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Staphylococcus aureus

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Good medicine is good economically, too

New studies validating and justifying surveillance for methicillin-resistant Staphylococcus aureus

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Although microbiologists and infection control preventionists may be convinced of the positive patient care benefits of methicillin-resistant *Staphylococcus aureus* (MRSA) surveillance, implementation of the best practices (a rapid but more costly molecular assay compared with traditional slow and inexpensive culture) has been an uphill battle with hospital administrators and chief financial officers. Whenever the request to increase the laboratory's budget has come up, the answer from above has been "show me the money savings." It appears that a recent group of published studies has met that challenge. The papers discussed here can be used as part of a strategy to convince skeptics that good MRSA surveillance is good medicine, good patient safety, good public relations, and good economics.

A key champion for universal surveillance for MRSA is Dr. Lance Peterson, Director of the EpiCenter, Professor of Medicine and Pathology at Northwestern University, and Health Care Epidemiologist at NorthShore University HealthSystem, Evanston, IL. Dr. Peterson's lively presentations on the benefits of universal surveillance in his 3-hospital system have helped to galvanize this practice around the world. A review of Dr. Peterson's seminal publication on MRSA surveillance was presented in the first On Demand newsletter published early last year (available on line at www.cepheidondemand.com)[12]. The program in Dr. Peterson's hospital system includes extensive involvement of all stakeholders, production of a video on

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CEPHEID
ON-DEMAND
REPORT

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Good medicine is good economically, too

proper nares swab collection technique (which is important because sampling is often performed incorrectly), and pre-assembled kits for the nasal mupirocin decolonization protocol that is initiated by a positive nasal test result. The stunning 80% reduction of MRSA bloodstream infections was a triumph for both the infection control department and patients, but did the program actually save the Healthcare System any money? The answer, according to Dr. Peterson, is a resounding "yes" and the data are published in the Joint Commission Journal on Quality and Patient Safety. The financial analysis of the intervention and the results are welcome news: best practices save money as well as lives[10].

costs above the control group. Eliminating 50 such infections during the first year resulted in a reduction (cost-avoidance) of $1,200,000 in medical expenditures, clearly on the positive side of the bottom line. Dr. Peterson has stated that there was a return on investment of $3 for every $1 spent. Of course these calculations are not inclusive of individual reimbursement and other subtle financial differences among patients, but they reflect the actual experience of the hospitals. The administrators have remained fully supportive of the program. Interestingly, the analysis also showed that if only patients entering the intensive care unit had been tested, 78% of colonized patients would not have been detected and

> Dr. Peterson has stated that there was a return on investment of $3 for every $1 spent.

The surveillance program utilized a real-time PCR assay that was batched and performed twice daily, with an average turnaround time of 12 hours and an estimated total testing cost of $600,000 per year. The costs attributed to additional patient isolation days (approximately $30 per day) increased only 20% above baseline, a minor $44,000 annually. The authors estimated the net expense of the MRSA surveillance program to be $16 per patient admitted. The cost savings were based only on cohorts of patients who stayed at least 8 days in the hospital, comprising 178 patients with infections (bloodstream, skin and soft tissue, respiratory, or urinary tract) and 5,976 patients without infections (control group). The patients who developed an MRSA infection incurred $23,783 additional medical

the reductions in infections would have been much less impressive. Experts agree that to achieve excellent results, highly sensitive tests with rapid turnaround time must be used, basically mandating PCR technology.

What has the impact of universal MRSA surveillance been on the incidence of MRSA isolated from patient specimens in the 3-hospital system? A separate analysis of those findings was just reported by the Evanston Northwestern Healthcare group[4]. Results of cultures received in the laboratory during the 5-year period encompassing 2 years before any active surveillance was performed, through one year of ICU-only surveillance, and concluding with 2 years of universal surveillance were included in the analysis. Figure 1 shows the results. The August '04 to

