Impact of the Implementation of a Host-Response Sepsis Test on Sepsis Alerts and Laboratory Sepsis Resource use in the Emergency Department

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Introduction

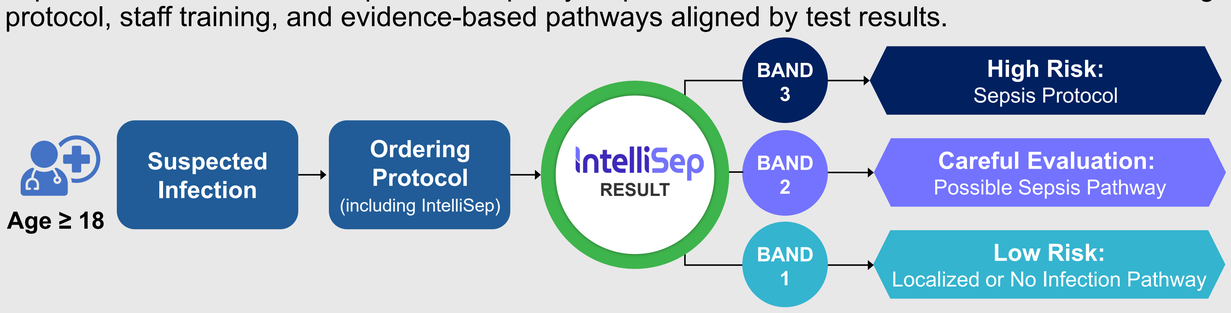
- Sepsis is a dysregulated host immune response to infection leading to organ dysfunction[1]
- There is substantial unmet need for rapid diagnosis to prevent resultant morbidity and mortality[2]
- Guidelines stress quick intervention[3], yet undifferentiated patients present to the Emergency Department (ED) and physicians must diagnose before objective diagnostic data are available
- This can lead to excess sepsis alerts and the over-use of laboratory and antibiotics resources
- A new host-response sepsis diagnostic (HRSD) test, recently cleared by the U.S. Food and Drug Administration (FDA) for early detection of sepsis, may aid in addressing this gap

This study evaluated the impact of implementing a hospital laboratory-based HRSD test for ED patients on code-sepsis alert activations, and the rate of antibiotics and blood culture utilization.

Methods

New Test Implementation:

On June 17, 2025, the Texas Health Resources Denton Hospital laboratory (Denton, TX) implemented an HRSD as part of a quality improvement initiative that included an ordering protocol, staff training, and evidence-based pathways aligned by test results.

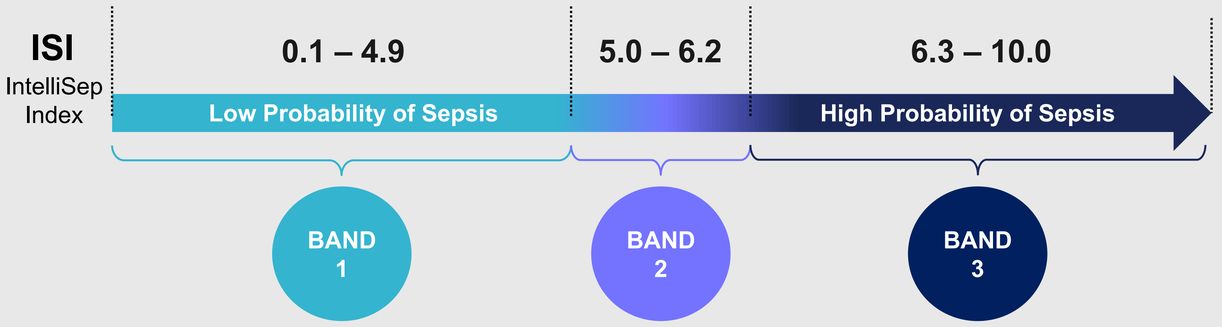


Laboratory and clinical leaders guided implementation and continued to monitor sepsis alerts, blood culture practices, and antibiotic utilization to ensure consistent protocol application, support antimicrobial stewardship, and promote patient safety.

	Pre-Implementation (Apr. 1 – May 15, 2025)	Post-Implementation (June 17, 2025 – Dec. 31, 2025)
ED Census	5,454 patients	26,913 patients
Sepsis Alerts (Vocera® System Data)	306 activations	803 activations

The Cytovale IntelliSep Test:

The IntelliSep test is an FDA cleared, semi-quantitative blood test that assesses the state of immune activation at the cellular level and is intended to aid in the early detection of sepsis with organ dysfunction manifesting within the first 3 days after testing for adults with signs and symptoms of infection presenting to the ED.



All results should be interpreted in the context of the other clinical observations and laboratory test results for the patient.

The test results in the IntelliSep Index (ISI), a single score between 0.1-10.0, in <10 minutes. Results are grouped into three interpretation bands reflecting increasing likelihood of sepsis, Band 1 (low) to Band 3 (high).

