be as well obtained by means of any one of our older, simpler and reliable methods.

The use of a clay-mixture poultice in pneumonia serves merely a single purpose, namely, a means for the application of heat to the chest wall. Aside from the demonstrated fact that a heated cotton pad or a flax-seed poultice is more efficient, the clay mixture has other serious disadvantages. Thus, I would point out that a thick layer of the heavy clay mixture applied to an infant's thin chest wall seriously impairs respiration; again, both in infants and in adults, the presence of the clay mixture makes it impossible to make with accuracy the careful physical examinations which here are especially needed, both to indicate the disease progress and as a basis for proper treatment. As a matter of fact, the use of heat in any form is rarely indicated in pneumonia, except when occurring in babies and in old people.

The use of cold by means of the icebag and coil is far more advantageous than heat. Cold not only relieves the pain as well as heat, but also relieves the cough and improves the breathing. Even in young children, a coil or light icebag, not kept on all the time, seems better than the use of heat, and in the cases above mentioned, where heat is useful, the cotton jacket should be used in preference to poultices. I may well end this discussion of the value of clay mixture and other poultices in pneumonia by quoting from Dr. Dock's article on "The Value of Internal Medication and Local External Applications in Pneumonia,"¹ in which he says:

Two or three years ago it would have been unnecessary to speak of poultices in the treatment of pneumonia. They often relieve symptoms, but can usually be substituted without loss by the cotton jacket. Within a short time the poultice has been revived in a new form under the stimulating influence of printer's ink and an amount of physiologic and therapeutic misinformation that would make Rabelais laugh, but must make all judicious therapists grieve.

THE ETIOLOGY AND THE PATHOLOGY OF BRONCHOPNEUMONIA COMPLICATING MEASLES.*

CHAS. F. CRAIG, M.D.

First Lieutenant, Assistant Surgeon, U. S. Army; Pathologist and Bacteriologist to the U. S. Army General Hospital.
SAN FRANCISCO, CAL.

Bronchopneumonia is recognized as the most fatal complication of measles. While the pathology of the condition has been thoroughly investigated, there is yet much to learn regarding the etiology and the more minute pathologic changes which occur in the tissues. Many epidemics of bronchopneumonia following measles differ markedly in their clinical and pathologic features, and it is impossible to believe that such epidemics are always due to the same etiologic factor.

The occurrence of an epidemic of measles in one of the posts of the Department of California, many of the patients being sent to the U. S. Army General Hospital at San Francisco for treatment, and the complication of this condition by bronchopneumonia which occurred in a considerable proportion of these cases, has given me an opportunity to study minutely the pathology of this condition. In all, 89 cases were sent

to this hospital for treatment; in 12 cases, nearly 13.5 per cent., bronchopneumonia developed, and, of these, 10 cases, nearly 84 per cent., terminated fatally.

On account of the high rate of mortality in this epidemic, and because of the similarity of the pathologic lesions in all the cases, I made a careful bacteriologic and pathologic study of each case, and I believe that the results obtained throw new light on the cause of this complication of measles. A complication which shows a mortality of nearly 84 per cent. certainly deserves a most careful study, in order to determine, if possible, the causation and character of the lesions present, in order that proper preventive and therapeutic measures may be taken to combat the disease. In this communication I shall not speak of the clinical phenomena present in these cases, but will give the pathologic conditions only.

All the cases occurred in young men between the ages of 21 and 30. In every case the disease began during the period of decline of the measles rash, although many authorities claim that bronchopneumonia is most apt to develop at the height of the eruption. The duration of the pneumonia in the fatal cases was as follows:

3 days.....	1 case	6 days.....	1 case
4 days.....	3 cases	7 days.....	1 case
4 days.....	2 cases	10 days.....	2 cases

The longest duration of the bronchopneumonia did not exceed ten days, while most cases proved fatal within a week. This epidemic was marked by great prostration of the patient and by all the symptoms of a septic intoxication. The pathology of the cases differed markedly, in many important respects, from that given by all authorities. Nine of the ten cases were accompanied by a purulent effusion into the pleura, which is stated by all authorities to be of very rare occurrence in bronchopneumonia following measles. Nine of the cases were also accompanied by abscess formation in the lung tissue, which by many good authorities is stated to be almost unknown in this disease. Beside these two marked differences in the pathology of the cases, there were numerous other pathologic lesions present in the organs which are of rare occurrence, and which show the intense virulence of the infection present in these cases. Because of these peculiarities, I believe that this epidemic is instructive, as showing what a terribly fatal disease bronchopneumonia may be in an adult when it complicates measles.

ETIOLOGY.

As I do not know the entire clinical history of these cases, I can not state whether or not exposure was a factor in producing the disease. In only three cases did the bronchopneumonia apparently originate in this hospital, and, in these cases, it was not due to exposure, as the ward was well heated and the patients were carefully nursed.

It is well known that the infecting poison in measles is especially active on the mucous membranes of the respiratory tract, and the accompanying bronchitis and coryza are dependent on as initial symptoms in the disease. This peculiar action of the infective agent no doubt assists very greatly in the production of bronchopneumonia.

