In April of 1961 an outbreak of a severe and frequently fatal respiratory disease was observed among swine on a farm belonging to the O'Grady brothers near La Plata, Argentina. Outbreaks of respiratory disease occurring at the same time in swine on two other O'Grady farms were not observed personally, but were stated to be similar to the one seen. A total of some 4000 swine were distributed on the three separate farms and during a period of about 5 weeks approximately 260 of the animals died. Most of the deaths were among animals weighing 60 to 115 pounds, but a small number of adult hogs also succumbed. Deaths occurred among both cross-bred and pure-bred animals, and among both hog cholera-vaccinated and unvaccinated swine.

The outbreak seen was observed at a time when it had either almost run its course or when an effective therapy had been at last instituted. The seemingly successful treatment was a terramycin preparation known as TM 10 (Chas. Pfizer and Company, Inc., New York), which was fed to the swine in the proportion of 600 gm of TM 10 to each 100 kg of ground grain. In individual groups of animals placed on this therapeutic regimen, new cases ceased appearing in about 3 days and sick pigs began to recover.

The disease picture at the time the affected drove was seen was therefore modified from what it had been earlier in the outbreak. However, even at the end of the outbreak, there were numbers of affected animals still to be observed. It had been thought, when the O'Grady brothers had first told me of the disease, and before it had been actually seen, that it might be swine influenza. However, on direct observation, the condition differed from swine influenza in a number of respects. For one thing, the morbidity rate was much lower than that characteristically seen in swine influenza and the spread from case to case was slower (1). Even at the height of the outbreak, large numbers of the animals were stated to have appeared unaffected and at the time it was seen personally, only a small minority of the drove were obviously ill. The period of 5 weeks that the outbreak persisted gives some measure of its relatively slow rate of transmission.
spread. The picture shown by individual sick animals also differed from that seen in swine influenza. The signs of respiratory distress exhibited by the Argentine swine were more exaggerated and severe than in swine influenza and consisted in labored and extremely rapid breathing, frequently in a sitting posture, instead of prone as is usual in swine influenza. Although the animals apparently had great respiratory embarrassment, and were obviously dangerously ill, as evidenced by the speed with which they sometimes succumbed, they did not exhibit the early extreme prostration seen characteristically in swine influenza. High fevers were the rule in the sick swine, and temperatures in excess of 42°C were not uncommon.

Animals that became ill enough to show severe signs of respiratory distress usually died if untreated and death ensued in from 24 to 48 hours of the first signs of illness. Some died without having been observed to be ill. Sick animals that eventually recovered were those in which respiratory signs at the onset of illness were not particularly marked and ordinarily, if such animals survived for 4 days, they eventually recovered.

The lungs of four swine, obtained for me at postmortem by Dr. Oscar Massini from animals that were either freshly dead or that were sacrificed when extremely ill, were examined in the gross. All exhibited an extensive lobar pneumonia with an accompanying fibrinous pleuritis. The pneumonia was predominantly basal in its distribution. The postmortem picture was thus very unlike that of swine influenza in which the anterior lobes are primarily affected and the distribution of pneumonia is lobular. Also pleuritis is only exceptionally present in swine influenza. In brief, the autopsy picture shown by the Argentinian field cases seen was that of an extensive pleuropneumonia accompanied by marked pulmonary edema of non-pneumonic areas of lung, a picture that was later faithfully reproduced in experimental swine. A more complete description of the gross and histopathology of the condition will be given when the experimentally transmitted disease is discussed.

EXPERIMENTAL TRANSMISSION

Portions of the lungs of the four field cases autopsied were brought back to the laboratory in 50 per cent glycerol–tap water and came into the country under United States Department of Agriculture, United States Veterinary Permit No. 871, Organisms or Vectors. A 10 per cent suspension in 0.85 per cent saline was prepared by grinding portions of two of the lungs with sand in a mortar, and 10 cc of the supernatant of this suspension was administered intranasally to swine 38-84. The animal became extremely ill the next day, had markedly labored breathing, and a temperature of 41.5°C. It was moribund the following day and died during that night. At autopsy, the lungs showed a pleuropneumonia that faithfully reproduced in

2 Grade Berkshire or Landrace swine, 7 to 19 weeks of age, were used in this work. They were kept in individual isolation rooms of a type designed to maintain adequate protection against accidental or cross-infection or escape of the infectious agent. In an experience of over 35 years with isolation rooms of this type, in work with either influenza or cholera of swine or rinderpest of cattle, no instance of cross-infection, accidental infection, or escape of the infectious agent has been encountered.
both type and extent that seen in the field cases in Argentina. Another pig, swine 38-83, was
inoculated intranasally with 10 cc of a 5 per cent suspension of the pneumonic lung of swine
38-84. This animal became extremely ill the day after inoculation with rapid heavy breathing
in a sitting posture and a temperature of 41°C. It died that night and at autopsy exhibited an
extensive pleuropneumonia like that seen in the Argentine swine.

