The Marriage of Antimicrobial Stewardship and Informatics: Improving Patient Outcomes with Technology

Jamie Kisgen, Pharm.D., BCPS
Clinical Assistant Professor
University of Florida College of Pharmacy

Disclosure

• I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation

Objectives

• Upon completion of this activity, the participant should be able to:
  – Discuss opportunities for improving antimicrobial stewardship with your existing pharmacy system
  – Compare and contrast the various clinical decision support systems available for antimicrobial stewardship
  – Describe how pharmacists can utilize new microbiology technology to improve patient outcomes and decrease overall costs

Guidelines

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship


IDSASHEA Guidelines

“Health care information technology in the form of electronic medical records (A-III), computer physician order entry (B-II), and clinical decision support (B-II) can improve antimicrobial decisions through the incorporation of data on patient-specific microbiology cultures and susceptibilities, hepatic and renal function, drug-drug interactions, allergies, and cost.”

Speaking the Same Language

Pharmacy Clinical Systems
- Allscripts Sunrise Pharmacy
- Cerner PharmNet and PowerChart
- CPSI
- Epic Willow
- Healthcare Management Systems HMS Pharmacy
- McKesson Horizon Meds Manager
- Meditech's Pharmacy Solution
- Netsmart Technologies Rx Connect
- Siemens Pharmacy

Custom Stewardship Reports
- Antibiotic therapy greater than 5 days
- Bug-drug mismatch
  - Must have a link to Microbiology data
- Duplicate therapy
  - e.g., piperillin/tazobactam PLUS metronidazole
- IV to PO antibiotics
- Pharmacy consult for antibiotic dosing
- Restricted antimicrobials
  - Antibiotics, antifungals, antivirals

Antibiotic Therapy Greater than 5 Days

Bug-Drug Mismatch

Duplicate Therapy
Other Options

- Automatic stop dates or alerts
- IV to PO alerts
- Vancomycin trough < 10 mg/L or > 20 mg/L
- Aminoglycoside levels not at goal
- *Clostridium difficile* (+) and on non-CDI antibiotic
- WBC > 15 x 10^9/µL PLUS documented Fever
- Renal dosing alerts (e.g., Cefepime and CrCl < 30 ml/min)
- Vaccination eligibility (Influenza, Pneumococcal, Tdap)
- Vancomycin and culture positive for CoNS or MSSA

Time Commitment is Critical

<table>
<thead>
<tr>
<th>Type of Report</th>
<th>Estimated Time</th>
<th>Example Tasks</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 days of Antibiotic therapy</td>
<td>4 hours</td>
<td>Pull active orders, patient specific data</td>
</tr>
<tr>
<td>Bug-Drug Mismatch</td>
<td>8 hours</td>
<td>Pull lab (3 days) and patient specific data</td>
</tr>
<tr>
<td>Duplicate Therapy</td>
<td>4 hours</td>
<td>Pair active orders with AHFS class</td>
</tr>
<tr>
<td>Antibiotic Consult</td>
<td>8 hours</td>
<td>Pull active orders, patient specific data for anyone</td>
</tr>
</tbody>
</table>

Clinical Decision Support Systems (CDSS)

- Most were originally developed for infection control
  - Pharmacy was secondary goal
- Data sent to 3rd party software (HL7) where it is collated and analyzed based on pre-built algorithms
- 2 different types of systems available:
  - Passive: user queries the database for possible interventions
  - Active: pushes the information/alert directly to the user
- Relatively expensive, based on institution size, ranging from $100,000-$500,000 per year
Historic barriers

• Need all computer systems to speak the same language (microbiology, pharmacy, ADT, etc)
• Cost of implementation
  – Who is going to pay? (silo effect)
• Concern for liability if system not accessed or advice is not followed
• Does it truly augment current system/processes
• Need human resources to query and act on alerts
• Alert fatigue

CDSS Third Party Vendors

• Theradoc by Hospira Inc.
• MedMined by CareFusion
• SafetyAdvisor by Premier Inc.
• Sentri7 by Wolters Kluwer Health
• Quality Compass by The Advisory Board
• Vigilanz by Vigilanz Corporation
• ABX Alert by ICNet

Common Features

• IV to PO conversions
• Bug-drug mismatch
• Duplicate therapy
• Documentation of interventions
• External reporting and benchmarking to NHSN**
• Dosing rules**
• Drug interactions**