Cultures were made from the lungs, spleen and the contents of the lung abscesses, and in all cases examined the culture media showed a rather rapidly growing streptococcus, which in 6 cases was accompanied by the pneumococcus; in 1 case by the *Proteus vulgaris*; and in 3 cases by staphylococci. These bacteriologic findings

1. THE JOURNAL A. M. A. Dec. 10, 1904.

* Published by permission of the Surgeon General, U. S. Army. From the Annual Report of the U. S. Army General Hospital, Presidio San Francisco, Cal., 1904.

agree with those of most authors who have studied this disease. Thus Aufrecht states that the streptococcus pyogenes is the most frequent organism found in bronchopneumonia complicating measles, together with the pneumococcus. He says: "As the cause of secondary pneumonias following the infectious fevers the streptococcus is pre-eminent." He also mentions the staphylococci, pneumobacillus of Friedlander, colon bacillus and the tubercle bacillus as having been found by various observers. Williams states that the most frequent organisms found are the pneumococcus, *Streptococcus pyogenes*, and the *Staphylococcus pyogenes aureus*. Hale states that in secondary bronchopneumonia the pneumococcus appears in about 75 per cent. of the cases, but seems less potent in giving character to the disease than the streptococcus. He also mentions the occurrence of staphylococci, Friedlander's bacillus, tubercle bacilli and the colon bacillus. There can be no doubt that the streptococcal infection produced the symptoms which were most characteristic in these cases, and which were those of a septic condition. The organs presented the lesions of a profound septic poisoning which I believe without doubt was due to the streptococcal infection of the tissues.

I have not had time nor opportunity as yet to test the virulence of these cultures on animals, but I am satisfied that experiments will demonstrate that the lesions found in these cases can be reproduced in animals, if the proper methods of inoculation are pursued, and that it will be possible to show whether these lesions depend entirely on the streptococcus or on a combination of this micro-organism with the staphylococcus or with the pneumococcus. I intend also to determine, by experiment, the value of antistreptococcus serum in combating the lesions due to this organism.

I believe that the bronchopneumonia in these cases was due to a secondary infection of the respiratory tract by the streptococcus pyogenes, the tissue of the bronchi and lungs being especially susceptible to such infection because of the infecting agent of measles, and that the great mortality was without doubt due to the peculiarly favorable condition of the tissues to such infection.

PATHOLOGY.

The lesions of this disease first appear in the bronchi and bronchioles, being quickly followed by the appearance of a peribronchial pneumonia involving the air vesicles in the immediate vicinity of the bronchus. This peculiar distribution of the lesions gives rise to the involvement of lobules instead of lobes, as in croupous pneumonia, and while in a very few cases the distribution of the lesions may become lobar, in all the cases observed during this epidemic the distribution was lobular. In describing the macroscopic appearance of the lesions in the lung, I have used the terms red and gray splenization because in every case there was present the typical lesions which are ascribed to these two stages of the disease. I do not believe that it is possible in this disease, as it is in lobar pneumonia, to separate it into distinct stages, as the lesions found differ so widely in different portions of the affected tissue. While macroscopically such a distinction often can be made, when sections of the lung are studied, it will invariably be found that it is impossible to separate the lesions into these stages with any degree of accuracy. In describing the pathology I shall only speak of the pathology of the lungs, including the pleura, the kidneys, the liver, and the spleen, as it was in these organs that the most characteristic changes occurred. In or-

der to give an idea of the macroscopic appearances noted in the pleural cavity and in the lungs, the portions of the autopsy records describing them are here inserted.

CASE 1.—The right pleural cavity is filled with pus; the left pleural cavity is free from fluid. The right lung is partially collapsed, and the pleura is greatly thickened and covered with lymph. The lobes of the lung are adherent to one another by recent adhesions. The organ is not crepitant except at the upper lobe. Externally the lower lobe shows a marked atelectasis. On section of this lobe, condition present is that of bronchopneumonia in the stage of red splenization. A large abscess cavity measuring 2 cm. in diameter and filled with greenish pus is found at the lower border of this lobe. There are no other abscesses in any portion of the lobe. On section of the middle and upper lobes, condition present is that of bronchopneumonia in the stage of gray splenization. A small abscess cavity is present in the middle lobe measuring about $\frac{1}{2}$ cm. in diameter and filled with rather thick fluid. The quantity of pus in the right pleural cavity is 1,600 c.c.

CASE 2.—The right pleural cavity is filled with pus. The lung shows a marked atelectasis, large portions being collapsed. The pleura is greatly thickened and covered with lymph and the lobes are adherent one to another by recent adhesions. The lung is not crepitant. On section, the cut surface is greyish-red in color, the bronchi being very prominent and filled with pus. The appearance is that of bronchopneumonia in the stage of red splenization. There are no abscesses present. The left lung appears fairly normal except the lower lobe, which shows marked atelectasis and is not crepitant. On section of this lobe, the condition present is similar to that in the right lung. There is no evidence of abscess formation.

