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# EPIDEMIC OF ACUTE RESPIRATORY DISEASE ASSOCIATED WITH ATYPICAL PNEUMONIA

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(From the Minnesota State Department of Health)

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Recently, the concept has developed that atypical pneumonia is merely an incident in what is usually a mild epidemic disease of the respiratory tract (1 to 6). A group of workers (3) summarize this idea:

"There is thus no sharp dividing line, other than roentgen evidence . . . to differentiate cases of atypical pneumonia from cases of acute bronchitis resembling atypical pneumonia and from cases of other illness of the respiratory tract. . . . It seems probable that at least some of these minor illnesses may be milder infections of the same specific nature as atypical pneumonia. Proof of such a hypothesis depends on the demonstration of the causative agent."

Although numerous clinical and epidemiological descriptions (7 to 20) of the disease have appeared, etiological studies have been largely disappointing. A few of the cases, especially the more severe ones, have been demonstrated to be caused by ornithosis (21) and related agents, "Q" Fever (22) and lymphocytic choriomeningitis (23) but it was recently concluded that "a

virus responsible for a large proportion of the cases of so-called virus pneumonia has not been satisfactorily established (24)."

The present communication deals with an explosive outbreak of respiratory disease, associated with atypical pneumonia, the etiology of which has been indicated to be the virus described by certain investigators (25).

The epidemic started in the only grade school of Kasson, a town in southeastern Minnesota, the population of which in 1940 was 1,230 people and spread into households of the school children. There were a total of 191 cases.

Table I shows the symptomatology of the disease, with cases divided arbitrarily into 3 groups: "severe," those with fever and bed-rest of more than 3 days; "moderate," those with fever and bed-rest of 3 days or less; and "mild," those without fever or whose temperature was not taken and bed-rest of 3 days or less. The "severe" cases of this outbreak would actually correspond to a fairly mild form of the disease as commonly described; none were hospitalized and only 29 per cent of the "severe" cases were in bed longer than 2 weeks, none longer than 3 weeks.

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TABLE I  
*Symptomatology*

	"Severe" cases		"Moderate" cases		"Mild" cases		Total cases	
	<i>number</i>	<i>per cent</i>	<i>number</i>	<i>per cent</i>	<i>number</i>	<i>per cent</i>	<i>number</i>	<i>per cent</i>
No. of cases	31	100	47	100	113	100	191	100
Fever	31	100	47	100			78	41
Cough	31	100	37	79	74	65	142	74
Headache	25	81	21	45	14	12	60	31
Chest signs*	12	39					12	6
Sore throat	1	3	10	21	17	15	28	15
Coryza	1	3	12	26	54	42	67	35
Chest pain	2	6	1	2	1	1	4	2
Chilliness	6	19	3	6	1	1	10	5
G.I. symptoms	7	23	6	13	5	4	18	9
Days in bed								
1 to 3			28	60	9	8	37	19
4 to 7	12	39					12	6
8 to 14	10	32					10	5
15 to 21	9	29					9	5

\* Only 26 patients examined during the acute stage of the illness.

Of the 191 cases, 26 received chest examinations by a physician during the acute stage of the illness, these being the more seriously affected. Râles or dullness was noted in 12 of the 26 patients examined. The remainder of the cases did not of their own initiative consult a physician, usually because of the mildness of the symptoms. Information concerning these was gathered through interview of the children and their parents during the acute stage or within a few days thereafter by a public health physician and public health nurses. Only 7 of the more severe cases were examined by x-ray, usually during early convalescence, and evidence of pneumonia was present in 5.

TABLE II  
*Attack rate in grade school*

	Number in room	Number ill	Attack rate  <i>per cent</i>
First	23	9	39
Second	19	11	58
Third	19	10	53
Fourth and fifth	35	30	86
Fifth and sixth	36	22	61
Seventh	29	17	59
Eighth	25	18	72
<b>Totals</b>	<b>186</b>	<b>117</b>	<b>63</b>

Cough was the most common symptom, being present in 74 per cent of all cases; it was hacking in nature with little or no sputum and almost always persisted even in mild cases for 10 days or longer. This characteristic, persistent cough, to-

gether with the relative infrequency of coryza, served in general to distinguish the "mild" cases of the outbreak clinically from the common cold and to identify them with the more severe cases. It will be noted that the incidence of coryza and sore throat was somewhat higher in the milder cases than in the severe, and the incidence of cough lower. Some of these milder cases may have been common colds or minor bacterial infections. However, no dividing line would be found clinically or temporally between the mild and severe cases of the epidemic.

