

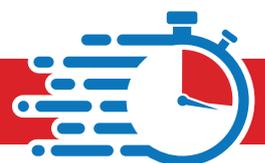
PATHFAST™ PRESEPSIN



The Sepsis Marker

- > Whole blood
- > Early prognosis
- > Risk stratification
- > Patient monitoring

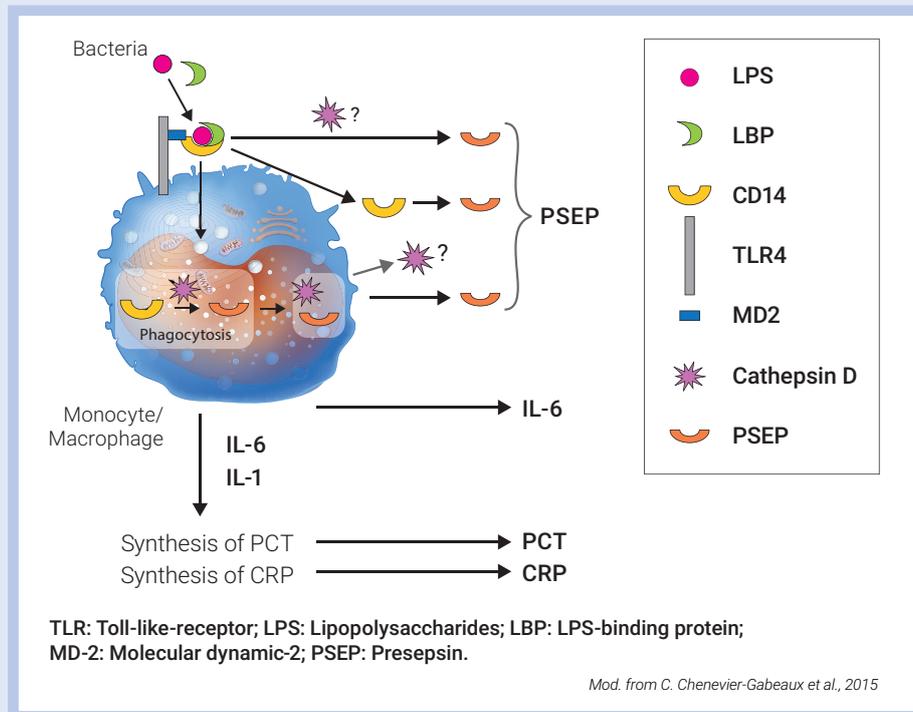
< 17 minutes for 6 samples



What is PATHFAST™ Presepsin?

PATHFAST™ Presepsin is a chemiluminescent enzyme immuno- assay (CLEIA) for the quantitative measurement of the Presepsin concentration in whole blood or plasma.

PATHFAST™ Presepsin improves the diagnosis and prognosis of sepsis defining its level of severity. It is a valid indicator of risk stratification in septic patients. Due to the fast analysis within 15 minutes and the high prognostic value even at patient's admission, PATHFAST™ Presepsin is useful in laboratories, emergency- and intensive care units and neonatal departments. An early diagnosis with an excellent prognostic performance and its ability to respond rapidly to the variety of clinical conditions make PATHFAST™ Presepsin the ideal tool for monitoring treatment, selecting the correct antibiotic-dose or changing it if ineffective.



Presepsin secretion (Fig.1)
 sCD14-ST is a 13k Da fragment derived from cleavage of CD14, a glycoprotein of 55k Da anchored to the membrane of monocytes, macrophages and polymorphic neutrophils. CD14 acts as a receptor for lipopolysaccharide (LPS) complexes and the specific LPS binding protein (LBP). It can bind to peptidoglycans and other surface structures present in both Gram- Positive and Gram-Negative bacteria. Once bound to the LPS-LBP complex, it activates the intracellular inflammatory response of the Toll-Like receptor 4 (TLR4)/MD2-complex, triggering the host's inflammatory cascade against the infectious pathogenic agent. Phagocytosis and activity of plasma proteases (lysosomal enzymes, cathepsin D) result in the formation of the fragment sCD14 subtype, in particular the 13 kDa fragment of sCD14-ST, known as Presepsin.