The disease has been maintained for study by serial intranasal passage in
swine, using pneumonic lung as inoculum at each passage. The record of these
passages shown in Table I makes it apparent that the causative agent of the
pleuropneumonia seen on the O'Grady farm survived in the material brought
back in glycerol and lost none of its killing potential in transit. All direct studies
to determine the etiological agent of the disease stemmed from the experi-
tentially infected passage swine and were designed to reveal the presence of either
a virus or a bacterium or both.

**Attempted Filtration of the Causative Agent.**—The history that the outbreak had responded
favorably to treatment with terramycin rather discouraged the thought that one of the small
viruses might be involved. However, the supernatant of a 10 per cent suspension of the lung
of swine 38-84 was filtered through a Seitz pad and 10 cc of the filtrate administered intra-
nasally to swine 38-85. The filtrate was also given intranasally to anesthetized white mice.
These mice remained normal, and serial passage of the lungs of some of them at 4 days also
resulted negatively. The surviving mice of both passages were found fully susceptible to swine
influenza virus when challenged after 2 weeks. Swine 38-85 remained normal throughout 3 days
of observation and was sacrificed at the end of this time. The lungs appeared normal at
autopsy, but were nevertheless saved in 50 per cent glycerol–saline. A suspension prepared
from the glycerol-stored lungs of swine 38-85 was administered later to two other experimental
animals, swine 39-06 and 39-08, who remained normal.

It seemed apparent, therefore, that the causative agent of the Argentine
pleuropneumonia was not one capable of filtration through a Seitz pad and that
swine influenza virus was not involved in the outbreak.

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**TABLE I**

**Serial Passage of Argentine Pleuropneumonia with Suspensions of Infected Lung
Administered Intranasally**

<table>
<thead>
<tr>
<th>Passage No.</th>
<th>Inoculum*</th>
<th>Glycerol storage days</th>
<th>Swine No.</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lungs of two natural Argentine cases</td>
<td>28</td>
<td>38-84</td>
<td>Died 3rd day</td>
</tr>
<tr>
<td>2</td>
<td>Lung swine 38-84</td>
<td>29</td>
<td>38-83</td>
<td>&quot; 2nd &quot;</td>
</tr>
<tr>
<td>2</td>
<td>&quot; 38-84</td>
<td>428</td>
<td>39-76</td>
<td>&quot; 5th &quot;</td>
</tr>
<tr>
<td>2</td>
<td>&quot; 38-84</td>
<td>588</td>
<td>40-07</td>
<td>Moribund 3rd day, killed</td>
</tr>
<tr>
<td>3</td>
<td>&quot; 40-07</td>
<td>19</td>
<td>39-96</td>
<td>&quot; 2nd &quot;</td>
</tr>
<tr>
<td>4</td>
<td>&quot; 39-96</td>
<td>47</td>
<td>40-33a</td>
<td>Died 2nd day</td>
</tr>
</tbody>
</table>

* 10 cc supernatant of 5 to 10 per cent lung suspension in 0.85 per cent NaCl solution
administered intranasally.
360  

PORCINE CONTAGIOUS PLEUROPNEUMONIA. I

BACTERIOLOGY

Pneumonic lung, bronchial and tracheal exudate, spleen, liver, heart blood, and lymph nodes from swine 38-83 and 38-84 were streaked on both blood and chocolate agar plates prepared with horse blood. Many of the blood agar plates appeared to support no growth unless a contaminating organism was present. The contaminating organism was a large thick bacillus which formed soft, grayish-white colonies, approximately 3 mm in diameter, on blood agar. In the immediate neighborhood of these colonies, and surrounding them in a satellite fashion, were smaller, smooth, glistening colonies. Those satellite colonies lying nearest the large grayish-white colonies were larger than those even only a few millimeters farther out, and as the distance from the larger colony increased, the satellites became smaller until several millimeters out they were so small as to be barely visible. The organism forming these satellite colonies was an extremely pleomorphic Gram-negative one which occurred as individual small bacilli, clumps of coccus-like forms, long thread-like forms, and bizarre club-shaped bodies, all within a single culture. The morphological appearance and the manner of growth of this organism on blood agar strongly suggested a close similarity to Hemophilus influenzae suis (2), the bacterial component of the swine influenza etiological complex (3). On chocolate agar, the same two types of organism were observed, except on this medium the small pleomorphic one, instead of forming tiny barely visible colonies as it did when growing alone on blood agar, formed larger colonies of about the same size as those seen growing satellitically on blood agar.

