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Author(s): Maxwell Finland and Mildred W. Barnes

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## Changing Ecology of Acute Bacterial Empyema: Occurrence and Mortality at Boston City Hospital during 12 Selected Years from 1935 to 1972

Maxwell Finland and Mildred W. Barnes

*From the Channing Laboratory (Epidemiology Unit),  
Thorndike Memorial Laboratory of the Harvard Medical  
Unit, and Laboratory for Infectious Diseases, Boston  
City Hospital; and the Department of Medicine, Harvard  
Medical School, Boston, Massachusetts*

The occurrence, etiology, and demography of acute bacterial empyema are presented to reflect the widespread use of sulfonamides, penicillin, and other active antibiotics. In community-acquired (C-A) cases *Streptococcus pneumoniae*, hemolytic streptococci, and *Staphylococcus aureus* were the most frequent single organisms identified in initial positive cultures of pleural fluid during 1935. *S. pneumoniae* declined steadily until 1953 but continued to occur frequently in C-A cases. Hemolytic streptococci became infrequent. *S. aureus* increased and became the most frequent organism in 1955 and declined to original levels after 1965 while gram-negative rods increased. *S. aureus*, aerobic gram-negative rods, and enterococci were most frequent in originally mixed infections, hospital-acquired cases, and superinfections. Anaerobes with or without aerobes were mostly seen in C-A cases and did not vary in incidence. Mortality increased with age. Overall mortality was greater during the 10 antibiotic years, associated with a marked decrease in the proportion of patients younger than 50 years and increase in those over 60 years old, and was greater in patients with serious underlying diseases subjected to more complicated surgical procedures.

In previous papers we presented data on the changes that have occurred during the antimicrobial era in the etiologic bacterial agents identified at the Boston City Hospital in patients with bacteremic infections [1], bacterial endocarditis [2], acute bacterial meningitis [3], and in the specific capsular types of *Streptococcus pneumoniae* isolated from various infections [4]. This paper deals with the changing etiology and some other features of 671 cases of acute bacterial empyema of the pleura observed at the Boston City Hospital during 12 selected years between 1935 and 1972; these years were chosen to represent the periods before and after the introduction and widespread clinical use of the succession of major antibacterial agents [1]. An earlier report by

Nowak [5] presented an analysis of 500 consecutive cases of empyema thoracis occurring in children and adults at the same hospital over a period of seven years, from 1932 to 1939. In a separate report, Strieder and Lynch [6] reviewed 90 cases of putrid empyema observed at this hospital from June 1934 to January 1941.

### Materials and Methods

The data presented in this paper are based on the hospital records of all patients admitted to the Boston City Hospital, during each of the 12 selected years, from whom a bacterial pathogen was identified in purulent pleural fluid obtained by thoracentesis, at operation, or at autopsy. The bacteriological examinations were carried out by standard methods in the Microbiology Laboratory of the hospital under the direction of Marion E. Lamb during the early years, and subsequently under the supervision of A. Kathleen Daly and Alice McDonald. Anaerobic and microaerophilic organisms were identified over the entire period but were not fully speciated.

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Please address requests for reprints to Dr. Maxwell Finland, Boston City Hospital, Boston, Massachusetts 02118.

Infections in the patients were classified as community-acquired (C-A) if the presence of empyema was recognized at the time of admission to the hospital or if the empyema was a complication of a bronchopulmonary infection that was present at that time. If the empyema was a complication of a pulmonary or bronchial infection that developed in the hospital or if the empyema occurred in a patient admitted to the hospital for trauma to the chest or followed cardiac or thoracic surgery, the empyema was classified as hospital-acquired (H-A). Only the demographic data, bacteriologic findings, and outcome were analyzed without reference to the type of medical therapy or surgical intervention.

**Results**

*Occurrence and mortality.* The total number of cases of empyema each year (table 1) at Boston City Hospital declined sharply during the first four selected years (1935-1951) associat-

ed with the successive introduction and wide use first of the sulfonamides, then of penicillin and streptomycin, followed by chlortetracycline, chloramphenicol, and polymyxin. The drop in the total number of cases each year was paralleled by, and was primarily accounted for by, a similar drop in numbers of C-A cases. No substantial change in the number of H-A cases occurred during this interval.

Over the last eight selected years the total number of cases each year fluctuated irregularly between 34 and 59. The number of C-A cases also varied irregularly but with a declining trend in the last four selected years, from 32 in 1963 to 15 in 1972. Over the last eight selected years, the number of H-A cases varied more widely and irregularly with a low of six in 1957 and a high of 34 in 1965.

The proportion of cases that were H-A increased more or less steadily in the selected years from 1935 (14.4%) to 1955 (57.8%). There was an unusually low proportion of H-A cases (17.6%)

**Table 1.** Occurrence of and mortality rate due to pleural empyema at Boston City Hospital during 12 selected years between 1935 and 1972.

Year	No. of cases (no. of deaths)			Percentage of total cases that were H-A	Mortality rate (%)		All cases	No. of cases/1,000 admissions	No. of deaths/100 hospital deaths
	C-A	H-A	Total		C-A	H-A			
1935	107 (39)	18 (9)	125 (48)	14.4	36	50	38.4	3.18	1.75
1941	75 (26)	19 (14)	94 (40)	20.2	35	74*	42.6	2.18	1.45
1947	40 (12)	23 (10)	63 (22)	36.5	30	44	34.9	1.64	0.76
1951	20 (12)	13 (6)	33 (18)	39.4	60	46	54.5	0.84	0.67
1953	23 (16)	14 (9)	37 (25)	37.8	70	64	67.6	0.98	0.57
1955	19 (7)	26 (16)	45 (23)	57.8	37	62	51.1	1.29	0.92
1957	28 (11)	6 (4)	34 (15)	17.6	39	67	44.1	1.04	0.66
1961	21 (15)	29 (11)	50 (26)	58.0	71	38†	52.0	1.52	1.25
1963	32 (10)	23 (11)	55 (21)	41.8	31	48	38.2	1.67	1.02
1965	25 (11)	34 (18)	59 (29)	57.6	44	53	49.2	1.80	1.46
1969	18 (6)	19 (11)	37 (17)	51.4	33	58	45.9	1.45	1.23
1972	15 (5)	24 (18)	39 (23)	61.5	33	75‡	59.0	1.85	2.16
Total (12 years)	423 (170)	248 (137)	671 (307)	37.0	40.2	55.2§	45.8	1.63	1.14
Subtotal (1935 + 1941)	182 (65)	37 (23)	219 (88)	16.9	35.7	62.2‡	40.2	2.66	1.62
Subtotal (1947-1972)	241 (105)	211 (114)	452 (219)	46.7*	43.6	54.0†	48.5†	1.51	1.01§

NOTE. C-A = community-acquired; H-A = hospital-acquired.

\*P < 0.01.

†P < 0.05.

‡P < 0.02.

§P < 0.001.

||P < 0.0001.

in 1957, but after that H-A cases constituted between 42% and 62% of all cases.

**Incidence of empyema.** In a previous paper [1] we noted that the total number of admissions to this hospital for all causes dropped steadily from a high of >43,000 in 1941 to slightly over 21,000 in 1972, with the greatest drop occurring after 1965. To adjust for these changes, the incidence or rate of occurrence of cases of empyema, expressed as cases per 1,000 admissions for all cases, is shown for each of the 12 years in the next to last column of table 1 and in the upper panel of figure 1. The figure shows a sharp and steady drop in rate from 3.18 cases per 1,000 admissions in 1935 to 0.84 in 1951. After that year there was an irregular rise to a high of 1.85 in

1972. The mean rate for the 12 years was 1.63 cases of empyema per 1,000 hospital admissions.

**Mortality.** The case-fatality ratio (CFR) for all cases fluctuated irregularly over the 12 selected years (figure 1, lower panel), with a low of 35% in 1947 and a high of 68% in 1953 (mean, 46% for the 12 years). In nine of the 12 selected years, the CFR was higher in H-A than in C-A cases, but the differences were statistically significant for only two of those nine years. In three of the years, the mortality was higher in C-A cases, and the difference was significant in one of those years (1961). The average CFR for the 12 years was significantly higher for H-A cases (55.2%) than for the C-A cases (40.2%) ( $P < 0.001$ ).