Fig. 1: Schematic production of Presepsin

Why choose PATHFAST™ Presepsin?

Presepsin is a reliable, specific and sensitive biomarker for sepsis and a valuable tool for the very early diagnosis of sepsis by Gram-negative and Gram-positive bacteria or fungi [1]. Presepsin rises earlier than other biomarker and does not show unspecific increases [2]. Presepsin values help to stratify the severity of the septic disease with excellent correlation to APACHE II-, GCS-, MEDS- and SOFA-score [3]. Presepsin exceeds the prognostic power of other sepsis biomarkers and is specifically useful when combined with clinical risk scores like e.g. qSOFA [4].

The time course of Presepsin can be used for monitoring: a decline demonstrates response to therapy and predicts a favorable outcome [5,6]. Presepsin is an accurate biomarker in the diagnosis of neonatal sepsis with higher cut off values [7,8]. In cardiac surgery elevated preoperative plasma Presepsin concentration is a strong predictor of postoperative mortality in cardiac surgery patients [9].

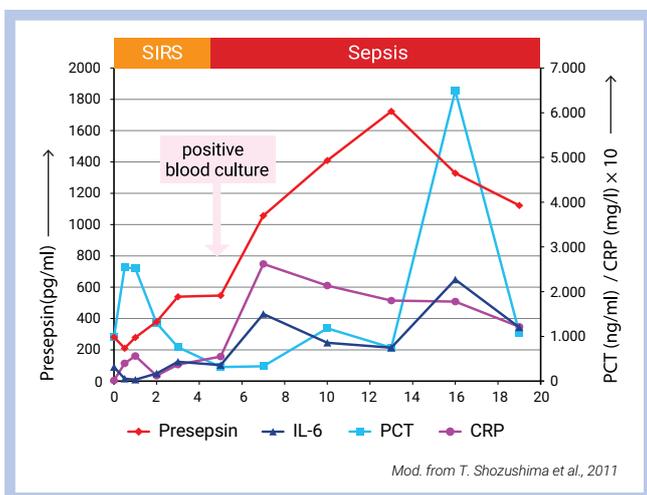


Fig. 2: Clinical course of each septic markers in a burn patient

Early marker of sepsis (Fig. 2)

The Presepsin molecule is characterized by rapid kinetics: activation time is only 2 hours following a bacterial or fungal event, with a peak concentration after 3 hours. This characteristic makes the Presepsin molecule the fastest biomarker for sepsis in relation to procalcitonin (PCT) and C-Reactive Protein (CRP), which have activation times of 6-12 hours and 12-24 hours, respectively. The half life of the molecule in plasma is 4-5 hours, compared to 12-24 hours for PCT, allowing more effective and earlier management of the pharmacological treatment.

Presepsin (in red) and other markers in post-traumatic patients following a serious burn were considered. It is well-known that Presepsin does not change after the trauma but there is an early increase in the values of Presepsin by day 2 following the occurrence of a bacterial infection confirmed by a positive blood culture of day 5. Effectiveness of antibiotic treatment is shown at day 13.

Moreover, when patients were divided into an infection group and a non-infection group and ROC curves of each of the markers were plotted to compare Presepsin with other markers, the results showed that Presepsin was the best, followed by CRP, IL-6, and PCT [2].

Diagnostic accuracy: sensitivity and specificity

The diagnostic validity of Presepsin has been evaluated in numerous clinical studies. Comparisons of different medical scores and relevant biomarkers in sepsis diagnosis revealed an important role for PATHFAST™ Presepsin.

Improved 30 day mortality prediction (Fig. 3)

Presepsin showed superior risk of 30 day mortality prediction at admission in septic patients compared to APACHE II, GCS, MEDS, SOFA and procalcitonin.

