bioMérieux CONNECTION
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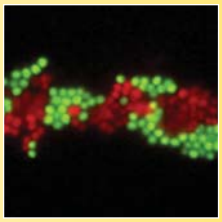

Message from bioMérieux

Herb Steward
Executive Vice President and General Manager, bioMérieux North America

Welcome to the August issue of the *bioMérieux Connection* newsletter. Inside you will find company news about exciting events taking place at bioMérieux as well as several product updates. bioMérieux is committed to helping the medical community face a number of growing challenges. We believe healthcare-associated infections (HAI) represent one of the most critical issues facing the healthcare industry today.

At any given time, 1.4 million people worldwide are suffering from an HAI[1]. Within the United States, nearly 90,000 people will die as a result of one of these infections[2]. In addition to these devastating numbers, longer hospital stays and rising healthcare costs associated with HAI generate up to $5.7 billion in expenses each year[1].

In June, bioMérieux sponsored the first World HAI Forum, which brought together more than 50 scientific experts from around the world to address current trends, prevention and control. The worldwide meeting will become a regular scientific event focused on HAI and will be organized every two years.

At bioMérieux, we are investing time and resources in the development of viable solutions to decrease the occurrence of HAI and resistant bacteria. We are aware of the seriousness of this issue and will continue to focus R&D efforts on finding ways to help our customers provide the best patient care possible.

As always, I thank you for the continued support of bioMérieux products. We appreciate your business and wish you a safe and successful year.

[1] *World Health Organization (WHO), 2005.*
[2] *Centers for Disease Control and Prevention (CDC), 2006.*

from diagnosis,
the seeds of better health

BIOMÉRIEUX

Superbug zapper recreates 'fresh air' indoors

A device that mimics the naturally disinfecting quality of fresh air could be used to purge hospital wards of superbugs, its makers claim.

The Air Disinfector, launched in London, UK, on 19 June pumps a continual stream of reactive hydrogen radicals into the atmosphere, killing microbes within minutes.

"The same results could be obtained simply by opening all the windows of hospital wards, but that's not practical," says David Macdonald, co-inventor of the device and chief scientific officer of Inov8 Science, which developed it.

Macdonald and co-inventor Derek Elwood identified the so-called open-air factor phenomenon more than 15 years ago through experiments at the UK government's chemical and biological defence labs at Porton Down in Wiltshire. They established that outdoors, microbes are killed by hydroxyl radicals, highly reactive agents constantly produced through natural reactions between airborne ozone and organic scented chemicals from plants such as pine trees.

Radical generation

Now, Macdonald, Elwood and collaborators say they have recreated this effect using a customised device the size of a flower vase that constantly generates the radicals. To do this, it draws in oxygen and exposes it to electric currents to produce a cold plasma rich in ozone. The hydroxyl radicals are generated by constantly reacting the ozone with pre-loaded supplies of scented chemicals, called terpenes, in cartridges that need renewing each month. The ozone and terpenes are retained within the device and not released into the room.

Bacteria, including methicillin-resistant Staphylococcus aureus (MRSA) and Clostridium difficile – two of the most notorious hospital-acquired superbugs – were undetectable within as little as an hour of the device being switched on, Macdonald says. "In earlier experiments, in which we flooded rooms with more than a billion bacteria, levels were effectively down to zero within an hour," he adds.

Although hydroxyl radicals are lethal to microbes – disrupting their ability to absorb nutrients – they appear harmless to humans.

The device is now on sale in the UK and is also being tried in wards at three hospitals. There are also plans to launch it in the US, where it is being tested at 17 veterans' hospitals.

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Sepsis Case Study

Within five hours, the BacT/ALERT detected a positive blood culture bottle and alarmed the microbiology staff.

Tricore Laboratories

An elderly woman was found down in her house and brought to the emergency room where she was quickly triaged. Blood cultures were performed in the emergency room. Approximately 10cc of blood was inoculated in each Standard Aerobic and Standard Anaerobic BacT/ALERT® blood culture bottles. Within five hours the BacT/ALERT detected a positive blood culture bottle and alarmed the microbiology staff. An initial gram stain was performed and demonstrated a small gram negative rod. With the VITEK® 2, we were able to rapidly confirm an identification of Yersinia pestis and had the susceptibility result autofiled to the electronic patient chart.

