

Major Regional Variation in *Haemophilus influenzae* Resistance in the Western Pacific: Results from SENTRY Western Pacific Plus (WP+) 1998-2000

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Abstract (updated)

Background: *Haemophilus influenzae* (HINF) remains an important cause of lower respiratory tract infection worldwide, and resistance to β -lactams is emerging in many countries. We examined the susceptibility of HINF to a broad range of antimicrobials as part of the SENTRY worldwide surveillance program in the WP+ (17 hospitals in 8 countries). **Methods:** Isolates from a range of sources, including respiratory secretions and blood were tested by broth microdilution to more than 25 antimicrobials, according to NCCLS criteria and breakpoints where available. Collections were made each year from 1998 to 2000. **Results:** At least 20 isolates were available for testing from each country except the Philippines (N=2) where this organism was an infrequent clinical isolate. Apart from these sites, β -lactamase production was demonstrated in 4% of HINF from mainland China to 27% in Singapore and Hong Kong. Resistance to tetracycline was low except in Hong Kong (7%) and mainland China (4%) and while resistance to trimethoprim-sulfamethoxazole was common in most countries except Japan (4%), ranging from 12% in Australia to 65% in mainland China. Resistance to chloramphenicol was common only in Hong Kong (10%) and Singapore (8%). β -lactamase-negative ampicillin-resistant (BLNAR) strains were noted in Japan, with 10% having MICs of 2 mg/L and 7% >2 mg/L. These strains resulted also in significant rates of resistance to cefuroxime in Japan (12% non-susceptible). Overall 63% of ampicillin-non-susceptible HINF in Japan were β -lactamase-negative. Similar strains were detected in South Africa, with 6% having an ampicillin MIC of 2 mg/L, none >2 mg/L, but 7% were non-susceptible to cefuroxime. **Conclusions:** There is marked regional variation in the resistance patterns of HINF in WP+, with each country demonstrating a distinctly different pattern. HINF is an uncommon isolate in some WP+ countries.

Introduction

Haemophilus influenzae is an important cause of upper and lower respiratory tract infection worldwide. Antimicrobial resistance, especially to β -lactams but also some other drug classes is gradually worsening in many countries. We examined the susceptibility of *H. influenzae* in the Asia-Pacific region to a broad range of antimicrobials as part of the SENTRY surveillance program

Methods

Isolates

Isolates of *H. influenzae* in the SENTRY surveillance program from a range of sources, including the upper and lower respiratory tract, and blood, were collected by 17 different hospitals from eight countries or locales over defined seasonal intervals between April 1999 and December 2000. All strains were sent to a central reference laboratory (Women's and Children's Hospital, Adelaide, Australia) for testing.

Susceptibility testing

All isolates were tested against more than 25 antimicrobials by the broth microdilution method using commercially prepared trays (TREK™ Diagnostic Systems Limited, UK), according to NCCLS standards [NCCLS, 2001]. Breakpoints for resistance were those recommended by the NCCLS.

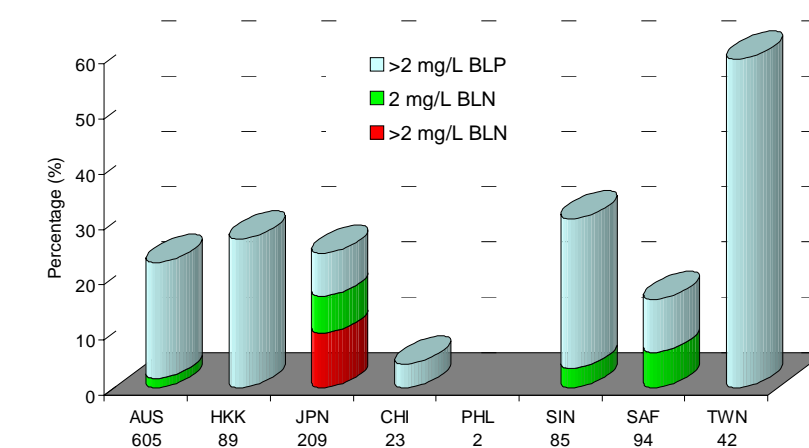
Results

- One site in the Philippines found only two isolates over the survey period. All other laboratories supplied at least 20 strains of *H. influenzae*.
- β -lactamase production rates ranged from 4% in Mainland China to 27% in Singapore and Hong Kong.
- Tetracycline resistance was only prevalent in Hong Kong (7%) and mainland China (4%)
- Resistance to trimethoprim-sulfamethoxazole was common in most countries, ranging from 12% in Australia to 65% in mainland China. Resistance was uncommon in Japan (4%)
- Chloramphenicol resistance was common in Hong Kong (10%) and Singapore (9%)
- β -lactamase negative, ampicillin-resistant (BLNAR) strains were found in Japan. 10% of strains had MICs of 2 mg/L and 7% > 2 mg/L. These strains contributed to the high rate of resistance to cefuroxime in Japan (12% non-susceptible).
- BLNAR were also detected in South Africa, 6% with an ampicillin MIC of 2 mg/L, none > 2 mg/L. 6% of strains from South Africa were cefuroxime non-susceptible.