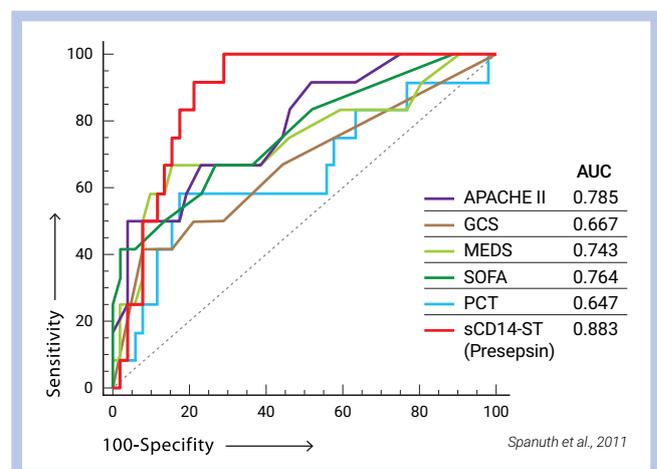


Fig. 3: Comparison of ROC curves for 30 day mortality at admission by Presepsin, PCT and medical scores

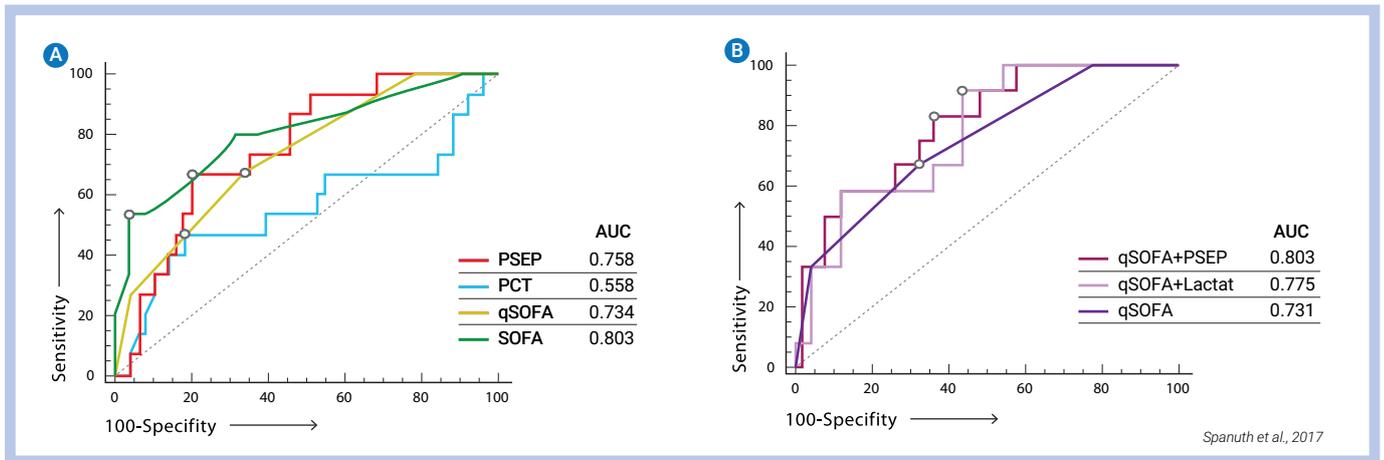


Fig. 4A: ROC curves for 30 day mortality at admission for Presepsin, PCT, SOFA, and qSOFA alone

Fig. 4B: ROC curves for 30 day mortality at admission for Presepsin, and Lactate combined with qSOFA

Support of medical scores (Fig. 4A+B)

Quick-SOFA (qSOFA) was defined by The Third International Consensus Definitions for Sepsis and Septic Shock in 2016 in order to provide a simplified version of SOFA without the need of laboratory tests. It can be directly assessed at patient admission. For discrimination between uncomplicated sepsis and severe sepsis or septic shock Presepsin showed superior discriminatory power compared to clinical scores and

biomarkers. Additionally simultaneous assessment by combining Presepsin and qSOFA improved the diagnostic validity significantly. Combination of Presepsin and qSOFA showed a detection rate for non-survivors of 93% and 67% and for patients with severe sepsis/septic shock of 92% and 58% whereas qSOFA alone only reached 67% and 58%, respectively. Presepsin showed also a predictive superiority compared to lactate and procalcitonin [4].