CASE 3.—The right pleural cavity is filled with grayish pus. The lung is collapsed and the pleura is greatly thickened and covered with lymph. Crepitation is absent, and on section the lung is found filled with abscesses varying in size from those hardly visible to the eye to one measuring 10 cm. in diameter. These abscesses are filled with greenish pus. A large abscess is found at the lower portion of the lower lobe, measuring 10 cm. in diameter. Another measuring 2 cm. in diameter is situated at the junction of the lower and upper lobe; and another 4 cm. in diameter, involves the lower portion of the upper lobe. Beside these larger abscesses there are numerous abscesses present throughout all the lobes measuring from .25 to .5 cm. in diameter. The left pleural cavity is free from fluid, and the lung crepitant throughout. There is some evidence of atelectasis in the lower lobe, and on section of this lobe the condition present is found to be that of bronchopneumonia in the stage of red splenization.

CASE 4.—The right pleural cavity is filled with a purulent fluid. The right lung is collapsed and the pleura greatly thickened and covered with lymph. On section of this lung cut surface is rather pale in color and the bronchi are filled with pus. There are numerous minute abscesses scattered throughout the organ, measuring about .25 cm. in diameter. The left lung appears normal.

CASE 5.—The right pleural cavity is filled with pus. The left pleural cavity is free from fluid. The pleura is greatly thickened. The lower lobe of right lung is of almost solid consistence, as is lower portion of the upper lobe. On section of the lower lobe, the cut surface is dusky red in color and streaked with pus, which oozes in large quantities from the bronchi. There are numerous areas of commencing abscess formation and a few well-defined abscesses. On section of the upper lobe, there is no evidence of abscess formation, but the lower portion of this lobe shows marked bronchopneumonia. The left lung appears normal.

CASE 6.—The left pleural cavity is filled with pus. The right pleural cavity is free from fluid. The left lung is adherent over the apex to the chest wall by old adhesions. The lower lobe of the lung shows considerable atelectasis, but is crepitant. On section of this lobe, condition present is that of bronchopneumonia in the stage of red splenization. The bronchi are filled with pus and there are a few small abscesses

scattered through the lobe. The right lung is crepitant, save in the lower portion of the lower lobe, which on section shows a condition of bronchopneumonia.

CASE 7.—The left pleural cavity is filled with pus, the right pleural cavity being free from fluid. The pleura, especially over the lower lobe of the left lung, is greatly thickened. The upper lobe of this lung is partially collapsed. The lower lobe is not crepitant and there are numerous firm tubercular feeling areas present at the lower portion of this lobe. On section of the lower lobe of the left lung numerous small abscesses are found filled with greenish yellow pus. The remainder of the lung tissue shows a condition of bronchopneumonia in the stage of red splenization. On section of the upper lobe, there is a marked atelectasis, but no evidence of very severe inflammation. The right lung is normal, save at the lower portion of the lower lobe, which shows a condition of bronchopneumonia, but there is no abscess formation.

CASE 8.—The left pleural cavity is filled with fluid, which is just becoming purulent. The right pleural cavity is free from fluid. The lower lobe of the left lung is of almost solid consistence. The upper lobe is crepitant in places, and in other places there is a marked atelectasis. The pleura over the lower lobe is very greatly thickened and inflamed. On section of this lobe, the cut surface is seen to be very dark red in color. The condition present is typical of bronchopneumonia. There are numerous irregular yellow areas present marking the site of small abscesses, the largest abscess found measuring 1.5 cm. in diameter. These abscesses are filled with greenish pus. The upper lobe of this lung appears normal, save for slight congestion. The lower lobe of the right lung is involved, the condition present on section being that of bronchopneumonia in stage of red splenization.

CASE 9.—The pleural cavities are free from fluid. The left lung is markedly congested externally. The pleura does not appear to be thickened, but there is considerable atelectasis present. On section, the cut surface presents typical appearance of bronchopneumonia. The remainder of this lung appears normal. The right lung is normal in appearance.

CASE 10.—*Clinical Findings.*—This case is of great interest, as beside the lung condition present this patient developed metastatic abscesses in the subcutaneous tissues throughout the body. An abscess was found lying beneath the clavicle, measuring 6 cm. in diameter and filled with greenish pus. This abscess did not involve the shoulder joint, but was situated in the muscular tissue. Another abscess was opened measuring 8 cm. in diameter lying in the subcutaneous tissue behind the scapula. A large abscess was opened in the psoas region, which contained nearly 500 c.c. of greenish pus. The entire subcutaneous tissue in the lower portion of the lumbar region and the upper portion of the gluteal was infiltrated with pus, and several abscesses were also present in the subcutaneous tissue of the thigh and leg.

Autopsy Findings.—The right pleural cavity is filled with pus, the left pleural cavity being free from fluid. The right lung is not crepitant and shows an extreme degree of atelectasis. The pleura is greatly thickened and covered with lymph. The lobes are adherent to one another by recent adhesions. On section of the lower lobe of this lung, the cut surface is seen to be very dark mahogany red in color; the bronchi are filled with pus. The condition present is that of unresolved bronchopneumonia. On section of the lower portion of the upper lobe, the condition present is similar to that of the lower lobe. An abscess is opened, which is about one cm. in diameter and filled with greenish pus. On section of upper lobe, upper portion, the condition present is normal. The left lung appears normal.