The attack rates in the various rooms of the grade school are given in Table II. Of the 186 pupils in the school, 117 or 63 per cent were affected. The attack rates in the different rooms ranged from 39 to 86 per cent.

Household occurrence of the disease, by age groups, is shown in Tables III and IV. In the 94 households affected there were 329 persons exposed to secondary attack, considering the first case in each household as the primary attack. Ninety-seven or 29 per cent of the 329 persons exposed in households contracted the disease. However, most of these (56 of the 97) who did become ill were in the age group 5 to 14 years so that they were also exposed in school. Only 41 cases occurred among the 230 persons who were exposed in households but not in the school, giving a corrected secondary household attack rate of 18 per cent, to be compared with an attack rate of 63 per cent in the school. This difference may have been due to an age factor in

TABLE III  
*Age and sex distribution in primary and secondary cases*

		Age years					Totals	
		0 to 4	5 to 9	10 to 14	15 to 19	20 or more		?Age
Primary cases:	Males	1	15	24	4	2	0	46
	Females	2	13	21	2	10	0	48
	<b>Totals</b>	<b>3</b>	<b>28</b>	<b>45</b>	<b>6</b>	<b>12</b>	<b>0</b>	<b>94</b>
Secondary cases:	Males	3	13	13	2	9	0	40
	Females	7	12	18	4	16	0	57
	<b>Totals</b>	<b>10</b>	<b>25</b>	<b>31</b>	<b>6</b>	<b>25</b>	<b>0</b>	<b>97</b>
Total cases:	Males	4	28	37	6	11	0	86
	Females	9	25	39	6	26	0	105
	<b>Totals</b>	<b>13</b>	<b>53</b>	<b>76</b>	<b>12</b>	<b>37</b>	<b>0</b>	<b>191</b>

TABLE IV  
Secondary household attack rate\*

		Age					
		0 to 4	5 to 9	10 to 14	15 to 19	20 or more	?Age
Males	Number exposed	8	17	22	9	93	8
	Number of cases	3	13	13	2	9	0
	Attack rate (A.R.)	38	76	59	22	10	0
Females	Number exposed	12	17	30	18	90	5
	Number of cases	7	12	18	4	16	0
	Attack rate (A.R.)	58	71	60	22	18	0
Totals	Number exposed	20	34	52	27	183	13
	Number of cases	10	25	31	6	25	0
	Attack rate (A.R.)	50	73	60	22	14	0

\* Higher rates in younger age groups, especially the 5 to 9 and 10 to 14 groups, may reflect spread within the school rather than differential age attack rates.

susceptibility or to some unknown factor favoring spread in the school.

Although dates of onset were found to extend from September 1 to November 2, 1942, as shown in Table V, over 90 per cent of the cases occurred from September 29 to October 26, and this latter probably represented the true epidemic period. Nearly half of the cases appeared during the week October 6 to 12. The outbreak may thus be said to have been explosive. In this respect, it differs from most of the epidemics which have been noted to extend over several months. One experience described (19) bears a close similarity to the present one.

The disease occurred indiscriminately among users of the one pasteurized milk supply, one public raw milk supply, and several private raw milk supplies, thereby eliminating milk from consideration as a possible source of infection. Water was excluded on similar grounds. Pigeons abounded in the school house and other nearby buildings. Investigation disclosed pigeons' droppings in the openings of the ventilating ducts into the school rooms, and 1 dead pigeon was found in the ventilating system. It was also stated that

live pigeons occasionally came through the ventilating system into the school rooms. In view of these facts, ornithosis was considered a possible etiology. Further investigation (detailed below) did not substantiate this hypothesis. The behavior of the disease in the households definitely suggested a respiratory mode of spread. The incubation period, estimated from the secondary occurrence in the household-exposed but non-school-exposed group, was from 8 to 21 days.

Throat washings taken early in the course of the disease from several typical cases were inocu-

TABLE V  
Dates of onset

Dates	Number of cases	Per cent of cases
September 1 to 7, 1942	2	1.2
September 8 to 14, 1942	1	0.6
September 15 to 21, 1942	3	1.8
September 22 to 28, 1942	5	3.0
September 29 to Oct. 5, 1942	28	16.6
October 6 to 12, 1942	79	46.6
October 13 to 19, 1942	32	18.9
October 20 to 26, 1942	16	9.5
October 27 to Nov. 2, 1942	3	1.8
Total	169	100.0
Date not stated	22	
Grand total	191	

lated<sup>2</sup> into mice. Pulmonary lesions occurred and some deaths after a few passages, but the responsible agent could not be differentiated from mouse pneumonia virus of Horsfall. It was not considered as having any etiological relation to the cases. Ten pairs of blood specimens showed no significant rise in titer between the acute-phase and convalescent specimens against influenza A (PR-8 strain) or influenza B (Lee strain).