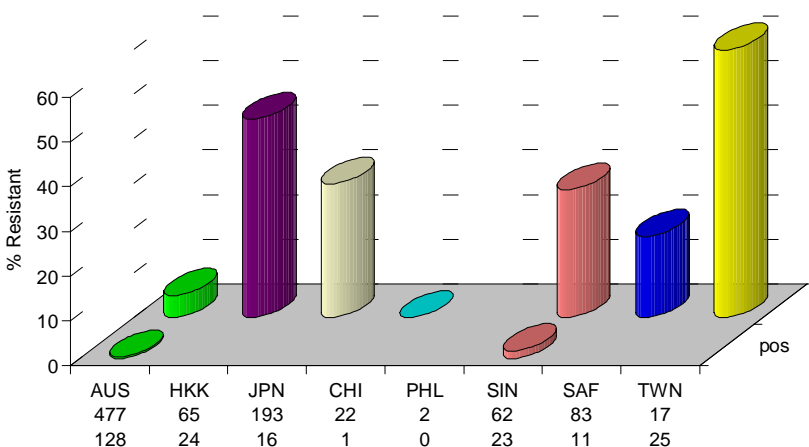
Table 1. *Haemophilus influenzae* Resistance

| Country | N | β lac | Amp >2 | Chl >4 | Tet >4 | Cfu >8 | SXT >0.5 |
|----------------|------|-------------|--------|--------|--------|--------|----------|
| Australia | 605 | 21.2 | 21.0 | 1.2 | 0.7 | 0.2 | 11.9 |
| Hong Kong | 89 | 27.0 | 27.0 | 10.1 | 6.7 | 0 | 28.1 |
| Japan | 209 | 7.7 | 17.7 | 2.1 | 1.4 | 12.0 | 4.3 |
| Mainland China | 23 | 4.3 | 4.3 | 0 | 4.3 | 0 | 65.2 |
| Philippines | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Singapore | 85 | 27.1 | 27.1 | 8.9 | 2.4 | 0 | 22.4 |
| South Africa | 94 | 11.7 | 9.6 | 2.1 | 0 | 0 | 28.7 |
| Taiwan | 42 | 59.5 | 59.5 | 35.7 | 14.3 | 0 | 61.9 |
| Region | 1149 | 19.8 | 21.4 | 4.3 | 1.9 | 2.3 | 15.0 |

