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In New York City the first recurrent epidemic of so-called influenza, now fortunately at an end, presented certain noteworthy differences from the pandemic disease which prevailed in the latter part of 1918. The recurrent disease, while it incapacitated thousands, pursued a milder course, complicating pneumonias were relately few, and the death rate, of course, did not approach the appalling figures of the previous eruption. On the other hand, the recurrent disease was characterized by a greater variety of pulmonary lesions—among other things, by concomitant semipurulent pleural exudates, by multiple pleural and subpleural abscesses, by frequent and extensive purulent invasion of the interlobar and interlobular septums of the lungs, by the formation of solitary, oftener multiple, discrete or confluent abscesses of the parenchyma, and by an extraordinary range of pneumonic lesions. The pathologic anatomy of the recurrent disease is important, not only from the standpoint of the diagnosis and treatment of the acute process, but also because the nature and distribution of the anatomic changes are such that we may expect both immediate and remote sequelae, some of which will probably demand operative interference.

The pandemic of 1918 is fresh in memory; but for purposes of comparison it may be recalled that the disease was strikingly abrupt in onset and that pneumonic complications were seldom absent, that they

occurred early, progressed with amazing rapidity, and yielded a high mortality. At necropsy, the changes in the lungs were so constant that the anatomic diagnosis of so-called influenzal pneumonia could be postulated with almost absolute certainty, even in the absence of any knowledge of the clinical history. Variations occurred, of course, but were numerically inconsiderable. For example, in the first epidemic, the pleura was almost invariably free from signs of exudate. The inflammatory changes in the lungs, commencing in the deeper portions of both lower lobes apparently simultaneously, and progressing rapidly toward the periphery, often spared many intervening or surface lobules. The pleura almost always escaped literally, it would appear, because death took place before the pleura had time to react. In certain localities, empyema frequently occurred as a sequel to pneumonia; but the rapidly fatal pneumonias were seldom actually accompanied by inflammatory changes in the pleura. In the recurrent epidemic, on the contrary, many hundreds came down with a disease of comparatively trifling proportions; pneumonic complications, when present at all, were late and progressed without unusual rapidity. In the recurrent disease, the anatomic picture was extremely variable, so much so that, in order to classify the pleural and pulmonary changes, one must resort to the process of grouping; and between groups and the individual members of different groups there are numerous gradations.

DEATH FROM ASPHYXIA WITHOUT PNEUMONIA

Near the close of the epidemic of 1918, one of us [1] described a variety of so-called influenzal infection which was characterized anatomically by generalized intense congestion of the viscera, without evidences of pneumonic lesions, or attended by lesions of such small size as to be negligible. Death was accompanied by signs of asphyxia and, at necropsy, the right side of the heart was found to be immensely distended by deep bluish black fluid and clotted blood. The lungs were large, heavy and deep bluish, and the pleura was thin, smooth and glistening. On section, the cut surface was of the smoothness of velvet, and pressure

1. Symmers, Douglas: The Significance of the Vascular Changes in the So-Called Pandemic Influenza, New York M. J. **110**: 789 (Nov. 15) 1919.

yielded large amounts of dark fluid blood with or without an admixture of dirty, pinkish, edematous fluid. The mucosa of the larger bronchi was covered by a thin sheeting of whitish exudate, beneath which the membrane was swollen and intensely injected. Virtually every other organ in the body was injected to a correponding extent. In the recurrent epidemic we have encountered five cases of identical nature. In all of them poisoning by wood alchohol was suspected because of the intense and widespread injection of the tissues, particularly the lungs and brain. Chemical investigation of the viscera in every case, however, was negative. Of the cases observed in 1918 and 1920—seven in all—the clinical histories were obtainable in six and showed that the patients had been ill for periods varying from a week to twenty-one days with cyanosis and generalized aches and pains, prostration, elevation of temperature, injection of the pharynx, and numerous moist and squeaky râles scattered over both sides of the chest. In two cases, signs of meningeal irritation were present in the form of muscular twitchings. In one case of the seven, death was sudden.

EMPYEMA AND PULMONARY ABSCESSES

In the recurrent epidemic, forty-five cases were investigated by necropsy at Bellevue Hospital. Of this number, the pleura was involved in twenty-seven (60 per cent.). Of the twenty-seven cases, effusions occurred into the pleural cavity in eighteen, or forty per cent. of the total number of cases observed at necropsy; in twelve cases (26.6 per cent.), the effusions were semipurulent and unilateral in distribution, and in two cases bilateral; the remaining four were frankly purulent—two bilateral and two unilateral. Of the twenty-seven cases of pleural involvement, mutiple small subpleural abscesses occurred twelve times (44.4 per cent.) and of these, six were associated with semipurulent effusions and one with frank empyema. All of the seven cases of small subpleural abscesses associated with pleural effusions were found to be accompanied by abscesses in the parenchyma of the lung, the latter being relatively much larger in size. In the remaining five cases of subpleural abscesses, purulent foci in the parenchyma of the