In our earlier paper [1] it was also noted that the CFR for all patients admitted to the hospital during the 12 selected years fluctuated between 6.2% and 7.6% through 1953 but subsequently showed a steady decline from 7.2% in 1955 to 5.0% in 1972. The last column in table 1 and the upper panel of figure 1 show the proportion of all deaths at Boston City Hospital that were associated with pleural empyema. The number of deaths of patients with empyema per 100 deaths from all causes declined steadily from 1.75 in 1935 to 0.57 in 1953 and varied in subsequent years between 0.66 and 1.46 until 1969 but was 2.16 in 1972 (mean, 1.14 for the 12 years).

**Comparison of occurrence of empyema and mortality before and after the general use of penicillin and other antibiotics.** The last two lines in table 1 show this comparison. The data indicate that (1) the proportion of cases of empyema that were H-A was significantly higher in the 10 years when antibiotics were available (46.7%) than in the two earlier years (16.9%) ( $P < 0.01$ ); (2) the CFR in H-A cases was higher than that in the C-A cases both before ( $P < 0.02$ ) and after ( $P < 0.05$ ) the antibiotics came into use; (3) although the mortality rate in all cases was higher during the 10 years antibiotics were used (48.5%) than in the two years before this time (40.2%) ( $P = 0.05$ ), neither the difference in mortality between the two periods in C-A cases ( $\chi^2 = 2.3$ ) nor that in H-A cases ( $\chi^2 = 0.55$ ) was significant; (4) the incidence of empyema at Boston City Hospital, expressed in cases per 1,000 admissions (figure 1), was much lower during the anti-

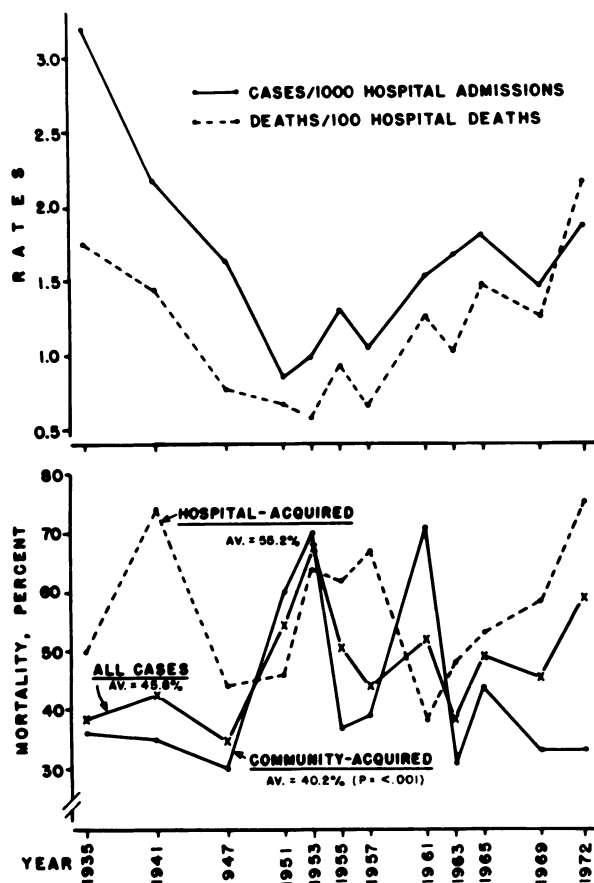


Figure 1. Acute bacterial empyema at Boston City Hospital during 12 selected years from 1930 to 1972. Cases per 1,000 hospital admissions and deaths per 100 deaths at the hospital (top) and case-fatality ratios in community-acquired, hospital-acquired, and all cases (bottom) are shown.

biotic years than in the earlier years ( $P < 0.001$ ); and (5) the number of deaths in patients with empyema per 100 deaths in patients at the hospital with all conditions was also significantly lower during the years when antibiotics were in use ( $P < 0.001$ ).

**Bacteriological findings. Initial positive culture of pleural fluid.** A single pathogen was identified from 473 patients (70.5%), and more than one species (mixed infection) were found in the other 198 patients (table 2). The order of frequency of the occurrence of the various pathogens differed in these two groups of cases and also in the C-A and H-A cases within each group.

**Cases with single organisms.** In cases with single organisms in the initial positive culture, the most frequent pathogens were *S. pneumoniae* (37.7%), *Staphylococcus aureus* (29.2%), and hemolytic streptococci (nearly all group A) (7.8%). *Haemophilus influenzae* accounted for 3.0%, viridans streptococci for 3.4%, and enterococci for 1.5% of the cases. Among the gram-negative rods, *Klebsiella-Enterobacter*, *Escherichia coli*, and *Pseudomonas aeruginosa* were the most frequent; they accounted for 5.1%, 4.0%, and 2.1% of the cases, respectively. Single anaerobes were identified infrequently; an anaerobic (or microaerophilic) *Streptococcus* was identified as the only organism in 1.7% of the cases.

Among the cases with single organisms, only 2% of the cases in which *S. pneumoniae* was the only pathogen found in the initial positive fluid culture were H-A. Likewise, H-A cases constituted relatively small proportions of cases in which hemolytic streptococci (12%), anaerobic streptococci (13%), *H. influenzae* (21%), and viridans streptococci (25%) were found singly. On the other hand, 48% of the cases with *S. aureus* alone, and  $\cong 50\%$  of the cases in which enterococci, various gram-negative rods, and other organisms were identified were H-A.

The CFR in the 473 cases with a single organism was 40.2%; it was 37.3% in the C-A cases as compared with 47.1% in the H-A cases ( $\chi^2 = 3.5$ ).

**Cases of mixed infections.** In cases with more than one organism in the initial positive pleural fluid culture, the order of occurrence of the various pathogens was different than in those with

a single organism. The most frequent were hemolytic streptococci (17.4%), anaerobic streptococci (10.6%), *S. aureus* (10.2%), and fusiform bacilli (9.8%). Other organisms, in order of descending frequency of occurrence were enterococci, *E. coli*, *Klebsiella-Enterobacter*, *Proteus*, *P. aeruginosa*, and *Bacteroides* species; each accounted for 8.8%–4.6% of the organisms isolated initially from fluids with mixed infections. *H. influenzae* accounted for 3.1% and *Clostridium* for 2.9%.

A majority (>60%) of the strains of *S. pneumoniae*, hemolytic streptococci, and viridans streptococci among the aerobes, and of anaerobic streptococci, *Bacteroides*, and fusiform bacilli among the anaerobes in cases with initially mixed infections, were from C-A cases. On the other hand, the great majority of strains of enterococci, various aerobic gram-negative rods, and *S. aureus* identified in the original mixed cultures were from H-A cases. Of the 218 strains from originally mixed infections in C-A cases, 96 (44.0%) were from fatal cases. By comparison, 214 (70.6%) of the 303 strains from the initial mixed cultures of H-A cases were from fatal cases ( $P < 0.001$ ).

The CFR in the 198 patients in whom more than one bacterial pathogen was identified in the first positive culture of pleural fluid was 59.1% as compared with 40.2% in cases with a single organism ( $P < 0.001$ ).

**"Superinfections."** The number and percentage distribution of 207 additional isolates that were not identified in the initial positive cultures of pleural fluid but were yielded from subsequent specimens from 104 patients are listed in the last two columns in table 2. These "superinfections" were as frequent among C-A cases (15.4%) as among H-A cases (15.7%) and only slightly less frequent in those with a single organism in the initial positive fluid culture (14.6%) than in those with originally mixed cultures (17.7%). In 39 of the 104 cases, the empyema had been classified as H-A in the first instance, and in 22 (56%) of these 39, the initial fluid showed mixed growth. Among the 65 C-A cases with superinfection, only 13 (20%) had mixed growth in the initial positive fluid ( $P < 0.001$ ).

