REASONS UNDERLYING ANTIMICROBIC MISUSE IN A UNIVERSITY HOSPITAL

by

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INTRODUCTION

Recent reports suggest an alarming degree of antimicrobic overuse and misuse in this country (1-6). Consuming 35% of the national expenditure for drugs (3,4), over 180 million prescriptions, nearly one for every man, woman and child, are filled in the U.S. every year(4). Approximately 40% of all hospitalized patients receive one or more antibiotics during their confinement, yet up to two-thirds of these have no evidence of infection (1-6).

Despite the unrestrained use of an ever increasing antimicrobic armamentarium, now exceeding 40 generic forms and over 300 proprietary preparations in this country alone, bacterial infection persists to be a major cause of morbidity and mortality (7). In fact the incidence of life-threatening infection, especially bacteremia caused by gram negative bacilli appears to be rising precipitously (7,8). Furthermore, emergence of drug resistance in previously susceptible species (9) such as Neisseria meningititis (sulfonamide), Staphylococcus aureus (penicillin and recently methicillin(10)), the gonococcus (to increasing levels of penicillin (9)), Pseudomonas aeruginosa (gentamicin (11) and carbenicillin (12)), Shigella (ampicillin (13)), and most recently Hemophilus

influenzae (ampicillin (14)), are now the unwelcome consequences of an era of antimicrobic excess. Superinfection by multi-resistant bacterial species or fungi, often lethal (15,16)or adverse toxic or hypersensitivity reactions (17,18) complicate antimicrobial therapy in up to 20% of courses. Most alarmingly, outbreaks within intensive care units caused by multi-resistant gram-negative bacilli, primarily *Klebsiella*(19-23),have been linked directly to heavy use of broad spectrum antibiotics, primarily for prophylaxis. In two instances epidemic infections could not be curtailed despite aggressive preventive measures until antibiotic use was restricted (22,23). In several outbreaks, the multi-resistant epidemic pathogen (19,22), and in one frightening report, the "epidemic episome" mediating drug resistance (24) spread to family members of cases following discharge from the hospital, confirming the far reaching sequellae of antimicrobic excess

Reasons offered for wide-scale overuse include "fear" of therapeutic failure in obscure illness, patient expectation (25),expense of diagnostic studies, heavy promotion by the pharmaceutical industry, and pharmacologic ignorance on the part of physicians (3,4). Although a number of studies have documented misuse, primarily in community (1,2)

or municipal hospitals (5), few (2,3) have examined specific patterns of usage, i.e. the possible reasons underlying irrational therapy.

This study carried out at a university hospital was designed to (1) determine in this type of hospital the patterns of antimicrobic use in hospitalized medical and surgical patients, especially the magnitude of inappropriate therapy, (2) quantitate where possible the immediate clinical sequelae and economic costs of overuse and (3) provide further understanding of reasons underlying inappropriate therapy. Programs aimed at upgrading the quality of antimicrobic use will depend heavily on identification of those factors influencing misuse.

METHODS

Background: The University of Wisconsin Hospitals is a 720-bed, acute care, referral hospital located in Madison, Wisconsin. It is the major teaching hospital of the University of Wisconsin Center for Health Sciences. It's Infection Control Unit conducts periodic prevalance surveys of nosocomial infection and antimicrobial use. Physicians from the Infectious Disease Service see in consultation most patients with complex infectious disease problems in the hospital. Use of cephalexin and oral carbenicillin are restricted (3). Justification to a member of the Infectious Disease Service by a prescribing physician must preceed therapy (26). The hospital's diagnostic bacteriology laboratory also provides an indirect, but substantial, favorable influence upon the quality of antimicrobic use in the hospital by it's policys on antimicrobic sensitivity testing (28). For instance, susceptibility to carbenicillin is routinely tested only with isolates of Pseudomonas aeruginosa, and urinary isolates of Enterobacter and indole-positive Proteus and chloramphenicol testing is done only on specific request. The Pharmacy and Therapeutics Committee has also been very active for a number of years in its attempts to implicitly improve antimicrobic use by control of the hospital formulary (27), specifically limiting it's size by excluding most combination drugs and other preparations

of equivocal efficacy, and redundant proprietary preparations. Since 1971, a registered pharmacist has been assigned to each patient care unit to administer all medications and to provide pharmacologic monitoring and consultation.

Study population: The neurosurgical ward, urology ward, a general surgical and a general medical ward were selected for study. All newly admitted patients to the four study units between February 1 and March 8, 1975 were followed longitudinally during their entire period of hospitalization. If transferred to non-study wards, patients remained in the study only if physicians from the original study unit maintained responsibility for medical care.