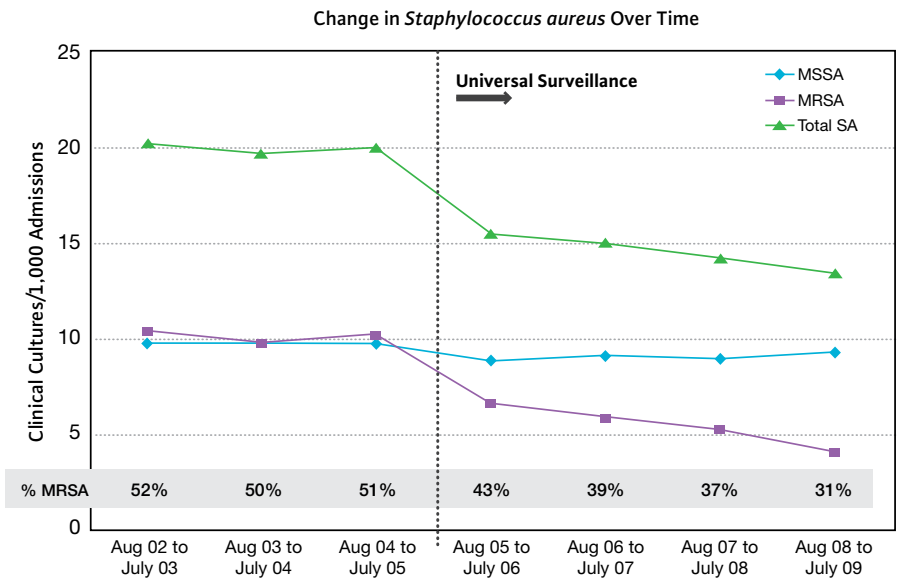

Figure 1. Annual numbers of inpatients with clinical isolates of *Staphylococcus aureus* (SA) admitted to NorthShore University Health System from August 2002 through July 2009.

July '05 bars cover the ICU-only surveillance program during which there was no reduction in numbers of *S. aureus* isolates. But the differences in MRSA isolate numbers between pre- and post-universal surveillance, where the MRSA incidence decreased, are highly statistically significant ($p<0.0001$). No differences in the rates of MSSA recoveries were detected; validating that MRSA surveillance and interventions were the only responsible factors. The majority of MRSA isolates (52%) came from wounds. The authors state that "rapid MRSA screening significantly reduced MRSA transmission within surgical wards..."

A different study from a Harvard-affiliated center, which evaluated the effect of MRSA surveillance on MRSA bloodstream infections, also found that their intervention program reduced MRSA bloodstream infections (BSIs) without impacting BSIs due to MSSA[6]. Both studies concluded that additional MSSA infections did not "fill the gap" left by decreases in MRSA, which was one worry that healthcare providers had voiced before the outcomes of MRSA surveillance interventions were available. The Evanston Northwestern (NorthShore) system findings take on even more significance when contrasted with major increases in MRSA detections reported from most other healthcare settings around the United States[8].

The Netherlands has long employed a national policy of "search and destroy," in which patients are preemptively isolated until shown to be culture-negative for MRSA using a very sensitive enrichment broth culture, probably similar in sensitivity to PCR, acknowledged most recently by a very new comparative study as the most sensitive method for detection of MRSA nasal colonization[16]. A recent analysis from one major Dutch medical center showed that the few MRSA-colonized patients who were admitted to the hospital without having their MRSA status determined, and thus were not isolated, were associated with a 10-fold higher rate (55%) of secondary transmission of MRSA[14]. During the 5-year study period, an annual average of only 6.7 healthcare associated transmissions per year occurred, a rate that most U.S. institutions would welcome.

Since 2004, Pofahl and colleagues have been screening the nares of all patients admitted to their North Carolina tertiary care hospital with a relatively rapid PCR test similar to that used by Peterson's group[11]. Those patients who were positive for MRSA were kept in isolation. The rate of MRSA carriage in their surgical patient population (5.8%) was on the low side of average for the U.S. population. Starting in 2007, patients were tested for nasal MRSA carriage before admission, and those found to be positive were given nasal mupirocin and chlorhexidine baths for eradication. The authors reported a decrease in MRSA surgical site infections (SSIs) after universal screening was implemented, with a statistically significant decrease in patients undergoing joint-replacement procedures ($p=0.004$). Importantly, among 4 patients who were screening test positive but went on to develop a MRSA infection, none received the protocol-mandated eradication intervention. Optimal outcomes were reported with pre-admission screening and intervention, similar to the results seen at New England Baptist Hospital, as reported in the second issue of the On Demand Newsletter (Volume 1, Issue 2). But exciting new results have just been published by two different groups of investigators for a strategy that does not rely on pre-admission detection and intervention.

