A Recent Epidemic of Acute Respiratory Infection at Camp Custer, Mich.

Preliminary Laboratory Report

WYNDHAM B. BLANTON, M.D.
(RICHMOND, VA.)
Captain, M. C., U. S. Army; Chief Laboratory Service

AND

ERNEST E. IRONS, M.D. (CHICAGO)
Lieutenant-Colonel, M. C., U. S. Army
CAMP CUSTER, BATTLE CREEK, MICH.

Reprinted from The Journal of the American Medical Association
Dec. 14, 1918, Vol. 71, pp. 1988-1991

A RECENT EPIDEMIC OF ACUTE RESPIRATORY INFECTION AT CAMP CUSTER, MICH.*

PRELIMINARY LABORATORY REPORT

WYNDHAM B. BLANTON, M.D. (RICHMOND, VA.)
Captain, M. C., U. S. Army; Chief Laboratory Service

AND

ERNEST E. IRONS, M.D. (CHICAGO)
Lieutenant-Colonel, M. C., U. S. Army

CAMP CUSTER, BATTLE CREEK, MICH.

From a knowledge of what other camps were experiencing with the epidemic of so-called "influenza," and in anticipation of an outbreak of a similar infection in this camp, certain preliminary bacteriologic work was attempted. Several days before any cases of influenza were reported at Camp Custer, a study was begun to determine the prevalent mouth flora of healthy individuals. For this purpose cultures were made from the throats of enlisted men of the Fourteenth Sanitary Train. Smears and cultures on plain blood agar plates were made from the nose and nasopharynx; in all, 357 cultures were taken. The usual mouth organisms were recovered. In addition, 75 per cent. of the cultures showed a hemolyzing streptococcus. In only five cases, or in a little more than 1 per cent., was the influenza bacillus identified. Before these studies could be extended, the epidemic broke. However, this much was apparent: A high percentage of healthy individuals were carrying hemolyzing streptococci somewhere in their respiratory tract. The influenza bacillus was not present in greater numbers than one is accustomed to find this organism in normal throats.

INFLUENZA

Influenza patients who showed no physical signs of pneumonia were first studied. Throat cultures, blood cultures, blood counts and urinalyses were made.

* Compilation to and including Oct. 22, 1918.

Throat Cultures.—Smears and cultures of the throat were made in 366 cases. Plain blood agar plates were employed, and special care was taken to identify the influenza bacillus. Organisms recovered were: hemolyzing streptococci, 34 per cent.; nonhemolyzing streptococci, 33 per cent.; pneumococci, 12 per cent.; influenza bacilli, 8 per cent.

Blood Cultures.—One hundred and forty cultures were made on these patients at various stages of the disease. In all cases the cultures remained sterile.

Blood Counts.—Five hundred and eighty leukocyte counts were made with the results as shown in Table 1. Seventy per cent. of these counts showed 8,000 cells or less per cubic millimeter. This leukopenia was the most impressive feature of the blood count. The polymorphonuclear leukocytes showed but slight increase over the normal. There has been no conspicuous lymphocytosis, nor other noteworthy features of the blood count.

Urinalyses.—Twenty per cent. of the urines examined have shown albumin. In the majority of cases this was recorded as a faint trace. Casts were an infrequent finding, occurring in 4.7 per cent. of the cases.

PNEUMONIA

It became apparent with the development of a large number of cases of pneumonia that the greatest importance attached to their study. Blood cultures, sputum typings, blood counts and urinalyses were made in as many cases as possible.

Blood Cultures.—Five hundred and ten blood cultures in cases of pneumonia have been made to date. Of these, eleven have shown organisms as follows: hemolyzing streptococcus in ten cases, *Pneumococcus mucosus* once. In other words, only 2 per cent. of pneumonia patients have shown a bacteremia. These cultures were taken from the sickest patients, the majority of whom died shortly after. Many cultures were sterile which were taken only a few hours antemortem. In seven of the eleven cultures that have shown organisms, the blood was taken just prior to death. The evidence clearly points to the fact that the infection of the lungs is only exceptionally accompanied by a bacteremia and that the blood stream is not invaded up to a very late period in the disease.