THE LUNGS.

One of the most interesting characteristics of this epidemic of bronchopneumonia was the almost constant occurrence of empyema. Of the 10 fatal cases, 9 presented this condition, and in only one case was the fluid semipurulent in character, in the others the material present being rather thick pus. All authorities

state that pleurisy and empyema in bronchopneumonia following measles are very rare. Thus Williams states that pleurisy with effusion is a very rare condition. Aufrecht, in his extensive article on bronchopneumonia,¹ does not mention the occurrence of this condition at all, while von Jurgensen states that effusions into the pleural cavity are not often observed in connection with bronchopneumonia, no matter in what way the latter may arise, and that the pneumonia in measles furnishes no exception to this general rule. He also states: "In my opinion, the occurrence at all of a pleuritic effusion during or following measles is a matter of chance."

The constant occurrence of empyema in these cases well illustrates the extreme severity of the infection, the quantity of pus present varying between 500 to 2,000 c.c., the average amount being 1,200 c.c. Five of the cases presented empyema on the left side and four on the right, only one case showing no pus in the pleural cavity. The pus was invariably of a greenish-yellow color, and of considerable consistence. The pleura was greatly thickened, especially over the lower lobes of the lungs, and covered with greenish-yellow lymph, which in some places had partly organized, binding the lobes together. On removal of this lymph the pleura presented a dark purple color, and numerous atelectatic areas were visible beneath it, in some places causing slight contractions of the pleura. The average thickness of the pleura was about .16 cm.

Macroscopic Appearance.—Externally the lung where empyema had developed presented the appearance which has just been described. Where empyema had not developed the lung externally was of a reddish-purple color and there was always present marked evidence of atelectasis. The areas of the lung showing this condition were greatly inflamed and collapsed. On incision the cut surface of the lung varied in appearance according to the stage of the infection. In those cases in which death occurred within three days the condition present was always that of red splenization. The bronchi were distinctly visible and presented the following structure: The cavity of the bronchus was filled with greenish-yellow pus, the walls standing out as dark reddish-purple areas surrounding this accumulation of purulent material. The surrounding peribronchial tissue presented a bright red appearance, the pneumonic condition being most marked in this situation.

In cases in which the pneumonic process had lasted for a longer time the cut surface of the lung did not present so many evidences of acute inflammation, the color being reddish-gray or grayish, and it was in these cases that abscess formation was most common. The bronchi invariably were filled with pus and the surrounding tissue was more or less inflamed. The areas showing atelectasis, which were especially frequent in those cases in which death had occurred within three days of infection, were distinctly outlined, due to the intense inflammation present.

Abscess formation: I have already spoken of the curious frequency with which empyema complicated bronchopneumonia in these cases, and shall now consider the most important complication observed, namely, abscess formation, which was metastatic in character. The occurrence of abscesses following bronchopneumonia is so rare that many authorities have denied that such a condition is possible. Aufrecht states: "No less doubtful is the appearance of abscesses in catarrhal pneumonia. They are confounded with collections of pus inside

1. Nothnagel's Encyclopedia of Medicine.

the bronchial lumen, which are not infrequently found: and if the bronchus undergoes saccular dilatation may assume a spherical form." Real abscess arising from destruction of the pulmonary tissue Damaschino had already declared to be exceedingly rare.

This statement, coming from so high an authority, illustrates the extreme rarity of abscess formation in the ordinary epidemics of bronchopneumonia, but this epidemic was characterized by the almost invariable appearance of multiple abscesses of the lung of the fatal cases, which could by no chance be confused with collections of pus in the bronchi. As will be seen from the autopsy excerpts, abscesses were present, varying in number from one to twenty or more, and in size from those just visible to the eye to those measuring 6, 8 or 10 cm. in diameter. The smaller abscesses were not well defined as regards an abscess wall and were irregular in shape. The contents did not consist of pus, but of necrotic lung tissue of a semi-fluid consistency. The larger abscesses had a well-defined wall and were filled with a thick greenish-yellow pus. Only one of the cases showed no abscess formation. The abscesses in most cases were situated in the lower lobe of the involved lung.

In one case a large abscess was opened in the upper lobe. Beside the distinct abscesses present in this case there were numerous irregular areas in which the lung tissue was necrotic for a considerable space, and so soft as to be of almost fluid consistency. These areas were no doubt gangrenous in character. The abscess invariably occurred where the atelectasis was most marked. In three of the cases abscess formation was so extensive that the cut section of the lung appeared to be entirely covered with pus, and it was only by removing it that the several abscesses present could be distinguished. In other words, the lower lobes of these lungs had been almost entirely destroyed by abscess formation. In those cases in which death occurred after the fifth day the cut section of the lung was generally of a grayish color and there were small areas present, standing out distinctly because of their light color. These gray areas are no doubt explained by the cutting off of the blood supply to the affected air vesicles, and the consequent softening and necrosis of the cellular elements.

Microscopic Appearance.—In considering the microscopic pathology of the lung in these cases the following structures have to be taken into account: The bronchi, the air vesicles, the blood vessels, the connective tissue and the pleura.