Patients at two major New York City hospitals were placed into a pilot study to determine if intervention at the time of contemplation of transfer to an ICU, rather than either after transfer or even before hospital admission, could impact outcomes[7]. The nasal colonization rate among patients in this setting was known to be high (many came from long-term care facilities) and the rate was even higher during the study (14.5%). Although rapid PCR tests, acknowledged by the authors as being the ideal, were not used, this pilot study paves the way for such tests to be implemented in the future. The study design assumed that patients determined to require ICU management were at increased risk of developing a serious MRSA infection. Because of the lack of a rapid test during the study period, patients being assessed by a critical care team prior to admission to an ICU

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Summaries of Selected Abstracts Presented

Ellen Jo Baron, Ph.D.

Summaries of selected abstracts presented at three recent meetings:

Infectious Diseases Society of America: *IDSA – Philadelphia, PA; Oct. 29–Nov. 1, 2009*

Association for Molecular Pathology: *AMP – Orlando, FL; Nov. 19–22, 2009*

Réunion interdisciplinaire de chimiothérapie anti-infectieuse: *RICAI – Paris, France ; Dec. 3–4, 2009*

IDSA

1. Huard, R.C., L. Lazzarini, J. R. Lapae Silva, J.L. Ho, and P. Della-Latta. Abstract 256. Rapid molecular detection of drug resistance in *Mycobacterium tuberculosis* strains from Rio de Janeiro, Brazil, using the AutoGenomics Infiniti™ Platform and MDRTB Test Kit.

357 isolates of *Mycobacterium tuberculosis* (Mtb) with known phenotypic resistance patterns from Brazilian patients were amplified using a multiplex PCR protocol (off-line). Amplified DNA was loaded onto special Biofilm chips for analysis in the AutoGenomics Infiniti microarray platform. Target genetic sequences included *katG*^{315} and *mabA-inhA*$^{1-15}$ promoter regions found in isoniazid (INH) resistant strains and *rpoB*$^{511-533}$ found in rifampin (RIF) resistant strains, as well as wild-type genes without mutations. Discrepancies were resolved by genomic sequencing. The collection included 19 multidrug resistant Mtb (MDR-TB) strains, 18 strains resistant to INH only, and 2 strains resistant to RIF only. Results from the chip analysis were available in approximately 3.5 hours after insertion into the instrument. 31 of 35 INH-resistant strains (88.6%), 20 of 21 RIF resistant strains (95.2%), and 18 of 19 MDR-TB strains (94.7%) were detected correctly. The strains that were missed by the assay had unusual mutations or mutations in non-target regions of the genome. Two phenotypically RIF-susceptible strains had resistance mutations that were detected accurately. The overall sensitivity of the assay was 91.1%, specificity 99.7%, positive predictive value 96.2%, and negative predictive value 99.2%.

Note from the Editor: Similar targets within the *rpoB* gene are used by the GeneXpert® CE-IVD MTB/RIF assay to identify Mtb and RIF resistant-Mtb as a predictor of MDR-TB. Key differences between the AutoGenomics assay and the Xpert® MTB/RIF assay are that the Xpert assay tests sputum directly, rather than requiring isolated colonies; there are no off-line high complexity amplification steps involved in the Xpert assay; and Xpert results are available within 2 hours, with a total of 15 minutes of operator time at the start of the assay procedure.

2. Brossette, S.E., S. Xiaowu, R.S. Johannes, P.A. Hymel, and P.T. Ying. Abstract 569. Economic Burden of Nosocomial Infection on Payers and Providers: Analysis of 272,143 Admissions in 2007.

MedMined™ is a proprietary hospital epidemiology database system with multiple data points per patient. The authors analyzed data from 129 hospitals with complete records to assess 28,694 hospital-acquired infection incidents identified in the database through a special "nosocomial infection marker" (NIM™) field. The most common infections, in order, were urinary tract (41.3%), respiratory (19.7%), blood (14.5%), surgical site (10.7%), *Clostridium difficile* (7.6%), and other sources (6.2%). The adjusted attributable cost per infection incident was $14,972 for respiratory; $12,763 for blood; $9,723 for surgical site; $8,117 for *Clostridium difficile*; $7,210 for urinary tract; and $8,985 for the other sources. The adjusted additional reimbursement per NIM from the Centers for Medicare and Medicaid Services was $8,310, $5,702, $3,945, $2,729, $2,439, and $4,098, respectively. The adjusted attributable net loss per NIM for hospitals after CMS reimbursement was $6,663; $7,061; $5,778; $5,388; $4,772; and $4,887; respectively. All p-values were <0.0001.

