INTRODUCTION

Drug use evaluation (D.U.E.) is a joint obligation of the medical staff, pharmacy staff, and other hospital departments such as health records and microbiology. It is a criteria-based, ongoing, planned and systematic process for monitoring and evaluating the prophylactic, therapeutic, and empiric use of drugs to help assure that they are used appropriately, safely, and effectively. A D.U.E. program is part of the Canadian Council of Health Facilities Accreditation Standards. The Ontario Hospital Association and the Ontario Ministry of Health have recommended the develop-
ment of such programs as having benefit to the patient and the hospital. Several reports in the literature have documented the success of D.U.E. programs in improving patient care while reducing drug expenditures.

Cefuroxime, a second generation cephalosporin, has been used extensively at our hospital. From April 1990 to March 31, 1991, cefuroxime accounted for $145,000 of the annual drug budget, making this agent the highest cost-generating drug at this hospital. Therefore, the need for a drug use evaluation of cefuroxime was apparent. Two separate evaluations were performed, one in adult patients and one in pediatric patients. The purpose of this paper is to present the evaluation of its use in pediatric patients.

The objectives were the following: (1) to evaluate if the prescribing of cefuroxime met the approved criteria for use; (2) to assess whether interventions made by a clinical pharmacist could influence the prescribing when therapy did not meet the criteria.

METHODS
From March 5, 1991 to May 15, 1991, the use of cefuroxime in pediatric patients was studied. During the concurrent use evaluation, interventions were made to influence the prescribing of cefuroxime according to approved criteria for use, through educational means, while the patient was receiving the drug. The approved criteria for use were developed by a pediatrician, medical microbiologist, a pediatric clinical pharmacist, and the D.U.E. coordinator based on their clinical experience and recently published recommendations. The criteria were approved by the Pharmacy and Therapeutics Committee and distributed to all the pediatricians prior to the evaluation.

The pediatric liaison pharmacist collected the demographic and clinical information about each patient on the nursing unit for whom cefuroxime was prescribed, and recorded it on the data collection form. The pharmacist assessed the initial cefuroxime therapy (i.e., route, dose, and interval), monitored the clinical progress of the patient (i.e., temperature, white blood cell count, renal function, and radiographic findings), culture and sensitivity data, and concomitant antimicrobial therapy. The pharmacist assessed each case according to the criteria for cefuroxime use within 72 hours after the prescription was written and determined whether intervention was warranted using the available clinical, and culture and sensitivity test data. Therapy was considered not to meet criteria if the physician did not change therapy when culture and sensitivity results showed that the organism was sensitive to a less expensive antibiotic which could have been as equally effective as cefuroxime. Therapy was also considered to not meet criteria if appropriate samples (blood, urine, wound, lumbar puncture, etc.) were not obtained for culture and sensitivity tests prior to the initial cefuroxime dose. The pharmacist could intervene by either telephoning or speaking directly with the prescriber. The pharmacist recorded the suggested change and the physician's response on the data collection form. After an intervention, the pharmacist followed the patient's progress for 48 hours. All data collection forms were returned to the Coordinator, D.U.E. after cefuroxime therapy was discontinued or upon discharge. All data collection forms were reviewed by the Coordinator, D.U.E., a medical microbiologist, and a pediatrician to assess whether or not therapy met the approved criteria for use and the outcome of pharmacist-physician interactions. Chart reviews were done on all cases that were designated as not meeting criteria.

RESULTS
Thirty-five pediatric patients were prescribed cefuroxime during the concurrent use evaluation. All courses of cefuroxime were empiric therapy (Table I). Community-acquired pneumonia accounted for 21 treatment courses in which cefuroxime was prescribed (60% of total). It was also prescribed empirically in otitis media (eight cases), meningitis (two cases), bacteremia/septicemia (one case), septic hip (one case), and exacerbation of asthma (two cases).

The mean duration of intravenous cefuroxime therapy in community-acquired pneumonia, otitis media, and meningitis were 3.0, 2.3, and 2.0 days respectively, after intravenous therapy, oral therapy was prescribed.

Whether cefuroxime therapy met criteria for use or not is also shown in Table I. Eighty-six percent (eighteen courses) of the empiric treatment of community-acquired pneumonia were deemed to meet criteria. Eighty-eight percent (seven courses) of the empiric use of cefuroxime in pediatric patients admitted for otitis media were deemed to meet criteria. None of the treatment courses for exacerbation of asthma met criteria because culture and sensitivity tests were not ordered, the chest x-ray was negative for pneumonia in one patient and was not done in the other. There were no other signs of infection.

