identified with the PASCO system (Difco Laboratories, Detroit, MI, USA) and susceptibilities to a range of antimicrobial agents were determined using the same system and according to the recommendations of the manufacturer. The susceptibility status was defined as outlined in NCCLS guidelines. Results were confirmed with the API Listeria kit (bioMérieux, Marcy L'Etoile, France) and a standard disc-agar diffusion antibiogram. The isolate was agglutinated with both listeria O polyvalent antiserum and listeria O antiserum type 4 (Difco). It exhibited resistance to gentamicin (MIC > 8 mg/L), streptomycin (MIC > 1000 mg/L), chloramphenicol (MIC > 16 mg/L), and clindamycin (MIC > 2 mg/L) and moderate susceptibility to tobramycin (MIC = 8 mg/L), while it remained fully susceptible to ampicillin (MIC < 2 mg/L), ampicillin/sublactam (MIC < 4/2 mg/L), erythromycin (MIC < 1 mg/L), tetracycline (MIC < 8 mg/L), co-trimoxazole (MIC < 4/76) and vancomycin (MIC < 4 mg/L). The strain also displayed susceptibility to amikacin and netilmicin as judged by the standard disc-agar diffusion antibiogram. The infant was given ampicillin/sublactam iv for 3 weeks and recovered without sequelae.

When plasmid DNA analysis was performed by the alkaline lysis method, a single plasmid of approximately 37 kb was visualized. However, conjugal transfer of the plasmid was not achieved because the resistance determinants were lost when the isolate was subcultured without antibiotic selection. In addition, the plasmid was not visualized when the isolate reverted to susceptible. Similar observations, concerning the instability of R-plasmids in listerial strains, have been reported by other authors.

This is the first case report of human infection with L. monocytogenes displaying reduced susceptibility to the aminoglycosides gentamicin and tobramycin. Previous reports have described plasmid-mediated resistance to tetracycline, chloramphenicol, erythromycin, clindamycin and streptomycin. In these studies, conjugal plasmids, although with discrepancies in their resistance determinants, were of approximately the same molecular weight as the one visualized in our isolate. These data, in conjunction with current observations of easily transferable R-plasmids from several Gram-positive donors to listeria might indicate the potential spread of multi-resistant L. monocytogenes strains. However, the relative instability of resistance determinants in listeria could partly explain the infrequent detection of resistant L. monocytogenes from clinical specimens.

References


Decreasing trend of multiresistant Salmonella typhi in Bangladesh

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Sir,

Increasing frequency of multi-resistant salmonella on the Indian subcontinent1–3 prompted the suggestion that ciprofloxacin5 or ceftriaxone6 should be the empirical choice of treatment for enteric fever. All these reports and suggestions prompted our clinical colleagues in the field of paediatrics to prescribe ceftriaxone. Ciprofloxacin is also prescribed as most of our patients cannot afford to buy ceftriaxone and the cost of hospital stay for its parenteral administration. In Bangladesh, the treatment of typhoid fever with intravenous ceftriaxone, in a child weighing 10 kg, costs US$150. On the other hand, therapy of the same child with oral ciprofloxacin costs only US$5.5. Further, in countries like Bangladesh, empirical therapy is a common practice as isolation of the organism is often jeopardized by lack of facilities or inadequate and/or improper antibiotic use before culture. Although caution has been expressed about routine use of ciprofloxacin,5 indiscriminate use of the available first-choice antibiotic is a common practice in Bangladesh.6

Since 1994, we have isolated another 576 strains of Salmonella typhi from the blood of paediatric patients at Dhaka Shishu Hospital (DSH) and the Popular Diag-
nostic Centre (PDC). The former is the only paediatric hospital at national level and the latter is one of the largest private diagnostic laboratories at Dhaka, with the highest number of referred patients from general practitioners. Both the centres have the same catchment area. Strains were isolated by the lysis–centrifugation method as described earlier.7 The minimum inhibitory concentrations (MICs) for the isolates, of six different antibiotics (ampicillin, co-trimoxazole, chloramphenicol, tetracycline, ceftriaxone and ciprofloxacin), were determined by a microbroth dilution method. Resistance to each drug was calculated on the basis of recommended breakpoints for Enterobacteriaceae.1,8 The results were analysed by EPI Info 6.02.

Yearly analysis of resistance among the strains revealed a remarkable decreasing rate of resistant strains. Multidrug resistant (MDR) strains were 46.5%, 29.7% and 17.8% in 1994, 1995 and 1996 in that order (P > 0.0001). When the PDC and DSH strains were analysed separately more resistance was noticed among the DSH strains. However, the decreasing trend of drug resistance was observed to be similar at both the institutes and for all antibiotics (Table, Figure).

This change is possibly a reflection of the decreased use of ampicillin, co-trimoxazole and chloramphenicol in treating enteric fever since the availability of ceftriaxone and ciprofloxacin in 1991, in Bangladesh. Present resistance patterns of S. typhi and their trends should also be monitored in other neighbouring countries. Further, in countries where typhoid fever is endemic, such as Bangladesh, investigation and treatment of typhoid fever cases at private laboratories and home, respectively, are the rule rather than exception. Usually, the patients are only admitted to the hospitals in case of initial treatment failure or complications. Therefore, strains isolated only from hospital in-patients, as shown in all previous reports including ours, may demonstrate higher rate of resistance which does not reflect the real picture in endemic areas of the particular country or community.

