VANCOUVER HOSPITAL & Health Sciences Centre

DRUG AND THERAPEUTICS NEWSLETTER

A Publication of the Department of Pharmacy

December 1997 *Volume 4, Number 4*

In This Issue...

Changes to Formulary	*1*
Updated Policies and Procedures	*1*
CSU Pharmaceutical Sciences Grants & Awards	*2*
Ceftriaxone and Ceftazidime IV-IV Stepdown	*2*
Home IV Antibiotic Program	*5*

Changes to Formulary

Additions

1. Sevoflurane 250mL (Sevorane®)

- inhalational anesthetic for maintenance of general anesthesia

2. Clodronate 400mg capsules (Bonefos®, Ostac®)

- oral bisphosphonate for management of hypercalcemia of malignancy, osteolytic bone metastases and Paget's disease
- cost: $1.87/400mg (comparison etidronate $2.82/400mg)

Deletions

1. Betaxolol 0.5% ophthalmic solution (Betoptic®)

- discontinued by manufacturer
- alternative: Betaxolol 0.25% ophthalmic solution (Betoptic® S)
- according to the manufacturer, both concentrations deliver the same clinical effect

Updated Policies/Procedures

1. Revised Drug Administration Policies

The following changes will be added to the next Parenteral Drug Therapy Manual update:

- **Atropine** may be administered **direct IV rapidly** over a few seconds. The direct IV route is still restricted to nurses in Special and Critical Care areas, the Telemetry unit and Palliative Care Unit. Physicians must administer the drug on other nursing units.

- **Streptokinase concentration** for treatment of occluded catheters has been changed to **25,000units/2mL** (effective December 1, 1997).

- **CSICU nurses may titrate infusions of propofol** downwards post cardiac surgery.

2. Vincristine preparation in minibags

Vincristine will be prepared in minibags unless specifically ordered otherwise, e.g. IV direct or via syringe, to further eliminate the risk of inadvertent intrathecal administration.

EDITORIAL STAFF:
Karen Shalansky, Pharm.D.
Peter Loewen, Pharm.D.
Rubina Sunderji, Pharm.D.
Peter Jewesson, Ph.D.
Any comments, questions or concerns with the content of the newsletter should be directed to the editors. Write to CSU-Pharmaceutical Sciences Vancouver General Hospital, 855 W12th Ave, Vancouver BC V5Z 1M9, send a FAX to 604-875-5267 or e-mail kshalans@vanhosp.bc.ca
Find us on the Web at **www.research.vhhsc.ubc.ca/pharmacy/**

Pharmacy Research Grant

The following group of investigators was awarded one of three grants by the Vancouver Hospital Interdisciplinary Research Grant competition:

- Dr. R. Sunderji, Dr. A. Fung, Dr. K. Shalansky, C. Davies, L. Schwartz, Dr. C. Carter, Dr. K. Gin for their project entitled:
  "A randomized trial of outpatient self-adjusted versus physician managed oral anticoagulation."

Pharmacy Awards

Several members of CSU Pharmaceutical Sciences were recipients of the Canadian Society of Hospital Pharmacists (CSHP), B.C. Branch annual provincial awards for excellence:

1. 1996/97 Highest Rated Hospital Residency Project (Hoechst Marion Roussel Award)

- *"Predictability of the Sheiner-Tozer equation for correcting phenytoin levels in hypoalbuminemic patients."*
  J. Conklin, Dr. K. Shalansky, Dr. J. de Lemos, Dr. M. Jones, Dr. M. Pudek

2. 1996/97 Highest Rated Hospital Pharmacy Resident (Hoffman-La Roche Award)

- Victoria Cox. Victoria is currently a Staff Pharmacist at VHHSC, VGH Site.

3. B.C. Branch Publication Award

- Dr. F. Marra, Dr. C. Marra, Dr. D. Patrick for their paper entitled:
  "Cost effectiveness analysis of azithromycin and doxycycline for Chlamydia trachomatis infection in women: A Canadian perspective." Can J Infect Dis 1997;8:202-8.