The colonies formed by the pleomorphic organism on chocolate agar were of two types. The one that seemed to predominate in early passage cultures was a rounded, dense, “waxy” colony. The other was a flatter, soft, glistening colony, and this type of colony predominated in cultures that had been maintained for several transfers on chocolate agar. So far as could be told by the examination of stained films of the two types of colonies, the organisms contained in each were morphologically the same.

The large thick bacillus and the pleomorphic organism found in the pneumonic lungs of swine 38-84 and 38-83, were transferred as pure cultures from individual colonies to a medium that has been employed in my laboratory for many years for the maintenance of Hemophilus influenzae suis (2), namely plain agar slants (pH 7.4) to which 1 cc of sterile defibrinated horse blood had been added at the base. In such media, the large thick bacillus formed a heavy grayish-white growth over the whole of the slant, while the small pleomorphic organism grew largely in the blood at the base of the slant and formed only tiny colonies on the agar, just above the level of the blood. In order to learn whether either of these organisms was etiologically important in the disease from which it was isolated, they were administered intranasally to experimental swine, as described in the next section of this paper.

**Pathogenicity of the Large Thick Bacillus for Swine.**—5 cc of a heavy saline suspension of a 48 hour culture of the large thick bacillus was administered intranasally to swine 38-75. This organism had been isolated originally from the lung of swine 38-84 and had been transferred on media three times since its initial isolation. Swine 38-75 developed no temperature elevation and no signs of illness and was considered negative. No further tests of the pathogenicity of the large thick bacillus were conducted.

**Pathogenicity of the Pleomorphic Organism for Swine.**—5 cc of the bloody fluid from the
bases of 24-hour agar slant cultures of the pleomorphic organism was administered intranasally to swine 38-90. One of the cultures used had been isolated from the lung of swine 38-83 and had been transferred on media three times since its initial isolation. The other cultures employed had been isolated from the lung and spleen of swine 38-84 and had been transferred on media three and six times respectively since their initial isolation. Swine 38-90 became quite ill on the afternoon of the same day it was inoculated, exhibiting respiratory distress and accelerated respirations. It died about midnight, approximately 15 hours after intranasal inoculation. At autopsy, the whole right side of the lung, apical, cardiac, and diaphragmatic lobes, was heavy, distended, and dark purple in color. On cut section, the involved lung was firm, bloody, edematous, and in an early stage of red hepatization. The right pleura contained a large amount of blood-tinged fluid without evident fibrin. The pericardium was also distended by blood-tinged fluid. The left lung and pleura were relatively normal.

With this suggestive lead that the pleomorphic organism might indeed be the causative agent of the Argentine pleuropneumonia, a second pig, swine 38-87, was inoculated intranasally with a culture of the organism.

This time a fourth passage culture isolated originally from the spleen of swine 38-84 was used and the bloody condensation fluid was diluted 1 in 10 with broth and administered in 3 cc amount in the hope that the smaller dose might result in a less acutely fatal illness. Swine 38-87 remained seemingly normal for 3 days after inoculation. On the 4th day, its temperature rose abruptly to 41.3°C and it appeared in respiratory distress. The following day the temperature was down slightly to 40.8°C and the animal was moribund. It was sacrificed at this time, rather than having it succumb during the night. Autopsy revealed a bilateral pneumonia involving portions of both diaphragmatic lobes with an accompanying fibrinous pleuritis involving only the pneumatic portions of lung. The pleomorphic organism was isolated in pure culture from the tracheal exudate and from both diaphragmatic lobes. The spleen, liver, and heart blood proved sterile.

In order to complete the fourth of Koch's postulates in incriminating the pleomorphic organism as the etiological agent of the Argentine pleuropneumonia, the cultures isolated from the pneumatic lung of swine 38-87 were transferred three times on media and then administered intranasally to another animal (swine 38-99).

0.05 cc of the bloody condensation fluid of 24-hour cultures was added to 10 cc of broth as the intranasal inoculum. Swine 38-99 became extremely ill the day after inoculation with a temperature of 41.1°C and marked respiratory distress. It was found dead the next morning and at autopsy showed an extensive right-sided pneumonia. The right pleura and the pericardium contained a large amount of yellowish gelatinous exudate. The pleomorphic organism was isolated in pure culture from the spleen and liver and in mixed culture from the heart blood and from the three pneumatic lobes of lung on the right side.