In addition to having the results already on the chart, the critical result was called to the physician and the antibiotic therapy was changed immediately. Yersinia pestis infections are seen in New Mexico as endemic organisms, however, the first line antibiotics used for gram negative sepsis do not cover Yersinia pestis in general. The communication between the microbiology laboratory and the treating physician lead to a quick change in therapy from Ceftriaxone to Gentamicin.

In addition to having the results already on the chart, the critical result was called to the treating physician when a change in antibiotic therapy was initiated immediately.

Yersinia pestis has bio-security implications as it is one of the Level A select agents that must be reported to the CDC immediately. Outcomes that may have changed due to rapid knowledge of the infecting organism:

1. Rapid change to the proper antibiotic was made possible by the knowledge of the infecting organism (in this case the plague bacillus).

2. Infection control procedures were instituted more quickly (the patient may have progressed to pneumonic plague and have become infectious to other patients and healthcare providers).

3. Department of Health (DOH) was notified quickly of the presence of plague and they immediately contacted family and friends to be sure that they are not infected. In addition, the DOH conducted an environmental survey of the patient's home area to determine the source of the plague organism (found to be an infected cat who probably acquired the plague from rodents around the patient's house).

4. CDC was also notified immediately by the DOH as this is a bioterrorism sentinel level A organism.

5. All of this knowledge was obtained in a short period of time because of the continuously monitoring blood culture instrument (BacT/ALERT® 3D), the rapid identification and susceptibility test instrument (VITEK 2), and the interfaced laboratory computer information system which was interfaced to the hospital computer system.

Larry Buck, Microbiology Manager, Tricore Laboratories
Dr. Gary Overturf, Infectious Disease, Medical Director, Tricore Laboratories

Data Driven Drug Decisions

In the scientific world of medicine where so much of our practice is evidence based, the choice and dosing of pharmaceuticals, particularly antimicrobials, should be very rigid. Instead, physicians rely on anecdotal or even less specific gut feelings to guide drug decisions.

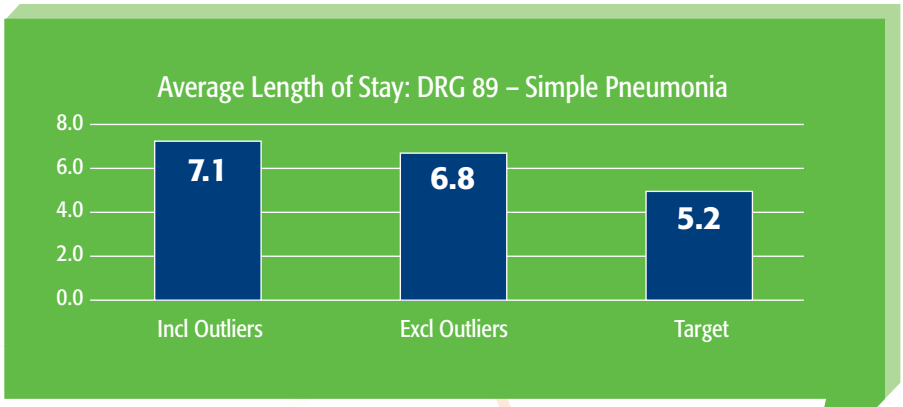
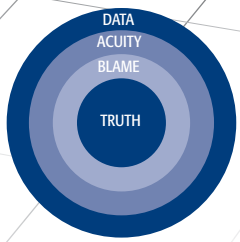


Table shows length of stay for patients with simple pneumonia, with and without outliers, versus target. Before intervention, this facility had a longer than expected length of stay for the complexity of its patients.

Aspen Healthcare Metrics is a healthcare consultancy and benchmark data company specializing in clinical service line improvement and supply chain continuum services for hospitals nationwide. In pharmaceuticals, Aspen works to assure that the use of high impact drugs is both clinically and fiscally appropriate. Recently, Aspen worked with a facility to improve the quality of care for its patients with simple pneumonia.

