A STUDY OF POTENTIAL CRITERIA FOR INITIATING ANTIMICROBIAL THERAPY IN PEDIATRIC PATIENTS

A Thesis

Presented to

The Faculty of the College of Pharmacy

University of Houston

In Partial Fulfillment

of the Requirements of the Degree

Master of Science

by

Homer Dwight Starr

May 1974

ACKNOWLEDGEMENTS

"Love of love, love of life and giving without measure
Gives in return a wondrous yearn of a promise almost seen.
Live hand-in-hand and together we'll stand on the threshold
of a dream."

Graeme Edge
from The Dream

To all my beautiful family and friends and especially to my wonderful wife, Margaret, I wish to express my sincere gratitude and joy for the realization of this one dream.

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ABSTRACT

This study was an attempt to delineate potential minimal criteria for initiating antimicrobial therapy in pediatric patients. A review of the literature indicated that there were two major concepts regarding the administration of antimicrobials to pediatric patients. The first concept required culture testing prior to any chemotherapeutic measures, and the second concept relied primarily on clinical judgment. The literature review provided no established criteria for initiating antimicrobial therapy in pediatric patients. Patients whose age ranges from six months through 16 years are considered pediatric patients at the study hospital.

This study was conducted in three phases. The first phase was to survey Staff general (family) practitioners and pediatricians at the study hospital regarding potential criteria for initiating antimicrobial therapy in pediatric patients. The second phase was to review the charts of discharged pediatric patients to attempt to determine potential criteria. The last phase was a comparison of the physician survey and the patient chart review in order to analyze and determine valid potential criteria for initiating antimicrobial therapy in pediatric patients.

The results of this study seemed to indicate that, although physicians are aware of the complexities involved,

they rely primarily on their clinical judgment when considering antimicrobial therapy in pediatric patients. The reasons for objecting to microbiological studies were time, patient cost, and questionable validity. The ideal procedure would seem to be for physicians to use their clinical judgment in initiating antimicrobial therapy and then consider clinical and laboratory evaluations for continuation of therapy. The laboratory tests to be evaluated should include complete and differential blood cell counts and culture and sensitivity testing.

TABLE OF CONTENTS

TABLE OF TABLES

TABLE OF ILLUSTRATIONS

CHAPTER I

INTRODUCTION AND SURVEY OF LITERATURE

INTRODUCTION AND OBJECTIVES OF THE STUDY

Antimicrobial therapy is one of the most common forms of therapy in use in current drug regimens. Some studies have indicated that approximately one-third of all hospitalized patients have received some type of antimicrobial agent on any given day.(1-5) The concept of clinical pharmacy hinges on the pharmacist monitoring drug therapy. The physician must weigh several factors, such as the patients' history and physical, the patients' signs and symptoms, the patients' laboratory tests, and the physicians' own clinical judgment before making a diagnosis and prescribing the appropriate drug therapy. The clinical pharmacist should aid the physician in determining the drug therapy to be followed. The pharmacist must be aware of potential criteria for a particular drug therapy in order to serve as a valid drug therapy consult to the physician. These criteria should be consistent with the current medical rationale.

Because antimicrobial therapy comprises such a large percentage of current drug regimens, a study of the potential criteria for initiating antimicrobial therapy would seem to be in order. These criteria could then aid the pharmacist in his role as a drug therapy consult. The next step would

be to define the age group in which to confine the study. In this study, the age group used was pediatric patients. For purposes of this particular study, a pediatric patient was defined as any patient whose age ranged from six months through 16 years.

A review of the medical and pharmaceutical literature indicated that there were two major concepts regarding the administration of antimicrobials to pediatric patients. Some reported studies (6,7) indicated that physicians required culture testing prior to any chemotherapeutic measures, while other studies (8,9,10) indicated that physicians relied primarily on clinical judgment to initiate chemotherapy.

From a survey of the literature, it appeared that a delineation of criteria for initiating antimicrobial therapy in pediatric patients might be of value. One of the objectives of this study was to attempt to formulate possible criteria for initiating antimicrobial therapy in pediatric patients. Another objective of this study was to determine if there was any significant relationship between the formulated potential criteria and the physician specialty and/or such factors as the patients' age, race, sex, course of therapy, and length of stay in the hospital.

SURVEY OF THE LITERATURE

In 1972, Rapkin (6) studied the patterns of care provided by pediatricians for respiratory infections and attempted to test the hypothesis that if the pediatrician regularly processed and utilized throat cultures, the patient received a higher degree of quality care. Questionnaires were mailed to all members of the New Jersey Chapter of the American Academy of Pediatrics. Of the 397 questionnaires mailed, 223 pediatricians replied and 196 (49%) completed the questionnaire. The replies were subdivided into four groups: 1) physicians processing and reading five or more cultures per day in their own office; 2) physicians processing and reading one to four cultures per day in their own office; 3) physicians having more than one culture per day processed and read by a laboratory outside of their office; and 4) physicians having less than one culture per day processed and read outside their office. In this study, 65% of responding pediatricians obtained more than one culture per day, 48% processed their own cultures, 27% self-processed five or more cultures per day, and 35% rarely used throat cultures in their practice.

In 1970, Rosenstein et al (7) published the results of a 15-month study designed to determine the accuracy of throat cultures processed in physicians' offices. The study was conducted from October 1, 1967 through January 31, 1968, and included children seen by 12 pediatricians in five private

practices in suburban Baltimore, Maryland. The physicians had received informal instruction in bacteriological techniques and had routinely processed throat cultures in their offices for several years prior to the study. The physicians used supplies and equipment readily adaptable to an office situation and no trained technical personnel were available to assist them during the course of the study. Throat cultures were obtained from children presenting signs and/or symptoms of a respiratory tract infection. After an incubation of 18 to 24 hours, the plates were read by the physicians for the presence of any colonies of beta hemolytic streptococci. The plates were then independently interpreted by both the Streptococcal Disease Laboratory, Sinai Hospital, and the Bureau of Laboratories of the Maryland State Department of Health. During the study period, throat cultures were obtained from 537 children presenting evidence of a respiratory infection. Of the cultures showing a moderate or confluent growth of Group A beta hemolytic streptococci, 90.3% were correctly identified by the physicians. While the over-all results showed that 18.9% of the positive isolates were missed by the physicians, it was significant that 10 of the false-negative readings were non-group A isolates and 13 were group A isolates with only a few or rare colonies.

The previous studies were concerned with upper respiratory tract infections. Weinstein (8) discussed the

use of common sense in the diagnosis and therapy of infections. He stated that even if microbiological proof of the identity of the organism and its sensitivity to various antimicrobial agents were absent, common sense was of great benefit in the diagnosis and treatment. He further stated that therapy should be based on such information as the detailed examination of the epidemiologic background of such diseases and of the manner in which they progress. He expressed his personal opinion that if these factors were considered, the use of an antimicrobial agent became rational. The author also stated that whether the etiology of an infection was determined on a clinical basis alone or by a combination of clinical and laboratory studies, the choice of chemotherapy should involve consideration of a number of factors to determine the safety, appropriateness and the effectiveness of the treatment. He expressed confidence in the fact that time and laboratory studies would prove these etiologic diagnoses correct and thus resolve diagnostic and therapeutic dilemmas.

Klein (9), in a general discussion, stressed the importance of clinical judgment. He stated that after therapy has been started, microbiological testing results and the patients' clinical course should aid the physician in determining if his diagnostic assumption was correct. In his opinion, if discrepancies occurred, the physician should rely on his common sense.