Note from the Editor: These are the most recent cost figures to realistically show the tremendous cost of hospital-acquired infections in a representative U.S. hospital cohort. Consider, for example, if screening a patient for MRSA before surgery allowed proper prophylaxis and prevented one post-surgical site infection. The cost of the screening test (if $45) would be 0.5% of the true cost of the infection. Looking at it another way, one could screen 128 patients before the cost of surveillance would equal the amount of money lost (after CMS reimbursement) from just one surgical site infection. Hospitals would only have to document a post-surgical infection rate of ≥0.8% to cost-justify implementing an MRSA surveillance system. If the cost of the test was $32, then hospitals would only need a post-surgical infection rate of ≥0.55% to cost-justify implementing an active pre-admission surveillance policy.

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at Three Recent Meetings

IDSA (continued)

3. Chang, A., J. Passick, S. Direnzo, J. Bondi, I. Echenique, D. Jungkind, P. Flomenberg. Abstract 424. What Is the Clinical Significance of *C. difficile* Antigen Positive, 2-Step Toxin Negative Stools?

The medical center's normal algorithm included an immunochromatographic assay (ICA) for glutamate-dehydrogenase antigen (GDH) and toxin A/B, followed by a cell culture cytotoxicity neutralization assay (CCNA). The authors analyzed the approximately one-third of samples that were positive for GDH but negative for toxin in both the ICA and CCNA toxin assays. A commercial PCR for toxin B gene and toxigenic culture (using CCNA to test isolates for toxin production) were used as the comparator assays. Of 55 evaluable samples, 24 were culture positive but toxin negative in the PCR or CCNA from culture (non-toxigenic strains). Ten samples were negative by both culture and PCR (false positive Ag tests). The authors also reported that among patients with toxin-producing strains who were treated for *C. difficile* infection, 2 of 3 received treatment prior to stool collection. Therefore, the sensitivity of the 2-step method was reduced when anti-infective therapy was initiated ≥1 day prior to stool collection, a common practice.

Note from the Editor: The value of the study could have been enhanced if the authors had tested the GDH-negative stools by toxigenic culture and PCR. Recent studies have shown that contrary to common belief, the GDH test fails to detect toxigenic *C. difficile* in some percentage of stools, depending on the strain types prevalent in the population. Although not explicitly stated, the data indicate that 21 strains must have been culture positive and toxin positive by the comparator assays, indicating that the ICA failed to detect toxin, necessitating performance of a second assay, with the associated delay in turnaround time, in 38% of patients who actually did have *C. difficile* infection and needed treatment.

AMP

1. M. Sabbath-Solitare, S.P. Marotta, R. Pulinthanathu, N.P. Zauber, T.C. Redondo. Abstract ID09. Is there clinical utility in strain-typing MRSA and correlating antibiotic susceptibility in a community hospital?

MRSA isolates from 53 cultures of nares, sputa, wounds, and tissues were evaluated using the Diversilab System, which utilizes molecular amplification followed by microfluidics separation and a web-based analysis tool, to characterize polymorphisms based on repetitive sequence-based PCR. The whole procedure can be accomplished within 24 hours. The web-based software allows users to generate dendrogram relatedness diagrams for their strains. Among the 53 isolates, strain-types and antibiotic resistance were correlated, particularly with USA100 strains, all 14 of which were clindamycin resistant. The authors stated that strain typing was available before antimicrobial resistance results, enabling faster time to appropriate therapy. In addition, the strain typing data identified spread within hospital units to facilitate more effective infection control activities.

2. C. Ginocchio, F. Zhang, R. Manji. Abstract ID62. Detection of the novel influenza A (H1N1) using the Luminex xTAG respiratory virus panel (RVP) assay.

