------|----------------|---------------------------|--------------|----------------|
| | | | S. Viridans | | Streptococcus Hemolyticus | | | | | |
| | | | Typical S. Viridans | Narrow Zone of Hemolysis after 24 Hrs. | | | | | | |
| Sputum..... | 13 | 8 | 46 | 80 | 8 | 23 | 0 | 8 | 0 | 100 |
| Throat..... | 125 | 12 | 20 | 70 | 10 | 64 | 17 | 13 | 12 | 80 |
| Nose..... | 22 | 0 | 10 | 5 | 0 | 18 | 0 | 0 | 0 | 91 |
| Pleural exu- date..... | 8 | 0 | 12 | 38 | 0 | 25 | 0 | 0 | 0 | 0 |
| Blood cul- tures..... | 105 | ... | 17 | 18 | | | | | | |
| Total..... | 273 | 5.5 | 20 | 41 | 4.4 | 32 | 8 | 7 | 4 | 46 |

* This table was kindly prepared by Dr. Katherine Howell, who will later make a detailed report of her studies.

PREGNANCY AS A COMPLICATION

Perhaps the saddest feature of the whole epidemic was the effect on pregnant women or women with very young children. These cases were unquestionably the most severe in our experience, and many of these patients died. At present it is impossible to collect our statistics. These patients very early became markedly cyanotic, dyspneic, had rapid pulse, and massive (often hemorrhagic) pneumonia, and many of them from the first day of the illness gave an absolutely unfavorable prognosis. One patient in particular, a healthy young woman with two children, seen early in the epidemic, was moribund in twenty-four hours from the onset.

CLINICAL COURSE

The clinical course ranged from a few days to two weeks of acute symptoms. The distressing feature in many cases was that when the patient seemed to be progressing favorably toward an uneventful recovery, suddenly like lightning from a clear sky he would develop an increasing cyanosis, high temperature, high pulse and respiratory rate, a severe toxemia and pass away in from twelve to thirty-six hours. Relapses did not occur, although in two instances that came to our notice, patients died one week later from what appeared to be pulmonary embolism.

Convalescence was often very greatly prolonged, so that at times two or three weeks were required before the patient felt well enough to be up and about.

PROGNOSIS

No disease has ever been encountered in which it was more difficult to outline a prognosis. Patients,

apparently mildly ill, suddenly on the third or fourth day would show a high temperature, cyanosis, rapid respiration and pneumonic consolidation, and would rapidly get worse. On the other hand, quite a number of our cases, especially those seen in the hospital, with cyanosis, lobar pneumonia and extremely toxic symptoms, pulled through to uneventful recoveries, without any special line of treatment. All the cases that were not complicated by pneumonia offer an absolutely good prognosis, but we had to be extremely cautious in all the pneumonic cases. Some factors which we considered of importance for prognosis are immediate taking to bed and keeping warm, with plenty of fresh air in the room and proper bedside care. By proper bedside care we mean absolute bed rest, the patient not being allowed to leave his bed for any purpose whatsoever. In several apparently mild cases pneumonia developed when the patient got up too soon, and it is our opinion that a certain percentage of the mortality from the epidemic might be prevented. Some patients die, no matter how excellent the care they obtain; but such a large proportion of the deaths occurred in patients apparently well who suddenly develop pneumonia, after exposure, that the impression of cause and effect is very definitely produced.

MORTALITY

The hospital statistics for the month of October show 269 admissions of all types, including moribund pneumonia patients. Of this number, forty-seven, or 17 per cent., died, but eleven of the forty-seven were in the hospital less than twenty-four hours, reducing the mortality to 13.4 per cent. From the hospital personnel of approximately 400 there were 107 admissions, of whom three, or 2.8 per cent., died.

TREATMENT

Prophylactic vaccination is as yet of unknown value. We know of at least three instances in which three doses of a vaccine had been given and influenza subsequently developed, and of over twenty instances in which one or two doses had been given, followed later by typical attacks of influenza and pneumonia.

We feel definitely that at present there is no special treatment. The two of us, working on independent services, gradually evolved an identical plan of practically leaving the patient alone and treating symptoms as they arose. We have used acetylsalicylic acid, 10 grains, or powder of ipecac and opium (Dover's powder) 10 grains, or both, with hot alkaline drinks and purgation for the first two days; then if there were any evidences of pneumonia, medication was removed and the patient treated purely for his symptoms. Heroin or morphin were found to be the best sedatives for the violent coughing and to keep the patient in comfort. We found that the administration of large quantities of fluids of all kinds by mouth, and when not retained, by rectum, either as plain tap water or with the addition of glucose, in 5 per cent. solution, and of urging the patient to take as much food as possible, with plenty of fresh air and warm coverings, were the most important factors in the treatment.

Early in the epidemic, we found that the administration of expectorants, salicylates, hexamethylenamin, quinin, etc., were of little value. Hexamethylenamin seems definitely contraindicated because of its tendency to produce hematuria. Cardiac stimulants, as digitalis, caffeine and sodium benzoate, by mouth or hypodermi-

cally, were used, but with questionable value. Camphor in oil, pituitary solution in 7 minim doses, epinephrin in physiologic sodium chlorid solution by hypodermoclysis, and atropin in $\frac{1}{60}$ to $\frac{1}{100}$ grain doses, especially when an edema of the lungs was imminent, did not seem to alter the course of the disease. Whisky, brandy and aromatic spirit of ammonia were all used, but except for a temporary stimulation seemed useless. Champagne served in teaspoonful doses, with ice pellets, was sometimes the only thing the severely ill patients could tolerate without nausea. Oxygen by inhalation relieved the cyanosis, but had no effect on the course.

