# Pathologic Similarity Between Pneumonia of Bubonic Plague and of Pandemic Influenza

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# PATHOLOGIC SIMILARITY BETWEEN PNEUMONIA OF BUBONIC PLAGUE AND OF PANDEMIC INFLUENZA

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Since the commencement of the present epidemic of influenza in New York City I have had occasion to investigate by necropsy at the Willard Parker and Bellevue Hospitals twenty cases of death from pneumonia occurring in the course of this remarkable infection. The changes in the lungs are those of a variety of confluent lobular exudative and hemorrhagic pneumonia in which the naked eye and microscopic features bear such a resemblance to the lesions in the pneumonic variety of bubonic plague as to provide an interesting study in similarities. There are, however, several features which serve as differential safeguards in separating the two diseases on anatomic grounds. If these should be eliminated or projected into the background—as not infrequently they are—then, indeed, the sum of the reactions of the pulmonary tissues to the prevailing infection is so nearly equivalent to that of pneumonic plague as described and depicted by investigators in the Far East that, were it not for the aid of modern bacteriologic methods, the pathologist of this climate might be tempted to the conclusion that the world is facing a pandemic of pneumonic plague in which, contrary to rule, the mortality is relatively low, rather than a pandemic of influenza with unusually frequent pneumonic complications and a far higher mortality than that exacted by any previous eruption of the same disease. The captious critic might object that an otherwise harmonious comparison is violated by the projection of superficial buboes into

the picture of pneumonic plague and their absence from that of influenza, to which it may be replied that the pneumonic variety of plague is seldom accompanied by those bubonic manifestations from which the disease takes its name and with which, erroneously, all of its several anatomic forms seem to be associated in the minds of most physicians resident in this latitude. As far, however, as participation of the deeper nodes is concerned, the extent and distribution of thoracic and abdominal adenopathies in both diseases bear out the analogy. Moreover, the similarity of the two diseases is enforced by the clinical features, which are remarkably alike in many respects, and by the pathology of certain tissues other than the lungs. However impressive these observations may be, it is comforting to recall that the bacteriology of the prevailing pandemic is vouched for by a number of exceedingly able investigators, and that *Bacillus pestis* has found no place in their results.

In the greater number of all the cases of pneumonia associated with the prevailing epidemic, our experience at the Willard Parker and Bellevue Hospitals is that the pleural cavities are free from excessive accumulation of fluid, only two exceptions having been found. In one of these the right pleural cavity was distended by cloudy, milklike fluid which had compressed the lung into an atelectatic mass scarcely larger than one's clenched fist, and the pleura was universally thickened. Obviously the empyema was one of long standing and had preceded the influenzal infection. In the second case, both pleural cavities were half filled with serofibrinous exudate, and the pleural membranes were extensively, although irregularly, obscured by collections of coarse, shaggy fibrin. In each of two other cases the pleura presented a localized, solitary patch of fibrinous exudate a few centimeters in diameter. In the remaining seventeen cases the pleurae were smooth, glistening and devoid of exudate. It is exceedingly important to note that, in this regard, the pathology of pneumonic plague is different from that of the existing pandemic influenza, Crowell, in twenty-five necropsies on subjects dead of plague in the Manchurian epidemic having found extensive pleural exudates in every one.

The naked eye appearances of the lungs themselves, however, are highly suggestive, and, for descriptive purposes, may be thus grouped:

1. Cases with (*a*) extensive confluent lobular solidification of the lower lobes; (*b*) circumscribed or partially confluent consolidation of the lobules of the upper lobe, and (*c*) areas of acute vesicular emphysema. These cases without exception represented examples of rapidly fatal pneumonia.

2. More prolonged cases characterized by complete or almost complete consolidation of all or most of the lobes of both lungs, areas of acute vesicular emphysema occurring as an inconspicuous feature.