Forty of the 104 patients died; the initial pleural infection was C-A in 23 of the 40 and H-A in 17. The CFR in C-A cases with superinfection

**Table 2.** Bacteriology of pleural empyema at Boston City Hospital during 12 selected years between 1935 and 1972.

Organism	Initial positive culture of pleural fluid								"Super-infections"	
	Single organism				Mixed infections					
	C-A	H-A	Percent- age of all patients	Percent- age of all patients	C-A	H-A	Percent- age of all organ- isms	Percent- age of all organ- isms	No.	Percent- age of all organ- isms
<b>Aerobes</b>										
<i>Streptococcus pneumoniae</i>	175 (64)	4 (3)	2	37.7	9 (7)	4 (3)	31	2.5	2	1.0
Hemolytic streptococci (not group D, mostly group A)	33 (12)	4 (2)	12	7.8	19 (9)	11 (5)	37	17.4	18	8.7
Viridans streptococci*	12 (6)	4 (2)	25	3.4	24 (8)	19 (13)	36	8.3	11	5.3
Enterococci	1 (1)	6 (1)	71	1.5	5 (3)	41 (26)	89	8.8	14	6.8
<i>Staphylococcus aureus</i>	71 (21)	67† (27)	48	29.2	26‡ (11)	38 (25)	59	10.2	40	19.3
<i>Haemophilus influenzae</i>	11 (7)	3 (2)	21	3.0	10 (3)	6 (4)	38	3.1	5	2.4
<i>Escherichia coli</i>	6 (4)	13 (6)	68	4.0	8 (5)	36 (30)	82	8.4	18	8.7
<i>Klebsiella-Enterobacter</i>	9 (5)	15 (9)	58	5.1	10 (7)	29 (24)	74	7.5	19	9.2
<i>Proteus</i>	2	3 (3)	60	1.1	7 (5)	28 (24)	80	6.7	18	8.7
<i>Pseudomonas aeruginosa</i>	1	9 (6)	90	2.1	6 (2)	26 (18)	81	6.1	21	10.1
<i>Serratia marcescens</i>	1 (1)	1	50	0.4	0	1 (1)	...	0.2	1	0.5
<i>Herellea vaginicola</i> ( <i>Acinetobacter cal- coaceticus</i> )	0	3	100	0.6	1 (1)	3 (1)	75	0.8	6	2.9
<i>Candida</i>	0	3 (2)	100	0.6	1	3 (2)	75	0.8	5	2.4
Miscellaneous	1 (1)§	1 (1)¶	50	1.1	0	3# (2)	...	0.6	5**	2.4
<b>Anaerobes</b>										
Streptococci††	7 (1)	1 (1)	13	1.7	34 (10)	21 (12)	38	10.6	7	3.4
<i>Bacteroides</i>	3 (2)	0	100	0.6	16 (5)	8 (6)	33	4.6	6	2.9
Fusiform bacilli	2	1	67	0.6	36 (14)	15 (9)	29	9.8	6	2.9
Spirilla	0	0	...	...	1 (1)	1 (1)	50	0.4	0	...
<i>Clostridium</i>	0	0	...	...	5 (5)	10 (8)	67	2.9	5	2.4
No. of strains	335 (125)	138 (65)	29.2	...	218 (96)	303 (214)	58.2	...	207	100
Total C-A plus H-A	473 (190)	...	100	...	521 (310)	...	100	...	...	...
No. of patients	335 (125)	138 (65)	...	...	...	...	...	...	104	...
Total C-A plus H-A	473 (190)	[40.2% died]	...	...	198 (117)	...	...	...	...	...
					[59.1% died] ‡‡					

NOTE. C-A = community-acquired; H-A = hospital-acquired. Numbers in parentheses indicate fatal cases (single organism) or organisms from fatal cases (mixed infections). "Superinfections" indicate new organisms (not present in original positive culture of pleural fluid grown from subsequent specimens).

\*Includes  $\alpha$ -hemolytic and  $\gamma$  (nonhemolytic) streptococci.

†Includes three cases due to *Staphylococcus epidermidis*, one each in 1965, 1969, and 1972. All were H-A and all recovered.

‡Includes one strain of *S. epidermidis* from a recovered case in 1935.

§*Salmonella typhimurium* in 1947.

¶*Nocardia asteroides* in 1972.

#All *Providencia stuartii*.

\*\**P. stuartii*, three; unidentified gram-negative rod, two.

††Includes microaerophilic streptococci.

‡‡ $P < 0.001$ .

was 35%, whereas in H-A cases with superinfection, it was 44% ( $\chi^2 = 0.5$ ). However, within each category, the CFR was not significantly different in cases with superinfection as compared with those without superinfection.

The most frequent new organisms identified in the pleural fluids of the cases with superinfection (table 2) were *S. aureus* in 40 cases; *P. aeruginosa* in 21; *Klebsiella-Enterobacter* in 19; hemolytic streptococci, *E. coli*, and *Proteus*, each

in 18; enterococci in 14; and viridans streptococci in 11. Other organisms each occurred in one to seven cases (*S. pneumoniae* in only two).

*Changing etiology of acute bacterial empyema. Initial positive culture of pleural fluid.* The pathogens isolated from these initial cultures are listed in table 3. In 1935, *S. pneumoniae* was the most frequent single organism initially identified in cases of acute empyema, accounting for 46% of the cases; hemolytic streptococci ranked second (18%) and *S. aureus* third (9%). *H. influenzae* and various single gram-negative rods were each identified in 3% of the cases, and other single aerobic streptococci in only 2%. Multiple aerobic pathogens (mostly gram-negative rods and *S. aureus*) and various anaerobes, with or without aerobes, together accounted for 19% of the cases in 1935.

The proportion of cases with *S. pneumoniae* dropped sharply in 1941 and 1947, but in four of the last nine selected years, pneumococci alone still accounted for 24%-29% of cases, and in the other five years, 13%-16% of the initial diagnostic pleural fluids yielded only *S. pneumoniae*.

Hemolytic streptococci were infrequent or absent after 1935, but other aerobic streptococci were somewhat more frequent in some years. The proportion of cases with *H. influenzae* alone in the initial positive culture of pleural fluid was low (2%-6% in six of the years), and this organism was not identified in any of the cases during five of the selected years after 1951.

On the other hand, the proportion of cases in which only *S. aureus* was found in the first posi-

tive culture of pleural fluid increased after 1935. Although, curiously, there were no such cases at all during 1953, *S. aureus* was the most frequent organism (32%-49%) during each of the next three selected years (1955, 1957, and 1961), and it accounted for 12%-27% of all cases in six of the other seven years.

Various gram-negative rods in initial pleural fluids increased in frequency after 1941 and in five of the last 10 years constituted 11%-25% of all cases. More than one aerobic organism or anaerobes, with or without aerobes, in the initial diagnostic pleural fluid accounted for an average of 31.7% of all cases during the 12 selected years and for 65% of all cases in 1953.

Over the entire 12 selected years of this study, the rank order of the common pathogenic bacteria found in the 671 cases of pleural empyema was as follows: *S. pneumoniae*, *S. aureus*, mixed aerobes, anaerobes with or without aerobes, single gram-negative rods, hemolytic streptococci, other aerobic streptococci, and *H. influenzae*.

*Distribution of common pathogens in mixed infections.* This distribution is shown in table 4 for each year and for all 521 strains identified in the initial positive culture of pleural fluid of 198 patients. The rank order of the pathogens for the 12 selected years was: aerobic gram-negative rods, streptococci other than group A  $\beta$ -hemolytic streptococci (i.e., viridans streptococci and enterococci), anaerobic gram-negative bacilli (*Bacteroides* species and fusiform bacilli), *S. aureus*, anaerobic streptococci (including microaerophilic strains), hemolytic streptococci (group

**Table 3.** Changing distribution of bacterial pathogens identified in initial positive cultures of pleural fluid obtained from patients with empyema during 12 selected years between 1935 and 1972 at Boston City Hospital.

Organism(s) in first positive culture of pleural fluid	Year												All 12 years*
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972	
<i>Streptococcus pneumoniae</i>	46†	33	21	27	27	13	15	24	29	12	16	15	26.7
Hemolytic streptococci	18	2	2	3	0	0	6	2	4	5	5	3	5.5
Viridans streptococci and enterococci	2	9	6	3	0	4	3	2	5	0	0	0	3.4
<i>Staphylococcus aureus</i>	9	22	16	12	0	49	47	32	27	15	22	8	20.1
<i>Haemophilus influenzae</i>	3	2	2	6	0	0	3	0	4	0	5	0	2.1
Gram-negative rods	3	2	13	6	8	4	3	8	11	25	19	21	9.4
Mixed aerobes‡	6	15	29	18	38	18	3	16	13	14	14	31	16.1
Anaerobes with or without aerobes‡	13	15	13	24	27	11	21	16	7	24	16	13	15.6
Total no. of patients	125	94	63	33	37	45	34	50	55	59	37	39	671

\*Eight of the patients (1.2%) had other organisms.

†Data are percentages of patients.

‡For distribution of these organisms, see table 2.

**Table 4.** Distribution of pathogens in mixed infections identified in the first positive culture of pleural fluid of 198 patients with empyema during 12 selected years between 1935 and 1972 at Boston City Hospital.