It was apparent by now that the picture, both clinical and postmortem, produced by the pleomorphic organism in pure culture, faithfully duplicated that seen in the naturally occurring disease observed in Argentina as well as the experimental disease induced in experimental swine inoculated with crude suspensions of the lungs of natural field cases. There was no evidence that a virus
was involved in association with the pleomorphic organism: acting alone it seemed completely capable of reproducing the highly fatal pleuropneumonia from which it was isolated.

Because of the peculiarly typical character of the pathological manifestations of the disease, because of its evident contagiousness, and because it is a definite etiological entity, it is proposed to designate it as porcine contagious pleuropneumonia (PCP). This designation will serve to differentiate it from other non-specific forms of pleuropneumonia occasionally seen randomly in swine.

To date, 37 swine have been inoculated intranasally either with pure cultures of the pleomorphic organism or with lung suspensions known to contain the organism. As shown in Table II, the mortality rate has approached 50 per cent.

**TABLE II**
Mortality of Experimental PCP Following Intranasal Infection with either Pure Cultures of *H. pleuropneumoniae* or Suspensions of Infected Lung

<table>
<thead>
<tr>
<th>Outcome of infection</th>
<th>No. of swine</th>
<th>Total (approximate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No illness</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Sick and recovered</td>
<td>10</td>
<td>27</td>
</tr>
<tr>
<td>Sick and killed</td>
<td>9</td>
<td>24</td>
</tr>
<tr>
<td>Died</td>
<td>16</td>
<td>43</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>100</td>
</tr>
</tbody>
</table>

The cultural, morphological, and biological characteristics of the pleomorphic organism have been studied by Dr. David White and Grace Leidy, and will be reported upon by them separately in a subsequent publication. From this work, as well as from some of its characteristics mentioned earlier in this paper, it is apparent that the organism belongs in the genus *Hemophilus*. Because of this, and in recognition of its uncanny propensity to cause pleuropneumonia in swine, it is proposed that it be designated *Hemophilus pleuropneumoniae*.

Contagiousness of PCP.---Naturally occurring PCP, as observed on the O'Grady farms in Argentina, gave the impression of being a disease of relatively low morbidity and slow spread. Because of this, it has been surprising to find that, under conditions of experimental pen contact, as shown in Table III, it transmitted fairly readily. Of the five swine exposed by pen contact, three became clinically ill and one of these died. The fourth animal failed entirely to become infected, while the fifth exposed animal, though showing no obvious signs of illness during observation, was found to have undergone a clinically inapparent infection, as evidenced by the presence of characteristic old unresolved lesions in its lungs at autopsy 49 days after its initial exposure. It seems entirely possible that the apparently low morbidity of the outbreak observed in
Argentina may have resulted from the frequent occurrence of subclinical infec-
tions during the natural outbreak. Certainly under conditions of experimental
pen exposure of individual normal swine to infected ones, *H. pleuropneumoniae*
transferred with considerable facility. Sometimes, as evidenced by the short
incubation periods shown by contact-infected swine 40-19 and 40-21, this trans-
fer of organisms from sick to normal swine must occur very promptly after
exposure.

**Gross and Histologic Pathology of PCP.**—The description of the gross and
histologic pathology of PCP is derived from experimental cases induced by
intranasal infection with suspensions of pneumonic lungs, either from original

<table>
<thead>
<tr>
<th><strong>TABLE III</strong></th>
<th><strong>Transmission of PCP by Contact</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infected swine</strong></td>
<td><strong>Exposed swine</strong></td>
</tr>
<tr>
<td>39-67 Sick 6 days, survived</td>
<td>39-75 Clinically negative, lesions at autopsy</td>
</tr>
<tr>
<td>39-84 &quot; 5 &quot; , &quot;</td>
<td>39-87 Sick for 5 days after 7-day incubation period, survived</td>
</tr>
<tr>
<td>40-10 &quot; 5 &quot; , &quot;</td>
<td>40-16 Negative</td>
</tr>
<tr>
<td>40-33a Dead 2nd day</td>
<td>40-19 Sick for 7 days after 2-day incubation period, killed</td>
</tr>
<tr>
<td>40-31 &quot; 1st &quot;</td>
<td>40-21 Dead 3rd day, 1-day incubation period</td>
</tr>
</tbody>
</table>

*Swine 40-33a was inoculated intranasally with a suspension of infected lung. The other
four swine serving as a source of contact infection were inoculated intranasally with pure
cultures of *H. pleuropneumoniae*. field cases or from experimental cases, or with pure cultures of *H. pleuropneu-
moniae*, or by pen exposure to intranasally inoculated swine. So far as could be
observed, the clinical course and pathology of all four categories of experimental
cases were identical with one another and with the cases of the field disease
observed in Argentina.

