BIOMEDICAL INFORMATICS

A PRELIMINARY STUDY OF AUTOMATED TOOLS TO MONITOR MICROBIOLOGICAL DATA AND IMPROVE COMPLIANCE WITH HOSPITAL INFECTION CONTROL POLICIES

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Thesis under the direction of Professor Randolph A. Miller

This Masters Thesis project had as its objectives: (1) to provide Vanderbilt University Hospital (VUH) with computerized tools for monitoring microbiological data; (2) to provide the VUH Infection Control Service with tools to help monitor and track infection-relevant patient-related data such as culture results, hospital location, current orders, and contact precautions status; and, (3) to initiate studies to improve compliance with VUH contact precautions policies – specifically, those for antibiotic-resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE). This project achieved its goals by developing and formatively evaluating the MicroTools suite of programs. MicroParse processes VUH microbiology laboratory reports, MicroDash provides infection control staff with aggregated information on patients with a history of antibiotic-resistant infections, and MicroGram generates antibiograms for VUH clinicians.

Approved _____ Date _____

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By

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Thesis

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

MASTER OF SCIENCE

in

Biomedical Informatics

August, 2007

Nashville, Tennessee

Approved:

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ACKNOWLEDGEMENTS

This work was funded by the National Library of Medicine Vanderbilt Biomedical Informatics training grant, T15 LM07450. Without their financial support, this work would not have been possible.

The three members of my Thesis Committee, Dr. Randolph Miller, Dr. Dario Giuse, and Dr. Tom Talbot, are likely three of the busiest people working at Vanderbilt, yet all three have always been willing to lend me their time and expertise whenever needed, and I am greatly indebted to all of them for their mentorship. None of this project would have been possible without their knowledge and assistance, and I have learned a great deal from working with all of them.

I was very fortunate to have the opportunity to work on a project that would provide real and immediate benefits to the Vanderbilt University Hospital, and there are many people that made that possible. Dave Staggs manages the StarPanel servers, and has provided a good home for MicroParse. Asli Ozdas, Joe Warner, Jonathan Grande, and Russ Waitman provided me with assistance in interfacing with WizOrder/HEO, Vanderbilt's CPOE system. Vanderbilt's Infection Control Practitioners, particularly Jan Szychowski, helped me shape the development of MicroDash. Narinder Midha gave me a great deal of guidance in creating antibiograms, and Dr. Titus Daniels, Dr. John Morris, and Dr. Addison May refined them with me. I am also grateful to the students in the Department of Biomedical Informatics. Whether discussing ideas or just going for lunch, their support is always appreciated.

Most importantly, I would like to thank my “assistant editors,” Stephany Duda, my parents, and my sister. The feedback on my writing that they provided to me was instrumental, but was nothing compared to their love and moral support. I cannot thank them enough.

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LIST OF ABBREVIATIONS

ADT ..... admit-discharge-transfer

CLSI ..... Clinical and Laboratory Standards Institute

CPOE ..... care provider order entry

EMR ..... electronic medical record

ICP ..... Infection Control Practitioner

MIC ..... minimum inhibitory concentration

MRSA ..... methicillin-resistant *Staphylococcus aureus*

NLP ..... natural language processing

VUH ..... Vanderbilt University Hospital

VRE ..... vancomycin-resistant *Enterococcus*

CHAPTER I

DETECTING AND PREVENTING ANTIBIOTIC RESISTANCE IN BACTERIA

Introduction and Study Overview

This Masters Thesis project had as its objectives: (1) to provide Vanderbilt University Hospital (VUH) with computerized tools for monitoring microbiological data; (2) to provide the VUH Infection Control Service with tools to help monitor and track infection-relevant patient-related data such as culture results, hospital location, current orders, and contact precautions status; and, (3) to initiate studies to improve compliance with VUH contact precautions policies – specifically, those for antibiotic-resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE). Prior to this study, VUH microbiology data were only available in plain text format from the microbiology laboratory system as individual culture or study results. Clinicians viewed microbiology study results in a single patient-specific manner through integration of the microbiology-result-containing laboratory system (GE's "Triple G"® system) with VUH's electronic medical record system ("StarPanel"). Access was limited to the text of the microbiology report only. For these reasons, antibiograms had to be constructed at VUH manually. Though this was done every six months for many years, time constraints ultimately forced bi-annual creation and distribution of antibiograms to be discontinued in 2005. As described in the remainder of this document, the project achieved success by creating and evaluating MicroTools, a suite of programs that address VUH's infection control needs.

Bacterial Sensitivity to Antibiotics

Antibiotic resistance in bacteria presents a growing problem to hospitals [1-9]. Antibiotic-resistant organisms such as MRSA and VRE cause infections that are more difficult or expensive to treat than their antibiotic-sensitive counterparts. Infections by resistant organisms often lead to more dire patient outcomes [7, 10-13].

The most common measurement used to determine the degree of antibiotic resistance present in a bacterial specimen is minimum inhibitory concentration (MIC) [14]. An MIC represents the lowest concentration of an antibiotic that is still able to prevent a microbe from growing during incubation on appropriate medium (such as an agar plate or agar broth containing specific nutrients) and is the current gold standard for determining susceptibility to antimicrobial agents [14]. Methods for calculating MICs include disk diffusion [15, 16], broth microdilution [17], agar dilution [17, 18], and the E Test (a newer method that tests many antibiotic concentrations simultaneously) [19]. Comparing MIC values for an organism/antibiotic pair with published breakpoints yields a determination of whether the organism is sensitive, intermediate, or resistant to the antibiotic [20, 21]. These breakpoints depend on pharmacokinetic and pharmacodynamic properties of the antibiotic, since to be effective and safe, the dosage given to a patient must effectively treat the infection without reaching a potentially toxic concentration in the body [22, 23]. When the MIC for an organism/antibiotic pair exceeds the level at which the body can safely tolerate the antibiotic (e.g., without substantial risk of ototoxicity or nephrotoxicity), the antibiotic cannot be used to safely treat the infection.

The Problem of Antibiotic-Resistant Bacterial Infections

A major problem occurs when an organism develops resistance to the most common current method of treatment (e.g., oxacillin/methicillin for *S. aureus*). Repeated use of an antibiotic to treat an infection exerts a selective pressure on an organism that is an important determinant in the emergence of new antibiotic resistance. [5, 24, 25]

Development of new antibiotics plays a small role in preventing resistance problems, since over-reliance on new antibiotics can lead to new resistance patterns. For example, linezolid, the first drug in a novel class of antibiotics, was approved for use in the United States in April of 2000 [26], but initial reports of resistance to linezolid appeared just one year later for both VRE [27] and *S. aureus* [28]. In addition, inter-species transfer of resistance by bacterial plasmids occurs commonly [29-32]. The plasmid transfer mechanism allows antibiotic resistance genes to be passed from adaptive but relatively benign bacteria to a more virulent species that may cause serious infections in patients. Ultimately, to control and prevent the spread of antibiotic resistance, hospitals must make a coordinated effort to both curtail the spread of currently antibiotic resistant organisms and prevent the emergence of new antibiotic resistant organisms [33].

Preventing the Emergence of New Antibiotic-Resistant Organisms

Attempts to inhibit or reverse antibiotic resistance in hospitals vary in their approach. The most basic method simply restricts the use of clinically important “potent” (and often expensive) antibiotics -- e.g., vancomycin or linezolid -- to cases where their use is strictly necessary on the basis of severity of infection, knowledge of the most likely causative organisms to treat before culture results are known, and actual patterns of

antibiotic sensitivity once culture results become available [33]. Careful use of antibiotics can lead to both decreased antibiotic costs and improvements in antibiotic susceptibility rates [34-37]. However, it should be stressed that limiting antibiotic use must be a coordinated effort hospital-wide; only limiting antibiotic use in single wards may not significantly reduce the incidence of antibiotic resistance for an institution [38]. Furthermore, antibiotics not covered by a hospital-wide antibiotic restriction policy tend to be misused more frequently, suggesting a real need for guidance from hospital administration [39].

The efficacy of antibiotic restriction is necessarily limited, however, as a given antibiotic must be available for the antibiotic to be useful. For this reason, several methods of restricting antibiotic use without outright discontinuation of their use have been proposed. One method involves limiting the antibiotics prescribed within the hospital via two common techniques. The first, antibiotic cycling, involves rotating the antibiotics used within the hospital [40]. In the second technique, combination antibiotic therapy, clinicians prescribe multiple antibiotics that can adequately treat an infection [41-43]. Thus, if a mutation yielding antibiotic resistance occurs in an organism, one of the other active antibiotics will prevent it from propagating. In general, antibiotic cycling is less efficient than combination antibiotic therapy at preventing antibiotic resistance [44, 45]. Furthermore, combination antibiotic therapy can reduce mortality rates in severely ill patients, thus providing additional therapeutic benefits that antibiotic cycling cannot [43, 46].

Newer techniques to improve antibiotic use involving computer-assisted antibiotic selection have shown promise [47-49]. Due to the extensive knowledge requirements

associated with antibiotic selection, taking all relevant factors into account is impossible without consulting outside sources [50]. The earliest developed antibiotic selection program was Shortliffe's pioneering MYCIN, a program that performed as well as or better than human physicians [51, 52] on paper-based evaluations, but which was never implemented in full-scale clinical practice. Later automated antibiotic selection efforts at LDS Hospital [53-55] and West Virginia [56, 57] achieved acceptable clinical performance in actual hospital settings.

Combining antibiotic restriction with combination therapy provides a currently effective means of slowing the development of new resistant organisms, and effectively incorporating computer assistance gives future opportunities for improvement. However, it is unlikely that even the strictest adherence to antibiotic restriction and combination therapy could completely prevent resistance from developing. Community-acquired antibiotic-resistant organisms provide an additional reservoir that lies beyond the reach of any single hospital's antibiotic stewardship program, and resistant organisms are already endemic in many areas. For these reasons, hospitals must also implement a plan to stop resistant organisms from spreading.

Preventing the Spread of Resistant Organisms

Basic infection control measures such as hand washing [58, 59] and staff cohorting (i.e., dedicating one group of nurses to working with all patients with a certain type of infection) [60-63] can help prevent MRSA, VRE, and other antibiotic-resistant organisms from spreading [64-66]. However, standard precautions are not always sufficient to avoid crossinfection [67]. For this reason, many hospitals dictate the use of

contact precautions for patients with antibiotic-resistant infections. Contact precautions give hospitals a relatively inexpensive and effective approach to avoid the spread of antibiotic-resistant organisms. Contact precautions aim to directly prevent the spread of resistant organisms by effectively isolating patients infected with resistant organisms [7, 68-70].

When starting contact precautions, the nursing staff first moves the infected patient into a private room. For infections spread by contact with infected or colonized patients and their environment (e.g., MRSA or VRE), all healthcare providers must wear gloves and gowns before entering the room and remove them as they exit [68-70]. Once the infection (or bacterial colonization) has been cleared, those who enter the patient's room no longer need to follow contact precautions.

If strictly implemented, contact precautions effectively prevent antibiotic-resistant infections from spreading and can help contain outbreaks as well [71-78]. Unfortunately, studies have also demonstrated that contact precautions may adversely affect the safety and outcomes of patients on contact precautions due to decreased patient observation time and lesser interaction with professional staff. These result from the increased demands (donning and removing protective attire) on providers caused by contact precautions protocols [79]. Nevertheless, contact precautions remain a key measure in infection control thanks to the patient safety benefits from reduced transmission of resistant organisms.

Non-compliance by caregivers limits the effectiveness of contact precautions. Hospital-based infection control practitioners often battle non-compliance even with relatively simple infection control interventions like proper hand hygiene [80, 81]. Thus,

it is not surprising that studies have demonstrated compliance problems with contact precautions. In one study conducted at the University of Iowa, hospital staff correctly followed the hospital-defined contact precautions protocols when dealing with patients only 41% of the time [82, 83]. Given the efficacy of contact precautions and the tendency of hospital staff to stray from them, hospitals should pursue methods capable of improving adherence to contact precautions policies.