Organism	Year												All 12 years
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972	
<i>Streptococcus pneumoniae</i>	2*	7	5	0	3	0	5	3	0	0	0	0	2.5
Hemolytic streptococci	13	17	3	8	0	3	0	3	4	7	0	0	5.8
Viridans streptococci and enterococci	13	16	26	24	23	25	11	8	14	13	6	16	17.1†
<i>Staphylococcus aureus</i>	9	19	13	11	10	19	16	22	11	9	6	2	12.1
<i>Haemophilus influenzae</i>	2	1	3	3	8	0	5	0	14	2	0	0	3.1
Gram-negative rods	13	17	31	23	28	34	16	31	29	31	56	63	30.3
Anaerobic gram-negative bacilli	34	17	8	16	11	16	21	11	11	16	9	7	14.2
Anaerobic streptococci	11	1	11	13	13	3	21	22	14	16	16	5	10.6
<i>Clostridium</i>	0	3	0	3	2	0	5	0	4	5	6	2	2.9
No. of strains	45	70	62	38	61	32	19	36	28	55	32	43	521‡

\*Data are percentages of strains.

†Viridans streptococci, 8.3%; enterococci, 8.8%.

‡Other organisms accounted for 1.3% of this total (seven strains).

A), *H. influenzae*, *Clostridium*, and *S. pneumoniae*. Particularly noteworthy is the paucity of pneumococci in the mixed infections; none were identified during six of the 12 selected years. Also notable is the increasing proportion of aerobic gram-negative rods during the last four selected years and the declining proportion of *S. aureus* during the same four years.

The numbers of different species of pathogens identified in the pleural fluids with mixed infections and superinfections are shown in table 5. In the latter category are listed only the new organisms not identified in the first positive culture. In the great majority (70%) of the patients, the initial culture yielded a single species, but in superinfections a single new organism was identified in 44%, and two or three species were identified in nearly half of all the cases. More

than three species were infrequent in both groups.

*Incidence and mortality by age and sex.* *Distribution by sex.* There was a great preponderance of males (61%–79%) in each of the 12 years, averaging 69% for all 671 patients (table 6 and figure 2). This predominance of males was seen for patients of each age group except those less than 10 years old, but it was most striking in the patients 30–69 year old (75%–81% males).

*Mortality by sex and age.* The CFR was slightly, but not significantly, greater among females in most age groups and in all cases combined. The CFR was high (28%) in patients under 10 years old; it was lowest (16%) in those 10–29 years old and then increased with age to 75% in patients 70 years of age or older. These trends are represented graphically in the left pan-

**Table 5.** Number of bacterial species identified in pleural fluids of patients with empyema at Boston City Hospital during 12 selected years between 1935 and 1972.

No. of species	Initial positive culture		Superinfections*	
	No. of patients (%)	No. of strains in mixed infections (%)	No. of patients (%)	No. of strains (%)
1	473 (70.3)		46 (44.2)	46 (22.2)
2	110 (16.7)	220 (42.4)	23 (22.1)	46 (22.2)
3	56 (8.3)	168 (32.2)	28 (26.9)	84 (40.6)
4	27 (3.9)	108 (20.7)	4 (3.8)	16 (7.7)
5	5 (0.8)	25 (4.8)	3 (2.9)	15 (7.2)
Total	671 (100)	521 (100)	104 (100)	207 (100)

\*Additional species identified in cultures of fluid obtained after the initial positive one.

**Table 6.** Distribution of cases and mortality rates due to pleural empyema by age and sex at Boston City Hospital during 12 selected years between 1935 and 1972.

Year	Age group (years)										All		Percentage				CFR (%)			
	<10		10-29		30-49		50-69		≥70		M	F	M	M	F	M	F	M	F	All
	M	F	M	F	M	F	M	F	M	F	M	F	M	M	F	M	M	F	All	
1935	13 <sup>1</sup>	15 <sup>5</sup>	17 <sup>3</sup>	13 <sup>4</sup>	26 <sup>13</sup>	11 <sup>3</sup>	21 <sup>11</sup>	2 <sup>2</sup>	3 <sup>3</sup>	4 <sup>3</sup>	80 <sup>31</sup>	45 <sup>17</sup>	64	39	38	38.4				
1941	3	10 <sup>5</sup>	11	9 <sup>1</sup>	19 <sup>10</sup>	7 <sup>4</sup>	21 <sup>11</sup>	3 <sup>1</sup>	4 <sup>4</sup>	7 <sup>4</sup>	58 <sup>25</sup>	36 <sup>15</sup>	61	43	42	42.6				
1947	0	4 <sup>3</sup>	4	5	15 <sup>4</sup>	3 <sup>1</sup>	18 <sup>4</sup>	5 <sup>4</sup>	7 <sup>4</sup>	2 <sup>2</sup>	44 <sup>12</sup>	19 <sup>10</sup>	70	27	53	34.9				
1951	1	0	1 <sup>1</sup>	0	4 <sup>2</sup>	3 <sup>2</sup>	16 <sup>7</sup>	10	4 <sup>3</sup>	3 <sup>3</sup>	26 <sup>13</sup>	7 <sup>5</sup>	79	50	71	54.5				
1953	0	0	1	0	6 <sup>3</sup>	5 <sup>3</sup>	13 <sup>9</sup>	2 <sup>1</sup>	8 <sup>7</sup>	2 <sup>2</sup>	28 <sup>19</sup>	9 <sup>6</sup>	76	68	67	67.6				
1955	3 <sup>1</sup>	0	0	3	11 <sup>4</sup>	3 <sup>1</sup>	11 <sup>7</sup>	6 <sup>3</sup>	6 <sup>5</sup>	2 <sup>2</sup>	31 <sup>17</sup>	14 <sup>6</sup>	69	55	43	52.3				
1957	7 <sup>2</sup>	1	2	2	4 <sup>1</sup>	1 <sup>1</sup>	6 <sup>2</sup>	4 <sup>2</sup>	5 <sup>5</sup>	2 <sup>2</sup>	24 <sup>10</sup>	10 <sup>5</sup>	71	42	50	44.1				
1961	1 <sup>1</sup>	1 <sup>1</sup>	2	1	8 <sup>4</sup>	2 <sup>2</sup>	18 <sup>9</sup>	4 <sup>3</sup>	8 <sup>3</sup>	5 <sup>3</sup>	37 <sup>17</sup>	13 <sup>9</sup>	74	46	69	52.0				
1963	2 <sup>1</sup>	6	5	1 <sup>1</sup>	6 <sup>3</sup>	3	14 <sup>5</sup>	6 <sup>3</sup>	8 <sup>6</sup>	4 <sup>2</sup>	35 <sup>15</sup>	20 <sup>6</sup>	64	43	30	38.2				
1965	5 <sup>1</sup>	1	5 <sup>1</sup>	2 <sup>2</sup>	9 <sup>4</sup>	0	20 <sup>7</sup>	5 <sup>5</sup>	3 <sup>2</sup>	9 <sup>7</sup>	42 <sup>15</sup>	17 <sup>14</sup>	71	36	82	49.2				
1969	0	1	1 <sup>1</sup>	2	8 <sup>3</sup>	1 <sup>1</sup>	13 <sup>6</sup>	3 <sup>2</sup>	1	7 <sup>4</sup>	23 <sup>10</sup>	14 <sup>7</sup>	62	43	50	45.9				
1972	1	0	3 <sup>1</sup>	2	4 <sup>3</sup>	1 <sup>1</sup>	17 <sup>10</sup>	3	7 <sup>7</sup>	1 <sup>1</sup>	32 <sup>21</sup>	7 <sup>2</sup>	82	66	29	59.0				
All 12 years	36 <sup>7</sup>	39 <sup>14</sup>	52 <sup>7</sup>	40 <sup>8</sup>	120 <sup>54</sup>	40 <sup>19</sup>	188 <sup>88</sup>	44 <sup>26</sup>	64 <sup>49</sup>	48 <sup>35</sup>	460 <sup>205</sup>	211 <sup>102</sup>	69	44.6	48.3	45.8				
Percentage of males	48*		57		75		82		57		69*									
Percentage of all patients	7.8	18.5	11.3	19.0	26.1	19.0	40.9	30.9	13.9	22.7	100	100								
	(11.2)†		(13.7)		(23.8)		(34.6)		(16.7)		(100)									
CFR (%)	19	36	13	20	45	48	47	59	77	73	44.6	48.3								
	(28)†		(16)		(46)		(49)		(75)		(45.8)									

NOTE. M = males; F = females; CFR = case-fatality ratio. Superscripts indicate deaths.

