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SPECIAL ARTICLE

Bacteremia at Boston City Hospital: Occurrence and Mortality during 12 Selected Years (1935–1972), with Special Reference to Hospital-Acquired Cases

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The cases of all patients hospitalized at Boston City Hospital during 1972 who had blood cultures positive for a clinically significant, aerobic bacterial pathogen or for *Candida* were analyzed with respect to incidence and mortality, sex, age, admission to medical or surgical services, and the causative organism. Similar data were obtained for 11 years between 1935 and 1969 selected to reflect the introduction and general use of various effective antibacterial agents. Comparisons were also made between hospital-acquired bacteremic infections (defined as those in which the first positive blood culture was obtained on or after the third day in the hospital) and community-acquired infections (defined as those with positive blood cultures on admission or within the first two days in the hospital). In 1972, the incidence of bacteremic infections (but not the case-fatality ratio) was significantly higher in males than in females. Bacteremic infections were more than twice as frequent on the medical than on the surgical services, but the case-fatality ratio was slightly but not significantly higher on the surgical services. Bacteremia was most frequent in the youngest (birth through nine years) and the oldest (≥ 60 years) age groups, whereas the case-fatality ratio was lowest in the youngest group and increased with each decade of life. *Streptococcus pneumoniae* was the most frequent organism causing bacteremia; next were *Escherichia coli*, *Klebsiella-Enterobacter*, and *Staphylococcus aureus*, in that order. The case-fatality ratio was lowest in cases due to *S. pneumoniae* and highest in those caused by *Pseudomonas aeruginosa*, *Proteus*, and *Klebsiella-Enterobacter*. The data for all 12 selected years indicate a rising incidence of bacteremic infections during the 1950s and most of the 1960s, with evidence of decline in 1969 and 1972. The greatest proportion of bacteremic cases on the medical services were community-acquired, whereas the majority of those on the surgical services were hospital-acquired; on both the medical and the surgical services, the rates of hospital-acquired infections continued to increase, and most of the recent decrease was in community-acquired cases on medical services. Case-fatality ratios were significantly higher among those with hospital-acquired infections than among those with community-acquired infections in all instances. In 1935 about one-fifth of all cases of bacteremic infection and about 30% of deaths from such infections were in patients ≥ 60 years old. The remaining cases were about equally divided among those < 30 years old and those 30–59 years old, but one-half of all deaths were among the latter age group. In the ensuing years the proportion of cases (and particularly of deaths) in those < 30 years old declined sharply, whereas cases and deaths in patients ≥ 60 years old increased to about one-half of all cases and to more than 60% (up to three-fourths) of all deaths in each of the selected years. In 1935, *S. pneumoniae* and β -hemolytic *Streptococcus* accounted for more than half of all cases of bacteremic infection and for nearly two-thirds of all deaths from such infections; *S. aureus* accounted for one-fifth of the cases and for one-sixth of the deaths. During the 1950s,

the number of *S. aureus* infections increased until this organism accounted for more than one-third of the bacteremic cases and deaths, but these proportions decreased in ensuing years to only one-eighth of all cases and deaths. Gram-negative bacilli have accounted for increasing proportions of cases since 1951 and now predominate as causes of bacteremic infection and of deaths from such infections.

Acquisition of infection within the hospital is being recognized as an increasingly serious problem [1-3]. Bacteremia accompanying such infection not only is one of the best criteria of severity but also offers the most reliable means of identification of the etiologic agent. Changes in the occurrence of and mortality rate from all bacteremic infections at Boston City Hospital during the antimicrobial era were first reported in 1959 [4] based on data for seven selected years between 1935 and 1957. The observations were subsequently extended to include three of the next eight years [5]; more recently, some features of cases from some of the same years and for 1969 were also reported [6].

The number of admissions to Boston City Hospital had been declining slowly but steadily since 1950 and more rapidly since 1965. In 1973 the bed capacity in the main hospital was deliberately reduced to 500, and professional care of patients was delegated to a single medical school (three Boston schools had previously been involved). In this paper we will present first an analysis of the cases of bacteremic infection at Boston City Hospital in 1972, the last full year of operation under the former regime. The data for 12 selected years from 1935 to 1972 will then be presented and analyzed in relation to age of the patients, their admission to medical or surgical services, and acquisition of infection in the community or in the hospital. The results will thus reflect the changes that occurred throughout the antibiotic era and the results of the use of the various antibacterial agents as they became

available and were used intensively within the hospital and in the community.

Methods

Patients were selected for inclusion in this study solely on the bases of (1) laboratory reports of blood cultures positive for bacteria considered to be pathogenic, and (2) clinical findings in the patients' records consistent with infection due to those organisms. Isolates identified as *Staphylococcus epidermidis*, diphtheroids, *Bacillus* species, and others considered by the bacteriologist to be contaminants were arbitrarily excluded from consideration. Likewise, strict anaerobic bacteria were also excluded because adequate methods for their detection were not used routinely during most of the period of this study.

In this paper we include among surgical patients those on the general surgical, pediatric surgical, thoracic surgical, urologic, gynecologic, neurosurgical, otorhinolaryngologic, ophthalmologic, and oral surgical services. Patients on all other services (general medical, pediatrics, obstetrics, neurology, psychiatry, and dermatology) are designated medical.

The designation community-acquired (C-A) is used for all cases in which the first culture with a significant bacterial pathogen was obtained before the third day of hospitalization. The term hospital-acquired (H-A) is applied to cases in which blood for the first culture positive for a significant pathogen was obtained on or after the third day of hospitalization. Analysis of the clinical, laboratory, and epidemiologic features of 910 of the bacteremic cases at this hospital in 1963 and 1972 (table 1) showed a good correlation between features that indicated H-A infection and the first detection of significant pathogens in cultures of blood drawn on the third day of hospitalization or later. In contrast, the findings in patients whose bacteremia was first

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Table 1. Day of hospitalization when first positive blood culture was obtained in 910 cases of bacteremia, and classification of infection as community-acquired (C-A) or hospital-acquired (H-A).

Hospital day	No. of cases (% of total)	Source	
		C-A	H-A
1	473 (52.0)	467	6*
2	25 (2.7)	18	7†
3	37 (4.1)	6‡	31
4	42 (4.6)	1§	41
5-7	82 (9.0)	0	82
8-14	87 (9.7)	0	87
≥ 15	164 (18.0)	0	164
Total	910	492 (54.1%)	418 (45.9%)#

NOTE. Of 910 cases, 20 (2.2%) deviated from the rigid classification of C-A (first positive culture on day 1 or 2) or H-A (first positive culture on or after day 3). The greatest number of deviants occurred on days 2 and 3 (13 of 62 cases, or 21.0%), as compared with only seven of 515 cases (1.6%) on days 1 and 4 and none after day 4. All deviants were readily classified based on clinical and laboratory data concerning the specimens submitted.

* Three cases followed catheterization of umbilical cord (one *Staphylococcus aureus*, one *Streptococcus viridans*, and one *Escherichia coli* [which was also cultured from the skin]). Three cases were due to group B *Streptococcus*; two of them followed prolonged labor, and one followed premature rupture of membranes.

† Five cases followed iv catheterization (one *S. aureus* after a negative culture, one *Klebsiella* with *Streptococcus hemolyticus* in blood on day 1, one *Klebsiella* associated with postoperative wound infection, one *Proteus mirabilis* with *Streptococcus pneumoniae* type 1 on day 1, and one *Herellea*). In the sixth case, *P. mirabilis* was grown from both an infected wound and urine. In the seventh case, *E. coli* bacteremia occurred after surgery.

‡ One patient was admitted with carbuncle; the first positive blood sample for *S. aureus* was obtained on day 3 after incision and drainage. One case was admitted with sepsis; *P. mirabilis*, *Providencia*, and *Pseudomonas aeruginosa* were cultured from the wound on admission. *P. mirabilis* and *Providencia* were grown from blood on day 1, and *P. aeruginosa* alone grew in blood on day 3. One case was admitted with lobar pneumonia and congestive heart failure; the first blood culture received on day 3 was positive for *S. pneumoniae* type 4. Two cases were admitted for "aspiration pneumonia"; the first positive blood culture was obtained on day 3. One case was admitted for pneumonia; *Klebsiella* was grown from sputum on day 1 and from the first positive blood culture received on day 3.

§ This case was admitted for *S. aureus* pneumonia (heavy growth in sputum and negative blood cultures on admission); the first blood culture was positive for *S. aureus* on day 4.

|| 16.2% of cases with the first positive blood culture on day 3 and 2.4% of those with the first culture positive on day 4 were classified as C-A.

1.3% of cases with the first culture positive on day 1 and 28% of those with the first blood culture positive on day 2 were classified as H-A.

demonstrated on admission or in cultures of blood drawn within the first 48 hr in the hospital were considered to be consistent with C-A infection. In all, 2.2% of positive samples were readily identified as deviants, but of the 62 cases (6.8%) in which the first positive sample was obtained on day 2 or 3, 21% were readily identified as deviants. Previous hospitalizations were not considered.

For the purposes of the analyses, the demographic data (namely, total numbers of patients and deaths each year and distribution by sex and age) were based on the numbers of patients. However, for the bacteremic infections, invasion by each organism is counted as a case. Thus, the number of cases exceeded the number of patients by 7%–9% in most years and by 11.0% and 16.1% in 1969 and 1972, respectively. A few patients each year (more in 1972 than in the other years) had three significant organisms cultured from the blood at different times but had no more than two in the same culture or at the same time.

