Maximizing the Use of the Advanced Expert System™ To Improve Patient Care

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The days of dropping antibiotic-containing disks on a culture plate inoculated with a clinical isolate, incubating the plate overnight, reading the zone sizes, interpreting the results as S, I or R, filling out the report, sending it to the clinician to be looked at 4-5 days after the culture was submitted are over.

We are now confronted with a dizzying array of resistance mechanisms that will have an impact on the way we interpret and report susceptibility data. In addition, we are constantly striving to improve the quality of data that we provide to clinicians while reducing the time required to generate and report this data. The critical care literature has been rife with references detailing that the earlier the correct antibiotic is used the better the outcome. Inappropriate initial therapy generally results in poorer patient outcomes, increased length of stay and increased hospital costs.\(^1\)\(^,\)\(^2\) The choice of empiric therapy depends on the clinician and the local antibiogram but delays in reporting the identification and susceptibility of a potential pathogen increase the likelihood that the patient is receiving inappropriate antimicrobial therapy. In addition, as soon as susceptibility data becomes available the clinician can streamline or de-escalate therapy which can decrease antimicrobial exposure, prevent the development of resistance, and result in cost savings.\(^3\)

**Identifying resistance – no easy task**

The Clinical and Laboratory Standards Institute (CLSI) have promulgated new breakpoints for some of the cephalosporins and the carbapenems. Whether to adopt these or not in place of elucidating the resistance mechanism(s) being expressed by a particular microorganism is up for debate. At our institution our Infectious Disease group wanted us to continue to provide them with information on the resistance mechanisms being expressed by the individual isolate. **Whatever the decision, one must keep in mind that expression of resistance is not always obvious.** Everyone is aware of MLS\(_S\) resistance in Staph and Strep. pneumoniae. For all isolates that test macrolide resistant and clindamycin susceptible, a “D” test must be performed to determine the nature of the macrolide resistance mechanism to ascertain if there will be inducible clindamycin resistance. The VITEK\(^\text{®}\) 2 will do that automatically for you and report the clindamycin result appropriately.

But what do you do with a *Klebsiella pneumoniae* that has a MIC to ertapenem of 4 and a MIC to imipenem of \(\leq 1\)? Do you report the ertapenem as resistant, imipenem as susceptible and forget about it? We have customized our VITEK\(^\text{®}\) 2 Advanced Expert System\(^\text{™}\) (AES) to withhold reporting this result and to alert the technologist to perform a PCR for the KPC genes. In this case the PCR was positive for KPC so we reported all of the beta-lactams as resistant. If your laboratory cannot perform a PCR for the KPC genes, a Modified Hodge Test may be used as a guide, but it is definitely not as accurate as the PCR. I would not feel comfortable reporting any KPC producing bacterial isolate as susceptible to any beta-lactam antibiotic.
We recently isolated an *E. coli* with a similar profile with the AES dictating that the KPC PCR assay be performed. In this case the result was negative for the KPC genes but when a MBL Etest was set up it was positive indicating that the *E. coli* was producing a metallo-beta-lactamase. In this case the Modified Hodge Test may not be positive as was described with isolates expressing the NDM-1 carbapenemase. This rather important finding, which was confirmed by the Centers For Disease Control (CDC), would have been missed had we not bothered to investigate the questionable susceptibility profile of this isolate.

“Regardless of what you decide to do, a good “Expert” system is an essential tool for clinical microbiologists.”

Results generated by any of the automated antibiotic susceptibility test (AST) systems may not always be correct from an in vivo standpoint, or there may be contraindications for a particular drug/bug combination. It is becoming more difficult in a busy laboratory to recognize these problems. In addition we need to make these results available in a timely fashion.

**Improving Susceptibility Reporting Workflow**

To maximize our use of the AES we customized bioART to help flag our local resistance issues. (bioART is the Advanced Reporting Tool for VITEK® 2 Systems that allows users to preprogram their own alerts and comments for specific results.)

We improved our workflow by setting up our isolates when the primary plates or subcultures are examined initially to allow them to be placed into the VITEK® 2 continually throughout the day as opposed to batch loading the isolates at the end of the shift.

We have also allowed the results to be auto-posted directly onto our Laboratory Information System (LIS) and then into the other systems utilized by the medical center. **Isolates that are “green-lighted” will go across the interface automatically.** This means that the susceptibility test result of the isolate is consistent with the organism identification and is expressing a recognized susceptibility profile.

We will also automatically attach statements to the report such as “this organism is an ESBL producer” or “…is producing a carbapenemase”. These are the types of isolates that we want to report as soon as possible both from a therapeutic and from an infection control point of view. An isolate that exhibits questionable results will be “yellow-lighted” meaning it requires review before release and any isolate that is totally inconsistent will be “red-lighted” and not sent across the interface. This means that the organism is expressing an unrecognized susceptibility profile and the results should be repeated or checked with an alternate method.