This facility had a longer than expected length of stay for the complexity of its patients. Simple pneumonia, DRG 89, was one of the highest volume admission diagnoses for the facility. Compounding the issue, the facility was often on diversion because it remained full. The administration and medical leaders recognized the quality of care and revenue loss concerns. Aspen's goal was to present data to the physicians to build the case for and then drive change.



This graphic demonstrates the layers of physician denial which must be penetrated to lead to the truth.

In order to present information to physicians to promote change, three layers of denial must be penetrated before the message can be heard. The first is data integrity. At this facility, the physicians were very skeptical of data that is presented by outside parties. Questions regarding data source, lag time, relevance to current practice, and control for outliers were all answered before we could move on.

The next layer was perceived acuity. When outcomes are in question, physicians look to acuity of illness to explain them. "My patients are sicker." is the phrase echoed at every facility. To use data to drive physician practice, acuity must be controlled. Risk factors must be adjusted to show the expected outcome in relationship to the acuity. Once this is done, the third layer of denial must be penetrated.

"It's not my fault. It's the (insert name of other department's) fault." Physician specific data supporting a physician's contribution to the outcome is required to deal with this denial. Once brought to this level of detail, the data is convincing enough to reveal the truth about the problem.

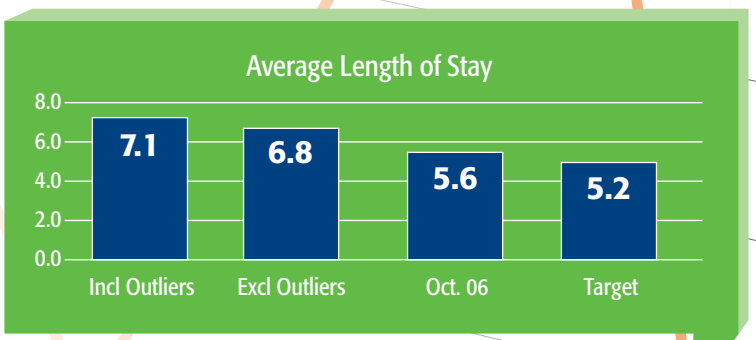
The truth is that this facility had no consensus on how to treat patients with simple pneumonia. Timing of appropriate cultures was not determined. Specialty consultation was over-prescribed. IV to PO protocols were not in place. Evidence based guidelines regarding antibiotic choice for treatments were not followed. All contributed to the problem of increased length of stay and lost revenue.

Antibiotic	Percent Utilized	Days of Therapy
Azithromycin 250mg oral	20%	5
Azithromycin 500mg IV	34%	4
Ceftriaxone 1G IV	41%	5
Ceftriaxone 2G IV	10%	5
Levofloxacin 250mg IV	8%	4
Levofloxacin 500mg IV	40%	4
Levofloxacin 500mg oral	20%	3.5
Piperacillin/tazobactam 3.375G IV	11%	5

This table shows the most common antibiotic choices at this facility. Even with the most appropriate choices, dose and route were not standard.

The table shows the most common antibiotic choices at this facility. Even with the most appropriate choices, dose and route were not standard. Also several simple pneumonia patients were treated with antibiotics designed for more complex infections. Aztreonam, caspofungin, cefepime, linezolid, meropenem, imipenem, and vancomycin were all used for varying amounts of time up to 8 days. IDSA guidelines are very clear that even in the presence of significant comorbidities that these drugs are not indicated for the treatment of simple pneumonia. Standardization of care was required to bring antimicrobial treatment in line with current guidelines.

Orders setting timing of cultures and administration of vaccines made performance measures automatic and a routine part of care were also written. Following implementation of the order sets to standardize care, the facility saw a precipitous decline in length of stay. The facility also experienced an improvement in performance measures.



Following implementation of the order sets to standardize care, the facility saw a precipitous decline in length of stay.

Antibiotics to be Administered Stat After Blood Culture and Within 4 Hours of Arrival.

(Record time administered here) _____

Antibiotics for Uncomplicated Pneumonia:
☐ Levofloxacin 750 mg ☐ IV ☐ PO Q24h
(further dosing per pharmacy as dictated by Renal function guidelines)

Switch to Levofloxacin 750mg PO Q 24h when pulse ox > 90%, and afebrile x 24h and tolerating oral intake

OR ☐ Ceftriaxone 1gm IV Q24h
Followed by _____ when pulse ox > 90%, and afebrile x 24h and tolerating oral intake

AND
☐ Azithromycin 500 mg ☐ IV ☐ PO Q24h

OR ☐ Other Antibiotic Therapy *(including for penicillin allergic or renally impaired patients)*

The above order sets were used to standardize care according to the IDSA guidelines.