Results

Bacteremic infections in 1972. During 1972, 28 (2.8%) of every 1,000 patients hospitalized at Boston City Hospital had a bacteremic infection, and 31% of all bacteremic patients died (table 2). Surgical patients accounted for about 42% of all admissions to the hospital but for only about one-fourth of patients with bacteremic infections. The case-fatality ratio (CFR) among bacteremic patients on surgical services was slightly but not significantly higher than that among bacteremic patients on medical services.

Slightly more males (51.7%) than females (48.3%) were admitted, but a much greater preponderance of males (58.5%) was noted among patients with bacteremic infections. The rate of bacteremia among males was also higher (31.7 per 1,000 male admissions vs. 24.0 per 1,000 hospitalized females; $P < 0.05$). The CFR was somewhat (but not significantly) higher among female bacteremic patients. The distribution of bacteremic cases by age differed considerably from that of all hospitalized patients. The age-specific rate was 3.2% for patients <10 years old, dropped for those in the two succeeding decades to 1.3% and about 1%, respectively, then rose steadily with each decade of life to 5% among

Table 2. Occurrence of and mortality rate from bacteremic infections at Boston City Hospital in 1972.

Analysis	No. of hospital admissions (%)	No. of bacteremic cases (%)	Rate/1,000 admissions*	Case-fatality ratio (%)
Service				
Medical	12,217 (57.8)	445 (75.3)†	36.4†	29.9
Surgical	8,916 (42.2)	146 (24.7)	16.4	34.2‡
Sex				
Male	10,924 (51.7)	346 (58.5)§	31.7§	30.1
Female	10,209 (48.3)	245 (41.5)	24.0	32.2‡
Age (years)				
0-9	3,713 (17.6)	119 (20.1)	32.0	5.9
10-19	1,981 (9.4)	26 (4.4)	13.1	11.5
20-29	3,960 (18.7)	39 (6.6)	9.8	17.9
30-39	2,436 (11.5)	39 (6.6)	16.0	20.5
40-49	2,086 (9.9)	44 (7.4)	21.1	34.1
50-59	2,003 (9.5)	81 (13.8)	40.4	35.8
60-69	1,831 (8.3)	87 (14.7)	47.5	35.6
≥ 70	3,123 (14.8)	156 (26.4)	50.0	53.2
Organism#				
<i>Streptococcus pneumoniae</i> (pneumococcus)		108	5.1	14.8
Hemolytic <i>Streptococcus</i> (not group D)		45	2.1	31.1
<i>Streptococcus viridans</i>		63	3.0	25.4
Enterococci		38	1.8	36.8
<i>Staphylococcus aureus</i>		87	4.1	35.6
<i>Escherichia coli</i>		97	4.6	38.1
<i>Klebsiella-Enterobacter</i>		94**	4.4	44.7
<i>Proteus</i>		32	1.5	59.4
<i>Pseudomonas aeruginosa</i>		22	1.0	63.6
<i>Candida</i> ††		30	1.4	62.1
Other		91	4.3	19.8
Total	21,133	591	28.0	31.0

* Specific rates for each category are listed in the first column, except under "Organism," for which the rate is given per 1,000 total admissions to the hospital.

† $P < 0.001$.

‡ $P > 0.05$.

§ $P < 0.05$.

|| Forty-five (38%) of these 119 patients were less than one year old, and 74 were one through nine years old; two of the former group (4.4%) and three of the latter group (4.1%) died.

More than one organism was grown from blood of 84 patients (generally at different times): two from 55 patients and three from 29 patients. The total number of organisms thus exceeds the total number of patients. Except for number of admissions and distribution by sex and age, "case" refers to infection with one organism.

** Of these 94 patients, 75 had *Klebsiella* isolated (of these, 35 [47%] died), and 19 had *Enterobacter* isolated (of these, seven [37%] died).

†† For convenience, candidemia is included among bacteremias throughout the text and tables.

patients ≥60 years old. The CFR in bacteremic patients was lowest (5.9%) in the youngest age group and increased with age; about one-third of patients 40-69 years old and one-half of those ≥70 years old died during the period of hospitalization in which their bacteremic infection occurred.

During 1972 *Streptococcus pneumoniae* (the pneumococcus) was the most frequent organism causing bacteremic infection; this organism was followed closely by *Escherichia coli*,

Klebsiella-Enterobacter, and *Staphylococcus aureus*, in that order. The CFR was lowest for cases of pneumococcal bacteremia and highest for cases due to *Pseudomonas aeruginosa*, *Proteus*, or *Candida*.

Hospital admissions and deaths. The total number of patients hospitalized at Boston City Hospital and the number of bacteremic patients during the 12 years between 1935 and 1972 selected for study are shown in table 3. The number of deaths and the mortality rate (CFR) and

Table 3. Mortality rate among all hospitalized patients and among bacteremic patients at Boston City Hospital during 12 selected years, 1935–1972.

Year	All hospitalized patients			Bacteremic cases				
	No. admitted	No. of deaths	CFR* (%)	No. of cases	Rate/1,000 admissions	No. of deaths	Rate/100 hospital deaths	CFR (%)
1935	2,749	39,274	7.0	291	7.4	168	6.1	57.7
1941	2,698	43,178	6.2	422	9.8	156	5.8	37.0
1947	2,904	38,463	7.6	469	12.2	143	4.9	30.5
1951	2,698	39,412	6.8	478	12.1	167	6.2	34.9
1953	2,617	37,557	7.0	571	15.2	201	7.7	35.2
1955	2,513	34,798	7.2	574	16.5	209	8.3	36.4
1957	2,276	33,604	6.8	598	17.8	234	10.3	39.1
1961	2,124	32,750	6.5	795	24.2	313	14.7	39.4
1963	2,061	32,976	6.3	910	27.6	361	17.5	39.7
1965	1,983	32,704	6.1	1,076	32.9	400	20.2	37.2
1969	1,379	25,643	5.4	665	25.9	260	18.9	39.1
1972	1,064	21,133	5.0	591	28.0	183	17.2	31.0

* CFR = case-fatality ratio.

the rates of bacteremic patients per 1,000 admissions and per 100 hospital deaths for each year are also shown. The total number of admissions and of deaths declined steadily in each of the years of study after 1951, and the decline accelerated after 1965. The steadily declining CFR for all hospitalized patients since 1955 is also evident from these figures.

The number and rate of all cases of bacteremic infection rose steadily during the successive years of this study through 1965 and dropped considerably during the last two years. The number and rate of deaths from bacteremic infection and the CFR in all bacteremic cases declined in 1941 after the sulfonamides came into general use and dropped still further in 1947 following the availability and widespread use of penicillin and streptomycin. After that year, the number and rate of deaths among bacteremic patients climbed steadily in successive years through 1965, despite the declining total number of hospital admissions and deaths and the declining death rate among all patients in the hospital; however, numbers and rates of bacteremic cases declined in 1969 and 1972. The CFR for all bacteremias dropped considerably in 1941 and again in 1947, but after that remained fairly steady (35%–40%), with an appreciable drop only in 1972.

C-A and H-A bacteremias. The above-mentioned changes were reflected in the steady

rise in the rates of both C-A and H-A bacteremic cases per 1,000 hospital admissions (table 4). Interestingly, the early declines in the number of all deaths due to bacteremia and in the mortality rate from bacteremia per 100 deaths in the hospital were accounted for entirely by the drop in the number of deaths among H-A bacteremic patients, while deaths among those with C-A bacteremias remained about the same at first and then rose more or less steadily after 1947. Only after 1965, coincident with the more rapid decline in both the total number of hospital admissions and the overall death rate in the hospital (table 3), did the number and rate of C-A bacteremic cases decline; at the same time, however, the rate of H-A cases continued to climb, with an increase of about 30% (from 10.6 to 13.2 per 1,000 admissions) in 1972 over the rate in 1969.

In 1935, CFRs were high and were about the same for C-A and H-A infections. Both rates declined sharply and to about the same extent in 1941. The mortality rate among patients with C-A, but not with H-A, bacteremias declined further in 1947 after the introduction and widespread use of penicillin and streptomycin. The CFR for C-A bacteremias increased after 1947, remained more or less constant at 30%–35% through 1969, and then dropped sharply to 23.5% in 1972. The CFRs for H-A bacteremic cases were higher (in most years significantly higher)

Erratum

In "Bacteremia at Boston City Hospital: Occurrence and Mortality during 12 Selected Years (1935–1972), with Special Reference to Hospital-Acquired Cases" by John E. McGowan, Jr., Mildred W. Barnes, and Maxwell Finland (September 1975), two headings in table 3 were inadvertently transposed. The heading of the second column in the table should read "No. of deaths," and the heading of the third column should read "No. admitted."

Table 4. Occurrence of and mortality rate from community-acquired (C-A) and hospital-acquired (H-A) cases of bacteremic infection at Boston City Hospital during 12 selected years, 1935–1972.

Category	Year											
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972
C-A												
No. of cases	144	315	349	362	404	385	358	537	606	772	394	311
Rate/1,000 hospital admissions	3.7	7.3	9.1	9.2	10.8	11.1	10.7	16.4	18.4	23.6	15.4	14.7
No. of deaths	82	118	95	122	126	118	103	197	212	250	130	73
Rate/100 hospital deaths	3.0	4.4	3.3	4.5	4.8	4.7	4.5	9.3	10.3	12.6	9.4	6.9
Case-fatality ratio (%)*	56.9	37.5	27.2	33.7	31.2	30.6	28.8	36.7	35.0	32.4	33.0	23.5
% of all cases	50.5	25.4	25.6	24.3	29.2	32.9	40.1	32.5	33.4	28.3	40.8	47.4
H-A												
No. of cases	147	107	120	116	167	189	240	258	304	304	271	280
Rate/1,000 hospital admissions	3.7	2.5	3.1	2.9	4.4	5.4	7.1	7.9	9.2	9.3	10.6	13.2
No. of deaths	86	38	48	45	75	91	131	116	149	150	130	110
Rate/100 hospital deaths	3.1	1.4	1.7	1.7	2.9	3.6	5.8	5.5	7.2	7.6	9.4	10.3
Case-fatality ratio (%)	58.5†	35.5†	40.0‡	38.8†	44.9‡	48.1§	54.6§	45.0	49.0§	49.3§	48.0§	39.3§
% of all deaths	51.2	24.4	33.6	26.9	37.3	43.5	56.0	37.1	41.3	37.5	50.0	60.1

* The case-fatality ratio for all 12 years combined was 32.9% for C-A and 46.7% for H-A cases ($P < 0.0001$).

