THE DEVELOPMENT AND IMPACT OF A PEDIATRIC
ANTIINFECTIVE DECISION SUPPORT TOOL

by

Charles J. Mullett

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SUPERVISORY COMMITTEE APPROVAL

Of a dissertation submitted by

Charles J. Mullett, M.D.

This dissertation has been read by each member of the following supervisory committee and by majority vote has been found to be satisfactory.

Chair: R. Scott Evans

Bruce E. Bray

Christenson

Reed M. Gardner
To the Graduate Council of the University of Utah:

I have read the dissertation of Charles J. Mullett in its final form and have found that (1) its format, citations, and bibliographic style are consistent and acceptable; (2) its illustrative materials including figures, tables, and charts are in place, and (3) the final manuscript is satisfactory to the supervisory committee and is ready for submission to The Graduate School.

Date

R. Scott Evans
Chair: Supervisory Committee

Approved for the Major Department

Reed M.
Chair

Approved for the Graduate Council

David S. Chapman
Dean of the Graduate School
ABSTRACT

Computerized medical decision support tools have been shown to improve the quality of care and have been cited as one method to reduce pharmaceutical errors by the Institute of Medicine. An existing adult antiinfective decision support tool was enhanced by adding medical logic to make it appropriate for pediatric patients.

Pediatric modifications to the medical logic and new antiinfective and dosage recommendations were implemented into the decision support tool. Measurements of appropriate antiinfective use, antiinfective costs, the rate of adverse drug events secondary to antiinfectives, antimicrobial-bacterial susceptibility mismatches, and pharmacy staff interventions for antiinfective agents were prospectively monitored during a six-month control and a six-month intervention period. Mandatory use of the decision support tool was initiated for all antiinfective orders in a 26-bed pediatric intensive (PICU) during the intervention period. Clinician opinions of the decision support tool were surveyed at the end of the intervention period.

The patient populations during both the control period (n = 809) and the intervention period (n = 949) were similar with respect to their PICU and hospital lengths of stay, severity of illness, risk of mortality, and total hospital costs. The intervention group was significantly younger (5.5 years vs. 6.2 years, p<0.05), and a greater percentage were treated with antibiotics (66.5 percent vs. 60.2 percent, p<0.01). There
was not a significant difference in type of antiinfectives ordered, or the number of antiinfectives, or antiinfective doses. Neither was there a difference in the rate of adverse drug events, or antibiotic-bacterial susceptibility mismatches. However, the rate of pharmacy interventions on erroneous drug doses declined by 59 percent from 35.5 to 14.5 interventions per 1000 patient-antiinfective courses (p < 0.01). The rate of antiinfective subtherapeutic patient days decreased by 36 percent from 7.4 to 4.7 subtherapeutic days per 100 patient days (p < 0.0001), and the rate of excessive-dose days declined by 28 percent from 8.5 to 6.1 excessive-dose days per 100 patient days (p < 0.0001).

Additionally, the number of orders placed per antibiotic course decreased 11.5 percent from an average of 1.56 to 1.38 orders/pt-antiinfective (p<0.01), and the robust estimate of the antiinfective costs per patient decreased 9 percent from $86.60 to $78.43 (p<0.05).

These data are supported by the surveyed clinicians who cited the dosage calculation assistance to be most helpful, and reported the program improved their antiinfective agent choices, increased their awareness of impairments in renal function, and reduced the likelihood of adverse drug events.

Use of the pediatric antiinfective decision support tool in a PICU was considered beneficial to patient care by the clinicians, and positively impacted the rates of erroneous drug orders and antiinfective sub- and supratherapeutic risk-days.
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INTRODUCTION
Errors in Medicine

The Institute of Medicine’s 2000 report, To Err is Human: Building a Safer Health System, focused on the unacceptable rate of patient injury from errors in healthcare.¹ This report cited studies published in the last 10 years which observed that error rates, when extrapolated to the nation as a whole, would account for 44,000 to 98,000 fatalities in 1997.²,³ These estimates would place medical errors as the eighth leading cause of deaths, ahead of motor vehicle crashes.¹ The Institute of Medicine’s report generated a great deal of interest in the lay press⁴-⁷ and triggered a call from President Clinton to mandate reporting of fatal medical errors and to create a new government Center for Patient Safety.⁸

The two studies cited above defined an adverse event as “an injury caused by medical management (rather than the disease process) that resulted in either a prolonged hospital stay or disability at discharge.” Negligence was defined as “care that fell below the standard expected of physicians in their community.” The more recent analysis,³ focusing on care provided in 1992 in the states of Utah and Colorado, found that although the greatest incidence of adverse events occurs in the operating room, a relative small percentage, 16.9 percent, were judged to have occurred secondary to medical negligence. This contrasts to the few adverse events that occur in the emergency department, where a high rate of negligence is found, 52.6 percent. The authors cite that most of these events were secondary to failed diagnoses. Consistent with the earlier study,² the second leading cause of adverse events was due to pharmaceutical agents, with antibiotics comprising
the greatest percent, 24 percent. Of these, 6.8 percent were judged to be due to negligence.

Errors in medicine are not unique to the system of care in this country. A recent study published in Australia described 805 medical “incidents” that could have or did harm a patient.\(^9\) Seventy-six percent of these were preventable, and 27 percent had the potential for severe harm. Over half involved pharmaceuticals. This study followed the earlier “Quality in Australian Health Care Study”\(^10\) that noted the rate of adverse events to be 13 percent of hospitalizations in their health system, significantly above the rates of 2.9 percent and 3.7 percent found in the Utah/Colorado and the New York studies. It is not known whether the difference represents actual disparity in the quality of care between these countries, or whether differences in the study definitions of adverse events and incidences account for a majority of the variance.

Errors in pharmaceutical therapy are recognized as a significant source of injury to hospitalized patients. Up to 2 percent of admissions in an adult, tertiary care university facility have been identified as suffering preventable adverse drug events, costing an average of $4700 per event.\(^11\) Others have investigated the error rate and published incidences of 3.99 errors per 1000 orders in one adult hospital.\(^12\) Factors associated with errors in this study were a decline in renal or hepatic function (13.9 percent), history of allergy to the same medication class (12.1 percent), use of the wrong drug name, dosage form, or abbreviation (11.4 percent), incorrect dosage calculation (11.1 percent), and atypical or unusual dosage frequency (10.8 percent). Studies in children corroborate these findings.\(^13,14\) One study found that those pediatric patients aged two years or less
and those requiring treatment in a PICU were at the greatest risk. The most common error cited was incorrect dosage, and of these, overdosage was more common than underdosage. Antibiotics were the most common class of pharmacotherapeutics with errant orders.

**Causes of Medical Errors**

The many studies cited above document that adverse events occur in the medical system and that these incidences are harmful to patients. Historically, blame has been placed on individuals, and efforts have focused on "weeding out" clinicians known to repeatedly cause harm. This citation of physicians is the original objective of departmental "Morbidity and Mortality" conferences where sentinel events are investigated for purposes of finding breaches in the current standard of care and providing feedback to the responsible party. More recently, these conferences have shifted intentions to the evaluation of the performance of the system of care, searching for "improvement opportunities." This change follows the general recognition that although it is often individuals that fail, it is the system of care that did not provide the safe environment.

Analysts define error as "the failure of a planned sequence of mental or physical activities to achieve its intended outcome when these failures cannot be attributed to chance." The Institute of Medicine defined error as "the failure of a planned action to be completed as intended (e.g., error of execution) or the use of a wrong plan to achieve an aim (e.g. error of planning).” These events are subcategorized into latent and active...
errors. Active errors are the final events that result in harm: for example, the act of the surgeon operating on the wrong knee. Latent errors are removed from the actual event and may be secondary to poor design or processes. In this example, the lack of a standard process whereby the physician and patient preoperatively label the correct knee for the arthroscopy is the latent error.

Human factors contribute significantly to medical adverse events. One study in the domain of anesthesia found that human error was involved in 82 percent of incidents that were deemed preventable.\textsuperscript{16} In the previously cited adverse pharmaceutical events study, essentially all events could be cited as occurring secondary to human error in either execution or monitoring failure.\textsuperscript{12} The title of the Institute of Medicine’s report cites an old adage “To err is human.” Thus, the task becomes designing a system of safety around individual health care providers. Many times this involves procedural changes such as requiring the surgeon and patient to jointly mark the operative site or mandating that the nurse repeat a verbal order back to the physician for verification. However, technology and information systems also provide methods to improve the performance of individuals in systems and positively impact the patient care environment.

**Technological Solutions to Medical Errors**

The realm of medical care can be divided into diagnostic and therapeutic pursuits. Similarly, clinical decision support systems can be divided into diagnostic and therapeutic support systems. The former are more likely to involve complex artificial
intelligence routines founded on probability networks (Bayesian Analysis) or neural networks. The latter, therapeutic decision support systems, are usually founded on rule sets. The potential impact of both types of clinical decision support systems will be reviewed.

Failure to make a proper diagnosis when the diagnostic information is available is a potentially harmful negligent medical error. In an ideal world, the most senior and insightful clinicians could consult on all patient cases, converting patient critical care diagnoses from "sepsis" and "multi-organ systems failure" to specific and therapy-guiding diagnoses such as "leptospirosis." Unfortunately, all-knowing senior clinicians are not always available and do not always contribute a correct diagnosis. With this in mind, many groups, including the University of Utah’s Department of Medical Informatics, developed computerized diagnostic decision support systems. Such systems are generally based on probability networks and are embedded with a broad and deep knowledge base of patient signs and symptoms and their estimated prevalence in disease states. These types of systems are developed through lengthy knowledge-engineering sessions with multiple domain experts. While possessing great potential, these tools have failed to make an impact. A 1994 comparison of four of these diagnostic systems found that no single system performed better than the others in every category, and as a whole, the mean proportion of relevant diagnoses was judged by experts to range from 0.19 to 0.37. On average, fewer than one half of the experts’ list of relevant diagnoses was suggested by any of the programs. This report of off-target diagnoses is congruent with this author’s personal and admittedly anecdotal experience with the Iliad system. Given
what was believed to be a classic pediatric case of diabetic ketoacidosis, Iliad did not return the correct diagnosis, and even "diabetes" was low on its ranking. This disparity underscores the restricted functionality of these diagnostic decision support tools when presented with cases that fall outside of the original development domain (pediatric medicine vs. adult internal medicine in the example).

Although broad diagnostic decision support tools have not had a great impact in medical care, narrow spectrum specialized tools are becoming more commonplace. Computer-aided diagnosis of breast lesions in mammography has been found to improve the sensitivity and specificity of radiologists screening mammograms for cancer. One such system is now in clinical use at the University of Chicago where a radiologist commented; "The world is not like the fictional Lake Wobegon, where all the children are above average. Only half of the radiologists are above average, this system should eventually make even the other half comparable to the experts."21

Diagnostic decision support tools have also been developed in many other domains. In fact, a Medline search on the MESH subject heading “diagnosis/computer-assisted” returns 11,165 papers possessing the topic. Interesting and clinically relevant diagnostic decision support systems have been developed in many domains: cytology screening of pap smears,22,23 electrocardiogram analysis,24-28 abdominal pain,29 lower gastrointestinal tract disorders,30 basal and squamous cell carcinoma,31 low back pain and sciatica,32 and pediatric strabismus.33 To my knowledge, on this list, only the computer-aided electrocardiogram analysis has made important inroads into clinical use. When coupled with automatic defibrillators, simplified versions of this decision support
technique is anticipated to be a great boon to services provided by lower-skilled emergency workers and travel-industry employees such as those attendant on airplanes and cruise ships.34-36

Although not of the same vein as the decision support tools mentioned above, telemedicine is another diagnostic informatics tool. Rather than applying artificial intelligence techniques, this technology enables a remote clinician and patient to consult a specialist located in a regional tertiary care facility using telecommunications equipment. Telemedicine has been growing tremendously, supported in large part by the military. According to Dr. Jay Sanders, the 1997 AMIA Fall Symposium plenary session speaker, nearly all 50 states have telemedicine facilities. Many project descriptions and technological details have been reported in the medical literature, but very few reports of controlled studies of its clinical benefit exist. This discrepancy is likely due to a combination of factors: one, its greatest benefit may be financial from saved transportation costs, rather than an improvement in clinical care; and two, the technology is not yet considered mature.

Greater inroads have been made in the category of clinical decision support systems for therapeutic choices. This type of decision support leaves the more complex and higher order task of making a diagnosis to the human mind, while bringing simpler, rule-based systems to bear on therapy choices.37

Computerized physician order entry systems for prescription of medications enable the presentation of standard dosages, automated dosage calculations, and presentation of clinically important and specific drug-drug, drug-allergy, and drug-lab
interactions at the time of the physician’s decisions. Additionally, these systems eliminate the inherent problems associated with handwriting interpretations and retranscription of orders. Not surprisingly, the rate of serious medication errors dropped 55 percent in one analysis of the impact of the implementation of a physician order entry system. Crude estimates by the authors of that paper suggest that the net savings to the study hospital through fewer adverse events and their sequelae amount to $5 to $10 million per year.

The National Library of Medicine’s Medline medical reference database provides valuable diagnostic and therapeutic clinical decision support through ready access of the medical literature for clinicians. Many informatics groups are pursuing methods that will enhance access to relevant articles by linking the hospitalized patient’s clinical data repository with the Medline search engine, thus automating searches and potentially providing timely alerts. The following is quoted from Geissmeuller’s paper presented at the American Medical Informatics Association’s 1998 Annual Symposium:

As described above, both diagnoses and medications are encoded as CUIs [concept unique identifiers] during the order entry process. It is therefore straightforward to lookup the co-occurrence information and issue warning messages, that, although non-deterministic, can indicate that “there are several citations in MEDLINE of (drug X) having adverse effects described along with (drug/diagnosis Y).” …WizOrder generates a fully formed MEDLINE query (e.g., “aspirin/adverse effects” AND “influenza”) which is sent to the PubMed Web-based search engine to retrieve current citations using the Web-browser built in WizOrder.

To my knowledge, studies of the clinical impact of these types of clinical search enabling tools have not yet been published.
Other therapy-based clinical decision support systems have been measured to improve the process of delivering care. Drug dosing systems have been documented to beneficially impact drug levels in the realms of aminophylline dosing, lidocaine infusions, and warfarin therapy. Computerized guidelines and protocols beneficially impact the quality of preventive care as measured in the domains of influenza and tetanus vaccinations, blood pressure screening, diabetes mellitus, and general preventive recommendations. Beneficial effects on patient outcomes have been measured when using a clinical decision support tool for advice on the therapy of urinary incontinence, obesity, and renal disease. Many of the above studies are nicely summarized in an evidence-based analysis of the effects of clinical decision support systems on clinician performance and patient outcomes published by Johnston and colleagues.

Alan H. Morris, M.D., and colleagues of LDS Hospital have expanded the role of computerized clinical decision support in the intensive care unit. Dr. Morris recently published a monograph on the impact of computerized protocols for standardization of clinical decisions. In it, he argued that humans have a limited ability to keep track of complex information and make reasoned decisions while considering multiple variables. This limitation contributes to nonstandard care and unnecessary medical errors. Computerized clinical decision support can be developed to depths not achievable by paper-based protocols and with implementation into hospital information systems, enables explicit, moment-of-decision therapy recommendations that can improve
adherence to published guidelines. Guideline adherence minimizes variance, potentially improves medical care, and enables rigorous evaluations of therapy.

Examples of recent work at LDS Hospital illustrate these points. Dr. Morris and his colleagues developed protocolized therapy for mechanical ventilation of patients with severe lung disease in order to homogenize the therapy given to patients in the control arm of a study designed to measure the beneficial effects of the application of extracorporeal carbon dioxide removal. What they found instead was that the patients randomized to receive computer-guided ventilatory care had a mortality of only 40 percent, rather than 80 percent as expected on enrollment in the study. The use of computerized protocols was given partial credit for the improvement in mortality. More recently, Tom East, Ph.D., and colleagues published the results of a multicentered, head to head trial of the clinicians plus computerized protocols versus clinicians alone in the therapy of adults with severe lung disease. These authors found a reduction in the morbidity suffered by the patients treated with the decision support tool as measured by multi-organ dysfunction and lung overdistension injury scores. The presence of a concurrent control arm in the study allowed attribution of the reduction in morbidity to be assigned to the use of the computerized decision support tool.

Given the success of these protocols, Dr. Morris and colleagues across the country are developing a computer-based decision support system that will provide fluid and cardiac therapy guidance in an NIH-sponsored, multicentered trial of the impact of pulmonary artery catheters in critically ill patients. As in the initial extracorporeal carbon dioxide removal trial, the authors anticipate that the use of the computer protocols will
homogenize the therapy given to the multiple patients at multiple sites, therefore
removing unnecessary variance that might mask the effects of the presence of the
pulmonary artery catheter. Given the increasing experience with the benefit of well-
designed decision support tools implemented in the complex environment of a modern
intensive care unit, many are interested in the simple effect of the computerized decision
support program on all the patients enrolled in the study. Better-than-expected outcomes,
attributable, in part, to care guidance by the online computerized decision support tool
would not be surprising.

Antiinfective Decision Support

Antiinfective decision support tools have been in development for the last three
decades. These “disease management systems” have shared techniques common to both
diagnostic and therapeutic expert systems. Like other diagnostic decision support tools,
they frequently possess probability- or statistics-based techniques, but like other
therapeutic systems, their recommendations are often based on rule-sets. A review of the
history of antiinfective decision support will show a growth of the field into tools that
possess the potential to impact quality of care.

In 1973, Shortliffe and colleagues published a monograph describing the
development of a rule-based infectious disease expert system designed to advise
physicians on the most rational antiinfective therapy.58 This computer tool, later named
MYCIN,59 was written in the LISP computer language and developed over a number of
years. In 1979, a comparison of MYCIN’s antiinfective recommendations in 10 cases of
meningitis revealed that its advice was judged by blinded experts to be at least as sound as, if not more sound than, the advice of several Stanford infectious disease specialists.\textsuperscript{60}

Other cited strengths included MYCIN's capability of explaining its reasoning, the recommendation of antimicrobial doses including consideration of age, weight, and renal function, and graphing of predicted serum concentrations of aminoglycosides with relation to the expected minimal inhibitory concentrations of the organism.\textsuperscript{61}

MYCIN's ultimate clinical impact was limited by a lack of an online clinical data repository.\textsuperscript{62} The absence of clinical databases mandated on-screen queries of the clinician for input of all relevant patient data. Necessary information included entry of such fundamental data as the name, age, and gender of the patient, plus domain-specific information like the known details of the suspected organism, the site of infection, and date of the culture specimens. Secondary to the manual entry of this data, MYCIN consultations were described to last from 15 to 20 minutes. This cost in time exceeds the perceived value of the information to the clinicians and prohibited MYCIN's adoption in the clinical arena.

The development of online clinical databases enabled advances in the field of antiinfective decision support. In 1984, Kilroy and colleagues reported the development of a computer-based tool that identified mismatches between culture sensitivities and concurrent antibiotic therapy.\textsuperscript{63} In a later report of one month's use,\textsuperscript{64} 12 patients were identified with important mismatches between pathogen sensitivities and antimicrobial therapy, and in all cases the patients' attending physicians changed therapy when notified of the inadequate coverage.
During the same time period, Evans and colleagues developed a Computer Infectious Disease Monitor (CIDM) that identified patients with hospital-acquired infections, infections in a sterile body site, a reportable disease, infections by antibiotic resistant organisms, patients treated with suboptimal therapy, unnecessarily expensive therapy, or unnecessarily long prophylactic therapy. The system took advantage of the breadth and depth of the clinical data housed in the LDS Hospital HELP (Health Evaluation through Logical Processing) hospital information system. The type of information available online at this facility at that time was relatively unique in the field of medicine and capitalized on more than one decade of development.

A two-month evaluation of the CIDM revealed that the tool identified 12 percent more hospital-acquired infections than the Infection Control Practitioners at LDS Hospital. Additionally, when CIDM was used by the infection control practitioners, they found more hospital-acquired infections in 65 percent less time. During the same study period, the CIDM found 37 different cases of ineffective therapy when compared to the susceptibilities of cultured pathogens. Thirty-one other instances were identified where unnecessarily expensive therapy was being administered. In one month's use, the tool noted 142 instances of unnecessarily prolonged cephalosporin prophylaxis.

Larsen, Evans, and colleagues next developed a tool to advise clinicians on the need for surgical perioperative prophylaxis. The LDS Hospital's surgical schedule, available in the online clinical database, provided the information necessary to enable computerized antibiotic alerting to clinicians prior to their elective surgery. The administration of perioperative antibiotics improved to 58 percent from a baseline of 40
percent in cases in which antiinfectives were considered advisable. Additionally, the rate of postoperative wound infections decreased by 50 percent, from 28 of 1621 patients to 16 of 1830. The authors concluded that computer-generated perioperative antibiotic reminders improved the prescribing habits and contributed to a decline in postoperative wound infections.

Other authors have shown that the most common inappropriate use of antibiotics occurs during surgical antibiotic prophylaxis and that in as many as 80 percent of the cases prophylactic use extends past the point of usefulness. Citing these studies, Evans and colleagues developed a prophylactic antibiotic duration report that provided the hospital's pharmacists with a list of postoperative patients still on antibiotics 48 hours after surgery without any evidence in the patient database of a possible infection. For the duration report, evidence of a possible infection included: (1) a positive or pending microbiology culture; (2) an admission diagnosis of an infection; (3) a gram stain showing the presence of bacteria or numerous white blood cells; (4) fever; (5) bacteriuria; (6) an operative infection classification of "contaminated" or "dirty"; (7) patient placement in infectious isolation. Upon receipt of the daily report, the hospital's clinical pharmacists visited each patient and reviewed the chart for other indications of an infection, and upon finding none, would place an antibiotic stop order on the chart. Six months of this type of computer-assisted interventions were compared to the same six-month period the previous year. The authors found that surgical patients meeting the report criteria received on average 19 doses of antibiotics the first year and 13 doses of antibiotics during the year of intervention. Additionally, the average cost of antibiotics
administered more than 48 hours after surgery decreased from $128 to $86 with the intervention. It was concluded that the computer system was an efficient tool for monitoring the use of antibiotics given to surgical patients and the use of the reporting program resulted in an improvement in surgical antibiotic prophylaxis.

Concurrent with the above work, other investigators developed decision support tools for the hospital antiinfective environment. Inaraja and colleagues from Pamplona, Spain, developed and described a DOS-based tool that reported on the use of antimicrobials and matched patients' antibiotic therapy with culture results. The resulting report facilitated review by pharmacists monitoring for agreement between therapy and published microbial susceptibility, the unnecessary use of restricted antimicrobial agents, the duration and monitoring of potentially toxic antimicrobial agents, the duration of surgical prophylaxis, the use of empiric treatments based on guidelines, inappropriate dosages or frequency of administration, and the appropriateness of antibiotic combination therapy. Although these authors reported success and compliance with the use of the decision support tool, they did not attempt to measure an impact.

The rising cost of medical care and the influence of government and third-party payers triggered interest in measuring the cost of equivalent therapeutic antibiotic regimens. Parr and colleagues reported in 1986 the development of a computer program for comparison of the total cost of intravenous antibiotic regimens. The program considered and calculated the unique cost of the dosage regimen, duration of therapy, the need for pharmacokinetic monitoring, the drug acquisition cost, and the specific
personnel and material cost. It then collated the information and printed the cost comparison of the two regimens under consideration. The authors used a recently published trial of ceftazidime versus tobramycin-ticarcillin for hospital-acquired infections as an example. Although the cost of the drug itself was very similar for the two regimens, the total cost considering all resource use greatly favored the ceftazidime monotherapy, a new cephalosporin at the time. These authors subsequently published monographs detailing the costs of therapy for nosocomial pneumonia and febrile neutropenia calculated by their computer program.  