Data collected: For uniformity, all primary data was collected by one of the co-authors (A.S.) utilizing a standardized form (Appendix I). Information obtained initially and where indicated serially included identifying data, age and sex, all major clinical diagnoses, any history of allergic illness, especially drug allergies, all surgical operations, daily temperature and any clinical signs or symptoms of infection, any preceding (prior to admission or transfer) antimicrobic therapy, all systemic antimicrobial drugs recieved, including the dose, route and duration, the

results of all Gram stained smears, bacteriologic cultures and antimicrobial sensitivity testing, and pertinent accompanying laboratory data (hemogram, platelet count, urinalysis, roentgenograms, radionuclear scans, serum urea nitrogen and creatinine, bilirubin and SGOT). Only systemic antibacterial drugs were studied; oral non-absorbable agents, topical preparations, antituberculous and anti-parasitic drugs were excluded from study. Aware that return of final bacteriologic reports to the patient's chart is not always done, the bacteriology laboratory's records for each patient were reviewed at least two weeks after hospital discharge.

From the patient's clinical record, it was determined whether therapy was intended for prophylaxis or for the treatment of suspected or obvious (presumptive) infection. Antimicrobial therapy without clinical evidence of infection or without a statement in the record indicating therapeutic goals was considered prophylaxis.

Whether the physician stated in the patient's record (1) that antibiotics had been started, and (2) the clinical rationale for antimicrobic therapy (i.e. specific treatment was aimed at presumptive infection or had a prophylactic goal) were noted.

Nursing notes, the narrative record and laboratory

data were regularly reviewed for evidence of temporally-related adverse toxic or hypersensitivity effects which might be related to antimicrobic therapy. The methodology of Cluff and his colleagues (17) were followed for monitoring and defining adverse effects. During each antibiotic course, other simultaneous drug therapy was examined to identify potentially significant drug interactions involving antimicrobics (29). The cost of antimicrobial therapy to the patient was determined from Central Pharmacy billing records.

Criteria and Definitions: Criteria for active infection at various sites are those followed by the CDC's National Nosocomial Infection Surveillance Program which have been published by one of the authors (30)

The appropriateness of antimicrobial therapy was assessed initially, based on the first drugs selected, and then finally after all antimicrobics comprising a continuous course of therapy had been discontinued. All decisions regarding appropriateness were made by the physician-coauthor (D.M.).

Appropriate therapy of presumptive infection required (1) clinical evidence suggesting infection at the outset of therapy, (2) rational drug choice(considering the host

state, the likely or known pathogens and the clinical pharmacology of the drug), and (3) modification of therapy when indicated by the clinical course and results of bacteriologic studies. Failure to obtain cultures before therapy was not considered grounds to designate therapy as inappropriate. A goal of the study was to determine whether performance of cultures implicitly influenced quality of antimicrobic use.

A uniformly accepted listing of clinical states where prophylactic antimicrobial therapy might provide benefit is not available although general guidelines have been published (31-33). Only those indications for medical prophylaxis published by the Medical Letter (33) were accepted in this study, i.e. considered appropriate. Classification of surgical procedures by likelihood of intraoperative contamination has been published in the 1963 National Research Council Study (34). Although recent studies now suggest for the first time efficacy of prophylactic antimicrobials in "clean" orthopedic surgery (35), no studies in other "clean" types of surgery have shown benefit, and in this study, surgical prophylaxis was considered inappropriate if employed for clean surgical procedures. Moreover, both animal experiments (36) and abundant clinical studies (34,37,38) now show that surgical prophylaxis begun post-operatively is valueless. Thus, in this study surgical prophylaxis was considered appropriate : 1) only when utilized for potentially contaminated (non-clean) operations, 2) if started before the anticipated exposure, i.e., preoperatively, 3) when the drug or drugs were likely to be effective against anticipated microbial contaminants and 4) when prophylaxis was not continued beyond 72 hours (39). Prophylaxis during prostatic resection (40) was considered acceptable if consonant with criteria 2 through 4 above. However, prophylaxis of cardiac catheterization was considered inappropriate (41,42).

Inappropriate therapy was subclassified in this study as follows:

- Inappropriate for suspected infection
  - No evidence of infection
  - Poor drug choice
    - Unlikely to be effective (pharmacologic reasons or probable microbial drug-resistance)
    - Dose
    - Route
    - Duration
    - Patient allergic by history
    - Spectrum unnecessarily broad
  - Failure to modify regimen when indicated
- Inappropriate for prophylaxis
  - Not indicated
  - Begun post-operatively
  - Poor drug choice
  - Duration of therapy too long

RESULTS

Incidence of Antimicrobial Use. Overall 24.2% of the 324 patients studied recieved one or more systemic antimicrobic agents during hospitalization (Table 1). Use was greatest in urology patients (35%) and lowest in neurosurgery (9%). The mean number of agents comprising a therapeutic course of therapy ranged from 1.3 in medical patients to 2.2 in neurosurgical patients.

(Table 2)

Four drugs, ampicillin (33%), cephalosporins (27%), penicillins G and V (26%) and gentamicin (16%) comprised part or all of over 90% of antimicrobic regimens. Parenteral cephalosporins were employed in 71% of prophylactic therapies, however, the oral cephalosporin cephalexin was used but twice during the entire period of study.