† $P > 0.05$. All P values are for comparisons of C-A and H-A cases.

‡ $P < 0.01$.

§ $P < 0.001$.

|| $P < 0.05$.

than those for C-A cases during the corresponding years through 1972. The CFR for H-A bacteremic infections rose steadily from a low of 35.5% in 1941 to a peak of 54.6% in 1957 and remained at nearly 50% through 1969; the CFR dropped below 40% in 1972.

From the bottom line under each category in table 4, it can be seen that in 1935, before the sulfonamides were first introduced, about one-half of all cases of bacteremic infection and a similar proportion of all deaths from such infections were H-A. By 1941, after the sulfonamides had achieved wide use but before penicillin and streptomycin became available, these proportions were cut in half; only about one-fourth of all bacteremic cases and deaths among these cases were H-A infections. After that time the proportion of both cases and deaths that were H-A increased steadily through 1957, remitted somewhat through 1965, and then again rose sharply; thus by 1972 nearly one-half of all bacteremic cases and 60% of deaths in these cases were H-A.

Bacteremias on the medical and surgical services. The total number of medical and surgical admissions in each of the 12 selected years, the number of cases and deaths from bacteremic infections, the rates per 1,000 admissions to the

respective services, and the CFRs are shown for C-A and H-A infections in tables 5 and 6, respectively. On the medical services (table 5), the case rates for all bacteremic infections increased in each of the years studied from 9.6 in 1935 to a peak of 41.8 per 1,000 medical admissions in 1965 and then dropped appreciably; most of the increases occurred among C-A cases, the incidence of which rose in each of the selected years from 5.0 per 1,000 medical admissions in 1935 to 33.6 per 1,000 in 1965 and then dropped to about 23% in each of the last two years, 1969 and 1972. Rates of H-A cases on medical services started at nearly the same level, dropped appreciably in 1941, and then increased more or less steadily in each of the remaining years to 13.4 per 1,000 medical admissions in 1972.

In contrast, the rates of C-A bacteremias on the surgical services (table 6) were much lower throughout the years of study; they were less than 2 per 1,000 admissions to surgical services in 1935, dropped to a low of 0.6 per 1,000 in 1947, then increased to a peak of about 6 in 1961 and 1963. The rates then dropped back during the following years to 3.4 per 1,000 in 1972. H-A case rates on the surgical services, on the other hand, more nearly followed the trend of cases on the medical services, beginning somewhat lower

Table 5. Community-acquired (C-A) and hospital-acquired (H-A) bacteremic infections on the medical services of Boston City Hospital during 12 selected years, 1935–1972.

Category	Year											
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972
C-A bacteremias												
Cases	111	287	340	343	359	347	331	468	538	724	348	281
Rate*	5.0	11.7	14.1	13.4	14.2	15.0	14.7	21.5	24.2	33.6	22.5	23.0
CFR (%)†	61‡	37‡	27	33	27	28	27	37	35	33	34	25
H-A bacteremias												
Cases	103	75	104	94	143	129	142	134	172	176	176	164
Rate	4.6	3.1	4.3	3.7	5.7	5.6	6.3	6.2	7.7	8.2	11.4	13.4
CFR (%)	53	29	40§	38‡	45	46	49	42‡	47§	45§	47§	39§
All bacteremias												
Cases	214	362	444	437	502	476	473	602	710	900	524	445
Rate	9.6	14.7	18.4	17.1	19.9	20.6	21.0	27.7	32.0	41.8	33.9	36.4
% H-A	48.1	20.7	23.4	21.5	28.5	27.1	30.0	22.3	24.2	18.9	33.6	36.9
CFR (%)	57	36	30	34	32	33	33	38	38	36	38	30
Total medical admissions	22,304	24,585	24,101	25,645	25,251	23,061	22,483	21,741	22,220	21,531	15,481	12,217

* Cases per 1,000 admissions to medical services.

† CFR = case-fatality ratio.

‡ $P > 0.05$. All P values are for comparisons of C-A and H-A cases.§ $P < 0.01$.|| $P < 0.001$.**Table 6.** Community-acquired (C-A) and hospital-acquired (H-A) bacteremic infections on the surgical services of Boston City Hospital during 12 selected years, 1935–1972.

Category	Year											
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972
C-A bacteremias												
Cases	33	28	9	19	45	38	27	69	68	48	46	30
Rate*	1.9	1.5	0.6	1.4	3.7	3.2	2.4	6.3	6.3	4.3	4.5	3.4
CFR (%)†	42	39	33	42‡	64‡	58‡	52	33	35	21	28	13
% surgical of all C-A cases	22.9	8.9	2.6	5.3	11.4	9.9	7.5	12.8	11.2	6.2	13.2	9.6
H-A bacteremias												
Cases	44	32	16	22	24	60	98	124	132	128	95	116
Rate	2.6	1.7	1.1	1.6	2.0	5.1	8.8	11.3	12.3	11.5	9.3	13.0
CFR (%)	70§	50‡	38‡	41	46	53	63‡	48§	52§	55	49§	40#
% surgical of all H-A cases	29.9	29.9	13.3	19.0	14.4	31.7	40.8	48.1	43.4	42.1	35.1	41.6
All bacteremias												
Cases	77	60	25	41	69	98	125	193	200	176	141	146
Rate	4.5	3.2	1.7	3.0	5.6	8.3	11.2	17.5	18.6	15.8	13.9	16.4
% H-A	57.1	58.3	64.0	53.7	36.1	61.3	78.4	64.2	66.0	72.7	67.4	79.5
CFR (%)	58	45	36	41	58	55	61	43	47	46	43	34
% surgical of all cases	26.5	14.2	5.3	8.6	11.9	17.1	20.9	24.3	22.0	16.4	21.2	24.7
Total surgical admissions	16,970	18,593	14,362	13,767	12,306	11,737	11,121	11,009	10,756	11,173	10,162	8,916

* Cases per 1,000 admissions to surgical services.

† CFR = case-fatality ratio.

‡ $P > 0.05$. All P values are for comparisons of C-A and H-A cases.§ $P < 0.05$.|| $P < 0.001$.# $P < 0.01$.

(2.6 per 1,000), reaching a lower trough (1.1) in 1947, but then rising steadily after that to about the same level (13 per 1,000) as the rate for medical H-A cases by 1972.

CFRs in C-A cases were about the same in medical and surgical patients during most of the selected years, but during the 1950s CFRs were appreciably higher among the surgical patients. For H-A cases the CFRs were higher among the surgical patients in 1935 and 1941 but were nearly the same among medical and surgical patients for most of the remaining years of the study. For all bacteremic cases, the CFRs were generally higher among surgical patients each year except 1935, when they were about equal to those among medical patients.

The proportion of all patients admitted to the hospital who went to surgical services dropped steadily from 1935 through 1953 and remained at about one-third of all admissions until 1963; this proportion rose again in the ensuing years until, in 1972, it was about the same as in 1935. The proportion of all bacteremic patients and of deaths in such patients on surgical services was smaller each year among C-A cases than among H-A cases (except in 1953), and the same was true (except for the years 1951, 1953, and 1955) for the proportion of deaths among bacteremic cases (third lines under C-A and H-A bacteremias, table 6).

The changes in the proportions of bacteremic cases that were on surgical services during the years of this study also differed among H-A and C-A cases. In 1935, somewhat fewer than one-fourth of the C-A bacteremias were in surgical patients; this level dropped to a low of 2.6% in 1947 and rose after that to various proportions (up to 13.2%). Of the H-A bacteremic cases, about 30% were on surgical services in 1935 and 1941; this proportion dropped to about 13% in 1947, rose to a peak of 48% in 1961, and remained at $\geq 35\%$ in subsequent years. The proportions of deaths from bacteremic infections in surgical patients followed trends that paralleled those for all C-A and H-A cases, respectively.

Age of bacteremic patients. One of the most striking trends among bacteremic infections was the decline in the proportion of cases in patients in the youngest age group and the corresponding increase (from about 20% in 1935 to about 50% in 1953 and thereafter) in the proportion of cases in

patients ≥ 60 years of age (table 7). Those of the middle age group showed a smaller but steady decline from over 40% in 1935 and 1941 to a low of 23% in 1957, with a moderate increase in the subsequent years. The same trends were demonstrated even more strikingly in patients with H-A bacteremia, among whom the proportion in the oldest age group was considerably higher than among patients with C-A infection in the same years. The reverse was true in the youngest age group except in 1935, when the proportion of C-A cases was the same as that of H-A cases. Thus, after 1947, those in the oldest age group accounted for the greatest share of both C-A and H-A bacteremic infections but for a greater proportion of the latter.