Addressing Information Needs in Infection Control and on the Wards

To determine the effectiveness of an intervention that attempts to improve contact precautions compliance rates for inpatients infected or colonized with resistant pathogens, one needs to be able to accurately identify when patients require contact precautions. However, monitoring and detecting cases of non-compliance with established contact precautions protocols can be difficult. Typically, most hospitals, even in the present information age, carry out compliance monitoring tasks by manual direct inspection of patient charts, of patients, and of patient isolation rooms. Data collected manually may be stored on paper forms, in electronic spreadsheets, or in localized PC-based databases. Infection control practitioners must consult many different information resources to detect non-compliance. They require current hospital census information to know who is currently admitted to or being evaluated in the hospital; microbiology culture data to determine which patients have drug-resistant infections or colonization; and information about which patients are currently isolated. Gathering such comprehensive data is daunting and time-consuming, particularly in hospitals lacking a good information technology infrastructure.

In clinical settings where existing electronic medical record systems (EMRs), admit-discharge-transfer (ADT) systems, laboratory information systems, and care provider order entry (CPOE) systems are in use, electronic dashboards can provide a potentially useful method for reducing the burden of data gathering [84-86]. Dashboards collect and summarize a large amount of information from different sources and display integrated and synthesized information for quick consumption. With the growth of information technology in medicine, dashboards are now available more frequently in the hospital setting [84, 86, 87].

Computerized reminders can help to improve compliance with hospital policies [88-93]. In a study at Indiana University Medical Center, Dexter et al. observed a large increase in physician ordering of preventive therapy measures after implementing computerized reminders [88]. Individual physicians' behaviors varied widely, however, with some following the recommended orders more than 80% of the time and others disregarding all or nearly all recommendations [89]. Litzelman et al. conducted a study measuring the effects of computerized reminders on physicians' ordering rates of preventive care measures at Regenstrief Health Center [90]. They found that the computerized reminders improved residents' ordering rates by 20-35%, though attending physicians' ordering rates did not change significantly. Neilson et al. also found that peer management in the form of computerized reminders reduced physician ordering rates of unnecessary tests, further suggesting that computerized reminders can be effective in changing physician behavior [91].

Kho et al. found that computerized reminders could help improve compliance with contact precautions policies at Indiana University Medical Center [92, 93]. After

identifying incoming inpatients who had past-documented MRSA or VRE cultures, Kho et al. generated a computerized alert reminding physicians to write a contact precautions order for those inpatients. Within that identified population, compliance with contact precaution policies rose from 33% to 89%.

Overall, the evidence suggests that providing useful information to clinicians at the proper time can often help improve their compliance with hospital policy. Thus, providing information on which patients require contact precautions when a clinician places orders could have a positive impact on overall contact precautions rates.

Detecting and Monitoring Antibiotic Resistance

A standard tool for monitoring antibiotic resistance patterns in hospitals is the antibiogram [94]. Antibiograms aggregate observed antibiotic sensitivities over a period of time for various organisms. Thus, they provide a basis for empiric therapy when new infections are identified. Currently, most antibiograms are created manually, including at VUH. Unfortunately, the data represented in manually created antibiograms are often immediately out of date, giving clinicians a less accurate indication of which antibiotics to use. Since antibiograms require a large amount of accurate, up-to-date information, computers systems to aid in their creation provide an immediate benefit for improved patient care [53, 57, 94-97]. Furthermore, eliminating the tedious and time-consuming task of collecting and organizing antibiotic resistance data allows infection control staff to spend their time more productively.

Among the earliest efforts at automating antibiotic resistance monitoring is the Computerized Infectious Disease Monitor (CIDM) created at LDS Hospital by Evans et

al. [96]. The CIDM was incorporated into LDS Hospital's larger HELP hospital IT system to integrate information from their microbiology laboratory system. The CIDM ran daily in the afternoon and generated a variety of alerts for infection control staff when it detected situations requiring attention. Overall, the CIDM performed quite well, detecting infections as accurately as infection control staff and making accurate and clinically useful antibiotic suggestions [97]. At Barnes Hospital in St. Louis, Kahn et al. developed GERMWATCHER, a computerized expert system used to detect nosocomial infections [95]. Though not technically used for tracking antibiotic resistance, the model they developed provided enough flexibility to do so. The microbiology laboratory system at Barnes Hospital generated microbiology reports in a semi-structured form, using natural-sounding language but backed by a limited terms dictionary. Leveraging the terms dictionary, they were able to use simple pattern matching to extract the portions of the report necessary for tracking nosocomial infections. Wright et al. developed a system that allowed infection control staff to set "control charts" that would generate an alert when certain organisms were detected [98]. The control charts allowed alerts to be displayed any time the organism was detected, only if it had certain antibiotic resistances, or only if it was in a certain unit. After configuring the control charts and analyzing retrospective data, the program was able to detect a number of outbreaks that infection control had missed, making this a potentially useful tool for surveillance. Brossette et al. developed a similar system but took a slightly different approach. Their program was designed to detect changes in resistance patterns as well, but the program ran independently; it was not informed of any preconceptions about what would constitute a clinically interesting pattern rather than an obvious pattern [99]. By observing differently

sized blocks of time, Brossette et al. were able to detect a number of interesting short-term and long-term changes in the resistance patterns shown by *Pseudomonas aeruginosa*.

Regardless of the methodology employed, hospitals must use resistance data when determining hospital antibiotic use policy and when making frontline antibiotic decisions. Without this information, clinicians can easily make mistakes that can result in an improperly treated infection or in the fostering of new antibiotic resistance.

CHAPTER II

DEVELOPMENT AND VALIDATION OF MICROPARSE

Introduction: Development and Validation of MicroParse

Providing VUH with automated tools for monitoring microbiological data first requires an accurate source of microbiological data. VUH uses a proprietary microbiology lab system (Triple G®) that does not allow access to its underlying database, thus making direct access to the microbiology data impossible. The plain text reports supplied by the microbiology lab system to physicians provide the only easily accessible method of output. For computerized tools to make use of the plain text reports, however, another tool must first parse the reports into a coded format. The MicroParse project aimed to provide the parsing functionality.

Methods: Development and Validation of MicroParse

Clinical Setting and Microbiology Data Source

Vanderbilt University Hospital is an 832-bed academic medical facility located in Nashville, TN. Its microbiology lab system, GE Medical Systems' Triple G®, processes over 20,000 unique microbiology culture and test reports per month. Unfortunately, the proprietary software underlying Triple G® generates microbiology reports in a human-readable format with variable structure that makes report parsing (by computer algorithms) to identify pathogen names and other characteristics less than straightforward

(Figure 1). Thus, to use VUH microbiology report data for decision support requires sophisticated parsing algorithms that "understand" the component parts of reports and that can recognize the underlying lexicons from which reports are generated.

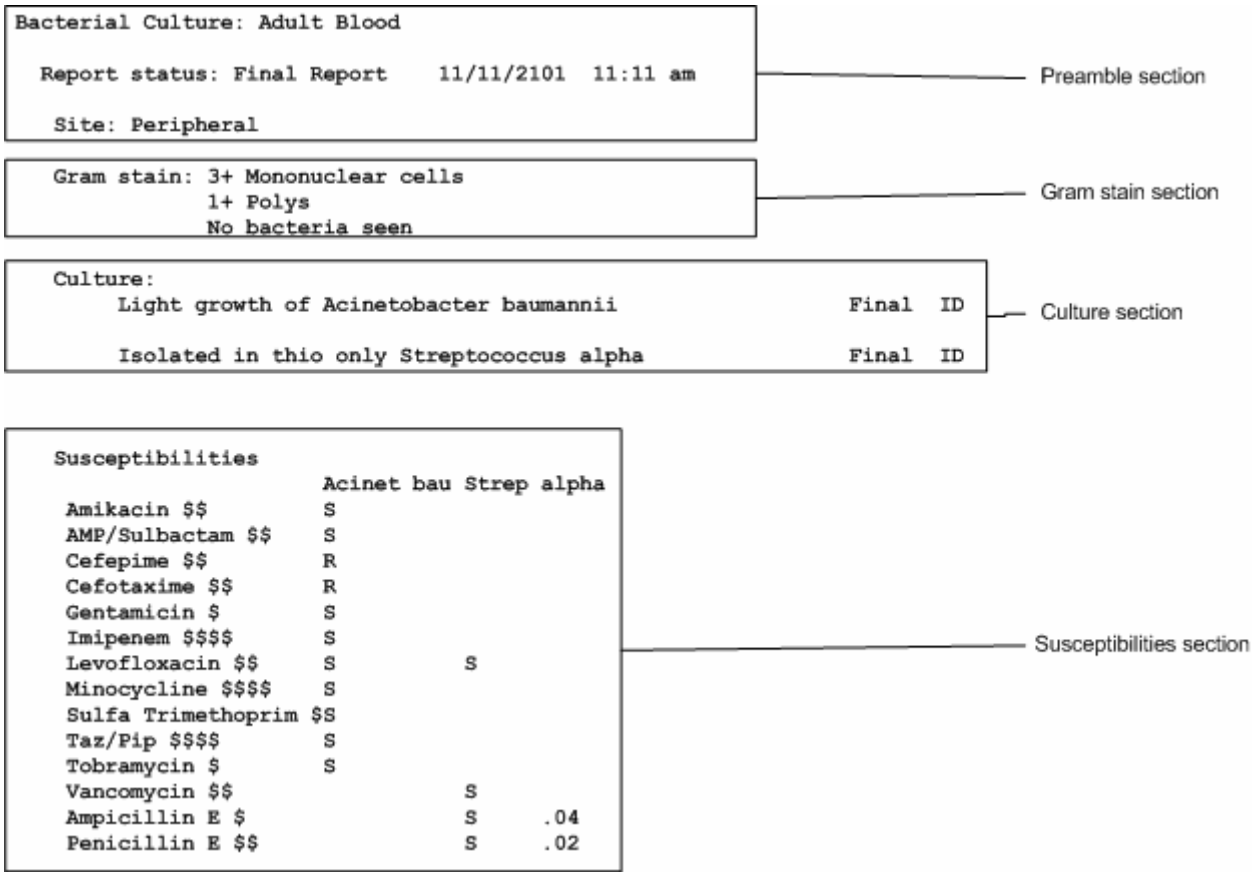


Figure 1: Sample plain text report from Triple G®

Description of MicroParse

The project (authors RC and RM) created a parser (MicroParse), written originally in Perl and later in PHP, to process the Triple G-generated microbiology text reports into usable microorganism-related data. At present, for purposes of security,

confidentiality, and convenience of data access, MicroParse runs on machines within the StarPanel cluster; StarPanel is VUH's electronic patient record. StarPanel was configured to regularly feed plain text Triple G® microbiology reports to MicroParse, which processes new reports every 10 minutes that are in turn passed back to StarPanel for storage.

MicroParse first decomposes each plain text Triple G® report into 4 potential sections (when present): preamble, Gram stain, culture, and susceptibilities (Figure 1). The preamble contains information about the culture result, including the culture category (e.g., blood, CSF, urine), the report time and date, the report status (i.e., preliminary or final), and the site from which the specimen was taken (e.g., arm wound, bone marrow). Because the preamble tends to follow a fairly specific order with common terms, this information is easily recognized using Perl-style regular expressions. For example, to extract the report's status, MicroParse uses:

```
/Report status:([a-zA-Z ]+)/
```

The Gram stain and culture sections are more difficult to parse since they more closely approximate natural language. However, text from these sections comes primarily from the dictionary of microbiology terms ("VUH Microbiology Thesaurus") stored within Triple G®. To generate reports, lab technicians simply select finding codes based on the results of the test or culture; Triple G® then enters a standardized phrase into the report, but combined in a manner with surrounding and intermingled English text phrases that make recognition of the original coded terms difficult. Fortunately, unlike most other data within the Triple G® database, the microbiology terms dictionary is externally

accessible. This allows MicroParse to use an externalized copy of the VUH Microbiology Thesaurus as an aid to parsing reports.

The susceptibilities section of VUH Microbiology reports contains a table that, in its top row, indicates an abbreviation for each isolated bacterium, and on subsequent rows, indicated only by column position, the results of testing each organism's growth in the presence of various antibiotics. The antibiotics for which susceptibilities were tested are named in the first (leftmost) column of the table rows (except the first row). The table columns are generally fixed-width fields, though complications can arise. For example, the abbreviated names often run together in the first row and the abbreviations are occasionally inconsistent (e.g., nonspecific coagulase-negative staphylococcus can appear with any of 6 different column headings). Without consistency in the column names, demarcating the column breaks can be difficult. Also, when the microbiology laboratory provides minimum inhibitory concentrations for a given isolated bacterium, unpredictable changes occur in the column alignments. When multiple bacteria grow from a single culture and their sensitivities are presented as side-by-side columns in a report, it is often the case that not all organisms were tested against all antibiotics, so the absence of testing is indicated by blank fields (extra spaces) within the table columns – further complicating the parsing task.