Physicians must often choose therapy based on the clinical suspicion of the site of the infection, the most likely pathogenic organisms at the site, and current susceptibility patterns of those pathogens in the community. Chung and Chung were the first to report the use of information management tools to facilitate the analysis of pathogens and susceptibility tests by culture site and age of the patient. They published the computer code of a series of programs that were written in BASIC. This code allowed hand entry of patient demographic information, culture results, and susceptibility patterns. On a monthly basis, the data was collated and published in various tables showing the most likely organisms by culture site, the susceptibility patterns for the most common pathogen at each culture site, and the most effective drugs by culture site. These authors published sample data based on 1209 positive cultures from clinical specimens. Contemporary clinicians would find their results interesting from a historical perspective. *Pseudomonas aeruginosa* was the most common isolate from the lower respiratory tract, and this group was sensitive to piperacillin 100 percent of the time and gentamicin 96.2
percent of the time. The authors did not publish the clinical impact, if any, their decision support tool had on their hospital’s antiinfective milieu. S.J. Chung later published a similar monograph giving updated culture results collated by software installed in an automated microbiology analyzer. 78

Citing studies that show that 35-39 percent of antimicrobial use is inappropriate, 79, 80 and that potential consequences of this practice include drug resistance, 81, 82 adverse drug reactions, 80, 83 increased costs, 84-89 and therapeutic failures, 85, 90 Pestotnik and colleagues described a computer system that monitored inappropriate antibiotic therapy relative to patient microbiology cultures and sensitivities. 91 The program, named therapeutic antibiotic monitor (TAM), checked hospitalized patients at 1 P.M. daily and generated an alert for patients with inconsistencies in their antibiotic therapies and their microbiology in vitro susceptibility test results. These alerts were reviewed by the clinical pharmacist who then contacted the patient’s attending physician to discuss the antimicrobial therapy. During a 12-month period, the TAM algorithms detected 696 instances of therapeutic mismatches, of which 420 were determined to be true positive alerts. Of these, notified physicians responded to the contact by the pharmacist by initiating or changing antimicrobial therapy in 30 percent of the cases. Physicians were found to be unaware of the published culture susceptibility results in 49 percent of the instances. The authors described several improvements in the microbiology susceptibility reporting process and to the computer algorithms that minimized the rate of false positive alerts. The authors concluded that computer-assisted monitoring systems could assist physicians in providing early and appropriate antimicrobial therapy.
Many patients, particularly the critically ill, need antimicrobial therapy prior to the discovery of the pathogen and antimicrobial susceptibilities. The effect of appropriate versus inappropriate therapy was recently measured in a retrospective study published by Leibovici and colleagues. This group compared the rate of mortality and median hospital stay for survivors in two comparison groups, those who received effective therapy and those who did not. Four hundred thirty-six of 2158 (20 percent) patients who received appropriate empiric therapy for their bloodstream infections died, compared with 432 of the 1255 (34 percent) patients who did not. Additionally, the survivors had a shorter length of hospital stay when initial appropriate therapy was rendered (9 vs. 11 days). The investigators used logistic regression techniques to control for other mortality risk factors and found that inappropriate empiric therapy remained statistically significant with an adjusted odds ratio of 1.6. Of note, pediatric patients benefited the most from appropriate empiric therapy with an odds ratio of 5.5 (95 percent C.I. = 2.4 – 10.7).

Recognizing that appropriate empiric therapy improves outcomes, yet unnecessarily broad therapy puts the patient at risk for the development of resistant organisms, adverse drug events, and increased cost, clinicians must strike a balance when choosing initial antimicrobial care. Investigators have sought to develop informatics tools to facilitate the clinician’s decision-making process. The first work in this field was by Shortliffe and partners with the MYCIN rule-based system. As described above, Chung and Chung used a statistical approach to publish a monthly list of most likely organisms and effective therapies by culture site. Evans and colleagues followed
with the first tool that automated the data-gathering process and reported to the physician the most effective therapy at the time he or she was making a therapeutic decision. This decision support system was titled the Antibiotic Assistant.93

The Antibiotic Assistant is comprised of a series of files.93 The first file extracts patient and microbiological data from the HELP system and collates the information by pathogen and by patient characteristics such as site of infection, gender, age, inpatient versus outpatient status, community- versus hospital-acquired infection, and the patient’s hospital service. The data analysis program calculates the probability of each pathogen for every combination of patient variables described above. The program then uses the hospital’s antibiograms to determine a rank order of the most effective single antibiotic or combination of antibiotics. A second level of logic then applies rules generated by infectious disease specialists to tailor the list of potential therapeutics. These pathogen and antibiotic rankings are then provided to the physician interface program. Prior to presentation on the screen, the antibiotic rankings are further modified by the program to take into account specific patient information such as allergic contraindications and impairments in renal function. The final therapeutic recommendation made to the clinicians is the most effective single antibiotic or combination of antibiotics that is not contraindicated. When two or more regimens are similarly effective, the least costly regimen is recommended.

Evans and colleagues demonstrated the effectiveness of the empiric antibiotic recommendations in a comparison of the recommended regimens versus the actual regimens ordered by clinicians in a set of randomly selected culture events.94 Antibiotic
regimens suggested by the Antibiotic Assistant covered all cultured pathogens for 94 percent of the culture results, yet the clinician-ordered regimens covered all pathogens only 77 percent of the time. With the use of the computerized tool, physicians ordered effective antibiotic regimens within 12 hours of the culture event significantly more frequently than before use of the computer.

Others have followed these results with the development of similar empiric antibiotic decision support systems. Leibovici and partners compiled a decision support tool that calculates the probability of a serious bacterial infection and the likelihood of a multiresistant organism. Therapy rules are then applied that generate antibiotic regimens that would cover the probable pathogens. These rules, called “arrays” in their system, account for local hospital susceptibility patterns. In a nonintervention comparison of this system versus the actual clinical care provided in their medical center, inappropriate antimicrobial treatment was provided by the clinicians in 42 percent of the patients, yet inappropriate care was recommended by the decision support system in only 23 percent of the patients. Additionally, superfluous therapy was prescribed in 15 percent of the cases, but recommended by the system in only 11 percent. An analysis of the data showed that the decision support system provided an advantage that was most evident in cases of multiresistant gram negative isolates, enterococci, and Staphylococcus aureus.

Another group led by Homer R. Warner, Jr., Ph.D., developed an empiric antibiotic decision support tool that used some of the relevant expert knowledge of Iliad, one of the comprehensive diagnostic decision support tools. Use of this expert knowledge enabled the tool to consider the patient’s signs and symptoms to determine the
probability of infectious disease, the expected or associated morbidity and mortality of each disease, the anticipated benefit to optimum therapy, and the costs of each intervention. Once the appropriate patient data had been entered, the tool provided therapeutic regimens ranked by their potential benefit to the patient, their toxicity, and their cost. In an evaluation presented at the 1999 American Medical Informatics Association Annual Symposium, an improvement over baseline was found when physicians selected antibiotics with the help of the tool. 97 A greater impact was noted on the more difficult cases.

Not all informatics applications must be complicated to potentially impact the quality of care. In light of the emergence of vancomycin-resistant enterococci, Shojania et al. reported the development of a computer application designed to minimize the unnecessary use of this antibiotic. 98 The authors arranged to have computerized vancomycin-use guidelines, published by the Centers for Disease Control and Prevention, presented to one-half of the hospital’s staff of resident physicians at the time the antibiotic was being ordered and then again after 72 hours of administration. This intervention led to 32 percent fewer orders for vancomycin and 28 percent fewer patients treated with this antibiotic when compared to the control group. The authors concluded that computerized guidelines were a promising tool for changing prescribing practices.
The Antibiotic Assistant: A Computerized Antiinfectives

Management Program

Evans and partners enhanced the antiinfective management program (AMP) at LDS Hospital with a number of new features. A patient data display screen was developed, showing the patient’s name, bedspace, admission diagnosis, maximum white blood cell count, maximum temperature, current renal function as estimated by the creatinine clearance, antibiotic allergies, current antibiotics and duration of administration (Figure 1). Computer code was written that searched the patient file for the patient’s microbiology results and pulled out and displayed any that were considered pathogens by the embedded knowledge base. These data take only seconds to gather and are displayed to the clinician on the AMP’s initial screen. Additionally, the patient’s dictated and transcribed chest radiograph results were searched for keywords that indicated the need for antiinfective therapy. If pneumonia was found, it was classified by whether it was community- or hospital-acquired. If the patient had been hospitalized more than three days, or had been hospitalized within the previous month, pneumonia was classified as hospital-acquired; otherwise it was community-acquired. Another subprogram searched the operating room schedule and determined if the patient has had a recent surgery. This data, admission diagnosis, the microbiology and chest radiograph results, and the list of surgeries were then used by the AMP’s knowledge base of algorithms to generate a list of suggested antiinfectives. This list was then screened for allergic, renal function, drug-drug and drug-lab contraindications, and appropriate
IHC ANTIBIOTIC ASSISTANT & ORDER PROGRAM

00000000 Doe, Jane Q E606 67yr F Dx: ABDOMINAL SEPSIS
Max 24 hr WBC=21.0 (21.3) Admit: 07/27/98. 14:55 Max 24hr Temp=38.7 (38.2)
Patient's Diff shows a left shift, max 24hr bands= 22 (11)
RENNAL FUNCTION: Decreased, CrCl = 50, Max 24hr Cr= 1.0 (1.1)
ANTIBIOTIC ALLERGIES: Ampicillin,
CURRENT ANTIBIOTICS:
1. 07/29/98 5DAYS TROVAFLOXACIN (TROVAN), VIAL 300. Q24 hrs
2. 08/01/98 2DAYS AMPHOTERICIN B (FUNGIZONE), VIAL 35 Q24 hrs
Total amphotericin given = 70mg K=3.6mg/dl 08/03/98 MAG = 2.5mg/dl 08/03/98
IDENTIFIED PATHOGENS SITE COLLECTED
p Gram negative Bacilli Peritoneal Fluid 07/27/98. 17:12
Yeast Peritoneal Fluid 07/27/98. 17:12
Torulopsis glabrata Peritoneal Fluid 07/27/98. 17:12
THERAPEUTIC SUGGESTION DOSAGE ROUTE INTERVAL
Imipenem 500mg IV *q12h (infuse over 1hr)
Amphotericin B 35mg IV q24h (infuse over 2hrs)
Suggested Antibiotic Duration: 10 days
*Adjusted based on patient's renal function.
ALT: Preim; Susceptibilities based on antibiogram or same pathogen w/suscept.
<1>Micro <2>Organism Suscept, <3>Drug Info, <4> Explain Logic, <5> Empiric Abx.
<6>Abx Hx, <7>ID Rnds, <8>Lab/Abx Levels, <9>Xray, <10>Input Screen,
<Esc>EXIT, <F1>HELP, <0>User Input, <>Outpatient Models, <+orF12>Change Patient
ORDER:<*>Suggested Abx, <ENTER>Other Abx, <D>C Abx, <>Modify Abx,

Figure 1. Patient Data Display and Antiinfective Recommendations Generated by the IHC Antiinfective Management Program of LDS Hospital

alternatives were then selected. Doses were calculated using the patient’s ideal body weight, renal function, and antibiotic indication.

Shortliffe has written that all medical decision support systems must be able to explain their reasoning to the physicians, or they will not be accepted for use in the clinical arena.58,59 He also argued that the ability to provide the rationale gives rule-based expert systems an advantage over probability-based systems that use Bayesian analysis. The AMP provides explanations of the rules used to derive the antiinfective suggestions. These are available from the main screen by choosing option <4>. Figure 2 displays a sample explanation.
LOGIC USED TO HELP SELECT SUGGESTED ANTIBIOTICS

- Patient should receive IV antibiotics
- Suggested antibiotics are not one of patient's known antibiotic allergies
- Renal function dictates that dosage should be adjusted
- Coagulase negative Staph. in sputum or urine was not considered a pathogen
- Cultures show fungi or yeast that were not considered pathogens
- Aminoglycosides potentiate ototoxicity if administered with loop diuretics
- Amphotericin B is suggested for serious fungal infections
- S. Maltophilia is generally not pathogenic unless found in sterile site
- A staph or gram + cocci reported in the blood was considered a contaminant
- Ceftazidime is usually suggested until gram negative bacillus is identified
- Suggested antibiotics should include Rx for possible abdominal anaerobes
- Suggest fluconazole for C. albicans in nonimmunosuppressed patients
- Prophylactic antibiotics are not suggested for this patient at this time
- Identified pathogens are covered by the suggested antibiotics
- Suggested antibiotic(s) are least expensive of the appropriate antibiotics

The antibiotic suggestions should not replace clinical judgement
Press the "Enter" key for next screen

**Figure 2.** Display of the Rules Used to Derive Antiinfective Suggestions

The hospital's antibiograms are made available to the clinician through option <2>. Because the data-gathering process permits association of a positive culture and susceptibility patterns to the patient from which it originated, it is possible to label the culture result as being from a particular patient unit in the hospital and from a community- or hospital-acquired infection. This association enables display of the antibiograms sorted by hospital unit of interest or by community versus hospital-acquired infections. A sample screen of an antibiogram is displayed in Figure 3.

Note that the cost/24-hour period is displayed in the antibiogram shown in Figure 3. The AMP also considers costs in its recommendations. When two or more antiinfectives are determined to be therapeutically equivalent, the program will select the less expensive agent.
LDS HOSPITAL ANTIBIOGRAM

BACTERIA: Escherichia coli
DURING THE PAST 5 YEARS

<table>
<thead>
<tr>
<th>ANTIBIOTIC</th>
<th>PERCENT SUSCEP.</th>
<th>TESTED 24HR</th>
<th>COST/NUM.</th>
<th>ANTIBIOTIC</th>
<th>PERCENT SUSCEP.</th>
<th>TESTED 24HR</th>
<th>COST/NUM.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Amikacin</td>
<td>100</td>
<td>7576</td>
<td>90.44</td>
<td>11. Cefuroxime</td>
<td>98</td>
<td>7515</td>
<td>27.81</td>
</tr>
<tr>
<td>2. Cefotaxime</td>
<td>100</td>
<td>7580</td>
<td>34.16</td>
<td>12. Amox/clav</td>
<td>94</td>
<td>7574</td>
<td>6.15</td>
</tr>
<tr>
<td>3. Imipenem</td>
<td>100</td>
<td>7581</td>
<td>75.92</td>
<td>13. Cefazolin</td>
<td>93</td>
<td>7578</td>
<td>11.22</td>
</tr>
<tr>
<td>5. Ceftriaxone</td>
<td>100</td>
<td>7581</td>
<td>48.62</td>
<td>15. Trimeth/sulfa</td>
<td>87</td>
<td>7548</td>
<td>6.40</td>
</tr>
<tr>
<td>6. Tobramycin</td>
<td>99</td>
<td>7565</td>
<td>20.78</td>
<td>16. Trimethoprim</td>
<td>86</td>
<td>6893</td>
<td>0.36</td>
</tr>
<tr>
<td>7. Aztreonam</td>
<td>99</td>
<td>7579</td>
<td>34.35</td>
<td>17. Sulfamethoxaz</td>
<td>72</td>
<td>6232</td>
<td>8.00</td>
</tr>
<tr>
<td>8. Levofoxacin</td>
<td>99</td>
<td>7307</td>
<td>32.26</td>
<td>18. Piperacillin</td>
<td>66</td>
<td>7345</td>
<td>49.08</td>
</tr>
<tr>
<td>9. Gentamicin</td>
<td>98</td>
<td>7580</td>
<td>8.56</td>
<td>19. Ampicillin</td>
<td>63</td>
<td>7546</td>
<td>1.76</td>
</tr>
</tbody>
</table>

The antibiotic costs are the exact cost to the hospital and calculated from the recommended dosage based on patient's renal function. The cost of laboratory tests to monitor the drug levels are included.

**Figure 3. A Sample Antiobigram**

The empiric culture-based antibiotic recommendations discussed previously are incorporated into the AMP and available for review by selecting option <5>. A sample screen is shown in Figure 4.

The evaluation of the AMP in the adult Shock/Trauma Intensive Care Unit (STICU) at LDS Hospital is the largest controlled trial on the use of computerized antiinfective decision support and is arguably the most important publication in this field since it was conceptualized by Dr. Shortliffe three decades earlier. Evans and colleagues reported the effect on various process and outcome measures of one year's use of the tool in the care of critically ill patients in the STICU compared to the care of patients during the preceding two years. The decision support tool beneficially impacted process measures such as antibiotic/bacterial susceptibility mismatches, orders for drugs
### LDS HOSPITAL EMPIRIC ANTIBIOTIC ASSISTANT

<table>
<thead>
<tr>
<th>Organism</th>
<th>%</th>
<th>$/24hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staph. Coagulase neg.</td>
<td>208(61)</td>
<td>116.33</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>28(8)</td>
<td>74.53</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>27(8)</td>
<td>46.67</td>
</tr>
<tr>
<td>Staph. aureus</td>
<td>18(5)</td>
<td>57.03</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>13(4)</td>
<td>50.24</td>
</tr>
</tbody>
</table>

**TOTAL 294 (86)**

**EMPIRIC ANTIBIOTIC SUGGESTION:** Vancomycin + Tobramycin

**ANTIBIOTIC ALLERGIES:** None reported

**RENAL FUNCTION:** Normal. CrCl: >120, Max 24hr Cr=0.6 (0.7). IBWeight: 67kg

Enter <*> to order suggested antibiotics, press <Enter> to continue...

---

**Figure 4.** Sample of Empiric Recommendations by Culture Result

to which the patient had reported allergies, and alerts of excessive dosage of antiinfective agents. Benefits to the patients were noted in the outcome measures, including fewer adverse drug reactions, fewer antiinfective doses, and less antiinfective costs.  

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**Pediatric Antiinfective Decision Support**

Relatively little work has been performed in the realm of computerized pediatric antiinfective decision support. Rocha and partners described the successful development of a rule-based expert system to assist hospital infection control practitioners by detecting the presence of hospital-acquired infections in newborn patients. In a retrospective examination, they reported that their system had an 84.5 percent sensitivity and a 92.8
percent specificity for detecting hospital-acquired infections when compared to a manual reviewer. This expert system has been successfully implemented to assist the infection control practitioners at LDS Hospital and was also modified for similar use at PCMC.

More recently, Shriger and colleagues described an implementation of computerized clinical guidelines for the care of febrile infants and children less than three years of age in the emergency department at the University of California at Los Angeles. This follows their earlier study that showed that clinical guidelines embedded in an electronic medical record can improve the quality and lower the cost of care provided to healthcare workers who have incurred occupational exposures to body fluid. In this pediatric study, the authors implemented existing guidelines from the medical literature into the electronic medical record being developed at their institution. During the second phase of the study, use of the tool was encouraged, but not mandated, for the care of febrile children in the emergency department. This time period was then compared to two control periods, before implementation, and after usage was discontinued. The authors report that the tool was used in 64 percent of the eligible patients and that a 13 percent improvement in the documentation of essential history details and physical findings was noted. However, there was no demonstrable change in the appropriateness of care or in the charges to the patient for care rendered. The authors concluded that the intervention improved documentation but did not effect the appropriateness of care.
Pediatric Antiinfective Management Program

Pediatricians must commonly choose therapy based on empiric notions of the etiologic agent, and suboptimal choices have been shown to increase the risk of mortality. Medical errors may occur in the execution of otherwise good therapy plans as doses may be miscalculated or may fail to be tailored to therapeutic indication (e.g., meningitis), the age and weight of the patient, the renal function, or the level of prematurity. As in adults, bacterial susceptibilities must be considered, and antibiograms change with both time and geographic location. An antiinfective decision support system, operating with the support of a rich clinical data repository, could provide expert advice to the clinician on antiinfective selection at the time the agent is ordered. Such a tool could minimize opportunities for medical errors due to a failure to consider important drug-drug and drug-lab interactions, and drug-allergy contraindications when selecting the patient’s therapy. The system could automatically consider the patient’s age, weight, therapeutic indication, and renal function when generating drug dosages and eliminate errors from hand-calculation. When agents are therapeutically equivalent, the least costly regimen could be selected to receive the recommendation. I therefore hypothesized that a clinical decision support system designed with these considerations would improve antiinfective choices, dosage selections, the rate of adverse drug events, and the cost of antiinfectives used in the care of critically ill infants and children. This report describes the development and clinical evaluation of a pediatric antiinfective management program.
METHODS
Background

Setting

Primary Children’s Medical Center is a 232 bed facility located on the University of Utah medical campus and owned and operated by Intermountain Health Care Corporation. PCMC is the primary pediatric teaching facility for the University of Utah School of Medicine. The hospital serves as the tertiary referral center for all of Utah and large portions of Nevada, Arizona, Colorado, Wyoming, and Idaho. In 1998, PCMC served 9700 admissions, 30,000 emergency department visits, and 104,000 outpatient visits. PCMC houses a PICU comprised of 26 beds and averaging 1700 admissions per year of a broad array of critically ill medical and surgical patients. Pediatric critical care specialists working together with critical care fellows-in-training, pediatric residents, and nurse practitioners staff the unit. This clinical team is primarily responsible for the medical patients, and comanages the surgical admissions.

Bedside computer terminals running the Health Evaluations through Logical Processing (HELP) hospital information system facilitate patient care. HELP was initially developed at LDS Hospital in Salt Lake City in 1967 and has expanded functionally and geographically since. It is now a fully integrated hospital information system providing data collection and storage at PCMC for a broad range of clinical arenas, including, laboratory, pharmacy, radiology and pathology (See Figure 5). The HELP system is installed at the largest Intermountain Health Care Corporation hospitals and is commercially implemented, through a partnership with 3M, in several other hospitals across the United States. At the time of implementation of the pediatric
antibiotic decision support tool, the physicians and nurse practitioners used the HELP system primarily for laboratory results review and the generation of a morning summary report of patient vital signs, labs, medications, radiology reports, and ventilator data. A blood product ordering module had been implemented for physicians, but in the PICU, the order entry was primarily performed by the nursing staff. Consequently, all patient care orders from the physicians were handwritten, with communication to the necessary ancillary services (pharmacy, lab, etc.) generally rendered through distribution of carbon copies. Handwritten antibiotic orders were typically interpreted by the clerk and rewritten onto the bedside medication administration record. Copies of the handwritten

**Figure 5.** Data Sources of the HELP System's Integrated Centralized Database at PCMC
order were also read by the pharmacist and entered via a keyboard into the HELP system's pharmacy module.

**System**

A detailed description of the adult version of the antiinfective decision support tool has been previously published. The availability of a detailed patient-specific database enhances the strength of the tool. For instance, the medical logic considers the patient's admission diagnosis, recent surgeries, dictated chest radiograph reports, microbiology culture results, white-blood cell count, temperature, serology, and pathology results when assessing for a need for antiinfectives. The tool also has access to the patient's laboratory results, current medication list, and allergic history available for providing alerts and reminders to the clinicians. Unlike at LDS Hospital, at PCMC the surgical schedule and patient vitals (temperature) are not always available online, necessitating modifications to the medical logic and display screens.

**Development of the Pediatric Antiinfectives Management Program**

**Empiric Medical Logic**

The task of developing the pediatric antiinfectives management program was started using the adult version as a template. Although the adult edition could be run at PCMC on pediatric patients, its advice was often incorrect and was sometimes potentially harmful. Thus, we sought to identify rules and logic in the adult version that would be safe and beneficial to keep in the pediatric edition, while maintaining the same code
framework and overall look and feel of the program. A text version of the adult logic was used to derive the new pediatric recommendations. The PCMC Antibiotic Assistant ad hoc committee reviewed each rule and recommended changes, additions, and deletions. Examples of our decisions on empiric antimicrobial recommendations are displayed in Table 1. Unique pharmaceutical toxicities in pediatric patients, variations between adult and pediatric culture practices and differences in pathogen virulence between pediatric and adult-aged patients necessitated modifications to the logic used to handle culture results. Examples of these logic changes are shown in Table 2.