Information on how best to treat illnesses is readily available, but physicians often don't know the degree to which they vary from best practice. Further, they don't understand how their variation affects outcome. By showing data specific to their practice patterns, and relating that to benchmarks, practice patterns can be influenced to conform to evidence based standards.

PNA FISH™

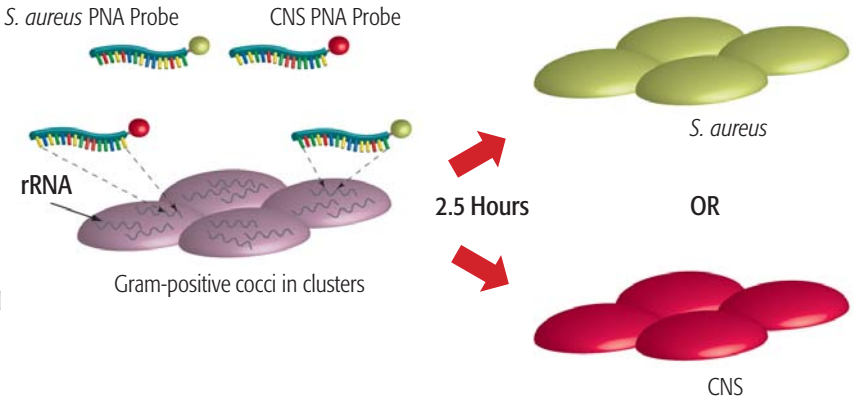
Rapid Tests to Improve Care for Patients with Bloodstream Infections

Rapid and accurate species identification from positive blood cultures using simple, molecular-based tests designed for routine laboratory use.

The rapid results with PNA FISH have been shown in clinical studies to:

- Reduce mortality and costs associated with *S. aureus* bacteremia[1]
- Reduce length of stay and unnecessary vancomycin use due to CNS contaminated blood cultures[2]
- Reduce time to correct therapy and mortality for *E. faecium* bacteremia[3]
- Reduce antifungal drug costs associated with *C. albicans* fungemia[4]

[1] *Ly et al. Poster 358. SHEA 2007. Baltimore, Maryland*
[2] *Forrest, G. N. J Antimicrob Chemother. 2006 Jul;58(1):154-8. Epub 2006 Apr 24*
[3] *Toombs et al. Oral Abstract Presentation #131. IDSA 2006. Toronto, Canada*
[4] *Forrest et. al. J Clin Microbiol. 2006 Sep;44(9):3381-3*



Managing bloodstream infections can be difficult and costly. Automated blood culture systems allow for rapid detection of the infection, but once the blood culture turns positive, physicians need to know what type of infection they are dealing with.

Is it *S. aureus* that requires aggressive therapy or coagulase-negative staph (CNS) contamination that often leads to unnecessary therapy, especially with vancomycin? Is it *E. faecalis* that is susceptible to ampicillin or another enterococci that is very likely vancomycin and ampicillin resistant (VRE)? Or, is it *C. albicans* that is fluoconazole susceptible or *C. glabrata* that might be fluconazole resistant?

Now microbiology labs can provide these critical species identification results in less than 3 hours after the blood culture turns positive and help physicians improve patient care. PNA FISH tests provide rapid species identification with high sensitivity and specificity using samples taken directly from positive blood culture bottles. The tests combine the latest in molecular-based diagnostic technology with the skills, equipment and materials available in today's clinical microbiology lab, and are designed for simple implementation and ease of use requiring minimal hands-on time.