After processing the report, MicroParse stores the information in a MySQL database, also located within the StarPanel machine cluster. Figure 2 shows an example of the parsed fields for one of the lines in the report shown in Figure 1. In this case, MicroParse stores the codes `IITO` ("isolated in thio only") and STRALP ("streptococcus alpha"), and labels their identification status as "final." The database then interfaces with

StarPanel to provide information about organisms identified in the report to other programs.

Parsing the Gram Stain and Culture Sections

Much of the text found in both the culture and Gram stain sections is drawn directly from the VUH Microbiology Thesaurus. For example, to identify an isolated bacterium in the culture section, it is common to see a term from the categories `QUANT` (quantity) and `FIDORG` (final identified organism) (Figure 2).

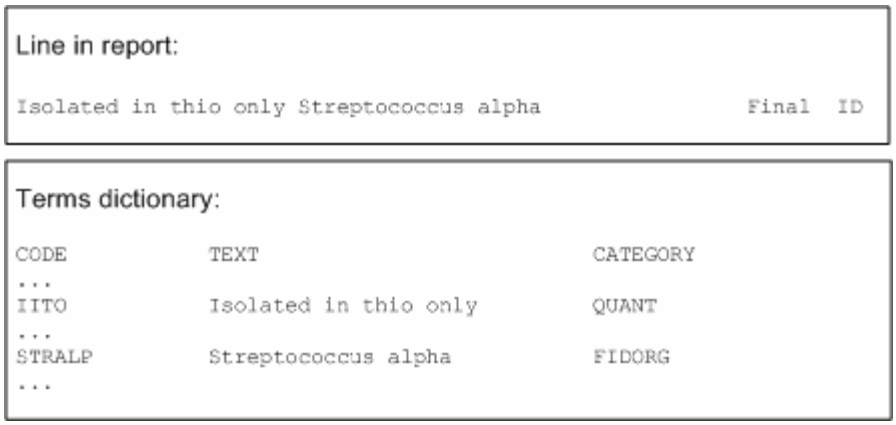


Figure 2: Breaking culture/gram stain sections into component terms

The Thesaurus helps MicroParse to process the Gram stain and culture results. The Gram stain segment of the report tends to be straightforward, as nearly all lines consist of a `STAINQTY` term followed a `STAINDESC` term, making the parsing process simple. The culture section often contains more complex information, however.

To parse the culture section, MicroParse first processes the VUH Microbiology Thesaurus into a compiled format nicknamed “the Microbiology Rosetta Stone.” To create the Microbiology Rosetta Stone, MicroParse breaks each phrase in the terms

dictionary into its constituent words. Starting with the first word in the phrase, MicroParse then creates a linked list from these words, thus storing the valid partial phrases along with an indication of where completed phrases end (Figure 3).

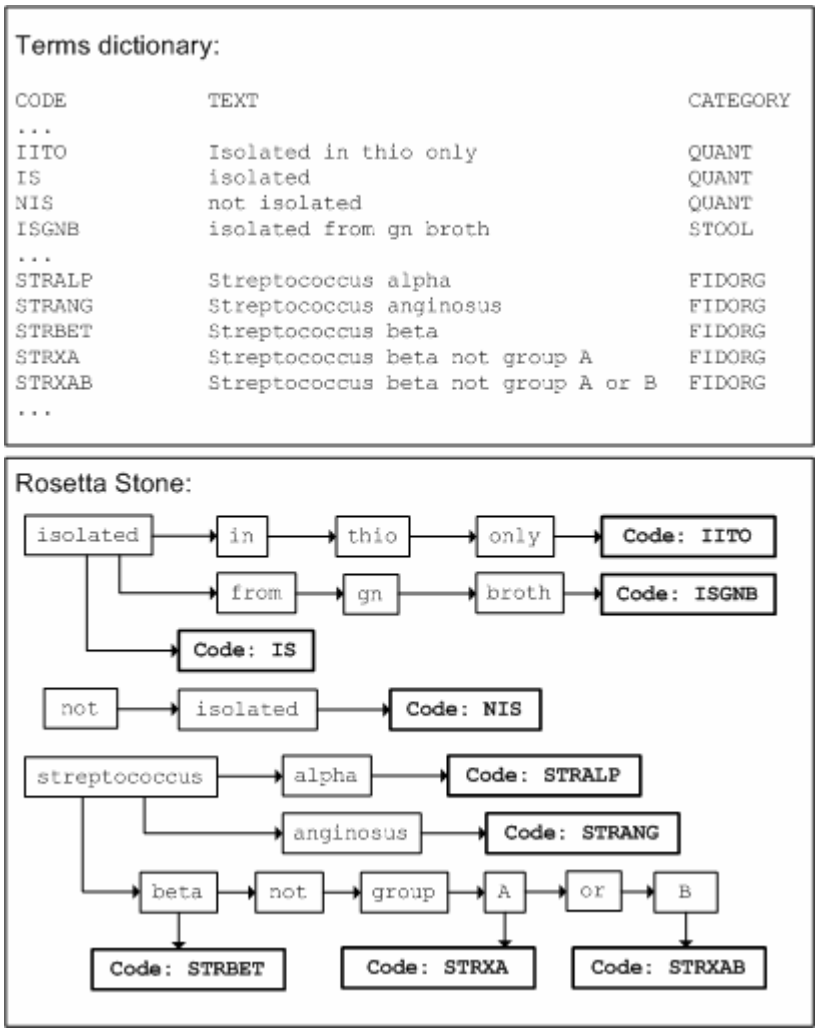


Figure 3: Creating the Microbiology Rosetta Stone

Once MicroParse has created the Microbiology Rosetta Stone as a reference source, it is ready to process the text in the culture section. Starting with the beginning of a microbiology report's culture segment, MicroParse matches one word at a time against the list of valid partial phrases until adding the next word from the report text would

create a phrase that does not exist in the terms dictionary. At that point, MicroParse takes the longest complete phrase it found and begins searching for the next phrase starting with the end of the previous one (see Figure 4). A placeholder entry in the Microbiology Rosetta Stone, `UNPARSED`, captures all phrases MicroParse encounters that do not have any valid matches in the dictionary.

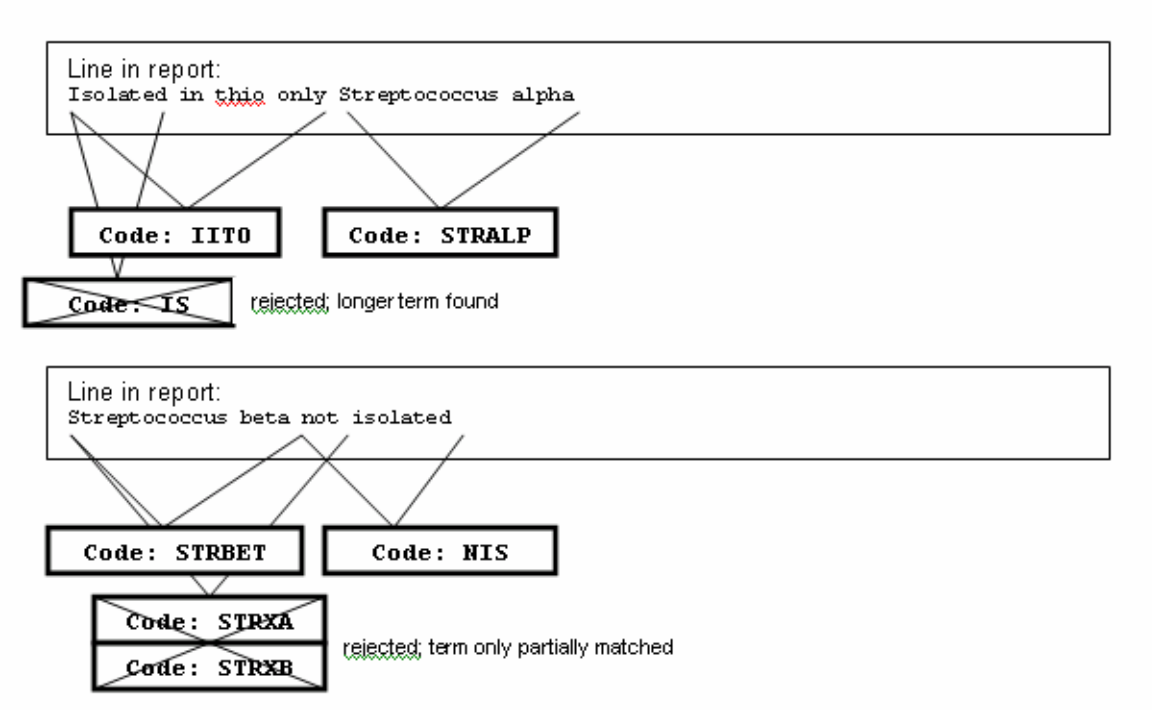


Figure 4: Parsing Text Using the Microbiology Rosetta Stone

Database Structure

The database centers around the `specimen` table. Each report issued by the microbiology laboratory system corresponds with one entry in `specimen`, and all general information about the report (e.g., time and date the specimen was received, time and date of the report, site the specimen was drawn from) is stored there along with a unique ID number, `specimen_id`.

The `specimen_id` directly links `specimen` to the `gramstain` table, which contains a quantity and finding for each entry listed in the Gram stain section of the report. The `specimen_id` also links `specimen` to the `specimen_result` table. Each result from the culture section of the report has one entry in `specimen_result`, with each parsed phrase from `specimen_result` stored in `specimen_result_rosetta`. Finally, `specimen_id` links `specimen` with the `sensitivity`. In `sensitivity`, each organism with antibiotic sensitivities given in the report has one entry, with individual results for each antibiotic/organism pair stored in `abxsuscept`. In this fashion, all portions of the standard report link together through `specimen`. Figure 5 graphically illustrates this linkage.

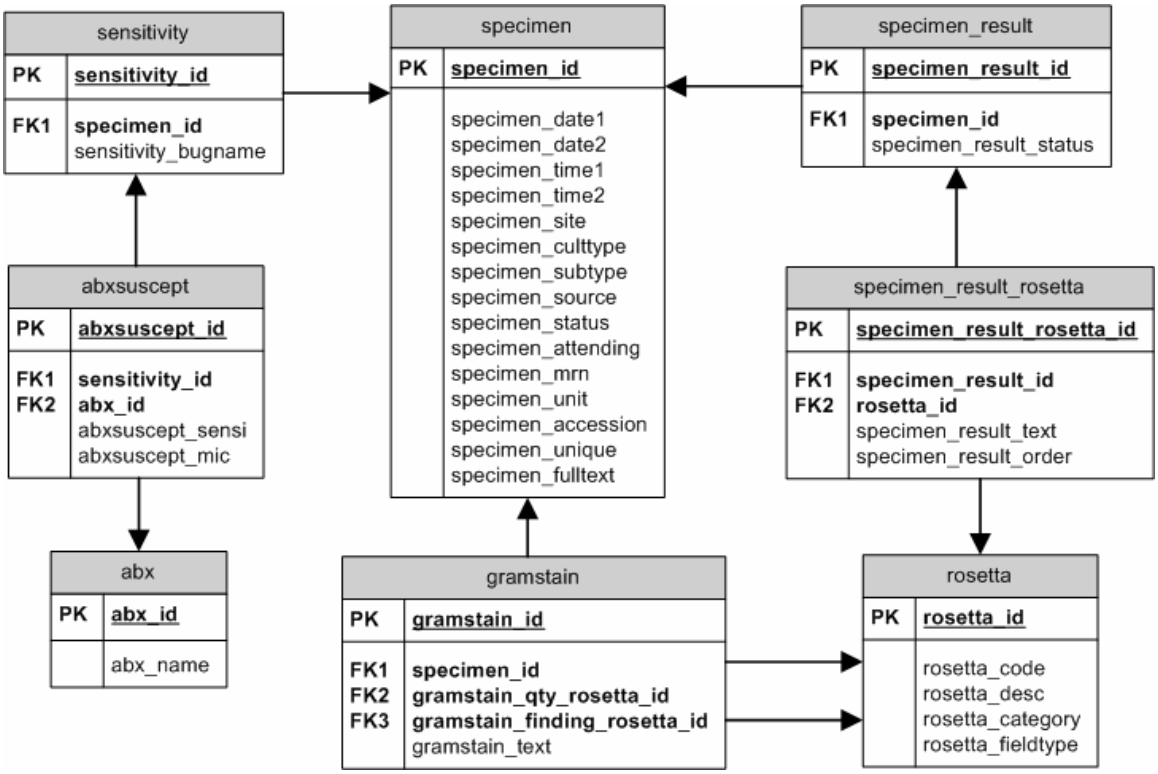


Figure 5: Relational Database Core Structure

The database structure works well with MicroParse, with each of the four report sections having a direct mapping to a table or set of tables within the database. Thus, after MicroParse processes the report, storing the information becomes a straightforward process.