\*P < 0.001.

†Percentage of males and females combined for each age group.

el of figure 2. The overall mortality in the 671 patients was 45.8%: 44.6% in males and 48.3% in females.

*Comparisons of distribution and mortality by age before and after the wide use of antibiotics.* These comparisons are shown in table 7 and in the right panel of figure 2. The CFR was essentially the same for each age group in 1935 and 1941, the two selected years before the introduction of penicillin, and in the subsequent 10 selected years from 1947 to 1972. However, the distribution by age was strikingly different in the two periods; the proportion of patients in the three youngest age groups (through 49 years) was much greater in the two prepenicillin years, whereas in the last 10 selected years, ~62% of the patients were older than 50 years.

*Comparisons of incidence and mortality by age from 1932 to 1939.* Data for 500 cases of acute empyema in those seven years, as reported by Nowak [5], and arranged to correspond to the age groups shown in tables 6 and 7, are given in

table 8. The overall mortality in these seven years was similar to that for 1935 and 1941. However, in patients younger than 10 years, the proportions of cases (32.4%) and deaths (18.2%) were higher than for the years 1935 and 1941 (18.7% of cases and 12.5% of deaths). The reverse was true for patients 70 years of age or older, who constituted 5.2% of cases and 12.4% of the deaths in Nowak's series, as compared with 8.2% and 15.9%, respectively, in 1935 and 1941 in the present study. The overall mortality in Nowak's series was 41.8%, whereas it was 48.5% for the 10 selected years from 1947 to 1972 in this study (P < 0.05).

*Age distribution and mortality for empyema in children younger than 10 years.* One-half of the 75 patients with empyema in the first decade of life were younger than two years of age. The mortality was 50% in infants, 22% in children one to two years old, and 13% in the older children (table 9). More than half of the cases and of the deaths occurred in the two prepenicillin

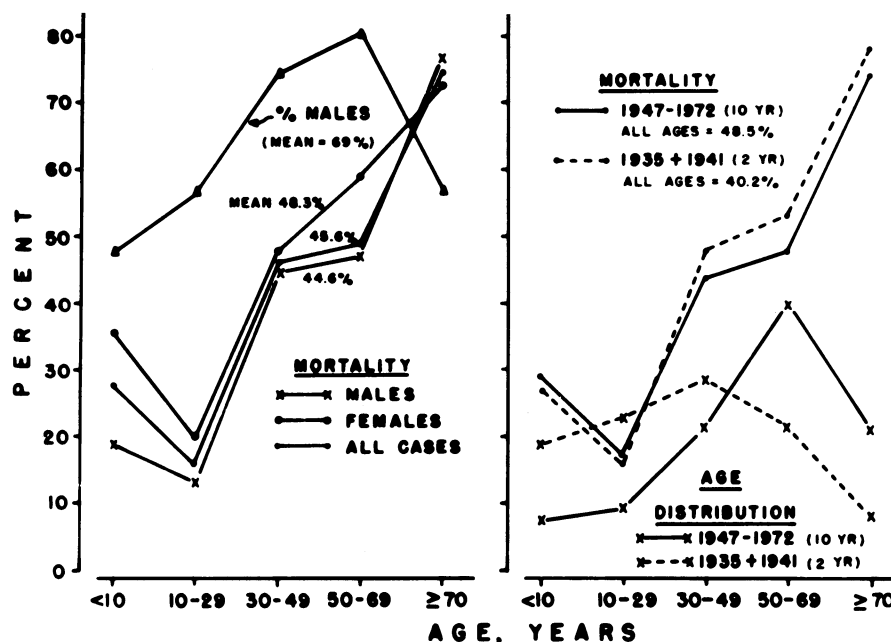


Figure 2. Incidence of and mortality from acute bacterial empyema, by age of patients, at Boston City Hospital during 12 selected years from 1935 to 1972.

years, and all but one of the 10 patients who died after 1941 were infants. There were five deaths among the six infants in the two selected years before the introduction of penicillin (83%) and nine deaths among the 22 infants who died during the 10 selected antibiotic years (41%).

### Discussion

Not many reports on acute empyema similar to this one and covering the same interval are available: the study by Weese and coworkers [7] covered all age groups at University of Iowa Hospitals during selected years in the pre-, early, and late antibiotic decades, whereas those of Lionakis et al. [8], Hoffman [9], Ravitch and Fein [10], Middlekamp et al. [11], and Beschamps et al. [12] include only cases in the pediatric age group over much of the same period. Ehler [13] reviewed the literature on nontuberculous empyema for the period from 1934 to 1939, whereas Yeh et al. [14] included brief mention of some later reports; however, these two papers are concerned chiefly with surgical management, which is not considered in the present report.

The selection of cases for inclusion in this study was based on the report of a significant bacterial pathogen demonstrated in purulent

pleural fluid obtained by thoracentesis, at operation, or at autopsy. Very few of the cases are in the last category, which includes mostly patients who died within the first day or two after admission to the hospital. Thus, no patients with empyema of "unknown or undetermined etiology" are included; such cases constitute a variable and often large proportion of the cases reported by others [7-9, 11, 14-18]. However, we did include a few patients in whom the first "positive fluid culture" was reported as "no growth," but microscopic examination of that purulent fluid showed bacteria which were morphologically compatible with organisms previously obtained from cultures of blood, tracheal aspirates, and/or sputum, the patient having received appropriate antibacterial therapy in the interim. All of the C-A cases of empyema in which the initial positive culture of pleural fluid yielded pneumococci or *H. influenzae* and most of those that yielded *S. aureus* or aerobic streptococci other than enterococci were complications of pneumonia. On the other hand, the cases with enterococci, gram-negative rod(s), mixed aerobes, or anaerobes were either post-traumatic or followed intrathoracic surgery, mostly in patients with pulmonary neoplasms, bronchiectasis, or lung abscess.

The data presented in table 1 and figure 1

**Table 7.** Distribution of cases of and mortality due to empyema by age at Boston City Hospital before (1935 and 1941, two years) and after (1947-1972, 10 selected years) antibiotics became available.

Years, age group (years)	No. of cases	No. of deaths	CFR (%)	Percentage of cases	Percentage of deaths
1935 + 1941					
<10	41	11	27	18.7	12.5
10-29	50	8	16	22.8	9.1
30-49	63	30	48	28.8	34.1
50-69	47	25	53	21.5	28.4
≥70	18	14	78	8.2	15.9
Total	219	88	40.2	100	100
1947-1972					
<10	34	10	29	7.5*	4.6†
10-29	42	7	17	9.3*	3.2‡
30-49	97	43	44	21.5	19.6§
50-69	185	89	48	40.9*	40.6‡
≥70	94	70	74	20.8*	32.0
Total	452	219	48.5#	100	100

NOTE. CFR = case-fatality ratio.

\* $P < 0.001$ .† $P < 0.05$ .‡ $\chi^2 = 3.5$ .§ $P = 0.01$ .|| $P < 0.01$ .# $P = 0.05$ .

show sharp declines in the total numbers of cases of empyema successively from 1941, after the sulfonamides had achieved wide use, to 1947, after penicillin and streptomycin had been extensively used, and to 1951, after chlortetracycline and chloramphenicol had been widely used for about three years and polymyxin had also been available. After 1951, in spite of the continued use of all of these agents and the introduction and use of erythromycin, new semisynthetic penicillins with an expanded spectrum or resistant to penicillinase, the cephalosporins, new and more effective aminoglycosides, lincomycins, and other active antibacterial agents, the total number of cases each year and the rate per 1,000 hospital

admissions increased more or less steadily over the following years.

The early sharp decline in numbers of cases and rates of empyema was limited to the C-A cases, that is, those in which the "infection" was acquired before admission to the hospital, whereas the H-A cases showed no such decline but fluctuated independently. The early decline in C-A cases may be a reflection of the extensive use of the antibiotics, particularly the oral forms, outside the hospital. Rates of empyema cases per 1,000 hospital admissions or discharges have been reported infrequently from general hospitals. At the University of Florida Hospitals [7], the incidence of empyema was 0.79 per 1,000 admis-

**Table 8.** Incidence of and mortality rate due to empyema by age among patients at Boston City Hospital during seven years, 1932 to 1939 (adapted from [5]).