**Gross Pathology.**—The gross pathological changes observed in the respiratory tracts
of acutely fatal cases of PCP have already been briefly described in connection with
accounts of individual experimental swine. In summary, the pneumonias have usually
been bilateral and limited to the diaphragmatic lobes of the lung. If unilateral, the
cardiac and apical lobes, as well as the diaphragmatic lobe on one side have been
involved. The pneumonic lobes have been purplish red in color, cut almost like liver,
and the cut surfaces were friable when grasped with forceps. Interlobular septa in
pneumonic areas were widened by bloody gelatinous fluid. Strands of loosely adherent
fibrin and sometimes a yellowish exudate overlay pneumonic areas of the lungs of
animals surviving for more than 24 hours. In animals that died before 24 hours had
elapsed, the pleurae contained blood-tinged fluid without a fibrinous pleuritis evident in the gross. Lobes of lung that were not consolidated were usually congested and edematous with interlobular septa widened by blood-tinged gelatinous fluid. The surfaces of such edematous lobes were glistening and showed no evidence of pleuritis. A picture of a lung illustrating the characteristic features of PCP is shown in Fig. 1.

In the rapidly fatal cases, the trachea and bronchi ordinarily contained a copious, frothy, blood-tinged, mucous exudate, and a similar exudate flowed from the nostrils and mouths at death. The bronchial lymph nodes were purple, glistening, swollen, and congested. Many cases in which there was a pleuritis also exhibited an excess of blood-tinged pericardial fluid, usually containing strands of fibrin.

Outside the chest, the gross pathological manifestations were less constant. Sometimes there was an excess of blood-tinged peritoneal fluid, occasionally containing fibrinous strands. The livers were ordinarily dark and engorged and the spleens swollen, soft, and dark. The kidneys were grossly negative, as were the gastrointestinal tracts. Mesenteric lymph nodes were sometimes swollen, purplish red in color, and diffusely congested.

Although many of the experimentally infected swine soon died, some have survived and eventually returned to apparent good health. In such recovered animals, the only pathology evident in the gross was in the lung and consisted of hard, rounded areas of consolidation, comprised of organizing connective tissue containing sequestra of inflamed or necrotic lung. These masses ranged in size from that of a marble up to that of a golf ball or larger. They were usually multiple and the pleurae overlying the consolidated areas were always adherent to the chest wall by dense strands of connective tissue. Recovered animals have not been held under observation for longer than 14 weeks but the residual respiratory tract lesions just described persist for at least that long. Swine bearing them have the outward appearance of being quite normal, and clinical signs referable to the respiratory tract are minimal or absent.

Histopathology. There was little of significance to observe microscopically outside the respiratory tract except in the lymph nodes and the heart. The mediastinal and mesenteric lymph nodes, which in acutely fatal cases were swollen and diffusely congested, exhibited histologically markedly dilated blood vessels packed with red blood cells, and red cells also were sometimes numerous throughout the parenchyma of the gland (Fig. 2). The hearts of pigs that survived 24 hours or longer ordinarily showed a gross pericarditis with excess fibrin-containing fluid in the pericardial sac. Histologically such hearts exhibited markedly dilated subpericardial blood vessels. Overlying the pericardium and loosely adherent to it, in the acutely fatal cases dying or killed between the 2nd and 4th days of illness, was a membranous exudate composed of fibrin and mononuclear cells which appeared to be predominantly lymphocytes (Fig. 3). Only very few polymorphonuclear leucocytes were present in the exudate.