The distribution of the fatal cases by age (table 7) changed similarly but even more strikingly. The proportion of deaths in the oldest (≥ 60 years) age group increased from less than one-third in 1935 to over three-fourths in the 1950s and still accounted for about two-thirds of the deaths in 1969 and 1972. These proportions were higher among deaths from H-A than from C-A infections in 1935 and 1941; they were lower in 1947 and 1951 but then tended to be similar in C-A and H-A cases in later years. Also noted was the high proportion of deaths in C-A cases (62.2%) in the middle age group in 1935; this proportion declined over the years. The proportion of deaths in the youngest age group declined after 1941 and was generally higher among H-A than among C-A cases.

The numbers of bacteremic patients and the CFRs for the three broad age groups in each of the 12 selected years are shown in table 8, which also gives the proportions of infections that were H-A. In each year the CFR increased with age among both C-A and H-A cases. In each age category among both C-A and H-A infections, there was a general drop in CFR during the first years of the study after 1935. In the youngest age group, the difference between the CFR for H-A cases and the lower value for C-A cases was statistically significant for most years, but in the other age groups, significant differences were not so frequently evident.

The proportion of all cases of and deaths from bacteremia that was H-A (as already noted in table 4) dropped from about one-half to about one-fourth from 1935 to 1951 and rose after that;

Table 7. Age distribution of cases of and deaths from bacteremic infections at Boston City Hospital during 12 selected years, 1935–1972: comparison of community-acquired (C-A) and hospital-acquired (H-A) infections.

Type of infection, age in years	Year											
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972
C-A cases (%)												
< 30	37.5	36.5*	27.2*	17.1*	19.1*	25.7†	38.0†	32.6†	23.8†	18.9*	26.9†	43.2†
30–59	47.2*	43.8*	37.0	34.8*	35.1‡	30.4	24.3*	25.9	36.1§	28.4*	24.4	23.2
≥ 60	15.3	19.7	35.8*	48.1	45.8	43.9	37.7	41.5	40.1	52.7	48.7	33.5
H-A cases (%)												
< 30	38.1*	31.8	20.0	16.4	13.8	14.8	11.7	12.0	12.2	18.1	15.5	17.8
30–59	36.1	43.0	50.0‡	33.6	25.7	27.5*	20.8	28.7*	27.3	27.0	29.5*	33.1§
≥ 60	25.8‡	25.2*	30.0	50.0*	60.5§	57.7‡	67.5†	59.3†	60.5†	54.9*	55.0*	49.1§
All cases (%)												
< 30	37.8	35.3	25.4	17.0	17.5	22.1	27.4	25.9	19.9	18.7	22.3	31.1
30–59	41.6	43.6	40.3	34.5	32.4	29.4	22.9	26.8	33.2	28.0	26.5	27.9
≥ 60	20.6	21.1	34.3	48.5	50.1	48.4	49.6	47.3	46.9	53.3	51.3	41.0
C-A deaths (%)												
< 30	13.4	21.6	6.3	3.3	2.4	2.6	7.8	7.6	7.9	5.6	4.6	9.6
30–59	62.2	46.6	34.7	21.3	22.2	15.5	17.5	24.4	27.2	26.5	25.4	24.7
≥ 60	24.4	31.9	58.9	75.4	75.4	81.9	74.7	68.0	64.9	67.9	70.0	65.8
H-A deaths (%)												
< 30	24.4	23.7	14.6	8.9	5.3	4.3	3.8	3.4	8.0	6.6	6.9	8.2
30–59	38.4	28.9	47.9	28.9	18.7	21.5	19.8	22.4	24.2	20.5	25.4	31.8
≥ 60	37.2	47.4	37.5	62.2	76.0	74.2	76.3	74.1	67.8	72.8	67.7	60.0
All deaths (%)												
< 30	19.0	22.1	9.1	4.8	3.5	3.3	5.6	6.1	8.0	6.0	5.8	7.7
30–59	50.0	42.2	39.2	23.4	20.9	18.2	18.8	23.6	25.9	24.3	25.4	29.0
≥ 60	31.0	35.7	51.7	71.8	75.6	78.5	75.6	70.3	66.1	69.8	68.8	62.3

NOTE. The number of cases and the case-fatality ratios are listed for the corresponding age groups in table 8. *P* values for total period of study (12 selected years) by age group were: <30 years, *P* < 0.001; 30–59 years, *P* > 0.05; ≥60 years, *P* < 0.001.

* *P* > 0.05 (χ^2 test). All *P* values are for comparisons of C-A and H-A cases.

† *P* < 0.001.

‡ *P* < 0.05.

§ *P* < 0.01.

the most striking rise was in 1969 and 1972, when the proportion of deaths that were H-A reached 50% and 60%, respectively, and the proportion of bacteremic cases that were H-A reached 41% and 47%, respectively.

Bacterial etiology. The changing ecology of serious bacterial infections at Boston City Hospital was reviewed in general terms in the papers referred to earlier [4, 5]. Similar data concerning the changing etiology of bacterial endocarditis for the same selected years through 1965 have also been reviewed [7]. The number of cases of C-A and H-A bacteremic infection and the mortality rate among those cases for the 12 years are shown for selected gram-positive bacteria in table 9 and for some of the gram-negative bacilli and *Candida* in table 10. The incidence of cases per 1,000 hospital admissions is shown graphi-

cally in figure 1 for both C-A and H-A cases due to the same organisms.

Pneumococcus. There were 100 cases of pneumococcal bacteremia in 1935 and roughly that number in most of the other years, but there were as many as 140 cases in 1941 and as few as 76 in 1955. The CFR dropped sharply from 78% in 1935 to 25% in 1947 after penicillin came into wide use. In subsequent years, the CFR ranged up to 22%–42% but was only 15% in 1972. About one-third of the cases in 1935 were H-A, but after that time ≥90% of the cases were C-A. The CFR was generally about the same in C-A and H-A cases. Of interest is the rising rate of C-A bacteremic pneumococcal infections since 1951 (figure 1) despite the steadily declining number of hospital admissions during the same period (table 2).

Table 8. Occurrence of and mortality rate from community-acquired (C-A) and hospital-acquired (H-A) bacteremic infections by age group at Boston City Hospital for 12 selected years, 1935–1972.

Age in years, type of infection	Year											
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972
<30												
C-A												
Cases*	54	115	95	62	77	99	136	175	144	146	106	134
CFR (%)	20	22	6	6	4	3	6	9	11	10	6	5
H-A												
Cases	56	34	24	19	23	28	28	31	37	55	42	50
CFR (%)	38†	26‡	29§	21‡	17†	14†	18†	13‡	32§	18‡	21§	18§
% H-A												
Cases	51	23	20	43	23	22	17	15	21	27	28	27
Deaths	66	26	54	50	59	59	38	21	43	42	60	56
30–59												
C-A												
Cases	68	138	129	126	142	117	87	139	219	219	96	72
CFR (%)	75‡	39‡	26	21	20	15	21	35	25	30	34	25
H-A												
Cases	53	46	60	39	43	52	50	74	83	82	80	93
CFR (%)	62	24	38‡	33‡	33‡	38	52	35	43§	38‡	41‡	38‡
% H-A												
Cases	43	25	32	24	23	31	36	35	27	27	46	57
Deaths	39	17	41	67	67	53	58	35	40	32	50	66
≥60												
C-A												
Cases	22	62	125	174	185	169	135	223	243	407	192	105
CFR (%)	91‡	60	45	53‡	51	56‡	57	60‡	58‡	42	47	46
H-A												
Cases	38	27	36	58	101	109	162	153	184	167	149	137
CFR (%)	84	67‡	50‡	48	56‡	63	62‡	56	55	66	59†	48‡
% H-A												
Cases	63	30	22	25	35	38	55	55	43	29	43	57
Deaths	62	33	24	23	38	42	56	39	44	39	49	58
All age groups												
C-A												
Cases	144	315	349	362	404	385	358	537	606	772	394	311
CFR (%)	59	37	27	34	31	31	29	37	35	32	33	23
H-A												
Cases	147	107	120	116	167	189	240	258	304	304	271	280
CFR (%)	57	36	40	39	45	48	55	45	49	50	48	39
% H-A												
Cases	51	25	26	24	29	33	40	32	34	28	41	47
Deaths	51	24	34	27	37	47	56	37	41	38	50	60

NOTE. *P* values for total period of study (12 selected years) by age group show a case-fatality ratio (CFR) higher for H-A than for C-A for all groups: <30 years, *P* < 0.0001; 30–59 years, *P* < 0.001; ≥60 years, *P* < 0.001.

* "Cases" is used here to indicate patients.

† *P* < 0.05. All *P* values are for comparisons of C-A and H-A cases.

‡ *P* > 0.05.

§ *P* < 0.01.

|| *P* < 0.001.

Hemolytic Streptococcus. Most of the strains tested were group A, some in 1969 and 1972 were group B, but all β-hemolytic strains other than enterococci are included. There were 53 cases due to these organisms in 1935; the

number of cases declined to a low of four in 1955. Thereafter, the number each year varied from 21 to 58. The CFR for all bacteremic cases of hemolytic streptococcal infections was high (72%) in 1935 and dropped to 36% in 1947. There

Table 9. Occurrence of and mortality rate from community-acquired (C-A) and hospital-acquired (H-A) bacteremic infections due to some gram-positive cocci at Boston City Hospital during 12 selected years, 1935–1972.