The Bronchi: In all microscopic sections it was found that the bronchioles and the smaller bronchi were occluded by material consisting of leucocytes, blood corpuscles, and more or less necrotic material, unrecognizable as regards structure. This occlusion of the bronchioles was evidently produced by inflammation of the bronchial walls, leading to a proliferation of the columnar epithelium lining them and to the exudation of serum into the bronchial canal. The sections showed an extension of this inflammatory condition into the muscular tissue and the infiltration of this tissue by large numbers of leucocytes. Where the inflammatory process had gone no farther this was the only noticeable change in the bronchioles. In the majority of cases, however, the inflammation had extended to the peribronchial tissue, involving the air vesicles surrounding the bronchioles. In every case properly stained, immense numbers of streptococci could be observed in the exudation within the bronchioles, and in those cases in which pneumococci

were obtained by culture, these organisms also were present in this situation. The blood vessels in the vicinity of the bronchi were invariably engorged, in many places they were entirely occluded by plugs consisting of red blood corpuscles, lymphoid cells and leucocytes. In every case examined rupture of the smaller capillaries had occurred, and hemorrhagic areas were formed, filled with red blood cells.

Air Vesicles: The sections showed that the air vesicles in the immediate vicinity of the bronchi—that is, in the peribronchial region—were first involved. The surrounding capillaries were entirely filled with blood and were greatly distended; in some places so much so that rupture had occurred, resulting in the destruction of numerous air vesicles which were replaced by great collections of red blood corpuscles, lymphoid cells and leucocytes.

Where rupture had not occurred, however, the air vesicles were distinctly outlined by these congested capillaries. In the immediate vicinity of the bronchi the outline of the air vesicles was lost; this was due, probably, to the extension and accumulation of cellular material similar to that contained within the air vesicles. Where the air vesicles were distinctly outlined they seemed in the early stages of the process to be entirely filled with a cellular exudate composed of the epithelium lining the air vesicles; numerous leucocytes and a few red blood corpuscles which had penetrated the surrounding capillaries. As the process extended, this cellular exudation was so great that in places rupture of the walls of the air vesicles occurred, and large areas of the lung tissue were composed of this material alone. Beside the cells which I have mentioned as occurring in the air vesicles there occurred two peculiar forms of cells, one resembling the giant cell in structure, being irregular in shape and containing several nuclei. These, however, were not giant cells, but were produced by the destruction of numerous cells which became merged in each other, thus giving the giant-cell appearance. The other peculiar cell noticed was mononuclear in character and filled with pigment. This pigment occurred in the form of minute granules or slender rods of a brownish-yellow color, and in many instances almost filled the cell. These pigment cells were especially numerous in the peribronchial tissue, as were also the giant cells. The cells lying within the air vesicles were undergoing various forms of degeneration, the most common being a vesicular swelling of the nucleus. In fact, this form of degeneration was present in almost every cell lying within the air vesicles. Fatty degeneration of the protoplasm and albuminoid degeneration were almost invariably present. There was also great distortion of the individual cells, and globular cells were especially frequent. The occurrence of mononuclear cells, both large and small, was very characteristic in all the sections. In fact, the vast majority of the cells present in the affected areas were mononuclear in character.

Where atelectasis had occurred the walls of the air vesicles had collapsed and were lying together, and at such places there was always a marked accumulation of small mononuclear and polynuclear cells.

The microscopic examination showed numerous places in which there was marked focal necrosis, evidenced by extensive degeneration of the tissue and by the accumulation of immense numbers of leucocytes, and a large amount of granular necrotic material. These areas no doubt in time would have given rise to abscesses, as the structure of the smaller abscesses exactly resembled these

areas, save that the necrotic material was greater in amount; the larger abscesses were composed of a well-marked abscess wall, fibrous in character, but always showing a marked infiltration by leucocytes. Numerous streptococci could be demonstrated in the areas of focal necrosis and also in the contents of the smaller abscesses.

The cells lying within the air vesicles, at some distance from the peribronchial tissue, had undergone hyaline degeneration; they presented a homogeneous appearance as the nucleus had entirely disappeared. This form of degeneration is undoubtedly due to the action of the toxic materials.

Blood Vessels: I have already spoken of the intense engorgement of the blood vessels, which include both the larger vessels and the capillaries. In some places this engorgement had been so great that extensive hemorrhages had occurred from the capillaries, producing areas composed entirely of red blood corpuscles and leucocytes. This condition resulted in the destruction of the lung tissue in such areas.

Connective Tissue: The connective tissue was not increased in amount, but rather decreased except where the larger abscesses were situated and around some of the larger blood vessels. In these regions the newly-formed connective tissue was invariably densely infiltrated by young connective tissue cells and leucocytes.

The Pleura: Sections of the lung showing the pleura invariably presented marked thickening of this structure and infiltration by leucocytes and young connective tissue cells. A characteristic and peculiar lesion present was the formation of cystic areas, which were filled with blood and degenerated cellular material, at the junction of the pleura and the lung. These cystic areas were no doubt due to the rupture of capillaries and the consequent collection of the contents of such capillaries in cavities lying between the connective tissue fibers and the pleura. In many sections these cystic cavities were so numerous as to form an almost unbroken chain at the junction of the lung tissue and the pleura. The outer layer of the pleura was invariably found to be covered with necrotic material and in this material streptococci and other bacteria were demonstrated. In all sections of the lung the absence of fibrin was very noticeable, even in those areas where resolution was commencing. It was but seldom that bacteria could be demonstrated in the contents of the air vesicles.