The most striking histological changes were in the lungs and pleurae and their character was dependent upon the time following infection that they were observed. In the case of animals dying or killed during the first 3 or 4 days of illness, lung sections

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1 I am very grateful to Dr. Eugene L. Opie for advising and guiding me in these studies of the microscopic pathology.
from areas of consolidation cut in such a way as to include small bronchi, terminal bronchioles, and overlying pleura presented a rather constant picture with the following features. Examined in the gross, these sections showed bizarre designs, circles, bands, and irregularly shaped areas that were discretely outlined along their margins by more deeply staining tissue components (Fig. 4). Examined under the microscope, these bizarrely shaped areas were found to represent widely dilated lymph sinuses containing coagulated lymph in which there was much fibrin and many lymphocytes. They were seemingly lying in the interlobular septa. Along these lymphatic channels and apparently outside them, both free in the septa and in the adjacent pulmonary alveoli were dense accumulations of round cells comprised largely of lymphocytes (Fig. 5). Only a few polymorphonuclear leucocytes were to be seen. It was this dense cellular exudate paralleling the lymphatic vessels that accounted for the more deeply staining designs that were so evident when one looked at the sections in the gross. While the alveoli adjacent to the lymphatic channels were frequently packed with lymphocytes, those lying deeper in the lung contained only few cells but much fluid (Fig. 6). The small bronchi and bronchioles usually contained a moderate cellular exudate, largely lymphocytic, and the atria and alveoli immediately adjacent to them were frequently packed with cells of the same types (Fig. 7). The bronchial walls were infiltrated with lymphocytes and the lining bronchial epithelium was usually fragmented and partially desquamated (Fig. 8). Throughout the areas of pneumonia, there was much congestion; small blood vessels were dilated and packed with red blood cells, and the capillaries lying in the alveolar walls were similarly packed (Fig. 9). The alveolar walls themselves were thickened and folded and infiltrated with scattered lymphocytes.

The subpleural lymph channels, like those in the interlobular septa, were widely dilated and filled with fibrin-containing lymph and lymphocytes. Below these, the underlying pulmonary alveoli were densely packed with many lymphocytes and a few leucocytes as had been those lying along the lymphatic channels in the interlobular septa. Overlying the pleural lymphatic channels were accumulations of lymphocytes, few leucocytes, and fibrin both in the space between the lymph channels and the pleural surface, as well as overlying the pleura (Fig. 10).

In those swine that survived, the histopathological picture shown by the lung was that of an attempt at healing by fibrosis and sequestration. The pleura was thickened by whorls and strands of fibroblasts (Fig. 11) and similar zones of fibroblastic proliferation extended down along the interlobular septa. Scattered throughout the areas of fibrosis were irregularly rounded areas containing alveoli packed with inflammatory cells (Fig. 12). These areas were closely encased by zones of intense fibroblastic reaction and in some the cells of the alveolar walls were necrotic. Lymphocytes were still prominently present, although at this stage polymorphonuclear leucocytes were more numerous than earlier. The lungs of swine convalescent for more than 3 weeks have not been studied histologically, so that the ultimate fate of these areas of seeming sequestration or of the fibrotic pneumonia is unknown.

DISCUSSION

It has been found that a frequently rapidly fatal respiratory disease occurring in swine in Argentina has as its causative agent a bacterium of the genus...
Hemophilus (H. pleuropneumoniae). No virus could be shown to be associated with the disease as it occurred in nature, and indeed none need be hypothesized because the bacterium alone in pure culture regularly induces infections in experimental swine that faithfully reproduce the natural condition.

The fact that a Hemophilus can serve unaided as an effective respiratory pathogen in swine is perhaps of itself not particularly remarkable. However what is probably worthy of additional comment in this connection is the fact that, in another respiratory disease of swine, swine influenza, a Hemophilus acts in concert with a virus (3) to exert what is usually a much milder pathologic effect (1). The Hemophilus associated with swine influenza, H. influenzae suis (dubbed H. suis some years after its discovery for reasons not clear to me), administered alone to swine is completely without deleterious effect (2). In this regard, H. influenzae suis differs markedly from H. pleuropneumoniae.

Work with H. influenzae suis since its original description as one of the components of the swine influenza etiological complex (3) has shown it to be more heterogeneous in its growth requirements than was at first thought. In the beginning, and as first described (2), H. influenzae suis was thought to require both “X” and “V” factors for growth. Further study by Leidy, Hahn, and Alexander (4) has shown that some strains of the organism require V factor (diphosphopyridine nucleotide) (DPN) but not X factor (hemin) for growth. Furthermore, Leidy (5) has found that some strains have very complex growth requirements and must have as yet unidentified factors, present in horse plasma, for satisfactory growth. Factors V and X are not adequate to assure the growth of these more fastidious strains. Both the DPN-dependent strains of H. influenzae suis as well as those with more fastidious growth requirements occur in both the encapsulated and non-encapsulated forms.

