

DRUG USE PATTERNS OF AN ORAL CEPHALOSPORIN IN  
AMBULATORY PATIENTS AT THE TUCSON  
VETERANS ADMINISTRATION HOSPITAL

by

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## ABSTRACT

A study was conducted at the Tucson Veterans Administration Hospital in compliance with the Drug Utilization Review Requirements of the Joint Commission on Hospital Accreditation and the Veterans Administration Chief Medical Director's letter to determine the drug use patterns of antimicrobial agents. The use of expensive, widely used, broad spectrum class of antimicrobial agents, the oral cephalosporins, were studied in depth in ambulatory patients.

The surgical house staff were the most frequent prescribers of the oral cephalosporins (14 of the 25 prescriptions). Surgeons used oral cephalosporins in outpatients as 18.6 percent of their overall antimicrobial usage whereas internists used them 4.6 percent of the time.

Only 32 percent of the infections were defined by culture and sensitivity data. Overall, this was done least frequently by the surgery house staff (14.3 percent) and most frequently by the internal medicine attending physicians (50 percent). All microorganisms were routinely sensitive to cephalixin. Various recommendations to correct these prescribing deficiencies were acted upon by the Tucson Veterans Hospital. The only action which

demonstrated favorable results, as measured by volume of use, was the complete removal of oral cephalosporins from the hospital formulary.

## CHAPTER 1

### INTRODUCTION

The medical profession, as other professions, maintains that it is self-policing in that it acknowledges or censures its members through peer review. This process, however, has been criticized as lacking effectiveness (Knoben 1975). Consumers, through government legislation and third party pay programs, are demanding that a systematic approach to this internal review process be taken to assure high quality medical care (Kelly, White and Miller 1975) by the most economical means (Rucker 1970):

The Joint Commission on Accreditation of Hospitals (hereinafter referred to as Joint Commission) was formed as an independent, voluntary, non-profit corporation to render public service. The parent bodies of this commission are the American College of Surgeons, American College of Physicians, American Medical Association, and American Hospital Association. Their purpose is to assure continuing quality of care in hospitals which can be faithfully recommended to the public (McGibony 1969). While no hospital is required to become accredited, the American Medical Association will not approve a hospital for residency training unless it

meets commission standards. Congress further supported the commission's purpose by requiring accreditation of a hospital before it could qualify for Medicare programs (Joint Commission 1976).

Among the guidelines the commission has developed are internal hospital audits which are directed at quality assurance. A periodic review of the utilization and cost of bed facilities, and of the diagnostic, nursing and therapeutic resources of the hospital must be performed. More specifically, with respect to the use of medications within the institution, the accreditation manual states that "the development and surveillance of pharmacy and therapeutic policies and practices, particularly drug utilization within the hospital, must be performed by the medical staff in cooperation with the pharmacist and with representatives of both disciplines, as necessary. Such policies and practices should ensure optimal drug use, with a minimum potential for hazard to the patient" (Joint Commission 1976, p. 111).

In compliance with this requirement a drug utilization review committee was established at the Tucson Veterans Administration Hospital in October 1975. Members of the committee included the Chief of Staff at the Tucson Veterans Administration Hospital, the Department Head for Pharmacology at the College of Medicine, the Chief of

Infectious Disease at the Tucson Veterans Administration Hospital, a head nurse at the Tucson Veterans Administration Hospital, the physician chairman of the Hospital Utilization and Medical Records Committee and the clinical pharmacist.

From purchasing records the committee determined that antimicrobials represented a large dollar expenditure of the pharmacy budget and the committee decided to study this group of drugs first. Of all the antimicrobials used at the Tucson Veterans Administration Hospital, the oral and parenteral cephalosporins accounted for approximately 25 percent of the total pharmacy budget for drugs (Newman 1975).

This information was of concern to the committee since the cephalosporin antimicrobials are not considered drugs of first choice for any infection although they provide reasonable alternate therapy or drugs of second choice in a few instances (The Medical Letter 1976).

When the Drug Utilization Committee further studied purchasing records, it was found that the use of cephalexin, the only oral cephalosporin on the Tucson V.A. Hospital formulary, accounted for approximately 25 percent of the total cephalosporin cost. Since oral antimicrobials are convenient to use in an ambulatory population, it became the concern of the committee that extensive use of these agents for the treatment of relatively uncomplicated

infections might lead to the selection of resistant strains of microorganisms with the eventual loss of these agents for the treatment of life-threatening infections.

Thus, concern over cost and effectiveness of the oral cephalosporin, cephalexin, provided the impetus for this study.

### Purpose

The purpose of this study was to determine drug use patterns for the oral cephalosporin, cephalexin, in outpatients at the Tucson Veterans Administration Hospital. The specific objectives of this study were to seek answers to the following questions.

1. What was the incidence of cephalexin use in outpatients and what was the relative frequency of use in relation to other antibiotics?
2. Which physicians were prescribing cephalexin to their ambulatory patients?
3. What doses of cephalexin were prescribed and what was the prescribed duration of therapy?
4. For what indication was cephalexin being used in outpatients?
5. Was cephalexin being used after appropriate culture and sensitivity testing?
6. Were there less expensive yet efficacious alternatives to the use of cephalexin in outpatients?

### Definitions

Antimicrobial agents are those drugs used to destroy microorganisms or suppress their multiplication or growth.

Physician category is defined for the purpose of this study as a combination of the physician's specialty or current specialty rotation or status, that is, whether he is an attending physician or in training (i.e., intern or resident).

Culture data resulted from the identification of microorganisms obtained from specific sites of human infection.

Drug use patterns included such information as which physicians were prescribing what drugs for what conditions at what dose and for what duration of treatment. The patterns that were compiled from this information provided a method for individual evaluation of overall appropriateness of therapy.

Drug utilization review was defined as the process of collecting data relevant to the clinical use of a drug for a given disease. Drug utilization review defines drug use patterns.

