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2024. Modeled Impact of Rapid Diagnostics on the Treatment of Gram-Negative Bacteremia at a Tertiary-Care VA Medical Center

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Background. Gram-negative pathogens take 24–72 hours to be identified (ID) and for antimicrobial susceptibilities (AS) to be obtained from blood cultures. Rapid molecular diagnostic tests (RDT) can shorten time to pathogen identification and antibiotic optimization. We compared our current processes with the predicted impact of an RDT system, to assist with an institutional decision to invest in RDT. The Accelerate PhenoTest™ BC Kit, which provides pathogen ID within 90 minutes of positive growth and AST within 7 hours, was selected as an example of a commercially available system for study purposes.

Methods. A retrospective review of adult patients between January 2016 and September 2017 with ≥1 positive blood culture with a Gram-negative organism detectable by the RDT system was conducted. Subject characteristics and organisms identified were recorded. Primary endpoints of the study were potential change in times to ID and AS with use of RDT. Standard laboratory procedures were used for ID and AS (pre-intervention period). The same subject population was used to calculate a theoretical time to ID and AS if RDT were used (modeled post-intervention). Patients were excluded if they expired or were discharged prior to culture results, on hemodialysis, were an outpatient at the time of + culture, or if time of ID or AS was not reported in the electronic record.

Results. A total of 156 subjects met inclusion criteria. The most common organisms isolated were *E. coli* (45%) and *K. pneumoniae* (22%). The pre-intervention mean time to ID and AS in the medical record were identical at 56 hours (using VITEK™). The mean times to effective (covering) and optimal (targeted/consolidated) therapy for the pre-intervention group were 8 and 75 hours, respectively. For the modeled post-intervention period, RDT could decrease time to ID by 54 hours (95% CI: 50.5–59.1, $P < 0.001$) and AS by 49 hours (95% CI: 45.1–53.5, $P < 0.001$).

Conclusion. Time to optimal therapy of Gram-negative bloodstream infections at our facility was ~3 days (within a day of final organism ID and AS). This demonstrates excellent communication protocols between our microbiology and clinical departments, suggesting that our modeled benefit to RDT for organism ID and AS has good potential to be translated into clinical benefits.

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2025. Procalcitonin Reference Cutoff and Specimen-Type Validation

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Investigation: The primary objective of this study was to validate that the clinical cutoff of 0.3 ng/mL is appropriate in our population of patients. The secondary objective of this study was to compare procalcitonin results in plasma and serum specimens to prove that both sample types gave similar results.

Background. Our institution started performing procalcitonin testing on November 29, 2017. The Roche package insert indicated that in a population of 282 self-reported healthy individuals, the 95th percentile, upper reference range limit was calculated at 0.08 ng/mL. This 95th percentile cutoff seemed to be much lower than published clinical cutoffs of 0.25 and 0.30 ng/mL. Upon extensive literature review and discussion with pediatric and adult infectious disease physicians, we decided to use the clinical cutoff of 0.3 ng/mL to indicate invasive bacterial infection in our institution.

Methods. Two hundred and fifty patients with normal renal and hepatic function, white blood cell counts and C-reactive protein below 5.0 mg/L were selected for the validation of procalcitonin clinical cutoff. An additional 100 patients with paired plasma and serum specimens drawn at the same time were selected for the plasma vs. serum comparison study. All results were analyzed using the R statistical program.

Results. Blood specimens from 128 females and 122 male patients ranging from 10 to 84 years old were utilized in this study. Out of the 250 specimens, 128 were plasma and 122 were serum specimens. The procalcitonin 95th percentile upper reference range limit based on our population was 0.08 ng/mL, which validated the Roche package insert claim. Only one out of 250 patients (0.4%) had procalcitonin result above 0.3 ng/mL. The paired plasma and serum specimens in 100 patients yielded procalcitonin results that correlated with a Pearson's R value of 0.999. The linear regression equation for the correlation was $y = 0.94x$.

Conclusion. This result confirmed that a procalcitonin clinical cutoff of 0.3 ng/mL is appropriate in our patient population. It also showed that both plasma and serum specimens can be used for procalcitonin measurement.