3. Those cases in which the pneumonic process is obviously subsiding.

### THE ACUTE CASES

(*a*) The lower lobes of both lungs were always involved in company, never, in my experience, alone. The lower lobes were enlarged, heavy and extensively, often almost completely, consolidated. The involved areas presented a deep slate blue color mottled at intervals by slightly elevated pinkish or cream colored subpleural patches in which the inflammatory process had not progressed to its customary conclusion, or by areas of vesicular emphysema in which the dilated vesicles appeared as streaks or patches of minute, glistening, beadlike bodies. Petechial hemorrhages into the pleura or larger, splotchlike extravasations of blood were practically constant. As a rule, the extreme edges of the lung were spared by the solidifying process, the air vesicles undergoing, however, marked compensatory emphysematous changes. On section the substance of the lung cut readily. The cut surface presented a deep bluish or bluish black appearance, the substance was friable but less easily broken than that of the lung in croupous pneumonia, and the surface was of the smoothness of velvet, not a trace of fibrin being seen or felt. Scattered over the deep slate blue background were occasionally to be seen small, pinkish, granular-looking, firm patches in which, however, no suggestion of fibrinous granulations were apparent to the touch or microscopically. Pressure on the consolidated lobe released huge quantities of deeply blood stained serum in which there was a distinct milky tint

due to the escape of leukocytic exudate from the vesicles. The cut ends of the smaller bronchi were sometimes to be distinguished by the escape of droplets of pus, oftener by frothy serum. The mucosa of the trachea and larger bronchi was greatly swollen, deep bluish red, and velvety, with an occasional grayish fleck of pseudomembrane lying on the surface. The peribronchial lymph nodes were markedly edematous and hyperemic, forming a mass around the root of the lung that sometimes attained remarkable proportions.

Microscopic examination of the deep bluish, firmly solidified portions of the lower lobe revealed the presence in the alveoli of huge numbers of red cells and polymorphonuclear leukocytes, either alone or in combination, and coagulated serum. Fibrin was absent. In many alveoli were quantities of large, rounded cells corresponding to desquamated vesicular epithelium. The interalveolar capillaries were intensely injected, as were those in the walls of the bronchi and bronchioles. The bronchioles were, for the greater part, filled by polymorphonuclear leukocytes, among which were clumps of desquamated epithelium.

(*b*) The upper lobes presented a somewhat different picture. The lowermost portions were divided into lobules of different sizes, some of them bluish and firm, others pinkish or reddish and less firm in consistence, while the uppermost parts and the extreme edges were markedly emphysematous and feathery. The microscopic changes in the solidified lobules varied, according to the degree of consolidation, from simple exudation of serum to distention of the vesicles by red cells or leukocytes or both. In other words, the pneumonic process in the upper lobes may be found in all stages of advancement, but the richly injected interalveolar capillaries and the frequent and abundant escape of red cells into the vesicles are apt to dominate the picture as a whole.

I shall not risk repetition in order to afford verification from an independent source of the similarity between the pulmonary changes in pneumonic plague and those of the prevailing pandemic of influenza as we have observed them at Bellevue Hospital. Suffice it to say that one has only to consult the admirable description of the lungs contained in Crowell's mono-

graph[1] on plague, as he saw it in the Manchurian epidemic, to confirm the impression that the pulmonary changes in pandemic influenza are of the same essential variety, the constant pleural exudate in plague and the almost constant acute vesicular emphysema in influenza serving as the main points in the anatomic differentiation. Moreover, the colored illustrations that accompany Crowell's paper substantiate the resemblance to which I have ventured to call attention.

(*c*) The areas of acute vesicular emphysema so constantly to be found in association with the lobular pneumonia of pandemic influenza are of considerable clinical interest. For example, in two of our cases, rupture of distended air vesicles had taken place, probably near the apex of the lung, and the soft tissues in the supraclavicular spaces were crepitant with infiltrated air. In another case rupture had occurred, apparently in the vicinity of the root of the lung, since the soft tissues of the posterior aspect of the pericardium were permeated by myriads of emphysematous bullae varying in size from the head of a pin to that of a small marble. Gaseous particles extended thence into the soft tissues of the precordial area, downward toward the pericardial attachment to the central tendon of the diaphragm, forward into the retrosternal region, and thence through the upper aperture of the thorax into the neck and to the lower portions of the face and downward into the subcutaneous tissues as far as the crest of the ilium on the left and the lower level of the costal slope on the right. In still another case, rupture had occurred directly into the left pleural cavity with the production of pneumothorax. In none of these cases was it possible for us to demonstrate at necropsy the actual point of rupture.

