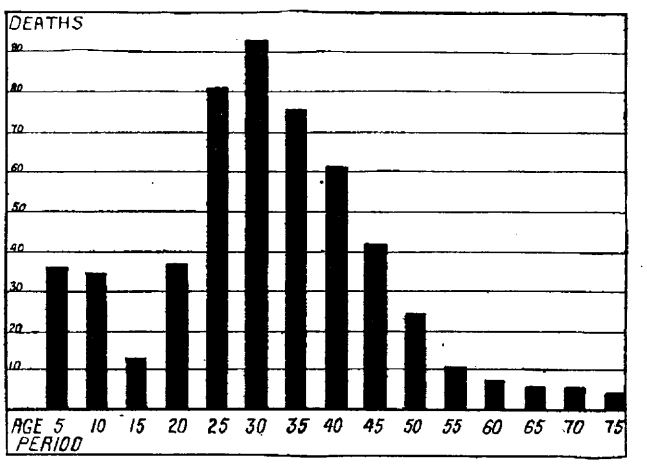
PANDEMIC INFLUENZA AND PNEUMONIA IN A LARGE CIVIL HOSPITAL *

JOHN W. NUZUM, M.D.; ISADORE PILOT, M.D.; F. H. STANGL, M.D., AND B. E. BONAR, M.D.
CHICAGO

Following the reports of a rapidly spreading and highly fatal pandemic of influenza and pneumonia in the Eastern States, and while the epidemic of influenza was raging at the Great Lakes Naval Training Station, a severe outbreak of this disease appeared among the civil population of Chicago. During the past five weeks, from September 23 to October 29, more than 2,000 patients were admitted to the wards of Cook County Hospital. Of these, 642 died, a mortality of 31 per cent. In the accompanying chart, of the first 500 deaths, it will be noted that the age period of highest mortality falls between 25 and 30 years.

Among the total number of admissions during this period there were 122 soldiers, and thus far twenty-one cases have terminated fatally—a mortality of 16 per cent. So far as the admissions to a large charity institution, such as the Cook County Hospital, may be regarded as an index to the prevalence of the recent epidemic in Chicago, it appears that the disease is now definitely on the decline. Accordingly, it seems pertinent to report the results of an intensive study conducted during the past five weeks in the morgue and the laboratory of the Cook County Hospital.



Age period of highest mortality in the first 500 deaths. The ordinates represent the ages in five year periods, the abscissas the total number of deaths per period. It will be noted that the period of highest mortality is between 25 and 30 years.

CLINICAL PICTURE

The incubation period varied from a few hours to one or two days. Shortly after the arrival of the first fifty soldiers, five of the nurses in attendance on these patients became violently ill, and during the following two weeks more than fifty nurses and twelve of the resident physicians contracted the disease. Three of the nurses died. Blood cultures, nasopharyngeal and tonsil swabs and cultures of the washed bronchial secretion were immediately taken by the laboratory staff, and four of the laboratory assistants were suddenly taken ill within the next forty-eight hours.

The onset is sudden, with complaint of severe headache, dull, aching pains in the muscles and joints, general weakness and quite commonly dull pains in the lumbar region. Conjunctivitis is not infrequent in the initial stages. Sore throat is unusual. The patient takes to bed with chilly sensations, and the fever rises rapidly from 101 to 104 F. Early prostration is the rule. Epistaxis occurs in a considerable number of patients, in one person as much as a pint of bright red blood gushing from the nostrils. The pulse is accelerated and the respirations vary from 20 to 36 a minute. The second to the fourth day marks the critical period for the average patient. Remissions may occur, but among our cases more frequently following the crisis the temperature rises rapidly again and a slight bronchial cough develops, productive of small amounts of thick yellow or yellowish brown sputum teeming with gram-positive encapsulated pneumococci. There can be no doubt that the bronchial secretions are highly infectious at this time and that the disease is transmitted by personal contact and by droplet infection occasioned by coughing and sneezing.