Apparent or suspected infection prompted antimicrobic therapy in 70% of instances, whereas prophylaxis was the specifically stated or presumed therapeutic goal in 30% of courses (Table 1). Infection, when suspected, was confirmed in 33 of 57 instances overall (55%). Confirmation occurred in 72% of surgical patients but in only 39% of suspected infections on medicine units. Treatment of presumed infection could be judged as appropriate even if clinical infection was subsequently disconfirmed, if drugs were discontinued when it was apparent that infection was not the cause of the patient's clinical picture.

Diagnostic Studies Before Therapy. As seen in Table 1, pre-therapy cultures were obtained in 74% of presumed infections (80% on surgical units and 60% on medicine). Falilure to obtain cultures before treatment occurred most frequently in presumptive sepsis (3 of 5

cases), and surgical wound infections (58%) (Table 3). Gram stained smears of sputum preceded and guided therapy of presumed respiratory tract infection in 7 of 12 cases; all were in medical patients and appropriate therapy resulted in every instance.

Appropriateness of therapy. Therapy was judged appropriate in 56% of instances overall; 60% of the time when directed at presumed infection and in 42% of courses designated for prophylaxis (Table 4). Except for the neurosurgical service where all six courses of therapy were appropriate, appropriateness of therapy was comparable on the other three major medical services, ranging from 48% to 54%.

Primary reasons for inappropriate therapy of presumed infection (Table 4), were poor drug choice (in 15 of 23 inappropriate courses), and an absence of clinical evidence suggesting infection (8 of 23). In eight of the 15 designations of poor drug choice, the agent selected was unlikely at the outset to be clinically effective considering the pathogens most likely to be encountered; this was confirmed in 4 instances clinically (e.g. by continued infection), and in 5 others by in vitro sensitivity testing. Therapy of respiratory tract infections (50%) and sepsis (60%) were least frequently judged appropriate (Table 3). It is noteworthy (Table 3), that pre-therapy cultures were obtained in 30 of 34 (88%) appropriate courses, but in only 57% of inappropriate courses ($p < .05$).

Prophylaxis was judged inappropriate because of being initiated too late (6 of 7 inappropriate courses, all in surgical patients) was not clinically indicated (5 courses), or was unduly prolonged i.e. greater than 72 hours (5 courses, also all on surgery).

Of the five drugs most heavily prescribed during the study, except for tetracycline (25% of use deemed appropriate), appropriateness of use was very comparable(Table 2).

Physician's Notes in the Patient Record. As seen in Table 1, the physician indicated in the patient's narrative record at the outset of therapy that antibiotics had been initiated only 42% of the time and a written justification for therapy appeared in only 20% of courses. General surgical physicians were least likely (12%) to include mention of antimicrobial therapy in the clinical narrative.

Adverse Sequelae of Therapy. Adverse reactions (Table 5) including super-infection (7% of antimicrobic courses), phlebitis (4%) and severe gastrointestinal symptoms (5%), occurred in 17% of patients receiving antibiotic therapy. Potentially harmful drug interactions were detected in 2 patients: combined therapy with tetracycline and ampicillin occurred in a patient with severe H. influenzae pneumonia and another patient was receiving concurrent tetracycline and antacids; however, adverse effects did not develop in either instance, primarily due to early recognition by the ward pharmacist which led to therapeutic modification. Sixty-two percent of adverse reactions developed in patients receiving inappropriate therapy.

Cost of Antimicrobial Therapy. Based on cost data from approximately 85% of patient receiving antimicrobials, the average cost of appropriate usage was derived to be $55.30 and of an inappropriate course of therapy, $84.45. Applying these figures to the 14,650 patient admitted to our hospital in 1974, and considering that based on this

study one-quarter of patients getting antibiotics received them needlessly (Table 4), it can be projected that unnecessary antibiotic therapy costs patients in our hospital $70,465 each year.

DISCUSSION

The Joint Commission on Accreditation of Hospitals has charged hospitals with maintaining active programs of infection control including surveillance of nosocomial infection and antimicrobic use within the hospital (43). Moreover, an expert committee under the auspices of the American Medical Association recently advocated development within individual hospitals of intramural guidelines for antimicrobic use and mechanisms for antimicrobic utilization review (4). The data and conclusions of our study, the third of it's kind, conducted at University of Wisconsin Hospitals in the past 2 years, will be transmitted to the medical and pharmacy staff as a major step to upgrading antimicrobic use in our institution.

Before comparing rates of use found in our and other studies, it is important to be aware of the differences between prevalence and incidence. Most published studies, for obvious logistic reasons have been prevalence surveys (1,5,6,44,45) which determine the proportion of patients in the hospital on a given day who are recieving antimicrobics. Studies of incidence use, such as ours, require collection of data over the entire period of hospitalization and rates are usually expressed per hospitalization of 100 patients. Only if the durations of patients both receiving and not receiving antimicrobics are identical, will the 2 rates coincide. In that patients receiving antimicrobics, on the average, are probably hospitalized somewhat longer than non-recipients (2) prevalence ratios will somewhat exceed incidence rates in identical populations. Thus, the incidence of use in our hospital, 24.2%, and the University of Virginia hospital (3) 28.0%, indicate antimicrobic utilization very comparable to

municipal (5,45) and most community instistutions (1,2,6,44). The percentage of patients receiving antimicrobics with clinical evidence of infection is difficult to compare unless uniform criteria are employed, and in the various studies, results have ranged widely with no discernable pattern by type of institution; our experience (38.5%) was a median for the listed studies in Table 6.