The empiric recommendations were then distributed among the four other pediatric infectious disease faculty members of the University of Utah. Their comments and suggestions were reviewed and, where appropriate, incorporated into the computer code of the pediatric antiinfective management program. The most up-to-date version of the rules for empiric therapy of pediatric infectious illnesses is reproduced for examination and documentation in Appendix A.

Table 1. Examples of Recommended Changes in Medical Logic

<table>
<thead>
<tr>
<th>Medical Condition</th>
<th>Adult-based Empiric Therapy</th>
<th>Recommended Pediatric Therapy</th>
<th>Reasoning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urosepsis</td>
<td>Ciprofloxacin, or ofloxacin</td>
<td>Ampicillin &amp; gentamicin,</td>
<td>Better coverage for pediatrics; quinolones toxic in children</td>
</tr>
<tr>
<td>Fever &amp; neutropenia</td>
<td>Ceftazidime or imipenem plus tobramycin</td>
<td>Ceftazidime alone</td>
<td>Standard pediatric practice</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Ceftriaxone</td>
<td>Vancomycin plus cefotaxime or ceftriaxone</td>
<td>Vancomycin needed for risk of cephalosporin resistant pneumococci</td>
</tr>
</tbody>
</table>
Table 2. Examples of Recommended Changes to Culture Results Logic

<table>
<thead>
<tr>
<th>Culture Result</th>
<th>Adult Therapy Rule</th>
<th>Pediatric Therapy Rule</th>
<th>Reasoning</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. epidermidis</td>
<td>Need two positive blood cultures within 24 hours to be considered a pathogen</td>
<td>All isolates in the blood considered a pathogen</td>
<td>Due to fear of needlesticks and conservation of blood volume, pediatric patients commonly have only one culture drawn per day. Immature immune systems in neonates; gravity of infection; increasing resistance of pathogen to fluconazole, TMP-SMX a reasonable alternative when penicillin &amp; cephalosporin allergic</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>Fluconazole in non-immuno-suppressed patients</td>
<td>Amphotericin B for all Candida infections of blood and other sterile sites, except urine</td>
<td></td>
</tr>
<tr>
<td>N. meningitidis</td>
<td>In blood without susceptibilities yet: ceftriaxone</td>
<td>(descending order): Ceftriaxone, penicillin, trimethoprim-sulfamethoxazole</td>
<td></td>
</tr>
</tbody>
</table>

Neonatal and Pediatric Antibiotic Doses

In contrast to the decision support logic for infectious diseases and positive bacterial cultures, the recommended pediatric antiinfective doses are entirely new and separate from the adult doses. These dosage recommendations were generated in a stepwise manner. Pediatric pharmaceutical texts\textsuperscript{105,106} were first consulted, and the list of candidate dosages for infants and children were determined. The neonatal dosage recommendations were constructed using standard tables that take into account the postconceptional age (estimated gestational age at birth plus age in weeks since birth) and age in days since birth (postnatal age).\textsuperscript{107} The list and tables of candidate dosages were then reviewed by the infectious disease specialist, and modifications were made based on local experience and population considerations. Special doses were developed where indicated for severe disease such as meningitis or bacteremia or for atypical patient...
populations, such as those with cystic fibrosis. Dosage adjustments for impairments in renal function were also standardized for patients greater than six months of age. Younger patients were excluded from this benefit because the Schwartz formula for creatinine clearance estimation has been cited to be inaccurate in that age group. The ability to estimate the creatinine clearance requires that the patient’s age, gender, serum creatinine, and height all be available in the hospital’s information system. Height was problematic. Although measurement of length or height on admission was hospital policy and is mandated by the Joint Commission on Accreditation of Healthcare Organizations, it was not routinely done. In support of its own policy and the development of the pediatric antiinfectives management program, the PCMC administrative staff began a reeducation campaign of the nursing staff to ensure proper electronic documentation of patient height.

As with the empiric antiinfective recommendations, all dosage recommendations were distributed among the faculty of the University of Utah Division of Pediatric Infectious Diseases for review. These were then used to write the computer code of the pediatric antiinfective management program. The current versions of the pediatric and neonatal dosing regimens are available for review in Appendix B.

**Antibiotic Susceptibility Results**

Although the institutions within IHC have standardized on many processes, the philosophy behind the presentation of bacterial culture results to the physicians differs between LDS Hospital and PCMC. At the adult hospital, LDS, the susceptibility results
for a pathogen are presented for most of the antibiotics tested. This convention allows the clinician to choose the one or two that he or she believes is most appropriate for the patient under consideration. At the children’s hospital, PCMC, a series of decision rules govern which antibiotic susceptibility results will be reported on the HELP system. These rules consider the type of organism, the source of the culture, and, in some instances, host factors such as cystic fibrosis. For example, the bacterial susceptibility to the urinary tract agents, nitrofurantoin and sulfisoxazole, are reported for pathogens grown from urine specimens, but not for cultures from the blood where their use would be ineffective. These rules result in fewer antibiotic susceptibilities being reported to the hospital’s information system, and therefore to the clinicians. Limitation of information in the HELP system has both positive and negative consequences. A positive consequence is the improvement in medical decisions and minimization of therapy choice errors that result from these rules. A negative consequence is the loss of antibiotic sensitivity information that could be used in the aggregate analysis. For instance, in the antibiogram tabulated for *Streptococcus pneumoniae*, the susceptibility results for penicillin have been reported a total of 80 times, but the results for vancomycin a total of 100 times. The question then arises: Do the unreported culture sensitivities influence the aggregate susceptibility results to the point of clinical relevance? A review of the susceptibility results for all 40 pathogens reported in the AMP determined that the differences in reported susceptibilities between the raw data from the Sunquest lab information system and the refined information gathered by the AMP do not vary by more than 1-2 percent. This difference was judged to be clinically inconsequential.
Thus, neither a change in the laboratory protocol for reporting bacterial sensitivities nor in the automated method of collating the same data from the HELP system, was necessary for the initiation of the automated pathogen susceptibilities feature of the antiinfectives management program.

Development and Testing

The new infection and dosage logic was added to the pediatric antiinfective management program and loaded onto the HELP system at PCMC. The empiric medical logic for the infectious diagnoses was then tested on neonates, infants, and older children to confirm that the AMP generated the appropriate antiinfective recommendations. For example, the therapeutic recommendations for the admission diagnosis of “meningitis” were tested and confirmed to be correct for patients of varying ages (ampicillin and cefotaxime for neonates and infants, vancomycin and cefotaxime for children and adults). Additionally, all of the calculated drug doses were tested for each indication and weight range encompassed by the logic. For example, the pediatric AMP’s recommended vancomycin dose output was tested and confirmed to be correct on sample patients of neonatal, pediatric, and adult weights, and for all potential therapeutic indications: meningitis, ventriculitis, C. difficile colitis, and routine. During the summer and fall of 1998, the pediatric AMP was also tested daily on the population of patients admitted to the children’s hospital. Each child’s combination of admission diagnosis, chest radiograph results, allergies, and microbiology and other lab results was unique and could not be comprehensively tested without this trial implementation. Periodically,
suboptimal recommendations were noted, necessitating changes to the medical logic. Occasionally, outright “bugs” in the computer code were found and fixed. Once the daily tests ceased finding suboptimal recommendations and other improvement opportunities, the logic and underlying code were judged to be ready, and plans were made for rollout and testing of the value of the pediatric AMP in the PICU.

Preparation for Rollout

Prior to going “live” in the PICU, demonstrations were given to the Pharmacy and Therapeutics Committee, the Nursing Practice Council, the Surgical Quality Improvement Committee, a PCMC Medical Staff meeting, the Pediatric Executive Committee, and a pediatric residents’ noon conference. More detailed demonstrations with hands-on experience were given to the PICU staff of attending physicians, fellows, and nurse practitioners. The pediatric residents rotating through the PICU at the time of rollout were also given personal demonstrations with hands-on experience. These personal sessions were repeated every four weeks when new housestaff rotated through the unit. These tutorials were similar in content to the web-based tutorial reproduced in Appendix C and available on the PCMC Intranet:

http://ihcweb.co.ihc.com/pcmc/electroniclib/antibiotics/index.html

The nursing staff in the PICU was prepared through announcements in their newsletter and through placement of posters in the unit. The pharmacy staff was educated in a small group session.
The Impact of the Pediatric Antiinfectives

Decision Support Tool

Study Design

A study comparing a six-month baseline period with a six-month control period was planned. With an average of 1700 PICU admissions per year, and an estimation that 75 percent would be treated with antibiotics, we anticipated capturing 600+ patients in each arm of the study. The time periods were chosen primarily by the anticipated readiness date of the tool. However, these periods supported the clinical study by placing approximately one-half of the summer trauma season and one-half of the winter bronchiolitis season in each phase of the evaluation. The Institutional Review Boards of the University of Utah and PCMC approved the study protocol.

Via an agreement between the medical and nursing directors of the PICU, the staff of attendings of the PICU, and the pharmacy staff, mandatory use of the pediatric antiinfective management program for ordering antiinfectives within the PICU was initiated on January 22, 1999. During the last week of each set of resident rotations, the residents’ opinions of the decision support tool were surveyed using a questionnaire comprised of five-point Likert-type scales. They were also asked to rank five facets of the tool by “helpfulness.” The pediatric nurse practitioners were surveyed at the end of the six-month experimental period.
Analysis

Data was prospectively gathered through a number of mechanisms. The hospital’s information system tracks and stores all of the population parameters, such as age, gender, length of stay, mortality, and costs. These were analyzed at the end of the study. In conjunction with the pharmacy staff, the Joint Commission on Accreditation of Healthcare Organization’s requirement to monitor and record adverse drug events (ADEs) was emphasized with the unit’s staff of nurses. The three current methods of reporting adverse events were publicized via the staff newsletter and strategically placed bulletins. Quarterly reminders were also posted. The pharmacy staff continued to keep a log of their interventions on drugs and drug dosages. A computer alerting program that determines and reports mismatches of bacterial culture sensitivities and patient antiinfective therapy was modified for pediatrics and installed at the children’s hospital in June of 1998. This printed the potential therapeutic mismatches daily at 1 PM during both study periods. These mismatches were recorded, and the clinical team was notified of the need to change antibiotics.

A computer application was developed to review the PCMC patient files comparing all administered antiinfective agents to published therapeutic ranges with modifications for age and renal function. This program identified all doses that fell outside of the therapeutic ranges and generated a file containing subtherapeutic and overdosage risk-days. A copy of the relevant portions of the program that find the antibiotics and doses and then compare these to generated therapeutic dosage ranges is available for review in Appendix D.
Statistical Methods

Study data were stored and manipulated in Microsoft Access. Study-group comparisons were performed using Fisher's Exact Test for equality of proportions, chi-squared test for independence, and two-sided t tests for comparisons of means. During the latter analyses, consideration was given to logarithmic transformations and the use of Tukey's biweight estimator for skewed variances when appropriate for non-normally distributed data. All chi-squared analyses were performed using Microsoft Excel. The regression analyses were performed using SPSS, SPSS Inc., Chicago, IL. All other analyses were performed using Statit Custom QC, Statware Inc., Corvallis, OR. Statistical significance levels were set at p values of 0.05 a priori.
RESULTS
PICU Study

Patient Populations

During the 12-month study period, 1749 patients were admitted to the PICU. 809 patients were admitted during the preintervention period, and 949 admitted during the intervention period (Table 3). The intervention group was more likely to be treated with antimicrobials while in the PICU (66.5 vs. 60.2 percent; p<0.01), but the overall rate of antimicrobial use during the total hospital stay did not differ significantly.

Further comparisons are limited to “study patients,” defined as those patients with antiinfectives ordered while hospitalized in the intensive care unit during the two time-periods. The intervention patients were younger, with a mean age of 5.3 versus 6.2 years for the preintervention group (p<0.05; Table 4). However, the two groups were similar with respect to gender, PICU length of stay, total hospital length of stay, All Patient Refined Severity of Illness, All Patient Refined Risk of Mortality, percent mortality, and total hospital costs.

Table 3. PICU Patient Population Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preintervention</th>
<th>Intervention</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients admitted</td>
<td>809</td>
<td>949</td>
<td></td>
</tr>
<tr>
<td>No. of Pts with an Abx order while in PICU</td>
<td>487 (60.2%)</td>
<td>631 (66.5%)</td>
<td>P&lt;0.01*</td>
</tr>
<tr>
<td>No. of PICU pts treated w/abx sometime during hospital stay</td>
<td>609 (75.2%)</td>
<td>744 (78.4%)</td>
<td>NS*</td>
</tr>
</tbody>
</table>

* Fisher's exact test for equality of proportions
Table 4. Population Statistics for Patients with a PICU Antiinfective Order

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preintervention</th>
<th>Intervention</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female %</td>
<td>41.5</td>
<td>43.5</td>
<td>NS</td>
</tr>
<tr>
<td>Mean Age</td>
<td>6.2</td>
<td>5.3</td>
<td>P&lt;0.05†</td>
</tr>
<tr>
<td>PICU LOS</td>
<td>4.93</td>
<td>4.90</td>
<td>NS‡</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>10.76</td>
<td>10.76</td>
<td>NS‡</td>
</tr>
<tr>
<td>APR-DRG Severity of Illness category: Count and percent of total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: 96 (19.1)</td>
<td>1: 120 (19.1)</td>
<td>NS†</td>
<td></td>
</tr>
<tr>
<td>2: 128 (26.2)</td>
<td>2: 153 (24.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3: 142 (29.2)</td>
<td>3: 177 (28.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4: 124 (25.5)</td>
<td>4: 178 (28.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>APR-DRG Risk of Mortality category: Count and percent of total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: 228 (46.8)</td>
<td>1: 280 (44.6)</td>
<td>NS‡</td>
<td></td>
</tr>
<tr>
<td>2: 84 (17.2)</td>
<td>2: 135 (21.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3: 119 (24.4)</td>
<td>3: 139 (22.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4: 56 (11.5)</td>
<td>4: 74 (11.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>18 (3.7)</td>
<td>20 (3.2)</td>
<td>NS‡</td>
</tr>
<tr>
<td>Hospital Costs in 1999 dollars</td>
<td>$28,257.67</td>
<td>$250,321.11</td>
<td>NS‡</td>
</tr>
</tbody>
</table>

* Fisher’s exact test for equality of proportions
† Two tailed t test
‡ Chi-squared

Antibiotic Use

Table 5 shows that the per-patient antibiotic use measurements were also similar between the two groups, despite the implementation of the new management tool. Specifically, there were no differences in the PICU or total hospital count of antiinfectives or antiinfective doses used per patient. Neither was there a difference in the PICU or total hospital costs of antiinfectives. However, the number of orders placed per antibiotic course decreased 11.5 percent from an average of 1.56 to 1.38 orders/pt-antiinfective, p<0.01. Additionally, application of Tukey’s biweight estimator, which downweights extreme values in non-normal distributions, revealed an underlying 9 percent decrease in the costs of antiinfectives used for the average intervention group PICU patient (Table 5
Table 5. Per-patient Antiinfective Use Measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preintervention</th>
<th>Intervention</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Antibiotic Costs</td>
<td>$274.79</td>
<td>$289.60</td>
<td>NS*</td>
</tr>
<tr>
<td>Total Num. Abx Used</td>
<td>2.18</td>
<td>2.22</td>
<td>NS*</td>
</tr>
<tr>
<td>Total Doses Used</td>
<td>19.8</td>
<td>22.0</td>
<td>NS*</td>
</tr>
<tr>
<td>PICU Abx costs</td>
<td>$177.03</td>
<td>$183.53</td>
<td>NS*</td>
</tr>
<tr>
<td>(PICU Abx doses)</td>
<td>($86.60)</td>
<td>($78.43)</td>
<td>P&lt;0.05†</td>
</tr>
<tr>
<td>PICU Num. Abx</td>
<td>1.85</td>
<td>1.97</td>
<td>NS*</td>
</tr>
<tr>
<td>PICU Abx Orders per Pt-Abx course</td>
<td>1.56</td>
<td>1.38</td>
<td>P&lt; 0.01*</td>
</tr>
</tbody>
</table>

* Two tailed t test
† Tukey’s biweight estimator

Application of Tukey’s biweight estimator did not change the interpretations of the other baseline population or antibiotic-use measurements between the two groups.

Total antiinfective use, by a comparison of the count of patients treated with each antiinfective, was also similar between the two groups by chi-squared analysis (Table 6). This comparison remained without a significant difference with the categories collapsed for expected values less than two, as is commonly recommended in chi-squared analysis.

Antibiotic/Bacterial-susceptibility Mismatches

Therapeutic mismatches between pathogens cultured in the microbiology lab and the antimicrobials being used to treat the patients were assessed by a time-driven computer alerting program at 1 PM on the day of published sensitivities. There was no difference in the incidence of mismatches between the two groups. Only one event was noted during the control period—a *Staphylococcus epidermidis* blood culture that was initially perceived as a contaminant and therefore was not being treated. During the intervention period, only one event was noted as well—a *Enterococcus sp.* urinary tract infection.
Table 6. Count of Patients with a PICU Order for Each Labeled Antiinfective

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Preintervention</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>acyclovir</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>amikacin</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>amoxicillin</td>
<td>16</td>
<td>29</td>
</tr>
<tr>
<td>amoxicillin/clav</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>amphotericin B</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>amphotericin lipid complex</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>ampicillin</td>
<td>37</td>
<td>56</td>
</tr>
<tr>
<td>ampicillin/sulbactam</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>azithromycin</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>cefaclor</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>cefazolin</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>cefixime</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>cefotaxime</td>
<td>41</td>
<td>51</td>
</tr>
<tr>
<td>cefotaxime</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>ceftazidime</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>38</td>
<td>32</td>
</tr>
<tr>
<td>cefuroxime</td>
<td>260</td>
<td>339</td>
</tr>
<tr>
<td>cephalixin</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>ciprofloxacin</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>clarithromycin</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>clindamycin</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>doxycycline</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>erythromycin</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td>fluconazole</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>ganciclovir</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>gentamicin</td>
<td>68</td>
<td>86</td>
</tr>
<tr>
<td>imipenem</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>meropenem</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>metronidazole</td>
<td>15</td>
<td>19</td>
</tr>
<tr>
<td>nafcillin</td>
<td>11</td>
<td>19</td>
</tr>
<tr>
<td>penicillin</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>piperacillin</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>piperacillin/tazobactam</td>
<td>25</td>
<td>38</td>
</tr>
<tr>
<td>ticarcillin</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>ticarcillin/clav</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>tilmex</td>
<td>15</td>
<td>29</td>
</tr>
<tr>
<td>tobramycin</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>vancomycin</td>
<td>48</td>
<td>54</td>
</tr>
</tbody>
</table>
that was being treated with, but found resistant to, amoxicillin. In this instance, the resident physician caring for the patient had not consulted the pediatric antiinfectives management program for therapeutic recommendations after the culture results had been reported to the HELP system.

**Adverse Drug Reactions**

The total number of adverse drug reactions recorded in the PICU for the 12-month study period was 119, with 24 of those secondary to antiinfectives. Twelve events were recorded in each of the two study periods. A breakdown of the reactions into the categories of mild (requiring no therapy change), moderate (requiring a change in therapy), and severe (potentially life threatening), found no significant difference (Table 7). In each group, only one of the 12 was potentially preventable secondary to known allergic sensitivities (each assigned to moderate severity group). During the intervention period, the potentially preventable allergic reaction occurred when a surgery resident, not using the antiinfectives management program, ordered a cephalosporin on a PICU patient known to be allergic to penicillins (note: unlike pediatric residents in the PICU, the surgery residents were not involved in the study and did not routinely use the pediatric antiinfective management program). Had the decision support tool been used, it would

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preintervention</th>
<th>Intervention</th>
<th>Statistical Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (requiring no therapy change)</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Moderate (requiring a change in therapy)</td>
<td>16</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Severe (potentially life threatening)</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12</td>
<td>12</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Fisher's exact test
have alerted the potential for an allergic cross-reaction.

**Pharmacy Interventions**

Using both manual and computer-assisted methods, the pharmacists in the PICU at PCMC serve as a human "safety net" for ordered pharmaceuticals, making interventions on erroneous drug doses and other therapeutic improvement opportunities. In this capacity, the pharmacists keep a log of their interventions on the drugs ordered by the clinicians. During the study period, the interventions for all pharmaceuticals numbered approximately 1800, with antiinfectives comprising 30 percent. Analysis of these data revealed that there was no significant difference in the number or rate of interventions on antiinfectives ordered by nonusers of the decision support tool (Figure 6), but there was a significant 53.6 percent decrease in the total rate of interventions on those ordered by users (Table 8 and Figure 7). Additionally, a 59.2 percent decrease in the rate of intervention for the subcategory of erroneous drug doses was noted, and a 58.4 percent decrease was found in the rate of clinician requests for dosing help.

![Figure 6. Number of Interventions on Erroneous Drug Orders by Users and Nonusers](image-url)
Table 8. Rate of Pharmacy Interventions per 1000 Patient-Antiinfective Courses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preintervention</th>
<th>Intervention</th>
<th>Statistical Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose adjustments</td>
<td>35.5</td>
<td>14.5</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Requested dosing help</td>
<td>23.3</td>
<td>9.7</td>
<td>(58.4% decrease)</td>
</tr>
<tr>
<td>Suggestions for altering therapy</td>
<td>24.4</td>
<td>12.1</td>
<td>NS</td>
</tr>
<tr>
<td>Allergic contraindications</td>
<td>2.2</td>
<td>2.4</td>
<td>NS</td>
</tr>
<tr>
<td>Drug-drug interactions</td>
<td>1.1</td>
<td>1.6</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Total rate of interventions on orders</strong></td>
<td>86.6</td>
<td>40.2</td>
<td>P&lt;0.0901</td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test for equality of proportions

![Intervention Rate Graph](image)

**Figure 7.** Graph of Pharmacy Interventions on Users' Drug Orders per 1000 Patient-Antiinfective Courses

Subtherapeutic and Excessive-dosage Risk Days

An analysis of patient antiinfective doses compared to published minimum and maximum recommendations for age, weight, and renal function was also performed. Days of antimicrobial therapy that fell outside of these minimum and maximum recommendations are called subtherapeutic and excessive-dosage risk days, respectively. The count of out-of-range days was determined for each patient and analyzed by study
day. As shown in Table 9, a significant 36 percent improvement in the rate of subtherapeutic risk days was found for the intervention group when compared to the control group. Likewise, a significant 28 percent decrease was noted in the excessive-dosage risk days. The combined effect was a 32 percent improvement in the rate of antiinfective days that fall outside of the published recommended parameters.

User Surveys

Questionnaires were returned by 28 of the 31 pediatric residents (n=26) and nurse practitioners (n=5). Questions were formatted as five-point Likert-type scales, and a favorable response was defined as one on the “beneficial” or “positive effect” side of the neutral response. For most questions, the favorable response is identified as a score of a 4 or 5 on the five-point scale. For three questions, a favorable response is scored as a 3, 4, or 5 as the neutral response was assigned as a 1. See Appendix E for further details.