Moreover, very early after the onset, careful physical examination of the patient's chest will often reveal scattered râles with areas of consolidation over the lower lobes and especially the right lower lobe. The bronchopneumonic process begins as an intense acute hemorrhagic tracheobronchitis, rapidly extending to the finer bronchioles of the lung. In the acute fulminating cases the patients become markedly cyanosed, and death results from an asphyxiative bronchiolitis with large quantities of frothy blood-tinged fluid exuding from the mouth and nostrils.

In the more protracted cases, particularly in civilian patients, the bronchopneumonia extends gradually to the left lower, and right middle and upper lobes, and clinical evidence of a severe toxemia manifests itself. Blood counts taken early after the onset of the initial symptoms exhibit a striking leukopenia as low as 1,800 per cubic millimeter and averaging from 3,000 to 4,000 per cubic millimeter. With the onset of the pneumonia a definite leukocytosis quite commonly appears. The urine shows traces of albumin with hyaline and granular casts. Blood cultures taken early and late in the course of the disease and inoculated into glucose broth and plated in blood agar have remained uniformly sterile in forty-two instances.

MORBID ANATOMY

Of the first forty postmortem examinations made on the bodies of persons dying both early and late of bronchopneumonia, it was possible to obtain cultures from the nasopharynx, tonsils, washed selected bronchial sputum and from the lung parenchyma. Cultures were also obtained from these sites before death. The first eight necropsies were all of acute fulminating cases in young soldiers of excellent muscular development and physique. The course of the disease ranged from three to five days. Death was preceded by marked cyanosis and clinical evidence of acute asphyxiative bronchiolitis.

At necropsy the pleural cavities contained blood-tinged fluids remarkably free from fibrin content and varying from 300 to 1,000 c.c. in amount. The pleura of the lungs was fibrin free and regularly the seat of petechial and confluent hemorrhages. On cutting transversely across the trachea to reflect the viscera from the thoracic cavity, large quantities of blood-

* From the Laboratory of Pathology of the Cook County Hospital.

tinged, frothy fluid exuded from the air passages. The lining of the trachea and main bronchi presented a deep purplish red, and this intense inflammatory condition extended downward into the finest bronchioles. The consolidation was always lobular in type and involved most frequently the lower lobes, less often the entire midde and lower half of the right upper lobes. Marginal compensatory emphysema presented itself with striking regularity. The peribronchial lymph glands were acutely swollen and edematous. Cut surfaces of the lung presented a mottled, firm, granular appearance with intervening areas of dark red aerated lung tissue. Large quantities of bloody serum bathed the smooth, fibrin-free cut surfaces of the lung. The right heart was acutely dilated, in two instances the tricuspid valve ring measuring 13 and 14 cm., respectively, from cut edge to cut edge. In another body, bilateral symmetrical hemorrhage of rather huge dimensions was present in the tissues of the fatty capsules of both kidneys. The liver and kidneys were heavier than normal and the seat of fatty changes and parenchymatous degeneration. Passive hyperemia of the pia-arachnoidal vessels over the cerebral cortex, and edema of the leptomeninges were not uncommon. We desire to emphasize the fact that the amount of consolidated lung parenchyma was small as compared to the pneumonic consolidation quite regularly present in the more protracted cases among civilians. It will be noted that *B. influenzae* was isolated from only three of the lungs at necropsy in these eight early cases, in one instance in practically pure culture.

In the more protracted cases among civilians the bronchopneumonic process presents a rather uniform bluish gray hue with the cut surface bathed in grayish yellow pus—a massive, confluent, pseudolobar pneumonia. Fibrin is frequently present over the pleura of the lower lobes of the lungs. In only one case was an empyema present. The hemolytic streptococcus was isolated in pure culture and identified in direct smears from the pus.

BACTERIOLOGIC FINDINGS

A careful detailed bacteriologic study of the prevailing epidemic, especially among the civilian population, forms the basis of this paper. Bacteriologic reports of the pandemic in Europe show that the influenza bacillus was found only exceptionally while pneumococci, streptococci and *Micrococcus catarrhalis* were recovered with considerable regularity from the sputum, nose and throat cultures. In Germany a circular letter addressed to the leading bacteriologists requesting the results of their laboratory investigations brought forth the following replies[1]: "Pfeiffer had not examined a sufficient number of cases at Breslau, but found his bacillus in some while failing to recover it from others, and was still investigating the causes of this discrepancy." Gruber in Munich and Friedmann in Berlin failed to find the influenza bacillus, and report streptococci and pneumococci as the common agents of the complicating pneumonias. Kolle in Frankfort failed to find *B. influenzae* in any of the cases which he had thoroughly examined.