Indication is the circumstance which points to or shows cause for therapy. The indication for use of antimicrobials is an infection either defined, presumed or for prophylaxis. More specifically in an infection, the indication is the organism and site.

Oral cephalosporins are relatively new antimicrobial agents which are similar in structure and mechanism to the penicillins. Those which are currently on the market in this country are cephalexin monohydrate, cephaloglycin dihydrate and cephradine. For the purpose of this study cephalexin monohydrate, the only oral cephalsporin in the Tucson V.A. Hospital formulary, was used.

Outpatients and ambulatory patients were used synonymously to refer to nonhospitalized patients receiving care by physicians of the hospital or its clinics.

Peer was defined as a group of individuals represented by single and multidisciplinary health practitioners.

Peer review is the evaluation by practicing physicians or other health professionals of the effectiveness and efficiency of services ordered or performed by other physicians or other members of the profession whose work is being reviewed (peers).

Sensitivity data was obtained by in vitro testing of cultured microorganisms and demonstrated the degree of susceptibility of the microorganisms to a given antimicrobial agent.

#### Assumptions

Three assumptions were made for this study. First, it was assumed that the prescriptions written for cephalexin

during the study period were representative of other periods of equal duration. Second, since patients must have had their outpatient prescriptions filled at the Tucson V.A. Hospital, where they received them free of charge, it was assumed that all prescriptions written for cephalexin were filled at the Tucson V.A. Hospital Pharmacy and were therefore entered into the study. Finally, it was assumed that all data collection and tabulation were accurate and complete.

#### Limitations

This study had two limitations. First, studies performed within this research were limited to outpatients receiving prescriptions for the oral cephalosporin filled at Tucson V.A. Hospital. No attempts were made to relate these findings, conclusions or recommendations to other antimicrobials, patient populations or institutions.

Second, the degree to which this study reflects the normal prescribing habits of the physician must be under suspect since the physicians knew they were being monitored. This is the effect of the observer on the observed.

## CHAPTER 2

### RELATED LITERATURE

Antimicrobial agents are among the most commonly prescribed drugs. In 1973 it was estimated that 11 billion dollars were spent on 2.8 million prescriptions and other drugs in the United States (Rucker 1974). Thirty to 40 percent of those costs were for antimicrobials (Kunin, Tupasi and Craig 1973; McGowan and Finland 1974a). When one considers that several independent studies have shown that over 50 percent of antimicrobial usage in this country is inappropriate due to lack of need or wrong agent selected (Kunin et al. 1973, McGowan and Finland 1974b, Simmons and Stolly 1974, Roberts and Visconti 1972), it can be seen that tremendous unwarranted expenditures are being made.

As a result, physicians have often been criticized for poor antimicrobial prescribing practices (Neu and Howrey 1975, LeFrock et al. 1976, Kunin et al. 1973). In support of this observation it has been documented that a group of drugs which essentially are not a first choice for any infection, the cephalosporins, hold 21.5 percent of the entire antimicrobial market (Brady 1976). Finally, adverse

reactions secondary to antimicrobial therapy are frequently encountered and may be severe or fatal ("Mission Possible" 1973). It has been estimated by surveillance studies that five percent of all hospitalized patients exposed to antimicrobials will have an adverse drug reaction: 47 percent of these will be rated moderate and 14 percent severe or life-threatening (Simmons and Stolley 1974). In addition, over-use of antimicrobials may lead to selection of resistant strains and thus limit the usefulness of the agent when it is needed (Simmons and Stolley 1974).

Antimicrobial therapy can therefore be considered expensive, dangerous, excessive and prescribed by physicians who probably should know more about the appropriate use of these drugs. It is no wonder that Professional Standards Review Organizations will be nationally required (Public Law 92-603, 1972) and that the Joint Commission on Hospital Accreditation requires therapeutic utilization for accreditation of hospitals and that the Veterans Administration requires internal drug audits (Chase 1975).

One of the tools used by the Professional Standard Review Organizations (PSROs) is drug utilization. Drug utilization review has been described by Pierpaoli and Bowman (1972, p. 46) as "the sum of the components of drug selection and prescription, dispensing, administration and effectiveness." Further, in any drug program, utilization

review is a dynamic process aimed at rational prescribing, improvement of the quality of health care, and at minimizing needless expenditures.

In many hospitals, staff committees of experts have long taken the responsibility of reviewing the records of their fellow physicians and offering advice or taking disciplinary action as they demand necessary. During the past two years, utilization review programs have been instituted to improve the quality of medical care under the hospital program of Medicare.

It should be the responsibility of a program administration to institute a drug utilization review, and provide the necessary data and whatever statistical analysis may be required.

But the implementation--the establishment and improvement of guidelines, the provision for acceptable deviations, the limitations of irrational prescribing, the prevention of fraudulent practices, and other professional judgments--should be mainly the responsibility of clinicians, pharmacologists, and pharmacists who are widely respected as objective, well-informed and appreciative of the needs of both physicians and patients, and who would work with their colleagues at the state or local level (Health, Education and Welfare Task Force on Prescription Drugs 1968, p. 3).

Brodie (1972) indicated that a utilization review is a study of the frequency of changes to determine patterns. The goal of a utilization review is to improve the quality of patient care and is based on sound medical judgment and a minimal cost consistent with an acceptable level of care.

Published drug utilization review studies have obviously interpreted drug utilization review in various ways. In two studies, Food and Drug Administration approved

usage was compared with actual usage (Gibson, Hanley and Newton 1973; Kelly et al. 1975). In another study the drug utilization review efforts consisted of pharmacy collected data on the number of doses administered to patients in comparison with adverse drug reaction data collected by the department of medicine (Lantos and Stewart 1970). Maronde et al. (1969) looked at the quantity of individual drugs issued to patients and incidence of inappropriate concurrent prescriptions. Roberts and Visconti (1972) collected data on hospitalized patients' antibiotic usage. They studied indication, drug, dose, duration, culture and sensitivity data and route of drug administration. These data were individually reviewed and evaluated on each patient by a pharmacy resident, a Ph. D. pharmacist and then an infectious disease physician for appropriateness. It was the intent of this research, however, to study drug utilization relevant to drug use patterns.