Ceftriaxone and Ceftazidime IV-IV Dosage Stepdown Initiative

Amy Wai, B.Sc. (Pharm)
VHHSC Home IV Antibiotic Program

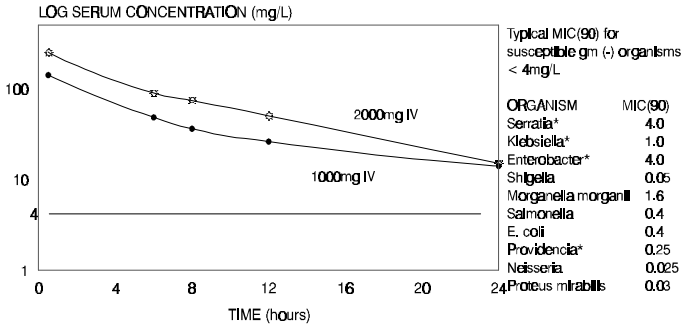
The ceftriaxone and ceftazidime IV-IV dosage stepdown initiative was launched by the CSU Pharmaceutical Sciences in January 1997. A similar program for BMT/leukemia patients has been in place since April 1995. The initiative promotes the stepdown of select intravenous (IV) antibiotics from an initial aggressive dose to a moderate dose for the treatment of serious infections in patients who are clinically stable and still require parenteral therapy. This initiative reduces drug costs while maintaining equivalent patient outcomes. Stepdown from 2g to 1g per dosage interval of ceftriaxone or ceftazidime will save approximately $35.00 in drug costs per day.

What is the rationale for IV-IV dosage stepdown therapy?

While initial aggressive antibiotic dosage regimens are often prescribed for the treatment of serious bacterial infections, subsequent stepdown to moderate doses will achieve adequate serum concentrations for the eradication of most bacterial pathogens. Figures 1 and 2 show typical serum concentrations over time following 1g and 2g IV doses of ceftriaxone and ceftazidime.

A single 30-minute infusion of ceftriaxone 1g will yield a peak serum concentration of approximately 150 mg/L.[1] At the end of a typical 24-hour dosing interval, the serum concentration remains greater than 10 mg/L which is in excess of the MIC_{90} of most susceptible organisms.[1-3]

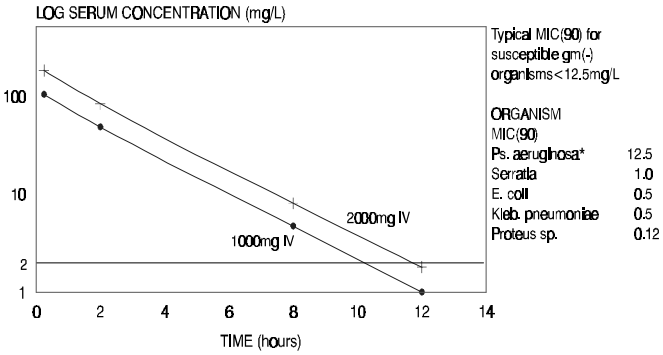
Figure 1. Ceftriaxone serum concentrations versus time



REPORTED MIC(90) VALUES FOR SENSITIVE ORGANISMS
Adapted from: Richards D et al. Drugs 1984;27:469-586

A single 1g dose of ceftazidime will yield a peak serum concentration of approximately 100mg/L.[4] At the end of a typical 8-hour dosing interval, the serum concentration remains greater than 2 mg/L which is in excess of the MIC_{90} of most susceptible organisms except *pseudomonas* species. Studies have also shown that tissue and fluid concentrations of both ceftriaxone and ceftazidime at 1g per dosage interval exceed the MIC_{90} for sensitive organisms.[1,5]

Figure 2. Ceftazidime serum concentrations versus time



Based upon a 1995 review of ceftazidime treatment courses in BMT/leukemia patients, IV-IV stepdown was initiated in 67% of the treatment courses. There was no evidence of any negative impact on patient outcome and an annual cost avoidance of $26,822 was projected.

Which patients are candidates for IV-IV dosage stepdown?

Patients are considered to be potential candidates for stepdown if they are clinically stable, afebrile for 48 hours and show signs of resolving infection. If the patient is able to tolerate oral therapy, stepdown to an appropriate oral antibiotic (IV-PO) is recommended. Patients being treated for central nervous system infections and severe *pseudomonas* infections should generally not receive stepdown therapy.

How is the IV-IV stepdown initiative promoted?

All ceftazidime and ceftriaxone treatment courses for non-BMT/leukemia patients are identified daily using the pharmacy computer. All 2g per dosage interval treatment courses are then reviewed daily by a clinical pharmacist in collaboration with the primary health care team to look for opportunities for stepdown.

What are the results of the IV-IV dosage stepdown initiative to date?