lung were absent, and there were no signs of pleural effusion, although the pleura was the seat of edematous fibrinous exudate in every instance. The association of multiple subpleural abscesses with pleural effusions and with abscesses in the parenchyma of the lung is of obvious surgical significance. On the other hand, it appears that multiple small subpleural abscesses may exist alone without giving rise to secondary effusions into the pleura. In the presence of such abscesses, however, it would be rather far fetched to assume that an accompanying effusion represents an independent infection of the pleura. While we have no anatomic evidence to offer that subpleural abscesses of the type described in this paper bear a direct causative relationship to empyema, it is quite probable that if an individual with small subpleural abscesses survives sufficiently long, rupture of or seepage through might readily infect the pleura with the secondary formation of seropurulent or purulent effusions. In short, in the recurrent disease there were cases of pleural effusion, purulent or semipurulent, which were associated with a combination of subpleural and parenchymal abscesses; there were other cases in which subpleural abscesses occurred alone and were not associated with effusions into the pleural cavity; in still other cases, pleural effusions occurred independently of abscess formation either in the pleura or in the lungs.

Of the forty-five cases, sixteen were associated with the presence of intrapulmonic abscesses (35.5 per cent.). In only one of these cases was the abscess solitary. The others were multiple, of irregular distribution, some bilateral, others unilateral, some in the lower lobes, others in the upper. The abscesses varied in size from minute affairs to purulent foci approximating 2 or 3 cm. in diameter. In one case, the upper lobe of the lung was almost completely replaced by multiple discrete or intercommunicating cavities.

THE PLEURAL CHANGES

The inflammatory changes in the pleura presented marked variations:

(*a*) In those cases of pneumonia in which the changes in the lung were obviously of the more acute variety, localized sheets of edematous fibrinous

exudate were scattered over the surface of the consolidated lung, and when stripped away left an opaque, finely granular, deep bluish surface, scattered through which innumerable minute hemorrhagic specks were often discernible. In such cases, the exudate was practically never attended by the excessive accumulation of fluid in the corresponding pleural cavity.

(*b*) A second group of cases was characterized by the extensive deposit of fibrinous material over the surface of the lung, the membrane being thick, tough, opaque, dirty yellowish white, firmly attached, and often thrown into innumerable small corrugations. These membranous deposits were obviously in process of organization, and were invariably associated with excessive accumulation of semipurulent fluid exudate in the pleural cavity.

(*c*) In a third group of cases, the pleura was the seat of diffuse or patchlike collections of succulent, yellowish exudate which penetrated the lung substance at irregular intervals. Section of the consolidated lung in such cases showed thick, edematous prolongations extending from the pleura and surrounding individual lobules or small groups of lobules, not alone at the periphery of the lung, but deep in its substance. In many instances the interlobar septums were extensively invaded, the lobes were firmly glued together, and not infrequently collections of fluid exudate were included between them.

(*d*) In a fourth group of cases, the pleura presented solitary or multiple, pea-sized or slightly larger, rounded projections which were yellowish, soft in consistency, and, on section, released moderately thick, yellowish, cloudy fluid. These small abscesses lay in or immediately beneath the pleura and were often associated with quantities of seropurulent fluid in the dependent portions of the cavity. The intervening pleura was usually the seat of irregular or diffuse collections of edematous fibrinous exudate The external covering of the abscesses was intact as far as the unaided eye could determine. Microscopic examination of the pleura in these cases showed the presence of rounded or elongated, circumscribed masses of polymorphonuclear leukocytes enclosed in a meshwork of finely fibrillated fibrin, the whole lying in or just beneath the pleura, sometimes surrounded

by a thin but distinct layer of connective tissue representing, apparently, the result of proliferation of the walls of the lymph vessels. In certain of these minute abscesses the limiting connective tissue contained small, injected blood vessels.

It is obvious that the changes in the pleura are of extreme importance, not only from the standpoint of immediate effects, but because they are such that, if the patient survives, sequelae may be expected in a certain proportion of cases in the form of organization of the pleural membranes, with complete or partial obliteration of the cavity and interference with the movements of the corresponding lung, chronic diffuse or sacculated pleural or interlobar empyemas, and chronic interstitial interlobar pleuritis or interlobular pneumonia following organization of the exudate in the pleural extensions. In the same way, one seems justified in the prediction that residuums of pulmonary abscesses may occasion trouble in a certain number of cases in the form of gangrene of the lung following invasion by putrefactive bacteria, organization of the abscess walls with the overgrowth of connective tissue, and the formation of bronchiectases, expectoration of pus from bronchial fistulas, and the like.

