NEW SEPSIS MARKER

PATHFAST® PRESEPSIN

- Diagnosis & early prognosis
- Risk stratification
- Patient monitoring

Fast and quantitative results out of whole blood in 17 minutes
For routine laboratory and point of care use
PATHFAST® Presepsin is a chemiluminescent enzyme immunoassay for the quantitative measurement of presepsin concentration in whole blood or plasma. PATHFAST® Presepsin can be used as an aid in the diagnosis and prognosis of sepsis, in the assessment of the degree of septic severity, and in the risk stratification of critically ill septic patients.

Introduction

CD14 is a glycoprotein expressed on the membrane surface of monocytes/macrophages and serves as a receptor for complexes of lipopolysaccharides (LPS) and LPS binding protein (LBP), activating the toll-like receptor 4 (TLR4) specific pro-inflammatory signaling cascade on contact with infectious agents. Simultaneously, CD14 is shed from the cell membrane into the circulation forming soluble CD14 (sCD14). However, plasma protease activity generates also another sCD14 molecule called sCD14 subtype (sCD14-ST) or presepsin. The levels of presepsin were significantly higher in septic patients than in patients with SIRS or apparently healthy individuals. Presepsin levels were elevated earlier than IL-6 and D-dimer along with occurrence of blood bacteria in animal model. The determination of the presepsin concentration can be used for diagnosis and prognosis of sepsis and also to monitor the course of the disease.

Mechanism of presepsin secretion

Clinical use of PATHFAST® Presepsin

» Early diagnosis and prognosis of sepsis
» Prognosis already at first presentation
» For emergency and intensive care use

Early diagnosis and prognosis

In a reference range study presepsin concentrations were determined in EDTA plasma samples from 119 healthy individuals (age: 21 – 69 years; 60 females and 59 males).

Arithmetic mean: 160 pg/ml (95% CI: 48 – 171 pg/ml); 95th percentile: 320 pg/ml (no influence of age and gender).

The presepsin values were determined at presentation in the emergency department in patients with sepsis.

Quartiles of presepsin showed a strong association with the 30 day mortality:

<table>
<thead>
<tr>
<th>Quartile</th>
<th>1st (n=37)</th>
<th>2nd (n=35)</th>
<th>3rd (n=35)</th>
<th>4th (n=33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presepsin (pg/ml)</td>
<td>177 – 512</td>
<td>524 – 927</td>
<td>950 – 1,810</td>
<td>1,850 – 15,757</td>
</tr>
<tr>
<td>Mortality (p&lt;0.0001)</td>
<td>2.7%</td>
<td>8.6%</td>
<td>17.1%</td>
<td>39.4%</td>
</tr>
</tbody>
</table>

mCD14: membrane CD14; sCD14: soluble CD14; sCD14-ST: soluble CD14 subtype (=Presepsin); LPS: lipopolysaccharide; LBP: lipopolysaccharide binding protein, TLR4: toll-like receptor 4; MD2: Co-Protein of TLR4.
Prognostic value of presepsin in emergency patients using the new assay PATHFAST® Presepsin

ROC analysis comparing the accuracy for the prediction of 30-day mortality revealed areas under the receiver operating characteristics curve (AUC) for presepsin, APACHE II score and procalcitonin of 0.878, 0.815 and 0.661, respectively."}

Interpretation of results

The following preliminary cut-off values were derived from first clinical study data:

- Exclusion of sepsis or infection: < 200 pg/ml
- Exclusion of severe sepsis or septic shock: ≤ 300 pg/ml
- Sepsis possible: > 300 pg/ml
- High probability of severe sepsis or septic shock: > 1000 pg/ml

For emergency and intensive care use

PATHFAST Presepsin can be measured out of whole blood and is due to the fast turn around time and high prognostic power already at admission suitable for the use in emergency and intensive care units.

- **Sample material:** anticoagulated (EDTA/heparin) whole blood or plasma
- **Turn around time:** 17 min

Disease monitoring

Presepsin was measured at presentation, at 24 hours and at 72 hours after admission. In patients with favorable outcome within 30 days after admission (n=104) presepsin levels decreased from baseline to 72 hours. In the patient group who experienced adverse outcome (n=36), presepsin levels showed an increasing tendency.