A majority of the users responded favorably to the decision support tool. Specifically, they reported improved overall antibiotic choices, increased awareness of

<table>
<thead>
<tr>
<th>Variable</th>
<th>Preintervention</th>
<th>Intervention</th>
<th>Statistical Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtherapeutic antiinfective days/100 pt. days</td>
<td>7.350</td>
<td>4.702</td>
<td>P &lt; 0.001*</td>
</tr>
<tr>
<td>Excessive-dosage antiinfective days/100 pt. days</td>
<td>8.454</td>
<td>6.063</td>
<td>P &lt; 0.001*</td>
</tr>
<tr>
<td>Total Risk Days/100 patient days</td>
<td>15.80</td>
<td>10.766</td>
<td>P &lt; 0.0001*</td>
</tr>
</tbody>
</table>

* Two tailed t-test
renal function, beneficial dosage calculation assistance, association with fewer adverse drug events, and improved quality of care (Table 10). The median estimation of how often the users ordered the recommended antibiotic was 50 percent, and the estimation of how often they ordered the recommended dose was 75 percent. Most (79 percent) reported that they learned something from the system, and nearly all (93 percent) would recommend it to others. A copy of the survey and detailed results, including hand-written comments are available for review in Appendix E.

The users were also invited to rank five facets of the decision support tool by “helpfulness.” The dosage calculation assistance and online antibiograms scored the highest, and the computerized drug ordering and printing was cited last (Table 11).

Regression Analysis

Two post-hoc analyses were performed to answer questions raised by the initial data. Is the younger age of the intervention patients responsible for the 5 percent increase in antimicrobial usage? Multiple linear regression does not find that variability in age explains PICU antibiotic usage variability, either alone, or when controlling for study

<table>
<thead>
<tr>
<th>Question</th>
<th>Percent Positive Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved overall antibiotic choices</td>
<td>81%</td>
</tr>
<tr>
<td>Increased awareness of renal function</td>
<td>79%</td>
</tr>
<tr>
<td>Beneficial dosage calculation assistance</td>
<td>96%</td>
</tr>
<tr>
<td>Associated with fewer adverse drug events</td>
<td>89%</td>
</tr>
<tr>
<td>Improved quality of care</td>
<td>81%</td>
</tr>
</tbody>
</table>
Table 11. User Ranking of Five Facets of the Antibiotic Assistant by “Helpfulness”

<table>
<thead>
<tr>
<th>Rank</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dosage Calculation Assistance</td>
</tr>
<tr>
<td>2</td>
<td>Online Antiograms (antibiotic susceptibility patterns)</td>
</tr>
<tr>
<td>3 (tie)</td>
<td>Antibiotic Suggestions</td>
</tr>
<tr>
<td>3 (tie)</td>
<td>Patient data review (micro results, allergies, renal function, etc)</td>
</tr>
<tr>
<td>5</td>
<td>Computerized drug ordering and printing</td>
</tr>
</tbody>
</table>

group. The second question raised by the data is whether the decrease in PICU antibiotic costs when analyzed using Tukey’s biweight estimator is secondary to the younger age of the intervention patients. Again, multiple linear regression does not find age to be a significant predictor of PICU antibiotic costs when controlled by study group, or the combination of study group, severity of illness, and risk of mortality.
DISCUSSION
Implementation of computerized antiinfective decision support, provided at the time of the ordering of the antiinfectives, increases the likelihood that the dose will be on target for the given age, weight, and renal function of the patient. The pediatric antiinfective management program provides support to the clinician in a number of ways that can account for the improvement. The renal function is automatically estimated and updated daily, and suggested doses are calculated with adjustments for evidence of impairment. Age and prematurity considerations are automatically considered, and doses are calculated without errors. Order legibility is also rendered a non-issue through the computer printouts. These mechanisms likely explain not only the decrease in pharmacy interventions for erroneous doses, but also the improvements in the number of days of therapy that fall outside of recommended therapeutic ranges.

Discussions held among the critical care faculty, fellows, and nurse practitioners also highlighted another beneficial aspect of the tool. The real-time decision support is also believed to result in antiinfective doses that are appropriately higher when the clinical indication calls for stronger therapy, such as in the case of meningitis. We were not able to devise a measurement that would document this clinical belief, as the clinician’s suspicions of meningitis were often not recorded in the computer database; however, it potentially accounts for some of the improvement seen in the pharmacists’ rate of interventions on erroneous or otherwise nonoptimal doses.

It is prudent to compare the results of this pediatric trial with the findings from the evaluation performed in the adult STICU of LDS Hospital. As shown in Table 12, in the STICU evaluation, a marked impact was noted in the number of mismatches between the susceptibility patterns of the cultured bacterial
Table 12. Comparison of AMP Impact in Adult and Pediatric Studies

<table>
<thead>
<tr>
<th>Measurement</th>
<th>PICU Impact</th>
<th>STICU Impact</th>
<th>Baseline Rates Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptibility-mismatch alerts</td>
<td>No change</td>
<td>Large reduction</td>
<td>18/100 admissions in STICU versus 0.2/100 admissions in PICU</td>
</tr>
<tr>
<td>Drug allergy alerts</td>
<td>No change</td>
<td>Large reduction</td>
<td>12/100 admissions in STICU versus 0.4/100 admissions</td>
</tr>
<tr>
<td>Excessive days of antinfective dose</td>
<td>Reduction</td>
<td>Reduction</td>
<td></td>
</tr>
<tr>
<td>Adverse drug events due to antiinfectives</td>
<td>No change</td>
<td>Large reduction</td>
<td>2.4/100 admissions in STICU versus 2.4/100 admissions in PICU</td>
</tr>
<tr>
<td>Pharmacists’ interventions</td>
<td>Large Reduction</td>
<td>Not measured</td>
<td></td>
</tr>
<tr>
<td>Antibiotic costs</td>
<td>11% reduction</td>
<td>20% reduction</td>
<td>$412/patient STICU versus $177/patient in PICU</td>
</tr>
<tr>
<td>Length of stay</td>
<td>No change</td>
<td>No change</td>
<td>6.3 days in STICU vs. 4.9 days in PICU</td>
</tr>
<tr>
<td>Mortality</td>
<td>No change</td>
<td>No change</td>
<td>22% in STICU vs. 3.7% in PICU</td>
</tr>
</tbody>
</table>

pathogens and the antibiotics used for therapy. An improvement was not noted in the PICU study. However, a comparison of the baseline rates of mismatch alerts shows that these occur far more frequently in the adult ICU. Thus, the opportunity for improvement in the PICU is relatively diminished. The measure of orders for drugs to which the patient was known to have a history of allergy was improved in the adult study but without change in the pediatric study. Again, these events are noted to occur at a much higher rate at baseline in the adult unit compared to the pediatric unit.

A large impact was noted in the rates of pharmacists’ intervention for erroneous drug orders in the pediatric study. However, this metric was not recorded in the STICU evaluation. In the two studies, a similar benefit was noted in the rate of reduction of
excessive drug dosage days. Additionally, a benefit was seen in under-dosage days in the PICU study but under-dosing is less of an issue in adults and was not measured in that study.

No change was noted in the rate of adverse drug events in the PICU, but a large benefit was found in the adult study. Interestingly, the baseline rate of events per 100 admissions was similar in both units. One might surmise that fewer of the events in children are preventable as they are less likely to be secondary to failing drug metabolism due to hepatic or renal dysfunction. The study data supports this notion, as only one of the 12 pediatric events at baseline could be judged preventable by retrospective evaluation, and none of these events was attributed to failed organs or otherwise poor drug metabolism.

A 20 percent reduction in the costs of antiinfectives used at baseline was found in the adult study, whereas the pediatric drug costs are 11% improved when analyzed with robust statistical techniques. The baseline analysis shows that antiinfective costs averaged $412 (1995 dollars) in the adult study and only $177 (1999 dollars) in the pediatric evaluation. Once again, it should be noted that there was less opportunity for improvement in the pediatric case. Lastly, although the measures of severity of illness used in the two studies are different and are not directly comparable, it is instructive to note the five-fold difference in incidence of death between the two units. The adult patients are far more likely to have terminal disease. One can therefore conclude that the pediatric and adult patients have different disease severity, and adults are likely to have more severe end organ dysfunction which affects their responses to and internal metabolism of the antiinfective therapy used in the study. Therefore, it should not be a
surprise that the impact of the two antiinfective management programs differs between the two units in the process and outcome measures evaluated.

The rate of administration of antiinfectives was approximately 5 percent higher in the intervention group than in the control group. Although the average age of the patients is younger in the intervention group, the patients remain similar in many other important categories such as PICU and total hospital lengths of stay, severity of illness and risk of mortality scores, and rate of total hospital administration of antiinfectives. For these reasons, we believe the populations are similar enough to credit the findings to the implementation of the computerized decision support system.

The last step in the system's antiinfective recommendations algorithm is to consider costs. The AMP recommends the less expensive agent, when two drugs are found to be equally therapeutically effective. We therefore anticipated a cost benefit, as was seen in the adult study. In this pediatric study, the average cost of antiinfectives was no different between the two groups. However, application of Tukey's biweight estimator, which downweights extreme observations in non-normal distributions, identified an 11 percent decrease in the robust estimate of the cost of antiinfectives used in the intervention group. Regression analysis found that the difference in age between the two groups did not account for any significant portion of the change in costs. Given that one of the tool's beneficial effects is to increase the doses administered where clinically indicated, and one of its documented effects is to minimize the number of subtherapeutic risk-days by increasing antibiotic doses, it would not have been surprising if we had found that the average antiinfective cost per patient was higher with the use of the program.
With the improvements in the rate of pharmacy interventions and the number of days outside of therapeutic ranges, one could anticipate a patient benefit in outcomes. Unfortunately, we were not able to document this given the insensitivity of our patient outcome measures: adverse drug events, length of stay, and mortality. However, one can conclude that although the incidence of adverse sequelae from medical errors is low, it is not zero, and minimization of outright errors and improvements in therapeutic dosing targets should impact both adverse events and the quality of care, given enough time. It is through considerations such as these that a majority of pediatric residents and nurse practitioners reported that they believed that the use of this clinical decision support tool should beneficially impact adverse drug events, and the quality of care. This is congruous with the adage that humans and computers working in tandem are better than either one alone.

Lastly, the findings of this study on the population of interest are likely to be the minimum that would be anticipated from wide-scale implementation of this computerized decision support tool throughout the children’s hospital. A significant percent of the antimicrobial therapy measured in this study was ordered without the use of the tool; either by pediatric residents on the floor prior to transfer of the patient to the PICU, or by surgery and surgery subspecialty residents transferring patients from either the floor or the operating room. Therefore, once these groups become users of the system, the doses ordered would also have the benefit of the elimination of calculation errors, plus the careful consideration of the indication, age, weight, and renal function rendered by the antiinfective management program.
Future Directions

Following the completion of this study, use of the pediatric AMP remained mandatory for ordering antiinfectives within the PICU at PCMC. This action was made by a joint decision of the members of the pharmacy, nursing, and medical staffs. The program was also made available for voluntary use by clinicians in the other areas of the children's hospital and was readied for use in additional hospitals within the IHC chain.

While recognizing the success of the current version, further development of the pediatric AMP could, and should, proceed along several lines. The empiric antibiotic recommendations feature, option <5> on the menu, has not been fully developed at PCMC and thus, is not yet available for use. In my opinion, it would be one of the most interesting features of the AMP for attending physicians as it provides a unique window into the patient database of culture results. The view it affords could potentially change common prescribing habits throughout the hospital's various units. See Appendix F for a further discussion of this issue.

Within PCMC, it would be interesting to study the effects of the use of the AMP in the Neonatal Intensive Care Unit. The antibiotic care provided to the neonates could potentially benefit from the automated gestational age considerations and the dosage calculation assistance. The AMP has been devised with the care of neonates in mind and could be implemented in that unit once training of the personnel was accomplished.

Use of the AMP improves the selection of antimicrobial doses through consideration of age, weight, and renal function at the time the agent is ordered. Continued, proactive use of the system allows for close monitoring of changes in renal function and the necessary modifications in drug doses to account for changes in drug
elimination. However, the AMP does not currently have a built-in alerting system that would signal clinicians when drug dosage alterations are indicated. This closure of the loop would potentially bring the benefit of the AMP knowledge base to patients whose physicians were not proactively monitoring renal function changes and making the necessary modifications in pharmaceutical therapy. Development of this type of program could further reduce the rate of subtherapeutic and excessive dosage days noted in this study. The first steps of this type of system have been initiated at LDS Hospital and were recently reported by Evans and colleagues. These authors designed a system to monitor the doses of five commonly used antibiotics and generate an alert to the pharmacist when a change of dose was indicated. Use of the tool reduced the incidence of excessive dosage days from 50 to 44 percent of the patients on one of these five antibiotics and decreased the average number of excessive dosage days from 4.7 to 2.9 days per patient. Additionally, adverse drug events from these antibiotics decreased from an incidence of 0.9 to 0.3 percent. The authors documented a financial savings from a decrease in the average cost of treatment of the patients with the study antibiotics, and one would expect a savings from the reduced need to pay for the therapy of the sequelae of the adverse drug events.

As the IHC Corporation migrates from the HELP system to the next generation hospital information system, provisions should be made to port the AMP as well. This may represent an opportunity to expand some of the core functionality by using current day information system tools to expand the reach of the AMP. For instance, a majority of patient care occurs in the outpatient setting. Development of a web-interface with links to the clinical data repository and to the area pharmacies could enable the AMP to assist
in the selection of cost effective antimicrobials with automated communication to the patient’s pharmacy of choice.

Lastly, the benefit of the AMP is not necessarily limited to the local population of patients treated in IHC’s facilities. Through standardized communication protocols and the use of the Internet, the AMP could provide decision support to clinicians all over the world. One can foresee a day when hospital medical information systems personnel have the opportunity to provide their clinicians with antiinfective and ventilator-management decision support from IHC, and other types of support from other centers with special expertise.

Conclusion

Implementation of a pediatric antiinfective decision support tool positively impacted the therapeutic milieu of a PICU through better dosage selection as documented by fewer pharmacy interventions on antiinfective orders and fewer antiinfective subtherapeutic and excessive-dosage risk-days. These findings are supported by the survey of users who reported that use of the tool would result in fewer adverse drug events and improved quality of care. Clinical decision support tools can beneficially impact patient care and should be further developed to provide support for a greater variety of clinical domains.
APPENDIX A

PEDIATRIC EMPIRIC THERAPY BY INFECTIOUS ILLNESS
## Pediatric Antibiotic Assistant -- Initial Empiric Therapy by Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age</th>
<th>Etiologies</th>
<th>First choice top row, allergy alternatives below</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS/HIV</td>
<td>all</td>
<td></td>
<td>Recommend ID consult</td>
</tr>
<tr>
<td>appendicitis, bowel perforations (nosocomial)</td>
<td>all</td>
<td>enterobacteriaceae</td>
<td>piperacillin/tazobactam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enterococci</td>
<td>meropenem(alone)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bacteroides</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>P. aeruginosa</td>
<td></td>
</tr>
<tr>
<td>appendicitis, bowel perforations (community acquired)</td>
<td>all</td>
<td>enterobacteriaceae</td>
<td>ampicillin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enterococci</td>
<td>gentamicin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bacteroides</td>
<td>clindamycin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P. aeruginosa</td>
<td></td>
</tr>
<tr>
<td>bite, cat or dog</td>
<td>all</td>
<td>Pasteurella multocida</td>
<td>amoxicillin/clavulanic acid (mild cases)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. aureus</td>
<td>ampicillin/sulbactam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>viridans group, streptococci</td>
<td>cefuroxime</td>
</tr>
<tr>
<td>cellulitis</td>
<td>all</td>
<td>group A streptococci</td>
<td>cefuroxime or cefazolin or cephalaxin (mild)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. aureus</td>
<td>clindamycin</td>
</tr>
<tr>
<td>cellulitis in varicella</td>
<td>all</td>
<td>group A streptococci</td>
<td>clindamycin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>cefuroxime or cefazolin or cephalaxin (mild)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>vancomycin</td>
</tr>
<tr>
<td>Condition</td>
<td>Pathogen(s)</td>
<td>Initial Antibiotics</td>
<td>Other Antibiotics</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>------------------------------------</td>
<td>---------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Central line infection</strong></td>
<td><em>S. aureus</em></td>
<td>vancomycin</td>
<td>Gentamicin</td>
</tr>
<tr>
<td></td>
<td><em>S. epidermidis</em></td>
<td>clindamycin</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Enterococcus spp.</em></td>
<td>TMP/SMX</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Enterobacteriaceae</em></td>
<td>Meropenem</td>
<td></td>
</tr>
<tr>
<td><strong>Cholangitis, cholecystitis</strong></td>
<td><em>Enterobacteriaceae</em></td>
<td>Piperacillin/lazobactam</td>
<td>Cefoxitin</td>
</tr>
<tr>
<td></td>
<td><em>Enterococci</em></td>
<td>Cefoxitin</td>
<td>Meropenem</td>
</tr>
<tr>
<td></td>
<td><em>Bacteroides</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Colitis, antibiotic associated</strong></td>
<td><em>Clostridium difficile</em></td>
<td>Metronidazole</td>
<td>Vancomycin PO (requires ID approval)</td>
</tr>
<tr>
<td><strong>Cystic fibrosis</strong></td>
<td><em>Clostridium difficile</em></td>
<td>Metronidazole</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Clostridium difficile</em></td>
<td>Metronidazole</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Vancomycin</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>PO (requires ID approval)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cytomegalovirus infection</strong></td>
<td><em>CMV</em></td>
<td>Ganciclovir</td>
<td></td>
</tr>
<tr>
<td><strong>Endocarditis</strong></td>
<td><em>Viridans group, Streptococci</em></td>
<td>Vancomycin</td>
<td>Gentamicin</td>
</tr>
<tr>
<td></td>
<td><em>S. aureus</em></td>
<td></td>
<td>Nafcillin</td>
</tr>
<tr>
<td></td>
<td><em>Enterococci</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Epiglottitis</strong></td>
<td><em>Group A streptococci</em></td>
<td>Cefuroxime, Cefotaxime or Ceftriaxone</td>
<td>Ampicillin/Sulbactam</td>
</tr>
<tr>
<td></td>
<td><em>H. influenzae</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EVD/VP shunt prophylaxis</strong></td>
<td><em>S. aureus</em></td>
<td>Cefuroxime</td>
<td>Vancomycin</td>
</tr>
<tr>
<td></td>
<td><em>S. epidermidis</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fever and neutropenia</strong></td>
<td><em>Enterobacteriaceae</em></td>
<td>Ceftazidime</td>
<td>Meropenem</td>
</tr>
<tr>
<td></td>
<td><em>S. aureus</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Fungi</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** The table above provides guidance on initial antibiotic selection for various medical conditions. The listed antibiotics are typical initial choices, and specific regimens may vary based on clinical context and patient history. Always consult with a healthcare provider for personalized medical advice.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Age</th>
<th>Pathogens</th>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile neonate</td>
<td>&lt; 2 mo</td>
<td>group B streptococci, <em>Escherichia coli</em>, <em>Listeria monocytogenes</em></td>
<td>ampicillin, gentamicin</td>
</tr>
<tr>
<td>Herpes</td>
<td>all</td>
<td><em>Herpes simplex virus</em></td>
<td>acyclovir</td>
</tr>
<tr>
<td>Liver transplant, post-op</td>
<td>all</td>
<td>prophylaxis</td>
<td>cefuroxime, ganciclovir, nystatin</td>
</tr>
<tr>
<td>Meningitis</td>
<td>&lt; 1 mo</td>
<td>group B streptococci, <em>Escherichia coli</em>, <em>Listeria monocytogenes</em>, <em>Enterococcus spp.</em></td>
<td>ampicillin, gentamicin</td>
</tr>
<tr>
<td>1 - 3 mo</td>
<td></td>
<td><em>S. pneumoniae</em>, group B streptococci, <em>H. influenzae</em>, <em>Neisseria meningitidis</em>, <em>Enterobacteriaceae</em>, <em>Listeria monocytogenes</em></td>
<td>ampicillin, cefotaxime or ceftriaxone, meropenem, aztreonam</td>
</tr>
<tr>
<td>3 mo - &lt; 5 yr</td>
<td></td>
<td><em>S. pneumoniae</em>, <em>Neisseria meningitidis</em>, <em>H. influenzae</em></td>
<td>vancomycin</td>
</tr>
<tr>
<td>5 yr - Adult</td>
<td></td>
<td><em>S. pneumoniae</em>, <em>Neisseria meningitidis</em></td>
<td>vancomycin</td>
</tr>
<tr>
<td>Meningitis/ventriculitis with shunt</td>
<td>all</td>
<td><em>S. epidermidis</em>, <em>S. aureus</em>, <em>Enterobacteriaceae</em>, <em>Propionibacterium acnes</em></td>
<td>vancomycin, cefotaxime or ceftriaxone, gentamicin &amp; aztreonam</td>
</tr>
<tr>
<td>Condition</td>
<td>Age</td>
<td>Organisms</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>---------</td>
<td>-----------------------------------------------</td>
<td>--------------------------------------------------------------------</td>
</tr>
<tr>
<td>Meningococcemia</td>
<td>all</td>
<td><em>N. meningitidis</em></td>
<td>Ceftriaxone&lt;br&gt;Penicillin G&lt;br&gt;TMP/SMX&lt;br&gt;*&lt;/br&gt;&lt;br&gt;Penicillin G</td>
</tr>
<tr>
<td>Necrotizing enterocolitis</td>
<td>all</td>
<td><em>E. coli</em>&lt;br&gt;<em>S. epidermidis</em>&lt;br&gt;<em>P. aeruginosa</em>&lt;br&gt;<em>C. perfringens</em></td>
<td>Ampicillin&lt;br&gt;Vancomycin&lt;br&gt;Meropenem</td>
</tr>
<tr>
<td>Necrotizing fascitis</td>
<td>all</td>
<td>Group A streptococci</td>
<td>Clindamycin&lt;br&gt;Penicillin G</td>
</tr>
<tr>
<td>Omphalitis</td>
<td>all</td>
<td>Group A or B streptococci&lt;br&gt;<em>S. aureus</em>&lt;br&gt;<em>Clostridium</em></td>
<td>Clindamycin&lt;br&gt;Nafcillin</td>
</tr>
<tr>
<td>Orbital cellulitis</td>
<td>all</td>
<td><em>S. pneumoniae</em>&lt;br&gt;<em>H. influenzae</em>&lt;br&gt;<em>S. aureus</em>&lt;br&gt;Anaerobes&lt;br&gt;Group A streptococci</td>
<td>Cefuroxime&lt;br&gt;Ticarcillin/clavulanate&lt;br&gt;Piperacillin/tazobactam&lt;br&gt;Ampicillin/sulbactam&lt;br&gt;Vancomycin &amp; aztreonam</td>
</tr>
<tr>
<td>Osteomyelitis, hematogenous</td>
<td>&lt;4 mo</td>
<td><em>S. aureus</em>&lt;br&gt;Group B streptococci&lt;br&gt;Enterobacteriaceae</td>
<td>Nafcillin&lt;br&gt;Vancomycin&lt;br&gt;Cefotaxime&lt;br&gt;Gentamicin</td>
</tr>
<tr>
<td></td>
<td>&gt;4 mo</td>
<td><em>S. aureus</em>&lt;br&gt;Group A streptococci</td>
<td>Cefuroxime&lt;br&gt;Nafcillin &amp; Gentamicin&lt;br&gt;Clindamycin</td>
</tr>
<tr>
<td>Medical Condition</td>
<td>Age</td>
<td>Pathogens</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>-----------</td>
<td>------------------------------------------------</td>
<td>-------------------------------------------------</td>
</tr>
<tr>
<td>peritonitis, primary</td>
<td>all</td>
<td>enterobacteriaceae, S. pneumoniae, Enterococci</td>
<td>cefotaxime or ceftriaxone, vancomycin &amp; gentamicin</td>
</tr>
<tr>
<td>peritonitis, assoc. with CAPD</td>
<td>all</td>
<td>S. aureus, S. epidermidis, P. aeruginosa, enterobacteriaceae</td>
<td>vancomycin, meropenem(alone), gentamicin, cefazolin</td>
</tr>
<tr>
<td>pertussis</td>
<td>all</td>
<td><em>Bordetella pertussis</em></td>
<td>PO: erythromycin or azithromycin or clarithromycin, TMP/SMX (PO)</td>
</tr>
<tr>
<td>pharyngitis</td>
<td>all</td>
<td>group A, C, G streptococci</td>
<td>Pen V PO, erythromycin PO, cephalaxin PO</td>
</tr>
<tr>
<td>Pneumocystis infections</td>
<td>all</td>
<td><em>P. carinii</em></td>
<td>TMP/SMX, pentamidine, atovaquone</td>
</tr>
<tr>
<td>pneumonia, aspiration</td>
<td>all</td>
<td><em>Bacteroides sp.</em>, <em>Peptostreptococci</em>, <em>Fusobacterium sp.</em></td>
<td>ampicillin/sulbactam, clindamycin</td>
</tr>
<tr>
<td>pneumonia, community acq. (also neonatal RDS &amp; HMD)</td>
<td>&lt; 1 mo</td>
<td>group B streptococci, <em>Escherichia coli</em>, <em>Listeria monocytogenes</em></td>
<td>ampicillin, vancomycin, gentamicin, cefotaxime</td>
</tr>
<tr>
<td></td>
<td>1 mo - 5 yr</td>
<td><em>S. pneumoniae</em>, <em>S. aureus</em></td>
<td>cefuroxime, ceftriaxone or cefotaxime, vancomycin &amp; aztreonam, erythromycin IV, clarithromycin or azithromycin</td>
</tr>
<tr>
<td>Condition</td>
<td>Age Group</td>
<td>Pathogen(s)</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----------</td>
<td>--------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Pneumonia, nosocomial</td>
<td>5 - 10 yr</td>
<td>H. influenzae, C. pneumoniae, Mycoplasma pneumoniae</td>
<td>Cefotaxime or ceftriaxone, vancomycin &amp; aztreonam, erythromycin IV, clarithromycin or azithromycin, doxycycline</td>
</tr>
<tr>
<td></td>
<td>10 yr - Adult</td>
<td>Mycoplasma pneumoniae, S. pneumoniae, C. pneumoniae enterobacteriaceae</td>
<td>Cefotaxime or ceftriaxone, vancomycin &amp; aztreonam, erythromycin IV, PO: doxycycline</td>
</tr>
<tr>
<td></td>
<td>PCA &lt; 44 weeks</td>
<td>Enterobacteriaceae, S. aureus</td>
<td>Piperacillin or ticarcillin, imipenem (alone)</td>
</tr>
<tr>
<td></td>
<td>infants - adults</td>
<td>Enterobacteriaceae, S. aureus</td>
<td>Pip/tazo or ticar/clav, vancomycin &amp; aztreonam, meropenem (alone)</td>
</tr>
<tr>
<td>Pyelonephritis, urosepsis, UTI</td>
<td>all</td>
<td>Enterobacteriaceae, Enterococci</td>
<td>Ampicillin, gentamicin, cefotaxime, ceftriaxone, aztreonam, meropenem</td>
</tr>
<tr>
<td>(community acquired)</td>
<td>all</td>
<td>Enterobacteriaceae, Enterococci</td>
<td>Piperacillin/tazobactam, meropenem (alone)</td>
</tr>
<tr>
<td>Pyelonephritis, urosepsis, UTI</td>
<td>all</td>
<td>Enterobacteriaceae, Enterococci</td>
<td>Gentamicin, aztreonam</td>
</tr>
<tr>
<td>(nosocomial)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Age</td>
<td>Pathogens</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------</td>
<td>------------------------------------</td>
<td>------------------------------------</td>
</tr>
<tr>
<td>Sepsis/septic shock</td>
<td>&lt; 2 mo</td>
<td>Group B streptococci</td>
<td>nafcillin</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. aureus</em></td>
<td>vancomycin</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Escherichia coli</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Klebsiella spp.</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Enterobacter spp.</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>H. influenzae</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 2 mo -</td>
<td><em>S. pneumoniae</em></td>
<td>cefotaxime or ceftriaxone</td>
</tr>
<tr>
<td>Adult</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Neisseria meningitidis</em></td>
<td>vancomycin &amp; aztreonam</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. aureus</em></td>
<td>meropenem</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>H. influenzae</em></td>
<td></td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>&lt; 3 mo</td>
<td><em>S. aureus</em></td>
<td>nafcillin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Group B streptococci</td>
<td>vancomycin and meropenem (alone)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>enterobacteriaceae</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Neisseria gonorrhoeae</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Kingella spp.</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 mo - 14 yr</td>
<td><em>S. aureus</em></td>
<td>cefuroxime</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. pyogenes</em></td>
<td>vancomycin &amp; gentamicin</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. pneumoniae</em></td>
<td>meropenem (alone)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>H. influenzae</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Kingella kingae</em></td>
<td></td>
</tr>
<tr>
<td>Sinusitis, community acq.</td>
<td>all</td>
<td><em>S. pneumoniae</em></td>
<td>amoxicillin</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>H. influenzae</em></td>
<td>cefuroxime</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>M. catarrhalis</em></td>
<td></td>
</tr>
<tr>
<td>Sinusitis, nosocomial</td>
<td>all</td>
<td><em>enterobacteriaceae</em></td>
<td>ampicillin/sulbactam</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>S. aureus</em></td>
<td>meropenem</td>
</tr>
<tr>
<td>Infection Type</td>
<td>Pathogens</td>
<td>Antibiotics</td>
<td></td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>------------------------------------------------</td>
<td>-------------------------------</td>
<td></td>
</tr>
<tr>
<td>tetanus</td>
<td><em>C. tetani</em></td>
<td>Metronidazole</td>
<td></td>
</tr>
<tr>
<td>thoracotomy/sternotomy prophylaxis</td>
<td><em>S. aureus</em>, <em>S. epidermidis</em></td>
<td>Cefuroxime, Vancomycin</td>
<td></td>
</tr>
<tr>
<td>toxic shock syndrome</td>
<td><em>S. aureus</em>, <em>S. aureus</em> group A,B,C,G streptococci</td>
<td>Nafcillin, Vancomycin, Clindamycin</td>
<td></td>
</tr>
<tr>
<td>TSS, streptococcal</td>
<td><em>S. aureus</em>, <em>S. aureus</em> group A,B,C,G streptococci</td>
<td>Clindamycin, Cefuroxime, Vancomycin</td>
<td></td>
</tr>
<tr>
<td>tuberculosis</td>
<td><em>M. tuberculosis</em></td>
<td>Consult ID</td>
<td></td>
</tr>
<tr>
<td>wound infection/laceration</td>
<td><em>S. aureus</em>, <em>S. aureus</em> group A streptococci, Enterobacteriaceae</td>
<td>Cefazolin, Ampicillin/Clavulanic Acid, Clindamycin, Meropenem</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX B