Culture and sensitivity tests
Table I. Patterns of Cefuroxime Use

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>COURSES OF THERAPY* n=35</th>
<th>MEAN DURATION THERAPY (days (range))</th>
<th>CRITERIA MET/CRITERIA NOT MET</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Community- acquired pneumonia</td>
<td>21 (60%)</td>
<td>3.0 (1-7)</td>
<td>18/3</td>
</tr>
<tr>
<td>2. Otitis media</td>
<td>8 (20%)</td>
<td>2.3 (1-3)</td>
<td>7/1</td>
</tr>
<tr>
<td>3. Meningitis</td>
<td>2 (6%)</td>
<td>2.0 (1-3)</td>
<td>0/2</td>
</tr>
<tr>
<td>4. Bacteremia/ Septicemia</td>
<td>1 (3%)</td>
<td>1.0</td>
<td>1/0</td>
</tr>
<tr>
<td>5. Septic hip</td>
<td>1 (3%)</td>
<td>14.0</td>
<td>1/0</td>
</tr>
<tr>
<td>6. Exacerbation of asthma</td>
<td>2 (6%)</td>
<td>2.0</td>
<td>0/2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>35</strong></td>
<td><strong>27/8</strong></td>
<td></td>
</tr>
</tbody>
</table>

* all courses of therapy were empiric

were ordered on various samples. In 25 cases, no organism was isolated, and in five cases no cultures and sensitivity tests were ordered. Four organisms were isolated. The throat swab of a patient suspected of having meningitis grew Streptococcus Group D. It was sensitive to amoxicillin but not to cefuroxime. Another throat swab of a patient with otitis media showed growth of Streptococcus Group A and the sensitivities were not reported. In both circumstances, the streptococcus species were not reported. Respiratory syncytial virus (RSV) was isolated from the nasopharyngeal aspirate of a patient with pneumonia and cefuroxime was subsequently discontinued. Streptococcus pneumoniae was isolated from a blood culture of a patient with pneumonia. Cefuroxime was discontinued and therapy with intravenous penicillin G was instituted.

The pediatric clinical pharmacist intervened in six therapeutic courses which did not meet criteria after available clinical, culture and sensitivity test data were assessed. Three of these interventions were successful. These included changing therapy for suspected meningitis in a thirteen month-old child from cefuroxime to ceftriaxone; discontinuing cefuroxime therapy in a patient with community-acquired pneumonia to 75 mg/kg/day. Interventions were unsuccessful in two cases of suspected pneumonia where the physician was reluctant to discontinue intravenous cefuroxime therapy after the patients had been afebrile for 72 hours and culture and sensitivity tests were negative. The pharmacist suggested the option of switching the patient to oral cefaclor therapy if antibiotic therapy was still needed. The physician did not accept the recommendation but preferred to continue intravenous cefuroxime therapy for seven days. In the other case, the pharmacist suggested discontinuing cefuroxime therapy in a patient that had received 72 hours of intravenous therapy for otitis media. The patient's signs and symptoms had subsided and was afebrile. The physician preferred to continue intravenous therapy for seven days.

**DISCUSSION**

During the evaluation, the most common indication for the use of cefuroxime was community-acquired pneumonia. Eighty-six percent of the cases were considered to meet approved criteria for use and these cases showed radiographic and clinical evidence of pneumonia.

Cefuroxime was prescribed in eight cases of otitis media. Therapy was considered to meet criteria in seven cases because the patients had recurrent otitis media resistant to out-patient therapy or the patient relapsed on cefaclor or other oral antibiotics. Therapy was also considered to meet criteria if the patient was not able to tolerate oral antibiotics due to nausea or vomiting. Therapy was considered not to meet criteria because culture and sensitivity tests were not ordered prior to cefuroxime therapy.

Cefuroxime was prescribed as initial therapy in two patients suspected of having meningitis. In one case, the pharmacist noted the diagnosis and intervened and the drug therapy was changed to ceftriaxone. The lumbar puncture was negative and the patient was treated for six days with ceftriaxone. In the other case, the patient was treated for three days with ceftriaxone and subsequently discharged. These two cases were considered not to meet criteria because cefuroxime is currently not recommended at our hospital for the treatment of meningitis in pediatric patients.

The pediatric clinical pharma-
cist intervened in six therapeutic courses and was successful in three courses. Some of these interventions were made to therapy which initially met criteria before culture and sensitivity data were available, and some involved suboptimal dosage or therapy. Interventions were not made in every cefuroxime order that did not meet criteria because culture and sensitivity results were not back within three days of therapy or upon discharge, no pathogen was isolated in many cases, and therapy was changed by the staff physician after culture and sensitivity tests were available.

In summary, the prescribing of cefuroxime in pediatric patients was evaluated against approved criteria for use. The results of this study indicate that cefuroxime is mainly prescribed for the empiric treatment of community-acquired pneumonia and otitis media.