PULMONARY LESIONS

In the pandemic of 1918, pneumonia was an almost constant occurrence. The prevailing type was a confluent lobular hemorrhagic and exudative lesion of bilateral distribution associated with areas of acute vesicular emphysema. In the recurrent disease, as we saw it at Bellevue Hospital, the attendant pneumonia conformed to no anatomic type. Of the pulmonary changes, the nearest approach to uniformity was found in the five cases marked by diffuse and intense congestion of the lungs and of virtually every other organ in the body, with dilatation of the heart and death from asphyxia without signs of pneumonia, or with pneumonic foci which were numerically and geographically insignificant. Of the forty-five cases, only three were sufficiently charateristic to be classified with the variety of pneumonia that prevailed in the pandemic sweep. The remaining thirty-seven cases represented a conglomeration of pneumonic lesions, scarcely

any two of which bore the same essential features. Among these, however, we were enabled to recognize a group, the members of which seemed to bear a certain general resemblance to the confluent lobular pneumonia of 1918. In these cases both lungs were involved, the lower lobes to a greater extent than the upper. The pleura covering the consolidated areas was irregularly strewn with fibrinous exudate and more or less richly sprinkled with hemorrhagic petechiae, and areas of acute vesicular emphysema were occasionally to be observed. The splotchlike hemorrhagic extravasations in the pleura, so frequently encountered a year ago, were seldom discernible. On the other hand, the consolidated portions not uncommonly showed large nodular or streaklike, firm, dark slate-blue elevations which, on section, revealed a smooth, velvety, bluish black surface, rich in blood—the so-called marantic infarctions or, better, massive hemorrhagic extravasations. The cut surface of the lungs as a whole presented extreme variations both in appearance and in consistency, owing to different combinations of dull reddish or deep bluish or grayish red lobular consolidations, confluent lobules of dull white appearance and semifluid consistency, inflammatory edema, abscess cavities varying in size from the head of a large pin to that of a crabapple, and filled with moderately thick whitish pus, the picture being still further complicated on occasions by the intersection of cream colored bands of infiltrated pleura that surrounded lobules or groups of lobules or that bound one lobe to another. In addition, the mucosa of the larger bronchi was swollen, deep bluish red, and of velvety smoothness. In three cases, large portions of a lobe were consolidated in such fashion as to resemble ordinary croupous pneumonia.

We do not mean to convey the impression that any single group of pneumonias in the recurrent epidemic presented the above described features with anything approaching regularity. On the contrary, as we have already stated, no two sets of pneumonic lungs presented the same essential features in the same essential combination as did the prevailing pneumonia of the pandemic year. Nevertheless, it is possible to select individual features from the array of pneumonias

that accompanied the recurrent epidemic, and from them to reconstruct a composite picture of the pneumonia which characterized the pandemic.

Microscopically, the changes in the lung were correspondingly variable. The capillary vessels were universally engorged, intra-alveolar hemorrhages were frequent—sometimes discrete, at other times confluent. Certain vesicles were partially or completely filled by coagulated serous fluid, entangled in which were a few red cells or an occasional round cell. Other vesicles were filled by polymorphonuclear leukocytes and fibrin, and through necrosis and confluence of these, the majority of abscesses appeared to arise. The frequent and abundant appearance of fibrin was in contrast to the lungs of the pandemic disease, in which fibrin threads were rarely demonstrable and then in isolated localities and small numbers. The interlobar pleural extensions were frequently enormously thickened through the infiltration of polymorphonuclear leukocytes and the deposition of variable quantities of fibrin. Most of these prolongations were ribbon-like in shape but not infrequently became oval or rounded and centrally necrotic; in this way, other abscesses were formed. In still other instances, the intervesicular venules and arterioles were thrombosed, and the exudate in the immediate vicinity showed large areas of necrosis. The smaller bronchi were distended by polymorphonuclear leukocytes, and their epithelial cells were desquamated.

HEART

In the pandemic of 1918, the heart muscle in the majority of cases was deeply congested but otherwise well preserved, both as far as the naked eye and microscopic changes were concerned. In the recurrent epidemic, acute parenchymatous degeneration occurred with great frequency, the heart muscle being flabby, opaque and friable. The immediate cause of death in both epidemics was to be found in immense dilatation of the heart, particularly the right side, the cavities of which were often filled to the point of distention by deep bluish red fluid and partially clotted blood. In one of the Bellevue Hospital cases during the recurrent epidemic, the pericardium was the seat of a semi-

purulent effusion out of which a pure growth of pneumococcus was secured. With this exception, the pericardium showed no changes worthy of record.