Kagan (10) also stated that initial therapy should be determined by clinical diagnosis; however, before antibiotic therapy is initiated, a gram stain should be obtained. He emphasized that even though the result of the culture testing was secondary to the clinical response, the culture results could aid the physician should the clinical course prove unsatisfactory. He also stressed that if the clinical response was favorable, the therapy should be continued even if the culture and sensitivity test results indicated that the drug used was among the least effective or was even without effect *in vitro*.

A serious and controversial question has arisen in recent years as to the validity of chemoprophylaxis of infections. McCraken *et al* (11) have stated that since the advent of the antimicrobials, mortality and morbidity have been reduced in a great number of infections. These researchers noted that as a result of this success antimicrobial agents have been used prophylactically, at times with questionable logic. Examples of some of this prophylaxis include usage in viral upper respiratory infections, in post-operative care, in burn therapy, in chronic illnesses, and for urinary catheterizing or tracheostomies. McCraken *et al* (11) were of the opinion that this type of broad coverage was not only ineffective but it encouraged acquired resistance, altered normal bacterial flora of the mucous membranes of the gastrointestional and respiratory tracts,

allowed for the overgrowth of potentially pathogenic organisms, and/or increased the probability of drug toxicity or hypersensitivity. The authors stated that there were instances where prophylaxis could be directed toward a single pathogen such as hemolytic streptococci or meningococci. They cited the following examples: 1) the use of penicillin to prevent group A streptococci infection in patients with a history of rheumatic fever; 2) the use of penicillin prior to and after dental or surgical procedures in patients with valvular heart disease to prevent bacterial endocarditis; 3) the use of antibiotic ophthalmic ointments in newborn infants to prevent ophthalmic neonatorum; and 4) the administration of tetracycline to household contacts of a patient with cholera. They stressed that the physician must be cognizant of the fact that antibiotics administered prophylactically may mask a serious disease state and may in turn lead to the delay or neglect of important therapeutic measures.

Wolman (12) discussed laboratory techniques and applications in clinical pediatrics, as well as several laboratory values and their interrelationships. However, he did not discuss any specific criteria, he only stated his opinion of the applications of certain laboratory tests and their results. The tests that Wolman was primarily concerned with were both complete and differential blood cell counts.

The previous studies, although they contain a wide range of therapy rationale, appeared to lack specific criteria for

initiating antibiotic therapy in pediatric patients. If one were to consider the obtaining of throat cultures as the proper procedure before deciding if antibiotic therapy should be initiated then only 65% of responding physicians were correct.(6) Rosenstein et al (7) reported that because of the high degree of accuracy of throat culture testing by informally trained pediatricians in their offices, 90.3% correct, a greater utilization of this procedure was warranted. Other physicians stressed the importance of careful clinical evaluation as the procedure to follow in diagnostic and therapeutic dilemmas.(8,9,10) These latter physicians stated that the reliability, accessibility and time factors involved in culture testing did not warrant the delay in chemotherapy until the culture results were reported.

The preceeding studies and opinions were concerned with pediatric patients. The literature also contains reports of studies which were concerned with patients of all age groups. Some studies have indicated that approximately one-third of all hospitalized patients have received some type of antimicrobial agent on any given day. (1-5) As a result of this extensive and possible indiscriminate use of antimicrobial agents, several researchers have conducted drug utilization review studies in an attempt to define such factors as appropriateness of therapy, incidence of adverse reactions, the cost of the therapy, and trends of usage.(13-15)

In 1972, Roberts and Visconti (13) attempted to define the extent and trends of use of antimicrobial agents from the standpoint of: the appropriateness, the incidence of adverse reactions, and the cost factors involved in this therapy. The therapy was reviewed and evaluated first by a hospital pharmacy resident, then a Ph.D. pharmacist and finally by one of two physician specialists. Irrational therapy was defined as those cases where: 1) the antimicrobial agent was contraindicated in the particular patient; 2) the patient was allergic to the agent; 3) the medication was inappropriate for the infectious agent as defined by culture and sensitivity testing results; 4) there was no culture and sensitivity testing performed; and 5) the medication was administered in the wrong strength, dosage form and/or for the incorrect duration of therapy. The therapy judged irrational by these researchers accounted for 1) 65.6% of the antimicrobial therapy administered in this study; and 2) 76.8% of the total cost to the patient, hospital or third party payers. In this study, 14.1% of the patients receiving antimicrobial therapy experienced some adverse drug reaction. These authors concluded that the patients receiving antimicrobial therapy tended to be older and stayed in the hospital longer.

In 1966, Ruedy (14) and in 1972 Hanley (15), in patient chart review studies, attempted to delineate between rational and irrational antimicrobial therapy on the basis of agreement

between the initial antimicrobial therapy and the culture and sensitivity testing results. In their studies, the authors defined interim antimicrobial therapy, i.e. therapy prescribed until culture testing results can be obtained, as irrational therapy.

The review of the literature indicated that physicians and pharmacists are concerned with the use of antimicrobials. The physician studies were directed more toward therapy rationale and not specific criteria to be considered before initiating antimicrobial therapy. The drug utilization studies in which the pharmacists were involved were directed toward trends in antimicrobial usage, adverse drug reactions and cost.

CHAPTER II

METHODOLOGY

DEFINTIONS OF TERMS

The terms used in this study conform to the definitions of an accepted medical dictionary.(18) The laboratory test ranges used in this study were those recommended in a text on pediatric laboratory applications.(7) The normal ranges listed in this text conformed to those normal ranges used in the study hospital. The statistical terms and formulas were obtained from an accepted text on statistical methods.(21)

Antimicrobials are agents which destroy microorganisms or suppress their multiplication or growth.(18)

Culture and sensitivity testing is a laboratory procedure used to define the infectious microorganism and determine its sensitivity to various antimicrobial agents.(18)

General (family) practice is that branch of medicine which specializes in the diagnosis and treatment of illnesses affecting all age groups.

Criteria are values by which something can be judged.

Pediatric patients are persons whose ages ranged from six months through 16 years.

Prophylaxis is that therapy directed toward preventing the growth or spread of the microorganism.

T-test is a statistical method for determining the relationships' level of significance. The formula for this test is

$$t = \frac{\bar{X}_1 - \bar{X}_2}{S_{\bar{X}_1 - \bar{X}_2}}$$

$S_{\bar{X}_1 - \bar{X}_2}$ = the standard error of the difference between the means

$$S_{\bar{X}_1 - \bar{X}_2} = S_{\bar{X}_1}^2 + S_{\bar{X}_2}^2$$

$$S_{\bar{X}} = \frac{\tilde{\sigma}}{N-1}$$

t = the numbers of deviation units from the mean.(21)

The 0.01 level of significance means that there is a 99% probability that the relationship stated is correct.

Basophilia is a condition characterized by the presence of basophilic erythrocytes.(18) The range used was above 50 cells/mm^3.

Endothelia, blast or histocyte cells are leukocytic components usually present during chronic infections or during subacute bacterial endocarditis.(18)

Eosinophilia is a condition characterized by the presence of an unusual number of eosinophil cells in the blood.(18) The range used was above 200 cells/mm^3.

Hyperthermia is an abnormally high body temperature.(18) The range used was greater than 99.4°F.