“In our institution, this has made a huge impact on patient care. The clinicians, especially in Infectious Diseases, now know that when they make their rounds in the afternoon, new data on their patients are already available.”
Faster Reporting Through Auto-Posting Improves Quality of Patient Care

Changes in therapy, including de-escalation to narrower spectrum antibiotics, can be made at this time resulting in better patient management/outcomes and potentially decreasing length of stay. **If these results were not auto-posted they would not be released until the following day.** As an example of the difference in auto-posting or waiting until the next day to release results, prior to auto-posting the average time to reporting the identification and susceptibility of a bacterial isolate obtained from a positive blood culture was 54.3 hours. After instituting auto-posting that time declined to 34.9 hours from the time the blood culture turned positive (Table 1). This would not be possible without the confidence in results provided by AES.

### TABLE 1

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<th>AUTO-POSTING VITEK® 2 RESULTS FROM POSITIVE BLOOD CULTURES TO THE LIS</th>
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When we compared the time required to identify non-albicans Candida species using conventional methodologies to the VITEK® 2, with auto-posting **the decrease was dramatic with a reduction from an average of 91 to 44 hours** (Table 1) from the time the blood culture became positive with a yeast.

“This decrease in turn-around-time (TAT) is significant and has been acknowledged by our clinicians.”

Reviewing the results from the VITEK® 2

**Results with a green light**

As stated above, results that are exhibited with a green light show consistency between the identification and the susceptibility profile obtained. The organism itself could range from a wild type (a susceptibility profile normally found in a particular organism), susceptible to all agents, resistant only to those antibiotics to which the organism is intrinsically (naturally) resistant, to a multi-drug resistant strain. As long as it is consistent with a known resistance mechanism or mechanisms, the isolate will be reported with a green light in AES. This is based on an extensive body of literature.
These results can be auto-posted directly to your LIS, thus made available to clinicians in significantly reduced time frames.

Results with a yellow light

These results will require attention and any potential discrepancy should be resolved prior to reporting results. A yellow light is listed as consistent with changes but results with a yellow light will not be auto-posted to your LIS. This means that one antibiotic for the identified organism had an MIC that is not consistent with an expected susceptibility profile. This results in AES recommending a change to that single antibiotic to make the entire susceptibility profile consistent with an expected profile.

- An example of this is a *Staphylococcus aureus* that is cefoxitin screen negative but has a MIC to oxacillin ≥4. The AES will change the cefoxitin screen to positive. However, this is a result that needs to be verified either by performing an assay to detect PBP2a or repeating the oxacillin using an Etest and repeating the cefoxitin screen.

- Another example of a “yellow light” result would be a Klebsiella that has an elevated MIC to ertapenem and a MIC to imipenem of ≤1. This would be held for review with a note to the microbiologist to refer this isolate for a PCR to detect the KPC genes. The AES can be set to automatically change the imipenem to resistant, however the production of a KPC or MBL should be verified in a case such as this.

These results will require attention and any potential discrepancy should be resolved prior to reporting results.
Results with a red light

→ These are results that will not be accepted because the observed phenotype (susceptibility profile) does not match anything that is contained in the AES database.

• As an example, we recently had a *Serratia marcescens* identified at an 89% probability that gave us a red light. The isolate was resistant to the first, second and third generation cephalosporins and had a MIC to cefepime of ≤1. This by itself would be totally consistent with a stably derepressed AmpC producer. However the isolate had a MIC to ertapenem of ≥8 and MIC to imipenem of ≤1 and was very resistant to levofloxacin and very susceptible to ciprofloxacin. This susceptibility profile just did not make sense and should not be released. The probability was also below what we would feel comfortable accepting. In this case a check of the purity plate revealed that the isolate was mixed.

This is a perfect example how the AES prevented the release of data on a mixed isolate or erroneous results.

In general with red light results, first check the purity plate, then repeat the identification and susceptibility test paying close attention to the age of the culture, the inoculum density, and the time between the preparation of the inoculum and the time the card is placed into the instrument. The majority of the red light organisms can be corrected in this manner. In some instances, using an alternate identification and susceptibility test method may be helpful.

Results with a purple light

These are organisms that, while the identification and susceptibility can be interpreted by the VITEK® 2, will not be contained in the AES database due to the infrequency in which they are isolated and therefore lack of data pertaining to their antibiotic profiles. In this instance the results will be held up for review in our laboratory.

→ For these organisms it might be prudent to check the literature or reference books for assistance in interpreting the results.
Conclusions

In an era where resistance profiles are changing rapidly and workloads are increasing, the VITEK® 2 with the Advanced Expert System gives clinical microbiologists the tools that are needed to deliver quality patient care in a timely, cost efficient manner.

However, it is up to us to take advantage of these tools. Although the thought of auto-posting results without first checking them is contrary to the way most clinical microbiologists were brought up, in this day and age with such emphasis on rapid testing and bed management, it behooves us to become part of the solution and not part of the problem. When one realizes that the majority of the isolates that we put through the VITEK® 2 can be reported the same day they were set up without technologist intervention, and have a positive impact on patient care, one might think twice about not taking advantage of this. Remember auto-posting is not auto-verification. The technologist must still verify and finalize all culture results. Auto posting is merely a way to provide faster results to clinicians, results that have been thoroughly checked against an extensive database of known organism susceptibility profiles. Verification on the other hand, a step that none of us would ever want to skip, gives us the final power of approval.

“Since we are all responsible for the results we generate, utilizing the VITEK® 2 and AES to its full potential will help us deliver the type of quality care that we owe to our patients. “

REFERENCES