Validation of MicroParse Data Capture

To confirm that MicroParse can properly parse reports and retrieve the clinically relevant information from them, we conducted a validation study. We first selected 3 dates that fell on different days of the week to analyze: Saturday, January 6, 2007, Monday, January 15, 2007, and Friday, January 19, 2007. We then acquired a complete data dump of all reports issued on those three days from the microbiology laboratory system.

Taking this information, a computer program matched the reports to records in the MicroParse database. We collected all of the matched reports and displayed them on a webpage containing 4 panes: the upper left displayed the report text MicroParse received and parsed, the upper right displayed the parsed output stored in the MicroParse database, the lower left displayed the data from the microbiology lab system, and the lower right contained controls allowing the reviewer to input comments on the displayed report and to navigate to the other reports to review. Figure 6 shows a screenshot from the validation webpage.

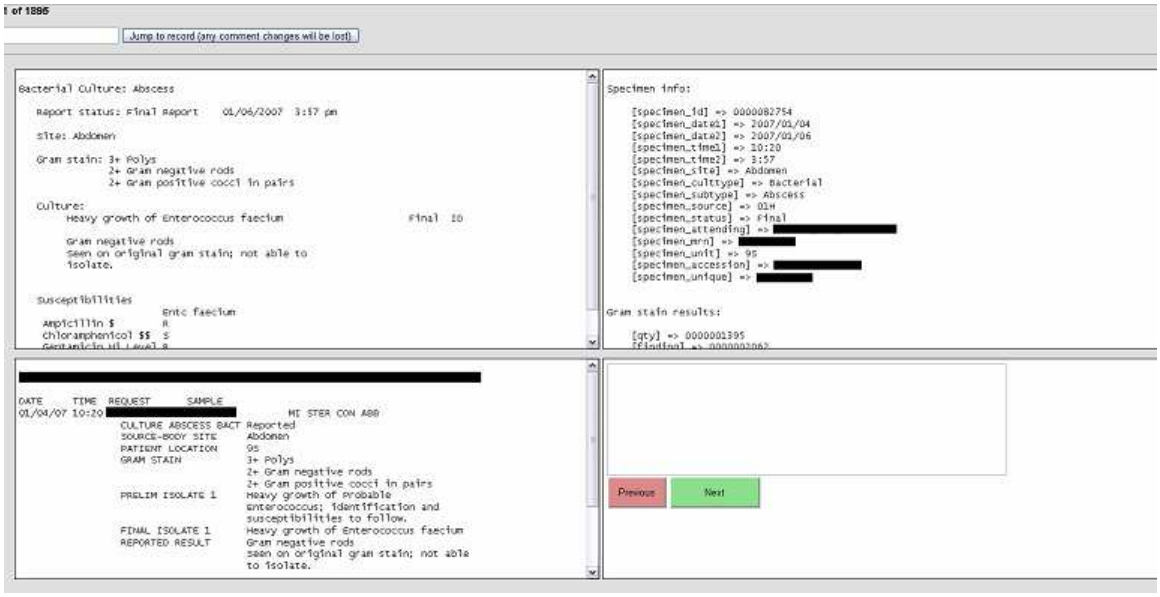


Figure 6: Webpage designed for the MicroParse validation

We chose our most clinically experienced collaborator, Dr. Thomas Talbot, to conduct the actual validation. Dr. Talbot reviewed all of the matched records from the above-mentioned sample to confirm that the information stored in the MicroParse database accurately reflected all relevant content found in the original microbiology lab report.

Results: Development and Validation of MicroParse

MicroParse Results

MicroParse currently handles approximately 500-900 VUH microbiology reports per day. It is able to process and store reports at a peak rate of approximately 15 reports per second, yielding a theoretical limit of over 1,000,000 reports per day. MicroParse

identifies a phrase in the Microbiology Rosetta Stone for over 98% of the text contained in the culture section and nearly 100% of the text in the Gram stain section.

Figure 7 shows the number of unique MRNs with an MRSA-positive inpatient culture result by month. As the trend line shows, the rate of MRSA at VUH approximately doubled between January 2001 and January 2006.

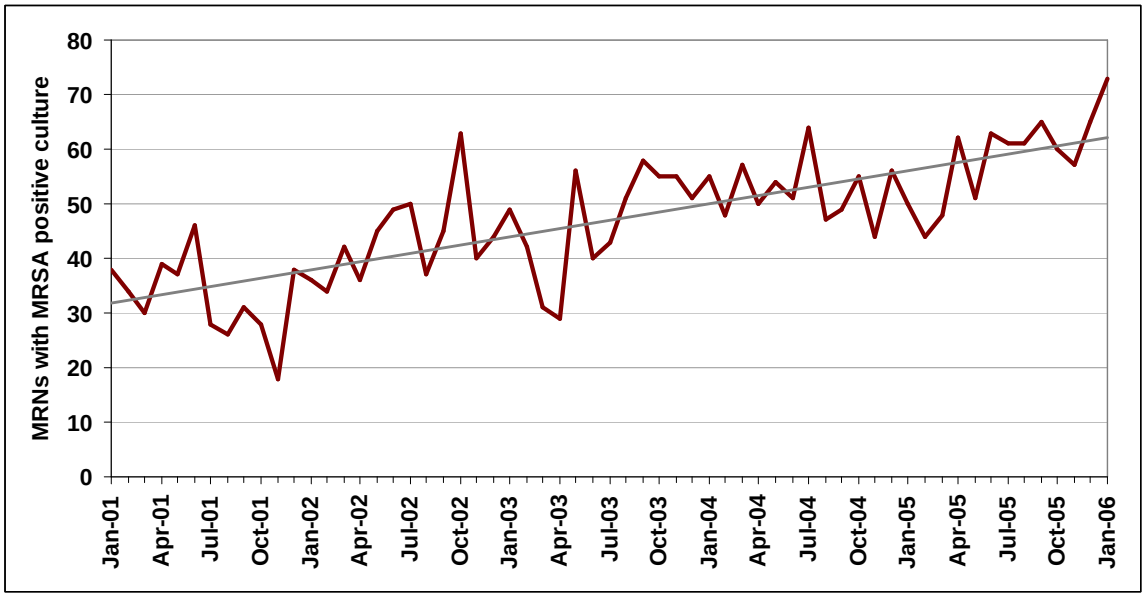


Figure 7: Unique MRNs with MRSA-positive inpatient culture by month

MicroParse Validation Study Results

Figure 8 shows the results of the MicroParse validation study. Out of the 1,895 reports reviewed, 28 had expert reviewer-generated comments (1.5%). Of the commented reports, 17 were problems in MicroParse, 2 were problems where a preliminary report was matched to a final report, 1 was a Triple G®-related problem, and 8 were general comments and questions. Overall, the validation process demonstrated that the core functionality of MicroParse was working as expected, with problems occurring in three

main areas: Microbiology Thesaurus term labeling, positive/negative culture tagging, and report linking.

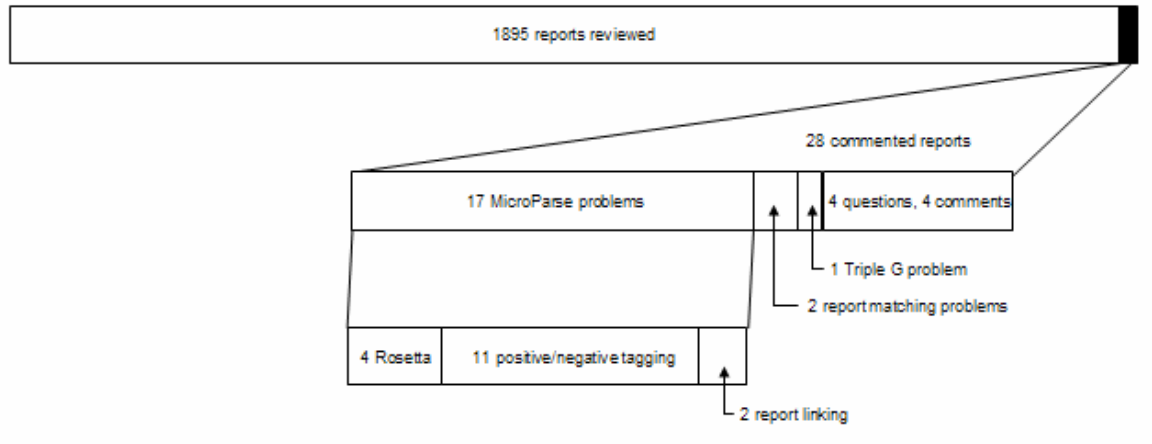


Figure 8: Validation results

Out of 1895 reviewed reports, 28 had comments. 17 comments related to problems within MicroParse, 2 were problems in the report creating the validation set, 1 was a Triple G® problem, and 8 were questions and comments that did not indicate problems. Of the 17 MicroParse problems, 4 were Microbiology Thesaurus term issues, 11 were problems with the positive/negative tagging system, and 2 were problems with linking related reports.

The MicroParse Microbiology Thesaurus term labeling problems primarily involved the redisplay of parsed information. Since the creation of the Microparse version of Microbiology Thesaurus terminology involves stripping most punctuation from the "raw" feeds from Triple G® to create canonical terms, displaying the descriptions associated with the resulting codes stored by MicroParse can be somewhat misleading. For example, the `QUANT` code `1025k` is associated with the text "10-25k", but the Microbiology Thesaurus entry for it appears as "10 25k" without the dash. Because the MicroParse version of the Microbiology Thesaurus originally only stored the canonical, "stripped down" version of the text in the database at the time of the validation study, that information was the only piece the reviewer was shown. Thus, the reviewer

was concerned that the code might not correctly represent the report. These problems were easily solved by adding the original text into the Microbiology Thesaurus as an extra field to be shown when redisplaying the parsed report results.

The positive/negative tagging problems centered on the system devised for MicroParse to identify positive cultures. Some of the Microbiology Thesaurus term entries are somewhat ambiguous as to whether or not they represent a positive, negative, or indeterminate culture. For example, one could argue that “no growth; reincubate” could be counted as a negative result or as an indeterminate result. As the most commonly occurring problem discovered in the validation, we are currently working on a new, more flexible tagging system that should alleviate some of the encountered problems.

The report linking problems identified in the MicroParse validation study arose when there were free text entries in the report telling the user to refer to another report for more detailed information about the current report (often sensitivity information). As free text, the instruction is worded differently in different reports, and the methods used to reference other reports vary as well. However, in many of the observed cases, the references cited a portion of the accession numbers given to all reports from a given patient sample.

Summary and Conclusions: Development and Validation of MicroParse

Principal Findings of MicroParse Validation

As demonstrated by the validation study, MicroParse performed quite well. MicroParse processes and stores reports very quickly and should scale well even if the number of reports processed by VUH increases significantly. Most of the issues encountered by the reviewer took little effort to fix. The problem with linking reports based on free text references within one of the reports presents a more difficult obstacle, but more sophisticated parsing techniques could potentially extract the information contained in the references.

