Diagnosis of infection utilizing Accellix CD64

Charles L. Sprung, Ricardo Calderon Morales (Hadassah Hebrew University Medical Center, Jerusalem, Israel); Harvey Kasdan, Allon Reiter, Yael Himmel, Julien Meissonnier (LeukoDx, Jerusalem, Israel)
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• Despite great progression in ICU therapies, the diagnosis of infections and sepsis remains elusive.
• The signs of infection and inflammation are similar, making diagnosis of bacterial infections difficult.
• Traditional markers for infection and sepsis (temperature, leukocytosis and CRP) suffer from the lack of sensitivity and specificity.
Antimicrobial Use in the ICU: Indications and Accuracy—An Observational Trial

- Intensivist infection certainty was recorded when starting antibiotics.
- Independent ID specialist determined if infection was present.
- Empirical antimicrobial therapy was justified by infection in 67/125 (54%) occasions.
- Infection was defined on 6/19 (31%) occasions when ICU clinician certainty was low and antimicrobials were prescribed even when clinician certainty was minimal.
- Antimicrobial course length was similar whether infection was defined or not (11.5 vs 10.7 days; p = 0.65).

Levin P. J Hosp Med 2012;7:672-8
Several laboratory tests have been assessed to differentiate between infected and non-infected ICU patients and to improve antibiotic administration.

Procalcitonin (PCT) has been compared to other biomarkers and been shown to be superior.

Most of the benefit of using PCT in ICU patients derives from a decrease in unnecessarily long course lengths of antibiotic therapy, rather than an improved diagnostic ability in determining which patients have active infection.

Bouadma L. PRORATA trial. Lancet. 2010;375:463-74

There is still a need for better markers of the presence of infection.
CD64 in Sepsis

• Improved diagnosis should be based on a marker that is specifically and rapidly activated upon infection.
• CD64 is constitutively expressed on the cell surface of PMNs and monocytes.
• Upon invasion of a pathogen into the circulation, the expression level of PMN-CD64 on neutrophils increases dramatically.
• The value of CD64 has been supported by numerous clinical studies that used the Trillium – Neutrophil - CD64 as an assay for diagnosis of bacterial infection and sepsis.
• Measurement of CD64 expression is equal or superior to other common tests (CRP, PCT, leukocyte count, etc) for sensitivity and specificity.

CD64 Sepsis Studies

- 300 unselected ICU patients
- CD64, PCT and sTREM-1 assessed for diagnosing sepsis in the critically ill patients - the best ROC curve being obtained for the PMN CD64 index.
- CD64 expression seems unchanged in patients with inflammatory states from non-infectious origin

Gibot S. Am J Respir Crit Care Med 2012;186:65-71
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Background/Purpose

- Preliminary studies have shown that the cartridge-based Accellix system determined CD64 levels are comparable to standard laboratory FACS.

![CD64 results: Accellix vs. FACS](chart.png)
CD64 Sepsis Studies

- CD64 & CRP were measured within 24 hours of admission.
- 103 (22%) of 468 ICU patients with serial data had sepsis.
- Septic patients had higher CD64 than non-septic patients ($p < .001$).
- A cutoff admission CD64 expression of 230 MFI identified sepsis with a sensitivity of 89% and specificity of 87%.
- When combining CRP and CD64 expression, an abnormal result for both was associated with a 92% probability of sepsis, whereas sepsis was ruled out with a probability of 99% if both were normal.

Dimoula A. Clin Infect Dis 2014;58:820-9
CD64 Monitoring Tool

- Septic patients receiving inappropriate antibiotics had persistently elevated CD64 expression.
- CD64 expression decreased over time in patients receiving appropriate antibiotics.
- In non-septic patients, an increase in CD64 expression $\geq 40$ MFI predicted ICU-acquired infection.

Dimoula A. Clin Infect Dis 2014;58:820-9
Diagnosis of infection utilizing Accellix CD64

Background/Purpose

• Differentiating ICU patients who are infected or not can be very difficult.
• Present diagnostic tests remain inadequate.
• CD64 has been found to be a potentially useful marker to identify infected patients.
• Unfortunately, CD64 measured by standard flow cytometers in a laboratory takes hours to perform.
• The purpose of this study was to evaluate the Accellix CD64 instrument which provides results in 20 minutes in ICU patients with and without infections.
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Methods

• Infected (ICUi) and non-infected ICU patients (ICU Control-ICUc) and normal volunteers (C) had CD64 levels measured by the Accellix CD64 instrument.

• Measurements were calculated as 'CD64 index', i.e. the ratio between the fluorescence of the PMN population and the fluorescence of control beads.
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Results

• 72 subjects were studied (ICUi- 27, ICUc-22 and C-23).

• CD64 Index levels were higher (mean ± SEM) in ICU infection patients then ICU control and normal control patients (2.62 ± 0.39 vs. 1.31 ± 0.24 vs. 0.46 ± 0.04, p = 0.009).
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Results

CD64 Index

** P<0.001

** P<0.01

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<tr>
<th>Group</th>
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<tbody>
<tr>
<td>Normal Controls</td>
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<tr>
<td>ICU Controls</td>
<td>22</td>
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<tr>
<td>ICU Septic</td>
<td>27</td>
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Conclusions

• CD64 Index levels are higher in infected than non-infected ICU patients.

• Accellix CD64 is a promising instrument to differentiate infected from non-infected ICU patients in a timely manner.
European CD64 Sepsis Study

- Study: Calibration and Validation Studies of the Accellix-CD64 system as an aid in the diagnosis of sepsis in critically ill patients

- Objective:
  - A calibration study to determine the optimal cut-off value of the CD64 index as an aid in the diagnosis of infection in critically ill patients.
  - A validation study testing the determined cutoff in the target population.

- Design: Prospective-retrospective, observational, delayed cross-sectional, open label

- Current Sites: Profs. Sprung, Reinhart, Vincent