Reagent cartridge

Sample well

- Magnetic particles
- ALP-conjugated antibody
- Chemiluminescent substrate (CDP-Star with Sapphire II)
- Sample diluent
- Washing buffer

Correlation of presepsin values and patient outcome

Course of mean values of presepsin (error bars 95% CI) in patients with worse outcome (orange line) and favourable outcome (blue line).
PATHFAST® Presepsin
Early prognosis of sepsis is key for improved clinical outcome

Analytical performance data

Analytical performance was evaluated on PATHFAST system with whole blood and plasma.

<table>
<thead>
<tr>
<th>Assay range</th>
<th>20 – 20,000 pg/mL</th>
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<tbody>
<tr>
<td>Correlation between whole blood and plasma on PATHFAST</td>
<td>y = 1.04 x - 10.8 ; r = 0.986 ; n = 104 (y: EDTA whole blood, x: EDTA plasma)</td>
</tr>
<tr>
<td>Total % CV in plasma</td>
<td>QC-LL = 4.4%, QC-L = 4.0%, QC-M = 3.8%, QC-H = 5.0%</td>
</tr>
</tbody>
</table>

The PATHFAST® System

The PATHFAST analysis system combines the accuracy of a full-scale lab with the flexibility of a mobile solution. Best prerequisites for fast differential diagnosis at the point of care. Easy to operate, install and network. Highest precision make this device an adequate „outpost“ of a full-scale lab on intensive care or emergency ward. Parallel processing enables the examination of six samples in only 17 minutes.

Six parallel channels. Six quantitative analysis simultaneously. Six results in 17 minutes. This gives PATHFAST its unique speed.

Its compact design and low weight make PATHFAST the ideal analysis system in emergency labs, hospitals and medical offices. Applied wherever fast quantitative results with full-scale lab quality provide decisive diagnostic advantages. Directly at the point of care.

PATHFAST is a fully automatic immunoassay analyzer, which combines the progressive chemiluminescence technology with the patented Magtration® technology. Small sample volumes can be detected with high accuracy and precision.

Insert the reagent cartridge, apply the samples and press the „Start“ button. PATHFAST takes care of everything else fully automatic. A simple 3-step method provides results in lab quality.

References


5) Internal data


PATHFAST® The highly precise, fast and compact chemiluminescence immunoassay analysis system

PATHFAST® Test Principle

**IMMUNOREACTION**
- Sample (whole blood, plasma)
- Magnetic particles coated with antibody
- ALP labelled antibody

**SEPARATION**
- Magnet
- Magtration® technology

**ENZYME REACTION**
- Chemiluminescent substrate

**DETECTION**
- Photomultiplier
- Measurement of light emission

**PATHFAST® Technical Specifications**

Instrument type: Desktop Immunoassay Analyzer

Throughput: Up to 6 samples or parameters per run

Measuring time: Less than 17 min for 6 samples using PATHFAST® Presepsin

Sampling material: Whole blood, plasma, serum

Measuring principle: Analysis takes place with the help of the chemiluminescence enzyme immunoassay technology (CLEIA) and Magtration® technology.

Reaction temperature: 37.5 °C

Sample volume: 100 µl

Wavelength: 300 – 650 nm

Data storage:
- Patient data: 1000
- QC data: 1800
- CAL data: 300

Data transfer: ASTM standard

Dimensions: 375 (w) x 570 (d) x 510 (h) mm

Weight: 33 kg

El. requirements: 100 - 240 V AC (50/60 Hz)

Power consumption: 360 VA

Monitor/keyboard: LCD touch-screen

Printer: Integrated

PC: Integrated

Interface: RS-232C

Calibration:
- Factory calibration
- 2-point calibration every 4 weeks

24-h operation (stand-by): recommended
# Product List

<table>
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<tr>
<th>SYSTEM</th>
<th>Item number</th>
<th>Pack size</th>
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<tr>
<td>PATHFAST® Immunoanalyser</td>
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<tr>
<th>CONSUMABLES AND ACCESSORIES</th>
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<tr>
<td>PATHFAST® pipette tips</td>
<td>1114-1000</td>
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<td>PATHFAST® waste box</td>
<td>1114-1001</td>
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<tr>
<th>REAGENT KITS FOR SEPSIS DIAGNOSTICS</th>
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<td>PATHFAST® Presepsin</td>
<td>1110-4000</td>
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<tr>
<td>PATHFAST® Presepsin control set</td>
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<th>REAGENT KITS FOR CRITICAL CARE DIAGNOSTICS</th>
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<tr>
<td>PATHFAST® HCG</td>
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