These findings agree with the apparent method of development of the pulmonary lesions and add weight to the belief that a preexisting bronchitis usually unassociated with marked sore throat gives rise to a bronchopneumonia by a process of direct extension. These results are not entirely in keeping with our experience with streptococcus pneumonias of last winter, which usually developed on the basis of a severe primary sore throat and were accompanied by positive blood cultures in 13 per cent. of the cases. It is of interest to note that of the first 430 blood cultures taken, only

TABLE 1.—RESULTS OF 1,580 LEUKOCYTE COUNTS MADE BEFORE AND AFTER THE DEVELOPMENT OF PNUEMONIA

Leukocytes per C.Mm.	Prepneumonia Stage		Pneumonia	
	No. of Cases	Per Cent.	No. of Cases	Per Cent.
4,000- 6,000	96	16.5	288	28.8
6,000- 8,000	306	52.7	390	39.0
8,000-12,000	113	19.5	177	17.7
12,000-16,000	48	8.3	83	8.3
16,000-20,000	14	2.5	29	2.9
20,000-30,000	3	0.5	33	3.3
Totals.....	580	....	1,000	
Differential Counts: Occurrence of polymorphonuclear leukocytes: Per Cent.				
40-50	6	2.6	35	3.5
50-60	40	17.4	112	11.2
60-70	60	26.0	260	26.0
70-80	97	42.2	459	45.9
80-90	27	11.8	134	13.4
Totals.....	230	....	1,000	

four showed organisms, less than 1 per cent.; while seven of the last eighty cultures have been positive; this agrees with other later developments in the epidemic.

Sputum.—The character of sputum produced by pneumonia patients was often unsatisfactory for typing because of the extremely critical condition of the patients at the time the collections were attempted. When sputum could be procured it was usually abundant, mucopurulent, and greenish yellow. A fair proportion of sputums were blood streaked, and quite a number were described as rusty. An attempt was made to trace some relation between the type of sputum and the organisms recovered from the sputum

during life and the lungs postmortem. None appeared to exist. Rusty sputums were found as often in cases of streptococcus as of pneumococcus infection, and mucopurulent sputums occurred as frequently with one organism as with another. As many sputums were typed as time would permit. From the original specimens smears were made, blood plates streaked, and Avery's rabbit's blood broth inoculated. Agglutinations and precipitations were done after from six to eight hours with the broth suspension. Bile solubility was determined and the results were checked by plain blood agar plates. In all, 740 sputums of pneumonia patients have been typed. The preponderance of strep-

TABLE 2.—TYPES OF ORGANISMS RECOVERED FROM THE SPUTUM OF PNEUMONIA PATIENTS

	Number of Cases	Per Cent. of Total
Pneumococcus:		
Type I	11	1.5
Type II	16	2.15
Type III	16	2.15
Type IV	148	20.00
	191	25.8
Streptococcus:		
Hemolytic	126	17.0
Nonhemolytic	325	43.9
	451	60.9
Influenza	38	5.2
Unsatisfactory	60	8.1
Total	740	

tococci is apparent, especially the nonhemolytic variety. Of the total of 451 streptococci recovered, 30 per cent. were hemolytic and 70 per cent. nonhemolytic. The common mouth pneumococcus was isolated in far higher percentage than usual, Type IV occurring 148 times. The remaining pneumococci were relatively infrequent. The influenza bacillus was identified in thirty-eight instances. In these cases the organism was seen in smears and subsequently recovered from the blood agar plates. In the majority of cases the influenza bacillus was associated with the streptococcus. In only eight instances was it found alone.

That these results do not accord entirely with the postmortem bacteriology of the lungs and blood is explained by the fact that many patients became rapidly moribund after entering the hospital, and before material could be collected for laboratory examination. From many of the patients sputum could not be had.

Therefore, pneumonias caused by the more fatal types of pneumococcus had their bacteriology worked out postmortem, while patients with the less severe infections with the pneumococcus for the most part recovered, and the type was determined during life.

Blood Counts.—A study of 1,000 leukocyte counts in pneumonia patients disclosed a striking lack of reaction on the part of the bone marrow; 67.8 per cent. showed 8,000 or fewer leukocytes per cubic millimeter, and 85.5 per cent. were 12,000 or under per cubic millimeter. These counts agree with those obtained in the prepneumonia period. The secondary invasion of the lungs is apparently without effect in arousing the bone marrow, as is commonly the case in pneumonia. Leukocyte counts have, therefore, been of no value in indicating the onset of pneumonia.

Urinalyses. — Urinalyses on pneumonia patients showed the presence of albumin in 40 per cent., about double the incidence in uncomplicated "influenza" cases. Casts have likewise been a much more frequent occurrence, being present in 22 per cent. of the urines examined.