Age group (years)	No. of cases	No. of deaths	CFR (%)	Percentage of cases	Percentage of deaths
<10	162	38	24	32.4	18.2
10-29	99	22	22	19.8	10.5
30-49	129	66	51	25.8	31.6
50-69	84	57	68	16.8	27.3
≥70	26	26	100	5.2	12.4
Total	500	209	41.8	100	100

NOTE. CFR = case-fatality ratio.

**Table 9.** Incidence of empyema in patients younger than 10 years old at Boston City Hospital during 12 selected years between 1935 and 1972.

Age (years)	Years (no. selected)			No. (%) of males
	1935– 1941 (2)	1947– 1972 (10)	1935– 1972 (12)	
0–1	6 <sup>5</sup>	22 <sup>9</sup>	28 <sup>14</sup>	14 (50)
1–2	5 <sup>2</sup>	4	9 <sup>2</sup>	5 (55)
2–10	30 <sup>4</sup>	8 <sup>1</sup>	38 <sup>5</sup>	17 (45)
<10 (total)	41 <sup>11</sup>	34 <sup>10</sup>	75 <sup>21</sup>	36 (48)

NOTE. Superscripts indicate deaths.

sions in 1937–1938, dropped to 0.52 per 1,000 by 1947–1948, and remained at about that level through 1967–1969. In our cases the CFR fluctuated irregularly and at higher levels, and those of C-A and H-A cases varied independently (figure 1).

At Boston City Hospital the overall mortality in the 671 cases (45.8%) was considerably higher than that reported by Weese et al. [7] and by most other authors [14, 15, 17–21]. However, in the series of Snider and Saleh [16], there were 49 deaths in 105 cases (47%); most of those deaths were in patients with serious underlying diseases, and only five were attributed directly to the empyema. In other reports that dealt mostly or entirely with adults [7, 14, 15, 18–21], the mortality rate ranged from 4% [21] to 30% [15], and in most of these reports, the deaths occurred chiefly in patients with serious complicating diseases, and few of them were attributed to the pleural infection (table 10).

Empyema was present at the time of death in all of the fatal cases reported here and was demonstrated post-mortem in those with autopsies. These patients died with purulent empyema regardless of the actual cause of death or the presence of other complications or underlying diseases, which were also frequent in our cases in all 12 years of the study. However, during the interval covered, increasing numbers of older patients and patients with serious cardiac and pulmonary diseases were subjected to thoracic operations and to antitumor and immunosuppressive agents. These factors, except for age, were not evaluated.

The overall mortality in the 122 cases reported by Weese and coworkers [7] was 15.6%; it was 10% in 106 C-A cases and 50% in the 16 H-A

cases ( $P < 0.01$ ). In our cases the CFR was 40.2% in the 423 C-A cases and 55.2% in the 248 H-A cases ( $P < 0.001$ ).

Mortality from empyema was generally related to the age of the patients (table 6 and figure 2); it was lowest in those 10–29 years old, considerably higher in infants and children (birth to nine years old), but rose with increasing age after the second decade of life. This trend was even more striking in the earlier series from this hospital (table 9). The proportion of cases in the various age groups is one of the important determinants in evaluating mortality before and after the antibiotic years. In our cases in 1935 and 1941, there were already fewer cases in the youngest age group and more in older patients than in Nowak's earlier series, and these changes were even more striking in the 10 selected years from 1947 to 1972 (table 7 and right panel of figure 2). Such data for adults are not available in the reports from other general hospitals (table 10).

For the pediatric age group (ages ranging up to 12 or 16 years in different hospitals), such data are available. They show that the incidence of empyema and mortality from the disease were both highest in patients younger than one year, or even six months old or younger, and both declined with increasing age (table 11). Of our 671 cases, 75 (11.2%) were less than 10 years old, and 37 of them were younger than two years; the CFR was 50% in those under one year and declined with increasing age. This was true in both the years before and the years after antibiotics became available, but in each age group to age 10, the CFR was lower in the antibiotic years, and, in addition, the proportion of patients less than one year old was significantly higher in the latter period. Several reports noted a high incidence of empyema due to *S. aureus* [11, 23, 24] predominantly in infants; in the study by Koch et al. [23], which dealt exclusively with empyemas due to *S. aureus*, 73% of the patients were less than one year old.

The preponderance of males over females in cases of empyema has been noted in all reports in which distribution by sex was mentioned, but data on the relation of age to this predominance of males were not provided. Our analysis in tables 6 and 9 and figure 2 (left panel) is therefore of some interest. The surprising result was that the

Table 10. Mortality rates due to acute bacterial empyema reported from general hospitals.

Author(s)	Years	Age (years)	No. of patients*	CFR (%)	Comments
Maes et al. [20]	1924-1933	All	682 <sup>117</sup>	17.1	CFR ranged from 8% to 23% in different years; mortality not correlated with that of pneumonia or influenza.
Nowak [5]	1932-1938	All	500 <sup>209</sup>	41.8	Incidence range of 29%-53% in different years; Boston City Hospital (see table 9 and figure 4).
		<10	162 <sup>38</sup>	24	
		≥70	26 <sup>26</sup>	100	
Poth and Mathes [21]	1934-1940	All	55 <sup>2</sup>	4	Consecutive cases treated by tidal irrigation. Fatal cases: 7 months and 18 months old.
		<2	9 <sup>2</sup>	22	
		2-60+	46 <sup>0</sup>	0	
Weese et al. [7]	1937-1969	0-79	122 <sup>19</sup>	16	Selected years for 4 decades; C-A cases: 106 <sup>11</sup> (10%); H-A cases: 16 <sup>8</sup> (50%) ( $P < 0.01$ ). Cases with initially sterile fluid, 35 <sup>1</sup> (3%); single organism, 63 <sup>8</sup> (13%); multiple organisms, 17 <sup>7</sup> (41%) ( $P < 0.01$ ).
	1937-1938		29 <sup>6</sup>	21	
	1947-1948		20 <sup>2</sup>	10	
	1957-1958		24 <sup>1</sup>	4	
	1967-1969		49 <sup>10</sup>	21	
Snider and Saleh [16]	1952-1967	Adults (all males)	105 <sup>49</sup>	47	Only 5 deaths from empyema; others due to underlying diseases; 53 patients >60 years old.
Geha [17]	1954-1967	0-89	85 <sup>10</sup>	12	Includes 9 cases of tuberculous empyema; 5 deaths attributed to empyema, and 5 to other diseases.
		0-9	12 <sup>2</sup>	17	
Yeh et al. [14]	June 1956-January 1963	0-79	111 <sup>14</sup>	13	Five deaths from empyema, 9 from other causes.
Simmons et al. [18]	July 1957-June 1971	All	62 <sup>7</sup>	11	
		0-9	5 <sup>1</sup>	20	
		10-49	17 <sup>0</sup>	0	
		≥50	40 <sup>6</sup>	15	
Emerson et al. [15]	1960-1970	All	50 <sup>15</sup>	30	Age of patients <10 years old who died: 9 weeks, 18 months, and 18 months; 17 <sup>1</sup> with initially sterile fluid, and 5 <sup>2</sup> with tuberculous empyema are omitted.
		<10	11 <sup>3</sup>	27	
Vianna [19]	June 1964-June 1968	20-79	41 <sup>8</sup>	20	All 8 deaths in 25 patients with serious complicating disease (32%).
This report	1935-1972 (12 years)	All	671 <sup>307</sup>	45.8	C-A cases, 425 <sup>170</sup> (40.2%); H-A cases, 248 <sup>137</sup> (55.2%) ( $P < 0.001$ ).
		<10	75 <sup>21</sup>	28	
		10-29	92 <sup>15</sup>	16	
		30-69	392 <sup>187</sup>	48	
		≥70	112 <sup>84</sup>	75	
	1935-1941	All	219 <sup>88</sup>	40.2	Two selected years: 8.2% ≥70 years; 29.7% ≥50 years ( $P = 0.05$ ). Ten selected years: 20.8% ≥70 years; 61.7% ≥50 years ( $P < 0.001$ ).
	1947-1972	All	452 <sup>219</sup>	48.5	

NOTE. CFR = case-fatality ratio; H-A = hospital-acquired; C-A = community-acquired.

\*Superscripts indicate deaths.

proportion of males with empyema increased steadily with age to 69 years and declined in the older patients. Among the children from birth to nine years old, the numbers of males and females were equal (48%); males were more frequent

(57%) in the 10- to 29-year-old groups, but the difference was not significant. The higher proportion of males in 30- to 49-year-old patients (75%) was statistically significant ( $P < 0.01$ ), although the further increase to 82% in the 50- to 69-year-

Table 11. Mortality rates due to acute empyema reported from pediatric hospitals.