Organism, type of infection	Year											
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972
<i>Streptococcus pneumoniae</i> (pneumococcus)												
C-A												
Cases	66	129	96	100	104	73	76	90	118	119	96	99
CFR (%)*	76	36	25	43	28	24	25	36	21	28	29	15
H-A												
Cases	34	11	3	4	3	3	6	10	9	8	8	9
CFR (%)	82	45	(1)	(1)	(0)	(2)	(4)	20	33	38	38	11
Total												
Cases	100	140	99	104	107	76	82	100	127	127	104	108
CFR (%)	78	36	25	42	27	26	28	34	22	28	30	15
β -hemolytic <i>Streptococcus</i> (not group D)												
C-A												
Cases	15	10	13	10	8	3	20	24	49	30	14	25
CFR (%)	80	90	38	60	38	0	16	29	45	30	43	36
H-A												
Cases	38	8	1	0	2	1	1	8	9	14	14	20
CFR (%)	71	25†	0		(2)	0	0	38	44	64	36	25
Total												
Cases	53	18	14	10	10	4	21	32	58	44	28	45
CFR (%)	72	61	36	60	50	0	14	31	45	41	39	31
<i>Streptococcus viridans</i>												
C-A												
Cases	22	39	41	34	31	37	49	36	41	43	30	34
CFR (%)	55	33	17	9	29	8	29	22	27	16	20	21
H-A												
Cases	20	14	9	11	5	8	10	10	8	18	14	29
CFR (%)	40	29	44	18	0	38	20	20	0	22	21	31
Total												
Cases	42	53	50	45	36	45	59	46	49	61	44	63
CFR (%)	48	32	22	11	25	13	27	22	22	18	20	25
Enterococci												
C-A												
Cases	0	2	6	25	14	15	15	29	24	40	25	11
CFR (%)		(1)	(2)	20	29	33	20	55	50	40	48	18
H-A												
Cases	0	2	5	8	10	9	8	16	20	21	22	27
CFR (%)		(1)	(4)	50	30	44	50	38	35	38	59	44
Total												
Cases	0	4	11	33	24	24	23	45	44	61	47	38
CFR (%)		(2)	54	27	38	38	30	49	43	39	53	40
<i>Staphylococcus aureus</i>												
C-A												
Cases	37	106	68	80	120	134	107	81	76	97	44	31
CFR (%)	54	26	18	29	28	28	27	41	41	21	32	32
H-A												
Cases	29	39	32	37	61	82	118	102	103	95	60	56
CFR (%)	38	38	22	43	33	44‡	51†	54	50	45†	53‡	38
Total												
Cases	66	145	100	117	181	216	225	183	179	192	104	87
CFR (%)	47	30	19	33	29	34	40	48	46	33	44	36

NOTE. For all 12 years combined, $P < 0.001$ for *S. pneumoniae*; $P > 0.05$ for all other *Streptococcus* species; and $P < 0.0001$ for *S. aureus*. Where statistical difference between case-fatality ratios (CFRs) for C-A and H-A infections is not indicated, $P > 0.05$.

* Where number of cases is small, the number of deaths is shown instead (in parentheses).

† $P < 0.001$. All P values are for comparisons of C-A and H-A cases.

‡ $P < 0.05$.

Table 10. Occurrence of and mortality rate from community-acquired (C-A) and hospital-acquired (H-A) bacteremic infections due to some gram-negative bacilli and *Candida* at Boston City Hospital during 12 selected years, 1935–1972.

Organism, type of infection	Year											
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972
<i>Escherichia coli</i>												
C-A												
Cases	10	23	46	30	38	46	44	42	79	86	60	48
CFR (%)*	30	53	26	43	39	35	48	52	34	38	35	23
H-A												
Cases	17	23	24	15	25	22	17	25	35	54	33	49
CFR (%)	41	26	42	27	60†	59	53	44	69‡	38	36	53§
Total												
Cases	27	46	70	45	63	68	61	67	114	140	93	97
CFR (%)	37	39	30	38	48	43	49	49	45	36	35	38
<i>Klebsiella-Enterobacter</i>												
C-A												
Cases	0	0	22	18	24	21	21	22	30	39	31	22
CFR (%)			23	22	54	43	57	59	57	38	32	32
H-A												
Cases	0	0	24	23	21	32	27	36	41	41	65	69
CFR (%)			63†	48	57	69	48	44	61	46	54†	45
Total												
Cases	0	0	46	41	45	53	48	58	71	80	96	91
CFR (%)			42	37	54	58	52	50	59	43	47	42
<i>Proteus</i>												
C-A												
Cases	0	6	25	38	33	31	19	15	20	29	22	13
CFR (%)		(2)	34	21	24	45	53	47	85†	66	41	54
H-A												
Cases	6	1	16	22	23	34	30	18	12	21	30	19
CFR (%)	(5)	(1)	44	41	65§	56	73	50	42	48	70†	63
Total												
Cases	6	7	41	60	56	65	49	33	32	50	52	32
CFR (%)	(5)	(3)	39	28	41	51	65	48	69	58	58	59
<i>Pseudomonas aeruginosa</i>												
C-A												
Cases	0	0	4	8	8	7	4	4	19	15	0	7
CFR (%)			(2)	13	25	57	(1)	(2)	32	47		43
H-A												
Cases	1	5	4	8	9	7	16	16	29	35	26	15
CFR (%)	(0)	(3)	(3)	75†	67	71	69	38	59	74	81	73
Total												
Cases	1	5	8	16	17	14	20	20	48	50	26	22
CFR (%)	(0)	(3)	63	44	47	64	55	40	48	66	81	64
<i>Candida</i>												
C-A												
Cases	0	0	0	0	16	9	7	5	1	6	5	2
CFR (%)					13	22	29	40	(0)	33	40	(1)
H-A												
Cases	0	0	0	0	6	6	8	9	8	9	23	28
CFR (%)					50	50	63	44	73	56	52	59
Total												
Cases	0	0	0	0	22	15	15	14	9	15	28	30
CFR (%)					23	33	47	43	67	47	50	57

NOTE. For the total of all cases in the 12 selected years, $P > 0.05$ for *E. coli*; $P < 0.05$ for *Klebsiella-Enterobacter*; $P < 0.01$ for *Proteus*; $P < 0.001$ for *P. aeruginosa*; and $P < 0.001$ for *Candida*. Where statistical difference between case-fatality ratios (CFRs) for C-A and H-A infections is not indicated, $P > 0.05$.

* Where number of cases is small, the number of deaths is shown instead (in parentheses).

† $P < 0.05$. All P values are for comparisons of C-A and H-A cases.

‡ $P < 0.001$.

§ $P < 0.01$.

|| See footnote 1 to text (p. 329).

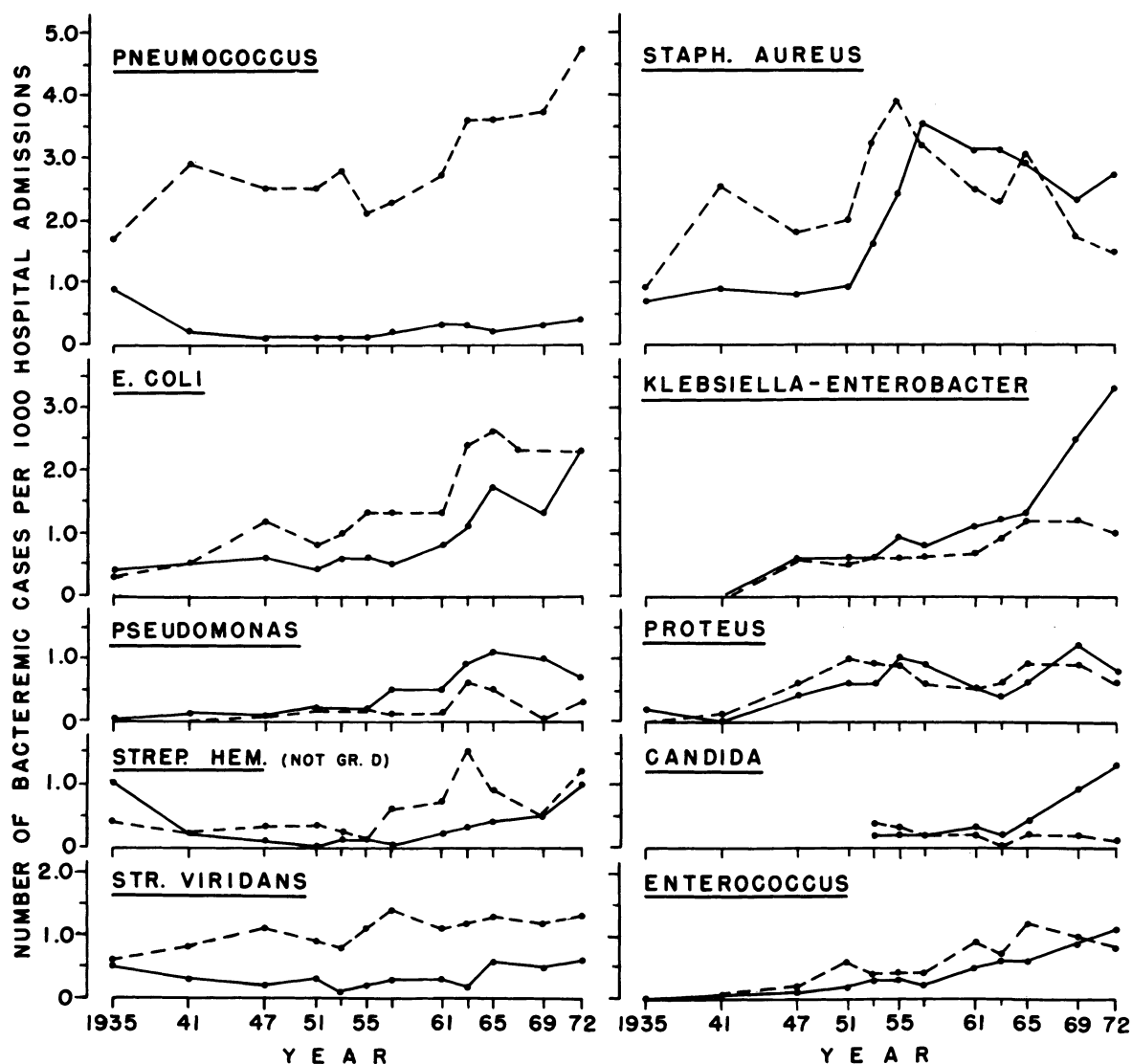


Figure 1. Incidence of community-acquired (broken lines) and hospital-acquired (solid lines) bacteremic infections due to some common pathogenic organisms at Boston City Hospital during 12 selected years, 1935-1972.

were no deaths in 1955, but subsequently the CFR increased when the number of cases increased; it rose to 45% in 1963 and then dropped to 31% by 1972. In 1935, nearly three-fourths of the cases were H-A, but after 1947, H-A cases were rare or did not occur until after 1957. After that year, the proportion of cases that were H-A increased. The CFR was generally similar in C-A and H-A cases. The early decline in incidence of H-A hemolytic streptococcal bacteremic infections is clearly evident in figure 1, which also shows the steady rise in incidence of C-A bac-

teremic infections in the late 1950s and early 1960s and the steady increase in H-A cases after 1957.