POSTMORTEM BACTERIOLOGY

The attempt has been made to secure as large a number of lung and heart's blood cultures as possible from fatal cases. A total of 280 fatal cases were thus studied. When necropsies were not performed, lung and heart's blood punctures were made and smears and cultures procured. In all cases examined postmortem, two blocks of consolidated lung were taken in sterile Petri dishes under sterile precautions, and carried to the laboratory for cultures. Plain blood agar plates were streaked and broth cultures inoculated. A number of fresh smears were made from each lung. The heart's blood was cultured in every case. In smears and in cultures particular care was taken to identify all gram-negative bacilli. All bile-soluble gram-positive diplococci that did not come down in pneumococcic serums of Types I, II and III were put through mice for verification. In a number of instances agglutinations were obtained from the mice after failure with rabbit's blood broth suspensions, indicating the importance of the mouse method as a check in Group IV diagnosis.

The result of these cultures is shown in Table 3. No one organism stands out above the others as peculiarly the etiologic factor. Streptococci have been present 142 times in the lungs, and pneumococci seventy-eight times. Hemolytic and nonhemolytic streptococci have appeared about equally as the causative factor. Type II has occurred about twice as frequently as any other type of pneumococcus. Type III has been recovered eighteen times. Small gram-negative bacilli have been recovered five times from the lungs, and three times from the heart's blood. As a usual occurrence only one organism was found in a given case. In three instances in the lungs, the influenza bacillus was found

TABLE 3.—BACTERIOLOGIC FINDINGS AT NECROPSY FROM THE LUNGS AND HEART'S BLOOD OF PNEUMONIA PATIENTS

	No. Recovered from Lungs	No. Recovered from Heart's Blood
Pneumococcus	78	77
Type I	8	6
Type II	34	33
Type III	18	16
Type IV	18	22
Streptococcus	142	110
Hemolytic	76	62
Nonhemolytic	66	48
Influenza	8	3
Unsatisfactory	30	29
Sterile	22	86

in conjunction with the streptococcus. In two cases it was the sole organism recovered. In the heart's blood it was once present with the streptococcus, once with staphylococcus, and once alone.

The occurrence of such a variety of organisms in pneumonic lungs suggests that they are secondary invaders, the field being prepared by the lowering of resistance incident to a preceding disease, which in this epidemic was in most instances influenza, and that in each instance the invader is probably the organism of which each individual is at the time a carrier. The high percentage of positive heart's blood cultures, taken in conjunction with contradictory antemortem findings, indicates how rapidly and at what a late period in the course of the disease the defense factors in the blood of the patient break down to allow invasion.

Table 4 shows the sugar reaction of forty-two organisms recovered from the lungs and the heart's blood at necropsy and chosen at random. All of these organisms were bile insoluble, produced no hemolysis on

TABLE 4.—SUGAR REACTION OF FORTY-TWO ORGANISMS FROM THE LUNGS AND THE HEART'S BLOOD

Streptococcus	Fermentation Reactions *					
	Saccharose	Inulin	Salicin	Mannite	Lactose	Raffinose
1	—	+	+	—	—	—
2	+	—	+	—	—	+
3	+	—	+	—	—	—
4	—	—	+	—	—	—
5	..	—	..	—	+	
6	..	—	..	—	+	
7	—	—	—	—	+	—
8	—	—	—	—	—	—
9	..	—	..	—	+	
10	—	+	—	—	—	—
11	+	—	—	—	+	—
12	..	+	..	—	+	
13	+	—	+	—	+	+
14	—	+	+	—	+	+
15	..	—	..	—	+	
16	—	+	+	—	+	+
17	+	+	—	—	+	—
18	—	+	+	—	+	+
19	..	—	..	—	+	
20	..	+	..	—	+	
21	..	+	..	—	—	
22	+	—	+	—	+	—
23	..	+	..	—	+	
24	—	—	+	—	+	—
25	+	—	—	—	+	+
26	—	—	+	—	—	—
27	—	—	+	—	—	—
28	..	+	..	—	+	
29	..	+	+	—	+	+
30	—	+	+	—	+	—
31	+	—	—	—	+	+
32	—	—	—	—	+	—
33	..	—	..	—	+	
34	..	+	..	—	+	
35	..	+	..	—	+	
36	—	—	—	—	+	—
37	+	—	+	—	+	+
38	—	+	+	—	+	—
39	+	—	+	—	—	—
40	—	+	+	—	—	—
41	—	—	+	—	+	—
42	—	—	—	—	—	—

* In this table — indicates no fermentation, and + indicates fermentation.

blood mediums, occurred in chains or in pairs, and retained the gentian violet when stained by Gram's method. The variability of inulin fermentation is particularly evident. The absence of mannite fermenters, strains corresponding to *Streptococcus fecalis,* is also noteworthy.