Among the English observers, Gotch and Wittingham[2] isolated *Micrococcus catarrhalis,* with which they claim to have produced the disease in man. Little, Garofalo and Williams[3] found a gram-positive coccus which they believe to be the etiologic agent of the disease. From the Eastern States Keegan[4] in Massachusetts and Park[5] in New York have isolated the influenza bacillus in a high percentage of cases. These reports concern soldiers and sailors chiefly. Our study was made principally of the civilian population.

During the present epidemic in Chicago, more than 3,000 blood agar plate cultures have been made from swabs of the nasopharynx, tonsils and washed selected bronchial sputum and from the viscera and body fluids at necropsy in search for the influenza bacillus or other micro-organisms of possible etiologic significance. Blood agar plate cultures were made from the swabs of the nasopharynx and tonsils in more than 100 patients approximately equally divided into early and late cases. The washed bronchial secretions from the same patients were both plated and streaked on the surface of blood agar plates. Control cultures from the nose and throats of normal individuals were also made. In both groups a peculiar gram-positive coccus growing in grayish white colonies and exhibiting marked pleomorphism in stained smears was present with considerable frequency. The smaller coccal bodies passed Mandler filters in two instances. This coccus was nonpathogenic both for man and the ordinary laboratory animals.

TABLE 1.—PERCENTAGE INCIDENCE OF VARIOUS BACTERIA ISOLATED FROM THE SPUTUM, NASOPHARYNX AND TONSILS IN 100 CASES OF INFLUENZA

	Pneumococcus %	B. Influenzae %	Streptococcus Hemolyticus %	Staphylococcus %	Micrococcus Catarrhalis %	B. Mucosus-Capsulatus %	Miscellaneous
Washed bronchial sputum..	70	4	20	40	5	1	Diphtheroids 1%
Nasopharynx	38	0	4	65	5	1	Leptothrix 2% Meningococcus 2% Diphtheroids 1%
Tonsil.....	74	0	37	37	7	1	Diphtheroids 1%

In Table 1 is shown the percentage incidence of the various organisms isolated from the nose, throat and sputum of 100 patients. The influenza bacillus was recovered in four cases from the washed sputum—in three instances in predominating cultures, but always in symbiosis with staphylococci. It was not present in the nose or throat swabs. The predominating organism was the pneumococcus isolated from the washed sputum in 70 per cent. and from the throat in 74 per cent. of the cases. *Streptococcus hemolyticus* occurred in the washed sputum in 20 per cent., or twenty patients.

To determine how early and with what frequency the various bacteria invade the lungs, a series of lung punctures was made both before and after clinical evidence of pneumonia presented itself. A sterile needle attached to a glass syringe was passed through the intercostal spaces into the lung parenchyma, and lung tissue plus serum was aspirated sufficient to streak the surfaces of blood agar plates at the bedside. In addition, some of the aspirated material was inoculated into poured blood agar plates in each instance. Of thirty-six consecutive lung punctures taken during life, twenty-one were sterile. Eleven yielded the results given in Table 2. Thus the pneumococcus was present

1. Quoted from Bacteriology of the "Spanish Influenza," Lancet, London, 1918, **2**, 177.
2. Gotch, O. H., and Wittingham, H. E.: Brit. Med. Jour., 1918, **2**, 82.
3. Little, T. H.; Garofalo, C. J., and Williams, P. A.: Lancet, London, 1918, **2**, 34.
4. Keegan, J. J.: The Prevailing Pandemic of Influenza, The Journal A. M. A., Sept. 28, 1918, p. 1051.
5. Park, W. H.: New York Med. Jour., 1918, **108**, 621.

in pure culture in 72.6 per cent.; hemolytic streptococcus in 19.8 per cent., and *Micrococcus catarrhalis* in 6.6 per cent.