Convalescent serum (400 c.c.) was administered in one case, without preventing a fatal termination.

CONTAGIOUSNESS

A word as to the element of contagion. All of the interns who became ill had been in close contact with the patients, and many of the nurses who attended influenza patients subsequently became patients themselves, despite the fact that they took precautions to wear face masks while on duty taking care of patients, and to wash their hands in antiseptic solutions before leaving their patients. The air in one of the wards, on culture, yielded the hemolytic streptococcus.

CONCLUSIONS

1. The present epidemic of "influenza" or "influenzal bronchopneumonia" or "epidemic pneumonia" is as yet of unknown etiology.
2. The course of the disease, apparently mild at first, is treacherous, and not associated with any symptoms that might indicate the intensity or the severity.
3. In our hands no specific treatment seemed to have greater value than the induction of symptomatic relief, which we believe should be the hub of the treatment.

TWO CASES OF HUMAN ANTHRAX AT CAMP JACKSON*

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Anthrax, a disease of relatively rare occurrence in civil life in this country, has assumed a certain degree of importance because of scattered cases that have appeared in Army camps. A few cases have occurred in camps in this country, and in the British army the cases have been more numerous. Usually it is possible to trace the infection to contaminated shaving brushes. The occurrence of two cases in Camp Jackson within a very short period of each other, the first reported from this camp, appears worthy of record, especially in view of the fact that the first case was so atypical clinically that the nature of the condition could not be suspected without the laboratory findings.

REPORTS OF CASES

CASE 1.—*Clinical Course*.—A private of the One Hundred and Fifty-Sixth Depot Brigade, white, aged 23, was admitted to the base hospital, July 17, 1918. The family and previous history were negative. July 14, while shaving, he noticed a small pimple on the neck. He squeezed out a small amount of fluid; the lesion began to swell and grew worse from this

time. By July 16 the swelling had extended well down on the chest. On admission both sides of the neck were swollen, the swelling extending downward on the chest to 1 inch below the nipple line. There was a small abrasion on the left side of the neck anteriorly. The pulse was weak, the skin was somewhat cyanosed, and respiration was sighing in character. The temperature on admission was 97.2, the pulse 124, respiration 26. The white blood cells numbered 16,500, of which 78 per cent. were neutrophils, 2 per cent. basophils, 13 per cent. small mononuclears, 5 per cent. large mononuclears, and 2 per cent. transitionals. The diagnosis made at this time was cellulitis of the neck. The patient's condition rapidly became worse. At 3 p. m. of the day of admission the swollen tissue was incised and drained, the incision consisting of a 4 inch median longitudinal incision, with a 4 inch subclavicular incision at each side. No pus was present. The incised tissue was edematous. Smears and cultures were made from the fluid that exuded from the incision. A blood culture was taken on the evening of the day of admission; the blood at this time was very thick and dark and coagulated quickly. When the dressing was changed at 3:30 a. m. of the next day a large amount of serum was present, and the swelling of the chest had decreased slightly. The patient appeared very ill. Examination of the cultures made from the incision and of the blood culture showed the presence of *B. anthracis*. At 9 a. m., July 18, the dressing was changed again, a large amount of serum being present. The patient failed rapidly and died at noon, July 18.

Necropsy.—This was done four hours after death. In the region of the upper chest was an open crucial incision that extended through the skin and soft parts to the underlying bone. The longitudinal limb of the incision extended from the sternal notch to the middle region of the sternum. The horizontal limb extended from the middle of the left clavicle to the middle of the right clavicle. The margins of the incision were retracted, and the exposed tissue was found to be covered by a thin layer of grayish white material. Slightly to the left of the midline of the neck and 5 cm. above the clavicular line was an oval superficial skin lesion, 0.5 by 1 cm., covered with a dark crust. The neck was swollen, the swelling extending laterally on each side to the line of the mastoid region. The skin of the swollen region was slightly reddened and felt boggy. The cervical glands were not palpable. In the inferior chest region, below the lower end of the longitudinal incision, the subcutaneous tissue was edematous and gelatinous. The loose tissue of the upper anterior mediastinum was edematous. The spleen was increased in size to about four times the normal. The capsule was tense, free of adhesions, and bluish. The tissue on section was dark red and moderately firm. The malpighian bodies stood out as grayish translucent points up to 1 mm. in diameter.

Microscopic Examination.—In sections from the edematous subcutaneous tissue of the chest, the collagen fibers were swollen, fibrillated and granular, and the tissue spaces were filled with granular, eosin stained, structureless material in which a fibrin meshwork was present. The tissue was richly infiltrated with polymorphonuclear leukocytes, and contained many large gram-positive bacilli, which often formed long threads. In the underlying muscle, some fibers were swollen and faintly stained, and others were compressed and hyaline; most of the fibers had lost their cross striations. Sections of organs and tissues other than the subcutaneous tissue contained a few scattered, large, gram-positive bacilli in the capillaries. In the subcutaneous tissue the bacilli were numerous.

Bacteriologic Examinations.—Cultures from the small local lesion of the neck and from the fluid of the incision, made at the time of operation, gave a pure culture of a gram-positive, nonmotile bacillus, morphologically *B. anthracis*. A blood culture made on the evening of the day before death gave a pure culture of the same organism; 0.1 c.c. of this culture inoculated subcutaneously into a white mouse caused the death of the latter in twelve hours, and from the heart's blood of the mouse *B. anthracis* was again isolated. Smears from the spleen and liver at necropsy showed the same organism

* From the laboratory of the Base Hospital, Camp Jackson, Marshall A. Barber, Captain, S. C., U. S. Army, Chief of Laboratory.