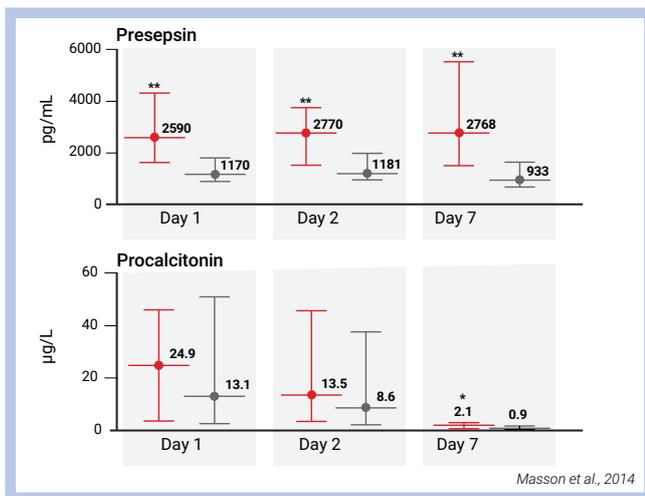


Fig. 5: Time course of plasma concentrations of Presepsin and procalcitonin during ICU stay by survival status. Decedents are shown in red and survivors in black

Presepsin and procalcitonin levels for mortality prediction (Fig. 5)

Evolution of Presepsin levels over time in survivors was significantly different from that in deceased patients in the ICU. PCT levels decreased rapidly and similarly in survivors and non-survivors whereas Presepsin clearly differentiates already after 24 hours between the two cases. In comparison to survivors Presepsin levels in non-survivors stayed constantly high over the time period observed. Conversely, PCT levels fell rapidly and similarly from day 1 to 7 in survivors and non-survivors. Presepsin appears as an early marker of mortality with better prognostic performance than PCT and can be used as an aid in risk stratification strategies in septic patients [6]. Patients with decreasing levels of Presepsin over 7 days in ICU were more likely to have received an early appropriate first-line empirical antibiotic therapy on day 1 than those with increasing levels [5].

Presepsin (pg/ml)	Diagnosis
< 200	Exclusion of sepsis
< 300	Systemic infection not probable
< 500	Systemic infection (sepsis) possible
< 1000	Significant risk of the systemic infection progression (severe sepsis), increasing risk of unfavorable outcome
≥ 1000	High risk of the systemic infection progression (severe sepsis/septic shock). High risk for mortality after 30 day comparable with a SOFA score ≥ 8

Fig. 6: Decision thresholds of PSEP for early risk stratification in patients with sepsis

Negative Predictive Value and cut off values (Fig. 6)

An important diagnostic factor is the high Negative Predictive Value (NPV) of Presepsin. In fact for healthy individuals, not affected by a clear bacterial outbreak, the values of Presepsin are below 200 pg/mL. A Presepsin cut off value of 1.622pg/ml excludes 30 day mortality by a Negative Predictive Value (NPV) of 98,5% [9]. Presepsin concentration is already related to the severity of the disease at the time of first presentation and may be useful in the differential diagnosis in patients presenting with clinical signs of SIRS and sepsis in the emergency department. In summary, based on the Presepsin values measured in the study patients with different disease severity degrees (SIRS, sepsis, severe sepsis or septic shock) and the close relationship between Presepsin and outcome decision thresholds for risk stratification could be established [1,10].

Evaluation of Severity

Presepsin correlates significantly with the degree of severity of the infection as its quantitative results increase proportionally. In fact, the studies reveal maximum correlation with the SOFA score values (clinical scoring used most frequently to evaluate organ failure). Higher values on the first day of monitoring are closely associated with a higher incidence of new organ failure and hemodynamic instability in the first 24 hours.