Viridans streptococci. The number of bacteremic cases due to this group of α - or non-hemolytic streptococci other than enterococci has fluctuated within moderate limits. The mortality rate among these cases was nearly 50% in 1935 but dropped to a low of 11% by 1951; since then it has ranged between 13% and 27%. Although nearly one-half of the cases in 1935 were considered to be H-A by the criteria used, only about one-sixth of the cases were H-A each year

after that (figure 1). The CFRs were not greatly different in C-A and H-A cases.

Enterococcus (group D Streptococcus). Bacteremias due to enterococci were rarely encountered before the sulfonamides came into wide use, but such cases subsequently became quite frequent, particularly after 1947, when penicillin and streptomycin achieved wide use. From 1947 on, the number of cases of enterococcal bacteremia in the selected years varied irregularly between 23 and 61, and the CFR varied between 27% and 54%, with a median of about 40%. The proportions of these cases that were H-A also varied widely, and the CFR among C-A cases was similar to that among H-A cases each year and also varied considerably. The incidence per 1,000 admissions rose more or less steadily and, interestingly, was generally higher for C-A cases (figure 1).

S. aureus. The number of bacteremic infections due to *S. aureus* increased fairly steadily during the first seven years of this study and rose from 66 in 1935 to a high of 225 in 1957; since then, the number has fluctuated (generally downward) and was 87 in 1972. The CFRs for all cases dropped from 47% in 1935 to a low of 19% in 1947 and since then have ranged between 33% and 48%. H-A cases represented anywhere from less than one-third to nearly two-thirds (in 1972) of bacteremic infections due to *S. aureus*. Except in 1935, the CFRs were generally higher among the H-A than among the C-A cases, and the differences were significant in four of the years. The incidence (figure 1) of H-A staphylococcal bacteremias was relatively constant during the first four selected years, rose sharply during the 1950s, and dropped slowly but steadily after that time. C-A cases had higher incidences than H-A cases until 1953 but have been lower since then, although both types followed the same downward trend.

E. coli. Bacteremic infections due to *E. coli* were the only ones due to gram-negative bacilli (other than *Salmonella*) that were seen with any frequency before the sulfonamides came into use. There were 27 cases at this hospital in 1935, and in subsequent years the numbers ranged from 46 to 70 until 1961; in each of the last four years their number varied from 93 to 140 cases. The CFRs in all cases of *E. coli* bacteremia dropped from 37% and 39% in the first two years

to 30% in 1947 and since then have ranged between 35% and 49%. In the first two years and again in 1972, one-half or more of the cases were H-A, but in the other years, most of the cases (up to 72%) were C-A. The incidence rose for both groups from 1957 through 1965 and then tended to stabilize (figure 1). The CFRs fluctuated over about the same range in both the C-A and H-A cases and were higher in H-A cases; the differences were statistically significant in 1953, 1963, and 1972.

Klebsiella-Enterobacter. Except for occasional cases of bacteremic "Friedländer's pneumonia" (due to *Klebsiella pneumoniae*, now classified as type 1 or 2), bacteremic infections due to either *Klebsiella* or *Enterobacter* were rarely encountered, and none was identified or reported in 1935 and 1941.¹ In 1947 there were 46 cases, and in the ensuing years selected for this study, the numbers increased from 41 in 1951 to a high of 96 in 1969; there were 91 cases in 1972. CFRs ranged from 37% to 59% for all cases. About one-half to more than three-fourths of these cases were H-A. CFRs were higher among H-A than among C-A cases in several years, but the difference was statistically significant ($P < 0.05$) only in 1947 and 1969. The incidence of C-A cases remained low and stable throughout the 1950s (figure 1), while the incidence of H-A cases was rising; the incidence of the latter increased sharply in 1969 and 1972, while the rates for C-A cases remained stable.

Proteus. Small numbers of cases of bacteremic infection due to *Proteus* were encountered in 1935 and 1941. From 1947 on there were 32–65 cases per year in the 10 selected years of the study. The CFRs ranged between 28% and 41% in 1947–1953 but then varied from 48% to 69% (median, 58%) in the last seven years. The proportion of cases that were H-A varied from 37% to 61% in different years, and the CFRs were generally higher among H-A cases than

¹ There were two cases of such bacteremic Friedländer's pneumonia (with one death) in 1935 and three cases (all fatal) in 1941; these cases are not listed in table 10. There were also six such cases with only one survivor in 1947 (included among the 22 C-A cases shown in table 10). Similar cases are included among *Klebsiella-Enterobacter* for subsequent years in table 11.

among C-A cases; the difference was statistically significant in 1953 ($p < 0.01$) and 1969 ($p < 0.05$), but the CFR was significantly higher among C-A cases in 1963 ($p < 0.05$). The incidence of C-A cases was very similar to that of H-A cases throughout the 12 years, showing broad peaks in the early 1950s and again in the late 1960s (figure 1).

P. aeruginosa. As with proteus infection, cases of bacteremia due to *P. aeruginosa* were quite rare before penicillin and streptomycin came into wide use at this hospital. Between 1951 and 1972 there were 14–26 cases in each of the selected years except in 1963 and 1965, when there were 48 and 50 cases, respectively. From 50% to 100% of these cases were H-A. CFRs ranged from 44% to 81%; CFRs among H-A cases were generally not significantly different from those among C-A cases. Figure 1 shows the regularly higher incidence for H-A than for C-A cases.

Candida. Bloodstream invasion by *Candida* was not reported in the first four selected years, but after 1953 the number of cases of candidemia ranged from nine to 30. Except in 1953 and 1955, most of the cases were H-A. The CFRs in all cases varied from 23% to 67% and were generally higher among H-A cases, but the differences were not statistically significant. The incidences stayed low for both C-A and H-A cases through 1963, after which the rates of the latter rose steadily (figure 1).

Relative frequency of etiologic agents. The distribution of pathogens in all cases of bacteremic infection² and the fatal cases for each of the 12 selected years are shown in tables 11 and 12, respectively. The pneumococcus was the most frequent organism causing bacteremia at Boston City Hospital in 1935, accounting for nearly one-third of all cases and for > 40% of all deaths from bacteremic infection that year. After 1941 these proportions dropped to a low of 12.5% of cases and 9% of deaths in 1955 and subsequently remained within that range, except for an increase in the proportion of cases with a lower percentage of deaths in the last year of the study.

² Each significant pathogen is here equated with one case to provide a total of 100% of cases.

β -Hemolytic streptococci other than enterococci accounted for more than one-sixth of all bacteremic cases and one-fifth of all deaths among these cases in 1935. This proportion dropped precipitously after the introduction of sulfonamides and then more gradually until 1955, when 1% of all bacteremic cases and no deaths were due to β -hemolytic streptococci. Since that year the proportion of such cases has been rising until, in 1972, they accounted for about 6% of all cases and deaths.

The proportion of cases caused by viridans streptococci dropped from nearly 14% in 1935 to a low of about 6% of all cases in 1953. Deaths due to these organisms accounted for nearly 11% of all bacteremic deaths in 1935 and 1941; this proportion dropped to a low of 3% in 1951. After this time the proportion of both cases and deaths associated with *Streptococcus viridans* bacteremia stabilized at or about these low levels. There were no bacteremic enterococcal infections in 1935, but a small proportion of cases was due to these organisms in 1941; the proportion increased to a peak of nearly 7% of cases and 5.4% of deaths in 1951 and fluctuated at or below this level in subsequent years.

Bacteremia due to *S. aureus* showed the most striking changes. Beginning with more than one-fifth of all bacteremic cases and one-sixth of all the deaths due to bacteremic staphylococcal infections in 1935, the proportions increased to nearly 36% of all cases and deaths in 1957 and then dropped steadily to a low of about one-eighth of all cases and deaths in 1972. The high proportion of cases and of deaths in 1941 was associated with a high incidence of staphylococcal infections complicating influenza A, which occurred in epidemic form in that year [8].

E. coli was responsible for about 9% of all bacteremic cases and about 5% of all deaths in 1935. The proportion of cases increased somewhat, ranging from about 10% to 14% during the other years of the study. *E. coli* accounted for 10.2%–15.4% of all the deaths in each of the 11 subsequent years.