Table 3 gives the findings in cultures of the lung tissue streaked and plated on blood agar at necropsy. *B. influenzae* was isolated in three cases, or 8.7 per cent., in one instance in practically pure culture from both lungs. Again the predominating organism was the pneumococcus, occurring in 75 per cent. of the lungs at necropsy, from ten cases in pure culture, eleven times in predominating culture and in five instances in mixed culture. Of the various types of pneumococci recovered, Type II was present in 30.5 per cent. of the lungs, and Type IV in 50 per cent.

TABLE 2.—LUNG PUNCTURES DURING LIFE *

	No. of Cases	Per Cent.
Pneumococcus, Type I	1	6.6
Pneumococcus, Type II	2	13.2
Pneumococcus, Type III	3	19.8
Pneumococcus, Type IV	5	33.0
Hemolytic streptococcus	3	19.8
Micrococcus catarrhalis	1	6.6

* Incidence of the various bacteria isolated from fifteen lung punctures during life. Pneumococci predominated in pure culture in eleven cases, a total of 72.6 per cent.

TABLE 3.—LUNG CULTURES AT NECROPSY *

	No. of Cases	Per Cent.
Pneumococcus, Type I	2	7.6
Pneumococcus, Type II	8	30.5
Pneumococcus, Type III	3	11.5
Pneumococcus, Type IV	13	50.0
Influenza bacillus	3	8.7
Hemolytic streptococcus	15	43.0
Staphylococcus	18	40.0
Micrococcus catarrhalis	0	0.0

* Incidence of the various bacteria isolated from thirty-four lung cultures at necropsy. Pneumococci were recovered in pure culture in twenty-six patients, a total of 75 per cent.

TABLE 4.—NUMBER OF INSTANCES THE VARIOUS BACTERIA WERE ISOLATED FROM THE TISSUES AND BODY FLUIDS IN THE FIRST THIRTY-SIX NECROPSIES

	Pneumococcus	B. Influenzae	Streptococcus Hemolyticus	Micrococcus Catarrhalis	Staphylococcus
Heart's blood	7	0	8	0	0
Pleural fluid	15	0	8	0	2
Pericardial fluid	8	0	8	0	0
Tracheal mucosa	19	1	14	1	15
Lung	26	3	15	1	18
Spinal fluid	2	0	1	0	3
Peritoneal fluid	0	0	1	0	0
Middle ear	2	0	1	0	0
Frontal sinus	1	0	1	0	0
Spleen	0	0	3	0	4

The various strains of pneumococci were identified by morphology, cultural reactions, inulin fermenting properties, bile solubility and, finally, biologically with immune serums. Pneumococcus, Type IV, and allied green producing organisms were found to vary greatly both as regards bile solubility and inulin fermentation. Subsequent study of this heterogeneous group may extend it to include numerous strains of *Streptococcus viridans*. Hemolytic streptococci appear as late secondary invaders and were isolated from 43 per cent. of the lungs at necropsy. Staphylococci were frequently present.

THE INFLUENZA BACILLUS

It is evident from the tables that the influenza bacillus was isolated in only a relatively small percentage of the cases. Thus *B. influenzae* was present in four washed sputums—three times in predominating cultures growing typically as transparent minute colonies in symbiosis with staphylococci. It was recovered in one instance from the tracheal mucosa and three times from the lung cultures at necropsy. Influenza bacilli were never isolated from the lung punctures during life taken by preference from the early cases. On the other hand, the bacilli were recovered both in smears and in practically pure cultures from each lung in the case of a young soldier dying the fifth day of the disease. It appears that the Pfeiffer bacilli may have been the cause of the pneumonia in this case. In contrast to this single case we have not been able to isolate the bacillus in any considerable percentage of the civilian patients either during life or from acute fulminating cases at necropsy. The early results indicate that the technic employed should have sufficed to recover the organism if it were present in any considerable number of patients.

Furthermore, the high percentage of pneumococci obtained during life and at necropsy and predominating in the sputum, tracheal mucosa and lung tissue both early and late in the course of the disease suggest that this organism is at least the most important secondary invader and is responsible for many of the rapidly fatal pneumonias. It may be that we are dealing with a highly virulent strain of pneumococci sufficient in themselves to produce a rapidly fatal lobular pneumonia.