Summary.—The pathologic lesions present may be summed up as follows: A marked inflammation of the bronchioles followed by extension to the peribronchial tissue; in many cases the process did not stop here, but extended further into the lung tissue, producing an almost lobar pneumonia, in that nearly the entire lobe was involved. The peculiar lesions found in this epidemic were the occurrence of empyema and abscess formation in the lung.

LIVER.

Macroscopic Appearance.—The liver was invariably enlarged. The capsule was smooth, color of the organ yellowish red and consistence decreased. On section, in every case, fatty degeneration was found present; generally it was of localized extent and was especially marked near the capsule. Congestion of the organ was invariably present. The lobules were indistinct and the cut surface presented a rather cloudy appearance.

Microscopic Appearance.—The examination of sections of the liver showed a condition of fatty degeneration and acute venous congestion. The capsule was not thickened, but the connective tissue in the portal spaces

was increased slightly in amount and was infiltrated by young connective tissue cells, and by mononuclear and polynuclear leucocytes. The capillaries were congested in many places, so much so that rupture had occurred, and large portions of the liver lobules were replaced by red blood corpuscles and leucocytes which had escaped from the ruptured vessels.

A peculiar condition present was the great accumulation of mononuclear leucocytes in the intralobular capillaries. This condition occurred in every case and was observed in every section of the liver. It was so marked as to resemble the condition found in lymphatic leukemia. The mononuclear cells did not present any evidence of degenerative changes. It is impossible to explain the occurrence of this variety of cell in such great numbers in the liver capillaries, but that it is of some practical significance I can not doubt, as it occurred in every case and in every section which was examined.

In the cases in which fatty degeneration was present the protoplasm of the liver cells was replaced by fat granules and the nucleus had been destroyed or stained poorly. When this form of degeneration was not present various other forms of degeneration were noticed in the liver cells, the most common being the albuminoid and the peculiar forms of hyaline degeneration which I have mentioned as occurring in the cells of the air vesicles. The liver cells were invariably distorted and swollen, and in many marked pigmentary deposits were observed, the pigment being in the form of minute granules or slender rods resembling that which has been described as occurring in the pigment cells in the lung. Many of the liver cells showed an entire destruction of the nucleus and a loss of staining properties.

Summary.—The microscopic pathology of the liver may be summed up in marked degenerative changes in the liver cells, great congestion of the capillaries, the occurrence of large numbers of lymphoid cells in the intralobular capillaries, and pigmentary deposits in the protoplasm of the liver cells and areas of focal necrosis.

THE KIDNEYS.

In every case sections of the kidneys showed the lesions of a very severe hemorrhagic nephritis.

Macroscopic Appearance.—In each case the kidney was somewhat enlarged and appeared greatly congested externally. None showed the presence of cystic degeneration, and in all the capsule was not adherent, and the stripped surface was very greatly congested. On section the cut surface in all the cases was intensely congested, but the cortex and pyramids were distinct. The cortex was considerably thickened and the malpighian bodies greatly enlarged, standing out very prominently as bright red dots in the cortex. The intertubular capillaries were engorged, giving the cortex a markedly striated appearance. The pyramids were intensely congested. The mucous membrane of the pelvis in all cases was considerably congested and the pelvis contained more or less urine almost semipurulent in character.

Microscopic Appearance.—The connective tissue of the kidney was not increased in amount, and the capillaries, especially the intertubular capillaries, were greatly engorged with blood. A characteristic lesion in all the sections was the presence of immense collections of blood lying between the tubules and in them, these collections being due to the rupture of the over-distended capillaries. In many sections this hemorrhage into the tubules was so marked as to constitute the chief pathologic picture present. The epithelium lining the tubules showed various forms of degeneration, the most common

being fatty, albuminoid and hyalin. The cells were distorted in shape and could be seen in all stages of detachment from the basement membrane. Large numbers of granular, epithelial and blood casts were present in the sections, and the hyaline degeneration mentioned was a characteristic lesion occurring in the cells of the tubules and in the glomeruli. These cells stained homogeneously and poorly. No structure could be distinguished, even with the highest power of the microscope, nor could the distinction be made out between the separate cells. Where this condition had occurred in the glomerulus the structure was entirely lost, the capillary tuft appearing as a homogeneous, structureless, faintly staining mass. In many places the tubules were greatly dilated and entirely empty, the entire epithelial lining of the tubule having been destroyed and removed.

The changes in the glomeruli consisted in great congestion of the capillary tuft, in many instances leading to rupture, and the occurrence of hemorrhage, filling the entire glomerular space. Where this condition was not present there was marked proliferation of the epithelium covering the tuft and lining Bowman's capsule, resulting in an entire obliteration of the capsular space. Areas of focal necrosis were observed in the glomeruli and rarely in the tubules and surrounding tissue. In two cases, metastatic abscesses, microscopic in size, were observed, consisting of a collection of necrotic material, mononuclear and polynuclear leucocytes, and bacteria, chiefly streptococci. In the capillaries were observed the same preponderance of mononuclear cells which were so conspicuous in the capillaries in the sections of the liver.