Hypothermia is an abnormally low body temperature.(18) The range used was less than 97.5°F.

Immature or juvenile neutrophils or bands are luekocytic components present whenever leukocytosis is severe or prolonged.(18)

Leukocytopenia is a decrease in the total number of leukocytes in the blood.(18) The range used was below 5,000 cells/mm^3.

Leukocytosis is an increase in the total number of leukocytes in the blood.(18) The range used was greater than 10,000 cells/mm^3.

Lymphocytopenia is a reduction in the number of lymphocytes in the blood.(18) The range used was below 1,000 cells/mm^3.

Lymphocytosis is an excess of normal lymphocytes in the blood.(18) The range used was above 3,000 cells/mm^3.

Monocytopenia is an abnormal decrease in the proportion of monocytes in the blood.(18) The range used was below 200 cells/mm^3.

Monocytosis is an increase in the proportion of monocytes in the blood.(18) The range used was above 500 cells/mm^3.

Neutropenia is a deficiency of neutrophil leukocytes in the blood.(18) The range used was below 2,500 cells/mm^3.

Neutrophilic leukocytosis is an excess of neutrophil leukocytes in the blood.(18) The range used was above 6,000 cells/mm^3.

Study Phases

Permission was obtained to conduct this study in a short-term, general, non-profit hospital of over 500 beds, which serves the Houston metropolitan population. The study consisted of three phases. The first phase was a survey of 205 Senior, Active, and Associate medical staff physicians in the study hospital regarding criteria used for initiating antimicrobial therapy in pediatric patients. The second phase was a review of the charts, 200 discharged pediatric (ages six months through 16 years) patients to obtain data regarding antimicrobial prescribing. The final phase was a computerized (16) comparison of the data derived from the

physician survey and the patient chart review. The following flow charts (Figures 1 and 2) illustrate the methodology involved in this study.

PHYSICIAN SURVEY

Letters of explanation of the study (Figure 3), questionnaires (Figure 4) and self-addressed stamped envelopes were mailed to all members of the Senior, Active, and Associate medical staff whose specialities were either general (family) practice or pediatrics. General (family) practitioners were included because they admit and attend pediatric patients. In the study hospital, the qualifications for these staff categories are: 1) Senior medical staff, a physician who has served on the Active Staff for a minimum of 20 years; 2) Active medical staff, a physician who regularly admits patients to the hospital and has served on the Associate staff for a minimum of two years; and 3) Associated medical staff, a physician who regularly admits patients to the hospital and complies with all other standards for medical staff membership.(17) The categories of the 205 physicians included in the physician survey portion of this Study are shown in Table 1.

FIGURE 1

FLOW CHART SHOWING DATA ACQUISITION AND ANALYSIS OF PHYSICIAN RESPONSES TO THE QUESTIONNAIRE SURVEYING POSSIBLE CRITERIA FOR INITIATING ANTIMICROBIAL THERAPY IN PEDIATRIC PATIENTS

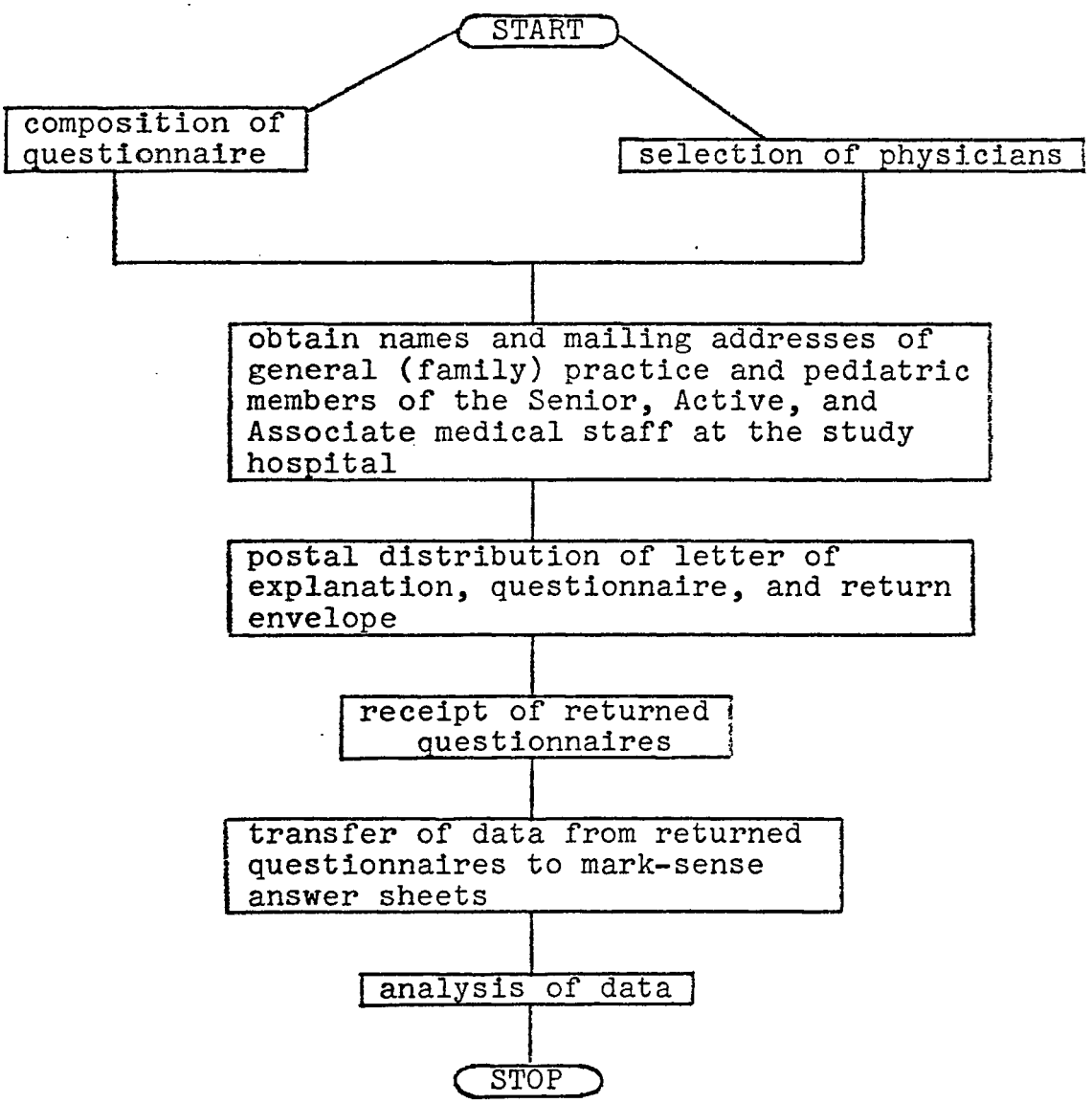
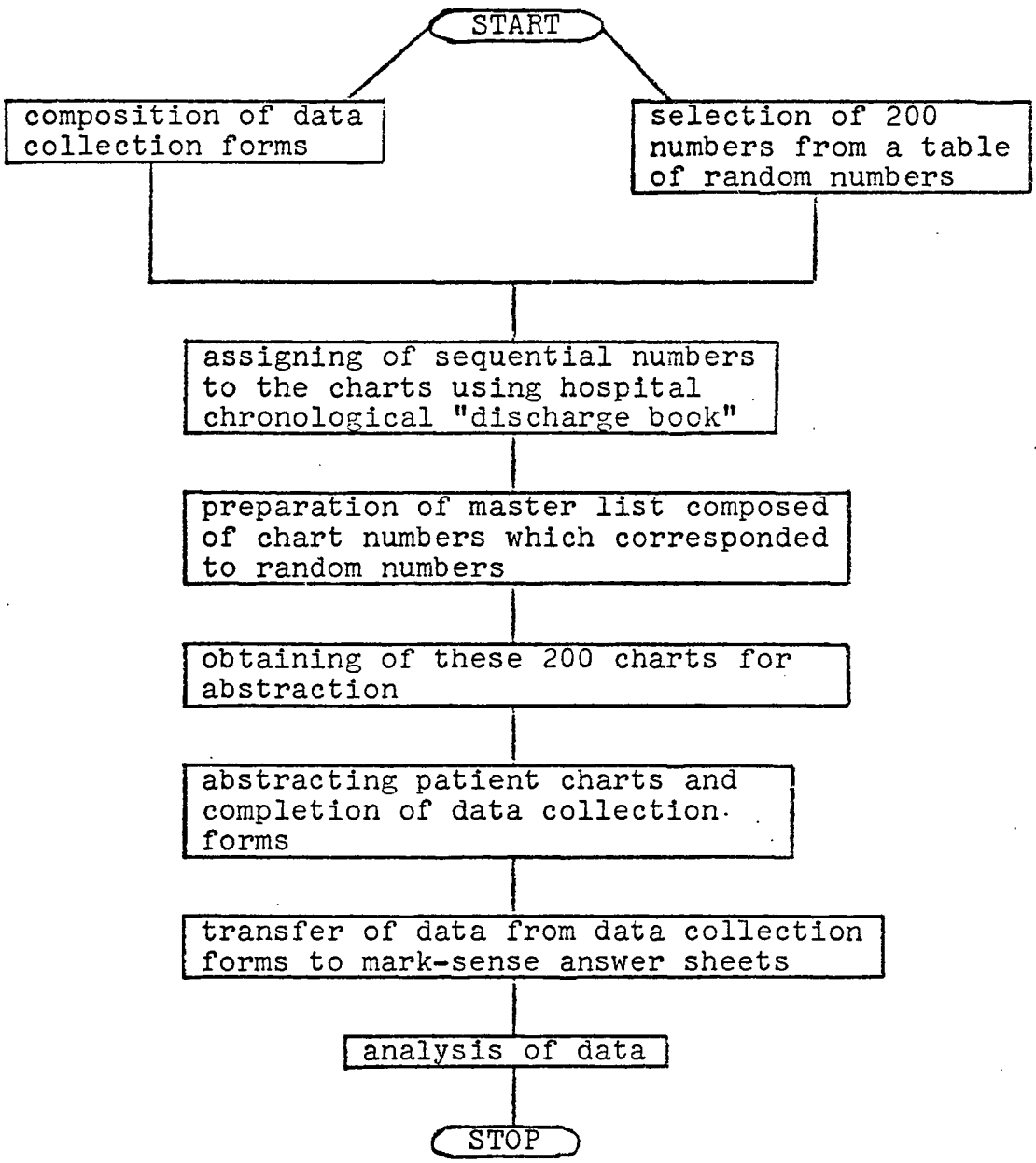