Relatively few studies have examined appropriateness of antimicrobial use. Even in those studies evaluating this parameter, it can be statistically hazardous to compare results because of differing representations of specialty services in hospitals studied, and nonuniformity of survey teams, protocols, and criteria for appropriate use. However, as seen in Table 6, the differences are so striking as to probably circumvent nonuniformity. Antimicrobics appear to be used in university hospitals much more appropriately (48% at the University of Virginia Hospitals (3) and 56% in our institution), than in community hospitals((13%) in Roberts and Visconti's institution (2)).However, misuse nearly one-half of the time is disappointing and indicates substantial need for improvement in teaching(ie university)hospitals as well as community hospitals.

The incidence of adverse reactions to antimicrobic therapy in our study (17%) compares very closely to previous studies (2,17,18). Nearly two-thirds of adverse reactions occurred in patients receiving inappropriate therapy even though inappropriate therapy made up only 44% of all antimicrobic use. Moreover, extrapolating our usage data, which are quite conservative compared with other studies, and our cost figures

for inappropriate therapy, which are very comparable to Roberts and Visconti's (2), to the 40 million patients admitted to U.S. hospitals every year suggests that approximately 2.5 million hospitalized Americans receive unneeded antibiotics, costing over 200 million dollars annually.

Based on this study, several factors appear to heavily influence inappropriate use of systemic antimicrobics:

1. Therapy designated for prophylaxis was least likely (42%) to be appropriate. Misguided prophylaxis, almost solely in surgical patients and divided equally between being clinically unwarranted and nonoptimally applied made up 1/3 of all inappropriate antimicrobic courses. Both Roberts and Visconti (2) and Kunin, et al (3), found misguided prophylaxis comprised over one-half of inappropriate therapy. Only 2 medical patient in our study received antimicrobic prophylaxis, both for cardiac catheterization which was judged inappropriate; prophylactic antibiotics in this procedure have been clearly shown to be ineffective and unnecessary (41,42).

2. Treatment of presumed infection, the indication for therapy in 70% of instances, was more likely (60%) than prophylaxis to be appropriate. However, based on the proportionally larger number of patients receiving antibiotics for this indication, inappropriate therapy of presumed infection made up two-thirds of all instances of misuse. Most telling, purely clinical-pharmacologic shortcomings underlie the majority of inappropriate courses, including selection of drugs unlikely to be effective against probable existant pathogens, or ineffective for pharmacologic reasons (i.e. nitrofuran for wound infection), or drugs

contraindicated because of host factors (i.e. tetracycline in severe uremia); use of inappropriate doses or routes; and failure to modify therapy based on the subsequent clinical course or culture results.

3. Roberts and Visconti stated that performance of cultures had little effect on the likelihood of therapy being rational (2); however, they did not exclude prophylactic regimens in their evaluation. With rare exception, there would appear to be little reason to expect culturing to be done prior to prophylaxis. Considering only therapy instituted for presumed infection, we found culturing was significantly associated with appropriate therapy (Table 3, $p < .05$). Whether the association indicates that physicians who regularly obtain cultures are implicitly more skilled antimicrobic therapists, or the availability of bacteriologic data facilitates later, clinically indicated alterations of the regimen, or both, remains conjectual. Our data suggests that both hypotheses may be correct. The diagnostic value of Gram-stained smears is well established, especially for differentiating bacterial from non-bacterial respriatory tract infection and for selecting initial therapy (46), and was affirmed in this study. Gram-stained smears of sputum were uniformly associated with appropriate therapy of suspected respiratory tract infection ($p < .01$).

4. Our program of restriction of cephalexin and oral carbenicillin was highly effective in limiting use of these drugs (2 courses of cephalexin in 324 patients). In fact, our yearly consumption of cephalexin is over 10-fold less than that of a small community hospital studied by a member of our hospital pharmacy staff this past year. We have found restriction can be accomplished effectively and efficiently without compromising

medical care or the prescribing physician's therapeutic prerogative. Restriction upon use of certain antibiotics within hospitals by requiring "justification before use" has been demonstrated by McGowan and Finland (26) and Ridley, et al (47) to be highly effective in limiting antibiotic use. Several hospitals have shown a substantial decline in prevalence of certain drug-resistant nosocomial pathogens, especially resistant S. aureus (47) and carbenicillin-resistant Pseudomonas (12) coincident with restricted use of specific antimicrobics. Also hospital outbreaks with multi-resistant organisms have been aborted only by stringent restrictions upon antimicrobic use (22,23). Antimicrobics which warrant consideration for categorization as requiring justification before use include drugs: (1) with significant potential for toxicity, (2) which are investigational, (3) with potential for rapid emergence of drug resistance or where resistance could be clinically or epidemiologically disasterous, (4) which are very expensive, and (5) which are in short supply. We intend to expand our list of drugs requiring justification in the near future.