There have been many published articles in the recent literature concerning drug utilization review. Many of these were studies done on antimicrobial usage on hospitalized patients (Scheckler and Bennett 1970; Roberts and Visconti 1972; Pierpaoli, Coarse and Tilton 1976; McGowan and Finland 1974a, 1974b; Gibson et al. 1973; Deliganis and Johnson 1973; Zeman, Pike and Samet 1974). Although several studies indicate that the overall quality

of hospital care is far superior to office-based care (Payne and Lyons 1973a, 1973b; Brook 1974), very few studies have been done on ambulatory patients. Stolley and Lasagna (1969) studied all types of drug therapy in a community of 112,000 people. They found that 15.5 percent of all out-patient prescriptions were written for antimicrobials. No attempt was made to determine how or why the drugs were prescribed. Hemminki, Forsman and Hemminki (1974) studied antimicrobial use in outpatients by general practitioners in Finland. One thousand five hundred eleven patients were studied and 594 antimicrobial agents were prescribed (39 percent of the patients). In their conclusion they stated that selection of the individual antimicrobials were often inappropriate especially for the broad spectrum drugs. Maronde et al. (1969) have developed an electronic data processing system at Los Angeles County-University of Southern California Medical Center for processing prescriptions as part of the dispensing function. A committee of five physicians and two pharmacists adopted definitions of prescribing practices based on information normally attainable from prescriptions. The definition of inappropriate included single prescriptions for large quantities of a drug, multiple prescriptions allowing an individual to possess large quantities of a drug and inappropriate concurrent prescriptions. From their data it was concluded

that measures must be taken to improve prescribing practices. However, most of our current data on drug use in ambulatory patients comes from marketing research firms. For instance it has been found that 95 percent of physicians issued one or more prescriptions to a patient diagnosed as having a common cold; 60 percent of these were for antimicrobials. (Stolley and Lasagna 1969). Analysis of trends in antimicrobial therapy done by Simmons and Stolley (1974) indicated that antimicrobial usage is widely increasing and that much of this increase was accompanied by inappropriate prescribing without prior cultures and prophylactic use where it is not proven beneficial.

Pharmacists and clinical pharmacists should be involved with physicians in collecting and evaluating data on drug usage (Brodie 1970, Joint Commission 1976, Zeman et al. 1974, Reilly 1972, Lantos and Stewart 1970, Hassan 1969). Traditionally the pharmacist in both the retail and hospital setting has reviewed the prescription for obvious errors prior to dispensing the medication (Knoben 1976). More recently the clinical pharmacists are reviewing the drugs with the physician prior to initiation of the order (Brodie 1970). The use of the pharmacist in drug utilization review creates a challenge in the interdisciplinary team approach to medical practice which will be an interesting test of the concept.

## CHAPTER 3

### DESIGN

#### Introduction

The study was conducted as part of an ongoing, comprehensive antimicrobial surveillance project established at the Tucson V.A. Hospital, a 329-bed, Dean's Committee teaching facility. The purpose of comprehensive antimicrobial surveillance was to document the use of a highly prescribed, over-used (Kunin et al. 1973) and expensive (Brady 1976) class of drugs while complying with drug utilization review requirements (Joint Commission 1976, Chase 1975).

Cephalosporin antimicrobials were selected because of the high percentage of budgeted funds expended on these drugs. This class of antimicrobials was further narrowed down for intensive study based upon the following considerations.

1. There was one oral cephalosporin, cephalexin, on the Tucson V.A. Hospital formulary. This allowed for an in-depth study of essentially one drug.
2. Cephalosporins are not the drug of first choice for any infection although they are considered to

provide a reasonable alternate therapy in a few instances (The Medical Letter 1976).

3. Oral antimicrobials are convenient to use in outpatients. The ambulatory patient is generally seen just once by the physician for an acute complaint, such as an infection. In this case the physician may not base his therapeutic decision on culture and sensitivity results that take several days to obtain unless he reschedules the patient. Because of this convenience and the nature of the ambulatory patient, antimicrobial therapy for outpatients has been described as less than optimal (Fekety 1976, "Antibiotic Use" 1976, "Usage of Cephalosporins and Other New Antimicrobials" 1975).
4. The cost of the oral cephalosporin, cephalexin, has been documented to be approximately six percent of the total pharmacy budget for drugs (Newman 1975).

#### Methodology

Prior to initiation of the study a specially selected panel was formed for the Drug Utilization Review Committee. The Chief of Staff issued a professional services memorandum to the entire hospital staff (Appendix A) explaining the purpose of the study and what their expected roles would be. The memorandum requested the physicians to write the suspected microorganism and the site of infection on all

antimicrobial prescriptions. The investigator, a full-time employee at the Tucson V.A. Hospital, met with the individual clinical service chiefs to explain the study and urge their support. In addition, the investigator explained the purpose and methodology of the study to each Tucson V.A. Hospital pharmacist on an individual basis. Each pharmacist agreed to conform to the proposed methodology.

The study included all consecutive new prescriptions for outpatients who received oral cephalosporin antimicrobials for one calendar month of 31 days. The basic study design was relatively simple and to assure that all prescriptions written for cephalexin during the study period were entered into the study, a small number of pretrained personnel were utilized in the recording of data. The pharmacy filled prescriptions for oral cephalosporin antimicrobials in the usual manner. After dispensing the drug, however, the prescription was not entered in the patients' profiles but was filed in a separate, conveniently located box. These prescriptions were collected, screened for entry criteria and data extracted onto the study form (Appendix B) by the investigator. Additional information was collected retrospectively from patient charts. Data were collected and coded for subsequent computerization. The specific information to be recorded on each order for an oral cephalosporin was as follows.