FIGURE 2

FLOW CHART SHOWING AQUISITION AND ANALYSIS OF DATA OBTAINED FROM 200 RANDOMLY SELECTED CHARTS OF DISCHARGED PEDIATRIC PATIENTS AT THE STUDY HOSPITAL



UNIVERSITY OF HOUSTON
CULLEN BOULEVARD
HOUSTON, TEXAS 77004

COLLEGE OF PHARMACY
OFFICE OF THE DEAN

Dear Doctor:

In a project for partial fulfillment of the requirements for a Master of Science Degree in Hospital Pharmacy, I am conducting a survey regarding criteria for initiating antimicrobial therapy in pediatric patients. Would you be kind enough to take a few minutes to complete the enclosed brief check list and return it in the enclosed envelope. Anonymity will be observed.

Any comments you desire to add will be gratefully appreciated.

Thank you most sincerely for your cooperation.

Respectfully,

H. DWIGHT STARR, R.Ph.

FIGURE 3

Letter of Explanation of the Study Mailed to 205 Members of the Pediatric and General (Family) Practice Senior, Active and Associate Medical Staff of the Study Hospital

FIGURE 4

CRITERIA FOR INITIATING ANTIMICROBIAL THERAPY IN PEDIATRIC PATIENTS

Your Specialty: GP____ Pediatrics____ Family Practitioner____

	YES	NO	OTHER-PLEASE SPECIFY
1. Do you initiate antimicoribal therapy if:			
a. Hyperthermia, above 99.4			
b. Hypothermia, below 97.5			
c. Leukocytosis, above 10,000 cells/mm^3			
d. Leukocytopenia, below 5,000 cells/mm^3			
e. Neutrophilic leukocytosis, above 6,000 cells/mm^3			
f. Neutropenia, below 2,500 cells/mm^3			
g. Presence of immature or juvenile neutrophils and/or bands			
h. Lymphocytosis, above 3,000 cells/mm^3			
i. Lymphocytopenia, below 1,000 cells/mm^3			
j. Monocytosis, above 500 cells/mm^3			
k. Monocytopenia, below 200 cells/mm^3			
l. Basophilia, above 50 cells/mm^3			
m. Presence of endothelia, blast or hisocyte cells			
n. Eosinophilia, above 200 cells/mm^3			
o. Known contact with infectious disease			
p. Prophylactic use in emergency case related to injury			
q. Positive culture			
r. Chest x-ray indicating infiltrate			
s. Other clinical symptoms of infection, e.g. abdominal tenderness, chest rales, purulent nasal discharge, inflammation discernible upon gross observation_)			

FIGURE 4 - Continued

	YES	NO	OTHER-PLEASE SPECIFY
t. Patient history indications: 1) Valvular disorders			
2) Rheumatic fever			
u. Pre-dental or surgical procedure			
v. Post-dental or surgical procedure			

2. Do you have access to supplies and equipment for processing throat cultures in your office or within close proximity?_____

3. Have you ever experienced any difficulties in processing throat cultures in your facilities?_____

   If so, explain._____

4. Have you ever experienced any difficulties in processing throat cultures in an outside facility?_____

   If so, explain._____

ADDITIONAL COMMENTS:

FIGURE 4

Questionnaire Mailed to 205 Members of the Pediatric and General (Family) Practice Senior, Active and Associate Medical Staff of the Study Hospital to Survey Possible Criteria for Initiating Antimicrobial Therapy In Pediatric (Ages Six Months Through 16 Years) Patients

TABLE 1

STAFF CATEGORY OF 205 PHYSICIANS TO WHOM QUESTIONNAIRES WERE MAILED TO SURVEY POSSIBLE CRITERIA FOR INITIATING ANTI-MICROBIAL THERAPY IN PEDIATRIC PATIENTS

STAFF CATEGORY OF PHYSICIANS	GENERAL (OR FAMILY) PRACTITIONER	PEDIATRICIAN
SENIOR	1	11
ACTIVE	30	21
ASSOCIATE	98	44
TOTAL	129	76

PATIENT CHART REVIEW

A review of the charts of discharged pediatric patients was conducted at the study hospital. Charts of discharged pediatric patients for the fiscal year, July 1, 1972 through June 30, 1973, were chosen as the total population to be reviewed. From this total population of 2,435, a sample population of 200 charts was randomly selected. At the study hospital, the chart number of each discharged patient is recorded chronologically in a book designated as the "Discharge Book". After assigning sequential numbers to the charts of discharged patients for the study time period, chart numbers corresponding to 200 random numbers selected from a table of random numbers (18) were obtained for a master list of cases to be reviewed.