PATHOLOGY

Without exception the deaths from this respiratory epidemic have been due to secondary pneumonia. In no instance has a case come to necropsy in which death occurred from influenzal infection alone. The bodies have been those of well nourished young men, the termination having been reached too quickly for gross external changes. Many of the bodies have shown a moderate degree of corpulence. Reference to Table 5 will show the associated chronic lesions manifested. These have occurred in sufficient number to warrant the belief that in a fair proportion of fatal cases the patients were seriously handicapped beforehand in the battle with their infection.

For the most part there has been a striking similarity in the appearance of the respiratory organs in the 123 bronchopneumonias coming to necropsy. The mucous membrane of the trachea and bronchi has appeared intensely red, swollen and covered with a mucopurulent exudate. The bronchial glands have been enlarged, soft and reddened on section. The majority of the lungs have been voluminous and heavy. As a general rule the posterior lobes have varied from the remaining lobes, and have presented a surface dark purplish red, sometimes smooth, sometimes roughened and dull from collections of fibrin. They have felt firm throughout, and only occasionally could areas of greater density be made out.

The remaining lobes have shown a greater proportion of air-containing tissue. They have usually presented pale, nonresilient emphysematous patches interspersed with dark red, firm and slightly depressed areas which were to be felt as irregular consolidations extending to various depths into the lung substance. Section of the lung through the lower lobes usually displayed an exceedingly moist cut surface, the slightest pressure forcing to the surface quantities of blood-tinged fluid. This may exist to such a degree as to obscure the underlying process. Again, the confluence of separate patches of consolidation may be so complete as to be confusing, but careful study has usually made evident the bronchial distribution of the process. As a general occurrence, however, patchy areas of consolidation clustered about the bronchi were easily

made out. Mucopurulent plugs filled the bronchi and bronchioles. Section of the remaining lobes showed a much drier lesion. Here islands of dark red, often hemorrhagic, consolidated lung showed against a paler background of nonelastic emphysematous pulmonary tissue.

Only one case of lobar pneumonia has occurred. This was caused by a Type I pneumococcus. It appeared during the first days of the epidemic, and its occurrence was undoubtedly fortuitous. Four cases showed the changes of an interstitial bronchopneumonia. Here the white, thickened, pus-filled bronchioles surrounded by hemorrhagic, edematous or indurated areas of consolidation presented a very distinctive picture, entirely different from the great majority of the pneumonic processes seen.

Microscopically, a variety of pulmonary changes have been found, but nothing has been encountered beyond what one is accustomed to expect in bronchopneumonia. The accumulation of inflammatory cells may be patchy, or so massed as to present, in a limited number of sections, an appearance indistinguishable from lobar pneumonia. The exudate may be very dense or it may be thin; in either case edema and congestion have been marked, and so greatly compromised the remaining lung tissue. Polymorphonuclear leukocytes have, as a rule, greatly predominated in the exudate. In other sections, however, the presence of many mononuclear wandering cells and epithelial cells has been noted. Often great quantities of erythrocytes have been massed together in the air cells, sometimes presenting a very striking picture, especially when contiguous to the other air cells stuffed with the inflammatory exudate. Fibrin has not been a prominent part of the exudate except in one case. In a few cases, wide stretches of exudate appear from which all remains of alveolar walls have disappeared. In several such cases, focal areas of disintegration were in process, evidenced by poorly stained, fused masses of cellular débris in which many remains of destroyed nuclei appear. The terminal bronchioles usually contain the same type of exudate described in the alveoli. The mucous membrane is often separated off, and tangled fragments appear free in the exudate. Smears of the lungs usually showed enormous numbers of gram-positive diplo-

cocci. It was rare to find organisms arranged in chains. Microscopic study of the remaining organs has not led to any noteworthy disclosures. Seventy-four of the 123 cases of pneumonia examined post-mortem showed an associated pleurisy. Thirty-four were described as serofibrinous, twenty as serofibrino-purulent and twenty as fibrinous.

Strange as it may seem, there was no difference to be made out in the nature of the process caused by the streptococcus, pneumococcus or influenza bacillus. It was not difficult to distinguish Type III pneumococcus by the sticky exudate and the greater tendency toward confluence, but no matter what the infecting organism, each appeared to produce the same type of pulmonary lesion with equal facility.