1. The generic name of the oral cephalosporin prescribed--in all cases, cephalixin.
2. The patient's name and last four digits of his social security number. These were later combined into a patient code. The patient code was the first initial of his first and last name and the last four digits of his social security number.
3. The prescribing physician's code number--a list of all physicians at the Tucson V.A. Hospital broken down by specialty and status (i.e., faculty, interns and residents) was obtained through the Chief of Staff's office. A four digit code was designed that would readily identify the physician's specialty or status as well as make it possible to identify the specific physician. The first digit classified the physician's specialty.

1 = Internal Medicine

2 = Surgery

3 = Anesthesiology

4 = Dentist

5 = Neurology

6 = Psychiatry

9 = Any other

The second digit classified the physician as to his status in the hospital.

1 = Attending or faculty physician

2 = An outside consultant physician

3 and 4 = House staff, interns and residents

0 = Represents any physician not covered in one of the above categories.

The third and fourth digit identified the specific physician written the above classification.

4. The date the prescription was written.
5. The organism being treated as specified by the physician--all organisms were coded with a three-digit code adopted from Standard Nomenclature of Pathology for subsequent computerization (see Appendix C).
6. The site of the infection as specified by the physician--the site was coded with a single letter giving an anatomically forced classification (see Appendix D).
7. The organism(s) cultured by the clinical microbiology laboratory at the specific site--these microorganisms were also coded by the three-digit code (Appendix C).
8. The sensitivities of the organism(s) cultured--the antimicrobials to which the microorganism cultured was sensitive were coded with a letter code (see Appendix E).

9. The dose, in grams per day, of the oral cephalosporin, cephalexin.
10. The duration of therapy prescribed, including refills if any.

Generally the only information collected that was not available directly from off the prescription was Items 7 and 8, the culture and sensitivity data. This information was gathered retrospectively from microbiology laboratory records or directly from the culture and sensitivity reports placed in the patient's chart. If no record of culture and/or sensitivities existed in the laboratory or in the patient's chart it was assumed that none was obtained and the organism being treated was unknown to the prescribing physician. Also, it was anticipated that occasionally the physician would neglect to supply Items 5 and 6 (the microorganism being treated and the site of infection). Under these circumstances the information was extracted from the patient's chart.

Since all antimicrobials were later to be considered for a comprehensive surveillance program, information concerning other antimicrobial agents prescribed for study patients were also collected.

These data were organized and tabulated. Specific trends and differences between variables were observed and appropriate statistical analysis was applied where applicable.

## CHAPTER 4

### RESULTS AND DISCUSSION

The Tucson V.A. Hospital in compliance with the Joint Commission on Accreditation of Hospitals requirements and the V.A. Chief Medical Director's Letter (Chase 1975) established a Drug Utilization Review Committee. The committee reviewed pharmacy purchase records and decided to study the use of antimicrobial agents. Cooperation with the study by all hospital staff was mandated by the Chief of Staff.

During the hospital-wide antimicrobial utilization program a more comprehensive study was conducted on cephalosporins in outpatients. This group of drugs has been recognized as expensive and widely used while having very few accepted indications. Since the only oral cephalosporin on the Tucson V.A. Hospital's formulary was cephalexin, a more intensive study to determine the drug usage patterns of essentially one drug was performed. Since the purpose of this study was to identify existing prescribing practices and not to directly determine appropriateness of therapy or influence quality of patient care, the results of this research have been forwarded to the Infectious Disease

Department and the Drug Utilization Review Committee for further action.

### Physician Categories

Physicians were examined by service and status (category) of practitioners prescribing cephalexin. Prescriptions were written by seven surgical house staff physicians, two internal medicine attending, six internal medicine house staff, one ambulatory care attending, one ambulatory care house staff and one anesthesiology house staff. For the purpose of data analysis, physician categories were grouped by specialty or service and status. The resulting groupings are shown below.

#### Forced Condensed Categorization of Physicians Who Actually Prescribed Cephalexin During the Study Period:

<u>Original Service</u>	<u>Condensed Classification</u>
House Staff:	
Internal Medicine)	Internal Medicine
Anesthesia )	
Surgery	Surgery
Attending:	
Internal Medicine)	Internal Medicine
Ambulatory Care )	
Ambulatory Care--)	
Consultant )	

It was felt that grouping data was appropriate since all ambulatory care physicians were internists. The one anesthesia resident who wrote a prescription for cephalexin was completing an internal medicine rotation at the time of

the study. This physician was also classified as internal medicine house staff physician since the categorization of house staff is based on current specialty rotation. The consultant physician in ambulatory care is also an internist and classified as an internal medicine attending.

#### Incidence of Prescriptions for Cephalexin

A total of 319 outpatient prescriptions for antimicrobial drugs were written at the Tucson V.A. Hospital during the 31-day study period. A breakdown by drug and prescribing physician category is presented in Table 1.

Of the 319 outpatient prescriptions for antimicrobials, 25 (7.8 percent) were for cephalexin. Seven surgical house staff physicians wrote 14 (56 percent) of the prescriptions for cephalexin, seven different internal medicine house staff physicians prescribed cephalexin 7 times (28 percent) and four different internal medicine attendant physicians prescribed cephalexin 4 times (16 percent). There were no prescriptions from surgical attendings or any other specialty during the study period (Table 2).

It was assumed by the Drug Utilization Review Committee that most of the cephalexin usage was in outpatients since generally hospitalized patients are more acutely ill and would be receiving parenteral cephalosporins. The pharmacy purchase records were used as a guide and indicated that approximately \$1,000 per month was expended on

Table 1. Outpatient antimicrobial usage patterns by physician category, total number of prescriptions and average daily dose during the study period.