The epidemiological evidence suggested ornithosis. Four pairs of blood specimens were submitted to Dr. K. F. Meyer, Hooper Foundation for Medical Research, San Francisco, California who reported that the complement-fixation test showed no increase in antibodies against psittacosis antigen. Ornithosis virus was isolated<sup>3</sup> from the organs of 10 out of 35 pigeons captured at the school. However, no real connection between the

<sup>2</sup> This work was carried out at the Rockefeller Influenza Laboratory, Division of Preventable Diseases, Minnesota Department of Health, under the direction of Dr. Carl Eklund.

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human disease and the pigeon virus could be established. The fact that this virus can ordinarily be isolated from throat washings of patients and established in mice suggests that the epidemic was not due to ornithosis. Also if the epidemic had been due to ornithosis, a higher proportion of severe cases would have been expected.

Recently, a group of workers (25) have described a virus which they isolated from cases of atypical pneumonia. Specimens of sera which have been saved from cases of the Kasson epidemic were submitted to Dr. Monroe D. Eaton for neutralization test with the new virus. He reports that specimens of the sera showed a significant rise in antibody titer as shown in Table VI. Paired serum specimens from 7 cases were tested. In 5 of these cases a 4-fold increase in antibodies was demonstrated. In one case (P. S.) a 2-fold increase was found, and in the remaining case (J. B.) titers of both the acute-phase and convalescent serum specimens were above 64, suggesting recent infection with the virus of atypical pneumonia. Most of these cases were among the "severe" cases of the epidemic but were not severe in comparison with the usual accounts of the

TABLE VI  
Neutralization tests with the virus of atypical pneumonia  
(strain De, amniotic passage)

Patient	Sex	Age	Date of onset	Date of specimen	Serum dilutions*				Horse serum control**	Normal amniotic***	Test animal
					1:4	1:8	1:16	1:64			
B. B.	M	11	10/ 8/42	10/10/42 10/22/42	3/4	2/3 0/3	0/3		5/7	0/7	C.R.† C.R.
J. B.	F	35	10/20/42	10/23/42 11/17/42	0/4 0/4		0/4 0/4	0/4 0/4	2/4	0/4	C.R. C.R.
D. K.	F	9	10/10/42	10/12/42 11/ 3/42	2/2 0/3	2/3	0/6	0/3	3/6	0/3	C.R. C.R.
J. A.	M	14	10/ 7/42	10/10/42 12/ 7/42	3/4 0/4		0/4		3/4	0/4	C.R. C.R.
R. E.	M	13	10/11/42	10/12/42 11/ 3/42	2/4 0/4		2/3 0/4		2/4	0/4	C.R. C.R.
E. S.	M	35	11/ 1/42	11/ 3/42 11/17/42	2/4 0/4	0/4	2/4		7/8	0/8	H.‡ H.
P. S.	F	11	10/11/42	10/12/42 11/ 3/42	4/4 0/4	2/4	4/4				H. H.
J. W.	M	10	10/ 6/42	10/10/42 11/ 3/42	3/4 0/4		0/4		3/4	0/4	H. H.

\* Numerator of fraction = number of animals with pulmonary lesions; denominator = number of animals tested.

\*\* Control for virus activity.

\*\*\* Control for intercurrent respiratory infection in animals.

† C.R. = Cotton rat.

‡ H. = Hamster.

disease. Although no sera from the extremely mild cases (those who were not in bed at all) were tested, it seems reasonable to assume from the clinical and temporal similarity of the cases that only one agent was involved in the outbreak.

## DISCUSSION

The neutralization test thus indicates that the virus described by a group of investigators (25) was responsible for the Kasson epidemic. Further study of the virus should elucidate its relationship to that group of cases among the minor respiratory diseases characterized by a lingering cough.

Present evidence suggests that a disease entity is being established as a segment of the common respiratory diseases to take its place along side the common cold and influenza. As was pointed out as early as 1940 (1), the disease is probably not primarily a pneumonia, nor in view of the work accomplished (25) can it any longer be said that its etiology is unknown. The designation "atypical pneumonia" seems to exaggerate what is probably only an incident in the disease. Before this concept can be considered established, it will be necessary to isolate the virus from cases in which thorough clinical study excludes pneumonia, demonstrate its etiological relationship to the cases by neutralization test, and finally show its correspondence to virus isolated from cases with atypical pneumonia.

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