Culturally, H. pleuropneumoniae is quite different from those strains of H. influenzae suis that have the more complex growth requirements. However, as will be reported in a later paper, it is very similar culturally to some of the strains of H. influenzae suis that are DPN-dependent and that do not have a requirement for factor X. Furthermore, as will also be detailed in a subsequent paper, the application of more critical tests for relatedness between H. pleuropneumoniae and DPN-dependent strains of H. influenzae suis, involving transformation, suggests a close relationship between the two organisms.

This seemingly close relationship between H. pleuropneumoniae and DPN-dependent strains of H. influenzae suis makes the more remarkable the great difference shown by the two organisms in their pathogenicity for swine. The one, H. influenzae suis, induces, with the swine influenza virus (3) an interstitial type of bronchopneumonia, seldom with an accompanying pleuritis, which has a fatality rate of less than 4 per cent. The other, H. pleuropneumoniae, induces alone, and without an associated virus, a fulminating type of lobar pneumonia, always with an accompanying pleuritis, which has a fatality rate approaching
50 per cent. The great lethality of *H. pleuropneumoniae* for swine makes it unique among the *Hemophilus* which are not ordinarily known to be highly fatal for the animal species they normally parasitize. Only encapsulated strains of *H. influenzae* injected intraperitoneally, with mucin in mice (6) show a lethality approximating that of *H. pleuropneumoniae* in its natural porcine host.

The readiness with which PCP was found to transmit from sick to normal swine under experimental conditions of pen contact contrasted with the apparently low morbidity and slow spread of the natural disease as observed in Argentina. A possible explanation of this seeming discrepancy, suggested by the experimental findings, may be that under natural conditions of field exposure, a relatively high proportion of infections is either mild or subclinical and would be recognized only by the residual lung lesions encountered at slaughter. Based solely upon manifest illness, the disease would then appear to have a lower morbidity rate than it actually has.

Study of the microscopic pathology of PCP has suggested that in its pathogenesis, the disease is one in which the lymphatics of the lung and pleura are primarily involved. The cellular reaction, initially at least, is one in which lymphocytes mainly participate. Pneumonia, as manifested by cellular exudation, seems to proceed from those alveoli that lie either adjacent to the interlobular septa or below the pleural surface and bears a relationship to the cellular reaction about the lymphatic channels in those regions. Deeper in the pulmonary lobules, the reaction is one that elicits edema with fewer cells participating in the reaction except that atria and air sacs adjacent to bronchi and bronchioles frequently exhibit as marked an inflammatory cellular reaction as do those along the lymphatics. The ultimate result of this sort of an inflammatory response is a fulminating pleuropneumonia participated in by lymphocytes, fibrin, and fluid which usually proceeds so rapidly as to overwhelm fatally the host in from 1 to 3 days. If the host does not succumb, healing appears to take place by a process of fibrosis and attempted sequestration of the areas of pneumonia.

It is perhaps of some interest from the standpoint of comparative disease that PCP, in its healing phase, is strikingly similar in both its gross and histopathological aspects to bovine contagious pleuropneumonia. This disease of cattle, which is extensively prevalent in various parts of the world, most notably in Asia and Africa, is caused by *Asterococcus mycoides*, an agent that has served as the morphological and cultural model of the PPLO (pleuropneumonia-like organisms) group of organisms. Strangely enough, the PPLO's, other than the original one causing bovine contagious pleuropneumonia, are not associated etiologically with pleuropneumonia and hence bear a completely meaningless group designation. The suggestion of the name, *Hemophilus pleuropneumoniae*, for the etiological agent of PCP is not made with any intent to cloud further the nomenclatural situation, but rather to designate the primary pathologic manifestation of infection of swine with this particular *Hemophilus*. 
SUMMARY

An acute frequently rapidly fatal respiratory illness occurring as an epidemic disease in Argentine swine has been shown to have a bacterium of the genus Hemophilus as its causative agent. This organism, for which the name *Hemophilus pleuropneumoniae* is suggested, causes a singular, fulminating pleuropneumonia in experimental swine. The very marked effectiveness of *H. pleuropneumoniae* as a respiratory pathogen contrasts strikingly with the relatively mild pathogenicity of the well known swine *Hemophilus, H. influenzae suis*, which, in concert with a virus, causes a less highly fatal respiratory ailment, swine influenza. Porcine contagious pleuropneumonia (PCP) is contagious under experimental conditions. In the pathogenesis of the disease, histopathological studies of early cases suggest that the lymphatics of the lung and pleura may be primarily involved and that the pneumonia and pleuritis then proceed from these initial sites of reaction.