EXPERIMENTAL

Early in the course of our investigations we were impressed with the paucity of the bacteria in the nasopharynx at the onset of the disease and the marked degree of prostration exhibited in many of the patients. The possibility of a filtrable virus as the cause of the disease suggested the following experiments:

EXPERIMENT 1.—Oct. 2, 1918, the nose and throat of a patient having a typical case of influenza of forty-eight hours' duration was washed with 40 c.c. of sterile physiologic sodium chlorid solution, and the collected washings were diluted to a total bulk of 60 c.c. and shaken for twenty minutes in a sterile bottle containing glass beads. The fluid was immediately filtered through two small tested Mandler filters of medium porosity. The clear Filtrate A was inoculated into the anterior nares of three volunteers in amounts varying from 0.5 to 1 c.c. in each nostril. One of the men thus inoculated complained of slight headache, and presented a moderate conjunctivitis and a temperature of 99 F. twenty-four hours after the inoculation. These symptoms rapidly disappeared, and no further symptoms developed in any of the three subjects.

EXPERIMENT 2.—Oct. 4, 1918, the nasopharyngeal washings in two typical cases of influenza were mixed together and agitated in a sterile bottle containing glass beads for a period of fifteen minutes. The first patient had been ill only ten hours while the second patient was in the fifth day of the disease. The mixture of washings was immediately passed through a Mandler filter as Filtrate A and a second smaller portion filtered through a small Berkefeld candle N as Filtrate B. Filtrate A was inoculated into the anterior nares of two volunteers, and Filtrate B was similarly inoculated into the noses of two additional volunteers. One of the four subjects complained of a slight headache and presented himself twenty-four hours after the experiment with a definite coryza, conjunctivitis and lacrimation. These symptoms had completely disappeared by the following morning, and the men had all remained well when seen two weeks later. Cultures of the clear filtrates were inoculated into glucose broth and in the anaerobic tissue ascitic fluid culture medium of Noguchi. All tubes remained sterile after the expiration of two weeks. From these observations, which confirm those recently reported by Keegan, it may be assumed that the etiologic agent is not filtrable.

EXPERIMENT 3.—Oct. 4, 1918, at 4 p. m., the trachea and main bronchi secured at necropsy from a patient dying on the fifth day of the disease was split parallel to its lumen and the swollen dark red mucosa curetted off and thoroughly ground up with sterile sand in a mortar to make a turbid

suspension in 50 c.c. of sterile saline solution. The suspension was centrifuged at slow speed to throw down the gross particles, and half of the resulting red emulsion was passed through a Mandler diatomaceous earth candle of 12 pounds positive pressure. A *Macacus rhesus* monkey received 5 c.c. of the unfiltered suspension in each nostril, and 20 c.c. of the clear filtrate were injected at the same time very slowly intravenously. No symptoms developed.

EXPERIMENT 4.—Oct. 8, 1918, the monkey received 2 c.c. of the mixture of the nasopharyngeal washings in four early cases of influenza in each nostril after previous swabbing and washing out the protective mucus in the nares. No symptoms developed after seven days' observation.

COMPLICATIONS AND SEQUELAE

During the past five weeks of the present epidemic there were eighty-six pregnant women admitted to the obstetric wards of the hospital affected with influenza or pneumonia. Of this number twenty-one died shortly after miscarriage. Twenty additional deaths occurred before miscarriage could result, and forty-five patients recovered with or without miscarriage. The total maternal mortality has been 45.5 per cent.

Among other complications of the disease, eleven patients have developed a unilateral or bilateral purulent otitis media. Pure cultures of pneumococci were isolated from eight discharging ears, the hemolytic streptococcus in two patients and the *Streptococcus viridans* in the remaining case. One child developed an acute and fatal mastoiditis. Purulent frontal sinusitis was encountered in one instance at necropsy, and cultures yielded pure hemolytic streptococci. It is to be expected that sequelae of still more diverse nature may subsequently develop.