Klebsiella-Enterobacter were not encountered or were not recognized as pathogens in 1935 and 1941 (except for the occasional cases of Friedländer's pneumonia with bacteremia, as already noted), but from 1947 on they accounted

Table 11. Percentage distribution of selected pathogens in cases of bacteremic infection at Boston City Hospital during 12 selected years, 1935–1972.

Organism	Year											
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972
<i>Streptococcus pneumoniae</i> (pneumococcus)	32.5	31.3	20.9	21.1	18.3	12.5	13.1	14.3	14.6	12.9	15.5	15.3
Hemolytic <i>Streptococcus</i> (not group D)	17.2	4.0	3.0	2.0	1.7	0.7	3.3	4.6	6.7	4.5	4.2	6.4
<i>Streptococcus viridans</i>	13.6	11.8	10.6	9.1	6.1	7.4	9.4	6.6	5.6	6.2	6.8	8.9
Enterococci	0	0.9	2.3	6.7	4.1	3.9	3.7	6.4	5.1	6.2	3.7	5.4
<i>Staphylococcus aureus</i>	21.4	32.2	21.1	23.7	30.9	35.4	35.9	26.1	20.6	19.5	15.5	12.3
<i>Escherichia coli</i>	8.8	10.2	14.8	9.1	10.8	11.1	9.7	9.6	13.1	14.2	13.9	13.7
<i>Klebsiella-Enterobacter</i>	...*	...	9.7	8.3	7.7	8.7	7.7	8.3	8.2	8.1	14.3	13.3
<i>Proteus</i>	1.9	1.6	8.7	12.1	9.6	10.7	7.8	4.7	3.7	5.1	7.7	4.5
<i>Pseudomonas aeruginosa</i>	0.3	1.1	1.7	3.4	2.9	2.3	3.2	2.9	5.5	5.1	3.9	3.1
<i>Candida</i>	3.8	2.5	2.4	2.0	1.0	1.5	4.2	4.2
Other	4.2	7.1	7.2	4.5	4.3	4.9	3.8	14.6	16.0	16.7	10.6	12.9

* Leaders indicate cases not reported. See also footnote 1 to text (p. 329) regarding *Klebsiella*.

for about 8% of all cases until 1969; in that year the proportion increased to 14.3%, and it was 13.3% in 1972. Fatal cases due to these organisms accounted for 9%–14% of all fatal bacteremic infections each year but increased to 17% and 17.5% in 1969 and 1972, respectively.

Proteus (all species) accounted for a small percentage of all cases and deaths in 1935 and 1941, but this proportion increased to between 9% and 12% of cases between 1947 and 1955, dropping irregularly to about 4% in most of the ensuing years. *Proteus* accounted for 10%–13% of deaths between 1947 and 1957 and for a smaller proportion in most of the subsequent years.

P. aeruginosa bacteremia was rare in 1935 but increased in incidence to about 3% of all bac-

teremic cases in 1951; the proportion remained at or around that level until 1961 and was somewhat higher in most of the years after that. The proportion of fatal cases attributed to *Pseudomonas* followed the same pattern except at a somewhat higher level, associated with the high fatality rate of these infections (table 10). Candidemia either was not occurring or was ignored prior to 1953; it constituted only a small proportion of blood-invasive infections until 1969 and 1972, when about 4% of all cases and about 5% and 8% of all deaths were associated with candidemia.

The “other pathogens” included the less common aerobic infections such as *Salmonella*, *Haemophilus influenzae*, *Neisseria*, *Providencia*, atypical pseudomonads, Mimosae, *Serratia*, *Listeria*, and others. The occurrence of systemic

Table 12. Percentage distribution of selected pathogens in fatal cases of bacteremic infection at Boston City Hospital during 12 selected years, 1935–1972.

Organism	Year											
	1935	1941	1947	1951	1953	1955	1957	1961	1963	1965	1969	1972
<i>Streptococcus pneumoniae</i> (pneumococcus)	41.7	32.5	17.5	26.3	14.4	9.0	9.2	11.9	8.0	10.0	11.7	6.7
Hemolytic <i>Streptococcus</i> (not group D)	20.9	7.0	3.5	3.6	2.5	0	1.2	3.5	7.4	5.0	4.2	5.8
<i>Streptococcus viridans</i>	10.7	10.8	7.7	3.0	4.5	2.7	6.4	3.5	3.1	3.0	3.4	6.7
Enterococci	0	1.3	4.2	5.4	3.5	4.0	2.8	7.7	5.4	6.7	4.5	5.8
<i>Staphylococcus aureus</i>	16.6	27.4	13.3	23.4	26.2	33.2	35.8	30.8	23.6	17.5	17.4	12.9
<i>Escherichia coli</i>	5.3	11.5	15.4	10.2	14.9	13.0	12.0	11.5	14.5	14.1	12.5	15.4
<i>Klebsiella-Enterobacter</i>	...*	...	14.0	9.0	12.4	13.9	10.0	10.1	11.9	9.4	17.0	17.5
<i>Proteus</i>	2.7	1.9	11.2	10.2	11.4	14.8	12.9	5.6	6.3	8.0	11.4	7.9
<i>Pseudomonas aeruginosa</i>	0	1.9	3.5	4.2	4.0	4.0	4.8	2.7	6.5	9.1	7.6	5.8
<i>Candida</i>	2.5	1.8	2.8	2.1	1.7	1.9	5.3	7.9
Other	2.1	5.7	9.8	4.8	4.0	3.6	2.0	10.5	11.7	15.2	4.9	7.5

* Leaders indicate cases not recorded.

Table 13. Occurrence of bacteremic infections due to *Mima*, *Herellea*, and *Serratia* at Boston City Hospital during five selected years, 1961–1972.

Organism	Year				
	1961	1963	1965	1969	1972
<i>Herellea vaginicola</i>	16/32*	24/55	15/58	4/15	8/39
<i>Mima polymorpha</i>	0/7	3/12	6/27	0/7	0/1
<i>Serratia marcescens</i>	...†	5/13	5/12	2/4	5/20

* Number of fatal cases/total number of cases.

† None reported.

salmonellosis during the same 12 selected years at this hospital was documented recently [9], as were some aspects of infections with *H. influenzae* [10], *Serratia* [11], and *Mimeae* [12]. The proportion of all "other" bacteremic infections fluctuated over a wide range and was associated in some years with the endemic appearance of certain uncommon pathogens. Table 13 shows the occurrence of bacteremia due to three species of gram-negative bacilli during each of the last five years of the study.

Discussion

The study reported here is unique in several ways. It covers changes in occurrence of and mortality from serious bacterial infections over the entire era of modern antimicrobial therapy. It is based on the "hardest" available data, namely, the demonstration of pathogenic bacteria by uniform and standard methods and the analysis of "nonjudgmental" data concerning the patients in whose blood the organisms were cultured (i.e., age, location in the hospital by service [medical or surgical] to which the patient was assigned, the time after admission when the first blood was drawn for the culture that yielded the pathogen, and the final outcome [survival or death] during the episode when that organism was cultured). The conditions under which the material was collected and the methods used have remained the same, and the study has been done under the continuous direction of the same individuals since the first report that covered the selected years through 1957 [4].

In that report, data were presented on the increasing numbers of cultures processed in the bacteriology laboratory and the percentage of autopsies in fatal cases during the period covered; it

was thought, however, that most of the increase in number of cultures was due to the replicate cultures made before, during, and after therapy (related to the selection and control of specific therapy) rather than to an increase in the number and kinds of patients from whom blood and other materials were taken for culture. Infections due to strictly anaerobic bacteria were all excluded for the reasons given. Distortions were avoided by arbitrary exclusion of all organisms generally considered to be contaminants, even when multiple cultures from infected sources were obtained, as in some cases of verified infection with *S. epidermidis*. Although not given, the annual number of cultures had stabilized and had been declining more recently with the drop in the number of admissions.

The particular years included in this study were selected to reflect the changes in occurrence of and mortality from serious infections associated with the introduction and intensive use of the succession of new and effective antibacterial agents, beginning with sulfanilamide and extending through the new tetracyclines, penicillinase-resistant and "broad-spectrum" penicillins, cephalosporins, aminoglycosides, antifungal agents (flucytosine), lincomycins, and nalidixic acid. During the period covered, however, other important changes have taken place in the practice of medicine. Our understanding of disease processes has increased greatly, the diagnostic and other therapeutic procedures available to the physician have greatly increased, and important changes have occurred in the demographic character of the patients treated in large, inner-city hospitals such as Boston City Hospital [1]. The data presented here do not permit assessment of the contributions of these important factors to the changes documented in this report.

In recent years, increasing attention has been given to the distinction between infections acquired in the community and those acquired within the hospital. Some studies have suggested that different types of infection affect different kinds of patients, have different causative organisms, and differ in severity of the illness and mortality [1, 2, 13, 14]. Data from the present study of bacteremic infections afforded a good opportunity to document such changes in the oc-

currence and character of H-A and C-A bacteremic infections during the years in which increasing numbers of effective antibacterial agents were introduced and used extensively. The empirical observation, based on a review of records of 910 cases from 1963 and 1972, indicated that classification of cases into those in which the first positive blood culture was obtained before the third day in the hospital and those whose first positive blood culture was obtained on or after the third day in the hospital correlated well with clinical and laboratory features of C-A and H-A infections, respectively, particularly if certain obvious deviations, such as those noted in table 1, are allowed. This fact permitted a simple and effective way to classify the cases presented here and provided a fairly reliable approximation of the marked differences between the characteristics of these infections. A recent study of the susceptibility of gram-negative bacilli isolated during 1972 from patients with C-A and H-A infection, with use of the same criterion for distinguishing types, also showed clear differences between organisms isolated in the two categories of infection [15].