### MORE PROLONGED CASES

In the Willard Parker and Bellevue Hospital necropsies we have several times observed almost complete consolidation of both lungs, particularly in individuals who had presented clinical indications of pneumonia for a relatively prolonged period. It was in two of these cases that the pleura presented localized patches of fibrinous exudate. In all of them the pulmonary substance was so extensively involved by the inflam-

1. Crowell: Philippine Jour. Sc., B, 1912, **7**, 203.

matory process that the peripheral areas of vesicular emphysema were scarcely noticeable. In cases of this sort, also, the cut section of the lung sometimes showed pinhead sized or larger, rounded or irregularly outlined, grayish or cream colored bodies corresponding to confluent vesicular exudations of leukocytes, or there were areas in which, scattered over a considerable extent, the cut surface of the consolidated lung was marked by a network of grayish or grayish red lines surrounding deeply congested islands of consolidated tissue.

### CASES IN WHICH PNEUMONIC PROCESS IS SUBSIDING

I have had an opportunity to study the lung in one case in which the pneumonic process was obviously subsiding. The patient was a man, about 30 years of age, who gave a history of having passed through a typical siege of influenzal pneumonia. He returned to work at an ill advised moment of convalescence and died suddenly. At necropsy the right side of the heart was greatly dilated and the muscle tissue was flabby. Both kidneys were large and congested, the tufts standing out as minute, reddish points. The spleen was enlarged and congested, weighing 275 gm. Both lungs were greatly increased in size. The upper lobes were emphysematous and feathery in consistence. The lower lobes were congested. In the lower lobe on the right side was a patch of consolidated tissue about the size of one's thumb, and similar but smaller areas were found to the number of two or three lying in different parts of both lower lobes. These patches were deep bluish, firm, airless, and, on section, presented a perfectly smooth, velvety appearance, and quantities of semipurulent fluid could be squeezed from them. Scattered over the lower lobe, beneath the pleura, were several thumb-nail sized, pinkish patches, and it was observed that the pleura covering each of them was finely wrinkled. Evidently these patches represented areas in which the lung had undergone acute emphysematous alterations without complete loss of tone in the elastic fibrils, and that restitution was progressing. Microscopic examination of the solidified patches in the lungs revealed intense congestion of the interalve-

olar capillaries together with the presence in the air vesicles and smaller bronchi of dense collections of polymorphonuclear leukocytes. No red cells were apparent, and no fibrin.

Finally, I may be permitted to call attention to the occurrence of one instance in which the changes in the lungs of a soldier dead of influenza were identical with those originally described by Delafield as constituting an acute productive bronchopneumonia, and more recently studied by MacCallum[2] among the American troops in Texas. This variety of pneumonia is fairly common as a sequel of measles, and, according to MacCallum and Cole, is caused by a hemolytic streptococcus. It is marked by the presence in the lung of myriads of pin head sized, grayish white foci which are irregularly rounded or angulated and in the center of which a minute opening or depression may be discerned. In the case that I had an opportunity to study these spots were present literally in countless numbers scattered through both lungs, lying in a deep bluish red background and bearing a resemblance to miliary tubercles. On microscopic examination it was found that each whitish spot corresponded to a small bronchus whose lumen was partially or completely filled by polymorphonuclear leukocytes and clumps of desquamated epithelium. The connective tissue framework of the bronchus supported numbers of dilated and deeply injected capillary vessels between which were round cells. The alveoli in the vicinity or at a distance were filled either by polymorphonuclear leukocytes or by leukocytes and desquamated cells, some of the latter containing brownish yellow pigment granules. The interalveolar capillaries were universally injected. In short, the histologic changes were those of a very early stage of Delafield's acute productive bronchopneumonia, the later stages of which, according to the original observations of the distinguished American pathologist,[3] are attended, among other things, by the growth of connective tissue in the smaller and medium sized bronchi, in the interalveolar septums and thus by permanent changes of a productive nature.

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2. Cole, Rufus, and MacCallum, W. G.: Pneumonia at a Base Hospital, THE JOURNAL A. M. A., April 20, 1918, p. 1146.
3. Delafield: Lectures on the Practice of Medicine, Part 2, p. 229.