Author(s)	Years	Age (years)	No. of patients*	CFR (%)	Percentage of patients		Comments
					<1 year	<2 years	
Penberthy and Benson [22]	1926-1935	0-12	407 <sup>44</sup>	11	7.6	31	Numbers estimated from text figure. Mortality of empyema related directly to type and virulence of antecedent pneumonia.
		0-1	31 <sup>11</sup>	35			
		1-2	95 <sup>8</sup>	8			
		2-8	259 <sup>25</sup>	10			
		8-12	22 <sup>0</sup>	0			
Lionakis et al. [8]	1932-1956	0-13	133 <sup>22</sup>	17	11	23	78 <sup>13</sup> (17%) without chemotherapy; 49 <sup>9</sup> (18%) received chemotherapy (and/or antibiotics).
		0-1	14 <sup>7</sup>	50			
		1-2	17 <sup>8</sup>	47			
		2-8	84 <sup>7</sup>	8			
		8-13	18 <sup>0</sup>	0			
Ravitch and Fein [10]	1934-1958	"children"	214 <sup>40</sup>	18.7			Patients <2 years (CFR) Most of deaths <1 year old.
		1934-1938	82 <sup>23</sup>	29	66	45 <sup>17</sup> (38%)	
		1939-1942	43 <sup>5</sup>	12	55	32 <sup>4</sup> (13%)	
		1943-1946	31 <sup>5</sup>	16	74	21 <sup>5</sup> (24%)	
		1947-1958	58 <sup>6</sup>	10	68	43 <sup>5</sup> (12%)	
Beschamps et al. [12]	1935-1965	0-15	138 <sup>26</sup>	19		26	CFR of empyema complicating other serious diseases, 59%.
		1935-1938	51 <sup>7</sup>	14		22	
		1939-1942	24 <sup>3</sup>	13		8	
		1943-1946	20 <sup>3</sup>	15		15	
		1947-1965	43 <sup>13</sup>	30 <sup>†</sup>		47 <sup>‡</sup>	
Hoffman [9]	1942-1958	0-12	125 <sup>5</sup>	4		37	46 <sup>2</sup> (4%) 0-2 years old.
Koch et al. [23]	1944-1958	0-12	83 <sup>10</sup>	12	73	86	Only <i>Staphylococcus aureus</i> empyemas.
		<6/12	37 <sup>9</sup>	24			
		1-2	10 <sup>1</sup>	10			
		>2	36 <sup>0</sup>	0			
Stiles et al. [24]	1955-1969	0-15	152 <sup>5</sup>	3.3	35		51 (58%) <i>S. aureus</i> 27 (42%) <i>S. aureus</i>
		1955-1961	88 <sup>4</sup>	4.5	52		
		1962-1969	64 <sup>1</sup>	1.6	11		
Middlekamp et al. [11]	1944-1961	0-11	82 <sup>9</sup>	11	43	60	<i>S. aureus</i> pneumonia 43 <sup>5</sup> (12%); 5 deaths <2 years old.
Cattaneo and Kilman [25]	1960-1969	2/12-16	69 <sup>5</sup>	7	39	61	
This report	1935-1972	0-9	75 <sup>21</sup>	28	37	49	12 selected years (see table 10).
		0-1	28 <sup>14</sup>	50			
		1-2	9 <sup>2</sup>	22			
		2-10	38 <sup>5</sup>	13			
	1935-1941	0-1	6 <sup>5</sup>	83			2 selected years.
		1-2	5 <sup>2</sup>	40			
		2-10	30 <sup>4</sup>	13	15	27	
	1947-1972	0-1	22 <sup>9</sup>	41			10 selected years.
		1-2	4 <sup>0</sup>	0			
		2-10	8 <sup>1</sup>	13	65 <sup>‡</sup>	76 <sup>‡</sup>	

NOTE. CFR = case-fatality ratio.

\*Superscripts indicate deaths.

† $P < 0.05$ .

‡ $P < 0.001$ .

old group was not. The decline to 57% in the patients of age 70 and older was highly significant ( $P < 0.001$ ). The difference between the proportion of males in the group from birth to

nine years old and that in all other age groups was highly significant ( $P < 0.001$ ).

Since similar data were not found in other reports, a comparison was made between the re-

Table 12. Sex distribution of cases of empyema in adults and children.

Source of report, authors	No. of patients	Age (years)	No. of males	Percentage of males	Comments
General hospitals					
Emerson et al. [15]	72	All	60	83	Includes 11 cases (15%) under age 10.
Geha [17]	85	4/12-80	61	72	Includes 13 cases (15%) under age 10.
LeRoux [26]	500	Adults	372	74	
Nowak [5]	500	1-78	351	70	Includes 162 cases (34%) under age 10.
Simmons et al. [18]	62	All	51	78	
Sullivan et al. [27]	226	All	189	84	
Weese et al. [7]	122	4/12-77	84	67	23 (19%) in 0-9 age group.
Yeh et al. [14]	110	0-79	82	75	24 (22%) in 0-9 age group.
This report	671	All	460	69	75 (11%) <10 years (table 11).
Total	2,384	All	1,710	71.7*	
Pediatric hospitals					
Beschamps et al. [12]	138	0-15	78	57	36 (26%) 0-2 years old.
Cattaneo and Kilman [25]	69	2/12-16	35	51	42 (69%) <2 years old.
Hoffman [9]	125	2/12-12	71	57	46 (37%) 0-2 years old.
Lionakis et al. [8]	777	Pediatric	471	61	31 (23%) of 133 cases <2 years old.†
Middlekamp et al. [11]	82	0-11	50	61	35 (43%) <1, 49 (60%) <2 years old.
Total	1,191	0-16	705	59.2*	190/547 (35%) <2 years old.

\* $P < 0.001$ .

†Includes author's series of 133 cases (63.1% males) and four series from other hospitals: 41 cases from 1945-1953 (59% males) and three other series from 1920 and 1932 with 204, 89, and 310 cases, of which 60.8%, 59.5%, and 60.0%, respectively, were males. The number under age 2 is not given.

ports on distribution of cases of empyema by sex in pediatric hospitals and in general hospitals in which children were either not admitted or constituted only a small proportion of all cases. Table 12 lists the data on 2,384 cases from nine general hospitals, including Boston City Hospital. The proportion of males ranged from 67% to 83% and averaged 71.7%. The number and percentage of patients younger than 10 years old are given where they were available. Similar data contained in reports from nine pediatric hospitals, including five listed by Lionakis et al. [8], are also provided in table 12. The proportion of males among the children ranged from 51% to 63% and averaged 59.1% ( $P < 0.001$ ). The relation to age is not given in any of these reports, but it is interesting to note that in the series with the highest proportion of patients under two years old, the sexes were equally represented [25]. Table 12 also shows the proportion of patients under age two in the other reports in which this information was given.

Although no explanation for the sex difference is offered, these observations suggest that some factor(s) increasing susceptibility to empyema may be related to the development, maturation, and deterioration in production of androgens,

perhaps mediated by anatomical changes. A similar sex distribution was noted in the cases of meningitis reported from this hospital [3]; the greatest predominance of males in those cases was in the 20- to 39-year-old group (75%), with a decline from 64% at 60-69 years to 55% in those 70 years old and older.

In our cases, the mortality was slightly higher among females in each age category except the  $\geq 70$ -year-old group, but none of the differences was statistically significant. Data on the relation of mortality to sex were not found in other reports.

The relative frequency with which bacterial pathogens were isolated in the initial positive culture of empyema fluid varied markedly depending on whether that culture yielded a single organism or more than one (mixed culture), whether the empyema was C-A or H-A, or whether the culture was the first one from a superinfection. As shown in table 2, over the entire 12 selected years, by far the most frequent single organism initially identified was *S. pneumoniae*; *S. aureus* ranked next, and hemolytic streptococci ranked third but caused many fewer cases. In the H-A cases, *S. aureus* was by far the most frequent single pathogen, with gram-negative

rods (the most frequent being *Klebsiella-Enterobacter* and *E. coli*) ranking next.

The originally mixed infections in C-A cases included many putrid empyemas; anaerobic organisms, including anaerobic or microaerophilic streptococci, fusiform bacilli, and *Bacteroides*, were most prominent, but among aerobes in the mixed C-A cases, *S. aureus*, viridans streptococci, and hemolytic streptococci were the most frequent. In the H-A cases of originally mixed infections, aerobic gram-negative rods and gram-positive cocci were about equally prevalent; enterococci and *S. aureus* were the most frequent of the latter, and *E. coli* was the most frequent of the former, but *Klebsiella-Enterobacter*, *Proteus*, and *P. aeruginosa* were each identified in almost similar numbers.