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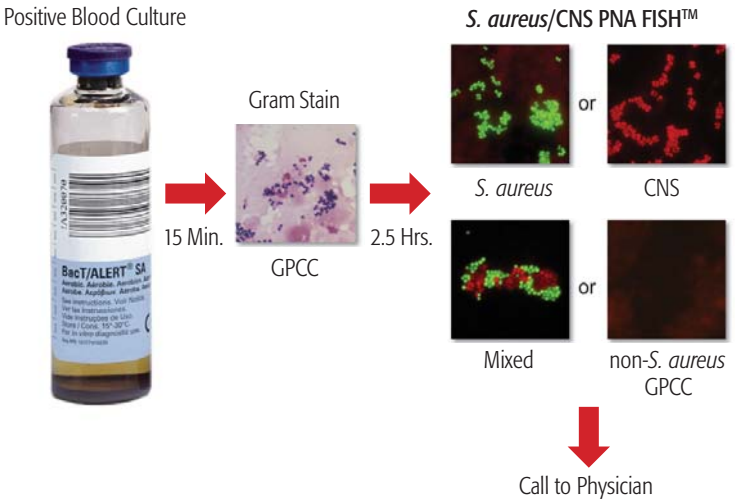

About PNA FISH™

PNA FISH is a qualitative nucleic acid hybridization assay intended for identification of bacteria and yeast species from blood cultures. The fluorescence in situ hybridization (FISH) assay uses fluorescence-labeled peptide nucleic acid (PNA) probes that target the species-specific ribosomal RNA (rRNA) in bacteria and yeast. Results are visualized using fluorescence microscopy.

Results Reporting

Once a blood culture turns positive, a Gram stain is performed. Depending on the Gram stain result, the appropriate PNA FISH test is performed. For example, *S. aureus*/CNS PNA FISH for GPCC-positive blood cultures. Within a few hours, results are available and can be reported to the attending physicians to help guide appropriate care.

Microbiology Software Updates

Are You Running the Most Current Software?

Listed below are the current software levels and/or upcoming software updates for the VITEK 2, VITEK 2 Compact, BacT/ALERT, and OBSERVA Data Management Systems.

VITEK® 2 CC Computers

VITEK 2 users should have received and loaded version 4.03 (part number 27862) for their CC. Please contact local bioMérieux representative to request your copy if one has not arrived.
Improvements include:

- Vancomycin Screen for S. aureus
- Fluconazole susceptibility testing for many clinically significant species of Candida spp.
- Tigecycline

VITEK® 2 Compact – Coming Soon

PC software version 2.01 software should begin shipping Mid-May providing access to the following tests:

- NH Identification card
- For S. aureus
  - Screen test for vancomycin resistance
  - Cefoxitin screen test for MRSA
- Rapid, automated approach for providing Fluconazole susceptibility testing for many clinically significant species of Candida spp.
- Tigecyline

OBSERVA®

Beginning in August and running through September, users of OBSERVA Data Management (those with either VITEK 2 Compact and/or BacT/ALERT signature) will receive an update (3.01).

- Its main purpose will be to enhance connectivity and improve speed during searches.
- Instruments will need to be at version B.25 for BacT/ALERT 3Ds and PC 2.01/OBSERVA 2.01 for VITEK 2 Compacts to load this update.

BacT/ALERT® 3D

BacT/ALERT 3D users should have received and loaded the B.25 (Part number 95068) software update for their control module.
Improvements include:

- Ability to view and print calibration history
- Bottle reading gap detection and notification

Friendly tips for loading software:

- Review instructions carefully, calling should you have questions.
- Gather all materials necessary to perform the update; including backup media.
- For optimal customer service and support, it is suggested that you load software during business hours Monday thru Thursday.

These software updates represent our continued efforts to improve the functionality and reliability of our products and to ensure customer satisfaction at all times. As with all software updates that assist in keeping your system current, we would recommend that you load them at your earliest possible convenience. ▮

2007 SHOWS AND CONFERENCES

Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)
Chicago, IL • Sept. 17-20

Infectious Disease Society of America (IDSA)
San Diego, CA • Oct. 4-7

American College of Emergency Physicians (ACEP)
Seattle, WA • Oct. 8-11

Association of Molecular Pathology (AMP)
Los Angeles, CA • Nov. 7-10

American Society of Health-System Pharmacists (ASHP)
Las Vegas, NV • Dec. 2-6
Booth #3217

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Please share your comments and suggestions with us through your local account manager or by emailing us at the address above.
As always, we thank you for being a bioMérieux customer.