All together, Presepsin concentration increased with the SOFA score, the number of prevalent organ dysfunctions or failures, and the incidence of new failures of the respiratory, coagulation, liver, and kidney systems, therefore Presepsin is an early predictor of host response and mortality in septic patients. Changes in concentrations over time seem to reflect the appropriateness of antibiotic therapy^[5].

Time

- > Results in 15 minutes
- > Fast kinetics (2/3 hours after onset of the infectious event)^[1]
- > Short half-life: 4/5h^[11]

Sensitivity

- > Chemiluminescent enzyme immunoassay
- > No interference
- > "All-in-one" single use cartridges

Presepsin

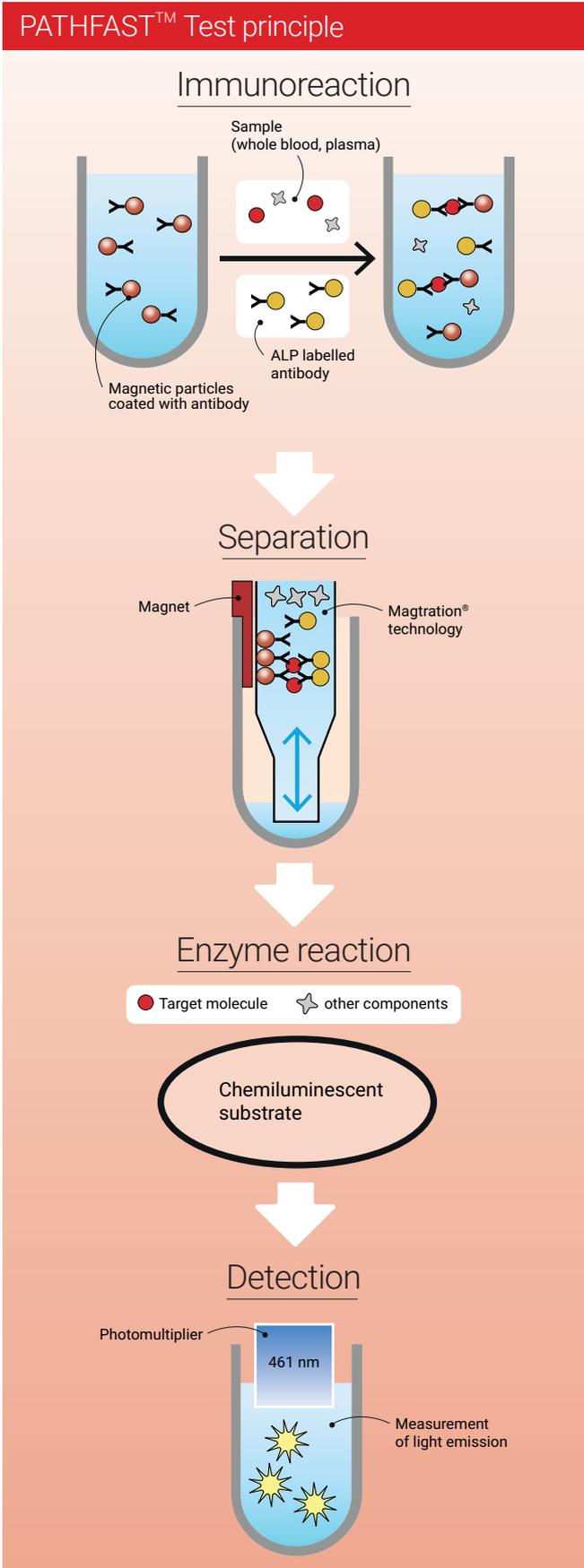
Practicality

- > Whole blood or plasma (100 µL)
- > Up to 6 tests in parallel (all in 15 min)
- > Ideal for Emergency Units