Information from various sections of each patient chart was abstracted utilizing a data collection form (Figure 5) which was assigned a number corresponding to the master list of patient chart numbers. The essential sections of the patient chart examined and abstracted were: 1) nursing records such as the Nurses' Notes, Nurses' Medication Sheet, the Nurses' Treatment Sheet, the Temperature, Pressure and Respiration (TPR) Record, and the Graphic Chart; 2) physician records such as the Chart Summary Sheet, the History and Physical Form, the Physicians' Order Form, and the Progress Notes; and 3) special report forms such as the Clinical Laboratory Report, the Radiology Report, the Electrocardiogram

FIGURE 5

DATA COLLECTION FORM

Master #____Adm.Date___Dischg.Date_____Age____Sex___Race____

Wt._____Provisional Diagnosis_____

Final Diagnosis_____

Other_____GP (Family Practitioner)_____Pediatrician_____

		YES	NO	OTHER-PLEASE SPECIFY
1.	a. Hyperthermia, above 99.4			
	b. Hypothermia, below 97.5			
	c. Leukocytosis, above 10,000 cells/mm^3			
	d. Leukocytopenia, below 5,000 cells			
	e. Neutrophilic leukocytosis, above 6,000 cells			
	f. Neutropenia, below 2,500 cells			
	g. Presence of immature or juvenile neutrophils and/or bands			
	h. Lymphocytosis, above 3,000 cells			
	i. Lymphocytopenia, below 1,000 cells			
	j. Monocytosis, above 500 cells			
	k. Monocytopenia, below 200 cells			
	l. Basophilia, above 50 cells			
	m. Presence of endothelia, blast or histocyte cells			
	n. Eosinophilia, above 200 cells			
	o. Known contact with infectious disease			
	p. Prophylactic use in emergency case related to injury			
	q. Positive culture			
	r. Chest x-ray indicating infiltrate			
	s. Other clinical symptoms of infection, e.g. abdominal tenderness, chest rales, purulent nasal discharge, inflammation discernible upon gross observation			

FIGURE 5 - Continued

	YES	NO	OTHER-PLEASE SPECIFY
t. Valvular disorder history			
u. Rheumatic fever			
v. Pre-dental or surgical procedure			
w. 1) Post-dental or surgical procedure			
2) If yes, was there culture & sensitivity testing?			

2. Antimicrobial Therapy: Yes_____ No_____

   a. Medication, strength & form_____

      Dose_____ Started_____ D.C.'d_____

   b. Medication, strength & form_____

      Dose_____ Started_____ D.C.'d_____

   c. Medication, strength & form_____

      Dose_____ Started_____ D.C.'d_____

   d. Medication, strength & form_____

      Dose_____ Started_____ D.C.'d_____

3. Discharge antimicrobial(s): Yes_____ No_____

4. Culture & Sensitivity Testing: Yes_____ No_____

DATE	TYPE	DID THERAPY AGREE WITH C&S RESULTS?		IF NOT, WAS THERAPY CHANGED ACCORDINGLY?	
		YES	NO	YES	NO

FIGURE 5

Data Collection Form Utilized In Abstracting 200 Discharged Pediatric (Ages Six Months Through 16 Years) Patient Charts for Possible Criteria for Initiating Antimicrobial Therapy In Pediatric Patients

Report, the Electroencephalogram Report, and the Pathology Report. Other sections examined when they appeared in the patient chart were: 1) Authorization for Surgery; 2) Pre-op Check List; 3) Surgery Report; 4) Recovery and Intensive Care Observation Report; 5) Transfer Forms; 6) Special Admitting Forms such as Emergency Room Report; 7) Discharge Summary; and 8) Death Summary.

The information from these data collection forms were transferred to mark-sense answer sheets to facilitate: 1) the summarization and statistical comparison of criteria by physician speciality; and 2) determination of significant relationships between stated criteria and such factors as the patients' age, sex, race, course of therapy and length of stay in the hospital.

DATA COMPARISON

The final phase of this study was a computerized (16) comparison of the data drived from the physician questionnaire survey and the patient chart review. This comparison was an attempt to formulate possible criteria for initiating antimicrobial therapy in pediatric patients in the study hospital.

In this study, all of the data was transferred to mark-sense answer sheets. These sheets were then analyzed by a Univac 1108 computer.(16)

CHAPTER III

RESULTS AND DISCUSSION

At the present time, the format for drug utilization reviews, such as this study, is not clearly defined. With the advent of clinical pharmacy and increased involvement of pharmacists as contributing members of the health care team, this situation should change and, therefore, studies of this type will be more relevant and significant.

Several problems that can occur in this type of study are: 1) determining normal laboratory values for an age group when age can be a factor effecting the value of laboratory results; 2) determining which criteria to include in the survey; 3) receiving a significant quantity of completed questionnaires; 4) determining the size of a valid sample population; and 5) abstracting data from patient charts.

The criteria selected for use in this study resulted from: 1) a review of medical literature; 2) consultations with physicians; and 3) a review of 12 randomly selected patient charts, not used in this study, in an attempt to formulate all potential criteria for initiating antimicrobial therapy in pediatric patients and to avoid a biased set of criteria. The listing of the criteria was not designed to determine any one criteria for initiating antimicrobial therapy. Each criteria can be a possible indication of

several disease states, but the combination and comparison of all of the criteria must be used in the diagnosis and treatment of any one patient. In addition to these numerous criteria, the physician must consider other variables such as the family history and the patients' history of related disease states. In the current study, this was substantiated by the existence of significant relationships,(22) at the 0.01 level, between each physician response to the stated criteria, except between patient history of valvular disorder and presence of immature or juvenile neutrophils and/or bands. This lack of relationship is consistent with opinion expressed by Wolman.(12) Therefore, even though the establishment of absolute criteria is not practical, this study was an attempt to formulate potential minimal criteria for initiating antimicrobial therapy in pediatric patients.

PHYSICIAN SURVEY

A total of 205 questionnaires were mailed to 76 pediatricians and 129 general (family) practitioners. A total of 135 (65.9%) of the questionnaires were returned. Sixteen (11.9%) of those returned could not be used in this study for various reasons. Six (4.4%) of the returned questionnaires could not be used because the speciality status of the physician was not noted. Nine (6.7%) of the returned questionnaires could not be used because the general (family) practitioner no longer treated pediatric patients. One (0.7%) of the returned questionnaires could

not be used because the general practitioner no longer practiced in the study area. The usable questionnaires in the survey totaled 119 (57.6%). This represented 51 (67.1%) of the 76 pediatricians and 68 (52.7%)of the 129 general (family) practitioners surveyed.

Table 2 summarizes the responses, by physician speciality, to each stated criteria on the questionnaire. Beside each stated criteria, a space labeled "other-please specify" was provided for the physician to note any comments. It was found that when this space was used by the physician, it indicated that he or she only considered this a valid criteria if some other criteria existed. Therefore, both the "yes" and the "other-please specify" responses were considered as positive responses.