Drug	No. of Rx's	Average Daily Dose	Internal Medicine	Surgery	Others
Ampicillin, po	72	1.53 gm	53	14	5
Carbenicillin, po	0		--	--	--
Cephalexin, po	25	1.55 gm	10	14	1
Clindamycin, po	0		--	--	--
Dicloxacillin, po	30	3.73 gm	19	8	3
Erythromycin, po	21	1.27 gm	15	3	3
Gentamicin, inj.	1	210 gm	--	1	--
Methenamine Mandelate	3	2.67 gm	2	--	1
Methenamine Hippurate	1	2.0 gm	--	1	--
Metronidazole	0		--	--	--
Nalidixic Acid	0		--	--	--
Nitrofurantoin	15	306.2 gm	8	7	--
Bicillin - CR	4	1.2 mu	4	--	--
Phenoxymethyl Pen.	18	1.38 gm	11	4	3
Sulfasoxizole	6	3.63 gm	6	--	--
Septra (Bactrim)	25	3.12 tab/day	14	10	1
Tetracycline, po	98	1.22 gm	76	13	9
Total	319		218	75	26
Total Inpatient	409		148	184	77
Grand Total (Dec)	728		366	259	103

Table 2. Inpatient cephalosporin antimicrobial use by physician service in relation to total antimicrobial usage during the study period.

Drug	No. of Rx's	Average Daily Dose	Internal Medicine	Surgery	Others
Cefazolin	2	6.0	1	--	1
Cephalexin	42	1.98	9	32	1
Cephalothin	9	8.17	10	37	2
Total Cephalosporin			20	69	4
Other Antimicrobials			128	115	73
Total 409			148	184	77

cephalexin. It was projected that if all cephalexin had been used in outpatients in the usual adult dose of one gram per day for a ten-day course (Physicians' Desk Reference 1977) and the use remained consistent with other months, there would have been approximately 110 prescriptions for cephalexin during the study period. However, study results demonstrated that there were only 25 outpatient prescriptions written for cephalexin during the study period which accounted for \$525.14 worth of cephalexin (52.5

percent of the total cost for cephalexin prescribed). On the other hand, a total of 42 orders for cephalexin for hospitalized patients (9 by internal medicine physicians, 32 by surgery physicians and 1 by another physician) were written during the study period (Table 2). The reasons for this apparent discrepancy between number of orders and prescriptions and cost can be explained by the larger mean daily dose prescribed (1.55 grams per day) and longer duration of therapy (17.9 days) in outpatients. It was unknown how many grams of drug or dollars this figure represents. So it cannot be stated that the usage of cephalexin remained constant, increased or decreased during the study period (Table 2).

It is of interest to note that 14 of the total 75 prescriptions for antimicrobial drugs (18.7 percent) written by the surgery service for outpatients were for cephalexin, whereas 11 of the total 218 prescriptions (5.0 percent) written by internal medicine were for cephalexin (as seen on page 23). A marked difference in outpatient usage of this drug between the two services can be seen and when monitoring inpatient drug usage, a similar trend can be noted (Table 2).

#### Dose and Duration of Therapy

The recommended daily dosage of cephalexin is from one to four grams or more (Physicians' Desk Reference 1977).

The overall dose of cephalixin prescribed per day in this study ranged from 500 mg to two grams per day with a mean of 1.59 grams per day. Those dosing regimens were well within the therapeutic range except for two cases where doses of 500 mg and 750 mg per day were prescribed for urinary tract infections. Both were 30-day courses of therapy and were prescribed by a surgery house staff physician and an internal medicine attending physician. Table 3 compares the actual mean and median daily dose of cephalixin prescribed by each physician specialty.

Table 3. Mean and median cephalixin dosage in grams per day by physician category.

	Surgery House Staff	Internal Medicine House Staff	Internal Medicine Attending	Overall
Mean Daily Dose	1.80	1.43	1.13	1.55
Median Daily Dose	2.00	1.00	1.00	2.00

The duration of therapy varied widely from two days for prophylaxis at the time of a procedure to 90 days for a sinus infection. The overall mean duration of therapy was 17.9 days and the median was ten days. The ten-day course was prescribed eight times out of the 25 prescriptions (32.0 percent) monitored. A breakdown of the duration of therapy by physician's specialty is presented in Table 4.

Table 4. Mean, median and range of duration of therapy in days by physician category.

	Surgery House Staff	Internal Medicine House Staff	Internal Medicine Attending	Overall
Mean,	12.5	30	15.5	17.9
Median	8.75	10	11	10
Range	29	84	21	89

The range of duration of therapy is much greater in the internal medicine staff group. Two very long treatments, one of 75 days and one of 90 days, were prescribed for sinus infections on two different patients by two different physicians. These two courses of therapy skewed the distribution greatly in this group. No course of therapy was prescribed for under seven days which was not for prophylaxis, however, one course of therapy for prophylaxis was prescribed for 14 days in a patient with an open fracture of the toe.

#### Indications for Therapy

The indications for antimicrobial therapy included (1) some clinical evidence of an infection such as fever, elevated white blood cell count, or purulent drainage from a wound, (2) determination of an obvious or suspected site of infection, and (3) suspicion or culture of a microorganism. These circumstances lead to at least a presumptive indication for antimicrobial therapy. Another possible indication for antimicrobial therapy was prophylaxis, or treatment to prevent an infection when the circumstances indicated that the risk of causing an infection was great. Since it was assumed that the clinical evidence for an infection had been evaluated by the physician and in his judgment an infection existed before he prescribed antimicrobial therapy, this study was only concerned with the

site of the infection and the microorganisms cultured from that site. If no microorganisms had been cultured an accepted indication for treatment included either "unknown" or "prophylaxis" as the microorganism being treated. The indication for treatment by infecting microorganism is shown in Table 5. Since two patients had two known infecting microorganisms cultured, the 25 study cases actually represented 27 infecting organisms. The most frequently treated defined infection was caused by *Klebsiella* which occurred in four cases (16 percent).

Table 5. Incidence of indications for treatment by microorganism.