Dr. Ginocchio's laboratory in Long Island had extremely high numbers of samples submitted for detection of influenza during the 2009 novel H1N1 influenza outbreak, allowing extensive evaluation of existing diagnostic platforms. In this report, 2,715 respiratory samples were evaluated. After extraction using the NucleSENS easyMag (bioMérieux, Durham, NC), all samples were tested on the xTAG RVP (Luminex Molecular Diagnostics, Toronto, Canada) and, in addition, 60 samples were tested using the CDC-specific PCR assay for novel H1N1. Almost half of the samples (46.6%) contained influenza A, 87.6% of which were novel H1N1. Many additional viruses were found singly and in combination. The most common co-infections with influenza A were rhinovirus and enterovirus. The xTAG system accurately identified the novel H1N1 and helped the laboratory assist the local health departments to quickly identify cases and monitor the outbreak.

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Summaries of Selected Abstracts

AMP (continued)

3. H. LaRue, L. Travnik, L. Swyers, JM. Balada-Llasat, J. Mangino, P. Pancholi. Clinical Evaluation and Impact of Xpert™ MRSA/SA Real-time PCR Testing for the Detection of *Staphylococcus aureus* and Methicillin Resistant *S. aureus* (MRSA) in Positive Blood Cultures

Microbiology laboratory, infection prevention, pharmacy, and clinicians at Ohio State University Medical Center worked together to evaluate the effect of implementing the Xpert® MRSA/SA blood culture identification assay for staphylococci combined with direct reporting of results to both clinicians and the infection control practitioners. Results indicating the presence of either MRSA or *Staphylococcus aureus* were available and communicated to clinicians within a few hours after gram-positive cocci in clusters were initially visualized in a positive blood culture broth. For the 290 blood cultures yielding gram-positive cocci in clusters that were evaluated in the study period, the Xpert MRSA/SA correctly detected and identified all 41 *S. aureus* and 53 MRSA, giving sensitivity, specificity, predictive positive and predictive negative values of 100%. Results were available 24-48 hours sooner than reporting by the prior conventional culture-based method. Antibiotic management, infection control practices, and patient outcomes were improved, and as presented in another session at the meeting, overall costs to the institution were also reduced.

RICAI

(Note that these posters were exhibited at a European meeting and presented data on the CE-mark Xpert® MTB/RIF product which is not currently available in the U.S.)

1. B. Malbruny, G. Le Marrec, R. Leclercq. Abstract 520. Detection of *Mycobacterium tuberculosis* DNA with the GeneXpert MTB/RIF Assay; preliminary results.

Thirty-seven samples (21 from pulmonary and 14 from extra-pulmonary sites) from 30 patients were tested using the GeneXpert MTB/RIF Assay and by conventional mycobacterial culture methods. Acid-fast smears that were positive by auramine fluorescent stain were confirmed by Ziehl-Neelsen staining. Cultures were inoculated into MGIT liquid medium (BD) and onto Lowenstein-Jensen agar. The Hain test was used for isolate identification and drug resistance testing, and patients also had a Quantiferon Gold test (QFT) performed. Among the respiratory samples, 5 were positive in both the Xpert assay and culture, 2 of which were smear-negative. An additional bronchial aspirate from a QFT + patient was positive in GeneXpert only. No culture-positive samples were reported negative by the GeneXpert assay. Among non-respiratory tract sites, there were 6 specimens (including 2 joint fluids, 1 cerebrospinal fluid, 1 bone tissue, 1 abdominal nodule, and 1 lymph node) positive by both Xpert and culture, 3 of which displayed negative smears. The positive CSF had insufficient volume to perform a smear at all. One pleural fluid and one lymph node were culture positive but GeneXpert negative. No rifampin resistance was detected by the Xpert MTB/RIF assay or by comparator methods. Given the very poor sensitivity of CSF smears and cultures in particular, these results are promising and merit further studies.

2. L. Deforges, JM. Le Glaunec, N. Launay, R. Vergne, A. Minaret, M. Marzouk, P. Legrand. Application of rapid detection system for *M. tuberculosis* complex and resistance to rifampicin by the test Xpert® MTB/RIF.