SUMMARY

A severe and rapidly spreading epidemic of influenza and bronchopneumonia first appeared at the Cook County Hospital, September 23. During the past five weeks more than 2,000 patients were admitted to the hospital. The disease is highly contagious, and the mortality among our patients has totaled 31 per cent. The epidemic has seriously crippled the medical and more especially the nursing staff of the hospital. More than fifty of the nurses and twelve of the physicians have contracted the disease, three deaths occurring among the total number.

The influenza bacillus was isolated in only 8.7 per cent. of the total cases and chiefly from a small number of soldiers. In one instance it appears that the influenza bacillus may have caused the fatal bronchonpneumonia. Influenza bacilli were isolated only exceptionally from the civilian patients. Pneumococci were the predominating organisms in the sputum, throat cultures and in the lung cultures both during life and at necropsy. Pneumococci of unusual virulence were the most important early secondary invaders, and have sufficed to cause many of the fatal pneumonias.

Experiments indicate that the disease is apparently not due to a filtrable virus.

Liability for Performing Unauthorized Postmortem Examination.—It is held in the Minnesota case of *Woods* v. *Graham*, 167 N. W. 113, annotated in L. R. A. 1918 D, 403, to be no defense to an action to recover damages caused by a necropsy performed on the body of the daughter of plaintiff, without the consent of the next of kin, that defendant, as the attending physician, was unable to ascertain the cause of death and performed the necropsy for that purpose, so as to be able to give a certificate, as required by law, stating the cause of death.—*Legal Notes.*

INCORRECTNESS OF THE DIAGNOSIS OF DEATH FROM INFLUENZA

PRESENCE OF BRONCHOPNEUMONIA IN PRACTICALLY ALL PERSONS SEVERELY ILL WITH INFLUENZA *

HENRY A. CHRISTIAN, M.D.
Hersey Professor of the Theory and Practice of Physic, Medical School of Harvard University; Physician-in-Chief, the Peter Bent Brigham Hospital
BOSTON

Boards of health, as indicated by newspaper reports, very generally are subdividing their mortality reports from epidemic influenza into deaths from influenza and deaths from pneumonia or bronchopneumonia. This is no doubt based on the death certificate return handed in by the physician in charge of the patient. Is it a correct return? In my opinion it is not. The correct return should be bronchopneumonia and (epidemic) influenza. Whether the bronchopneumonia is part of the influenza or is a complication of that disease; whether the disease is due primarily to the influenza bacillus; whether the pulmonary consolidation is caused primarily by the *Bacillus influenzae* or is the result of concomitant bacteria are questions that cannot be answered on the basis of our present information. However, my own observations on patients suffering from epidemic influenza do justify a vigorous protest against a statistical subdivision of death reports into those dying from influenza without pneumonia and those dying from bronchopneumonia or pneumonia and influenza.

My reasons for believing that in practically all fatal cases of epidemic influenza there is a pneumonic process in the lungs before death are as follows:

1. In 126 consecutive fatal cases of epidemic influenza observed by me and my assistants at the Peter Bent Brigham Hospital, not a single patient failed to show physical signs justifying a clinical antemortem diagnosis of bronchopneumonia.

2. In twenty-two consecutive necropsies at the Peter Bent Brigham Hospital in fatal cases of this group, no single case failed to show pathologic changes in the lung justifying the diagnosis on the part of the pathologist of bronchopneumonia.

3. In patients submitted to necropsy, pulmonary changes are as a rule more extensive than physical signs during life had indicated.

4. Clinical study of nonfatal cases of epidemic influenza justify the belief that with very few exceptions, patients with fairly severe to severe cases have bronchopneumonia.

In making the foregoing statements I do not deny that influenza patients may die from an overwhelming toxemia without pulmonary involvement or from influenzal meningitis or encephalitis or from some other manifestations of the disease. Such fatal cases did not occur at the Peter Bent Brigham Hospital, and in conversation with my colleagues who have had postmortem experience in this disease I have found that their views have seemed to coincide with those expressed here by me. In our admissions to the hospital of patients sent in with the diagnosis of influenza, I have seen cases of meningitis; one case was due to the meningococcus and apparently did not have any com-

* From the Medical-Clinic of the Peter Bent Brigham Hospital.