Microorganism	Incidence
Unknown	13
Prophylaxis	4
<i>Klebsiella</i>	3
<i>Hemophilus influenza</i>	2
<i>Escherichia Coli</i>	1
<i>Staphylococcus</i> (coagulase positive)	1
<i>Enterococcus</i>	2
<i>Streptococcus</i> Group A (Beta)	1
Total	27

When treating prophylactically the organism was also unknown; thus the unknown microorganisms treated with cephalixin represented 17 out of 25 cases or 68 percent (Table 6). The rate of therapy with cephalixin to treat an unknown infection appears to be much greater on the surgical service by these data.

Table 6. Incidence in number and percent of therapy for prophylaxis or for unknown organism by physician category.

	Surgery House Staff	Internal Medicine House Staff	Internal Medicine Attending	Overall
Number	12	3	2	17
Percent of Category	85.7	43	50	68

The sites of infection are tabulated in Table 7. Again there were 27 sites for the 25 cases due to micro-organism cultured from two sites on two patients. Urinary tract infections were the most frequently treated of the infection sites with 11 cases (40.7 percent), and lung infections determined from sputum samples, comprised the second largest category of infection sites with five (18.5 percent) while the remaining 11 sites involved bone, skin, chest, vascular, eye, sinus and joint.

Table 7. Number of infections by site of infection.

Site	Incidence
Sputum (lung)	5
Urine	11
Bone	2
Skin	3
Chest	1
Vascular	1
Eye	1
Sinus	2
Joint	1
Total:	27

Culture and Sensitivity

Eight of the 25 cases studied (32 percent) had cultures ordered. Twelve microorganisms were grown from these eight cultures of which eight had sensitivities recorded on the chart. The frequency of culturing a suspected microorganism by physician category is presented in Table 8. These data indicate that cultures are acquired less frequently by the surgical house staff (14.3 percent) than the other physician categories.

Table 8. Frequency and percent of cultures by physician category.

	Surgical House Staff	Internal Medicine House Staff	Internal Medicine Attending	Overall
Number	2	4	2	8
Percent of Category	14.3	57	50	32

All organisms cultured were sensitive to cephalosporins. The cultured organisms were all sensitive to other oral antimicrobials. Also, all of the other oral antimicrobials are less expensive than cephalexin (see Tables 9 and 10).

#### Cost of Therapy

The cost to the Veterans Administration Hospital of a course of cephalexin therapy varied from \$3.66 to \$82.26 with a mean cost of \$21.01 and a median of \$13.71. Table 11 shows the cost for cephalexin during the study period by physician category. The mean, median, range and total cost of therapy is the lowest in the internal medicine attending category while it is the highest in the internal medicine house staff group. If the average expenditure for cephalexin remained \$1,000 per month, the total expenditures for outpatients then comprises 52.5 percent of the cephalexin usage. If this is the case, then the 42 inpatient orders for cephalexin during the study period had a mean cost of \$11.30 and, since the mean daily dose is higher (see Table 2), the inpatient duration of therapy is less than that for outpatient.

#### Patients Receiving Other Antibiotics

Patients for whom other antimicrobial agents were prescribed were especially scrutinized to determine if

Table 9. Organisms cultured by site of infection and sensitivity to alternate oral antimicrobial agents.

Microorganism Cultured	Site		UTI Drugs***	Drugs*						
	UTI**	Non-UTI		1	2	3	4	5	6	7
Klebsiella Species		x	NA****				x			x
Hemophilus Influenza		x	NA	x	x					x
Staphylococcus (coagulase +)		x	NA			x	x	x	x	x
Staphylococcus (coagulase +)		x	NA			x		x	x	x
Hemophilus Influenza		x	NA			x	x			x
Klebsiella Species	x		xx				x			x
Escherichia coli	x		xxxx	x						x
Klebsiella Species	x		x							x

\* 1 = Penicillin; 2 = Ampicillin; 3 = Dicloxicillin; 4 = Tetracycline; 5 = Erythromycin; 6 = Clindamycin; 7 = Chloramphenicol.

\*\* UTI = Urinary Tract Infection.

\*\*\* UTI drugs are those which are generally not effective in systemic infections. They include sulfisoxazole, cotrimoxazole, nitrofurantoin, nalidixic acid, and oral carbenicillin.

\*\*\*\* NA = Not Applicable.

Table 10. Organism cultured without sensitivities by site of infection and percent chance of organism susceptibility to alternate oral antimicrobial agents.

Microorganism Cultured	Site		UTI Drugs***	Drugs*						
	UTI**	Non-UTI		1	2	3	4	5	6	7
Alpha Streptococcus		x	NA****	99.2	99.1	93.1	61.8	97.4	97.4	99.1
Hemophilis Species		x	NA	58	98	83	100	66	2	99
Streptococcus (Group A--Beta)	x		UNK*****	100	100	100	78	94	100	97
Enterococcus	x		UNK	96.8	99.4	8.0	24.7	39.1	9	98.4

\* 1 = Penicillin; 2 = Ampicillin; 3 = Dicloxicillin; 4 = Tetracycline; 5 = Erythromycin; 6 = Clindamycin; 7 = Chloramphenicol.

\*\* UTI = Urinary Tract Infection.

\*\*\* UTI drugs are those drugs which are usually not effective in systemic infections. These include sulfisoxazole, cotrimoxazole, nitrofurantoin, nalidixic acid, and oral carbenicillin.

\*\*\*\* NA = Not Applicable.

\*\*\*\*\* UNK = Unknown.

Table 11. Mean, median and range of therapy cost by physician category.

	Surgical House Staff	Internal Medicine House Staff	Internal Medicine Attending	Overall
Mean	18.12	31.34	13.03	21.01
Median	13.71	18.28	12.34	13.71
Range	52.18	76.86	10.14	79.70
Total	253.68	219.36	52.10	525.14

cephalexin, as a broad spectrum antimicrobial agent had been used temporarily until culture and sensitivity data returned allowing more specific therapy. This was not the case.