### References


### Table. Resistance pattern of *S. typhi* strains in Bangladesh, 1994–1996

<table>
<thead>
<tr>
<th>Year</th>
<th>Medical centre</th>
<th>(no. of strains)</th>
<th>ampicillin</th>
<th>co-trimoxazole</th>
<th>chloramphenicol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1994</td>
<td>DSH</td>
<td>(n = 59)</td>
<td>76.3</td>
<td>93.2</td>
<td>71.2</td>
</tr>
<tr>
<td></td>
<td>PDC</td>
<td>(n = 214)</td>
<td>42.1</td>
<td>54.2</td>
<td>40.7</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>(n = 273)</td>
<td>49.5</td>
<td>62.6</td>
<td>47.3</td>
</tr>
<tr>
<td>1995</td>
<td>DSH</td>
<td>(n = 52)</td>
<td>65.4</td>
<td>88.5</td>
<td>55.8</td>
</tr>
<tr>
<td></td>
<td>PDC</td>
<td>(n = 141)</td>
<td>31.2</td>
<td>36.9</td>
<td>30.5</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>(n = 193)</td>
<td>40.1</td>
<td>50.5</td>
<td>37.0</td>
</tr>
<tr>
<td>1996</td>
<td>DSH</td>
<td>(n = 12)</td>
<td>41.7</td>
<td>41.7</td>
<td>33.3</td>
</tr>
<tr>
<td></td>
<td>PDC</td>
<td>(n = 89)</td>
<td>16.9</td>
<td>18.0</td>
<td>18.0</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>(n = 101)</td>
<td>19.8</td>
<td>20.8</td>
<td>19.8</td>
</tr>
</tbody>
</table>

a All the strains were sensitive to ceftriaxone and ciprofloxacin.

b DSH, Dhaka Shishu Hospital; PDC, Popular Diagnostic Centre.
Intravenous desensitization to ceftazidime in cystic fibrosis patients

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Sir,

Most patients with cystic fibrosis (CF) are colonized with *Pseudomonas aeruginosa* from a very early age and this organism is responsible for much of the morbidity and mortality of the disease. P. aeruginosa colonization is extremely difficult to eradicate and regular intravenous courses of antibiotics are necessary in most patients to maintain lung function. Ceftazidime monotherapy is currently our first-line anti-pseudomonal antibiotic because of the lack of a need for blood level monitoring, the favourable sensitivity profile and the good therapeutic response. However, a number of patients develop allergy to this antibiotic. Desensitization to ceftazidime was, therefore, attempted when alternative parenteral antibiotics became limited.

During a 4-year period, 13 patients (of whom seven had previously received ceftazidime) developed allergic reactions on 16 occasions. These ranged from maculopapular rash (nine patients) and urticarial rashes (three patients), muscular pain (two patients), bronchospasm (one patient) and hypotension (one patient). The antibiotic was stopped in seven patients; others continued the course with antihistamine and steroid cover. The reactions were seen immediately after the first dose in two patients but were delayed for 2–12 days in the others. While four of the 13 patients tolerated ceftazidime on subsequent occasions and two patients received alternative antibiotics, seven required desensitization.

The protocol for intravenous desensitization we adopted was similar to that used previously for other *β*-lactam antibiotics. On the first day ceftazidime, 50 mg dissolved in 500 mL of 0.9% saline (0.1 mg/mL), was infused in a stepwise manner (steps 1–8) to give an approximately doubling dose of ceftazidime every 15 min (Table). Subsequently the concentration of ceftazidime was increased to 1 mg/mL (500 mg/500 mL 0.9% saline) and steps 9–14 were followed. Pulse, respiration and oxygen saturation were monitored and patients were observed for adverse reactions such as rash, anaphylaxis or bronchospasm. If a reaction occurred, the infusion was stopped, antihistamines and corticosteroids were given if required and the infusion was restarted cautiously two stages below the earlier infusion rate. On the second day the ceftazidime concentration was doubled (1 g/500 mL 0.9% saline) and the rate increased stepwise. A normal therapeutic dose was next administered as an infusion over 1 h and, if tolerated, patients were discharged to complete their antibiotic course at home supervised by the CF nurse practitioner.

A total of seven patients had nine desensitizations performed over a period of 4 years. The patients experienced no problems with the procedure and no major systemic reactions were observed. One patient had a recurrence of bronchospasm but desensitization was continued and completed successfully after treatment of the bronchospasm with salbutamol, hydrocortisone and antihistamines. Following desensitization, two patients again developed rashes on the seventh and twelfth day of their therapeutic course; these patients were desensitized for a second time and this was successful in one patient but the other had a recurrence of the rash and treatment was discontinued.

In serious respiratory exacerbations in patients with CF, broad-spectrum penicillins and third-generation cephalosporins may be the drugs of choice according to bacterial sensitivities. If allergic reactions are encountered during a course of treatment, an alternative antibiotic is usually chosen. Alternatively, the same antibiotic can be continued together with drugs to suppress the reaction, or desensitization considered when alternative antibiotics are unavailable.

Intravenous desensitization was preferred over the subcutaneous route because serial dilutions could be administered and altering the rate and concentration of drug infused was straightforward. Infusions also avoid repeated needle pricks, an important consideration in paediatric patients.

We did not use skin testing in our study because antibodies to third-generation cephalosporins appear to be directed against the side chains rather than the common ring structure. Thus despite a negative skin test, an allergic reaction to the drug is still possible.

Successful desensitization to broad-spectrum penicillins and aminoglycosides has been reported in patients with CF. This report demonstrates that intravenous desensitization to cephalosporins is a safe and effective procedure and the technique described may be adapted for use with other antibiotics.