Study Limitations during MicroParse Validation

The phrase-matching algorithms employed by MicroParse are quite simple and can be prone to error. When MicroParse encounters free text in a report, it will still attempt to match the text to phrases in the Microbiology Rosetta Stone and could potentially find spurious matches. For example, if the text "not consistent with *Pseudomonas aeruginosa*" appeared in a report, MicroParse would lump "not consistent with" into an `UNPARSED` phrase, but would match "*Pseudomonas aeruginosa*" to the encoded phrase `PSAER`, incorrectly suggesting that *P. aeruginosa* was present in the culture. Furthermore, important information such as the report linkage free text cannot be retrieved simply by using the phrase matching.

Nonetheless, the phrase matching technique provides several advantages as well. Since the vast majority of the text is made up of Microbiology Rosetta Stone phrases,

MicroParse correctly interprets a great deal of the report without any of the potential ambiguity that a more powerful natural language processing (NLP) technique might produce. In addition, implementing NLP techniques to parse `UNPARSED` phrases could allow MicroParse to take advantage of the benefits of both phrase matching and more advanced techniques.

The database structure is well-suited for interoperating with MicroParse, but from a database design standpoint, the structure is not optimal. In particular, the database has not been fully normalized. Database normalization involves moving redundant information within one table to a new table [100]. In general, database designers should strive for highly normalized tables, as normalization reduces data redundancy and prevents data anomalies.

In this database design, for example, an entry in the `specimen` table corresponds with a report received from the microbiology laboratory system. However, multiple entries in `specimen` are linked by `specimen_accession`, a value that uniquely identifies the sample from which the report was generated. Thus, when MicroParse processes multiple reports from a single specimen, it stores in the database redundant information such as medical record number (`specimen_mrn`), hospital unit (`specimen_unit`) and culture type/subtype (`specimen_type` and `specimen_subtype`), among others. To better normalize the database, we could thus add an `accession` table that stores an accession number with all shared information that links to several entries in `specimen`.

However, database normalization carries several side effects. First, database normalization requires consistent information. For example, if it was discovered that a

patient had mistakenly been assigned a second medical record number and the error was fixed between a preliminary culture result and the final result for a specimen drawn from that patient, the normalized database design would either (1) have a second entry in `accession` for the new accession number/medical record number combination or (2) discard either the new or old medical record number. In the first case, we would lose the convenient mapping of one entry in `accession` to one patient sample, making working with the database more difficult. In the second, we would needlessly discard information. Under the current design, each the two entries in `specimen` would still share the same `specimen_accession` value but would have different `specimen_mrn` values. This inconsistency is not problematic for our purposes since we can still link the two results to the same patient sample, and we maintain the one `specimen` entry to one culture result model without discarding any information.

In addition, since normalization creates more tables in a database, when retrieving information, the database package must perform more table joins, reducing reading performance. Since MicroParse only writes to the database once per report but other applications may perform many read attempts on each report, read access to the tables needs higher priority than write access.

Significance of Results of MicroParse Validation Study

MicroParse provides VUH with new opportunities. Studies and monitors involving microbiology data that would have previously involved chart reviews no longer require this potentially costly and time-consuming activity. Informatics staff have already begun a study on Group B streptococcal infections in pregnant women using the data

from MicroParse, and a monitor for *Bordetella pertussis* runs in association with an infection control study. MicroParse also provides the basis for the rest of this Master's Thesis project.

CHAPTER III

A RETROSPECTIVE ANALYSIS OF CONTACT PRECAUTIONS FOR VUH INPATIENTS WITH METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) AND VANCOMYCIN-RESISTANT ENTEROCOCCUS (VRE) ISOLATES

Introduction: Retrospective Analysis of Contact Precautions

The long-term objective of this project is to design, build, implement, and determine the efficacy of an intervention that increases contact precautions ordering rates for inpatients with MRSA or VRE infections. Yet to accomplish this task requires baseline infection rate information. For this reason, we conducted a retrospective study to measure the overall compliance with VUH's contact precautions policy for patients with MRSA and VRE isolates. As an adjunct to this retrospective study, and in preparation for the overall goal, the current project developed a dashboard to help VUH Infection Control staff to track information and notifications on patients with MRSA and VRE isolates and to allow project staff to collect retrospective and real-time information on contact precaution status and clinician isolation ordering rates.

Background: Retrospective Analysis of Contact Precautions

VUH Infection Control Service

The VUH Department of Infection Control and Prevention manually conducts surveillance "walk rounds" to determine and verify the actual contact precautions status of patients, and to monitor their progress. Both MRSA and VRE infections are often

acquired within hospitals. Hospital policy at VUH (and many other institutions) requires contact precautions for patients who have recent culture isolates for these organisms. Thus, the VUH Infection Control team monitors for patients colonized or infected with these organisms with a two-step process. First, Infection Control Practitioners (ICPs) compile the list of all inpatients with newly identified isolates of MRSA, VRE, and other drug-resistant or CDC-reportable organisms. The ICPs compile the list based on information that the microbiology lab delivers manually via telephone calls. The data from phone calls is supplemented by review of individual patient records in StarPanel. Then, ICPs conduct work rounds by walking through the hospital to determine which patients should be, and currently are, on contact precautions. Combining the results of these surveys with the microbiology data allows ICPs to identify those patients who require isolation but who are not yet isolated. For appropriate patients, the Infection Control team then recommends initiation or discontinuation of contact precautions to the clinicians caring for those patients.

Though the current Infection Control MRSA/VRE surveillance process works well, potential for improvement exists. Because the ICPs only can survey culture results and contact precautions status via rounding once per work day, day-long or weekend-long time lapses can occur between the first identification of a drug-resistant organism and the ICP taking appropriate actions, such as recommending contact precautions when isolation has not been ordered. In many cases, microbiology laboratory technicians act as a safety net, and will inform the ICPs of any particularly unusual results with a phone call. Nevertheless, gaps in this manual system can still occur, which might potentially

result in the spread of MRSA or VRE from an infected patient if contact precautions are not followed.

The project was able to externalize relevant data available from MicroParse to create a Web-based, real-time automated monitor to help ICPs follow inpatients with antibiotic-resistant bacterial isolates. The monitor concurrently tracks and displays this information for all relevant patients throughout VUH. This can potentially make identifying patients who require isolation a more straightforward process, providing the ICPs with access to the most up-to-date antibiotic resistant culture result information available.

By monitoring active CPOE system orders on inpatients, it is possible to capture another relevant aspect of contact precaution information. Generally, based on evidence accumulated by ICPs on their rounds, if a physician issues an order for contact precautions for a patient, it is a safe assumption that hospital staff will properly follow the order and initiate contact precautions for the patient, making a manual check less important. Unfortunately, the converse cannot be automatically assumed. In other words, the lack of an order for contact precautions does not necessarily indicate that a patient was not placed on contact precautions.

A patient on contact precautions may not have an active contact precautions order for several reasons. After learning of a patient with a new MRSA or VRE positive culture result, nursing unit personnel may act independently to initiate contact precautions per protocol (through hospital policy). Alternatively, an ICP may issue a recommendation to institute contact precautions for a patient without placing an order in the CPOE system. Similarly, if a physician gives a verbal contact precautions order, unless a staff member

remembers to enter the order into the CPOE system later, the contact precautions order may never be registered in the CPOE system, even though it is carried out. Another potentially problematic scenario might occur when a physician or nurse enters a CPOE order to initiate contact precautions, but does so as a free-text nursing order, rather than using the encoded order (e.g., "Nursing: please place this patient in a room with appropriate supplies and precautions to insure hospital protocol for MRSA infections is followed"). In such cases, the task of correctly identifying a patient's contact precaution status becomes substantially more difficult to do algorithmically than simply searching for an encoded contact precautions order.

For all of the above-listed reasons, the order data stored within the CPOE system may not necessarily represent a patient's true contact precautions status. Thus, accurately determining the overall contact precaution status for all hospitalized patients requires some degree of manual confirmation. However, CPOE order data can provide a good "first pass," yielding a starting point that will reduce the ICPs' workload.

Methods: Retrospective Analysis of Contact Precautions

MRSA/VRE Infection Control Dashboard

As described previously, the current method that the ICPs use to track patients' contact precautions status starts by checking all hospital rooms. With the data available from MicroParse, however, the ICPs could instead start by checking patients with known antibiotic-resistant infections or colonization and would thus reduce their workload. The

MRSA/VRE Infection Control Dashboard (MicroDash) facilitates the process of finding patients with MRSA or VRE to allow them this opportunity.

MicroDash consists of several functional units. The first is the data aggregator. The aggregator queries MicroParse for all culture results positive for MRSA or VRE and merges this information with current census data drawn from VUH's ADT system to determine which patients with a current or past positive culture for MRSA or VRE are presently hospitalized. For each inpatient on the merged list, the aggregator draws information from VUH's CPOE system to determine if they have an active contact precautions order. The results are cached on the StarPanel servers.

The next functional unit, the dashboard webpage, displays the cached data. It sorts the list of inpatients by nursing unit. Information about the patient's contact precautions status is displayed in 3 columns. The first is automatically populated and shows whether the aggregator identified a contact precautions order. The other two columns display whether the patient should be isolated and whether they are currently isolated; both fields are editable by the ICPs to reflect the results of their manual reviews. Figure 9 shows a screenshot from the dashboard webpage.

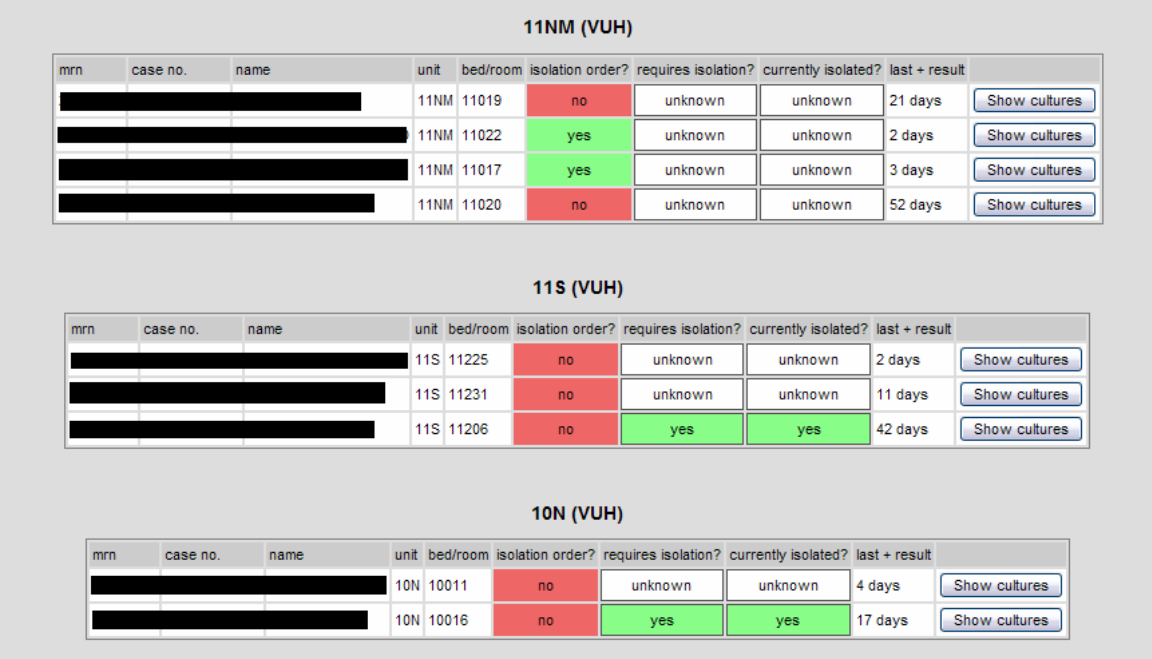


Figure 9: MRSA/VRE Infection Control Dashboard webpage

Retrospective Study of Contact Precautions Implementation

The study described in this section was reviewed by Vanderbilt University's Institutional Review Board in March 2006 with approval number #060237. To establish a baseline rate at which VUH clinicians order contact precautions for patients with MRSA or VRE isolates, we reviewed all VUH adult inpatient microbiological cultures from January 2001 through January 2006.

First, the "raw" Triple-G® microbiology reports in StarPanel were passed through MicroParse. Next, an automated program identified all inpatient and outpatient cultures which were positive for MRSA or VRE. Since patients could have multiple positive MRSA/VRE cultures during one hospitalization, we used a program that reviewed VUH CPOE log file data to compare the positive culture dates with hospital admission and

discharge dates, and determined the first positive MRSA/VRE isolation date for each patient admission in which a positive culture occurred.