Three patients who received cephalexin during the study period also received another antibiotic. In one case the patient had been started on treatment with cotrimoxazole for a urinary tract infection which the cultures reported to be Klebsiella and sensitive to cotrimoxazole. The therapy was changed eight days later to cephalexin to which the microorganism was also susceptible. Another patient was begun on tetracycline and changed to cephalexin the following day for a sinus infection with staphylococcus (coagulase

positive). The organism was sensitive to a wide variety of other oral antimicrobials. The cephalixin was prescribed in a 90-day course by an internal medicine house staff physician. The third patient to receive another antimicrobial agent had been treated for a urinary tract infection with cephalixin by an internal medicine attending. A 30-day course had been prescribed. Fourteen days after initiation of the cephalixin, cotrimoxazole therapy was initiated, also for a urinary tract infection by a different internal medicine attending physician.

## CHAPTER 5

### SUMMARY AND RECOMMENDATIONS

Drug utilization review studies have been mandated by the Joint Commission on Accreditation of Hospitals as a requirement for hospital accreditation. Recognizing this requirement, the Veterans Administration Chief Medical Director prepared a letter (Chase 1975) ordering immediate implementation of such a project at all V.A. hospitals.

In order to determine the most appropriate class of drugs to review, the Drug Utilization Review Committee studied purchase records and determined that the cephalosporin antimicrobials constituted approximately 25 percent of the total budget for drugs (Newman 1975). Additionally, the cephalosporins have been described as over-used (Kunin et al. 1973), expensive (Brady 1976) and not the drug of first choice for any infection (The Medical Letter 1976). These facts led Kunin et al. (1973) to describe the cephalosporins as "drugs of fear" since the physician, by wanting to provide his patient with the best therapy, may prescribe these broad spectrum and relatively safe agents out of fear of failure.

### Summary

This investigation was conducted to determine drug use patterns for an oral cephalosporin, cephalexin, in outpatients. The study was designed to identify the physician prescribing cephalexin and observe the incidence, dose, duration, indication and cost of each prescription written for outpatients.

The results showed fewer prescriptions than anticipated secondary to higher mean dose, longer duration and a higher fraction of inpatient use than expected. When treating an infection the usual expected practice is to define the organism by doing cultures of the infected site and determine the antimicrobial agents to which the organism is sensitive. This was not done routinely by the physicians studied. Only 32 percent of the infections were defined in such a fashion. Overall, this was done least frequently by the surgery house staff (14.3 percent) and most frequently by the internal medicine attending physicians (50 percent). When culture and sensitivity data was obtained the organisms were routinely sensitive to cephalexin, however they were all sensitive to other more specific and less expensive antimicrobial agents.

The surgical house staff were the most frequent prescribers of the oral cephalosporins (14 of the 25 prescriptions) and prescribed it with greater frequency when

overall usage was reviewed. Fourteen of the 75 outpatient prescriptions written by the surgery house staff (18.6 percent) were for cephalexin, while the internal medicine group prescribed cephalexin ten times out of 218 prescriptions for antimicrobials (4.6 percent) for outpatients.

Since the surgery house staff appears to be the highest users of cephalexin and the least frequently have culture and sensitivity data to support their use, it appears that this category of physician is the greatest abuser of this expensive drug.

#### Recommendations

After these and other data became available to the Drug Utilization Review Committee it was recommended that an extensive inservice education program be carried out to influence the prescribing practices of physicians in regard to their use of antimicrobial agents. This was done through the Department of Infectious Disease. Additional controls were implemented in that all antimicrobials were maintained on ward stock for inpatient use except the cephalosporins. These were dispensed only upon written orders for specific patients. These methods had little apparent success when evaluated by pharmacy purchase records.

The Pharmacy and Therapeutics Committee, in an effort to reduce usage of this drug class, changed the

parenteral cephalosporin from cephalothin to cefazolin. Later it was recommended that the Pharmacy and Therapeutics Committee change oral cephalosporins from cephalixin to cephradine. Those changes were based on cost savings on equivalent doses but had no effect detectable on incidence of use.

The final recommended action that was taken was the removal of all oral forms of cephalosporins from the Tucson V.A. Hospital's formulary. This action was not a popular one for the Pharmacy and Therapeutics Committee to take. These antimicrobial agents are now available only through the New Drug Request procedures which requires the signature of the chief of the clinical service before the drugs may be dispensed. It is evident that the short-term effects of this recommendation has not met with favorable results although the long-term impact on prescribing and cost of the oral cephalosporins remains to be evaluated.

## APPENDIX A

### MEMORANDUM FROM CHIEF OF STAFF, TUCSON V.A. HOSPITAL

Professional Services  
Memorandum No. 119-75-7  
November 18, 1975

#### ANTIBIOTIC UTILIZATION REVIEW

1. GENERAL: Drug Utilization Review (DUR) is an important component of the Systematic Internal Review (SIR) quality of care assessment program being carried out by individual VA Hospitals. The major value of such programs is that they supply a means of overall self-reflection for the DM&S staff and afford them the opportunity to pinpoint areas which may show less than optimal drug usage and improve them. DUR will require a concerted effort by all concerned so that accurate and reliable information may be obtained. The subject of this particular aspect of DUR is antibiotic usage. Periodic reports to DM&S will be prepared as data is accumulated.
2. PURPOSE:
  - a. To evaluate the current physician prescribing patterns and patient drug consumption.
  - b. To better patient care by utilizing this audit as a teaching tool to improve medical prescribing.
  - c. To appraise and assure management that expenditures for pharmaceutical care are making the maximum possible contribution to health care delivery.
3. MEMBERSHIP:

Rubin Bressler, M.D., Chairman  
Carl Diener, M.D., Chairman, HUMRC (Hospital Utilization  
and Medical Records Committee)

Henry Perlmutter, M.D., Chief of Staff  
Robert Hyland, M.D., Chief, Infectious Disease Section  
William Fritz, R.Ph., Clinical Pharmacy  
Mable Howell, R.N., Nursing Service

4. PROCEDURE:

- a. This study will include all VA patients receiving antibiotics, both hospitalized and ambulatory care patients.
- b. Antibiotics will no longer be ward stock drugs; they will be available in the pharmacy and issued to a specific patient on prescription when needed.
- c. All prescriptions for antibiotics must contain the specific problem for which it is being prescribed before the pharmacy may dispense it. Specifically, the information required would be:
  - (1) The organism being treated.
  - (2) The site of the infection.
  - (3) Whether the diagnosis is presumed or the organism isolated.