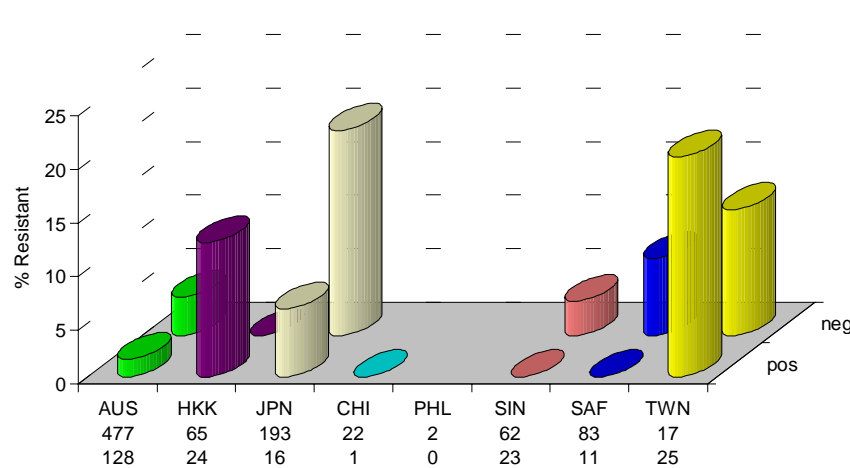
Amp(amox)icillin



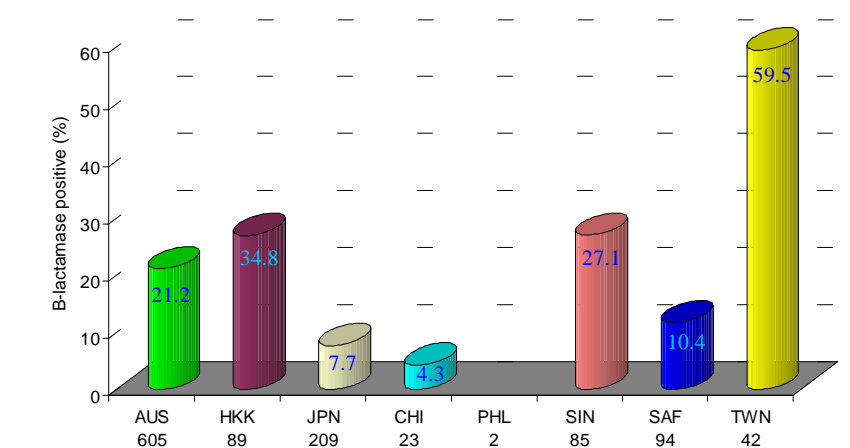
Chloramphenicol



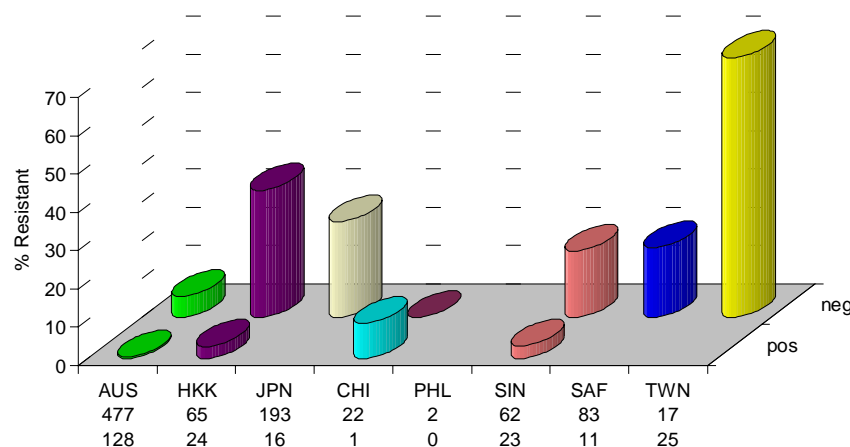
Cefuroxime



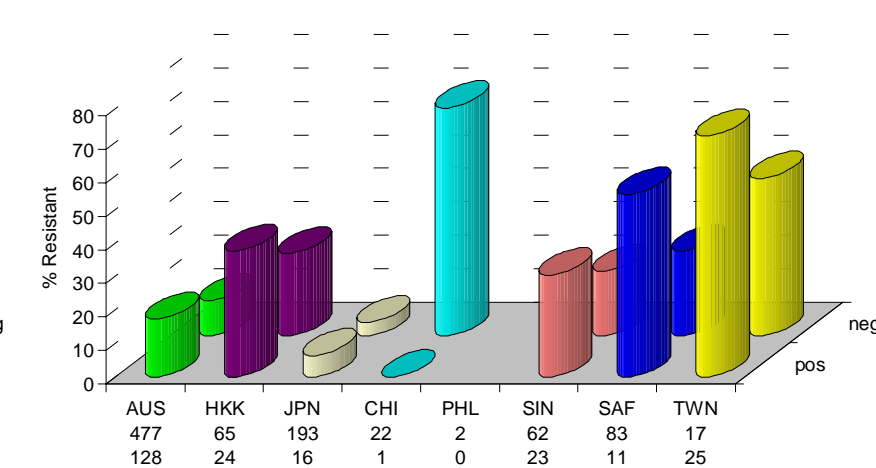
β -lactamase



Tetracycline



Trimethoprim/sulphamethoxazole



Discussion and Conclusions

- There is marked regional variation in the resistance profiles of *H. influenzae* in the Asia-Pacific region
- BLNAR were increasingly found in Japan
- Cefuroxime resistance was associated with the emergence of BLNAR strains
- Over 60% of isolates from Taiwan were β -lactamase producers, and many were multi-resistant

References

- 1 National Committee for Clinical Laboratory Standards. Methods for Dilution Antimicrobial Susceptibility Testing for Bacteria That Grow Aerobically, 4th Ed. Approved Standard M7-A4. National Committee for Clinical Laboratory Standards, Wayne, Pa.
- 2 NCCLS. Performance standards for Antimicrobial Susceptibility Testing; 11th Informational Supplement. M100-S11. NCCLS 2001; Wayne, Pa

Acknowledgments

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