Summary.—The pathologic changes in the kidney consist, then, of lesions of a very severe acute nephritis, characterized by the occurrence of hemorrhage into the tubules and glomeruli, and by the occurrence of areas of focal necrosis and hyaline degeneration. A peculiar condition found in the tubules in which the hemorrhage had occurred consisted in the entire destruction of the epithelium lining the tubules and the covering of the basement membrane by a row of red blood corpuscles. In every section this appearance was observed, the kidney tubule appearing to be lined by red blood corpuscles instead of by tubular epithelium.

THE SPLEEN.

The pathologic lesions in the spleen consisted in acute venous congestion and the crowding of the splenic sinuses with various forms of cells, the most common being mononuclear leucocytes and macrophages.

Macroscopic Appearance.—In all the cases the spleen was greatly enlarged, generally being about twice as large as when normal. The capsule was tense and the organ of a dark reddish-purple color externally. The consistence was decreased, and the weight increased. On section the cut surface was dusky red in color, with numerous areas of a dark mahogany color marking the site of hemorrhages into the parenchyma. The malpighian corpuscles were invisible, or very slightly visible as light reddish areas, although microscopically these were found to be considerably enlarged. The substance of the spleen was almost diffident in character.

Microscopic Appearance.—The cells in the splenic sinuses contained a large amount of pigment. The sections showed that the capillaries of the organ were greatly congested, and here again hemorrhages were very frequent, resulting in the production of large hemorrhagic areas replacing the normal splenic tissue. The connective tissue of the spleen was not increased in amount. The malpighian corpuscles were invariably enlarged and

contained numerous pigmented cells resembling those found in the lungs and in the liver. The lesions in the spleen were not so characteristic as those found in the other organs, but were typical of an acute septic condition. In three cases small areas of focal necrosis were present in the spleen, resembling those found in the lungs, liver and kidneys.

FOCAL NECROSIS AND HYALINE DEGENERATION.

On account of the constant appearance of areas of focal necrosis in the lung, liver, kidneys and spleen, a more detailed description of this condition may be of interest. These areas were situated in the lung, in the exudation in the air vesicles, and also involved, in many instances, the capillaries and walls of the vesicles. In the liver they were situated within the lobules and involved the liver cells in the locality affected. In the kidney they were found chiefly in the cortex, involving, in some instances, the tubules alone, and in others both the tubules and the glomeruli, and in still other instances, portions of the glomeruli alone were affected. In the spleen they were found in the malpighian corpuscles, and also involved the splenic sinuses and the cells within them. This condition has been observed in some of the infectious diseases, such as typhoid, tuberculosis, and in forms of poisoning due to chemical agents; in these cases the focal necrosis was undoubtedly due to some toxic material circulating in the blood, as in very few of the areas showing this form of degeneration could any bacteria be demonstrated. The chief pathologic lesions present were degeneration of the nuclei of the cells in the region involved, and the hyaline or granular degeneration of the protoplasm, with loss of distinction of the separate cellular elements. The nuclear changes consisted in the breaking up into a number of particles and granules of the chromatin and dispersion of these chromatin particles throughout the entire affected area. In many instances the nucleus, while it retained its form, had lost its staining properties, due largely to the destruction of the chromatin. The cells in the involved areas were distorted in shape, and where the process had extended still further they were entirely destroyed, all that remained being a mass of granular deposit entangled in some peculiar material resembling fibrin. While these changes were noticeable in the cells of the tissues involved, the most marked change consisted in a great accumulation of leucocytes which infiltrated the mass of necrotic material. Many of these leucocytes showed granular, fatty and hyaline degeneration, some of them being almost entirely destroyed. In none of the areas observed was there any evidence of regeneration of the tissue. Microscopically these areas consisted of a mass of more or less degenerated cellular material derived from the cells normally found in the connective tissue infiltrated by leucocytes, and in a few instances by bacteria, chiefly streptococci. I believe that the cause of this condition was toxic material in the circulating blood, this material probably being present in the form of toxalbumins. The condition also may have been produced in part by thrombosis occurring in the capillaries, thus cutting off from the affected tissue its source of nutrition. Whether these areas of focal necrosis were due to the toxins produced by the streptococci or to poisonous materials produced during the measles infection it would be impossible to say, but I am inclined to believe they were due to the secondary infection by streptococci.

The form of degeneration which I have called hyaline, occurring so frequently in the cellular elements of the

lungs, liver, kidney and spleen, consisted in a peculiar degeneration of the protoplasm and nucleus, evidenced by great swelling and distortion of the cell, disappearance of the nucleus, and peculiar staining reactions. Areas showing this form of degeneration stained homogeneously, and the most careful examination did not demonstrate any peculiar structural change except the entire disappearance of the cell, nucleus, and the replacement of the normal protoplasm by a mass of hyaline material without distinct structure. Such areas were clearly mapped out in sections from the areas surrounding them by the fact that they took the stain homogeneously throughout, all trace of distinction between the cells being entirely lost. The name hyaline degeneration is generally applied to a peculiar change occurring in the connective tissues, and it is necessary to differentiate this form of hyaline degeneration from the form widely known as hyaline change.