KIDNEYS

In the recurrent epidemic, acute parenchymatous degeneration of the kidneys occurred more frequently and in a more severe form than in the previous disease, the kidneys often being swollen, edematous and flabby, easily torn, and their markings obscured or irregular in distribution. Microscopic examination revealed, in addition to widespread congestion, granular changes in the epithelial cells of the convoluted tubules, occasionally in those of the glomerular tufts.

JAUNDICE

Of the forty-five cases investigated postmortem at Bellevue Hospital, jaundice occurred in only four, and was slight in extent, being limited to the face and upper portions of the chest. At necropsy, a number of factors appeared to participate in its production, namely, congestion and edema of the papilla of Vater and the surrounding mucous membrane of the duodenum, and the presence of mucoid secretions in the larger bile ducts, together with congestion and parenchymatous degeneration of the liver proper.

MISCELLANEOUS COMPLICATIONS

In the recurrent epidemic, degenerative changes in the rectus muscles were observed in Bellevue Hospital only once, and were of mild degree (Zenker's degeneration). In the previous epidemic, this variety of muscle change was encountered in a considerable proportion of cases, and not infrequently was attended by rupture and extravasation of large quantities of blood into the sheath of the muscle, occasionally followed by secondary infection and abscess formation. In another case in the recurrent epidemic, an abscess was found at the hilum of the right testicle associated with a solitary abscess of the upper lobe of the right lung occurring in a hemorrhagic variety of lobular pneumonia. The same patient presented multiple effusions into the joints.

BACTERIOLOGY

Bacteriologic examination of the pleural fluid removed surgically and sent to the laboratory, together with that encountered at necropsy, revealed streptococci in most instances, occasionally *Staphylococcus aureus* and pneumococci. Bacteriologic examination of the pus in the intrapulmonary abscesses almost invariably yielded a pure growth of *Streptococcus hemolyticus*, but occasionally *Staphylococcus aureus*. In three cases, *Streptococcus hemolyticus* was isolated in pure culture from the blood. In the pneumonic exudates themselves, the prevailing micro-organism was a streptococcus. In occasional instances, influenza bacilli and pneumococci were isolated in combination with one another or with streptococci. There were three cases in which massive portions of a lobe were consolidated in such fashion as to resemble ordinary croupous pneumonia. In all of these the exudate was sticky. In two, *Bacillus mucosus-capsulatus* was isolated, in the other *Streptococcus mucosus*. In three other cases, streptococci were isolated from the blood during life; and all of them, at necropsy, presented abscesses of the lungs.

SUMMARY AND CONCLUSIONS

1. The first recurrent epidemic of so-called influenza in New York presented anatomic variations from the pandemic disease of a year before, (*a*) in the form of frequent and widespread inflammatory involvement of the pleura characterized by semipurulent and purulent exudates occurring in immediate association with pneumonic changes; (*b*) by multiple small pleural or subpleural abscesses; (*c*) by purulent infiltration of the interlobular and interlobar pleura, and (*d*) by solitary, oftener multiple, discrete or confluent intrapulmonary abscesses varying in size from a few millimeters to several centimeters.

2. In the pandemic disease of 1918, the participation of the pleura in the pneumonic process was conspicuous by its rarity. In the recurrent epidemic, pleural involvement occurred in 60 per cent. of all cases; and in 40 per cent., purulent or semipurulent effusions were present.

3. In the epidemic of 1918, intrapulmonary abscesses were virtually unknown accompaniments of the pneu-

monic process. In the recurrent epidemic, they were encountered in 35.5 per cent. of all cases. Of the total number of cases attended by pleural involvement (twenty-seven in all), multiple small pleural or subpleural abscesses occurred in twelve, or in 44.4 per cent.

4. As a result of the recurrent disease, sequelae may be expected in the form of (*a*) organization of the inflamed pleural membranes with partial or complete obliteration of the cavity and interference with the excursions of the corresponding lung; (*b*) delayed, diffuse or sacculated pleural or interlobar empyemas; (*c*) fibrosis of the lung following organization of exudate in the interlobar and interlobular septums of the pleura, and (*d*) gangrene of the lung and bronchiectatic cavities following secondary changes in intrapulmonary abscesses.

5. In the epidemic of 1918, pneumonia was virtually constant, both in point of incidence and in conformation to type. In the recurrent disease, pneumonia was a relatively infrequent event, and the anatomic vagaries in the distribution and structure of the lesions were so numerous that no two sets of lungs were similar in appearance, and often one lung differed markedly from its fellow.

6. In the pandemic disease of 1918, acute degenerative changes in the heart muscle, liver and kidneys were neither frequent nor intense. In the recurrent disease, they were both common and severe. In the pandemic, the blood cultures were almost invariably sterile; in the epidemic, streptococcal septicemia occurred, we estimate, in about 10 per cent. of all pneumonias.