Ceftriaxone

A summary of the outcome of the ceftriaxone IV-IV dosage stepdown initiative is shown in Figure 3. During the first 6 months, there were 220 treatment courses involving initial regimens of 2g per dosage interval initiated in non-BMT/leukemia patients. Of the 96 treatment courses considered eligible for stepdown, 52 (54%) were successfully stepped down in collaboration with the primary health care team, 21 (22%) were discontinued, 13 (14%) were changed to another antibiotic, and 10 (11%) remained on the original regimen.

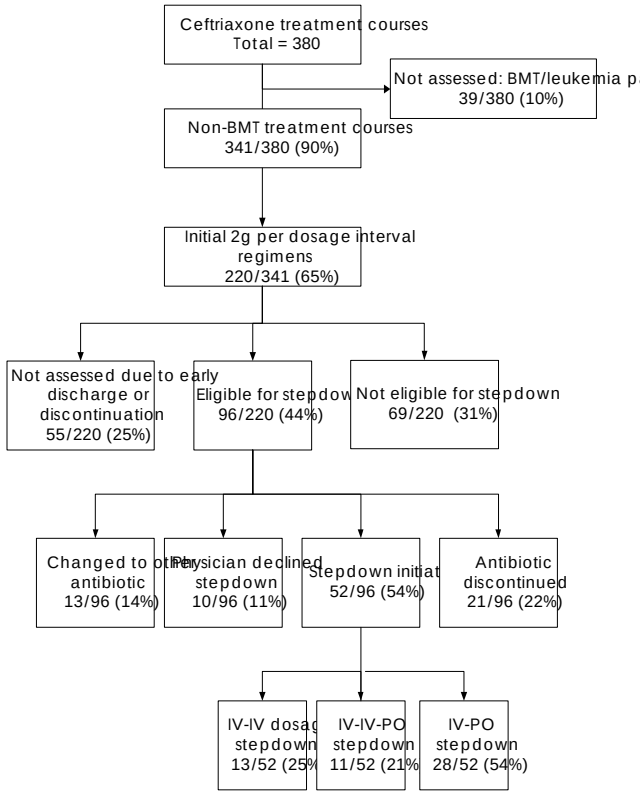


Figure 3. Ceftriaxone treatment course outcomes

Of the 52 stepdown treatment courses, 13 (25%) were IV-IV dosage stepdown only, 11 (21%)

further stepped down to oral (IV-IV-PO) stepdown), and 28 (54%) were converted directly to oral therapy. Stepdown was directly facilitated under the initiative in 60% of these treatment courses. Fifty-one (98%) of the stepdown treatment courses resulted in clinical cure or improvement. This was similar to the outcomes for non-stepdown patients. The treatment course duration for IV-IV stepdown patients was 8.3 days (range 3-21 days), similar to the mean treatment duration of non-stepdown courses (8.7 days, range 4-16 days).

Ceftazidime

A summary of the outcome of the ceftazidime IV-IV dosage stepdown initiative is shown in Figure 4. During the first 6 months, there were 50 treatment courses involving initial regimens of 2g per dosage interval initiated in non-BMT/ leukemia patients. Of the 11 treatment courses considered eligible for stepdown, 6 (55%) were successfully stepped down in collaboration with the primary health care team, 1 (9%) was discontinued, and 4 (36%) remained on the original regimen.