Next, for each of these hospital admissions where an MRSA or VRE positive culture occurred, an automated program retrieved all CPOE nursing orders from each relevant patient's hospital stay. An automated program identified all contact precaution orders based on having unique orderable ID codes. The program further searched all free-text nursing orders for words and phrases suggesting that a given order was a contact precautions order (e.g., containing "contact", "precaution*", or "isolat*"). Finally, an automated program calculated the time that elapsed for that patient during that admission from the time of the first positive MRSA/VRE culture until the time of issuing the first contact precautions order. Patients with contact precautions orders antedating the first positive culture isolate were excluded from this portion of the analysis and analyzed separately. We set a maximum possible contact precautions order delay of 14 days to prevent extreme outliers from skewing the aggregate results. An automated program also cataloged all instances when no isolation order was issued during the admission, before or after a positive culture isolate.

Results: Retrospective Analysis of Contact Precautions

During the 61-month study period, there were 384,957 inpatient culture results. Of these culture reports, 3,303 (0.86%) contained MRSA and 530 (0.14%) contained VRE. Eliminating multiple positive cultures during the same admission yielded 2,268 MRSA/VRE cases. Matching these to contact precautions data from the VUH CPOE system yielded 1,019 patients properly placed on contact precautions before or after a

positive MRSA/VRE isolate, for an overall rate of 45.1%. This aggregate figure of 45.1% includes 132 patients placed on contact precautions prior to the culture result and 887 patients with precautions following the culture. An average time of 3.6 days elapsed between the positive result and the contact precautions order for the 887 patients who had a contact precautions order after the result. Figure 10 shows the average time lapse between a positive culture and the contact precautions order.

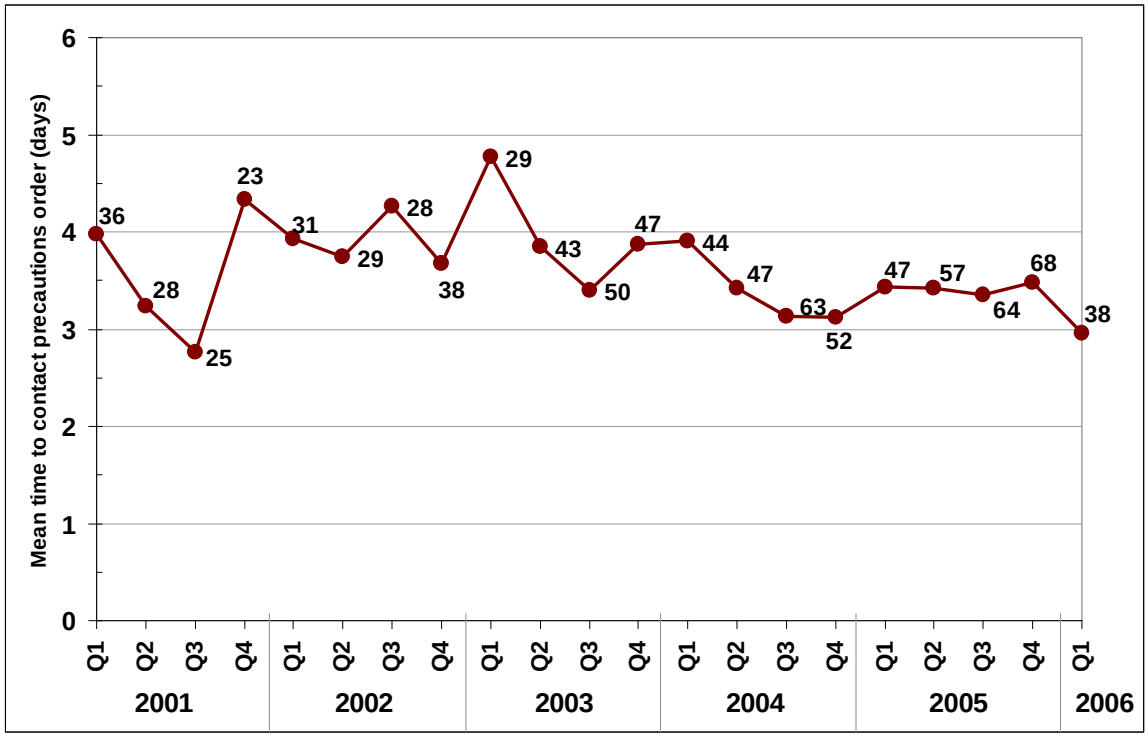


Figure 10: Time elapsed between MRSA/VRE positive culture result and contact precautions order for 887 patients isolated following a culture result by quarter

We attempted to estimate the true rate of contact precaution implementation, since, as previously noted, some patients without isolation orders nevertheless have appropriate precautions implemented on the hospital ward. An automated program identified all inpatient positive MRSA and VRE cultures from May-June 2007. Again,

with IRB approval, the project leader (R.C.) manually cross-checked those patients for whom an automated program indicated no contact precautions order had been entered in the CPOE logs against the manually generated ICP contact precautions records that had been stored in MicroDash. Of the 127 inpatients during the time period who had at least one positive MRSA or VRE culture (107 with MRSA and 20 with VRE), review of CPOE records indicated that contact precaution orders were present for 65 (51.2%). For the 62 culture-positive patients without a CPOE contact precautions order, review of ICP records indicated that 42 (67.7% of the 62, and 16.6% overall) of the patients had indeed been placed on contact precautions at some point during their hospitalization, yielding a total of 107 of the original 127 patients (84.3%) who were correctly placed on contact precautions.

We assumed that the rate determined by our audit of 67.7% of all culture-positive patients who did not have an identified contact precautions order but were actually on contact precautions was a valid approximation for use on retrospective data. Thus, out of the initial 2,268 patients in our previously described retrospective study, 1,019 had contact precautions orders identified from the CPOE system logs, and we then estimated that 846 had contact precautions orders that could not be detected, yielding an overall contact precautions implementation rate of 82.2%. Figure 11 shows the CPOE-ordered and estimated overall contact precautions implementation rates by quarter for the study period. Because the ICPs do not collect information on the time contact precautions were initiated, we cannot evaluate the time lapse between the positive culture to the contact precautions order in the group for which we could not automatically detect the order.

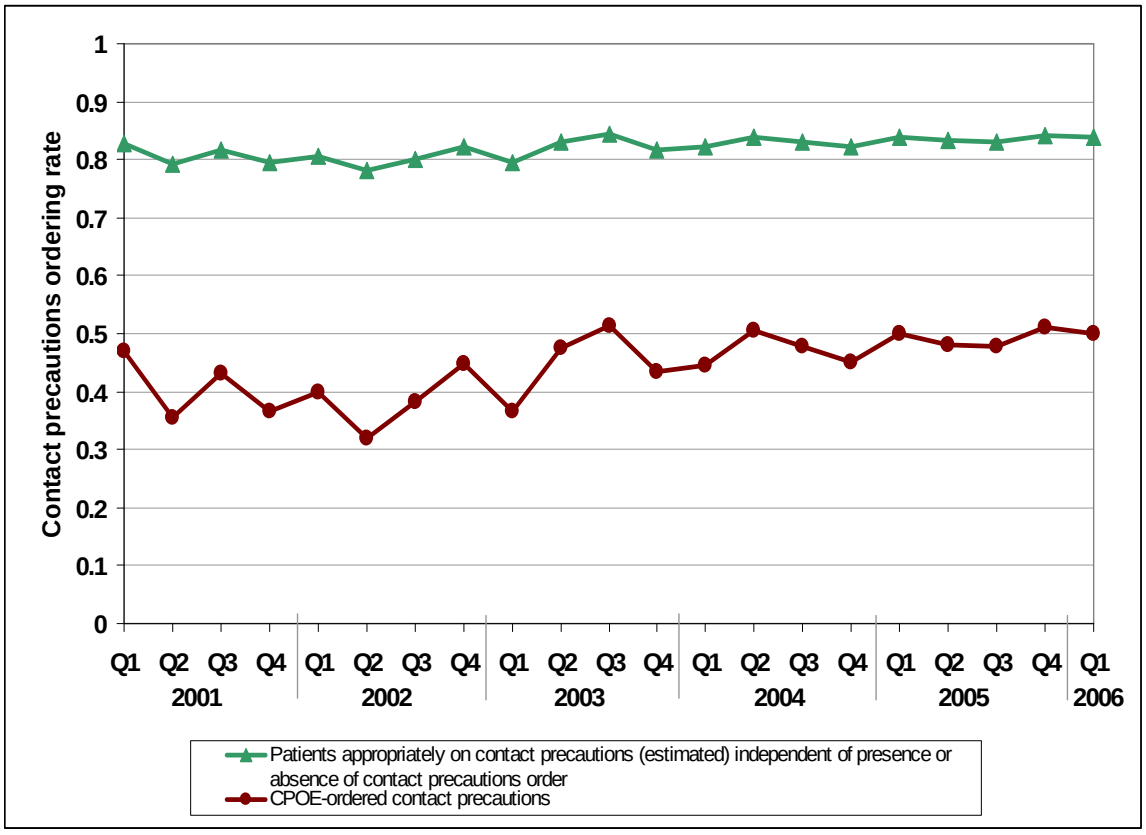


Figure 11: Contact precautions implementation rates for inpatients with MRSA or VRE positive culture

Summary and Conclusions: Retrospective Analysis of Contact Precautions

Principal Findings

Though VUH clinicians generally follow contact precautions policy correctly, the retrospective study suggests that approximately 1 out of every 5 patients with a new MRSA or VRE positive culture does not receive the proper hospital-policy-recommended contact precautions. Even when staff correctly initiate contact precautions, the orders are not always implemented immediately following a positive culture. Failing to follow

contact precautions for any length of time might potentially lead to an outbreak of infections.

Because contact precautions are an infection control measure rather than a method of treating an individual patient's symptoms, a clinician may not remember to order them without some external reminder. The ICPs often provide reminders, but using highly skilled and already busy ICPs to perform clerical duties such as telephoning clinicians is a tedious use of their time. Given the importance of contact precautions and the current lack of a better way to remind clinicians, however, the ICPs currently do not have any other options.

MicroDash has anecdotally helped the ICPs in the identification of patients with MRSA or VRE positive cultures. Feedback from the ICPs has suggested that the real-time dashboard provides them with earlier notice of antibiotic-resistant infections than relying on the telephone calls from the microbiology lab. On several occasions, microbiology lab staff called several hours after the new report appeared on MicroDash. In addition, during the study, clinical staff notified the ICPs that one patient on contact precautions did not have an antibiotic-resistant infection. MicroDash showed this patient as having MRSA. After closer examination, the ICPs determined that the original Triple-G® microbiology report contained a methicillin-sensitive *S. aureus* isolate that was incorrectly labeled as methicillin-resistant. Searching the MicroParse database yielded 7 additional cases of methicillin-sensitive *S. aureus* labeled in Triple-G® as MRSA, along with 8 cases of methicillin-resistant coagulase positive *Staphylococcus* (i.e., *S. aureus*) that had not been labeled as MRSA in Triple-G®.

Study Limitations

The high rate (67.7%) of missed contact precautions implementation for those culture-positive patients lacking CPOE orders for precautions suggests that the methods MicroDash currently uses to retrieve orders may be systematically missing orders. Clinicians may also frequently forget to use the CPOE system to place orders, instead issuing them informally as verbal requests. However, given the CPOE system's central role in the VUH medical culture, it seems surprising that nearly half of the contact precautions orders initiated at VUH are not being entered into the CPOE system. Further study into how physicians order contact precautions could provide valuable insight that might help MicroDash better judge contact precautions status for a patient.

When measuring the time between the positive culture result and the initiation of contact precautions, we used the time of the contact precautions order. If contact precautions generally start before clinicians enter the contact precautions orders into the CPOE system, however, the study may have systematically overestimated the time lapse. Nonetheless, driving down the time between the positive culture result and the CPOE order still represents a helpful goal. If clinicians always enter their contact precautions orders in the CPOE system and on time, the ICPs would no longer need to conduct walking rounds to accurately assess a patient's contact precautions status.

