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# A 5-Year Surveillance Study of 44,691 Isolates of *Haemophilus influenzae* Project Beta-Alert 1993–1997

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**Beta-Alert is a surveillance program developed in 1993 to monitor the percentage of β-lactamase-producing *Haemophilus influenzae* isolates obtained from specimens submitted to regional commercial laboratories. The results of this study demonstrate that levels of β-lactamase producers have remained between 31 and 38% in the United States over the past 5 years.**

*Haemophilus influenzae* causes a variety of community-acquired infections, including acute otitis media, sinusitis, bronchitis, and pneumonia. *H. influenzae* was considered to be susceptible to all β-lactam antibiotics until 1974, when β-lactamase-mediated ampicillin resistance was first reported (5). In a national surveillance study of 5,750 isolates of *H. influenzae* conducted in 1993, the percentage of β-lactamase producing *H. influenzae* isolates was 33% (10). In a study of 1,539 clinical isolates of *H. influenzae* collected in 1994 to 1995 from 30 U.S. centers, a prevalence of β-lactamase-mediated ampicillin resistance of 36% was reported (4).

The purpose of this analysis was to identify trends in the percentage of β-lactamase producers. Thousands of *H. influenzae* isolates are identified by SmithKline Beecham Clinical Laboratories (SBCL) each year from a variety of clinical specimens. Data from isolates of *H. influenzae* were collected at regional SBCL sites between 1993 and 1997. Atlanta (Ga.), Philadelphia (Pa.), Seattle (Wash.), St. Louis (Mo.), and Los Angeles (Calif.) sites participated in the study from 1993 through 1997. Dallas (Tex.) and Chicago (Ill.) sites participated beginning in 1994. In 1997, 10 additional laboratories were added to the list of study sites. The new study sites were located in Detroit (Mich.), Houston (Tex.), Lexington (Ky.), Minneapolis (Minn.), New Orleans (La.), Nashville (Tenn.), New York (N.Y.), San Francisco (Calif.), Tampa (Fla.), and Boston (Mass.).

Specimens were collected from several locations, including physician offices, clinics, and hospital clinical microbiology laboratories. The specimens were transported to one of the 17 regional SBCL sites described above. Specimens were processed, plated, and incubated according to standard microbiological methods (6).

Isolates of *H. influenzae* were identified by standard methods in specimens from blood, sputum, eye, nasal, ear, sinus, and throat (7). *H. influenzae* isolates were not serotyped. *H. influenzae* was identified from throat specimens if the isolate was present as the predominating organism or as "heavy" growth. All isolates were assessed for β-lactamase production by using the nitrocefin β-lactamase test (Cefinase; Becton-Dickinson Microbiology Systems, Cockeysville, Md.) as established by the National Committee for Clinical Laboratory Standards (9). Daily quality control testing was performed according to manufacturers' recommendations. Patient results were reported only when quality control results were acceptable.

A total of 44,691 isolates of *H. influenzae* collected during a 5-year period (1993 to 1997) were analyzed. The isolates were analyzed to determine the overall percentage of β-lactamase production. In addition, the data provided the percentages and numbers of isolates that produce β-lactamase categorized by specimen source, patient age, month of collection, SBCL site, state, and zip code. The percentage of β-lactamase producers ranged from 31% (1994) to 38% (1996). The number and percentage of β-lactamase-producing *H. influenzae* isolates analyzed per year are shown in Table 1. Seven regional SBCL sites participated in the Beta-Alert surveillance program from 1993 to 1997 (Table 2). A total of 35,963 isolates were collected from these seven regional SBCL sites. The percentage of *H. influenzae* isolates producing β-lactamase were 33, 31, 37, 38, and 36%, for each year from 1993 to 1997, respectively.

Children 6 years old and under provided the majority of specimens, accounting for 39% of the isolates, and had the highest percentage of β-lactamase-producing isolates: 35, 41, 41, and 37%, respectively, during the period from 1994 to 1997. In 1993, the age group with the highest percentage of β-lactamase producing *H. influenzae* was the 22- to 60-year-old group (37%). The results of this study are consistent with previously published data (5), in which isolates from children 5 years old and under had the highest frequency of β-lactamase production. This may be related to high enrollment of children in day care centers, increased use of antimicrobial agents in children, lack of patient compliance, and/or inadequate dosing schedules (1, 3). Of the 44,691 *H. influenzae* isolates collected

TABLE 1. Number and percentage of β-lactamase producing *H. influenzae* isolates, by year

| Year | No. of participating labs | No. (%) of isolates | |
|---|---|---|---|
| | | Total | Producing β-lactamase |
| 1993 | 7 | 5,750 | 1,901 (33) |
| 1994 | 7 | 5,426 | 1,691 (31) |
| 1995 | 7 | 8,306 | 3,105 (37) |
| 1996 | 7 | 8,646 | 3,298 (38) |
| 1997 | 17 | 16,563 | 5,643 (34) |
| Total | 17 | 44,691 | 15,638 (35) |