**Available now from several vendors, future release in others

Theradoc Key Features

• Founded in 1999 (one of the oldest commercial systems)
• Modules for infection control, pharmacy, and physicians
  – Modules for anticoagulation, adverse drug events, and MD rounds are also available
• Real time alerts (can be sent via email or pager)
• On demand antibiogram, custom reports for MUE
• Can incorporate eMAR data for usage trending (DOT)
• Able to report and benchmark to NHSN
• Ranked #1 in 2012 by KLAS for “Infection Control & Monitoring software”

www.klasresearch.com

Theradoc Alerts

Rounds Assistant
MedMined Key Features

- Clinical data sent outside for analysis
  - Alerts/reports sent back to user for feedback and intervention
- Infection control and pharmacy are key users
- Automated system for finding patients with possible nosocomial infections based on clinical data
- Customizable stewardship alerts and antibiograms
  - Non-stewardship capabilities as well (e.g., TDM, anticoagulation)
- Able to report and benchmark to NHSN
- Financial analysis provided to clinical group and C-suite
- Ranked #2 in 2012 by KLAS

www.klasresearch.com

Patient Event Advisor

SafetyAdvisor

- Formally known as “SafetySurveillor”
- Real time alerts made up of predefined event library or customizable alerts defined by user
  - Have to determine “actionable alerts” to avoid alert fatigue
- Rounds support and NHSN reporting available
- Access to members of Premier Alliance (~2600 facilities) for sharing of best practices, education content
- Ranked #3 in 2012 by KLAS for “Infection Control & Monitoring software”

www.klasresearch.com

Prospective Audit and CDSS

- Quasi-experimental pre-/postintervention study
- Single center study over 6 months
- Prospective audit, intervention, and feedback by the ASP began following implementation of CDSS
- 3,153 alerts (30%) were considered actionable
- ASP intervention occurred on 75-92% of actionable alerts with an acceptance rate of 88%
- Significant amount of time required by ASP due to volume
  - 2-3 hours/day to review alerts
  - 1-2 hours for interventions on actionable alerts and documentation


Does CDSS Work?

- Single center, randomized controlled trial over 3 months
  - Standard of care group (even MRN): manual review of patients on antibiotics for possible interventions
  - CDSS group (odd MRN): 32 alerts created to detect potentially inadequate or inappropriate antibiotic use
- Interventions: 359 (16%) vs 180 (8%) patients
- Cost savings of $84,194 ~ $37.64 per patient
- One hour saved each day performing patient reviews
- No significant difference in mortality or length of stay

MRN: Medical record number
Questions to Ask Regarding CDSS

• What can your current system do for you?
• What is Infection Control using now for surveillance?
  – If so, will the vendor guarantee compliance with NHSN?
• What are the start-up and maintenance costs?
  – Which cost center will this come from? (Pharmacy, Quality)
• What is the real timeline for implementation?
• Is your IT department willing to take this on right now and devote resources?
  – Competing priorities (e.g., meaningful use)
• Will the data remain onsite or offsite?

Questions to Ask Regarding CDSS

• Who will have access (RPh, MD, RN, IC) and does the number of users affect costs?
• What else can it do beyond stewardship?
  – Infection Control, Anticoagulation, Core Measures, NPSG’s?
• Will the reports and alerts come pre-built or will they have to be created by you?
• Can it capture days of therapy or administration(eMAR)?
• What is coming next year? 5 years?
• Who else is using the software? (names, emails)
  – Consider a site visit to see it in action!

Current EMR vs External Vendor

Pros of using Current EMR
  – Less expensive in the long run (no outside fees)
  – Single system improves efficiency (one-stop-shop)
  – Customizable to your specific institutional needs
  – Less concerns with integration
  – Easy retrieval of data for research
  – More prescriber level alerts and education available


Current EMR vs External Vendor

Pros of External Vendor
  – Less upfront institutional investment (time, manpower)
  – Many parts come pre-built
  – Minimal maintenance by hospital IT
  – Can help Infection Control and Pharmacy at the same time
  – Constantly updating and improving due to competition, feedback
  – Many reports/alerts can be created by user instead of IT

Antimicrobial Stewardship and Rapid Diagnostic Tests

Geiger et al. Am J. Health-Syst Pharm. 2013; 70:335-42
New Rapid Assays

- Rapid PCR (e.g., Cepheid, BD GeneOhm, Genprobe, Roche Molecular Systems)
- PNA FISH (e.g., AdvanDx)
- MALDI-TOF (e.g., Bruker Daltonics Inc.)
- Nucleic Acid (e.g., Nanosphere)
- Bacteriophage (e.g., Micro-Phage)

Rapid Polymerase Chain Reaction (rPCR)

- Most are highly sensitive and specific (>90%)
- Quicker turnaround time compared to traditional culture methods (hours instead of days)
- Majority have been approved for surveillance and some available for active infections (wounds, blood)
- Higher cost compared to traditional methods
  - Most require you to purchase proprietary equipment
  - Lab technician time and training needs to be factored in as well

Rapid PCR Pathogens

Cepheid GeneXpert
- Chlamydia trachomatis and Neisseria gonorrhoeae
- Clostridium difficile
- Enterovirus
- Group B Streptococcus
- Influenza virus
- MRSA/MSSA in nares
- MRSA/MSSA/CoNS
- VRE – van A