Another objective of the physician survey was to attempt to determine if there was any relationship between the individual criteria and the physician speciality. Significance at the 0.01 level was chosen to evaluate the relationships. The simple t test was utilized for determining those relationships significant at the 0.01 level. The analysis of this portion of the study indicated that significant relationships (22) existed between all of the formulated criteria except between patient history of valvular disorder and presence of immature and juvenile neutrophils and/or bands.

It would appear from the percentage (65.9%) return of

TABLE 2

SUMMARY OF 123 RESPONDING PHYSICIANS' POSITIVE RESPONSES (EXPRESSED AS PERCENTAGE) TO PROPOSED CRITERIA FOR INITIATING ANTIMICROBIAL THERAPY IN PEDIATRIC (AGES SIX MONTHS THROUGH 16 YEARS) PATIENTS

CRITERIA	PERCENT OF PHYSICIAN SPECIALITY	
	GENERAL (FAMILY) PRACTICE	PEDIATRICS
I. Clinical Factors		
a. hyperthermia	47.5	38.3
b. hypothermia	35.6	33.9
c. known contact with infectious disease	54.3	59.6
d. prophylactic use in emergency case related to injury	71.2	59.6
e. chest x-ray indicating infiltrate	73.1	91.5
f. other clinical symptoms of infection, e.g. abdominal tenderness, chest rales, purulent nasal discharge, inflammation discernible upon gross observation	88.2	91.5
g. valvular disorder history	67.8	82.9
h. pre-dental or surgical procedure	62.7	68.1
i. post-dental or surgical procedure	61.0	70.2
j. rheumatic fever history	78.0	91.5
II. Laboratory Results		
a. leukocytosis	55.9	29.8
b. leukocytopenia	37.3	31.9
c. neutrophilic leukocytosis	45.8	31.9
d. neutropenia	52.3	40.4
e. presence of immature or juvenile neutrophils and/or bands	49.1	27.7
f. lymphocytosis	37.3	27.7
g. lymphocytopenia	37.3	27.7
h. monocytosis	39.0	27.7
i. monocytopenia	33.9	27.7
j. basophilia	35.6	27.7
k. presence of endothelia, blast or histocyte cells	35.6	27.7
l. eosinophilia	33.9	29.8
m. positive culture	88.2	91.5

self-appraisal type questionnaires that 1) the questionnaire was designed properly, and 2) the surveyed physicians were concerned with the problems involved when considering initiation of antimicrobial therapy in pediatric patients. The anonymity of self-appraisal type surveys prohibits the postal distribution of follow-up letters requesting a response. If the anonymity did not have to be protected, the percentage return could have been greater; but it was believed that a 65.9% response was valid for this study. The sex of the physicians was not noted on the physician questionnaire because only three of the physicians to be surveyed were female. The staff physicians surveyed represented those physicians most actively involved in admitting and treating pediatric patients in the study hospital. The data obtained from the survey of the Senior, Active and Associate Medical Staff of the study hospital and reported in Table 2 appears to indicate that the pediatricians, during the study time interval, prescribed antimicrobial therapy to the study sample population less often than did the general (family) practitioners.

Valuable comments were offered by 47 physicians, 17 pediatricians and 30 general (family) practitioners. A majority of the comments were of such a nature as to aid the study by further defining certain criteria. Several physicians stated that they considered clinical factors or observations as the primary criteria for initiating antimicrobial therapy.

Their reasons for this therapy rationale included: 1) questions as to the validity of laboratory results; 2) objections to the cost to the patient for laboratory testing; 3) problems of patient accessibility to laboratories' and 4) objections to the time required for processing laboratory tests. A few of the responsing physicians, primarily pediatricians, expressed the opinion that therapy should be delayed until all findings, both clinical and laboratory, were considered. These latter physicians stated that the destruction of the patients' normal protective flora of the respiratory or alimentary tract was the best reason not to initiate antimicrobial therapy unless required by culture results and/or other unequivocal signs.

The percentage response of the surveyed physicians seems to indicate that the members of the medical professions, at least those surveyed in this study, are willing to cooperate in studies of this nature. This should serve as encouragement for the members of the pharmacy profession to become involved in this type of research.

PATIENT CHART REVIEW

A total of 200 charts of discharged pediatric (ages six months through 16 years) patients were reviewed. A summary of the data obtained from this abstraction, separated by physician speciality, is shown in Table 3. The summations in this table represent the percent of times that each criteria was documented in the charts. In this portion of

TABLE 3

SUMMARY OF DATA (EXPRESSED AS PERCENTAGE) ABSTRACTED FROM 111 CHARTS OF DISCHARGED PEDIATRIC (AGES SIX MONTHS THROUGH 16 YEARS) PATIENTS INDICATING THE FREQUENCY OF DOCUMENTATION OF PROPOSED CRITERIA FOR INITIATING ANTIMICROBIAL THERAPY

CRITERIA	PERCENT OF PHYSICIAN SPECIALITY	
	GENERAL (FAMILY) PRACTICE	PEDIATRICS
I. Clinical Factors		
a. hyperthermia	45.8	56.8
b. hypothermia	1.4	0
c. known contact with infectious disease	1.4	0
d. prophylactic use in emergency case related to injury	1.4	2.7
e. chest x-ray indicating infiltrate	2.8	16.2
f. other clinical symptoms infection, e.g. abdominal tenderness, chest rales, purulent nasal discharge, inflammation discernible upon gross observation	70.8	48.6
g. valvular disorder history	0	0
h. pre-dental or surgical procedure	0	0
i. post-dental or surgical procedure	16.7	10.8
j. rheumatic fever history	0	0
II. Laboratory Results		
a. leukocytosis	26.4	48.6
b. leukocytopenia	6.9	0
c. neutrophilic leukocytosis	30.6	40.5
d. neutropenia	2.8	5.4
e. presence of immature or juvenile neutrophils or bands	25.0	43.2
f. lymphocytosis	62.5	64.9
g. lymphocytopenia	2.8	0
h. monocytosis	18.1	24.3
i. monocytopenia	1.4	0

[1]Numerals and lower case letters correspond to those used in Table 2.

TABLE 3 - Continued

CRITERIA	PERCENT OF PHYSICIAN SPECIALITY	
	GENERAL (FAMILY) PRACTICE	PEDIATRICS
j. basophilia	0	0
k. presence of endothelia, blast or histocyte cells	13.9	10.8
l. eosinophilia	20.8	8.1
m. positive culture	5.6	8.1

the study, it was found that 89 (44.5%) of the pediatric patients were treated by other specialists, e.g. neurologists, urologists, and/or plastic and general surgeons. These patients were eliminated from the study since they were not treated by the physicians surveyed, that is, pediatricians or general (family) practitioners.

The data obtained from the patient chart review of the sample population and reported in Table 3 appears to indicate that both the pediatricians and the general (family) practitioners in this study utilized laboratory results to substantiate their clinical judgments to initiate antimicrobial therapy. It appeared that if antimicrobial therapy was to be initiated then the primary indication was clinical judgement.

Another objective of the patient chart review was to attempt to determine if there was any relationship at the 0.01 level (22) between the variables; patient age, sex and/or race, and 1) the stated criteria and 2) the physician speciality. The analysis of the data indicated that no relationship existed between these variables and the stated criteria and/or the physician speciality.