In the first fluid in which additional organisms were subsequently identified, *S. aureus* was by far the most frequent, and the same gram-negative rods were each equally prominent and together were twice as common as the staphylococci. However, hemolytic and viridans streptococci were also common in superinfections.

The source and significance of the new organisms, here designated as superinfections, are difficult to evaluate. Some may represent colonization with organisms from chest tubes, dressings, or other environmental sources, but many, particularly in H-A cases that followed trauma or operations, probably originated in the lungs. They were more frequent in H-A cases than in C-A cases with mixed growth in the initial positive fluid. In some cases, superinfection was associated with rapid deterioration and death within one or two days, and the same organisms were predominant in cultures of the lungs and pleural fluid and in some instances were grown from cardiac blood at autopsy. The overall mortality was not significantly different in patients within some categories with and without superinfection. However, the mean duration of hospitalization in those who lived and the mean survival time in fatal cases after the first positive fluid culture were two weeks longer in C-A cases with superinfection and about six weeks longer in H-A cases with superinfection than in the corresponding cases with no superinfection.<sup>1</sup>

<sup>1</sup> M. Finland and M. W. Barnes, "Duration of Hospitalization for Acute Bacterial Empyema at the Boston City Hos-

The introduction and increasing use of sulfonamides and antibiotics were accompanied by marked changes in the frequency with which the various pathogens were isolated from pleural fluids in both C-A and H-A cases. *S. pneumoniae* was the most frequent organism in 1935 and declined in frequency progressively to 1953, but it was still quite common even after that time. Hemolytic streptococci ranked second in 1935 but have been infrequent or not seen in initial fluids since then. *S. aureus*, on the other hand, increased somewhat after 1935, gained the ascendancy in the middle and late 1950s, and then declined steadily to its original position in the years before chemotherapy. Mixed aerobic infections (mostly *S. aureus* and gram-negative rods) increased in incidence steadily until 1953, declined sharply in the years when *S. aureus* was most frequent, and then increased steadily after that time. *S. aureus* and gram-negative rods have been particularly prevalent in H-A cases and in superinfections. The relative incidence of anaerobes, with or without aerobes, fluctuated less than that of the other organisms over the entire 12 years. *H. influenzae* has been infrequent throughout the period studied, both in C-A and H-A cases. Single gram-negative rods became increasingly frequent as *S. aureus* declined. Superinfections were most often with more than one new organism.

More or less parallel changes have occurred in the relative incidence of the most common pathogens in cases of bacteremia [1] and of meningitis [3] at this hospital over the same period covered in this report, as shown in figure 3.

The great predominance of pneumococci in empyemas, generally as a complication of lobar pneumonia, and the frequent occurrence of hemolytic streptococci in the preantibiotic years have been noted by many authors [5, 7, 10, 12, 13]. The frequent occurrence and increasing prominence of *S. aureus* in the middle 1950s and in the 1960s were also reported from many hospitals, both in adults [7, 14, 16-19] and particularly in infants and children [10, 11, 23, 25], and the emergence of aerobic gram-negative rods as increasingly frequent causes of empyema during and after the 1960s has also been noted in many hospitals [7, 15-18].

pital during 12 Selected Years between 1935 and 1972," manuscript in preparation.

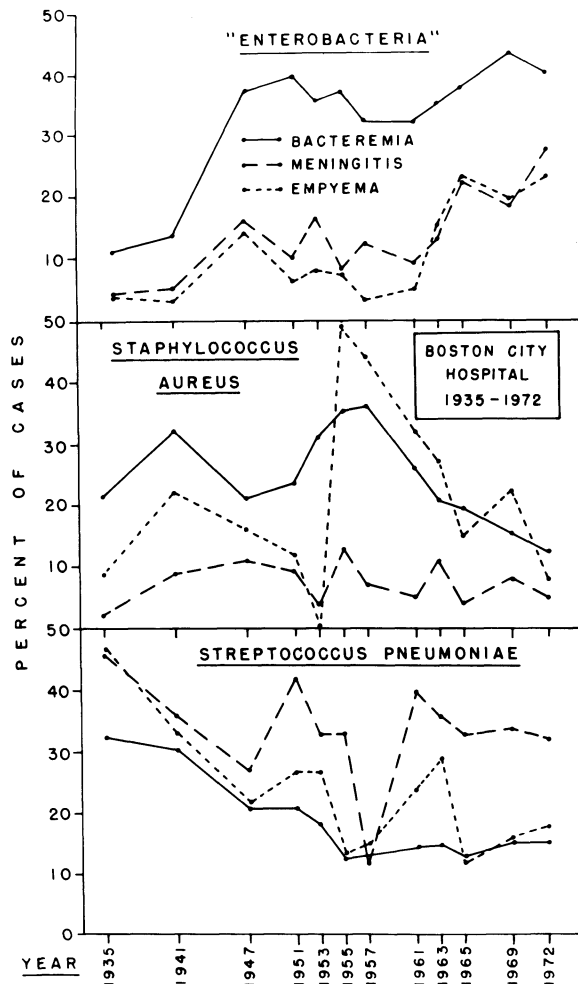


Figure 3. Percentage distribution of the most common bacterial pathogens identified in cases of bacteremia, meningitis, and empyema at Boston City Hospital during 12 selected years from 1935 to 1972.

The frequency of identification of anaerobic bacteria as the only infecting organisms or together with aerobic bacteria in mixed infections of pleural fluids has varied widely, from a low of 1%–3% [28] to as high as 76% [29] depending on the methods of handling and processing the specimens of pleural fluid. In the 226 “culture-proven cases” of empyema reported by Sullivan et al. [27], anaerobes with or without aerobes were cultured from 42 (19%). These authors listed 22 other reports of 100 or more cases of “culture-positive” nontuberculous empyema since 1940. The percentage of anaerobes is listed as “?” in two of these reports, “0” in 10, and 1%–11% in the other 10. In the 12 selected years of the present study, single anaerobes were identified

in 2.9% of cases yielding only one organism initially and constituted 23.8% of the organisms in the initial diagnostic pleural fluids with mixed infections; they also accounted for 11.6% of the organisms subsequently identified in the cases with superinfections. Cultures from cases with superinfections were frequently mixed (56% of cases) when they were first identified.

The mortality from bacterial empyema was higher in patients in whom culture of the initial diagnostic pleural fluid yielded a mixed infection (59%) than in those in whom a single organism was identified (40%) ( $P < 0.001$ ); 70% of the 671 patients were in the latter category.

Many changes in the management of empyema have occurred in our hospital, as in all others, over the last half century since the classic contributions of Graham et al. [30–32] and of others [13, 14, 21, 24, 26, 33]. The management of empyema at this hospital before antibiotics came into use was reported by Nowak [5] and Strieder and Lynch [6]. Sulfonamides may have prevented many cases after pneumonias in which they were used early in the course of the infection but had no effect when purulent exudate had developed because of the content of sulfonamide inhibitors in such exudates. We reported on the effects of topical and systemic penicillin [34, 35], and the influence of the use of all antibiotics has been reflected in the data on mortality previously cited. However, the increasing frequency with which penicillin-resistant staphylococci and increasingly resistant gram-negative rods have been encountered [36, 37] has reduced the beneficial effects of antibiotics. Recently, Barnes and Waterworth [38] described a new inactivating enzyme in the cells of empyema fluid which destroys various penicillins and cephalosporins, and de Louvois and Hurley [39] also found that purulent exudates from some human cases inactivate penicillin, ampicillin, and cephaloridine.

The surgical management of empyema at Boston City Hospital was reported by Nowak [5] for six years between 1932 and 1939 and for putrid empyemas by Strieder and Lynch [6] for the period from June 1934 to January 1941. More recently, Sherman et al. [40] reported on the management of 102 purulent, culture-positive, nontuberculous cases observed at this hospital for the 10 years from 1965 through 1974; 29 of those patients died, but in only three was the death consid-

ered "a consequence of sepsis from the pleural empyema." Not all of the cases for those years were included, even those we classified as H-A, for in three of those years that we included (1965, 1969, and 1972), there were 77 H-A cases with 47 deaths (61%) and 58 C-A cases with 22 deaths (38%).

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