Thirty-nine samples, including 15 respiratory, 1 skin biopsy, 1 urine, 2 bone biopsies, 5 CSFs, 10 pleural fluids, and 5 lymph nodes, were tested in the GeneXpert MTB/RIF assay and results were compared to detection by culture (Hain Biocentrix) and COBAS Taqman MTB test (Roche) and to identification of *M. tuberculosis* by GenProbe (bioMérieux). Nine samples (including 3 respiratory and 6 tissue samples) were positive for *M. tuberculosis* by all 3 methods: culture, TaqMan, and GeneXpert. There were no false negative results with either Xpert or TaqMan. The GeneXpert also correctly reported all rifampin results (only one resistant isolate was detected). The authors suggest that the GeneXpert platform is suitable for rapid results, and additionally propose the system for use with samples other than those obtained from pulmonary sites.

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were screened by nasal culture (obtained at the time of assessment) and placed on contact isolation if positive. The study was designed to determine if patients at risk for development of MRSA infection would benefit from timely detection of colonization (during initial assessment, during which transfer to an ICU was being contemplated) and subsequent decolonization. Twenty-nine of 200 patients enrolled were colonized with MRSA. Of 8 patients who developed MRSA infections ≥4 days after the nasal swab was obtained, 7 were colonized with MRSA (54-fold higher risk than for non-colonized patients) and the infection was conservatively deemed to have been preventable if timely decolonization had occurred. In fact, prevention of infection probably occurs even if decolonization procedures have just begun at the time of admission to the facility, as detailed below[3]. The New York City study concluded that the rate of preventable MRSA infections was 24.1% and that rapid initiation of eradication interventions would reduce infections by 50%. A prospective interventional trial using Xpert® MRSA has been proposed.

Exciting news on the value of immediate initiation of decolonization for nasal carriers of *Staphylococcus aureus* was just published in the New England Journal of Medicine[3]. With a group of >800 patients, Bode and colleagues used a rapid real-time PCR method to test for *S. aureus* in the nares of patients admitted for surgery and expected to stay in the hospital more than 4 days. Results were available within the first 24 hours, and colonized patients were assigned to receive either 5 days of nasal mupirocin and chlorhexidine baths or placebo decolonization treatment, which was started within the first day of hospitalization. The post-surgical site infection rate in the mupirocin-chlorhexidine treated patients was less than half of that in the placebo-treated patients. And, in patients with deep-seated infections, the most serious and costly, the immediate decolonization protocol reduced infections by 80%! In an accompanying editorial, Dr. Richard Wenzel noted that the decolonization strategy was particularly valuable for colonized patients undergoing cardiothoracic surgery, prosthesis implantation, and immunocompromised surgical patients[15].

Using a molecular test with 0.9 days turnaround time as the "rapid" admission surveillance test and culture as the standard test (3.3 days turnaround time), investigators from the United Kingdom showed that acquisition of MRSA occurred 1.49 times more often in surgical wards where the culture method was used (p=0.007) than in those where molecular testing yielded faster results[5]. Patients were re-tested every 4 days to assess new acquisitions and to decolonize them as quickly as possible. All patients were given decolonization treatment once their MRSA carrier status was reported and the study, which involved more than 10,000 patients over two years, was validated by reversing the wards in which the rapid test and culture were utilized halfway through. Because of low availability of single rooms, only 17% of patients actually were maintained in isolation, making it even more critical that the colonized patients be identified rapidly so that their risk of transmitting the organism could be reduced. Studies from institutions able to implement pre-emptive isolation have shown better results[10]. *(Editor's note: Use of an extremely rapid molecular test with turnaround times fast enough to yield results before patients have been assigned beds, such as the Xpert® MRSA Nasal assay with 45 minute time to results, could effectively facilitate infection control interventions for patients from the time of their presentation to the hospital.)*