The data presented in this paper confirm the general impression that the incidence of serious H-A bacterial infections, as evidenced by bacteremia first demonstrated on or after the third day of hospitalization, has increased markedly and steadily during the last two decades. The data also show that, since 1947, the CFRs in H-A bacteremic infections have been higher and, in nine of the 10 selected years, significantly higher than in C-A cases (table 4). Important differences between the changes in incidence and mortality in C-A and H-A cases were shown in patients on the surgical services as well as in those on medical services (tables 5 and 6).

The striking changes in the age distribution and in the mortality rate for different decades of life during the first 10 selected years were shown in the previous report [5]. In this paper, we compared three broad age groups (< 30, 30–59, and \geq 60 years old) in relation to distribution and mortality for all cases, for C-A cases, and for H-A cases of infection. In 1935, about one-fifth of all cases were in the oldest age group, and the other four-fifths were almost equally divided among the youngest and the middle age groups.

In that year, one-half of the deaths were among patients of the middle age group, about one-fifth were in the youngest group, and about 30% were in patients \geq 60 years of age. However, in the oldest age group, the proportion of all cases that were H-A was higher than that of C-A cases and was significantly higher for all 12 years combined and for five of the selected years from 1953–1963. On the other hand, the proportion of all cases that were in the young and middle age groups declined at first and then increased somewhat, and that in the oldest age group increased until the incidence in that group accounted for about one-half of the cases in 1953; the proportion then declined until 1972, when the oldest patients still accounted for 40% of the cases and patients in the other two age groups each accounted for about half of the other 60%. In this shift, the proportion of C-A cases was generally higher, and in most years significantly higher, than that of H-A cases in the youngest age group whereas the reverse was true in the oldest patients; among these patients the proportion of H-A cases was generally and significantly higher in most of the selected years (table 7).

In general, CFRs were higher and in several years significantly higher in H-A than in C-A cases among the younger and middle age groups; however, among the oldest patients (\geq 60 years), CFRs were high and generally about equal in C-A and H-A cases in each of the selected years (table 8).

The major changes in the occurrence of and mortality from bacteremic infections due to the most common bacterial species during the selected years from 1935–1965 were dealt with in previous papers [4, 5]. Most striking was the decline in the proportion of bacteremic cases and deaths due to pneumococcus and β -hemolytic *Streptococcus*, the rise during the 1950s of cases and deaths due to *S. aureus*, the relatively stable proportion of cases and deaths due to viridans streptococci, and the appearance of and increase in the numbers of cases and deaths due to enterococcus.

During the last two years of the study, the number of pneumococcal infections and of infections due to viridans streptococci remained stable, but the CFR of the former dropped in 1972. The number of bacteremic β -hemolytic strep-

tococcal and enterococcal infections and the CFR in those cases fluctuated somewhat, and the number of those due to *S. aureus* continued to decline, but the CFR in those cases did not change much (table 10). H-A infections provided only a minor portion of the cases due to pneumococci and viridans streptococci. Most cases of hemolytic streptococcal bacteremia in 1935 were H-A. This type of infection declined in incidence and essentially disappeared during the 1950s but has been occurring and increasing in incidence (though to a lesser extent among H-A than C-A cases) during the 1960s. There were more C-A than H-A infections due to *S. aureus* during the first four selected years; the number of both C-A and H-A cases due to this species increased after that. The number of H-A cases increased more than that of C-A cases, so that the number of H-A cases exceeded that of C-A cases during five of the last six selected years. Enterococcal infections increased in parallel among both C-A and H-A cases, but the former were generally more frequent (figure 1).

Among the gram-negative bacillary infections (table 10), C-A cases due to *E. coli* were more frequent than H-A cases, except in 1972, when the two categories were about equal in incidence. Bacteremias due to *P. aeruginosa* were mostly H-A, as were those due to *Klebsiella-Enterobacter*, particularly during the last two years studied. *Proteus* bacteremias were about evenly divided among C-A and H-A cases. *Candidemias* were predominantly H-A (figure 1). The CFRs were generally much higher in the gram-negative than in the gram-positive bacterial infections.

Comparisons of the data presented here with those reported from other hospitals have been difficult because of differences in the manner in which the data were collected and in the type of material presented; nor can the rates of C-A bacteremic infections (even those due to specific bacteria) be taken as an accurate reflection of the incidence of such infections in the community from which these patients are derived. In general, however, the relative decline in the proportion of bacteremias due to gram-positive organisms and the corresponding increase in the proportion due to gram-negative bacilli and *Can-*

didia, the changes in occurrence of *S. aureus* infections over the years, the high CFRs, and the increasing occurrence of H-A infections (particularly with gram-negative bacilli) have been noted by many others, as is pointed out by Eickhoff [2] and McCabe [16]. Eickhoff [2] noted the similarity between the distribution of pathogens during 1969–1970 in 68 hospitals included in surveys by the Center for Disease Control and the distribution in 1970 at Boston City Hospital; the exceptions were higher proportions of *E. coli* in the former and of *Klebsiella-Enterobacter* and *Pseudomonas* in the latter. At the University of Minnesota Hospitals, where there have been about one-half as many hospital admissions annually and an appreciably lower death rate for all admissions (4.2%–5.6%, as compared with 6.1%–6.8% at Boston City Hospital during about the same years), the rate for gram-negative bacteremia per 1,000 admissions was considerably lower, but the CFRs were very similar [13, 17]. About 84% of the gram-negative bacteremias at the University of Minnesota were H-A, and the mortality rate was higher in H-A than in C-A cases among adults but lower among children [17].

Although the data presented here show a rising incidence of serious bacteremic infections (particularly those due to gram-negative bacilli and *Candida*) in spite of the increasing availability and use of effective antimicrobial agents, they do not permit assessment of the effects of any possible misuses or abuses of these agents within the hospital. Indeed, attempts to evaluate the use of antibiotics in this hospital have suggested that, in general, they have been used properly and under good control [18, 19].

References

1. Brachman, P. S., Eickhoff, T. C. Proceedings of the International Conference on Nosocomial Infections, Center for Disease Control, 1970. American Hospital Association, Chicago, 1971. 334 p.
2. Eickhoff, T. C. Hospital infections. DM (Disease-a-Month). Year Book Medical Publishers, Chicago, September 1972. 40 p.
3. Alexander, J. W. Nosocomial infections. Curr. Prob. Surg. Year Book Medical Publishers, Chicago, August 1973. 54 p.
4. Finland, M., Jones, W. F., Jr., Barnes, M. W. Occur-

- rence of serious bacterial infections since introduction of antibacterial agents. *J.A.M.A.* 170:2188–2197, 1959.
5. Finland, M. Changing ecology of bacterial infections as related to antibacterial therapy. *J. Infect. Dis.* 122:419–431, 1970.
 6. McGowan, J. E., Jr., Barnes, M. W., Finland, M. Host-pathogen-drug interactions in surgical patients with bacteremia. *Surg. Gynecol. Obstet.* 138:50–54, 1974.
 7. Finland, M., Barnes, M. W. Changing etiology of bacterial endocarditis in the antibacterial era. *Ann. Intern. Med.* 72:341–348, 1970.
 8. Finland, M., Peterson, O. L., Strauss, E. Staphylococcal pneumonia occurring during an epidemic of influenza. *Arch. Intern. Med.* 70:183–205, 1942.
 9. Finland, M., Barnes, M. W. Salmonellosis and shigellosis at Boston City Hospital. Part 1. Relationship to bacteremic infections due to enterobacteria. *J.A.M.A.* 229:1183–1186, 1974.
 10. McGowan, J. E., Jr., Klein, J. O., Bratton, L., Barnes, M. W., Finland, M. Meningitis and bacteremia due to *Haemophilus influenzae*: occurrence and mortality at Boston City Hospital in 12 selected years, 1935–1972. *J. Infect. Dis.* 130:119–124, 1974.
 11. Wilfert, J. N., Barrett, F. F., Kass, E. H. Bacteremia due to *Serratia marcescens*. *N. Engl. J. Med.* 279:286–289, 1968.
 12. Daly, A. K., Postic, B., Kass, E. H. Infections due to organisms of the genus *Herellea*. *Arch. Intern. Med.* 110:580–591, 1962.
 13. Matsen, J. M. The sources of hospital infection. *Medicine (Balt.)* 52:271–277, 1973.
 14. Graybill, J. R., Marshall, L. W., Charache, P., Wallace, C. K., Melvin, V. B. Nosocomial pneumonia—a continuing major problem. *Am. Rev. Resp. Dis.* 108:1130–1140, 1973.
 15. McGowan, J. E., Jr., Garner, C., Wilcox, C., Finland, M. Antibiotic susceptibility of gram-negative bacilli isolated from blood cultures; results of tests with 35 agents and strains from 169 patients at Boston City Hospital during 1972. *Am. J. Med.* 57:225–238, 1974.
 16. McCabe, W. R. Gram-negative bacteremia. *DM (Disease-a-Month)*. Year Book Medical Publishers, Chicago, December 1973. 38 p.
 17. Dupont, H. L., Spink, W. W. Infections due to gram-negative organisms: an analysis of 860 patients with bacteremia at the University of Minnesota Medical Center, 1958–1966. *Medicine (Balt.)* 48:307–332, 1969.
 18. McGowan, J. E., Jr., Finland, M. Infection and antibiotic usage at Boston City Hospital: changes in prevalence during the decade 1964–1973. *J. Infect. Dis.* 129:421–428, 1974.
 19. McGowan, J. E., Jr., Finland, M. Usage of antibiotics in a general hospital: effect of requiring justification. *J. Infect. Dis.* 130:165–168, 1974.