5. The failure to mention, let alone, medically justify antimicrobial therapy in the narrative clinical record in an astounding 58% of instances points up a major factor underlying inappropriate antimicrobic use.

The seemingly more optimal use of antimicrobics in university compared with community hospitals should be expected econsidering the educational raison d'etre of these teaching institutions and their highly visible subspecialty infectious disease services. However, a number of additional influences existent in our and the University of Virginia hospitals, more rational use of antimicrobial therapy in the all of which contribute to

hospital are logistically feasible for implementation by community hospitals as well:

1. The findings of this and other studies (2,3) underscore the serious need for effective programs of postgraduate education for physicians which stress basic principles of clinical infectious disease, rational drug selection, elementary antimicrobial pharmacology, and especially guidelines for prophylaxis.

2. Further well controlled prospective studies of antimicrobial prophylaxis, especially in surgery are needed.

3. Periodic antimicrobial utilization reviews onthe order of this and other's studies (1-3,5,6,44,45), should figure heavily in programs of intramural education for physicians in the hospital and peer review. Zeman, et al (50) were able to effect a $60,000 saving in antimicrobic expenditures in the first year of an antibiotic utilization program in a community hospital. Hospitals ideally should evolve intramural guidelines for antimicrobial use (4).

4. Awareness and utilization of existant methodology to promote infection control in general, especially to prevent hospital-related infections can implicitly lessen antimicrobic overuse (49).

5. Means by which the hospital's diagnostic microbiological laboratory can indirectly promote more rational antimicrobic use have been published(28).

6. Control of hospital drug formularies and collaborative formation of community-wide formularies (27) are indirect, but effective means of lessening drug costs.

7. Direct participation of pharmacists in patient care, implicit in their assignment to hospital wards as carried out at University of Wisconsin Hospitals can substantially upgrade antimicrobial use. Vance in a controlled study demonstrated a 48% savings in antimicrobic expenditures directly attributable to the surveillance and consultative activities of ward pharmacists (50).

8. Antimicrobic justification programs, even modest ones such as our own, can significantly limit use of selected drugs.

9. The contradictory roles of the pharmaceutical industry as manufacturer and a major reference source concerning drug use for many physicians needs re-examination(48).

Table 1

ANTIMICROBIAL USE BY SPECIALTY SERVICE

Category	No. and Percent of Total				
	Neurosurgery	Urology	General Surgery	Medicine	Total
No. patients studied	67	66	95	96	324
No. patients received 1 or more courses of therapy (%)[1]	6 (9)	23 (35)	24 (25)	24 (25)	78 (24)
No. antibiotic courses	6	25	24	26	81
Note in patient record[2]:					
justifying use	1	4	1	6	12 (15%
therapy begun	4	9	5	15	33 (42%
neither	2	14	19	11	46 (58%
Therapeutic indication[2]					
Presumptive infection	5	20	8	24	57 (70%
Prophylaxis	1	5	16	2	24 (30%
Pre-therapy Cultures in Presumptive Infection[2] (%)	5 (100%)	15 (75%)	6 (75%)	16 (67%)	42 (74%)

[1] Percentages calculated on total number of patients

[2] Percentages based on total number courses of antimicrobial therapy; 77 patients received 81 courses.

Table 2

FREQUENCY AND APPROPRIATENESS
OF SYSTEMIC ANTIMICROBIAL AGENTS USED

Drug	No.[1] and Percent[2] of Therapeutic Courses			
	Presumptive Infection (N=57)	Prophylaxis (N=24)	Total (N=81)	Percent Use Appropriate
Ampicillin	25 (44%)	2 (8%)	27 (33%)	56%
Cephalosporins	5 (9%)	17 (71%)	22 (27%)	64%
Penicillin G or V	15 (26%)	6 (25%)	21 (26%)	48%
Gentamicin	13 (23%)	-	13 (16%)	62%
Tetracycline	5 (9%)	3 (13%)	8 (10%)	25%
Sulfonamide	4 (7%)	-	4 (5%)	50%
Methicillin or Cloxicillin	3 (5%)	-	3 (4%)	67%
itrofuran	4 (7%)	-	4 (5%)	100%
Trimethoprim-Sulfamethoxazole	3 (5%)	-	3 (4%)	67%
Chloramphenicol	1 (2%)	-	1 (1%)	-
Kanamycin	-	1 (4%)	1 (1%)	-
Clindamycin	1 (2%)	-	1 (1%)	-
Total Courses	57 (100%)	24 (100%)	81 (100%)	56%
one drug	38 (67%)	20 (83%)	58 (72%)	57%
2 drugs	19 (33%)	4 (17%)	23 (28%)	52%

[1] Seventy seven (77) patients received 81 therapeutic courses

[2] Because of multiple antimicrobial therapy, a summation of individual percentages will exceed 100 % overall.