NEONATAL AND PEDIATRIC ANTIINFECTIVE DOSES
Antibiotic Dosing for Pediatrics:

Definitions

**Neonate**: newborn infant less than 45 weeks postconceptional age (estimated gestational age plus age in weeks)

**Infant**: patients greater than 44 weeks postconceptional age and less than 1 year of age

**Child**: patients greater than 1 year and less than 18 years of age

Neonatal doses per tables factoring postconceptional and postnatal ages. Adult doses to be used for pediatric patients greater than 50 kg. Renal function adjustments are performed for pediatric patients greater than age 6 months only.

**Acyclovir (IV)**

**Neonates**

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;= 36</td>
<td>all</td>
<td>10</td>
<td>Q12</td>
</tr>
<tr>
<td>37 to 44</td>
<td>all</td>
<td>10</td>
<td>Q8</td>
</tr>
</tbody>
</table>

**Infants and Children**

- CNS dz & < 2mos
- CNS dz & > 2mos
- Varicella
- Mild – Mod

<table>
<thead>
<tr>
<th>Renal Impairment 106</th>
<th>20 mg/kg IV q8 max: none</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl 25-50</td>
<td>Change interval to q12</td>
</tr>
<tr>
<td>CrCl 10-25</td>
<td>Change to q24</td>
</tr>
<tr>
<td>CrCl &lt;10</td>
<td>Decrease dose by 50%, administer q24</td>
</tr>
</tbody>
</table>

**Acyclovir (oral)**

**Infants and Children**

- Oral

<table>
<thead>
<tr>
<th>Oral Dose Mapping for Age &gt; 7 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calculated dose</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>190 - 299</td>
</tr>
<tr>
<td>300 - 499</td>
</tr>
<tr>
<td>500 - 699</td>
</tr>
<tr>
<td>700 and up</td>
</tr>
</tbody>
</table>
Renal Impairment
CrCl < 10

Amikacin (requires ID approval):

Neonatal

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;= 29</td>
<td>0 to 28</td>
<td>7.5</td>
<td>Q24</td>
</tr>
<tr>
<td>&gt; 29</td>
<td>&gt; 28</td>
<td>10.0</td>
<td>Q24</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>10.0</td>
<td>Q24</td>
</tr>
<tr>
<td>&gt; 14</td>
<td>0 to 14</td>
<td>7.5</td>
<td>Q12</td>
</tr>
<tr>
<td>37 to 44</td>
<td>&gt; 7</td>
<td>7.5</td>
<td>Q8</td>
</tr>
</tbody>
</table>

Infants and Children

<table>
<thead>
<tr>
<th>Age (weeks)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 28</td>
<td>7.5</td>
<td>Q24</td>
</tr>
<tr>
<td>&gt; 28</td>
<td>10.0</td>
<td>Q24</td>
</tr>
<tr>
<td>0 to 14</td>
<td>10.0</td>
<td>Q24</td>
</tr>
<tr>
<td>&gt; 14</td>
<td>7.5</td>
<td>Q12</td>
</tr>
<tr>
<td>0 to 7</td>
<td>7.5</td>
<td>Q8</td>
</tr>
<tr>
<td>&gt; 7</td>
<td>7.5</td>
<td>Q8</td>
</tr>
</tbody>
</table>

Renal Impairment
CrCl < 50

Amoxicillin:

Infants and Children:

| Otitis Media, Sinusitis     | 27mg/kg PO q8   |
| Other                      | 15 mg/kg PO q8  |

max: 500 mg/dose

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 - 174 mg</td>
<td>125 mg</td>
</tr>
<tr>
<td>175 - 299 mg</td>
<td>250 mg</td>
</tr>
<tr>
<td>300 - 399 mg</td>
<td>375 mg</td>
</tr>
<tr>
<td>400 - and up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Renal impairment:
CrCl < 10

increase interval to q24

Amoxicillin/Clavulanate

Neonates and Infants (<3months) 15 mg/kg PO q12
Infants (>3 months) and Children 20 mg(amox)/kg PO q12
max 875 mg/dose
Oral Dose Mapping for age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 - 224 mg</td>
<td>200 mg</td>
</tr>
<tr>
<td>225 - 299 mg</td>
<td>250 mg</td>
</tr>
<tr>
<td>300 - 449 mg</td>
<td>400 mg</td>
</tr>
<tr>
<td>450 - 649 mg</td>
<td>500 mg</td>
</tr>
<tr>
<td>650 &amp; up</td>
<td>875 mg</td>
</tr>
</tbody>
</table>

Renal impairment
- CrCl 10-50
- CrCl <10

increase interval to q24
increase to q48

Amphotericin B

Neonates, Infants and Children:
- Test Dose: 0.1mg/kg IV to max of 1mg
- Usual: 1mg/kg IV qd
- Max: 1.5 mg/kg IV qd

Renal Impairment
- None

Amphotericin B Lipid Complex (requires ID approval):

Infants and Children
- Severe (meningitis): 5.0 mg/kg IV qd max: none
- Mild-Mod: 2.5 mg/kg IV qd

Renal Impairment
- None

Ampicillin

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>100</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>100</td>
<td>q8</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>100</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>100</td>
<td>q8</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>100</td>
<td>q12*</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>100</td>
<td>q8*</td>
</tr>
</tbody>
</table>

*meningitis dosed at q6 hour frequency
Infants and Children

Severe (meningitis)  
100 mg/kg IV q6  
max: 12 g/day

Mild-Mod  
50 mg/kg IV q6

Appy/bowel infection > 50 kg  
2 g IV q6h

Renal Impairment:

CrCl <30:  
Change interval to q12

Ampicillin/Sulbactam

Children (1 year and up)

Meningitis  
100 mg amp/kg IV q6h  
max: 8 g amp/day

Other  
50 mg amp/kg IV q6h

Renal Impairment

CrCl 15-29  
administer q 12h

CrCl 5-14  
administer q 24h

Azithromycin

Intravenous:  
12 mg/kg IV q day  
max: 500 mg/dose

Otitis Media

day 1  
10 mg/kg PO x 1  
max 500 mg/dose

day 2-5  
5 mg/kg PO x 1  
max 250 mg/dose

Pharyngitis/Tonsillitis

day 1-5  
12 mg/kg PO qd  
max 500 mg/dose

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>201 - 300 mg</td>
<td>250 mg</td>
</tr>
<tr>
<td>301 - 400 mg</td>
<td>375 mg</td>
</tr>
<tr>
<td>401 &amp; up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Aztreonam

Infants (> 1 mo) and children

Severe and/or Pseudomonas  
50 mg/kg IV q6  
max: 2.5 g/dose

Mild-Mod  
30 mg/kg IV q8
Renal Impairment:
CrCl 10-30
CrCl <10
decrease dose by 50%
decrease dose by 75%

Cefaclor:
Infants (> 1 mo) and Children:
Otitis media & pharyngitis
Other
20 mg/kg PO q 12h max: 2 g/day
10 mg/kg PO q 8h

Oral Dose Mapping for Age > 7 years
<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>201 - 400</td>
<td>250 mg</td>
</tr>
<tr>
<td>401 &amp; up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Renal Impairment
CrCl < 10
administer 50% of dose

Cefazolin:
Infants and Children
All
Renal Impairment
CrCl 10-30
CrCl <10
33 mg/kg IV q 8h max 12 g/day
Change Interval to q 12h
Change to q 24

Cefixime:
Children (1 year and up)
All
8 mg/kg PO q day max: 400 mg/day

Oral Dose Mapping for Age > 7 years
<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 - 149</td>
<td>100 mg</td>
</tr>
<tr>
<td>150 - 249</td>
<td>200 mg</td>
</tr>
<tr>
<td>250 - 349</td>
<td>300 mg</td>
</tr>
<tr>
<td>350 &amp; up</td>
<td>400 mg</td>
</tr>
</tbody>
</table>

Renal Impairment:
CrCl 21-60
CrCl < 20
administer 75% of standard dose
administer 50% of standard dose
Cefpodoxime:

Infants (> 6 mos) and Children:
- Uncomplicated gonorrhea: 200 mg PO x 1
- All Other: 5 mg/kg PO q 12h max: 800 mg/day

Renal Impairment:
- CrCl < 30: administer q 24h

Cefprozil:

Infants (> 6mo) & Children
- Pharyngitis/tonsillitis: 7.5 mg/kg PO q 12h max: 1 g/day
- Other: 15 mg/kg PO q 12h

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 - 149</td>
<td>125 mg</td>
</tr>
<tr>
<td>150 - 299</td>
<td>250 mg</td>
</tr>
<tr>
<td>300 - 399</td>
<td>375 mg</td>
</tr>
<tr>
<td>400 &amp; up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Renal Impairment
- CrCl < 30: Reduce dose by 50%

Cefotaxime:

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (davs)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>50</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>50</td>
<td>q8</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>50</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>50</td>
<td>q8</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>50</td>
<td>12*</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>50</td>
<td>q8*</td>
</tr>
</tbody>
</table>

*meningitis dosed at q6 hour frequency

Infants and Children
- Meningitis, resistant pneumococcus: 75 mg/kg IV q 6h max: 12g/day
- Mild-Mod: 50 mg/kg IV q 6h

Renal Impairment:
- CrCl < 20: decrease dose by 50 %
Cefoxitin

Infants and Children
Prophylaxis
50 mg/kg IV q 8h

Renal Impairment:
CrCl 30-50
change interval to q 12h
CrCl 10-30
change to q 24h
CrCl <10
change to q 48h

Ceftazidime:

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>50</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>50</td>
<td>q8</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>50</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>50</td>
<td>q8</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>50</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>50</td>
<td>q8</td>
</tr>
</tbody>
</table>

Infants and Children
Cystic Fibrosis
100 mg/kg IV q 8h
max: 12g/day
Severe (meningitis)
75 mg/kg IV q 8h
Mild-Mod
50 mg/kg IV q 8h

Renal Impairment:
CrCl 30-50
Change interval to q 12h
CrCl 10-30
Change to q 24h
CrCl <10
Change to q 48h

Ceftriaxone:

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>75</td>
<td>q24</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>75</td>
<td>q12</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>75</td>
<td>q24</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>75</td>
<td>q12</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>75</td>
<td>q24</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>75</td>
<td>q12</td>
</tr>
</tbody>
</table>
Infants and Children
Meningitis, resistant pneumococcus 50 mg/kg q 12 max: 4 g/day
Mild-Mod 75 mg/kg q 24
Renal Impairment:
No change necessary

Cefuroxime:

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>37 to 44</td>
<td>All</td>
<td>50</td>
<td>q12</td>
</tr>
</tbody>
</table>

Infants and Children
Pneumonia, resistant pneumococcus 75 mg/kg IV q 8h max: 4.5 g/day
Neurosurgery prophylaxis 70 mg/kg IV q8h
Mild-mod 50 mg/kg IV q 8h
Cardiothoracic prophylaxis 50 mg/kg IV q 8h

Renal Impairment
CrCl 10-20
CrCl <10
Change interval to q 12h
Change to q 24h

Cefuroxime axetil:

Infants and Children
All 15 mg/kg PO q12 max 500 mg/dose

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 - 187</td>
<td>125 mg</td>
</tr>
<tr>
<td>188 - 299</td>
<td>250 mg</td>
</tr>
<tr>
<td>300 - 399</td>
<td>375 mg</td>
</tr>
<tr>
<td>400 &amp; up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Renal Impairment
CrCl <10 Change to q 24h
Cephalexin:

Infants and Children:

Severe (osteo, septic arthritis) 25 mg/kg PO q6 max 1g/dose
Mild-Mod 12.5 mg/kg PO q6

Renal Impairment

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Oral Dose Mapping for Age &gt; 7 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-40</td>
<td>Calculated Dose</td>
</tr>
<tr>
<td>200 - 349</td>
<td>250 mg</td>
</tr>
<tr>
<td>350 - 599</td>
<td>500 mg</td>
</tr>
<tr>
<td>600 - 799</td>
<td>750 mg</td>
</tr>
<tr>
<td>800 - 1000</td>
<td>1000 mg</td>
</tr>
</tbody>
</table>

increase interval to q12

Ciprofloxacin (when recommended by ID service):

Children (1 year and up)

Cystic Fibrosis

IV: 10 mg/kg q8h max: 1.2 g/day
PO: 20 mg/kg q 12h max: 2 g/day

Other

IV: 10 mg/kg q 12h max: 0.8 g/day
PO: 15 mg/kg q 12h max: 1.5 g/day

Renal Impairment

<table>
<thead>
<tr>
<th>CrCl</th>
<th>Oral Dose Mapping for Age &gt; 7 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30</td>
<td>Calculated Dose</td>
</tr>
<tr>
<td>200 - 299</td>
<td>250 mg</td>
</tr>
<tr>
<td>300 - 399</td>
<td>375 mg</td>
</tr>
<tr>
<td>400 - 624</td>
<td>500 mg</td>
</tr>
<tr>
<td>625 &amp; up</td>
<td>750 mg</td>
</tr>
</tbody>
</table>

administer q 24h
Clarithromycin

Infants and Children

All

7.5 mg/kg PO q12  max 500 mg/dose

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 to 399</td>
<td>250 mg</td>
</tr>
<tr>
<td>400 &amp; up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Renal Impairment

CrCl<30

administer 50% of dose

Clindamycin

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>5.0</td>
<td>Q8</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>5.0</td>
<td>Q6</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>5.0</td>
<td>Q8</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>5.0</td>
<td>Q6</td>
</tr>
<tr>
<td>37 to 44</td>
<td>All</td>
<td>10.0</td>
<td>Q6</td>
</tr>
</tbody>
</table>

Infants and Children

Pneumonia, sinusitis, toxic shock syndrome, varicella associated cellulitis:

10 mg/kg IV q 6h max: 4.8 g/day

Other

7.5 mg/kg IV q 6h

Oral

10 mg/kg PO q 8h max: 1.8 g/day

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>125 - 224 mg</td>
<td>150 mg</td>
</tr>
<tr>
<td>225 to 349 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>350 &amp; up</td>
<td>450 mg</td>
</tr>
</tbody>
</table>

Renal Impairment

No change necessary
Dicloxacillin

Infants and Children
- Osteo, septic arthritis
- Other

25 mg/kg PO q6  max 500 mg/dose
6 mg/kg PO q6

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 - 299</td>
<td>250 mg</td>
</tr>
<tr>
<td>300 &amp; up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Renal Impairment:
No changes necessary

Doxycycline:

Children (>= 8 years)
- All

4 mg/kg IV/PO qd  max: 200 mg/day

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated dose</th>
<th>Suggested dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 - 74 mg</td>
<td>50 mg</td>
</tr>
<tr>
<td>75 - 124 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>125 - 174 mg</td>
<td>150 mg</td>
</tr>
<tr>
<td>175 &amp; up</td>
<td>200 mg</td>
</tr>
</tbody>
</table>

Renal Impairment:
No changes necessary

Erythromycin Lactobionate

Infants and Children:
- All

10 mg/kg IV q6  max 1g/dose

Renal Impairment:
CrCl <10
decrease dose by 50%
**Erythromycin Ethylsuccinate**

Neonates:

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>All</td>
<td>10</td>
<td>q6</td>
</tr>
</tbody>
</table>

Infants and Children:

| All | 10 mg/kg PO q6 | max 1 g/dose |

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>350 to 599 mg</td>
<td>400 mg</td>
</tr>
<tr>
<td>600 &amp; up</td>
<td>800 mg</td>
</tr>
</tbody>
</table>

Renal impairment

| CrCl < 10 | administer 50% of dose |

**Erythromycin Estolate**

Neonates:

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>All</td>
<td>12.5</td>
<td>q8</td>
</tr>
</tbody>
</table>

Infants and Children:

| Pertussis | 12.5 mg/kg PO q6 | max 500 mg/dose |

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>201 - 300</td>
<td>250 mg</td>
</tr>
<tr>
<td>301 - 399</td>
<td>375 mg</td>
</tr>
<tr>
<td>400 &amp; up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Renal impairment

| CrCl < 10 | administer 50% of dose and lengthen interval to q12 |
Erythromycin/Sulfisoxazole:

Infants (> 2mo) and Children  
All  
15 mg erythromycin/kg PO q8h max: 2g/day  
Renal Impairment:  
CrCl < 10 administer 50% of dose q12h

Fluconazole

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>6.0</td>
<td>q72</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>6.0</td>
<td>q48</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>6.0</td>
<td>q48</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>6.0</td>
<td>q24</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>6.0</td>
<td>q48</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>6.0</td>
<td>q24</td>
</tr>
</tbody>
</table>