For hospitalized patients this information may be written on the inpatient order, or, in the ambulatory care patient, on the back of the outpatient prescription. For the convenience of the medical staff, a specially imprinted card has been placed at each nursing station and in the outpatient clinic which identifies the information needed. For inpatients the card may be stamped on the pharmacist's copy of the physician's order (green copy), or, for outpatients, in the blank area labeled "calculations" on the reverse side of the prescription blank.

- d. For all inpatients, any unused portion of the drug must be returned to the pharmacy and must identify the patient for whom it was issued.
- e. Issues and returns will be recorded on each patient to determine amount used.
- f. Refilled outpatient prescriptions will be recorded in the same manner as new prescriptions.

5. IMPLEMENTATION: The project will begin officially December 1, 1975. All inpatients receiving antibiotics prior to this time will need to have that order re-written on or before November 28. These orders will be delivered to the nursing unit on December 1 at the time the ward stock is removed. To insure that the patient's antibiotic therapy not be interrupted, it is important that all antibiotic orders be sent to the pharmacy prior to November 28, 1975. All new orders written after November 28, 1975, must conform to the study protocol.
  
6. REFERENCE: Chief Medical Director Letter No. 10-75-52 dated 9/12/75

/s/ Henry A. Perlmutter, M.D.  
HENRY A. PERLMUTTER, M.D.  
Chief of Staff

DISTRIBUTION: B & D

APPENDIX B

STUDY FORM



## APPENDIX C

### BACTERIUM IDENTIFICATION CODE

- 100 Pseudomonas Sp.
- 101 Pseudomonas aeruginosa
- 103 Pseudomonas cepacia
- 104 Pseudomonas maltophilia
- 106 Aeromonas
  
- 310 Alcaligenes Sp.
- 331 Flavobacterium
- 340 Escherichia Sp.
- 341 Escherichia coli
- 350 Shigella
- 351 Shigella dysenteriae
- 352 Shigella flexneri
- 353 Shigella boydii
- 354 Shigella sonnei
- 356 Edwardsiella
- 360 Salmonella
- 370 Arizona
- 380 Citrobacter
- 390 Klebsiella
  
- 400 Enterobacter Sp.
- 404 Enterobacter agglomerans
- 420 Serratia
- 430 Proteus Sp.
- 431 Proteus vulgaris
- 432 Proteus mirabilis
- 433 Proteus morgani
- 434 Proteus rettgeri
- 440 Providencia
- 460 Pasteurella Sp.
- 463 Pasteurella multocida
- 465 Yersinia Sp.
- 490 Haemophilus Sp.
- 491 Haemophilus influenza
- 492 Haemophilus aegyptius
- 497 Haemophilus aphrophilus

- 520 Moraxella
- 540 Bacteroides Sp.
- 541 Bacteroides fragilis
- 542 Bacteroides melaninogenicus
- 550 Fusobacterium Sp.
- 551 Fusobacterium necrophorum
- 552 Fusobacterium nucleatum
- 590 Micrococcus Sp.
- 599 Peptococcus Sp.
  
- 600 Staphylococcus
- 601 Staphylococcus (coagulase positive)
- 602 Staphylococcus (coagulase negative)
- 631 Neisseria gonorrhoeae
- 632 Neisseria meningitidis
- 633 Veillonella
- 650 Acinetobacter
- 651 Acinetobacter calcoaceticus
- 670 Streptococcus
- 671 Streptococcus pneumoniae
- 681 Streptococcus--Group A (Beta)
- 683 Streptococcus Alpha
- 683 Enterococcus
- 684 Streptococcus--Group B (Beta)
- 685 Streptococcus--Non-group A or B (Beta)
- 686 Peptostreptococcus Sp.
  
- 705 Propionibacterium Sp.
- 706 Propionibacterium acnes
- 711 Listeria monocytogenes
- 740 Clostridium Sp.
- 741 Clostridium septicum
- 743 Clostridium perfringens
- 780 Actinomyces
- 785 Eubacterium Sp.
  
- 800 Corynebacterium Sp.
  
- 900 Unknown
- 901 Prophylaxis
- 910 Gram negative cocci
- 920 Gram positive cocci
- 930 Mixed flora
- 940 Gram negative rods
- 950 Gram positive rods
- 960 Anaerobes
- 997 Pneumocystis carini
- 998 Candida
- 999 Treponema pallidum

## APPENDIX D

### SITES OF INFECTION

- A = Abdominal Cavity
- B = Blood
- M = Bone
- S = Cellulitis or cutaneous abscess
- C = CSF
- E = Eye or Ear
- H = Head and mouth (non-CNS)
- J = Joint
- L = Lung
- T = Thoracic cavity (other than lung)
- K = Throat
- U = Urinary tract
- W = Wound/Surgical
- N = Wound/non-surgical
- O = Other
- X = Unknown

## APPENDIX E

### DRUG LIST

A = Ampicillin	S = Sulfisoxazol
Z = Carbenicillin	T = Tetracycline
C = Cefazolin	B = Trimethoprim $\bar{c}$ Sulfamethazole
C = Cephalexin	
C = Cephalothin	
X = Chloramphenicol	
L = Clindamycin	
D = Dicloxacillin	
E = Erythromycin	
G = Gentamicin	
K = Kanamycin	
H = Methenamine Mandelate	
M = Methicillin	
N = Nalidixic Acid	
F = Nitrofurantoin	
P = Penicillin G Aqueous	
P = Penicillin G Benzathine	
P = Penicillin G Procaine	
P = Phenoxymethyl Penicillin	

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