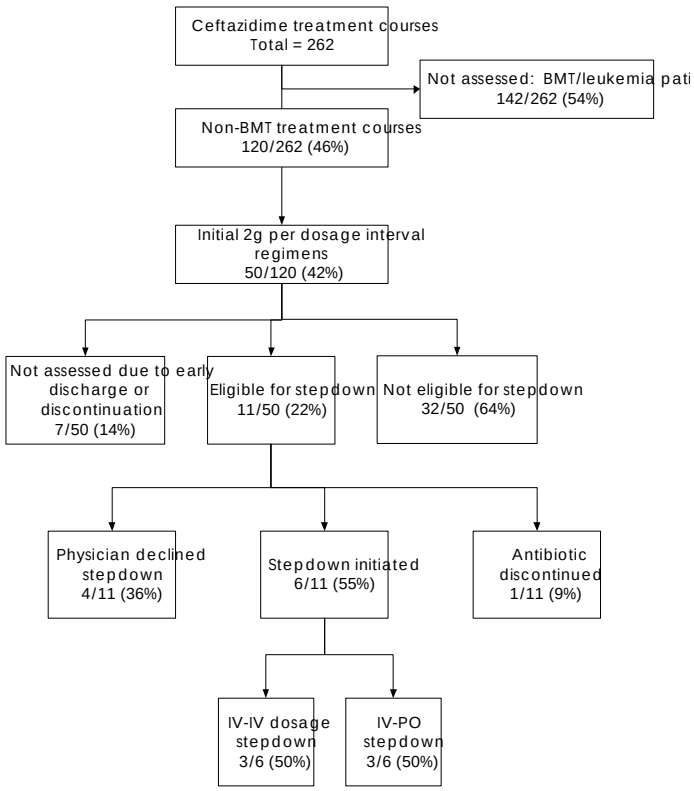


Figure 4. Ceftazidime treatment course outcomes

Of the 6 stepdown treatment courses, 3 (50%) were IV-IV dosage stepdown only, and 3 (50%) were converted directly to oral therapy. Stepdown was directly facilitated under the initiative in 67% of these treatment courses. Five (83%) of the stepdown treatment courses resulted in clinical cure or improvement. This was similar to the outcomes for non-stepdown patients. The treatment course duration of IV-IV stepdown patients was 12.7 days (range 8-20 days), and the mean treatment duration of non-stepdown courses was 8.7 days (range 6-10 days).

What are the estimated savings from this initiative?

Estimated drug treatment acquisition, preparation and delivery cost avoidance directly attributed to the IV-IV dosage stepdown initiative for both ceftriaxone and ceftazidime during the 6-month period was $9900.00. This initiative also resulted in further streamlining of antibiotic therapy by switching to another antibiotic when warranted or by facilitating timely discontinuation of the target antibiotics. Savings associated with these latter treatment modifications have not been quantified.

This latest IV-IV dosage stepdown initiative has proven to be a safe, effective and cost efficient process.

References

1. Brogden RN, Ward A. Ceftriaxone. A reappraisal of its antibacterial activity and pharmacokinetic properties, and an update on its therapeutic use with particular reference to once-daily administration. Drugs 1988;35:604-45.
2. Low DE, Mandell LA. A prospective open-label multicentre trial on the use of 1g, once daily cetriaxone in lower respiratory tract infections. Can J Infect Dis 1994;5 Suppl C:3C-7C.
3. Richards DM et al. Ceftriaxone. A review of its antibacterial activity, pharmacological properties and therapeutic use. Drugs 1984;27:469-586.
4. Smith BR. Cefsulodin and ceftazidime, two antipseudomonal cephalosporins. Clin Pharm 1984;3:373-83.
5. Rains CP, Bryson HM, Peters DM. Ceftazidime. An update of its antibacterial activity, pharmacokinetic properties and therapeutic efficacy. Drugs 1995;49:577-617.

Home IV Antibiotic Program: A Two Year Update

Amy Wai, B.Sc. (Pharm)
VHHSC Home IV Antibiotic Program

The Home Intravenous (IV) Antibiotic Program at VHHSC was successfully launched on June 1, 1995 as part of the "Closer to Home - Vancouver Regional Home IV Program". Over the past 24 months, this program has permitted medically stable patients to initiate or continue parenteral antibiotic therapy in the comfort of their own homes.

How many patients were screened and enrolled into the program over the two year period?

From June 1, 1995 to June 30, 1997, 245 patients were screened and 140 patients (57%) were successfully discharged on home IV antibiotics. Of these 140 patients, 80 were enrolled into the VHHSC program and the balance were transferred to a non-Vancouver region program. One hundred and five patients (43%) were found to be inappropriate candidates for home IV therapy. Of these 105 patients, 51 remained as inpatients, 29 were discharged on oral antibiotics, 16 were referred to medical daycare, 7 had their antibiotics discontinued, and 2 patients left the hospital against medical advice.

Patient referrals increased by 85% during the second year of the program while home IV enrollment doubled for the same period. The incidence of inappropriate candidates remained stable at 45%. The overall duration of treatment at home increased by 92% to 3421 days. Figures 5 and 6 illustrate the incidence of referrals and the number of treatment days at home per quarter respectively.