Infants and Children:  
Systemic/invasive disease  
Mucocutaneous dz (candidiasis)  
12 mg/kg IV qd max 600 mg/day  
6 mg/kg PO qd

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 - 74</td>
<td>50 mg</td>
</tr>
<tr>
<td>75 - 124</td>
<td>100 mg</td>
</tr>
<tr>
<td>125 - 174</td>
<td>150 mg</td>
</tr>
<tr>
<td>175 - 224</td>
<td>200 mg</td>
</tr>
<tr>
<td>225 - 274</td>
<td>250 mg</td>
</tr>
<tr>
<td>274 - 349</td>
<td>300 mg</td>
</tr>
<tr>
<td>350 &amp; up</td>
<td>400 mg</td>
</tr>
</tbody>
</table>

Renal impairment  
CrCl 20-50 administer 50% of dose  
CrCl < 20 administer 25% of dose

Ganciclovir

Children (1 year and up)  
All  
5 mg/kg IV q12h max: none
Renal Impairment

| CrCl 50-79 | administer 2.5 mg/kg IV q 12h |
| CrCl 25-49 | administer 2.5 mg/kg IV q 24h |
| CrCl < 25  | administer 1.25 mg/kg IV q 24h |

Gentamicin

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>2.5</td>
<td>q24</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>3.0</td>
<td>q24</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>3.0</td>
<td>q24</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>2.5</td>
<td>q12</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>2.5</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>2.5</td>
<td>q8</td>
</tr>
</tbody>
</table>

Infants and Children

All 7.5 mg/kg IV q 24h

Renal Impairment

CrCl < 60 Dose once at 2.5 mg/kg & check levels

Imipenem/Cilastatin (requires ID approval)

Neonates (per Pediatric Dosage Handbook106):

<table>
<thead>
<tr>
<th>Age (weeks)</th>
<th>Weight (grams)</th>
<th>Dose (mg/kg/dose)</th>
<th>Frequency (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>&lt;1200</td>
<td>20</td>
<td>Q18</td>
</tr>
<tr>
<td>&lt; 1</td>
<td>&gt;=1200</td>
<td>20</td>
<td>Q12</td>
</tr>
<tr>
<td>&gt;= 1</td>
<td>1200 to 2000</td>
<td>20</td>
<td>Q12</td>
</tr>
<tr>
<td>&gt;= 1</td>
<td>&gt; 2000</td>
<td>20</td>
<td>Q8</td>
</tr>
</tbody>
</table>

Infants and Children

All 15 mg/kg IV q6h max: 2 g/day

Renal Impairment

CrCl 30-70 decrease dose by 50%
CrCl 20-30 decrease dose by 63% & decrease frequency to q8h
CrCl <20 decrease dose by 75% & decrease frequency to q12
Loracarbef:

Infants and Children
Otitis media: 15 mg/kg PO q12h max: 800 mg/day

Other:
Renal Impairment:
CrCl 10-49: 7.5 mg/kg PO q12h
CrCl <10: 50% dose at same interval
usual dose q 3 days

Meropenem (requires ID approval):

Infants (>3 months) and Children:
Meningitis 40 mg/kg IV q 8h max: 6 g/day
Usual 20 mg/kg IV q 8h

Renal Impairment
CrCl 26-50 decrease frequency to q 12h
decrease dose by 50%; frequency to q 12h
decrease dose by 500/0; frequency to q 24h
CrCl 10-25
CrCl <10

Metronidazole

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>7.5</td>
<td>q48</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>7.5</td>
<td>q24</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>7.5</td>
<td>q24</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>7.5</td>
<td>q12</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>7.5</td>
<td>q24</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>7.5</td>
<td>q12</td>
</tr>
</tbody>
</table>

Infants and Children
Anaerobic infections 7.5 mg/kg IV/PO q 6h max: 4 g/day
C. difficile colitis 10 mg/kg IV/PO q 8h

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated dose</th>
<th>Suggested dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 - 299</td>
<td>250 mg</td>
</tr>
<tr>
<td>300 - 399</td>
<td>375 mg</td>
</tr>
<tr>
<td>400 - 599</td>
<td>500 mg</td>
</tr>
<tr>
<td>600 &amp; up</td>
<td>750 mg</td>
</tr>
</tbody>
</table>
Renal Impairment:
No change necessary (dosage decreased 50-67% in hepatic impairment)

Nafcillin:

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>50</td>
<td>Q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>50</td>
<td>Q8</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>50</td>
<td>Q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>50</td>
<td>Q8</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>50</td>
<td>Q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>50</td>
<td>Q8</td>
</tr>
</tbody>
</table>

Infants and Children
All
50 mg/kg IV q 6h
max: 12 g/day

Renal Impairment:
For combined severe renal and hepatic impairment decrease dose by 50%.

Penicillin G

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (units/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>100,000</td>
<td>Q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>100,000</td>
<td>Q8</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>100,000</td>
<td>Q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>100,000</td>
<td>Q8</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>100,000</td>
<td>Q12*</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td></td>
<td>Q8*</td>
</tr>
</tbody>
</table>

*meningitis dosed at q6 hour frequency

Infants and children
Meningitis, pneumonia
100,000u/kg IV q6h
max: 24 million u/day
Other
50,000 u/kg IV q6h

Renal Impairment:
CrCl 10-30: Change interval to q 8
CrCl <10: Change interval to q12
Penicillin V

Infants and Children

Septic arthritis, osteo 37.5 mg/kg PO q6h max 500 mg/dose
Mild-mod 12.5 mg/kg PO q6h

Pneumococcal prophylaxis in asplenia:
125 mg PO BID age < 5 years
250 mg PO BID age >= 5 years

Secondary rheumatic fever prophylaxis:
250 mg PO BID

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>201 - 300</td>
<td>250 mg</td>
</tr>
<tr>
<td>301 - 400</td>
<td>375 mg</td>
</tr>
<tr>
<td>401 &amp; up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Renal Impairment
No changes necessary

Piperacillin:

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>100</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>100</td>
<td>q8</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>100</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>100</td>
<td>q8</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>100</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>100</td>
<td>q8</td>
</tr>
</tbody>
</table>

Infants and Children

Cystic Fibrosis 100 mg/kg IV q 6h max: 24 g/day
Other 75 mg/kg IV q 6h

Renal Impairment:

CrCl 20-40 Change interval to q 8h
CrCl <20 Change to q 12h
Piperacillin/Tazobactam

Neonates:

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>50</td>
<td>Q8</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>80</td>
<td>Q8</td>
</tr>
</tbody>
</table>

Infants (< 6 mos )
- Cystic fibrosis: 100 mg pip/kg IV q 8h
- Other: 80 mg pip/kg IV q 8h

Infants (>6 mos) and Children
- Cystic fibrosis: 100 mg pip/kg IV q 6h
- Other: 80 mg pip/kg IV q 8h max 4g pip /dose

Renal Impairment:
- CrCl <40 decrease dose by 30%

Tetracycline

Children greater than 8 years old
- all: 12.5 mg/kg PO q6h max: 3 g/day

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 - 349</td>
<td>250 mg</td>
</tr>
<tr>
<td>350 &amp; up</td>
<td>500 mg</td>
</tr>
</tbody>
</table>

Renal Impairment
- no adjustment necessary

Ticarcillin:

Neonatal Dose

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>Weight (grams)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;= 7 days</td>
<td>&lt;= 2000</td>
<td>75</td>
<td>Q12</td>
</tr>
<tr>
<td>&lt;= 7 days</td>
<td>&gt; 2000</td>
<td>75</td>
<td>Q8</td>
</tr>
<tr>
<td>&gt; 7 days</td>
<td>&lt; 1200</td>
<td>75</td>
<td>Q12</td>
</tr>
<tr>
<td>&gt; 7 days</td>
<td>1200 to 2000</td>
<td>75</td>
<td>Q8</td>
</tr>
<tr>
<td>&gt; 7 days</td>
<td>&gt; 2000</td>
<td>100</td>
<td>Q8</td>
</tr>
</tbody>
</table>
### Ticarcillin/Clavulanate

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Frequency</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infants and Children</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>75 mg/kg IV q 6h</td>
<td>max: 24 g/day</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>50 mg/kg IV q 6h</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Renal Impairment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl 10-30</td>
<td>change interval to q 8h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl &lt;10</td>
<td>change to q 12h</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tenn Neonates (PCA &gt;= 37 weeks) and Infants &lt; 3 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual</td>
<td>100 mg/kg IV q 8h</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Infants (&gt; 3 mos.) and Children</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>100 mg/kg IV q 6h</td>
<td>max: 24 g/day</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>75 mg ticarcillin/kg IV q 6h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild-Mod</td>
<td>50 mg ticarcillin/kg IV q 6h</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Renal Impairment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl 10-30</td>
<td>decrease frequency to q 8h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl &lt;10</td>
<td>decrease to q 12h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl &lt;10 and hepatic impairment</td>
<td>decrease to q 24h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Tobramycin

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Frequency</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infants and Children</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>3.5 mg/kg IV q 8h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7.5 mg/kg IV q day</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Renal Impairment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CrCl &lt;60</td>
<td>dose once at 2.5 mg/kg and check levels</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Trimethoprim-Sulfamethoxazole

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose</th>
<th>Frequency</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infants and Children</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe (PCP)</td>
<td>5 mg/kg IV q6</td>
<td>max: none</td>
<td></td>
</tr>
<tr>
<td>Severe oral (PCP)</td>
<td>5 mg/kg PO q 6h</td>
<td>max 160 g/dose</td>
<td></td>
</tr>
<tr>
<td>Mild-mod</td>
<td>5 mg/kg PO q12</td>
<td>max 160 mg/dose</td>
<td></td>
</tr>
</tbody>
</table>
Renal Impairment
CrCl < 30

Vancomycin

Neonates

<table>
<thead>
<tr>
<th>Postconceptional Age (weeks)</th>
<th>Postnatal Age (days)</th>
<th>Dose (mg/kg/dose)</th>
<th>Interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0 to 28</td>
<td>20</td>
<td>q24</td>
</tr>
<tr>
<td></td>
<td>&gt; 28</td>
<td>20</td>
<td>q24</td>
</tr>
<tr>
<td>30 to 36</td>
<td>0 to 14</td>
<td>20</td>
<td>q12</td>
</tr>
<tr>
<td></td>
<td>&gt; 14</td>
<td>20</td>
<td>q12</td>
</tr>
<tr>
<td>37 to 44</td>
<td>0 to 7</td>
<td>15</td>
<td>q8</td>
</tr>
<tr>
<td></td>
<td>&gt; 7</td>
<td>15</td>
<td>q8</td>
</tr>
</tbody>
</table>

Infants and Children

Meningitis                   15 mg/kg q 6h                    max: 3 g/day
CNS shunt infections         20 mg/kg q 8h                    
Other                        15 mg/kg q 8h                    
C. difficile colitis          10 mg/kg PO q 6h                   max: 2 g/day

Renal Impairment (IV dosing only):

CrCl 46-70                   change interval to q 12h
CrCl 30-45                   change to q 18h
CrCl 15-29                   change to q 24h
CrCl <15                     dose once, follow serum levels

Oral Dose Mapping for Age > 7 years

<table>
<thead>
<tr>
<th>Calculated Dose</th>
<th>Suggested Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>61 - 109</td>
<td>80 mg</td>
</tr>
<tr>
<td>110 &amp; up</td>
<td>160 mg</td>
</tr>
</tbody>
</table>

administer 50% of dose
APPENDIX C

WEB-BASED ANTIBIOTIC ASSISTANT TUTORIAL
Author's Note: Following the completion of the clinical impact study, a web-based tutorial was designed and developed by the author to replace personal developer-to-user training sessions with self-training and/or guided peer-to-peer teaching. This tutorial is reproduced here, and can also be viewed on the PCMC Intranet: http://ihcweb.co.ihc.com/pcmc/electroniclib/antibiotics/index.html

Antibiotic Assistant Tutorial

The Antibiotic Assistant is an infectious disease management tool that was developed at LDS Hospital and found to be associated with an improved quality of care while simultaneously controlling costs. As a medical informatics project at Primary Children's Medical Center, the Antibiotic Assistant was modified for pediatrics and imported into the patient-care environment. Testing in the PICU revealed the tool to be safe and effective and associated with a nearly 50 percent decrease in the number of pharmacists' interventions on erroneous doses, and a 36 percent decrease in the number of subtherapeutic or excessive dosage risk-days.

The following pages are a tutorial in the use of the pediatric version of the Antibiotic Assistant.

Outline:
Introduction (this page)
Getting an ID and Password
Antibiotic Assistant's Main Screen
Ordering Antibiotics
Other Useful Features
Comments, Suggestions? Send an email: chuck.mullett@hsc.utah.edu.
Getting a User ID and Password

In order to use the Antibiotic Assistant, all clinicians must obtain a user ID and password. This can be accomplished by visiting the Information Systems department in the Northeast corner of the fourth floor of the hospital. Blank ID and password request sheets are hanging on the wall outside of the main office. Necessary information includes your name, social security number (for electronic signature), and supervisor. You must also sign the confidentiality agreement and have your supervisor (Residency director or chief resident) sign as well.

In general, pediatric residents have already been assigned IDs and passwords. To test yours, double-click on the "Tandem" icon and enter your social security number in the "Logon ID" spot and press enter. If the cursor jumps to the password space, you have been recognized. You must now remember and enter your password.

If you get an error message at the ID entry spot, or if you've forgotten your password, call the information system's help line at x-5678 and find out what you need to do to be successful at the login. For some of you, your password may need to be reactivated, for others, you may need to troop upstairs to fill out the request form. Once you've been successful at logging on, you're ready to try the Antibiotic Assistant.

Running the Antibiotic Assistant
Back to Introduction
Running the Antibiotic Assistant

Once you've logged on, the first screen that you come to is the "doctor's list" of patients. This page will be largely blank if you have never logged on before, or if you don't keep a running list of patients. To get to the "program menu" where the Antibiotic Assistant is located, press "shift" and "F6" simultaneously. These directions are also listed at the bottom of the screen. Start the Antibiotic Assistant by selecting from the list and entering the number at the prompt. Next, the Antibiotic Assistant will ask for a patient, choose one that is currently in the hospital by typing their last name or room number. Then press "enter" once to enter the information, and again to confirm.

The next screen (below) asks if the patient has had recent surgery. You can enter such information by choosing from the general list of surgical classifications (clean, clean-contaminated, dirty, etc). If your patient has not had recent surgery, you just press "enter" to get to the main screen.

The subsequent screen is the main screen of the Antibiotic Assistant:
The first line displays patient information from the hospital's database including name, hospital number, age, gender, and admission diagnosis. The second line shows the maximum white blood cell count today (compared to yesterday's max), the admission date and time, and the maximum 24hr temperature, if known. The third line displays the estimated renal function based on the Schwartz formula (1) which uses the maximum 24hr serum creatinine, and the patient's age, gender, and height. This estimation is used to adjust the recommended doses of the antibiotics where appropriate. As the Schwartz formula is less accurate for infants less than six months of age, an asterisk will indicate that the suggested doses have not been adjusted. If a timed urine specimen has been sent for actual creatinine clearance measurement, this will be automatically calculated and will override the Schwartz formula estimation. The most recent weight is displayed on the far end of the third line. Next, the antibiotic allergies are displayed, followed by the current antibiotics being administered in the hospital. The Antibiotic Assistant reviews the patient's microbiology data, and pulls out identified pathogens and makes recommendations based on (in order) the published sensitivities for this isolate, historical sensitivities for this pathogen when the current sensitivities are pending, and then lastly, simple, conservative rule sets when none of the above are available (i.e.: vancomycin for gram positive cocci in the blood when the identification and sensitivities are pending). The patient in the current example has grown Enterococcus faecium and coagulase negative staphylococci from the blood and the therapeutic recommendation is vancomycin and gentamicin at the doses indicated.

Next: Ordering Antibiotics
Back to Introduction

Reference:
Ordering Antibiotics

The Antibiotic Assistant can be quite helpful to the clinician who is considering initiating new antimicrobial therapy because it will alert the physician to potential allergic contraindications and drug-drug interactions while also suggesting recommended doses based on the provided indication, age, weight and renal function. For these reasons, use of the Antibiotic Assistant remains mandatory for ordering antibiotics in the PICU where the average patient is on many medications and is often on multiple antibiotics.

The directions for ordering antibiotics are in white at the bottom of the screen. To order the suggested agents at the recommended doses, press "*" on the keyboard and hit enter. The Assistant will then walk you through the remainder of the ordering steps. To order other antibiotics, press enter.

Next: Ordering Antibiotics II
Back to Introduction
After pressing 'enter' at the main screen, the next screen shows a list of the 43 antibiotics commonly ordered throughout the IHC chain of hospitals. After typing in the number of the desired antibiotic, you may see warnings of allergic contraindications or potential drug-drug interactions such as these:

Patient has a reported allergy/cross-reactivity to Ampicillin
Enter "*" to order this antibiotic, press <enter> to select another.

Erythromycin may increase carbamazepine levels.
Enter "*" to order this antibiotic, press <enter> to select another.

Pressing enter allows you to select another antibiotic. To override the warning, press '*' and proceed. You will then see a box asking for the desired drug route, followed by a screen regarding the therapeutic indication. The following screen appears in the ampicillin ordering pathway:
The Antibiotic Assistant has two doses for ampicillin, "routine" and "meningitis." To get the meningitis dose, type '1' and press enter. For the routine dose, you can just press enter, as it is the default option. Here you see the result:

If you agree that this is a good dose, press '*' and enter. If you would like to modify the amount, press enter and you will be given the option of typing in a new quantity. After finalizing the dose, you are sent back to the screen listing the 43 different antibiotics in case you want to order another. If so repeat the above steps.

Once you have selected all of the antibiotics that the patient needs, you merely press enter at the list of 43 antibiotics. It will then ask you for your Social Security Number as an electronic signature:

For confidentiality, the SSN does not appear as you type. Press enter then review the order:

If this is as you intend it, press '*' to confirm and print the order. If this is erroneous, press enter and start again.

Next: Completing the Order
Back to Introduction
Completing the Order

Once the order has been accepted and an '*' entered, a note appears stating that the order has been printed at the nearest printer:

These three sheets show the ordering information, and one is labeled at the top as "pharmacy copy", one as "chart copy", and one as "nurse copy".

02/10/00. 16:36 Antibiotic Order Pharmacy Copy

Train, Test NMI 30031371 N903 I 06/23/97 51 lly

Ampicillin 1700mg IV q6h (meningitis dose)

Ordered by: MULLETT, CHARLES J. M.D.
   (Electronic Signature)

The pharmacy copy is placed in the pharmacy box located at each nursing station. The pharmacist will pick this copy up per the usual routine. Stat orders should also be phoned to the pharmacist. Each nursing station has a three-hole punch, and this should be used on the "chart copy" prior to placing it in the chart in the "Orders" section. Additionally, the order should be flagged per the usual routine - in the ICU all orders should be communicated directly to the patient's nurse, on the floor the chart should be placed in the Orders rack. The "nurse copy" may be given to the nurse or placed in the local
recycle bin. This third copy of the order is somewhat redundant at Primary Children's Medical Center.

To reiterate, the antibiotic is not ordered until a copy has been placed in the pharmacy box, and a copy has been placed in the chart! Do not forget.
Other Useful Features

Note the options available at the bottom of the screen in green:

<1> Micro: this takes you to the patient's microbiology results using the usual lab lookup screen.
<2> OrganismSuscept: The PCMC bacterial sensitivities can be viewed through this option, with the results sorted by patient location if wished. Example.
<3> Drug Info: Here you can find monographs on the 43 antibiotics ordered through the Antibiotic Assistant. Useful information includes the recommended doses for neonatal and pediatric patients, the dose adjustments for impaired renal function, administration details, costs, pharmacokinetics, and adverse reactions. Example.
<4> ExplainLogic: The logic that founded the Antibiotic Assistant's current recommendations are viewable through this option. When making a recommendation, the assistant takes into account the admitting diagnosis, the dictated chest radiograph reports, the microbiology results, and any recent surgeries. Example.
<5> Empiric Abx: This option is disabled at PCMC.
<6> Abx Hx: The patient's antibiotic history during this hospitalization can be quickly viewed through this option.
<7> ID Rnds: Lists the patient's positive blood cultures, their maximum temperature, maximum WBC count, maximum serum creatinine, and antibiotic therapy by day over the duration requested by the user. A very nice feature.
<8> Lab/Abx Levels: This option connects the user to the patient's lab results using the usual HELP system screens.
<9> XRay: Connects you to the radiology results HELP screens. Interest is often triggered by a pneumonia therapy recommendation triggered by the Antibiotic Assistant's discovery of an infiltrate/opacity/pneumonia in the radiology reports.
<10> Data Input Screen: This option can be used to change or add information that the Antibiotic Assistant uses to make recommendations. Useful features include the ability to change the admission diagnosis as new information arises (changes only in the Antibiotic Assistant), or to add a serum creatinine value obtained at an outside institution.

This completes the Antibiotic Assistant tutorial! Good luck in your pediatric endeavors. Questions, comments, and suggestions can be emailed to Scott Evans (ldsevans@ihc.com). Live support can be obtained by calling x-5678.

Back to Introduction
Online Antibiograms

The Primary Children's Medical Center bacterial susceptibility patterns are viewable through option 2 of the Antibiotic Assistant. The first screen asks you to select a pathogen by typing a number:

Selecting a pathogen by typing in its number brings you to the following screen. Here you may decide to see the sensitivities from specimens sent from the whole hospital, or just one unit within the hospital.

We'll choose option '2' and then choose the PICU from the following screen:

This brings us to the actual susceptibilities. Here, the antibiogram for the *Psuedomonas aeruginosa* specimens sent from the PICU over the last 5 years is shown. Note that these are listed in descending order of susceptibility, and that the cost to the hospital for the typical daily dose for this patient is also shown.
On your own, with the live version of the Antibiotic Assistant, compare the susceptibility to ceftazidime and gentamicin of *Pseudomonas aeruginosa* in the PICU, to those specimens sent from the Med-Surg floor where the cystic fibrosis patients are housed. There's quite a difference!

Just a note. The costs displayed for tobramycin, amikacin, gentamicin, and vancomycin all have the cost for two drug levels over a ten-day course added.

![Antibiotic Susceptibility Table](image)

The antibiotic costs are the exact cost to the hospital and are calculated from the recommended dosage based on the patient's renal function. The cost of laboratory tests to monitor the drug levels are included.

Enter number of specific antibiotic to go directly to monograph, or Hit only the 'Enter' key to return to previous menu...  

**Back to Useful Features**  
**Back to Introduction**
Antibiotic Monographs

Below are screenshots of the monograph for vancomycin. Information is displayed regarding the recommended pediatric and neonatal doses, administration details, costs, surgical and other prophylaxis comments, pharmacokinetics, impaired renal function dosage adjustments, therapeutic serum concentrations, and adverse reactions.

Note item 6: Neonate dose. When making a dose and interval recommendation for neonates, the Antibiotic Assistant considers the patient's postconceptional age (PCA = estimated gestational age at birth + age in weeks since birth) and postnatal age (PNA = age in days since birth). As a user, you may be asked to enter the estimated gestational age at birth if it hasn't been entered yet for your patient under four months of age. The definition of a neonate used by the Antibiotic Assistant is any newborn 44 weeks postconceptional age or less. Infants of 45 weeks PCA and greater are treated with the pediatric dosage calculations.
The Recommendations Logic

An explanation of the rules that lead to the antibiotic recommendations for any patient can be viewed by selecting option '4' from the main screen. Here are the explanations for the nafcillin and gentamicin recommended in an adult-sized (90 kg) 11 year old girl.