Finally, while MicroDash can help make information gathering easier for the ICPs, the task of reminding clinicians to order contact precautions remains. We plan to create a CPOE-based alert to automatically remind clinicians to order contact precautions for patients who require them.

Significance of Results

The retrospective study of contact precautions demonstrated that compliance with VUH contact precautions policy can be improved. Future work in this area should target 3 areas: (1) increasing contact precautions ordering rates for patients with MRSA or VRE positive cultures, (2) increasing the number contact precautions orders entered through CPOE, and (3) decreasing the time between an MRSA or VRE positive culture and initiation of contact precautions.

MicroDash provides the ICPs with a real-time tool to monitor antibiotic resistance in the hospital. By building in more flexibility into MicroDash, it could replace some of their currently non-automated workflow (e.g., the daily contact precautions status spreadsheet).

CHAPTER IV

DEVELOPMENT OF A COMPUTERIZED ANTIBIOGRAM

Introduction: Development of a Computerized Antibiogram for VUH

An antibiogram is a table or chart that summarizes all patient culture sensitivity results for a given time period – by organism isolated -- for a hospital or for selected clinical units within a hospital or clinic. Antibiograms provide useful tools for determining which antibiotics to select when treating an infection especially before sensitivities are reported for the organism(s) causing a specific patient's infection. Because antibiotic resistance patterns can change drastically over time, a previously effective antibiotic for treating Gram-negative-rod related infections years or even months ago may be almost useless at the present time.

We developed a computerized antibiogram construction tool to give VUH clinical users the most up-to-date information about antibiotic resistance possible using electronically available resources. We hypothesized that the tool will help improve patient care, but have only begun to evaluate its effectiveness in a number of settings. Prior to this study, VUH microbiology lab staff had to manually collect all antibiotic resistance data from a given period of time in order to create antibiograms. With the large number of cultures conducted at VUH, this presented a very difficult and time-consuming task. Using cumulative microbiology data stored by MicroParse, we created an automated antibiogram tool, called MicroGram.

Methods: Development of a Computerized Antibiogram for VUH

Creating and Evaluating an Antibiogram

MicroGram constructs antibiograms following standard guidelines for doing so that are published by the Clinical and Laboratory Standards Institute (CLSI) [94]. First, MicroGram selects an appropriate window of time (3-6 months prior to the current date). It then retrieves all antibiotic sensitivity data from MicroParse for that time frame. The CLSI standard recommends using only the first isolated organism (of each type) per patient to generate the antibiogram to avoid counting a single isolated bacterium several times when a patient has several cultures positive for that organism within a short timeframe. Thus, MicroGram discards all sensitivities for which an earlier matching isolate (organism, not sensitivity pattern) exists from the same patient.

Whenever the time period of interest includes at least 10 unique case-isolates for a given organism/antibiotic pair, MicroGram calculates the percentages of isolates for that organism that were sensitive, intermediate, and resistant to each tested antibiotic. If MicroGram finds the time period contains fewer than 10 isolates for an organism/antibiotic pair, it queries the MicroParse database for all historical sensitivity data for that pair, not limited to the index time period. If MicroGram finds 10 isolates in the complete historical data set, it will perform the sensitivity rate calculations for the organism/antibiotic pair; otherwise, MicroGram skips the pair in calculating the antibiograms.

Once MicroGram has calculated all sensitivity percentages, it caches a table containing the organism names, antibiotic names, and sensitivity percentages on the

StarPanel servers and generates a graphical representation for the sensitivity patterns of each organism/antibiotic pair. To view the data, users can access either of two different MicroGram web interfaces. The first interface provides a standard grid (simple tabular) antibiogram, a form often used when manually constructing antibiograms. This view allows clinicians to compare the efficacy of an antibiotic on different organisms. The second interface provides a graphical view of the resistance patterns for one organism at a time. Both views allow the user to examine antibiograms for particular units or for certain culture types. Figure 12 and Figure 13 in Appendix A show the two interfaces.

To assess the validity of the antibiograms MicroParse generates, we selected two organisms and manually constructed an antibiogram for them using "raw" Triple-G® output. We chose *Acinetobacter baumannii*, since different isolates often have different resistance patterns, and *Morganella morganii*, a less commonly observed organism that would likely require more than 6 months of data to find 10 isolates.

To assess the clinical usefulness of each MicroGram interface, a formative evaluation enlisted several clinicians to review both versions of the antibiogram and to then complete a survey. The survey instrument is shown in Figure 14 in Appendix A.

Results: Development of a Computerized Antibiogram

Antibiogram Validation

Project member R.C. reviewed 171 VUH culture and sensitivity reports for *Acinetobacter baumannii* from January to July, 2007 and found 71 distinct medical

record numbers in that time period. Project member R.C. reviewed 11 VUH culture and sensitivity reports for *Morganella morganii* January to July, all from distinct medical record numbers. For several antibiotics (amoxicillin/clavulanic acid, ampicillin/sulbactam, ampicillin, cefazolin, imipenem, minocycline, and nitrofurantoin), retrieving 10 tested isolates required a search in a more than a year-long interval. The manually generated antibiograms matched those generated by MicroGram. Table 1 shows the corresponding MicroGram antibiogram for *A. baumannii* and Table 2 shows the MicroGram result for *M. morganii*. No antibiotics were consistently effective against *A. baumannii*, but amikacin and imipenem were always effective against *M. morganii*.

Table 1: Antibiogram for *Acinetobacter baumannii* in VUH as of July 23, 2007

Antibiotic	% sensitive	n	Days
Amikacin	34	71	180
Amox/Clav Acid	0	13	182
AMP/Sulbactam	31	64	180
Ampicillin	0	13	182
Cefazolin	0	13	182
Cefepime	4	71	180
Cefotaxime	1	71	180
Gentamicin	24	71	180
Imipenem	26	66	180
Levofloxacin	20	71	180
Minocycline	35	62	180
Nitrofurantoin	0	13	182
Pip/Tazo	18	71	180
Sulfa Trimethoprim	23	71	180
Tobramycin	30	69	180

Table 2: Antibiogram for *Morganella morganii* in VUH as of July 23, 2007

Antibiotic	% sensitive	n	Days
Amikacin	100	11	180
Amox/Clav Acid	0	10	399
AMP/Sulbactam	40	10	363
Ampicillin	0	10	399
Cefazolin	0	10	399
Cefepime	64	11	180
Cefotaxime	45	11	180
Gentamicin	73	11	180
Imipenem	100	10	363
Levofloxacin	64	11	180
Minocycline	20	10	363
Nitrofurantoin	0	10	399
Pip/Tazo	91	11	180
Sulfa Trimethoprim	55	11	180
Tobramycin	91	11	180

Clinician Formative MicroGram Survey Results

Nine volunteer clinicians (1 internist, 2 surgeons, 4 infectious disease specialists, 1 microbiologist, and 1 pulmonologist) received by e-mail a link to the sample MicroGram antibiograms with a second link to the survey instrument. After the nine volunteers shared the link with a few colleagues, we received 10 survey responses. Table 3 shows the responses to each of the survey questions. Feedback was largely positive, and all survey takers agreed that the data contained in the antibiogram appeared to be correct.

Table 3: Antibiogram survey results

Question	Mean response
1. Overall, this antibiogram would be useful (1=Strongly agree, 5=Strongly disagree)	1.1 (range:1-2)
2. The antibiogram is clear and easy to read (1=Strongly agree, 5=Strongly disagree)	1.4 (range:1-2)
3. View preference:	4 prefer grid view 2 prefer individual view 4 no preference
4. Antibiograms would provide data I need for patient care that is not currently readily available (1=Strongly agree, 5=Strongly disagree)	1.4 (range: 1-4)
5. Having an online antibiogram available will improve the care of my patients (1=Strongly agree, 5=Strongly disagree)	1.1 (range: 1-2)
6. If regularly available, I would use an antibiogram:	5 would use weekly 5 would use daily

Feedback on the free text sections of the survey suggested that clinicians would primarily use an antibiogram to keep abreast of antibiotic sensitivity patterns and to help in antibiotic selection, particularly when deciding on an early course of empiric therapy. The survey responses also contained several layout change suggestions (e.g., label Gram-positive and Gram-negative tables in the grid view, include antibiotic trade names to reduce the possibility of errors) that will be incorporated into future versions of MicroGram.

Summary and Conclusions: Development of a Computerized Antibiogram

Principal Findings

The positive survey results suggest that VUH clinicians recognize the potential for MicroGram to improve patient care once it is fully implemented. The results also

suggest that MicroGram can potentially provide an effective means of accessing antibiogram information. Based on the free text responses, some fine tuning, but no major changes, should be carried out for the two MicroGram (grid view and individual organism view) displays.

Study Limitations

Because we directly asked the clinicians to volunteer to participate in the informal formative evaluation of MicroGram, the survey results may be biased in favor of the importance of antibiograms. The clinicians who participated were primarily those who would stand to benefit most from having an antibiogram available (e.g., trauma surgeons and infection control physicians).

The current implementation of MicroGram is near real-time but slow enough to be of concern if physicians want to rapidly review a number of sensitivity patterns for various clinical settings. For the initial version of MicroGram, queries used to extract the information from the MicroParse database originally took approximately 5-10 minutes for each specific antibiogram (e.g. all VUH cultures, VCH urine cultures, 10N BAL cultures). Performing each query sequentially upon end-user requests for data would entail a slow and frustrating end-user experience. Creation of additional indices in the MicroParse database reduced the query time to 30-90 seconds each, but this performance level remains unacceptable for actual clinical use. The current plan is to improve MicroGram's response times by running all possible queries (possibly staggered in time) daily and caching the results. Then MicroGram could generate antibiograms from cached data much more efficiently. Alternative approaches include methods to cache portions of

the data while still retrieving new culture data when loading MicroGram, thus giving the user the most current antibiogram possible.

Significance of Results

MicroGram provides VUH clinicians with antibiograms that can help improve antibiotic selection and therefore patient safety. Since MicroGram can generate the antibiograms without requiring human assistance, there tedious work of constructing them at infrequent intervals is no longer an obstacle to clinical care.

CHAPTER V

SYNOPSIS AND CONCLUSIONS

Summary

This project provided VUH clinicians and staff with new computerized tools to improve patient care. The MicroParse tool allows its users to search the microbiology results database flexibly, facilitating a number of approaches to monitoring microbiological data. The MicroGram tool gives VUH clinicians important data that can assist in antibiotic selection and to monitor for new patterns of antibiotic resistance. The MicroDash tool provides VUH ICPs with a means of tracking inpatients with a history of antibiotic-resistant colonization or infection, and a rapid notification mechanism to identify new patients with these conditions. The retrospective analysis of compliance with VUH contact precautions policy demonstrated that there are opportunities to improve the ordering of contact precautions for eligible inpatients with MRSA or VRE isolates and to improve the timeliness of the contact precaution orders following a new positive MRSA or VRE culture result.

Future Directions

To take advantage of the opportunities to improve compliance with contact precautions policy, we plan to develop a CPOE-based alert that will remind clinicians to order contact precautions for patients who require them based on culture results. Because MicroParse can provide real-time microbiology results, the CPOE system, informed by

MicroParse, can generate these alerts during the first ordering session immediately following the positive culture result. Through this approach, we hope to not only improve the percentage of patients properly placed on contact precautions but also the timeliness of the orders.

Since the current method of storing the microbiology data in the MicroParse database uses the coded phrases from the VUH Microbiology Thesaurus, any programs created that using the data will not be interoperable with other systems. To remove this limitation, we hope to abstract out the VUH Microbiology Thesaurus by either finding or creating a basic microbiology terminology that we can then use to "tag" phrases. These tags will allow MicroParse to merge phrases referring to the same concept and to combine phrases logically (e.g., combining information about quantity with information about the organism isolated). Furthermore, it will allow VUH to share programs with other institutions if both sites are using the same terminology.

Finally, while MicroGram provides antibiogram data to VUH clinicians, it does not provide any active assistance in antibiotic selection. To provide this assistance, we would like to develop a computer-based antibiotic advisor. An antibiotic advisor similar to the kind developed at LDS Hospital in Salt Lake City [53, 55] could streamline the antibiotic selection process, from empiric therapy to final antibiotic selection once sensitivity information is available.