## THE CIRCULATORY SYSTEM

In the prevailing pandemic influenza, clinical indications of circulatory disturbances are numerous. For example, the nasopharynx is deeply congested, the skin is not uncommonly the seat of erythematous eruptions of various sorts, duskiness and cyanosis are common, the blood pressure is often alarmingly low, and the pulse is slow. At necropsy the signs of congestion are more intense and widespread than in any acute infective disease with which I am acquainted. The mucous membrane of the upper respiratory tract is swollen and deep red, the pulmonary capillaries, with scarcely a detectable exception, are crowded with red cells, and hemorrhages into the pleura and lung are common, the spleen is always deeply congested, the capillaries of the kidney from pelvis to capsule are filled to distention, the medulla of the suprarenals is frequently swollen and deep bluish red, the mucosa of the gastrointestinal tract presents isolated or diffuse areas of injection, sometimes giving rise to hemorrhage by diapedesis, the lymph nodes are swollen and hyperemic to an unusual degree, the capillaries of the liver are injected to their fullest capacity, and the smaller vessels of the brain are likewise involved. In addition, the right side of the heart is dilated, especially the auricle, and the heart muscle is diffusely bluish and its capillaries are universally distended. Both the naked eye and microscopic appearances of the heart muscle fibers, however, are in the majority of cases indicative of a surprisingly excellent state of preservation. Cloudy swelling, in my experience, is exceptional.

The anatomic and histologic changes in the circulatory apparatus are of importance as indicating the necessity for stimulation from the instant that the diagnosis of influenza is made. Clinically, there are excellent reasons for believing that these changes are present from the earliest moments of infection. Moreover, from the opportunity that I have had to observe these cases at necropsy and in the living patient, it appears to me to be probable that the prevailing pandemic influenza is attended by pneumonic lesions from the beginning. Thus it has been shown that patients in whom it is impossible to detect signs of consolidation by ordinary methods of diagnosis, if subjected to

roentgen-ray examination, reveal defects in the lower lobes that are to be interpreted only as areas of consolidation, subsequent developments confirming this view. Moreover, the distribution of the pathologic changes in the lungs is such as to suggest that the infection is introduced by way of the respiratory tract and that, in many cases, the initial lobular consolidations are situated deep in the substance of the lung, the process later developing in such fashion as to include the periphery. In those cases in which death has occurred twenty-four or thirty-six hours after the development of detectable pneumonic signs, it is scarcely conceivable that the massive solidification of the lungs found at necropsy could have taken place with corresponding rapidity. The suggestion naturally follows that, if one is to err at all let it be on the safe side, and that every case of pandemic influenza should be regarded from the outset as pneumonic, and so treated.

### THE KIDNEYS

Microscopic examination of the kidneys reveals diffuse congestion of the capillary network throughout the entire organ, together with cloudy swelling of the tubular epithelium, most marked in the convoluted tubules and not infrequently well marked in the epithelium of Bowman's capsule. In this way the lumina of the tubules become partly occluded by granular débris, and similar material is to be found in the interval between capsule and tuft.

### THE BRAIN

In those cases attended by delirium, the meninges of the brain are richly infiltrated by serous fluid and the capillaries are injected. Microscopic examination of the brain substance shows marked hyperemia. In one of our cases the convolutions of the brain were flattened and the brain tissues were noticeably dry. In another case purulent meningitis of pneumococcal origin was present.

### JAUNDICE

In seven of the twenty cases investigated postmortem at Bellevue and Willard Parker Hospitals, slight jaundice was present. Inquiry into this feature has shown that the mucous membrane of the duodenum is

congested and swollen and that the exit of bile through the papilla of Vater is impeded to an extent sufficient, in part at least, to account for retention in the bile capillaries and liver cells. Moreover, microscopic examination reveals the liver cells in such an advanced state of cloudy swelling that the bile capillaries are obstructed, the bile accumulating in the cells as minute greenish particles, finally being diverted, no doubt, into the circulation. In addition, the bile itself is extremely viscid, the contents of the gallbladder consisting of material of gelatinous consistence.

### THE SPLEEN

In seven of the twenty cases of fatal influenza the spleen was normal in size, in nine it was slightly increased, and in the remaining four the organ was distinctly enlarged, three times to the extent of 300 gm. or over. The organ is deep blue; there is, in fact, a strong resemblance between the color of the spleen and that of the consolidated lower lobes of the lungs as seen through the pleura. On section the substance of the spleen is deep blue, friable rather than grumous—in which respect the consistence differs from the spleen of sepsis as commonly observed—and the follicles are unusually numerous.

### ABORTION

The observation of Ball[4] that pregnant women are apt to abort as a result of influenzal infection is confirmed by our experience at Bellevue Hospital. The subject is now being investigated and will be made the object of a subsequent report.

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4. Ball, M. W.: Abortion as a Sequela of Influenza, THE JOURNAL A. M. A., Oct. 19, 1918, p. 1336.