Here are the explanations for the cefuroxime and erythromycin recommended for a patient with community-acquired pneumonia. Note the mention of the radiograph. The Antibiotic Assistant performs a keyword search on the dictated chest x-ray reports searching for evidence of pneumonia.

Lastly, when two or more antibiotics are determined to be therapeutically equivalent, the Antibiotic Assistant recommends the one which is least expensive.
APPENDIX D

"GET^DRUG" AND "GET^SUGG^DOSE" PROCEDURES
Author’s Note: At this point in the query, the PCMC patient file is opened and a PICU patient has been found by sorting through all of the patients and examining the room assignments. Sequential transactions have been assessed to find pharmacy data. This portion of the code examines the current string to find antibiotics and assigns values to the variables “Anti,” “mg,” “Interval,” “oral,” and “dcAtime.” Order details are then written to an external file “orderfile.” The current antibiotic order is then compared to a daily recommended maximum dose, “max’dose,” and a minimum dose, “min’dose,” by a loop in the code that calls the procedure which calculates these recommendations. This “get’sugg’dose” procedure then calls a second procedure, “get’crcl” which calculates the estimated creatinine clearance for the day under consideration. The “max’dose” and “min’dose” values are then calculated based on age, weight, and renal function and returned for comparison to the current dose. Orders that fall outside of these parameters are placed in a struct called “risk’days” and written to a file called “risk’file.”

CALL UNPACK‘TYPE‘1(CURRENT‘STRING,SCODE,B‘TYPE,VAL,50,ITEMS);

For J := 0 TO (ITEMS - 1) DO
BEGIN
LEV := STRCODE[J * 8 + 3];
FC := STRCODE[J * 8 + 2];
Noun := STRCODE[J * 8 + 4];
Adj := STRCODE[J * 8 + 5];
DCM := STRCODE[J * 8 + 7];
If dcm = 89 and lev = 4 and val[j] <> 0f then interval := $fixi(val[j]);
If dcm = 13 and lev = 4 and val[j] <> 0f then dc’time := $fixd(val[j]);
If lev = 4 and (dcm = 21 or dcm = 36 or dcm = 187 or dcm = 196 or dcm = 58) then oral := 1;
Anti := 0;
If FC = 54 then
Begin;
If Noun = 3 and (Adj = 14 or Adj = 13 or Adj = 16 or Adj = 19 or Adj = 152) then Anti := 6;
’gentamicin
If Noun = 3 and (Adj = 2 or Adj = 5 or Adj = 17 or Adj = 18 or Adj = 22) then Anti := 18;
’tobramycin
If Noun = 3 and (Adj = 7 or Adj = 8) then Anti := 19;
’amikacin
If Noun = 11 and (Adj = 27 or Adj = 28 or Adj = 29 or Adj = 36 or Adj = 48) then Anti := 46;
’ticarc/-clav
If Noun = 5 and (Adj = 1 or Adj = 16 or Adj = 17) then Anti := 30;
’cefaclor
If Noun = 6 and (Adj = 4 or Adj = 8 or Adj = 14) then Anti := 42;
’cephalexin
If Noun = 7 and (Adj = 2 or Adj = 10) then Anti := 47;
’aztreonam
If Noun = 5 and (Adj = 2 or Adj = 3) then Anti := 39;
’cefuroxime
If Noun = 7 and (Adj = 3 or Adj = 4 or Adj = 5) then Anti := 21;
’coamoxiclav
If Noun = 5 and (Adj = 150 or Adj = 151) then Anti := 23;
’cefotaxime
If Noun = 5 and (Adj = 154 or Adj = 156) then Anti := 40;
’ceftriaxone
If Noun = 5 and (Adj = 18 or Adj = 19 or Adj = 20) then Anti := 31;
’ceftizoxime
If Noun = 5 and (Adj = 9 or Adj = 37 or Adj = 60 or Adj = 152 or Adj = 153) then Anti := 32;
’cefoxitin
If Noun = 9 then Anti := 5;
’erythromycin
If Noun = 11 and (Adj = 1 or Adj = 2 or Adj = 3 or Adj = 4 or Adj = 5 or Adj = 7 or Adj = 8 or Adj = 12 or Adj = 13 or Adj = 17 or Adj = 18 or Adj = 152) then Anti := 9;
’penicillin
If Noun = 11 and (Adj = 150) then Anti := 10;
’amoxicillin
If Noun = 10 and (Adj = 1 or Adj = 6 or Adj = 7 or Adj = 9 or Adj = 10 or Adj = 11) then Anti := 1;
’ampicillin
If Noun = 11 and (Adj = 30 or Adj = 31 or Adj = 34) then Anti := 24; !piperacillin
If Noun = 13 and (Adj = 1 or Adj = 3 or Adj = 25) then Anti := 25; !vancomycin
If Noun = 13 and (Adj = 11 or Adj = 7 or Adj = 150) then Anti := 8; !clindamycin
If Noun = 17 and (Adj = 4 or Adj = 7 or Adj = 8 or Adj = 6) then Anti := 43; !ciprofloxacin
If Noun = 17 and (Adj = 9 or Adj = 12 or Adj = 13) then Anti := 50; !levofloxacin
If Noun = 7 and (Adj = 6 or Adj = 7 or Adj = 8 or Adj = 9) then Anti := 27; !imipenem
If Noun = 5 and Adj = 155 then Anti := 37; !cefezidime
If Noun = 18 and (Adj = 15) then Anti := 34; !loracarbef
If Noun = 22 and Adj = 22 then Anti := 36; !trimethoprim
If Noun = 30 and (Adj = 1 or Adj = 2 or Adj = 5 or Adj = 4) then Anti := 17; !tmp/smx
If Noun = 10 and (Adj = 24 or Adj = 25 or Adj = 26 or Adj = 27 or Adj = 28) then Anti := 38; !amoxicillin/clav
If Noun = 12 and (Adj = 2 or Adj = 3 or Adj = 8 or Adj = 9) then Anti := 13; !tetracycline
If Noun = 30 and (Adj = 3 or Adj = 6 or Adj = 7 or Adj = 11 or Adj = 15 or Adj = 23) then Anti := 44; !metronidazole
If Noun = 4 and (Adj = 15 or Adj = 42 or Adj = 21 or Adj = 151) then Anti := 11; !fluconazole
If Noun = 4 and Adj = 2 then Anti := 7; !amphotericin B
If Noun = 15 and (Adj = 1 or Adj = 151) then Anti := 52; !ganciclovir
If Noun = 15 and (Adj = 4 or Adj = 5 or Adj = 10 or Adj = 7 or Adj = 150) then Anti := 51; !acyclovir
If Noun = 4 and Adj = 43 then Anti := 73; !ampho B lipid complex
If Noun = 11 and Adj = 8 then Anti := 53; !loxacin
If Noun = 11 and Adj = 43 then Anti := 3; !pip/tazo
If Noun = 10 and (Adj = 4 or Adj = 8 or Adj = 23) then Anti := 12; !amoxicillin
If Noun = 12 and (Adj = 4 or Adj = 18 or Adj = 21) then Anti := 14; !doxycycline
If Noun = 10 and Adj = 29 then Anti := 22; !amp/sulbactam
If Noun = 9 and (Adj = 25 or Adj = 27) then Anti := 28; !azithromycin
If Noun = 7 and Adj = 16 then Anti := 33; !meropenem
If Noun = 5 and (Adj = 14 or Adj = 15) then Anti := 35; !cefixime
If Noun = 11 and Adj = 25 then Anti := 49; !ticarcillin
end;

If Anti and LEV = 2 and interval and j > 3 then
BEGIN
  case b^type[j] of
  begin
    240 -> @r240 := @val[j] 'i+2;
      If r240 < 5000e0 then mg := $int(r240 * !0e-1)
      else mg := 1;
    245 -> @r245 := @val[j];
      If r245 < 500010 then mg := $int(r245) else mg := 1;
      otherwise -> mg := $int(val[j]);
  end;

  orders ':= set for 10;
  orders.patnum := patid.primary^key.patnum;
  orders.abx := Anti;
  orders.order^time := s^time;
call write(order^file,orders,10);
  If interval < 48 and interval > 3 and mg > 1 then
begin
If interval <= 3 then interval := 4;
If interval <= 24 then
begin
dailydoses := $flt(24 / interval);
dose := $int($flt(mg) * dailydoses);
end
else
begin
dailydoses := $flt(interval / 24);
dose := $int($flt(mg) / dailydoses);
end;
If dc^time = 0d then dc^time := icu^out;
Anti := Anti + 100;
while s^time < dc^time do
begin
  call get^sugg^dose(Anti,s^time,sugg^dose,max^dose, min^dose, oral, kg, crc1);
  If kg > 50e0 and dose > sugg^dose then stri.risk^days := stri.risk^days + 1;
  riskdays := set for 44;
  If dose < min^dose then riskdays.min^day := 1;
  If dose > max^dose then riskdays.max^day := 1;
  If riskdays.min^day = 1 or riskdays.max^day = 1 then
  begin
    riskdays.patnum := patid.primary^key.patnum;
    riskdays.abx := Anti;
    riskdays.date^time := s^time;
    riskdays.mg := mg;
    riskdays.oral := oral;
    riskdays.interval := interval;
    riskdays.kg := kg;
    riskdays.age := patid.byte^stats.age;
    riskdays.age^unit := patid.byte^stats age^unit;
    riskdays.crc1 := crc1;
    riskdays.totaldose := dose;
    riskdays.min^dose := min^dose;
    riskdays.max^dose := max^dose;
    call write(risk^file,riskdays.44);
    riskdays.min^day := 0;
    riskdays.max^day := 0;
  end;
  s^time := s^time + 1440d;
end;
end;
END;

Get^Sugg^Dose Procedure called by the above.

proc get^sugg^dose(drug,time,sugg^dose, max^dose, min^dose, oral, kg, crc1);
int drug, oral, .crc1;
int .max`dose, .min`dose;
int(32) time;
real .kg;
begin
int bili := 0;
crl := 0;
call get`crl(crl,bili,.kg,.time);
If (patid.byte`stats.age`unit = "D") or (patid.byte`stats.age`unit = "M" and patid.byte`stats.age < 6) then
crl := 100;  !CrCl estimate less accurate for infants < 6 months
If crl = 0 then
begin
.min`dose := 1;
.max`dose := 25000;
return;
end;
.min`dose := 1;
.max`dose := 25000;
If .kg > 300e0 or .kg < 1e0 then
begin
return;
end;
case drug of
begin
  101 -> If crl > 30 then  !ampicillin
      begin
        min`dose := $int(.kg * 100e0);
        max`dose := $int(.kg * 420e0);
        If max`dose > 12000 then max`dose := 12000;
        If min`dose > 2000 then min`dose := 2000;
      end;
    If crl <=30 then
      begin
        min`dose := $int(.kg * 50e0);
        max`dose := $int(.kg * 210e0);
        If max`dose > 6000 then max`dose := 6000;
        If min`dose > 1000 then min`dose := 1600;
      end;
  102 -> If crl > 30 then  !clarithromycin
      begin
        min`dose := $int(.kg * 12e0);
        max`dose := $int(.kg * 16e0);
        If min`dose > 500 then min`dose := 500;
        If max`dose > 1000 then max`dose := 1000;
      end;
    If crl <=30 then
      begin
        min`dose := $int(.kg * 6e0);
        max`dose := $int(.kg * 8e0);
        If max`dose > 500 then max`dose := 500;
      end;
If min\textasciidoth{dose} > 250 then min\textasciidoth{dose} := 250;
end;

103 -> If crcl > 40 then

\hspace{1em} \textit{piperacillin/tazobactam}
\begin{verbatim}
begin
min\textasciidoth{dose} := \texttt{$\int(kg \ast 220e0)$};
max\textasciidoth{dose} := \texttt{$\int(kg \ast 400e0)$};
If max\textasciidoth{dose} > 12000 then max\textasciidoth{dose} := 12000;
If min\textasciidoth{dose} > 12000 then min\textasciidoth{dose} := 12000;
end;
end;
\end{verbatim}

113

If (patid\textunderscore byte\textunderscore stats\textunderscore agel\textunderscore unit = \textquotedblleft D\textquotedblright) or (patid\textunderscore byte\textunderscore stats\textunderscore age\textunderscore unit = \textquotedblleft M\textquotedblright and patid\textunderscore byte\textunderscore stats\textunderscore age < 7) then
\begin{verbatim}
begin
min\textasciidoth{dose} := \texttt{$\int(kg \ast 135e0)$};
max\textasciidoth{dose} := \texttt{$\int(kg \ast 315e0)$};
end;
end;
end;
\end{verbatim}

105 -> If crcl > 10 and not oral then

\hspace{1em} \textit{erythromycin}
\begin{verbatim}
begin
min\textasciidoth{dose} := \texttt{$\int(kg \ast 14e0)$};
max\textasciidoth{dose} := \texttt{$\int(kg \ast 55e0)$};
If max\textasciidoth{dose} > 4000 then max\textasciidoth{dose} := 4000;
end;
end;
end;
end;
\end{verbatim}

151

If oral and crcl > 10 then
\begin{verbatim}
begin
min\textasciidoth{dose} := \texttt{$\int(kg \ast 19e0)$};
max\textasciidoth{dose} := \texttt{$\int(kg \ast 55e0)$};
If max\textasciidoth{dose} > 3200 then max\textasciidoth{dose} := 3200;
end;
end;
end;
end;
end;
end;
end;
end;
end;
end;
end;
106 -> If (patid.byte^stats.age^unit = "D") or (patid.byte^stats.age^unit = "M" and patid.byte^stats.age < 6) then
  return; //eliminates consideration of crcl in infants

If crcl > 60 then
  begin
    !gentamicin
    min\dose := $int(kg * 4.7e0);
    max\dose := $int(kg * 8.0e0);
  end;
If crcl <= 60 then
  begin
    min\dose := $int(kg * 2.0e0);
    max\dose := $int(kg * 7.5e0);
  end;

107 -> min\dose := $int(kg * 0.5e0);  !amphotericin
max\dose := $int(kg * 1.6e0);

108 -> If not oral then
  begin
    !clindamycin
    min\dose := $int(kg * 23e0);
    max\dose := $int(kg * 43e0);
    If max\dose > 4800 then max\dose := 4800;
    If min\dose > 1200 then min\dose := 1200;
  end;
If oral then
  begin
    min\dose := $int(kg * 9.5e0);
    max\dose := $int(kg * 32e0);
    If max\dose > 1800 then max\dose := 1800;
    If min\dose > 450 then min\dose := 450;
  end;

109 -> If oral then
  begin
    !penicillin
    min\dose := $int(kg * 50e0);
    max\dose := $int(kg * 150e0);
  end;
If max\dose > 2000 then max\dose := 2000;
If min\dose > 500 then min\dose := 500;

110 -> min\dose := $int(kg * 47e0);  !nafcillin
max\dose := $int(kg * 212e0);
If max\dose > 12000 then max\dose := 12000;
If min\dose > 2000 then min\dose := 2000;

If (bili > 10) and (crcl < 20) then
begin
min\ dose := $\text{int}(kg \times 25e0);
max\ dose := $\text{int}(kg \times 100e0);
If \ max\ dose > 8000 \ then \ max\ dose := 8000;
If \ min\ dose > 1000 \ then \ min\ dose := 1000;
end;

111 -> If \ crcl > 50 \ then
   begin
     !fluconazole
     min\ dose := $\text{int}(kg \times 2.8e0);
     max\ dose := $\text{int}(kg \times 13e0);
     If \ max\ dose > 600 \ then \ max\ dose := 600;
     If \ min\ dose > 100 \ then \ min\ dose := 100;
   end;
   If (crcl <= 50) \ and \ (crcl > 20) \ then
   begin
     min\ dose := $\text{int}(kg \times 1.4e0);
     max\ dose := $\text{int}(kg \times 6.5e0);
     If \ max\ dose > 300 \ then \ max\ dose := 300;
     If \ min\ dose > 50 \ then \ min\ dose := 50;
   end;
   If (crcl <= 20) \ then
   begin
     min\ dose := $\text{int}(kg \times 0.7e0);
     max\ dose := $\text{int}(kg \times 3.3e0);
     If \ max\ dose > 150 \ then \ max\ dose := 150;
     If \ min\ dose > 100 \ then \ min\ dose := 100;
   end;
112 -> If \ crcl > 30 \ then
   begin
     !amoxicillin
     min\ dose := $\text{int}(kg \times 23e0);
     max\ dose := $\text{int}(kg \times 88e0);
     If \ max\ dose > 3000 \ then \ max\ dose := 3000;
     If \ min\ dose > 750 \ then \ min\ dose := 750;
   end;
   If \ crcl >= 10 \ and \ crcl <= 30 \ then
   begin
     min\ dose := $\text{int}(kg \times 16e0);
     max\ dose := $\text{int}(kg \times 58e0);
     If \ max\ dose > 2000 \ then \ max\ dose := 2000;
     If \ min\ dose > 500 \ then \ min\ dose := 500;
   end;
   If \ crcl < 10 \ then
   begin
     min\ dose := $\text{int}(kg \times 8e0);
     max\ dose := $\text{int}(kg \times 27e0);
     If \ max\ dose > 1000 \ then \ max\ dose := 1000;
     If \ min\ dose > 250 \ then \ min\ dose := 250;
   end;
114 -> min\ dose := $\text{int}(kg \times 1.8e0);
max\ dose := $\text{int}(kg \times 4.3e0);
!doxycycline
If max\(^\text{dose}\) > 200 then max\(^\text{dose}\) := 200;
If min\(^\text{dose}\) > 100 then min\(^\text{dose}\) := 100;

118 -> min\(^\text{dose}\) := $\text{int}(\text{kg} \times 2.3e0)$;  
   !tobramycin
max\(^\text{dose}\) := $\text{int}(\text{kg} \times 10.5e0)$;

119 -> min\(^\text{dose}\) := $\text{int}(\text{kg} \times 7.3e0)$;  
   !amikacin
max\(^\text{dose}\) := $\text{int}(\text{kg} \times 24e0)$;
If max\(^\text{dose}\) > 1500 then max\(^\text{dose}\) := 1500;

121 -> If crcl > 50 then  !cefoxitin
   begin
      min\(^\text{dose}\) := $\text{int}(\text{kg} \times 75e0)$;
      max\(^\text{dose}\) := $\text{int}(\text{kg} \times 170e0)$;
      If max\(^\text{dose}\) > 12000 then max\(^\text{dose}\) := 12000;
      If min\(^\text{dose}\) > 3000 then min\(^\text{dose}\) := 3000;
      end;
   If crcl > 30 and crcl <= 50 then
   begin
      min\(^\text{dose}\) := $\text{int}(\text{kg} \times 55e0)$;
      max\(^\text{dose}\) := $\text{int}(\text{kg} \times 110e0)$;
      If max\(^\text{dose}\) > 8000 then max\(^\text{dose}\) := 8000;
      If min\(^\text{dose}\) > 2000 then min\(^\text{dose}\) := 2000;
      end;
   If crcl > 10 and crcl <= 30 then
   begin
      min\(^\text{dose}\) := $\text{int}(\text{kg} \times 40e0)$;
      max\(^\text{dose}\) := $\text{int}(\text{kg} \times 80e0)$;
      If max\(^\text{dose}\) > 6000 then max\(^\text{dose}\) := 6000;
      If min\(^\text{dose}\) > 1500 then min\(^\text{dose}\) := 1500;
      end;
   If crcl <= 10 then
   begin
      min\(^\text{dose}\) := $\text{int}(\text{kg} \times 20e0)$;
      max\(^\text{dose}\) := $\text{int}(\text{kg} \times 40e0)$;
      If max\(^\text{dose}\) > 3000 then max\(^\text{dose}\) := 3000;
      If min\(^\text{dose}\) > 750 then min\(^\text{dose}\) := 750;
      end;
   If crcl > 29 then  !amp/sulbactam
   begin
      min\(^\text{dose}\) := $\text{int}(\text{kg} \times 95e0)$;
      max\(^\text{dose}\) := $\text{int}(\text{kg} \times 420e0)$;
      If max\(^\text{dose}\) > 8000 then max\(^\text{dose}\) := 8000;
      If min\(^\text{dose}\) > 3000 then min\(^\text{dose}\) := 3000;
      end;
   If crcl <= 29 and crcl > 14 then
   begin
      min\(^\text{dose}\) := $\text{int}(\text{kg} \times 48e0)$;
      max\(^\text{dose}\) := $\text{int}(\text{kg} \times 210e0)$;
      If max\(^\text{dose}\) > 4000 then max\(^\text{dose}\) := 4000;
      If min\(^\text{dose}\) > 1500 then min\(^\text{dose}\) := 1500;
end;
If crc1 <= 14 then
begin
  min\dose := $int(kg * 24e0);
  max\dose := $int(kg * 105e0);
  If max\dose > 2000 then max\dose := 2000;
  If min\dose > 750 then min\dose := 750;
end;

123 -> If crcl > 20 then !cefotaxime
begin
  min\dose := $int(kg * 95e0);
  max\dose := $int(kg * 320e0);
  If max\dose > 12000 then max\dose := 12000;
  If min\dose > 3000 then min\dose := 3000;
end;
If crcl <= 20 then
begin
  min\dose := $int(kg * 48e0);
  max\dose := $int(kg * 160e0);
  If max\dose > 6000 then max\dose := 6000;
  If min\dose > 1500 then min\dose := 1500;
end;

124 -> If crcl > 40 then !piperacillin
begin
  min\dose := $int(kg * 185e0);
  max\dose := $int(kg * 320e0);
  If max\dose > 24000 then max\dose := 24000;
  If min\dose > 6000 then min\dose := 6000;
end;
If crcl > 20 and crcl <= 40 then
begin
  min\dose := $int(kg * 140e0);
  max\dose := $int(kg * 240e0);
  If max\dose > 18000 then max\dose := 18000;
  If min\dose > 4500 then min\dose := 4500;
end;
If crcl <= 20 then
begin
  min\dose := $int(kg * 92e0);
  max\dose := $int(kg * 160e0);
  If max\dose > 12000 then max\dose := 12000;
  If min\dose > 3000 then min\dose := 3000;
end;

125 -> If (patid.byte\stats.age\unit = "D") or (patid.byte\stats.age\unit = "M" and patid.byte\stats.age < 6) then
return; !elminates consideration of inaccurate crcl
If not oral and crcl > 70 then !vancomycin
begin
min^dose := $int(kg * 37e0);
max^dose := $int(kg * 65e0);
If max^dose > 3000 then max^dose := 3000;
If min^dose > 2000 then min^dose := 2000;
end;
If not oral and crcl > 45 and crcl <= 70 then
begin
min^dose := $int(kg * 18e0);
max^dose := $int(kg * 33e0);
If max^dose > 1500 then max^dose := 1500;
If min^dose > 1000 then min^dose := 1000;
end;
If not oral and crcl > 30 and crcl <= 45 then
begin
min^dose := $int(kg * 12e0);
max^dose := $int(kg * 22e0);
If max^dose > 1000 then max^dose := 1000;
If min^dose > 660 then min^dose := 660;
end;
If not oral and crcl <= 30 then
begin
min^dose := $int(kg * 8e0);
max^dose := $int(kg * 16e0);
If max^dose > 700 then max^dose := 700;
If min^dose > 440 then min^dose := 440;
end;