Reference to Table 5 will show that there have been no particularly constant extrapulmonary complications. Nine cases have shown hemolytic jaundice, the majority of these appearing late in the epidemic. Four cases showed a massive interstitial emphysema, probably beginning in the multiple rupture of the emphysematous alveoli at the pulmonary hila. There were four cases of pneumococcus meningitis developing in the course of the disease, only two of which came to necropsy, however. There have been relatively few splenic tumors. A firm, congested organ not a great deal larger than normal has been the rule. Acute changes in other parenchymatous organs have been inconspicuous. Marked acute nephritis occurred only three times. Rupture of the rectus muscles was found in four instances. The bone marrow of the femur in all cases studied has appeared to gross examination pale and unreactive.

There has been a noticeable and instructive change in the course and manifestations of the disease in the last days of the epidemic. The leukopenia has disappeared in large measure, twenty of the last thirty-five leukocyte counts having averaged 20,000 cells per cubic millimeter. A far higher percentage of blood cultures show positive results. Of the total of eleven positive findings, seven have been obtained in the last eighty cultures. Synchronous with these changes, necropsy findings have shown older processes in the chest, more

fibrin and pus in the pleural cavities, collapsed lungs showing various stages of resolution and extension of the bronchopneumonia.

The average leukocyte count in the streptococcus pneumonias of last winter in this hospital was 17,000, and positive blood cultures were obtained in 13 per cent. of the cases. The duration of the present pneumonias to the time of death has been noticeably shorter

TABLE 5.—COMPLICATIONS OF ONE HUNDRED AND TWENTY-THREE CASES OF BRONCHOPNEUMONIA DISCLOSED AT NECROPSY

Pulmonary congestion and edema	98
Congestion of the spleen	71
Pleurisy	74
Serofibrinous	34
Serofibrinopurulent	20
Fibrinous	20
Cloudy swelling of the kidneys	21
Icterus	9
Lung abscess	5
Interstitial emphysema	4
Acute nephritis	3
Acute peritonitis	1
Meningitis, pneumococcus	2
Pericarditis, acute serofibrinous	3
Rupture of the rectus muscles	4
Cardiac dilatation	3
Cholecystitis	1
Abscesses of the kidneys	1
Myocarditis, acute	1
Abscess of the foot	1
Gastric ulcer	1
Status lymphaticus	1
Abscess of the right kidney	1
Congenital cystic kidneys	1
Pleural adhesions, marked	8
Pericarditis, chronic, adhesive	2
Cholelithiasis	1
Hydropericardium	1
Cirrhosis of the liver	1
Peritoneal adhesions	1
Endocarditis, chronic	1
Nephritis, chronic	1
Horseshoe kidney	1

than those studied last winter. There is possible significance in the fact that the few pneumonias of the present epidemic that presented a picture at necropsy most like those of last winter are those which have a period of longest illness, in this respect also corresponding to last winter's pneumonias.

In view of the high incidence of pneumonia in the Southern camps, the presence of large numbers of carriers of intestinal parasites has been suggested as possibly a predisposing factor. In search of such factors in the development of pneumonia in the recent Custer epidemic, the incidence of intestinal parasites was investigated. Out of 150 stools of pneumonia patients

taken at random and examined, no ova or worms were found. Previous to the outbreak of influenza, a survey of several thousand Southern troops stationed at this camp showed intestinal parasites in 3 per cent. of the cases studied.

To determine the pathogenicity for laboratory animals of various strains of hemolytic and nonhemolytic streptococci recovered at necropsy, mice, rabbits and rats have been inoculated. Of thirty-three inoculated mice, twenty-two died within twenty-four hours, the original organism being recovered postmortem in each instance. Hemolytic and nonhemolytic streptococci were equally fatal. Fourteen rabbits and twelve rats were injected intravenously and subcutaneously with hemolytic streptococci. With the exception of one rabbit and one rat, both of which died of a rapid septicemia, complicated in the case of the rabbit by bronchopneumonia, all of these animals are still living.

SUMMARY

The patient is attacked by a severe acute infection of unknown etiology. In the prepneumonia stage the principal objective signs are those of a marked mucopurulent bronchitis, with high temperature, generalized pains, prostration and a leukopenia. If the process advances, the peribronchial lung tissue is quickly involved by direct extension. A massive bronchopneumonia, in many cases accompanied by acute pulmonary congestion and edema, rapidly develops, which as quickly resolves or goes on to an early termination. The marked leukopenias are probably only one phase of a general overpowering of the defensive forces of the organism. The rarity of concurrent septicemias is doubtless explained by the rapid course of the disease and the mode of origin from the bronchi. The influenza bacillus has played a minor rôle in the production of bronchopneumonia. The infective cause of the antecedent respiratory infection remains undetermined.