This study was also an attempt to determine if there was any relationship between each of the stated criteria. Significance at the 0.01 level was chosen to determine relationships. The results of the analysis indicated that significant relationships (22) existed between:

1) hyperthermia and
   a) other clinical symptoms of infection, e.g. abdominal tenderness, chest rales, purulent nasal discharge, and inflammation discernible upon gross observation,
   b) leukocytosis,
   c) initiation of antimicrobial therapy,
   d) culture and sensitivity testing performed,
   e) post-operative antimicrobial therapy initiated;
2 known contact with infectious disease and
   a) leukocytopenia,
   b) lymphocytopenia;
3) prophylactic use in emergency case related to injury and
   a) chest x-ray indicating infiltrate,
   b) initiation of antimicrobial therapy;
4) chest x-ray indicating infiltrate and
   a) initiation of antimicrobial therapy,
   b) culture and sensitivity testing performed,
   c) post-operative antimicrobial therapy,
   d) known contact with infectious disease;
5) other clinical symptoms of infection and
   a) initiation of antimicrobial therapy,
   b) post-operative antimicrobial therapy,

6) leukocytosis and
   a) hyperthermia,
   b) initiation of antimicrobial therapy,
   c) post-operative antimicrobial therapy,
   d) neutrophilic leukocytosis,
   e) monocytosis,
   f) presence of immature or juvenile neutrophils and/or bands;
7) leukocytopenia and
   a) known contact with infectious disease,
   b) eosinophilia,
   c) post-operative antimicrobial therapy;
8) neutrophilic leukocytosis and
   a) leukocytosis,
   b) lymphocytosis;
9) presence of immature or juvenile neutrophils and/or bands and
   a) leukocytosis,
   b) post-operative antimicrobial therapy;
10) lymphocytosis and
   a) neutrophilic leukocytosis,
   b) post-operative antimicrobial therapy;
11) lymphocytopenia and
   a) known contact with infectious disease,
   b) monocytopenia,

12) monocytosis and
    a) lymphocytosis,
    b) eosinophilia,
    c) positive culture,
    d) initiation of antimicrobial therapy,
    e) culture and sensitivity testing performed,
    f) post-operative antimicrobial therapy,
    g) presence of endothelia, blast or histocyte cells;
13) monocytopenia and lymphocytosis;
14) presence of endothelia, blast or histocyte cells and monocytosis
15) eosinophilia and leukocytopenia;
16) positive culture and
    a) leukocytopenia
    b) initiation of antimicrobial therapy,
    c) post-operative antimicrobial therapy;
17) initiation of antimicrobial therapy and
    a) hyperthermia,
    b) prophylactic use in emergency case related to injury,
    c) chest x-ray indicating infiltrate
    d) other clinical symptoms of infection,
    e) leukocytosis,
    f) positive culture,
    g) culture and sensitivity testing performed;

18) culture and sensitivity testing performed and
    a) hyperthermia,
    b) chest x-ray indicating infiltrate,
    c) monocytosis,
    d) initiation of antimicrobial therapy,
    e) post-operative antimicrobial therapy initiated; and
19) post-operative antimicrobial therapy initiated and
    a) other clinical symptoms of infection,
    b) neutrophilic leukocytosis,
    c) presence of immature or juvenile neutrophils and/or bands,
    d) lymphocytosis,
    e) monocytosis,
    f) positive culture, and
    g) culture and sensitivity testing performed.

These significant relationships were consistent with the opinion of Wolman.(12)

In Table 4, all of the criteria included in the patient chart review are represented by "variable numbers". Those relationships which were significant at the 0.01 level are designated with an asterix. The information from this table was discussed in the preceeding paragraph. The key for this table is as follows:

Criteria	Variable No.
I. Clinical Findings	
a. hyperthermia	1
b. hypothermia	2
c. known contact with infectious disease	3
d. prophylactic use in emergency case related to injury	4
e. chest x-ray indicating infiltrate	5
f. other clinical symptoms of infection	6
g. valvular disorder history	7
h. pre-dental or surgical procedure	8
i. post-dental or surgical procedure	9
j. rheumatic fever history	10
II. Laboratory Results	
a. leukocytosis	11
b. leukocytopenia	12
c. neutrophilic leukocytosis	13
d. neutropenia	14
e. presence of immature or juvenile neutrophils and/or bands	15
f. lymphocytosis	16
g. lymphocytopenia	17
h. monocytosis	18
i. monocytopenia	19
j. basophilia	20
k. presence of endothelia, blast or histocyte cells	21
l. eosinophilia	22
m. positive culture	23
III. Antimicrobial therapy initiated	24
IV. Culture and Sensitivity testing performed	25

TABLE 4

SIGNIFICANT RELATIONSHIPS AT THE 0.01 LEVEL BETWEEN INDIVIDUAL CRITERIA AS DEFINED BY REVIEW OF 111 CHARTS OF DISCHARGED PEDIATRIC PATIENTS

Variable No.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
1						*			*		*													*	*
2																									
3												*					*								
4																							*	*	*
5						*									*			*						*	
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24	*			*	*	*					*												*		
25	*			*							*	*						*					*		

Another objective of the patient chart review was to ascertain by inspection if any interrelationship existed between the patients' length of stay in the hospital and such factors as 1) had the patient received antimicrobial therapy 2) was culture and sensitivity testing performed; and 3) was the patient discharged with an antimicrobial agent? The summary of these interrelationships is shown in Table 5.

Roberts and Visconti (13) concluded that the length of stay in the hospital and the percentage of patients receiving antimicrobial therapy were directly proportional. The data obtained in this study and reported in Table 5 substantiates this conclusion. The reason for this direct proportionality is that these patients were ill enough to warrant an increased length of stay in the hospital. This increased length of stay is not due to the patients receiving antimicrobial therapy. The length of stay would have probably increased if the antimicrobial therapy had not been initiated.

Table 6 summarizes the data abstracted to attempt to determine if the physician changed the chemotherapy when the results of the culture and sensitivity tests indicated that the initial chemotherapy was inappropriate.

The data in table 6 shows that seventy patients (63.1%) of the sample population received antimicrobial therapy; and 34 (48.6%) of these patients had culture and sensitivity testing performed prior to the initiation of this therapy.

TABLE 5

SUMMARY OF THE INTERRELATIONSHIP (EXPRESSED AS PERCENTAGE) BETWEEN THE LENGTH OF STAY IN THE HOSPITAL FOR 111 PEDIATRIC PATIENTS AND SUCH FACTORS AS PATIENTS RECEIVING ANTIMICROBIAL THERAPY, HAVING CULTURE AND SENSITIVITY TESTS PERFORMED, AND/OR DISCHARGED WITH ANTIMICROBIAL AGENTS

LENGTH OF STAY (DAYS)	TOTAL NUMBER PATIENTS	PERCENTAGE OF PATIENTS		
		RECEIVING ANTIMI-CROBIAL THERAPY	CULTURE AND SENSITIVITY TESTING PERFORMED	DISCHARGED WITH AN ANTIMI-CROBIAL AGENT
1	6	16.7	8.3	8.3
2	13	38.5	30.8	23.1
3	48	53.6	12.6	12.6
4	15	46.9	20.1	26.8
5	7	28.6	28.6	28.6
6	5	40.0	40.0	40.0
7	4	50.0	50.0	25.0
8	2	50.0	50.0	0
9	1	100.0	100.0	100.0
10	1	0	0	0
11	1	0	0	0
12	1	100.0	0	100.0
13	2	100.0	50.0	50.0
14	1	100.0	0	0
15	2	50.0	0	0
17	2	50.0	50.0	0