BIBLIOGRAPHY

5. Leidy, G., personal communication.

EXPLANATION OF PLATES

**PLATE 43**

**FIG. 1.** Dorsal aspect of lung in experimental PCP (swine 40-40). The left lung is completely consolidated and coated by a thick layer of fibrinous exudate. The right lung is edematous and its interlobular septa are widely dilated by blood-tinged fluid. Animal died on the 4th day following intranasal inoculation with $5.5 \times 10^6$ viable *H. pleuropneumoniae*. $\times \frac{3}{2}$. 
(Shope: Porcine contagious pleuropneumonia. 1)
Fig. 2. Section of a mesenteric lymph node in experimental PCP (swine 40-33a) showing dilated blood vessels packed with red blood cells. Animal died on 2nd day following intranasal inoculation with infected lung suspension. Hematoxylin-eosin. × 82.

Fig. 3. Section of heart in experimental PCP (swine 40-33a), showing dilated sub-pericardial blood vessels and a partially separated overlying membranous pericardial exudate made up of fibrin and mononuclear cells that appear to be mainly lymphocytes. Hematoxylin-eosin. × 82.
(Shope: Porcine contagious pleuropneumonia. I)
PLATE 45

Fig. 4. Section of lung in experimental PCP (swine 39-35) to show bizarre designs made by accumulations of deeply staining inflammatory cells. Animal died on the 3rd day following intranasal inoculation with $1.4 \times 10^3$ viable *H. pleuropneumoniae*. Hematoxylin-eosin. $\times 4$.

Fig. 5. Section of lung in experimental PCP (swine 40-33a) showing widened interlobular septa which contained coagulated lymph and scattered lymphocytes. There are dilated lymph sinuses in the septa. Pulmonary alveoli adjacent to the septa are packed with dense accumulations of inflammatory cells. These were largely lymphocytes with only a very few polymorphonuclear leucocytes. Hematoxylin-eosin. $\times 82$. 
(Shope: Porcine contagious pleuropneumonia. I)
PLATE 46

Fig. 6. Section of lung in experimental PCP (swine 39-30) showing pulmonary alveoli containing much fluid but only few inflammatory cells, largely lymphocytes. Animal died on the 4th day following intranasal inoculation with $1 \times 10^6$ viable *H. pleuropneumoniae*. Hematoxylin-eosin. $\times$ 82.

Fig. 7. Section of lung in experimental PCP (swine 40-33a) showing bronchus containing a lymphocytic exudate and adjacent atria and alveoli packed with inflammatory cells that are largely lymphocytes. Hematoxylin-eosin. $\times$ 82.
(Shope: Porcine contagious pleuropneumonia. 1)
PLATE 47

Fig. 8. Section of a small bronchus in experimental PCP (swine 40-33a) showing exudate that was largely lymphocytic, and fragmented and partially desquamated bronchial epithelium infiltrated with lymphocytes. Hematoxylin-eosin. X 280.

Fig. 9. Section of lung in experimental PCP (swine 39-35) showing dilated blood vessels packed with red blood cells in an interlobular septum, and similar dilation and congestion of capillaries in the adjacent pulmonary alveolar walls. Hematoxylin-eosin. X 202.
(Shope: Porcine contagious pleuropneumonia. I)
Fig. 10. Section of lung in experimental PCP (swine 39-35) to show the pleural inflammatory reaction. The pleural lymph sinuses are widely dilated, and in the adjacent pleural spaces are scattered inflammatory cells, largely lymphocytes. Fibrin and inflammatory cells overlay the pleura (top). The pulmonary alveoli just beneath the pleural lymph channels contain many inflammatory cells of the type present in the pleural exudate, while alveoli lying deeper in the lung contain only few cells but much fluid. Hematoxylin-eosin. X 82.

Fig. 11. Section of pleura in experimental PCP (swine 39-49) to show fibroblastic reaction occurring during the healing process. The pleura is markedly thickened by whorls and strands of fibroblasts. New blood vessels in the fibrotic area are dilated and packed with red blood cells. Inflammatory cells, largely lymphocytes, have accumulated along the pulmonary side of the pleura. Animal killed when apparently recovered on the 21st day following intranasal inoculation with $4.5 \times 10^4$ viable *H. pleuro-pneumoniae*. Hematoxylin-eosin. X 82.
(Shope: Porcine contagious pleuropneumonia. I)
FIG. 12. Section of lung in experimental PCP (swine 39-49) to show reaction during the healing process. An area of necrotic lung is surrounded by a dense zone of inflammatory cells, largely lymphocytes, and this, in turn, by an area of marked fibroblastic reaction. Hematoxylin-eosin. X 47.
(Shope: Porcine contagious pleuropneumonia. I)