The form of degeneration occurring in these cases affected the cellular elements as well as the connective tissue in the regions involved. It affected not only the cells in the connective tissue, but the capillaries also, the entire structure of the organ in such regions being lost and replaced by a homogeneous staining mass in which no structure could be recognized. There can be no doubt that this peculiar condition was due to toxic materials circulating in the blood. In all the organs the cellular elements were especially affected and the change was most noticeable in the kidneys, where the cortex showed the process in its greatest severity.

From a summary of the macroscopic and microscopic pathology of the organs from these cases of bronchopneumonia it is evident that the infection was of a septic character, producing very severe and rapidly fatal lesions in the organs mentioned. The peculiar pathologic lesions present were the occurrence of hemorrhages in all the organs, areas of focal necrosis, hyaline degeneration, empyema, and abscess formation in the lungs, kidney and spleen, and the occurrence in the capillaries of the liver and kidney, and in the air vesicles of the lung, of large numbers of lymphoid cells. I believe that it is justifiable, from the lesions present, to conclude that this epidemic of bronchopneumonia complicating measles, and showing such a high mortality, was due to secondary infection of the diseased mucous membrane of the respiratory tract by streptococci, with consequent production of a bronchopneumonia associated with a pyemic infection due to these organisms.

Special Article

IMMUNITY.

CHAPTER XII.

PRECIPITINS.

Because of their scientific importance and certain practical features the serum-precipitins should receive something more than the incidental mention which has been given them under agglutination and in other chapters.

In 1897 Kraus discovered that bouillon cultures of the organisms of typhoid, cholera and plague, from which the bacteria had been removed by filtration, would cause precipitates when mixed with their respective antisera. The reaction is specific.

As stated later, however, this specificity holds only when those quantitative relationships are observed which were found so essential for the agglutination test. The precipi-

tins of Kraus are the bacterial precipitins. He proposed their use for the identification of micro-organisms. If, for example, one has in hand a culture which he suspects to be that of the typhoid bacillus, it may be grown in a liquid medium, the cells removed by filtration, and the filtrate mixed with a known anti-typhoid serum; if a precipitate occurs when the serum is sufficiently diluted, the reaction indicates that the organism in question is the typhoid bacillus. Inasmuch as precipitins are formed during the course of some infections it may be possible to use them in clinical diagnosis, but for either bacterial or clinical diagnosis the agglutination test is more readily performed and interpreted.

In addition to bacterial precipitins we have also to recognize the phytoprecipitins. These are produced by immunization with albuminous substances of plant origin.

Phytoprecipitins and as ricin and albumin from grains, and their action is specific for the homologous substance.

Zoöprecipitins. Zoöprecipitins are those which are obtained by immunizing with an albuminous fluid from some animal. Through the work of Wassermann and Uhlenhuth, of Nuttall and others, it has been demonstrated as a general law that immunization with an albumin from whatsoever source gives rise to the formation of a precipitin which manifests its action only against the particular albumin used for the immunization. Hence, the albumin of a particular serum, in some unknown respect, is different from that of all others; it is special to the species.

Immunization with milk causes the formation of a precipitin which throws down the casein of the milk used for injection, but not that of milk from another species. The milk of the goat may be differentiated from that of the cow by the use of the lactoserum.

Likewise, after the injection of egg-albumin a precipitin is formed which is specific for the type injected.

Three substances are open to study in the precipitation reaction. First, the fluid or substance which is used for immunization; it bears the name of precipitogen, just as the analogous substance is called agglutininogen, as indicated in the preceding chapter. Second, the specific constituent of the precipitating serum-precipitin. Third, the precipitate, which is a consequence of the reaction between precipitogen and precipitin. We are able to recognize in this instance the actual end-product of a reaction, a condition which is not so easily realized in other "immunity reactions." It is true, of course, that little has been learned concerning the nature of the end-product; its chemistry is as dark as that of the proteids in general.

As stated in the chapter on "Natural Immunity," some serums normally have the power to cause precipitates in other serums. Precipitins for egg albumin and goat serum have also been found in extracts of organs, although at the same time they were absent from the serum of the animal.

Formation of Precipitin. In this case the active body exists normally in the cells in the form of sessile receptors, as they have been called, and by the process of extraction they are brought into solution. During immunization these same receptors are stimulated to overproduction and are thrown into the circulation as free precipitin receptors, or serum-precipitin.

The power of forming precipitins may be widely distributed among the organs; the leucocytes apparently have this function, and in one case they were formed locally in the anterior chamber of the eye.

For the artificial production of precipitins the precipitinogenous fluid may be injected into the veins, peritoneal cavity or the subcutaneous tissue. Within from four and a half to five days the precipitin has been formed to such an extent that it may be demonstrated in the serum of the immunized animal.

As in the case of agglutinin formation, not all animals have