TABLE 6

SUMMARY OF COMPLIANCE BETWEEN INITIAL CHEMOTHERAPY AND RESULTS OF CULTURE AND SENSITIVITY TESTS AS DEFINED BY REVIEW OF 111 DISCHARGED PEDIATRIC (AGES SIX MONTHS THROUGH 16 YEARS) PATIENT CHARTS

PHYSICIAN SPECIALITY	PERCENT AGREEMENT BETWEEN INITIAL CHEMOTHERAPY AND CULTURE AND SENSITIVITY TESTING RESULTS	PERCENTAGE OF TIMES CHEMOTHERAPY WAS CHANGED IN ACCORDANCE WITH CULTURE AND SENSITIVITY TESTING RESULTS
Pediatrics	30.0	0
General (Family) Practice	46.7	11.0

These 34 patients received interim antimicrobial therapy, i.e. therapy prescribed until culture testing results could be reported. The data from Table 6 indicates, however, that if this initial chemotherapy, based on clinical judgment, was shown to be inappropriate by microbiological testing results, the physician did not change the therapy accordingly. The therapy was only changed in accordance with the culture and sensitivity tests four times (11%). Since the physicians ordered the tests, the objection to patient cost of laboratory testing procedures would not appear to be pertinent. It would appear that the physicians who did not change the therapy to agree with microbiological testing results either doubted the validity of the tests or, like Kagan (10), felt that if the clinical response was favorable, the therapy should be continued even if the culture and sensitivity test results indicated that the drug was among the least effective or was even without effect *in vitro*.

COMPARISON OF INFORMATION DERIVED FROM RESPONDING PHYSICIANS WITH THAT DERIVED FROM PATIENT CHART REVIEW

Table 7 summarizes the comparison of data derived from 119 responding physicians with that derived from reviewing the charts of 111 discharged pediatric patients who were treated by either pediatricians (PED) or general (family) physicians (GP).

TABLE 7

COMPARISON OF POSITIVE FREQUENCY ANALYSES OF DATA ABSTRACTED FROM 111 DISCHARGED PEDIATRIC (AGES SIX MONTHS THROUGH 16 YEARS) PATIENT CHARTS AND 119 RETURNED PHYSICIAN QUESTIONNAIRES REGARDING POSSIBLE ANTIMICROBIAL THERAPY IN PEDIATRICS

CRITERIA	PERCENT OF PHYSICIAN SPECIALITY PATIENT CHART REVIEW		RESPONDING PHYSICIANS	
	GP	PED	GP	PED
I. CLINICAL FACTORS				
a. hyperthermia	45.8	56.8	47.5	38.3
b. hypothermia	1.4	0	35.6	33.9
c. known contact with infectious disease	1.4	0	54.3	59.6
d. prophylactic use in emergency case related to injury	1.4	2.7	71.2	58.6
e. chest x-ray indicating infiltrate	2.8	16.2	73.1	91.5
f. other clinical symptoms of infection, e.g. abdominal tenderness, chest rates, purulent nasal discharge, inflammation discernible upon gross observation	70.8	48.6	88.2	91.5
g. valvular disorder history	0	0	67.8	82.9
h pre-dental or surgical procedure	0	0	62.7	68.1
i. post-dental or surgical procedure	16.7	10.8	61.0	70.2
j. rheumatic fever history	0	0	78.0	91.5
II. LABORATORY RESULTS				
a. leukocytosis	26.4	48.6	55.9	29.8
b. leukocytopenia	6.9	0	37.3	31.9
c. neutrophilic leukocytosis	30.6	40.5	45.8	31.9
d. neutropenia	2.8	5.4	52.3	40.4

TABLE 7 - Continued

CRITERIA	PERCENT OF PHYSICIAN SPECIALITY PATIENT CHART REVIEW		RESPONDING PHYSICIANS	
	GP	PED	GP	PED
e. presence of immature of juvenile neutrophils or bands	25.0	43.2	49.1	27.7
f. lymphoctyosis	62.5	64.9	37.3	27.7
g. lymphocytopenia	2.8	0	37.3	27.7
h. monocytosis	18.1	24.3	39.0	27.7
i. monocytopenia	1.4	0	33.9	27.7
j. basophilia	0	0	35.6	27.7
k. presence of endothelia blast, or histocyte cells	13.9	10.8	35.6	27.7
l. eosinophilia	20.8	8.1	33.9	29.8
m. positive culture	5.6	8.1	88.2	91.5

The comparison of the data derived from the physician survey and the patient chart review (Table 7) would appear to indicate that the physicians were cognizant of the complexities of diagnosing and treating individual pediatric patients. Therefore, they appeared to rely primarily on clinical judgment, based on their own practical experience, to determine if and when to initiate antimicrobial therapy in pediatric patients.

Initially, it was estimated that the reviewing and abstracting would involve an average of 30 minutes per patient chart. However, several complex patient charts required in excess of three hours. Thus, the average time involved in reviewing and abstracting increased from the estimated 30 minutes to approximately one hour. The increase in this required time period was due to the lack of standardization of patient charts. There is little standardization as to the chart form upon which observations and data are noted and/or recorded, and likewise only slightly more standardization as to the arrangement of the forms within the patient chart.

CHAPTER IV

CONCLUSION

The results of this study to determine potential criteria for initiating antimicrobial therapy in pediatric patients allow for drawing conclusions from physician comments on a survey as well as from the statistical analysis of the data collected in the physician survey and the patient review. The comments from the physician survey indicated that the physicians were cognizant of the complexities involved in initiating antimicrobial therapy in pediatric patients. The percentage of completed questionnaires returned (57.6% of the 205) indicates that the physicians surveyed for this study were willing to cooperate with pharmacists in a study of this nature. Microbiological procedures are available for determining the sensitivity of specific infectious agents; however, the physician survey comments indicated that they objected to the patient cost of these tests and the time delay involved and were concerned about the validity of the results of such tests.

One conclusion can be drawn from the observation of the data collected in both the physician survey and the patient chart review. It appeared that physicians must and do rely primarily on clinical judgment based on their own practical experience.

The statistical analysis of the data collected from

the 119 returned physician questionnaires and the 111 discharged pediatric patient chart reviews did provide some relationships significant at the 0.01 level. (22) From the physician survey significant relationships existed between all of the physician responses to each stated criteria except between the presence of immature or juvenile neutrophils and/or bands and patient history of valvular disorder. The analysis of data from the patient chart review showed significant relationships existed between 63 of the stated criteria and thus it can be concluded that no single criteria is indicative of the need for initiating antimicrobial therapy.

In summary, it might be concluded that ideally physicians should use their clinical judgment in initiating antimicrobial therapy in pediatric patients and should consider clinical and laboratory evaluations for continuation of antimicrobial therapy. These laboratory tests to be evaluated include 1) complete and differential blood cell counts and 2) culture and sensitivity tests.

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ADDENDUM

Recommendations for Future Studies

In order for studies of this nature to be more relevant and valid, the following recommendations might be considered by future investigations: 1. It is recommended that a method of determining the physicians' training status be established in order to compare variables between the physicians' specialty and prescribing habits. 2. It is recommended that future drug utilization reviews be conducted concurrent with the patients' hospitalization provided the same investigator follows the patient throughout his or her hospital stay.