Many workers have asked whether extra-nasal sites must also be tested to detect all colonized patients. Different studies yield different results, depending on the patient populations tested. As many as 30% of nursing home patients, for example, may be colonized in extranasal areas[9]. Fortunately for the largest group of patients being screened for MRSA in the United States, those entering Veterans Administration (VA) medical centers, at least one study just released shows that nasal screening is likely to be adequate to establish MRSA colonization in a patient. Baker and colleagues, from the Boston VA hospital, used PCR for nasal swabs and culture on chromogenic agar for swabs obtained from other sites, including posterior pharynx, hands, axilla, perirectal area, and any wound site or indwelling intravenous or Foley catheter site[2]. The nasal PCR results by the Xpert MRSA assay showed 11% of patients were colonized with MRSA. Only 3 patients (2%) of the 150 patients evaluated had positive cultures from any other sites in the presence of a negative nasal PCR result. Extranasal swab samples were positive for MRSA on culture for 9 (56%) of 16 patients who tested positive for nasal MRSA colonization (p<0.001). For the Boston VA population, the strategy of nasal screening by PCR supports the approach adopted by VA medical centers nationwide. Their results mirror those published previously by a group from Ireland, who found that the Xpert MRSA assay on nasal swabs from patients new to the healthcare institution was the best sample for detecting carriers, detecting 100% of colonized new patients[13].

Although not addressing the cost-savings realized from an MRSA surveillance and intervention program, nevertheless very important findings have been published based on a rigorous cost analysis of the impact of MRSA and MSSA deep incision surgical site infections in seven Duke University Infection Control Hospital Network system institutions[1]. Over approximately 4 years, information on all patients who developed SSI due to either methicillin-susceptible *S. aureus* (MSSA) or MRSA were collected and analyzed. Extensive patient data including risk factors, glucose

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Good medicine

levels, co-morbidities, severity of illness, readmission within 90 days, and 90 day mortality were included in the analysis. Patients with SSIs caused by MRSA were compared to uninfected controls and to patients with SSIs caused by MSSA. To those familiar with the field, the conclusions are already predictable — however, the extent of the morbidity and severity of outcomes was surprising even to these seasoned authors. Among 141,345 total surgical procedures, 278 patients developed SSI with *S. aureus* (only 0.2%). This low percentage is not uncommon in well-controlled medical centers around the United States. One-hundred fifty of the patients were infected with MRSA (54%) and 128 patients had MSSA. The appropriate therapy was given to 70-71% of the patients in each group, so differences in outcomes are not based on correctness of treatment. The patients with MRSA infections were 30 times more likely to be readmitted to the hospital and 7 times more likely to die within 90 days than uninfected controls. Additionally, patients with MRSA infections were 2.6 times more likely to die than those with MSSA infections. The average length of stay for patients with SSIs due to MRSA was 23 days, much longer than uninfected patients, whose average stay was 5.2 days, and 6 days longer than those with MSSA infections. The overall excess hospital costs for patients with MRSA SSIs, above the baseline $50,463 cost for uninfected patients, was $61,681 compared with $38,681 in excess costs for the patients with MSSA infections. Although the patients who contracted MRSA SSIs had more risk factors to begin with, the authors of this study accounted for those differences in their analysis. By every measure, MRSA infections led to increased costs, a staggering $19 million for this hospital system over the course of the study. The authors have provided a benchmark for workers wishing to implement interventions, as quoted here. "We believe our estimate for the attributable impact of a single SSI due to MRSA of more than $61,000 can be used by administrators and infection control personnel to design and evaluate specific preventative interventions. For example, if an intervention (e.g., decolonization, screening, hiring of one FTE) costs less than $61,000 and leads to the prevention of only one SSI due to MRSA, then this intervention will likely be cost effective for the institution[1]."

The more reports of studies and interventions accumulate, the more evidence mounts that active surveillance using the fastest and most accurate method available, real-time PCR, is both good medicine and good monetary stewardship.