127 -> If crcl > 70 then !imipenem
begin
min^dose := $int(kg * 37e0);
max^dose := $int(kg * 65e0);
If max^dose > 4000 then max^dose := 4000;
If min^dose > 1000 then min^dose := 1000;
end;
If crcl > 30 and crcl <= 70 then
begin
min^dose := $int(kg * 18e0);
max^dose := $int(kg * 33e0);
If max^dose > 2000 then max^dose := 2000;
If min^dose > 500 then min^dose := 500;
end;
If crcl > 20 and crcl <= 30 then
begin
min^dose := $int(kg * 9e0);
max^dose := $int(kg * 16.5e0);
If max^dose > 1000 then max^dose := 1000;
If min^dose > 250 then min^dose := 250;
end;
If crcl <= 20 then
begin
  min\^dose := $\int$(kg * 4e0);
  max\^dose := $\int$(kg * 8.25e0);
  If max\^dose > 500 then max\^dose := 500;
  If min\^dose > 125 then min\^dose := 125;
end;

128 -> min\^dose := $\int$(kg * 4.7e0);        !azithromycin
    max\^dose := $\int$(kg * 13e0);
    If max\^dose > 500 then max\^dose := 500;
    If min\^dose > 250 then min\^dose := 250;

130 -> If crcl > 30 then  !cefazolin
    begin
    min\^dose := $\int$(kg * 47e0);
    max\^dose := $\int$(kg * 110e0);
    If max\^dose > 6000 then max\^dose := 6000;
    If min\^dose > 1500 then min\^dose := 1500;
    end;
    If crcl > 10 and crcl <= 30 then
    begin
    min\^dose := $\int$(kg * 31e0);
    max\^dose := $\int$(kg * 74e0);
    If max\^dose > 4000 then max\^dose := 4000;
    If min\^dose > 1000 then min\^dose := 1000;
    end;
    If crcl <= 10 then
    begin
    min\^dose := $\int$(kg * 15.5e0);
    max\^dose := $\int$(kg * 37e0);
    If max\^dose > 2000 then max\^dose := 2000;
    If min\^dose > 500 then min\^dose := 500;
    end;

132 -> If not oral and crcl > 20 then  !cefuroxime
    begin
    min\^dose := $\int$(kg * 70e0);
    max\^dose := $\int$(kg * 255e0);
    If max\^dose > 6000 then max\^dose := 6000;
    If min\^dose > 2250 then min\^dose := 2250;
    end;
    If not oral and crcl > 10 and crcl <= 20 then
    begin
    min\^dose := $\int$(kg * 48e0);
    max\^dose := $\int$(kg * 170e0);
    If max\^dose > 4000 then max\^dose := 4000;
    If min\^dose > 1500 then min\^dose := 1500;
    end;
    If not oral and crcl <= 10 then
    begin
    min\^dose := $\int$(kg * 35e0);
max\^{dose} := \text{int}(kg \times 130e0);
If max\^{dose} > 3000 then max\^{dose} := 3000;
If min\^{dose} > 1125 then min\^{dose} := 1125;
end;
If oral and crc1 > 10 then
begin
  min\^{dose} := \text{int}(kg \times 18e0);
  max\^{dose} := \text{int}(kg \times 32e0);
  If max\^{dose} > 1000 then max\^{dose} := 1000;
  If min\^{dose} > 500 then min\^{dose} := 500;
end;
If oral and crc1 <= 10 then
begin
  min\^{dose} := \text{int}(kg \times 9e0);
  max\^{dose} := \text{int}(kg \times 16e0);
  If max\^{dose} > 500 then max\^{dose} := 500;
  If min\^{dose} > 250 then min\^{dose} := 250;
end;
133 -> If crc1 > 50 then !meropenem
begin
  min\^{dose} := \text{int}(kg \times 55e0);
  max\^{dose} := \text{int}(kg \times 130e0);
  If max\^{dose} > 6000 then max\^{dose} := 6000;
  If min\^{dose} > 1500 then min\^{dose} := 1500;
end;
If crc1 > 25 and crc1 <=50 then
begin
  min\^{dose} := \text{int}(kg \times 37e0);
  max\^{dose} := \text{int}(kg \times 87e0);
  If max\^{dose} > 4000 then max\^{dose} := 4000;
  If min\^{dose} > 1000 then min\^{dose} := 1000;
end;
If crc1 > 10 and crc1 <=25 then
begin
  min\^{dose} := \text{int}(kg \times 18e0);
  max\^{dose} := \text{int}(kg \times 44e0);
  If max\^{dose} > 2000 then max\^{dose} := 2000;
  If min\^{dose} > 500 then min\^{dose} := 500;
end;
If crc1 <= 10 then
begin
  min\^{dose} := \text{int}(kg \times 9e0);
  max\^{dose} := \text{int}(kg \times 22e0);
  If max\^{dose} > 1000 then max\^{dose} := 1000;
  If min\^{dose} > 250 then min\^{dose} := 250;
end;
135 -> If crc1 > 60 then !cefixime
begin
  min\^{dose} := \text{int}(kg \times 7e0);
  max\^{dose} := \text{int}(kg \times 9e0);
If max\^dose > 400 then max\^dose := 400;
If min\^dose > 380 then min\^dose := 380;
end;
If crcl > 20 and crcl <= 60 then
begin
  min\^dose := \int(kg \* 5e0);
  max\^dose := \int(kg \* 7e0);
  If max\^dose > 300 then max\^dose := 300;
  If min\^dose > 280 then min\^dose := 280;
end;
If crcl <= 20 then
begin
  min\^dose := \int(kg \* 3.5e0);
  max\^dose := \int(kg \* 4.5e0);
  If max\^dose > 200 then max\^dose := 200;
  If min\^dose > 180 then min\^dose := 180;
end;

137 -> If crcl > 50 then !ceftazidime
begin
  min\^dose := \int(kg \* 95e0);
  max\^dose := \int(kg \* 240e0);
  If max\^dose > 6000 then max\^dose := 6000;
  If min\^dose > 2000 then min\^dose := 2000;
end;
If crcl > 30 and crcl <= 50 then
begin
  min\^dose := \int(kg \* 64e0);
  max\^dose := \int(kg \* 160e0);
  If max\^dose > 4000 then max\^dose := 4000;
  If min\^dose > 1400 then min\^dose := 1400;
end;
If crcl > 10 and crcl <= 30 then
begin
  min\^dose := \int(kg \* 32e0);
  max\^dose := \int(kg \* 80e0);
  If max\^dose > 2000 then max\^dose := 2000;
  If min\^dose > 700 then min\^dose := 700;
end;
If crcl <= 10 then
begin
  min\^dose := \int(kg \* 16e0);
  max\^dose := \int(kg \* 40e0);
  If max\^dose > 1000 then max\^dose := 1000;
  If min\^dose > 350 then min\^dose := 350;
end;

138 -> If crcl > 30 then !amoxicillin/clav
begin
  min\^dose := \int(kg \* 19e0);
  max\^dose := \int(kg \* 49e0);
  If max\^dose > 1750 then max\^dose := 1750;
  If min\^dose > 750 then min\^dose := 750;
If ercl <= 30 and ercl > 10 then
begin
  min\text逃生 dose := \text{int}(kg \times 9.5e0);
  max\text逃生 dose := \text{int}(kg \times 24.5e0);
  If max\text逃生 dose > 875 then max\text逃生 dose := 875;
  If min\text逃生 dose > 375 then min\text逃生 dose := 375;
end;
If ercl <= 10 then
begin
  min\text逃生 dose := \text{int}(kg \times 5e0);
  max\text逃生 dose := \text{int}(kg \times 13e0);
  If max\text逃生 dose > 450 then max\text逃生 dose := 450;
  If min\text逃生 dose > 200 then min\text逃生 dose := 200;
end;

140 -> min\text逃生 dose := \text{int}(kg \times 46e0); !ceftaxone
max\text逃生 dose := \text{int}(kg \times 110e0);
If max\text逃生 dose > 4000 then max\text逃生 dose := 4000;
If min\text逃生 dose > 2000 then min\text逃生 dose := 2000;

144 -> If bili < 10 then !metronidazole
begin
  min\text逃生 dose := \text{int}(27e0 \times kg);
  max\text逃生 dose := \text{int}(33e0 \times kg);
  If max\text逃生 dose > 4000 then max\text逃生 dose := 4000;
end;
If bili >= 10 then
begin
  min\text逃生 dose := \text{int}(kg \times 13e0);
  max\text逃生 dose := \text{int}(kg \times 17e0);
  If max\text逃生 dose > 2000 then max\text逃生 dose := 2000;
end;

146 -> If ercl > 30 then !ticar/cla
begin
  min\text逃生 dose := \text{int}(kg \times 185e0);
  max\text逃生 dose := \text{int}(kg \times 320e0);
  If max\text逃生 dose > 24000 then max\text逃生 dose := 24000;
  If min\text逃生 dose > 12000 then min\text逃生 dose := 12000;
end;
If ercl > 10 and ercl <= 30 then
begin
  min\text逃生 dose := \text{int}(kg \times 138e0);
  max\text逃生 dose := \text{int}(kg \times 240e0);
  If max\text逃生 dose > 18000 then max\text逃生 dose := 18000;
  If min\text逃生 dose > 9000 then min\text逃生 dose := 9000;
end;
If ercl <= 10 then
begin
min\(^*\)dose := $\text{int}(kg \times 92e0); 
max\(^*\)dose := $\text{int}(kg \times 160e0); 
If max\(^*\)dose > 12000 then max\(^*\)dose := 12000; 
If min\(^*\)dose > 6000 then min\(^*\)dose := 6000; 
end;

147 -> If crcl > 30 then !aztreonam 
begin 
min\(^*\)dose := $\text{int}(kg \times 85e0); 
max\(^*\)dose := $\text{int}(kg \times 205e0); 
If max\(^*\)dose > 8000 then max\(^*\)dose := 8000; 
If min\(^*\)dose > 2000 then min\(^*\)dose := 2000; 
end;

If crcl > 10 and crcl <=30 then 
begin 
min\(^*\)dose := $\text{int}(kg \times 43e0); 
max\(^*\)dose := $\text{int}(kg \times 105e0); 
If max\(^*\)dose > 4000 then max\(^*\)dose := 4000; 
If min\(^*\)dose > 1000 then min\(^*\)dose := 1000; 
end;

If crcl <= 10 then 
begin 
min\(^*\)dose := $\text{int}(kg \times 21e0); 
max\(^*\)dose := $\text{int}(kg \times 52e0); 
If max\(^*\)dose > 2000 then max\(^*\)dose := 2000; 
If min\(^*\)dose > 500 then min\(^*\)dose := 500; 
end;

149 -> If crcl > 30 then !ticarcillin 
begin 
min\(^*\)dose := $\text{int}(kg \times 190e0); 
max\(^*\)dose := $\text{int}(kg \times 320e0); 
If max\(^*\)dose > 24000 then max\(^*\)dose := 24000; 
If min\(^*\)dose > 4000 then min\(^*\)dose := 4000; 
end;

If crcl > 10 and crcl <=30 then 
begin 
min\(^*\)dose := $\text{int}(kg \times 143e0); 
max\(^*\)dose := $\text{int}(kg \times 240e0); 
If max\(^*\)dose > 18000 then max\(^*\)dose := 18000; 
If min\(^*\)dose > 3000 then min\(^*\)dose := 3000; 
end;

If crcl <= 10 then 
begin 
min\(^*\)dose := $\text{int}(kg \times 95e0); 
max\(^*\)dose := $\text{int}(kg \times 160e0); 
If max\(^*\)dose > 12000 then max\(^*\)dose := 12000; 
If min\(^*\)dose > 2000 then min\(^*\)dose := 2000; 
end;
151 -> If not oral and crcl > 50 then
    !acyclovir
    begin
    min\^dose := $int(kg * 28e0);
    max\^dose := $int(kg * 64e0);
    end;
If not oral and crcl > 25 and crcl <=50 then
    begin
    min\^dose := $int(kg * 19e0);
    max\^dose := $int(kg * 43e0);
    end;
If not oral and crcl > 10 and crcl <= 25 then
    begin
    min\^dose := $int(kg * 9e0);
    max\^dose := $int(kg * 22e0);
    end;
If not oral and crcl < 10 then
    begin
    min\^dose := $int(kg * 5e0);
    max\^dose := $int(kg * 11e0);
    end;
152 -> If crcl > 79 then
    !ganciclovir
    begin
    min\^dose := $int(kg * 4.7e0);
    max\^dose := $int(kg * 11e0);
    end;
If crcl > 50 and crcl <=79 then
    begin
    min\^dose := $int(kg * 2.35e0);
    max\^dose := $int(kg * 5.5e0);
    end;
If crcl > 25 and crcl <= 50 then
    begin
    min\^dose := $int(kg * 1.2e0);
    max\^dose := $int(kg * 2.75e0);
    end;
If crcl < 25 then
    begin
    min\^dose := $int(kg * 1.0e0);
    max\^dose := $int(kg * 1.5e0);
    end;
153 -> min\^dose := $int(kg * 95e0);
    !oxacillin
    max\^dose := $int(kg * 210e0);
If max\^dose > 12000 then max\^dose := 12000;
If min\^dose > 1000 then min\^dose := 1000;
173 -> min\^dose := $int(kg * 2.3e0);
    !ampho B lipid complex
    max\^dose := $int(kg * 5.5e0);
end;
APPENDIX E

USER SURVEY AND DETAILED SURVEY RESULTS
Antibiotic Assistant Questionnaire:

1. You are a (circle).
   resident  nurse practitioner  fellow  attending

2. Number of times that you have used the Antibiotic Assistant
   Less than five  Between five and ten  More than ten

3. Do you find the patient data display helpful (WBC count, max temperature, renal function, allergies, current antibiotics, pathogens from micro)?
   Very helpful  5  4  3  2  1  Not helpful

4. Does use of the Antibiotic Assistant increase your awareness of the patient's renal function?
   Yes, increased  5  4  3  2  1  No, already aware

5. By your estimation, when you ordered antibiotics, how often did you order the Antibiotic Assistant's recommended antimicrobial(s)?
   0 – 10%  25%  50%  75%  90 – 100%

6. Do you feel that use of the Antibiotic Assistant will result in better or worse overall choices of antibiotics?
   Much better  5  4  3  2  1  Much worse

7. By your estimation, when you ordered antibiotics, how often did you order the Antibiotic Assistant's recommended dose (excluding minor rounding adjustments)?
   0 – 10%  25%  50%  75%  90 – 100%

8. Do you believe that its dosage selection and calculation assistance are or are not beneficial?
   Very beneficial  5  4  3  2  1  Not beneficial

9. Do you perceive that use of the Antibiotic Assistant will result in more or less adverse drug events (allergic reactions, overdosing errors, etc)?
   Less adverse events  5  4  3  2  1  More adverse events
10. Do you feel that the quality of patient care will be improved through clinician use of the antibiotic assistant?

| Improved quality | 5 | 4 | 3 | 2 | 1 | Decreased quality |

11. How helpful are the following facets of the Antibiotic Assistant? Please rank from 1 – 5.

1 = most helpful
5 = least helpful

- Data review (WBC count, temperature, renal function, allergies, current antibiotics, positive cultures)
- Automatic antibiotic suggestions
- Organism susceptibilities from Primary Children’s micro lab
- Dose calculation assistance with consideration to renal function
- Computerized drug ordering & printing

Comments:

12. Learning to use the Antibiotic Assistant is easy or difficult:

| Very easy | 5 | 4 | 3 | 2 | 1 | Quite Difficult |

13. Would you recommend this program to your colleagues?

| Enthusiastically | 5 | 4 | 3 | 2 | 1 | Never |

14. Have you learned anything new from the Antibiotic Assistant?

Yes   No

Other Comments/Suggestions:

Thank you for your time and attention!
Detailed Survey Results by Question

3. Do you find the patient data display helpful (WBC count, max temperature, renal function, allergies, current antibiotics, pathogens from micro)?

<table>
<thead>
<tr>
<th>Response Category</th>
<th>Count of Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very helpful</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

4. Does use of the Antibiotic Assistant increase your awareness of the patient’s renal function?

<table>
<thead>
<tr>
<th>Response Category</th>
<th>Count of Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, increased</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>
5. By your estimation, when you ordered antibiotics, how often did you order the Antibiotic Assistant’s recommended antimicrobial(s)?

0 – 10% 25% 50% 75% 90 – 100%

6. Do you feel that use of the Antibiotic Assistant will result in better or worse overall choices of antibiotics?

Much better 5 4 3 2 1 Much worse
7. By your estimation, when you ordered antibiotics, how often did you order the Antibiotic Assistant's recommended dose (excluding minor rounding adjustments)?

<table>
<thead>
<tr>
<th>Ordered Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 10%</td>
</tr>
<tr>
<td>25%</td>
</tr>
<tr>
<td>50%</td>
</tr>
<tr>
<td>75%</td>
</tr>
<tr>
<td>90 - 100%</td>
</tr>
</tbody>
</table>

8. Do you believe that its dosage selection and calculation assistance are or are not beneficial?

<table>
<thead>
<tr>
<th>Dosage Calculation Beneficial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very beneficial</td>
</tr>
<tr>
<td>Not beneficial</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Count of Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10%</td>
</tr>
<tr>
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</tr>
<tr>
<td>50%</td>
</tr>
<tr>
<td>75%</td>
</tr>
<tr>
<td>90-100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Response Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10%</td>
</tr>
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<tr>
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</tr>
<tr>
<td>75%</td>
</tr>
<tr>
<td>90-100%</td>
</tr>
</tbody>
</table>
9. Do you perceive that use of the Antibiotic Assistant will result in more or less adverse drug events (allergic reactions, overdosing errors, etc)?

Less adverse events  5  4  3  2  1  More adverse events

10. Do you feel that the quality of patient care will be improved through clinician use of the antibiotic assistant?

Improved quality  5  4  3  2  1  Decreased quality
12. Learning to use the Antibiotic Assistant is easy or difficult:

Very easy 5 4 3 2 1 Quite Difficult

13. Would you recommend this program to your colleagues?

Enthusiastically 5 4 3 2 1 Never
14. Have you learned anything new from the Antibiotic Assistant?

Yes  No

11. How helpful are the following facets of the Antibiotic Assistant? Please rank from 1-5.

1 = most helpful
5 = least helpful

- Data review (WBC count, temperature, renal function, allergies, current antibiotics, positive cultures)
- Automatic antibiotic suggestions
- Organism susceptibilities from Primary Children’s micro lab
- Dose calculation assistance with consideration to renal function
- Computerized drug ordering & printing

<table>
<thead>
<tr>
<th>Facets of Antibiotic Assistant</th>
<th>Median Ranking by Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data Review</td>
<td>3</td>
</tr>
<tr>
<td>Automatic Antibiotic Suggestions</td>
<td>3</td>
</tr>
<tr>
<td>Organism Susceptibilities</td>
<td>2</td>
</tr>
<tr>
<td>Dose Calculation Assistance</td>
<td>1</td>
</tr>
<tr>
<td>Computerized Drug Ordering and Printing</td>
<td>5</td>
</tr>
</tbody>
</table>
Anonymous comments written about the program in the space at the end of the questionnaire:

- Great system. Can't wait to have it available on the wards.
- Nothing new, it's similar to program at LDS Hospital. It is VERY helpful. Could not figure out how to enter new data into the computer that might change antibiotic choices (aspiration, etc).
- Displaying dose in mg/kg would be helpful. I think this will be occurring soon.
- On one occasion dosing was delayed. The initial order was entered before the labs, wt, ht, etc were entered. The order never printed. Because we were busy putting in lines. I did not realize the antibiotics were not officially ordered. It may be helpful to emphasize that the ordering physician must ensure the orders are printed and make it to the pharmacy.
- Peak and trough easily omitted since P/T needs to be ordered on usual order sheet.
- Generally will be useful with appropriate modifications. Often doesn't give typical rule-out sepsis medications for newborns (often cefuroxime & erythromycin).
- At the time that most patients arrive, antibiotic assistant is usually of little help (in fact, it causes delays) in getting antibiotic ordered. Overall is more time consuming than ordering antibiotic by hand.
- Actually, I think it takes more time to use this, than to calculate yourself.
• My only concerns have been errors in the recommendations made which will likely be fewer as the program has been in place. (Author’s note: recommended antiinfectives are not always the best choice when other important information is known to the clinician but not to the computer.)

• Interface (e.g., *, then return) difficult to use at times Useful, enjoyed utilizing the program. A few times an order would be misplaced or lost, or not put on chart. Eliminate the "nursing copy" to save paper.

• Occasionally, the computer malfunctions & does not respond to dosage changes. (Author’s note: this is probably an instance where the pharmacists had not yet entered the antiinfectives into the computer.) The main disadvantage is that when the tandem is down, you cannot access the program.

• Attendings usually want different antibiotics anyway

• Took several times using the system to get used to the format but in the end very helpful and efficient

• The suggested antibiotics are often not ones we want to choose. It seems the computer isn't always up to date on the current diagnosis. It is a hassle not to be able to write antibiotic orders on rounds and to have to go back and play around with the computer. I learned less about the antibiotic by not having to look them up for dose, etc.

• Getting print-out from printer, punching holes remain tedious; however well worth the support provided by the Antibiotic Assistant
- It seems like the nurse copy is repetitious - two should be enough. I for pharmacy and 1 in order section. Also- I've been writing in orders "see antibiotic assist for" i.e. vanco, gent orders. Do we need to do this, or is this excessive? I really like the program - would like to see addition of empiric/prophylactic antibiotic.

- It would be nice to have it state mg/kg/day when giving the dose. Has the issue about amphotericin B test dose been worked out? Sometimes there is a lag between the information re: micro lab & the antibiotic assistant. For example - positive urine culture but Antibiotic Assistant states no indication for antibiotic. Good program.

- Overall, once I was experienced with the system, it was quite helpful.
APPENDIX F

EMPIRIC RECOMMENDATIONS BY CULTURE RESULT
Upon request, the empiric recommendations by culture result feature of the adult version of the antiinfective management program matches the patient of interest with a historical set of patients that are very similar in six significant categories (gender, age category, hospital location, site of infection, and whether nosocomially or community-acquired). It then presents collated culture results of the previous patients sorted by pathogen in descending order of frequency and makes antibiotic recommendations for the current patient based on a mathematical summation of the reported antibiotic sensitivities. This works well at LDS Hospital where nearly all antibiotic sensitivities for all positive cultures are reported, and those that are not displayed to the physician have been reported to the HELP system but flagged as hidden from the user. However, at the children’s hospital, the trimmed bacterial susceptibility testing and reporting influences the power of the mathematical summation. This results in unnecessarily broad spectrum therapy (i.e., vancomycin and tobramycin) being recommended a disproportionate amount of the time. As unnecessary use results in an acceleration of the rate of the development of resistance to these important, last-line-of-defense antibiotics, this option was disabled at PCMC.

This problem of the trimmed antibiotic susceptibility results reporting could be managed through a combination of a change in the practice of the microbiology lab and the development of a rule-set to fill in the remaining gaps. The microbiology lab would need to decide to report all susceptibilities to the HELP hospital information system, but flag only the desired antibiotics to show to the clinician. Additionally, a set of susceptibility rules would need to be developed to populate the database of potential antibiotic therapies to provide the greatest chance of finding commonly susceptible
antibiotics among the myriad of pathogens. For example, one rule might state that if an isolate of \textit{Streptococcus pneumoniae} is sensitive to penicillin, then it is also sensitive to ampicillin, ampicillin/sulbactam, amoxicillin, amoxicillin/clavulanate, piperacillin, cefazolin, vancomycin, etc. Another rule might state that if an isolate of \textit{Staphylococcus aureus} is not sensitive to methicillin, then it is also resistant to penicillin, ampicillin, etc. Through these two procedures, the strength and accuracy of the empiric recommendations by culture results could be recovered. This problem is significant and would be a worthy endeavor for another medical informatics student.


7. Gorman C. Mixed-up meds. Lots of drugs have similar-sounding names. How you can tell you're getting the right one. Time 1999; 154:117.


111. Grosbart SR. All patient defined diagnosis related groups. Salt Lake City, 1996:51.