BD GeneOhm
- Clostridium difficile
- MRSA in nares
- VRE – vanA and vanB
- Group B Streptococcus

Rapid PCR Comparison

<table>
<thead>
<tr>
<th>Test</th>
<th>Minimum Turnaround</th>
<th>Sample Sites</th>
<th>Sens/Spec</th>
<th>Min Test Cost</th>
<th>Cost/Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>GeneOhm MRSA/ACP</td>
<td>2 hr</td>
<td>Nasal, groin, wound</td>
<td>91-100/95-99</td>
<td>Not Available</td>
<td>$30</td>
</tr>
<tr>
<td>GeneOhm StaphSR</td>
<td>2 hr</td>
<td>Blood, nasal, wound</td>
<td>96-100/95-98</td>
<td>Not Available</td>
<td>$30</td>
</tr>
<tr>
<td>Xpert MRSA/SA BC</td>
<td>1 hr</td>
<td>Blood</td>
<td>75-98/99-100</td>
<td>$29,000</td>
<td>$65</td>
</tr>
<tr>
<td>Xpert MRSA/SA SST1</td>
<td>1 hr</td>
<td>Wound</td>
<td>97/96</td>
<td>$29,000</td>
<td>$65</td>
</tr>
<tr>
<td>LightCycler MRSA</td>
<td>2 hr</td>
<td>Nasal</td>
<td>92/99</td>
<td>$50,000</td>
<td>$50</td>
</tr>
<tr>
<td>KeyPath MRSA/MSSA</td>
<td>5 hr</td>
<td>Nasal</td>
<td>92/98</td>
<td>$0</td>
<td>$55</td>
</tr>
</tbody>
</table>

Staphylococcus aureus Bacteremia and ASP

- Single center retrospective study pre and post rPCR implementation
  - Test performed 24 hours per day/7 days per week
  - ID pharmacist contacted with results of rPCR
  - Appropriate antibiotics and ID consults recommended
- n=156 patients with Staphylococcus aureus bacteremia
  - MRSA rate was 59% pre vs 45% post rPCR (p=0.08)
  - Excluded pts with coagulase-negative Staphylococcus
- Multivariable regression assessed clinical and economic outcomes

Results

- Mean length of stay 6.2 days shorter (p=0.07)
- Mean hospital costs were $21,377 less (p=0.02)
Staphylococcus Bacteremia w/o ASP

- Retrospective, pre/post interventional cohort conducted at two 500-bed tertiary medical centers
  - Performed at 1000/1900 M-F and at 1500 on weekends
  - MRSA results called to floor RN, no pharmacy intervention
  - pre-PCR = 68 vs post-PCR = 58
- Time to identification reduced by 13.2 hours (p<0.0001)
- Time to optimal antibiotic therapy was not reduced
  - Overall: 23.8 hours pre-PCR vs 25 hours post-PCR (p>0.1)
  - MRSA: 10.7 hours pre-PCR vs 14.4 hours post-PCR (p>0.1)


Peptide nucleic acid fluorescence in situ hybridization (PNA FISH)

*DNA Molecular Structure*
- DNA and RNA have a negatively charged super phosphate backbone.

*PNA Molecular Structure*
- RNA has a non-charged polyethylene or “peptide” backbone.

DNA Probe Binding to PNA Target
- DNA probes must overcome a destabilizing electrostatic repulsion among hybridizing complementary nucleic acids.

DNA Probe Binding to PNA Target
- The non-charged backbone of PNA permits access to the minor groove of DNA duplexes.

www.advanx.com

PNA FISH Available Tests

**PNA FISH Tests (~90 min)**
- *S. aureus/Coagulase-negative staphylococcus*
- *E. faecalis/faecium/other*
- *E. coli/P aeruginosa*
- Gram negative rods Traffic Light®: *E. coli, Pseudomonas, Klebsiella*
- *C. albicans/C. glabrata kit*
- *Yeast Traffic Light® kit - C. albicans, C. parapsilosis, C. tropicalis, C. glabrata or C. krusei*

**QuickFISH (~20 min)**
- *Staphylococcus QuickFISH BC*
- *Enterococcus QuickFISH BC*
- *Gram-negative QuickFISH BC*
- *Candida QuickFISH BC*

Impact PNA FISH with Clinician Notification

- Single center, prospective, randomized controlled study
- n= 202 patients with gram-positive bacteremia
- Half were randomized to clinician-notification of PNA FISH result (NG)
  - *Staphylococcus aureus* in 29 usual care vs 32 in notification group (NG)
  - Test performed twice daily; results faxed to lab/clinician liaison in NG group