Table 3

APPROPRIATENESS OF ANTIMICROBIAL
THERAPY BY ANATOMIC SITE OF PRESUMPTIVE INFECTION

ite	No. and Percent Therapeutic Courses		
	No. Courses	No. (%) with Pre-Therapy Cultures[1]	No. (%) Appropriate Therapy[1]
inary tract	21	17 (81%)	14 (67%)
lmonary	16	12 (75%)	8[2] (50%)
und	12	7 (58%)	7 (58%)
stemic sepsis	5	3 (60%)	3 (60%)
her	3	3 (100%)	2 (67%)
l sites	57	42 (74%)	34 (60%)

Cultures prior to therapy were obtained in 30 of 34 appropriate courses (88%) but in only 13 of 23 inapporpirate courses of therapy, $x^2=3.07$, $p < .05$.

Gram-stained smears of sputum preceded 7 courses of therapy of presumed respiratory tract infection; every course turned out to be appropriate ($p < .01$ by Fischer's exact test).

Table 4

OVERALL ASSESSMENT OF ANTIMICROBIAL THERAPY IN 77 PATIENTS

	No. and Percent of Therapeutic Courses[1]				
	Neurosurg (N=6)	Urology (N=25)	Medicine (N=26)	Gen.Surg. (N=24)	Total (N=81)
Appropriate Therapy	6(100%)	12(48%)	14(54%)	13(54%)	45(56%)
Inappropriate Therapy[2]	0(-)	13(52%)	12(46%)	11(46%)	36(44%)
Inapp. for Presumptive Infection	-	10	10	3	23(28%)
No Evidence of Infection	-	2	6	-	8
Poor Drug Choice	-	8	4	3	15
Unlikely effective	-	4	3	1	8
Dose	-	1	1	-	2
Route	-	-	-	1	1
Allergic History	-	1	-	1	2
Duration	-	1	-	1	2
Failure to modify	-	2	2	-	4
Inappropriate Prophylaxis	-	3	2	8	13(16%)
Not indicated	-	-	2	4	6
Poor Drug Choice[3]	-	1	-	-	1
Begun post-exposure	-	3	-	4	7
Duration too long	-	1	-	5	6

1. Seventy-seven (77) patients recieved 81 courses of therapy.

2. Summation of individual factors may exceed 100%; therapy was not uncommonly judged inappropriate for multiple reasons.

3. Subcategories similar to Inappropriate for Presumptive Infection.

Table 5

FREQUENCY OF ADVERSE REACTIONS TO ANTIMICROBIAL THERAPY

Reaction	No. and Percent of Therapeutic Courses[1]		
	No.	Percent (N=81)	Drugs Implicated
Superinfection[2]	6	7%	Ampicillin(3), Penicillin(2), Penicillin and Gentamicin(1)
Phlebitis	3	4%	Cephalothin (3)
Gastrointestinal (vomiting or diarrhea)	4	5%	Ampicillin(2), Penicillin(1) Tetracycline(1)
Azotemia	1	1%	Gentamicin
All Reaction	14	17%	Ampicillin(5), Penicillin(4) Cephalothin(3), Gentamicin(2) Tetracyline(1)

1. Seventy-seven (77) patients received 81 courses of therapy.

2. Urinary tract, 4(19% of 21 treated presumptive urinary tract infections); Pneumonia, 1(of 16 treated presumptive respiratory infections); Candida Vaginitis,1.

Table 6

RECENT[1] STUDIES OF ANTIMICROBIAL USE

Authors (Ref.)	Type of Hospital	Type of Study	No. Patients Studied	% Receiving Antimicrobials	%On Antimicrobials with Infection	% Use Judged Appropriate
Scheckler &Bennett(1)	Community	Prevalence	5,256	30.6%	38%	N.S.[2]
Roberts & Visconti	Community	Incidence	1,035	32.8%	36%	13%
Kunin, et al (3)	University	Incidence	795	28.0%	21%	48%
McGowan and Findland (5)	Municipal	Prevalence	645	36.1%	76%	N.S.
Moody and Burke (6)	Community[3]	Prevalence	566	23.0%	52%	N.S.
Schuna and Maki	University	Incidence	324	24.2%	38.5%[4]	56%

1. Published since 1970.

2. Not Stated

3. Although a community hospital, the Later-day Saints Hospital is a major teaching hospital with house officers in all major specialties and is closely affiliated with the University of Utah School of Medicine.

4. Presumed infection underlay therapy in 70% of instances, but infection was ultimately confirmed in only 55%; if drugs were discontinued when infection was ruled out, therapy could be judged as appropriate.

DATE:	Pre-Rx																								
ANTIBIOTICS:																									
OPERATIONS:																									
TEMP > 100°																									
INFECTIONS:																									
CULTURES:																									
LAB: Hct																									
WBC																									
P/L																									
Plat																									
Bun/Creat																									
SGOT/Bili																									
other																									
SIDE EFFECTS:																									
Allergic/Rash																									
GI																									
Renal																									
Hema																									
other																									
Superinfection																									

NAME _____

APPENDIX I.

Service _____

Diagnoses _____

Allergies (specify) _____

Asthma or Hayfever _____

INTERACTIONS:

Date	Antibiotic	Other Drug	Cl Ef

APPENDIX II.