APPENDIX A

SUPPLEMENTARY FIGURES

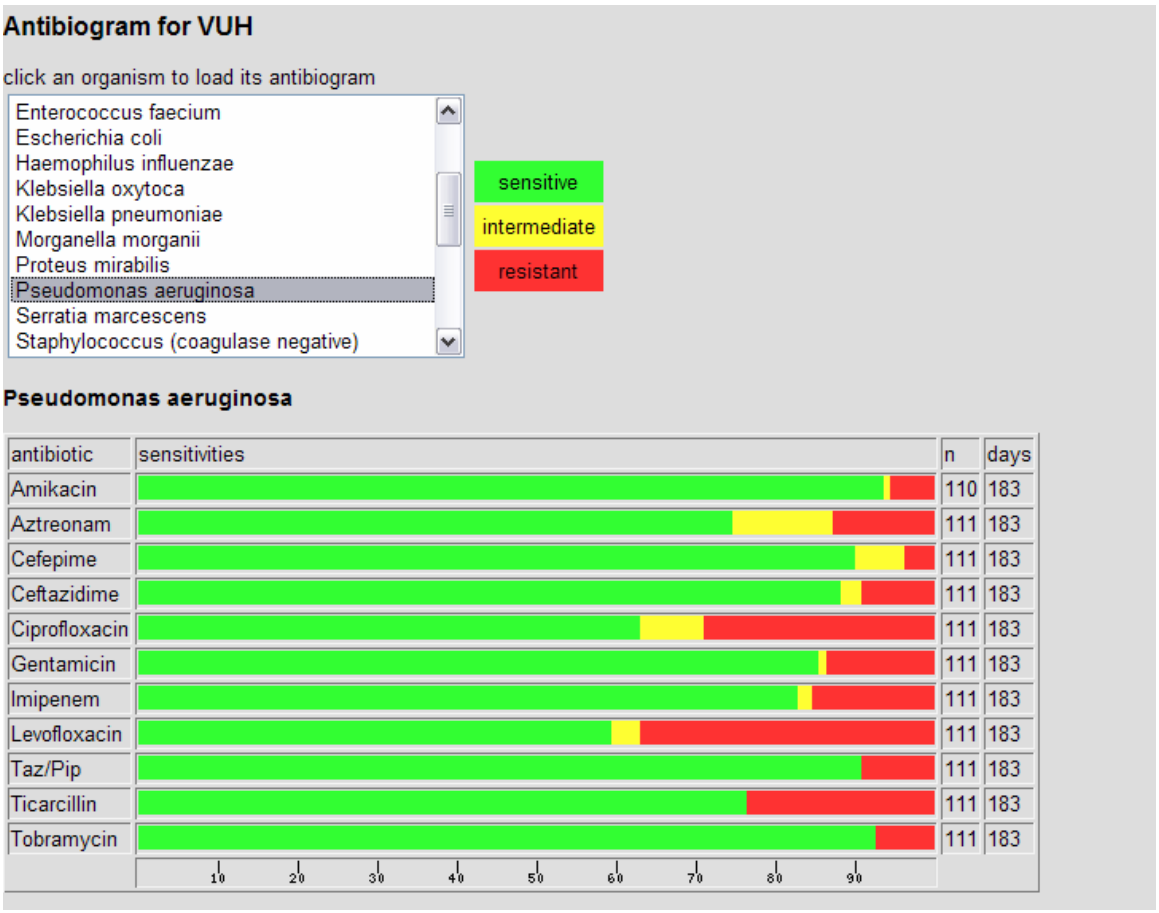
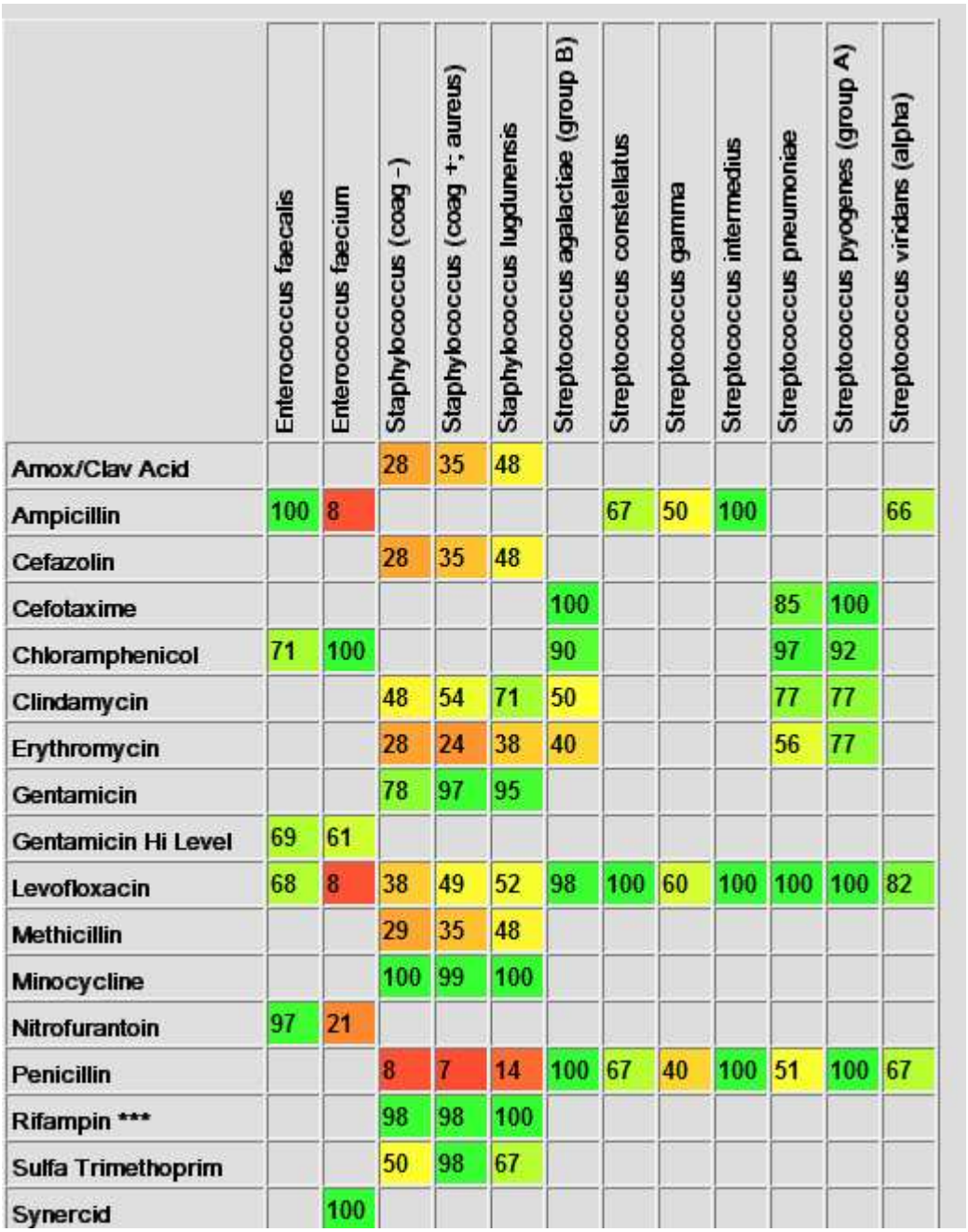


Figure 12: Individual organism view in MicroGram



	Enterococcus faecalis	Enterococcus faecium	Staphylococcus (coag -)	Staphylococcus (coag +; aureus)	Staphylococcus lugdunensis	Streptococcus agalactiae (group B)	Streptococcus constellatus	Streptococcus gamma	Streptococcus intermedius	Streptococcus pneumoniae	Streptococcus pyogenes (group A)	Streptococcus viridans (alpha)
Amox/Clav Acid			28	35	48							
Ampicillin	100	8					67	50	100			66
Cefazolin			28	35	48							
Cefotaxime						100				85	100	
Chloramphenicol	71	100				90				97	92	
Clindamycin			48	54	71	50				77	77	
Erythromycin			28	24	38	40				56	77	
Gentamicin			78	97	95							
Gentamicin Hi Level	69	61										
Levofloxacin	68	8	38	49	52	98	100	60	100	100	100	82
Methicillin			29	35	48							
Minocycline			100	99	100							
Nitrofurantoin	97	21										
Penicillin			8	7	14	100	67	40	100	51	100	67
Rifampin ***			98	98	100							
Sulfa Trimethoprim			50	98	67							
Synercid		100										

Figure 13: Grid view in MicroGram

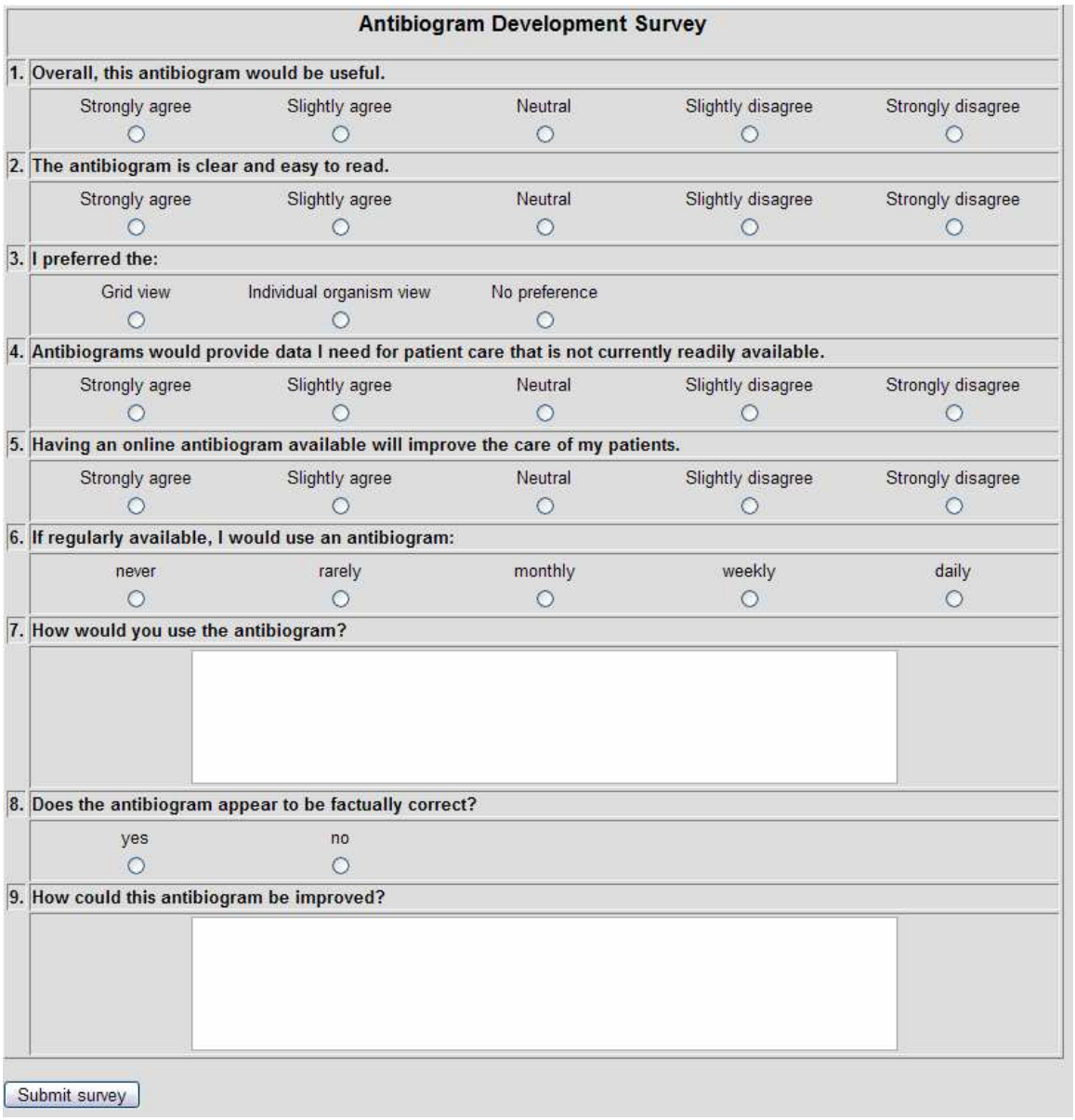


Figure 14: Antibiogram development survey

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