Impact PNA FISH with Clinician Notification

- Notification associated with decrease in:
  - Overall mortality 17% vs 8 % (p = 0.05)
  - ICU mortality 47.8% vs 9.5% (p=0.01)
  - Antibiotic use by 2.5 days (p=0.01)
- No significant difference:
  - Length of stay: 9 days each
  - Overall cost: $92,373.78 vs $72,932.41 (p=0.09)

Impact of PNA FISH without ASP Intervention

- Single center, retrospective study pre/post PNA FISH
- Single positive blood culture w/ coag-negative Staphylococci
  - n = 100 Pre PNA FISH (May 2005 to Oct 2006)
  - n = 99 Post PNA FISH (Dec 2006 to May 2008)
- Primary Outcome of overall length of stay
  - 18.7 days (pre) vs 20.9 days (post) p = 0.35
- Secondary outcome: Mean days of vancomycin:
  - 4.15 days (pre) vs 3.51 days (post) p=0.49
- Time to identification: 22.6 vs 15.1 hours (p<0.0001)

MALDI-TOF

MALDI-TOF MS instruments have 3 components

MALDI-TOF Clinical Data

- Intervention associated with decreased:
  - Time to organism ID: 36.6 vs 11.1 hrs (p < 0.001)
  - Time to final ID and susceptibility: 47.1 vs 24.4 hrs (p < 0.001)
  - Hospital length of stay: 11.9 vs 9.3 (p = 0.01)
  - Hospital cost: $45,709 vs $26,162 (p = 0.009)
- No significant difference in all-cause 30-day mortality
  - 10.7% versus 5.6% (p = 0.19)
- Independent predictors of hospital length of stay
  - Intervention (HR 1.38; 95 CI, 1.01-1.88)
  - Active therapy with 48 hours (HR 2.9; 95% CI, 1.15-7.33)

Matrix Assisted Laser Desorption Ionization Time-of-Flight (MALDI-TOF)

- Mass spectrometry is based on the acquisition and analysis of mass and charge values from an individual ionized sample
  - The mass to charge ratio serves as a unique “fingerprint”
- Can be used to identify organisms from colonies on solid media as well as positive blood and urine cultures
  - Testing can be performed directly from single colonies on primary culture plates, other methods may require subculture
- Improves turn-around time by an average of 1.5 days
- Subcultures and susceptibility testing are still needed

MALDI-TOF Clinical Data

- Single center, pre/post intervention study in patients with 1st episode of gram-negative bacteremia
- Pre group: gram stain, culture, ID, susceptibility and notification of RN and/or patient care team
- Post group: MALDI-TOF performed after gram stain 3-4 times/day, results called to ID pharmacist 24/7
  - 1000, 1300, 1900, and 0500(later in study) every day
  - ID pharmacist contacted physician to discuss results and determine appropriate antimicrobial therapy
- n = 201 patients (100 pre vs 101 post)

MALDI-TOF Advantages

- Ease of use
- Potential to automate
- Able to handle large volume of tests
- Rapid turnaround time (<1 min once setup)
- Low reagent costs ($0.10 to 0.40 per ID)
- Applicable to many pathogens including bacteria and fungi
MALDI-TOF Disadvantages

• Does not provide antimicrobial susceptibility
• Poor performance with polymicrobial samples
• Upfront instrument costs
• Misclassification (e.g., Shigella as Escherichia coli)
• Identification limited to what’s in the database
• Repeat testing may be required for 10% of isolates
• Not cleared by FDA yet
• Need more clinical outcome data

Challenges with Implementing Rapid Diagnostic Tests

• Cost of acquiring new equipment and tests
  – Which cost center will it come from?
  – Will you lease or own the new equipment?
  – Will you have enough volume to sustain it?
  – Reimbursement? (not usually covered by inpatient stay)
• What are the quality control requirements?
• How much technician time and complexity?
• How often will the test be done? (24/7 vs batch)
• How will results be reported and to whom?

References

• Delitt TH, Owens RC, Mcgowan JE Jr, et al. Infectious Diseases Society of
  America and the Society for Healthcare Epidemiology of America
  guidelines for developing an institutional program to enhance antimicrobial
• Owens RC. Antimicrobial stewardship: concepts and strategies in the 21st
• Kullar R, Goff DA, Schulz LF, et al. The EPIC Challenge of Optimizing
  Antimicrobial Stewardship: the Role of Electronic Medical Records and
• Hiller A. Technology helps hone antibiotic stewardship. Anesthesiology News
  2010; 35: 10
  decision support system on reducing inappropriate antimicrobial use: a

Conclusion

• Medical information systems play an important role in any productive stewardship program
• Clinical decision support can potentially save time and increase the number and complexity of interventions
• New rapid diagnostics can shorten the time to organism identification, which may improve patient outcomes and decrease antibiotic use and cost
• In the end though, someone needs to review the alert or lab result and act on the data for any benefit to be seen

References