ANTIBIOTICS _____
(dates) _____
_____

APPROPRIATE:
Initially _____
Overall _____

PHYSICIAN _____

STATUS _____

SERVICE _____

I. APPARENT PHYSICIAN INDICATIONS:

Note in Chart { indicating Rx begun _____ / justifying use _____ / neither _____

Indication: Obvious infection _____ / Suspected infection _____ / Prophylaxis _____

{ Infection proven? _____ / Cultures done Pre-Rx? _____

II. INVESTIGATOR'S ASSESSMENT OF APPROPRIATENESS OF ANTIBIOTIC Rx:

	INITIALLY (AT OUTSET)	OVERALL (AT CONCLUSION)
APPROPRIATE		
Infection		
Suspect Inf		
Prophylaxis		
INAPPROPRIATE		
No evidence Inf		
Poor Drug Choice		
Unlikely effective		
Dose		
Route		
Duration (Specifiy how)		
Less Expensive available		
Pt. allergic hx		
Failure to Modify		
Prophylaxis Misguided:		
Not indicated		
Begun p-exposure		
Poor drug choice (above)		

ANTIBIOTIC USE STUDY 1975

UNIVERSITY OF WISCONSIN HOSPITALS

Cultures pre-Rx _____

Adverse Effects _____
_____
_____

Interactions _____
_____
_____

Cost ($) of Antibiotics _____

BIBLIOGRAPHY

1. Scheckler WE and Bennett JV: Antibiotic Usage in Seven Community Hospitals, J Am Med Assoc 213:264-267, 1970.

2. Roberts AW and Visconti JA: The Rational And Irrational Use of Systemic Antimicrobial Drugs, Am J Hosp Pharm 29:828-834, 1972.

3. Kunin CM, Tupasi,T and Craig WA: Use of Antibiotics, A Brief Exposition of The Problem and Some Tentative Solutions, Ann Int Med 79:555-560, 1973.

4. Simmons HE and Stolley PD: This is Medical Progress? Trends and Consequences of Antibiotic Use in the United States, J Am Med Assoc 227:1023-1032, 1974.

5. McGowan JE and Finland M: Infection and Antibiotic Usage at Boston City Hospital: Changes in Prevalence during the Decade 1964-1973, J Inf Dis 129:421-428, 1974.

6. Moody ML and Burke JP: Infections and Antibiotic Use in a Large Private Hospital, January 1971, Arch Int Med 130:261-266, 1972.

7. Finland M: Changing Ecology of Bacterial Infections as Related to Antibacterial Therapy, J Inf Dis 122:419-431, 1970.

8. McCabe WR:Gram-Negative Bacteremia, Disease-a-Month, Year Book Medical Publishers, Dec 1973, p.1-62.

9. Finland M: Changing Patterns of Susceptibility of Common Bacterial Pathogens to Antimicrobial Agents, Ann Int Med 76:1009-1036, 1972.

10. Benner EJ: Growing Clinical Significance of Methicillin-Resistant Staphylococcus Aureus, Lancet 2:741-744, 1968.

11. Shulman JA, Terry PM and Hough CE: Colonization with Gentamicin-Resistant Pseudomonas aeruginosa, Pyocine Type 5, in a Burn Unit, J Inf Dis 124:S18-S28, 1971.

12. Lowbury EJL, Babb JR and Roe E: Clearance From a Hospital of Gram-Negative Bacilli That Transfer Carbenicillin-Resistance to Pseudomona Aeruginosa, Lancet 2:941-945, 1972.

13. Ross S, Controni G and Khan W:Resistance of Shigellae to Ampicillin and Other Antibiotics, Its Clinical and Epidemiological Implications, J Am Med Assoc 221:45-47, 1972.

14. Anon: Ampicillin-Resistant Hemophilus influenzae Meningitis, Morbidity and Mortality, 23:77-78, 1974.

15. Weinstein L, Goldfield M and Chang T:Infections Occurring During Chemotherapy, N Engl J Med 251:247-254, 1954.

16. Tillotson JR and Finland M: Bacterial Colonization and Clinical Superinfection of the Respiratory Tract Complicating Antibiotic Treatment of Pneumonia, J Inf Dis 119:597-624, 1969.

17. Seidl LG, Thornton GF, Smith JW, et al:Studies On the Epidemiology of Adverse Drug Reactions, Bull Johns Hopkins Hosp 119:299-315, 1966.

18.Caldwell JR and Cluff LE: Adverse Reactions to Antimicrobial Agents, J Am Med Assoc 230:77-80, 1974.

19.Adler JL, Shulman JA, Terry PM, et al:Nosocomial Colonization with Kanamycin-Resistant Klebsiella Pneumonia, Types 2 and 11, in a Premature Nursery, Journ Peds 77:376-385, 1970.

20.Hable KA, Matsen JM, Wheeler DJ, et al:Klebsiella type 33 in an Infant Intensive Care Unit 80:920-924, 1972.

21. Hill HR, Hunt CE and Matsen JM: Nosocomial Colonization with Klebsiella, type 26, in a Neonatal Intensive-care Unit Associated with an Outbreak of Sepsis, Meningitis, and Necrotizing Enterocolitis, Journ Peds 85:415-419, 1974.