Seventy-seven percent of the therapeutic courses were found to meet the established criteria for use. This is higher than is reported in the literature perhaps due to the involvement of the Department of Pediatrics in establishing the criteria which are specific to the clinical practice at our hospital. The problems identified with cefuroxime prescribing include its use as initial therapy for meningitis and the finding that in up to 14% of the treatment courses, no samples were sent to microbiology for culture and sensitivity testing. The results of this D.U.E. will be presented to the Pharmacy and Therapeutics Committee and the Department of Pediatrics. The pediatricians will be consulted for suggestions to eliminate the problems identified in the evaluation and ways to further optimize the prescribing of cefuroxime in pediatric patients.

REFERENCES


Appendix A. Criteria for Cefuroxime Use in Pediatric Patients

1. Empiric therapy of cellulitis, septic arthritis, osteomyelitis and pneumonia potentially caused by ampicillin-resistant strains of Haemophilus influenzae.
2. Empiric treatment of epiglottitis or bacterial tracheitis.
4. Treatment of infections (excluding meningitis) caused by ampicillin-resistant strains of Haemophilus influenzae.
5. Inappropriate for the treatment of bacterial meningitis.
6. The recommended dose in infants and children is 75 - 225 mg/kg/day IV or IM in three divided doses Q8H (maximum 1.5 g/dosage).
7. Dosage adjustments are required if estimated creatinine clearance is < 20 mL/min/1.73 m². (Increase dosing interval up to Q48H in moderate and up to Q72H in severe renal impairment).
8. Inappropriate if appropriate samples (sputum, blood, urine, wound, etc.) were not obtained for culture and sensitivity (C&S) prior to initial cefuroxime dose.
Appendix B. Cefuroxime Use Evaluation in Pediatric Patients

<table>
<thead>
<tr>
<th>DATA COLLECTION FORM</th>
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</thead>
<tbody>
<tr>
<td>PHARMACIST</td>
</tr>
<tr>
<td>CEFUROXIME START DATE</td>
</tr>
<tr>
<td>CEFUROXIME DOSE (mg/kg/day)</td>
</tr>
</tbody>
</table>

I. PATIENT DATA:
- Patient Name
- Hospital #
- Age
- Sex
- Weight (IBW) (Kg)
- Admission Date
- Unit
- Prescribing Physician
- Attending Physician

- Indication for Use: Pneumonia
- Bacteremia/Septicemia
- Other
- Date of onset of illness (if obtainable)
- Pertinent Past Medical History: DM
- Otitis Media
- Recurrent Pneumonias
- Other
- Where Infection Acquired: Community
- Hospital
- Allergies

II. CULTURE AND SENSITIVITY DATA
- Not Ordered

<table>
<thead>
<tr>
<th>III. LABORATORY DATA (Complete while patient is on Cefuroxime)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DATE</td>
</tr>
<tr>
<td>------</td>
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<tr>
<td></td>
</tr>
</tbody>
</table>

IV. ANTIBIOTIC THERAPY (Complete until cefuroxime D/C’d)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>Dosage Interval</th>
<th>Start Date</th>
<th>Stop Date</th>
<th>#Doses Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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</tbody>
</table>

V. INTERVENTION
- Therapy Meets Criteria: Yes
- No
- Why?
- If No, Physician Contacted: Yes
- No
- Why not?
- Date
- Physician
- Method of Contact
- Suggested Change
- Response

VI. HOSPITAL EXPENDITURE FOR CEFUROXIME
- 1987 - 1988 $133,000
- 1988 - 1989 $150,000
- 1989 - 1990 $145,000

DAILY DOSE DRUG COST COMPARISON OF FORMULARY ANTIMICROBIALS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost ($)/Day+</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPICILLIN 1-2 g Q6H</td>
<td>3.76 - 7.52</td>
</tr>
<tr>
<td>CEFAZOLIN 1 g Q8H</td>
<td>6.24</td>
</tr>
<tr>
<td>CEFUROXIME 750 mg Q8H</td>
<td>22.65</td>
</tr>
<tr>
<td>CEFUROXIME 1.5 g Q8H</td>
<td>39.96</td>
</tr>
<tr>
<td>CLINDAMYCIN 600 mg Q8H</td>
<td>46.44</td>
</tr>
<tr>
<td>CLINDAMYCIN 900 mg Q8H</td>
<td>6.08 - 6.48</td>
</tr>
<tr>
<td>CLOXACILLIN 1-2 g Q6H</td>
<td>6.08 - 6.48</td>
</tr>
<tr>
<td>AMIKACIN 300 mg/2 mL vial</td>
<td>7.79 *</td>
</tr>
<tr>
<td>PENICILLIN G 1 - 2 mu Q4H</td>
<td>6.36 - 12.72</td>
</tr>
<tr>
<td>VANCOMYCIN 1g Q12H</td>
<td>95.12</td>
</tr>
<tr>
<td>ERYTHROMYCIN 500 mg - 1 g Q6h</td>
<td>19.70 - 39.40</td>
</tr>
</tbody>
</table>

* cost does not include minibag
* cost per vial, not per day