REFERENCES

1. Anderson, D. J., K. S. Kaye, L. F. Chen, K. E. Schmader, Y. Choi, R. Sloane, and D. J. Sexton. 2009. Clinical and financial outcomes due to methicillin resistant Staphylococcus aureus surgical site infection: a multi-center matched outcomes study. PLoS One 4:e8305.
2. Baker, S. E., S. M. Brecher, E. Robillard, J. Strymish, E. Lawler, and K. Gupta. Extranasal methicillin-resistant Staphylococcus aureus colonization at admission to an acute care Veterans Affairs hospital. Infect Control Hosp Epidemiol 31:42-6.
3. Bode, L. G., J. A. Kluytmans, H. F. Wertheim, D. Bogaers, C. M. Vandenbroucke-Grauls, R. Roosendaal, A. Troelstra, A. T. Box, A. Voss, I. van der Tweel, A. van Belkum, H. A. Verbrugh, and M. C. Vos. Preventing surgical-site infections in nasal carriers of Staphylococcus aureus. N Engl J Med 362:9-17.
4. Hacek, D. M., S. M. Paule, R. B. Thomson, Jr., A. Robicsek, and L. R. Peterson. 2009. Implementation of a universal admission surveillance and decolonization program for methicillin-resistant staphylococcus aureus (MRSA) reduces the number of MRSA and total number of S. aureus isolates reported by the clinical laboratory. J Clin Microbiol 47:3749-52.
5. Hardy, K., C. Price, A. Szczepura, S. Gossain, R. Davies, N. Stallard, S. Shabir, C. McMurray, A. Bradbury, and P. M. Hawkey. 2009. Reduction in the rate of methicillin-resistant Staphylococcus aureus acquisition in surgical wards by rapid screening for colonization: a prospective, cross-over study. Clin Microbiol Infect.
6. Huang, S. S., D. S. Yokoe, V. L. Hinrichsen, L. S. Spurchise, R. Datta, I. Miroshnik, and R. Platt. 2006. Impact of routine intensive care unit surveillance cultures and resultant barrier precautions on hospital-wide methicillin-resistant Staphylococcus aureus bacteremia. Clin Infect Dis 43:971-8.
7. Keene, A., L. Lemos-Filho, M. Levi, J. Gomez-Marquez, J. Yunen, H. Said, and F. D. Lowy. The use of a critical care consult team to identify risk for methicillin-resistant Staphylococcus aureus infection and the potential for early intervention: a pilot study. Crit Care Med 38:109-13.
8. Miller, L. G., and B. A. Diep. 2008. Clinical practice: colonization, fomites, and virulence: rethinking the pathogenesis of community-associated methicillin-resistant Staphylococcus aureus infection. Clin Infect Dis 46:752-60.
9. Mody, L., C. A. Kauffman, S. Donabedian, M. Zervos, and S. F. Bradley. 2008. Epidemiology of Staphylococcus aureus colonization in nursing home residents. Clin Infect Dis 46:1368-73.
10. Peterson, L. R., D. M. Hacek, and A. Robicsek. 2007. 5 Million Lives Campaign. Case study: an MRSA intervention at Evanston Northwestern Healthcare. Jt Comm J Qual Patient Saf 33:732-8.
11. Pofahl, W. E., C. E. Goettler, K. M. Ramsey, M. K. Cochran, D. L. Nobles, and M. F. Rotondo. 2009. Active surveillance screening of MRSA and eradication of the carrier state decreases surgical-site infections caused by MRSA. J Am Coll Surg 208:981-6; discussion 986-8.
12. Robicsek, A., J. L. Beaumont, S. M. Paule, D. M. Hacek, R. B. Thomson, Jr., K. L. Kaul, P. King, and L. R. Peterson. 2008. Universal surveillance for methicillin-resistant Staphylococcus aureus in 3 affiliated hospitals. Ann Intern Med 148:409-18.
13. Rossney, A. S., C. M. Herra, G. I. Brennan, P. M. Morgan, and B. O'Connell. 2008. Evaluation of the Xpert methicillin-resistant Staphylococcus aureus (MRSA) assay using the GeneXpert real-time PCR platform for rapid detection of MRSA from screening specimens. J Clin Microbiol 46:3285-90.
14. Vos, M. C., M. D. Behrendt, D. C. Melles, F. P. Mollema, W. de Groot, G. Parlevliet, A. Ott, D. Horst-Kreft, A. van Belkum, and H. A. Verbrugh. 2009. 5 years of experience implementing a methicillin-resistant Staphylococcus aureus search and destroy policy at the largest university medical center in the Netherlands. Infect Control Hosp Epidemiol 30:977-84.
15. Wenzel, R. P. Minimizing surgical-site infections. N Engl J Med 362:75-7.
16. Wolk, D. M., J. L. Marx, L. Dominguez, D. Driscoll, and R. B. Schifman. 2009. Comparison of MRSASelect Agar, CHROMagar Methicillin-Resistant Staphylococcus aureus (MRSA) Medium, and Xpert MRSA PCR for detection of MRSA in Nares: diagnostic accuracy for surveillance samples with various bacterial densities. J Clin Microbiol 47:3933-6.