22. Eisenbach KD, Reber RM, Eitzman DV, et al: Nosocomial Infections due to Kanamycin-Resistant, (R)-Factor Carrying Enteric Organisms in an Intensive Care Nursery, Pediatrics 50:395-402, 1972.

23.Price DJE and Sleigh JD: Control of Infection Due to Klebsiella Aerogenes in a Neurosurgical Unit by Withdrawal of all Antibiotics, Lancet 2:1213-1215, 1970.

24. Damato JJ, Eitzman DV and Baer H: Persistence and Dissemination in the Community of R-Factors of Nosocomial Origin, J Inf Dis 129:205-209, 1974.

25. Muller C: The Overmedicated Society:Forces in the Marketplace for Medical Care, Science 176:488-492, 1972.

26. McGowan JE and Finland M: Usage of Antibiotics in a General Hospital: Effect of Requiring Justification, J Inf Dis 130:165-168, 1974.

27. Kunin CM and Dierks JW: A Physician-Pharmacist Voluntary Program to Improve Prescription Practices, N Engl J Med 280:1442-1446, 1969.

28. Kunin CM: Antibiotic Sensitivity Tests:How to Get the Most Out of Them, Wis Med Journ 70:206-208, 1971.

29.Kabins SA: Interactions Among Antibiotics and Other Drugs, J Am Med Assoc 219:206-212, 1972.

30. Garner JS, Bennett JV, Scheckler WE, et al:Surveillance of Nosocomial Infections, Proceedings of the International Conference on Nosocomial Infections, Center for Disease Control, pp.277-281. Aug 3-6, 1970.

31. Rammelkamp CH: Prophylaxis of Bacterial Disease with Antimicrobial Drugs, Am J Med 39:804-811, 1965.

32. Alford RH: Prevention of Bacterial Disease by Oral and Parenteral Antimicrobial Agents, S Med J 66:32-40, 1973.

33. Anon: Handbook of Antimicrobial Therapy, Med Letter 14:1-64, Issue340, 1972.

34. Anon:Postoperative Wound Infections:The Influence of Ultraviolet Irradiation of the Operating Room and of Various Other Factors, National Academy of Sciences-National Research Council. Ann Surg 160(supp): 1-192, 1964.

35. Boyd RJ, Burke JF, Colton T : A Double-Blind Clinical Trial of Prophylactic Antibiotics in Hip Fractures, J Bone and Joint Surg 55-A:1251-1258, 1973.

36. Burke JF: The Effective Period of Preventive Antibiotic Action in Experimental Incisions and Dermal Lesions, Surgery 50:161-168, 1961.

37. Bernard HR and Cole WR: The prophylaxis of Surgical Infection: The Effect of Prophylactic Antimicrobial Drugs on the Incidence of Infection Following Potentially Contaminated Operations, Surgery 56:151-156, 1964.

38. Fullen WD, Hunt J and Altemeier WA: Prophylactic Antibiotics in Penetrating Wounds of the Abdomen, J Trauma 12:282-289, 1972.

39. Polk HC and Lopez-Mayor JF: Postoperative Wound Infection: A prospective study of determinant factors and prevention, Surgery 66:97-103, 1969.

40. Miller AL, Scott FB and Scott R: An Evaluation of Antibiotics Prior to Prostatectomy, J Urology 92:711-713, 1964.

41. Kreidberg MB and Chernoff HL: Ineffectiveness of Penicillin Prophylaxis in Cardiac Catheterization, J Pediat 66:286-290, 1965.

42. Clark H: An Evaluation of Antibiotic Prophylaxis in Cardiac Catheterization, Am Ht Journ 77:767-771, 1969.

43. Anon: Standards for Accreditation of Hospitals, Joint Commission on Accreditation of Hospitals pp1-111,(Oct. 1969).

44. Edwards LD: Infections and Use of Antimicrobials in an 800-Bed Hospital, Public Health Reports 84:451-457 (May, 1969)

45. Shoji KT, Axnick K and Rytel MW: Infections and Antibiotic Use in a Large Municipal Hospital 1970-1972:A Prospective Analysis of the Effectiveness of a Continuous Surveillance Program, Health and Lab Sci 11:283-292, 1974.

46. Provine H and Gardner P:The Gram-Stained Smear and Its Interpretation, Hosp Practice pp. 85-91 (Oct 74).

47. Ridley M, Lynn R, Barrie D, et al:Antibiotic-Resistant Staphylococcus Aureus and Hospital Antibiotic Policies, Lancet 1:230-233, 1970.

48. Kunin CM: This is Medical Progress? In Comment, J Am Med Assoc 227:1030-1032, 1974.

49. Anon: Proceedings of the International Conference on Nosocomial Infections, Center for Disease Control, American Hospital Association, pp.1-334 (Aug 3-6, 1970).

50. Zeman BT, Pike M and Samet C:The Antibiotic Utilization Committee, Hospitals 48:73-76, 1974.

51. Vance PH: The Effect of a Pharmacist Drug Surveillance Program in an Acute Ward, Cand J Hosp Pharm pp.71-74 (Mar-Apr 1973).