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2026. Phenotypic and Molecular Characterization of Drug Resistance and Biofilm Production in *Stenotrophomonas maltophilia* Obtained in a 10-Year Period from a Mexican Hospital

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Background. *Stenotrophomonas maltophilia* is an emerging drug-resistant opportunistic pathogen related with healthcare-associated infections. The aim was to perform a phenotypic and molecular characterization of drug resistance and biofilm formation in *S. maltophilia* obtained in a 10-year period from a Mexican Hospital.

Methods. *S. maltophilia* isolates from a 10-year period from a tertiary care hospital in Mexico were identified by MALDI-TOF MS. Antimicrobial susceptibility was determined by the broth microdilution method. Drug resistance-associated genes were analyzed by PCR. Biofilm formation and its composition was assessed by crystal violet staining, and detachment assays, respectively. Biofilm production-associated genes were analyzed by PCR. MALDI-TOF mass spectra patterns were analyzed to search markers of drug resistance and biofilm production using the ClinProTools software.

Results. In the 10-year study period, 258 *S. maltophilia* isolates were identified, with high resistance detected for ceftazidime (48.4%), cefepime (31.6%), ciprofloxacin (25.0%), trimethoprim-sulfamethoxazole (18.8%), and lower resistance to chloramphenicol (13.6%) and levofloxacin (2.2%). Drug resistance was not associated to the presence of the *sul1* (4.1%), *sul2* (0.5%), *sul3* (0.0%) or ISCR (0.0%) genes. Overexpression of the SmeABC efflux pump was associated to higher drug resistance ($P < 0.05$). Overall, 97.7% isolates were biofilm producers, i.e., 41.7% were strong producers; 32.0% were moderate, and 26.2% were weak producers. Biofilm composition analysis showed similar percentages for carbohydrates, proteins and DNA in all isolates (36.0, 39.7 and 40.9%, respectively). Biofilm-associated genes *fsnR*, *rmlA*, *rpfF*, *xanB* and *spgM* were detected in 94.0, 75.3, 28.6, 17.2% and 0.0% of isolates, respectively. Four potential biomarker peaks were detected in *rmlA* positive biofilm-producing isolates ($P < 0.05$).

Conclusion. Most of *S. maltophilia* clinical isolates showed high antimicrobial resistance levels and were able to produce biofilm. Biofilm biomass composition of these isolates showed a similar proportion of polysaccharides, proteins, and DNA. The presence of the *rmlA* gene was associated with biofilm production. Four potential markers of the presence of the biofilm production-associated *rmlA* gene were detected by mass spectrometry.

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2027. Immune Correlates of Protection Against Herpes Zoster (HZ) in People Living with HIV (PLWH)

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Background. HZ has high morbidity in immune-compromised hosts, including PLWH. Two vaccines against HZ are available, but their efficacy in PLWH is unknown. A surrogate marker of protection against HZ would facilitate efficacy studies of HZ vaccines in PLWH, as compared with HZ clinical outcome studies. To this goal, our study investigated the association of cytotoxic T lymphocytes (CTL) and regulatory T cells (Treg) with incident HZ in PLWH.

Methods. The study used peripheral blood mononuclear cells (PBMC) cryopreserved at mean (SD) of 2.7 (2.5) months before HZ from 31 PLWH cases on ART with plasma vRNA < 200 c/mL, and CD4 counts ≥ 200 cells/ μ L. 31 non-HZ controls were matched to cases by CD4 count, age, sex, race, parent study, and ART duration. T cell subsets were measured by flow cytometry after ex vivo VZV- and mock-restimulation and in freshly thawed unstimulated PBMC using the following markers: CD3, CD8, CD25, CD28, CD39, CD57, CD127, CTLA4, FOXP3, IFN γ , IL10, KLRG1, LAG3, PD1, perforin, TGF β , TIM3 and TNF α . Data were analyzed by paired t-tests.

Results. At PBMC collection, PLWH had mean (SD) age 41 (10) years; 16 females; 28 White and 22 Black non-Hispanics; mean (SD) CD4 counts 501 (222) cells/ μ L; 56 (90%) vRNA < 50 c/mL; median ART duration 50 weeks. In unstimulated