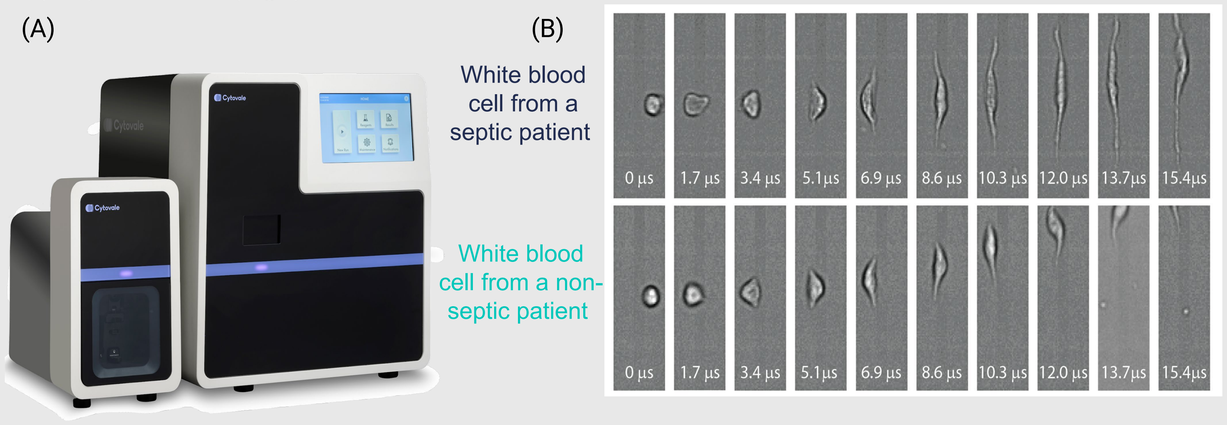


Figure 1: (A) Photograph of the Cytovale system, a benchtop instrument on which the IntelliSep test is performed; (B) Time series of cell deformation for a representative leukocyte of a septic Band 3 patient (top) and a non-septic Band 1 patient (bottom).

Methods (continued)

Study Design & Setting

- Retrospective pre-post cohort analysis at a single ED in Denton, Texas
- Pre-implementation spanned April 1, 2025, to May 15, 2025, and post-implementation spanned June 17, 2025, to December 31, 2025 (3 days in the pre-period [April 18–20, 2025] had missing sepsis alert data and were excluded from analysis)
- Daily code-sepsis alert activations were extracted from Vocera®

Activation Rate

$$\frac{\text{Daily Activations}}{\text{Daily ED Encounters}}$$

Activations per Sepsis Case

$$\frac{\text{Total Activations}}{\text{Sepsis Cases (ICD-10 @ discharge)}}$$

- To evaluate whether clinical care was preserved, we assessed the mean daily proportion of sepsis patients receiving 1) IV antibiotics, and 2) blood cultures ordered in the ED
- Between-period comparisons for proportional endpoints were performed using Pearson chi-square tests (two-sided α=0.05); continuous variables were compared using Welch's t-test

Results & Discussion

- 5,454 ED encounters occurred pre-implementation and 26,913 post-implementation, with similar mean daily census (130 patients/day pre vs 136 post)
- There were 306 sepsis alert activations pre-implementation and 803 post-implementation
- Confirmed sepsis cases totaled 172 pre-implementation and 734 post-implementation, with comparable average sepsis prevalence (3.14% pre vs 2.73% post)
- The mean daily activation rate decreased from 5.58% to 2.99% (46.4% relative reduction; p<0.001). Mean daily activations per confirmed sepsis case declined from 2.18 to 1.31 (39.7% relative reduction; p<0.01).
- Clinical management metrics among confirmed sepsis patients remained unchanged
  - Proportion receiving IV antibiotics (95.09% pre vs 95.45% post, p=ns)
  - Proportion with ED blood cultures (93.77% pre vs 91.44% post, p=ns)

Time Period	Pre 4/1/2025 to 5/15/025	Post 6/17/2025 to 12/31/2025	Relative Reduction	p-value
ED Census	5,454	26,913		
Mean ED Census per day	130	136		NS
Activations	306	803		
Sepsis Cases	172	734		
Average Sepsis Prevalence	3.14%	2.73%		NS
Mean Activation Rate (% per day)	5.58%	2.99%	46.4%	p < 0.001
Mean Activations per Sepsis Case (per day)	2.18	1.31	39.7%	p < 0.01
Sepsis Patients Receiving IV Abx (% per day)	95.09%	95.45%	-0.4%	NS
Sepsis Patients with a blood culture ordered in the ED (% per day)	93.77%	91.44%	2.5%	NS

Conclusions

Implementation of HRSD was associated with a substantial reduction in sepsis alert activations per day and per confirmed sepsis case, with mean activations moving closer to a 1:1 alignment with sepsis prevalence. Despite fewer alerts, IV antibiotic use and blood culture ordering among true sepsis patients were unchanged, indicating preserved care quality and patient safety. The reduced alert volume also lessened the operational burden on laboratory staff. **Overall, these findings suggest improved alert specificity and diagnostic efficiency while maintaining high-quality clinical management.**

Acknowledgements

We would like to thank the providers and nursing staff of the Texas Health Resources Denton Hospital Emergency Department for their tireless efforts in adopting new process and technology to improve the care of our patients who present with signs or suspicion of infection. We also thank the clinical laboratory staff who have worked with us over the last year to implement this test. Finally, we thank the THR Denton Quality and Safety team that works to ensure we are providing the best possible care to our patients.

References

[1] Singer, *JAMA*, 2016
[2] Wang, *Crit Care Med* 2017.
[3] Surviving Sepsis Campaign Declarations. 'Barcelona Declaration' [cited 2020].