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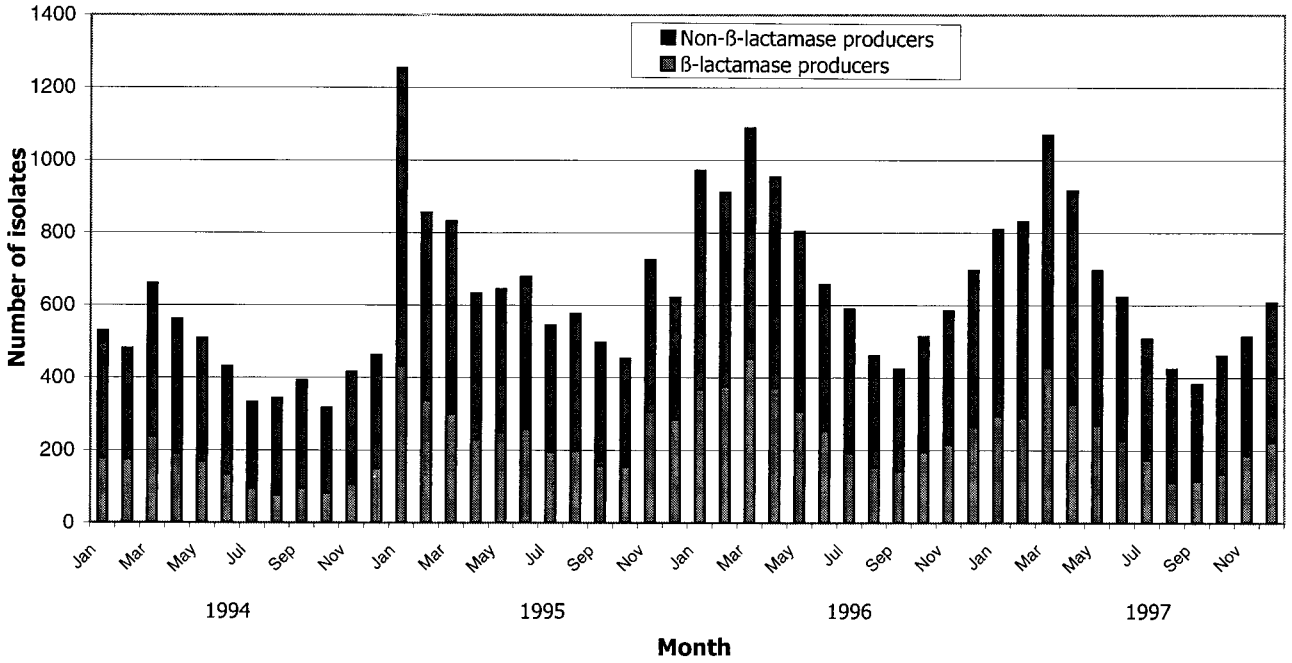


FIG. 1. Variation in the number of β-lactamase- and non-β-lactamase-producing *H. influenzae* isolates by month from 1994 to 1997 ($n$ = 38,941).

during the period from 1993 to 1997, 19,384 were throat isolates, 7,898 were sputum isolates, 5,007 were eye isolates, 5,212 were nasal isolates, 2,723 were ear isolates, 703 were sinus isolates, 102 were blood isolates, 2,408 were from other sources, and 1,254 had no source indicated. The source groups with the highest percentage of β-lactamase-producing organisms during the period from 1993 to 1997 were ear (46%), eye (49%), and sinus (46%). These results are consistent with previously published data (5). The high percentages of β-lactamase producers in ear specimens may have clinical significance, since *H. influenzae* is responsible for 20 to 35% of acute otitis media infections (2).

Seasonal variation in the isolation of *H. influenzae* from clinical specimens was observed. The isolation frequency was highest in January and March and lowest in October.

The numbers of β-lactamase- and non-β-lactamase-producing *H. influenzae* organisms isolated in each month of the surveillance period are shown in Fig. 1.

The percentage of β-lactamase-producing *H. influenzae* isolates was analyzed by zip codes along the U.S.-Mexican and U.S.-Canadian borders. The percentage of β-lactamase producers was not calculated for countries that had fewer than 10 isolates. During the period from 1994 to 1997, the percentage along the U.S.-Mexican border was 30% ($n$ = 331) and the percentage along the U.S.-Canadian border was 35% ($n$ = 248).

In conclusion, the results of this study demonstrate that the percentage of β-lactamase-producing *H. influenzae* isolates in the United States has remained high, between 31 and 38%, for the past 5 years.

TABLE 2. Percentage of isolates that produce β-lactamase, categorized by SBCL site from 1994 to 1997

| SBCL site[a] | % β-Lactamase producers ($n$)[b] | | | |
|---|---|---|---|---|
| | 1994 (5,426) | 1995 (8,306) | 1996 (8,646) | 1997 (7,835) |
| Atlanta | 40 | 44 | 43 | 39 |
| Chicago | 27 | 37 | 47 | 40 |
| Dallas | 42 | 41 | 37 | 33 |
| Philadelphia | 11 | 34 | 40 | 38 |
| Seattle | 34 | 35 | 33 | 26 |
| St. Louis | 32 | 46 | 42 | 39 |
| Los Angeles | 28 | 30 | 30 | 31 |
| Total | 31 | 37 | 38 | 36 |

[a] Atlanta, Philadelphia, Seattle, St. Louis, and Los Angeles participated in 1993 (number of isolates = 5,750); however, individual values for each laboratory are not available. Chicago and Dallas participated from 1994 to 1997.

[b] The total number of isolates was 30,213.

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