Figure 5. Incidence of referrals per quarter

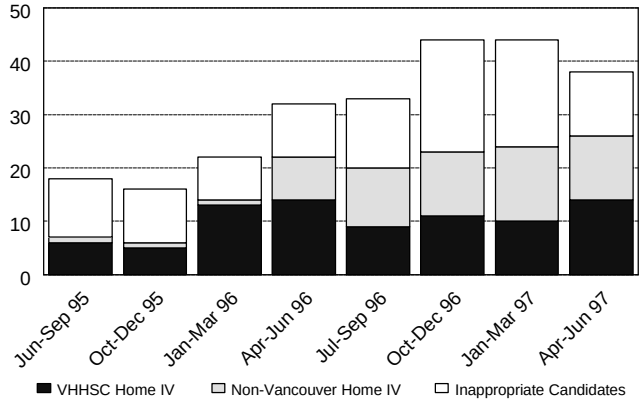
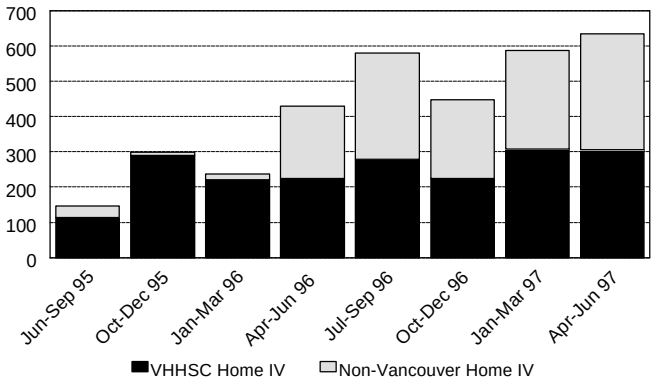


Figure 6. Total number of planned or completed antibiotic



days per quarter

What types of infections were treated?

Infections treated include bone and joint infections (45%), endocarditis (15%), skin and soft tissue infections (12%), respiratory infections (9%), cytomegalovirus (CMV) infections (6%), and others (13%).

What were the general characteristics of those patients enrolled?

The mean age was 53 years (range 19-83) and 61% were male. Inpatients were discharged after a mean hospital stay of 13 days (range 1-56) and received a mean of 12 days (range 1-50) of antibiotic therapy prior to discharge.

What types of antibiotics were used?

Several different antibiotic treatment regimens were administered at home. The 5 most common home IV antibiotics were vancomycin (27%), cloxacillin (23%), cefazolin (23%), ceftriaxone (11%) and penicillin (9%). The median duration of home parenteral therapy administered was 20 days (range 1-247).

What were the treatment course characteristics?

Of the 80 patients enrolled into the VHHSC program, 68 (85%) patients successfully completed their treatment course while 4 (5%) clinically deteriorated during therapy. The remaining 8 (10%) patients were discontinued from the program due to catheter-related complications (3), noncompliance (2), adverse drug reaction (1), an inappropriate home environment (1) and death due to an unrelated cause (1).

Were there any adverse drug reactions during therapy?

Thirteen (16%) of the 80 patients experienced an adverse drug reaction during their treatment course. The most common reactions were dizziness and loss of balance (4), nausea (2), and rash (2). The remaining 5 reactions included thrush, fever, vancomycin-induced redman's syndrome, diarrhea and interstitial nephritis. Two patients were unable to complete their antibiotic course due to vancomycin-induced drug fever, and cloxacillin-induced interstitial nephritis.

What types of IV access devices were used?

There were 77 (55%) peripherally inserted catheters (PIC), 29 (21%) peripheral lines, 15 (11%) port-a-caths, and 19 (13%) central lines.

What were the patients' perceptions of our program?

Since June 1, 1996, patients were asked to complete a patient satisfaction survey anonymously after completion of their antibiotic therapy. Seventy-one percent of the 42 mailed surveys were returned. Ninety-three percent of patients felt that the amount of time spent teaching them about their antibiotic treatment regimens was appropriate while 7% of the patients believed additional time was required. Patients typically claimed to be comfortable administering IV medications at home and felt it was more convenient than remaining in the hospital. While on the program, 80% of the patients were able to return to the majority of their normal activities. Patients were very satisfied with the quality of care they received and with the medication and supply delivery process. Over 95% of patients stated they would consider home IV antibiotic treatment again in the future should they require it.

How do I enroll a patient into the program?

A physician must request a Home IV Antibiotic Program assessment (on a standard physician order form) and notify the program pharmacist (pager 601-7899 at VGH site, 822-7249 at UBC site). Please contact Amy Wai, Home IV Antibiotic Program Pharmacist, if you have any questions or concerns regarding this program.

CSU Pharmaceutical Sciences wishes the Staff at VHHSC a safe and healthy holiday season and a happy new year.