Reliability

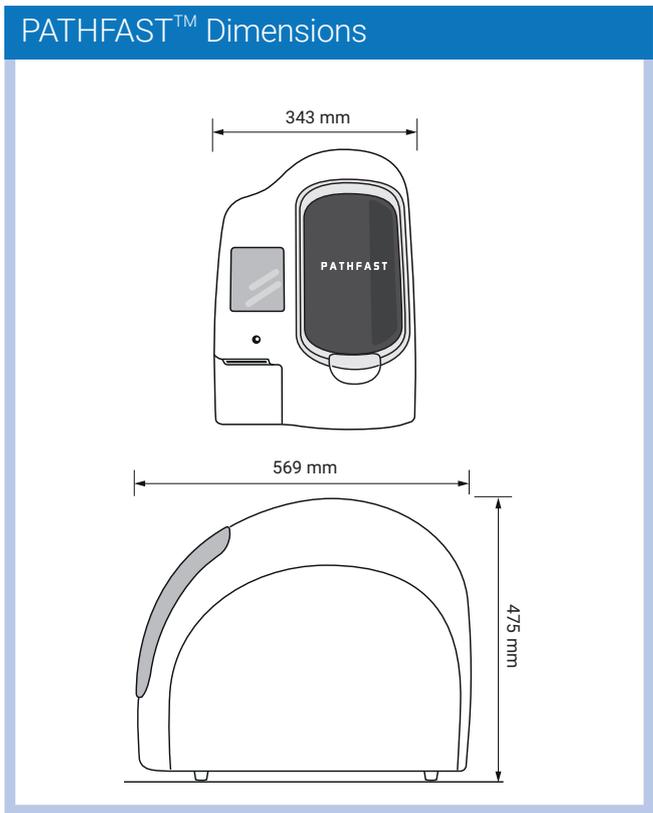
- > High Negative Predictive Values
- > No unspecific results
- > Excellent correlation with medical scores





PATHFAST™ Technical Specifications

Instrument type	Desktop Immunoassay Analyzer
Throughput	Up to 6 samples or parameters per run
Measuring time	<17 minutes for 6 samples using emergency markers or PATHFAST™ Presepsin
Sampling material	Whole blood, plasma, serum
Measuring principle	Chemiluminescence enzyme immunoassay technology (CLEIA) and Magtration® technology.
Reaction temperature	37 °C
Sample volume	100 µl
Data storage	Patient data: 1000, QC data: 1800, CAL data: 300
Datatransfer	ASTM and Fixed standard
Weight	28 kg
El. requirements	100 - 240 V AC (50/60 Hz)
Power consumption	360 VA
Monitor/keyboard	LCD touch-screen
Printer	Integrated
PC	Integrated, Handheld Barcodereader included
Interface	RS-232C and Ethernet Port
Calibration	Factory calibration, 2-point calibration every 4 weeks
24-h operation (stand-by)	Recommended



Product List

PATHFAST™ for critical care and sepsis diagnostics



	Item number	Pack size
SYSTEM		
PATHFAST™ Immunoanalyser Analyzer for the detection of cardiac and other emergency parameters and sepsis	300929	1 x 1
CONSUMABLES AND ACCESSORIES		
PATHFAST™ pipette tips	300936	5 x 42 units
PATHFAST™ waste box	300950	10 units
REAGENT KITS FOR CRITICAL CARE DIAGNOSTICS		
PATHFAST™ hs-cTnl	PF1241-K	60 tests
PATHFAST™ Myoglobin	PF1021-K	60 tests
PATHFAST™ CK-MB	PF1031-K	60 tests
PATHFAST™ D-Dimer	PF1051-K	60 tests
PATHFAST™ NTproBNP	PF1061-K	60 tests
PATHFAST™ hsCRP	PF1071-K	60 tests
REAGENT KITS FOR SEPSIS DIAGNOSTICS		
PATHFAST™ B-R-A-H-M-S PCT	PF1221-K	60 tests
PATHFAST™ B-R-A-H-M-S PCT control set	PF0221C	4 x 1 ml
PATHFAST™ Presepsin	PF1201-K	60 tests
PATHFAST™ Presepsin control set	PF0201-C	4 x 1 ml

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