LSI Medience Corporation

Presepsin: Summary of clinical studies in Japan

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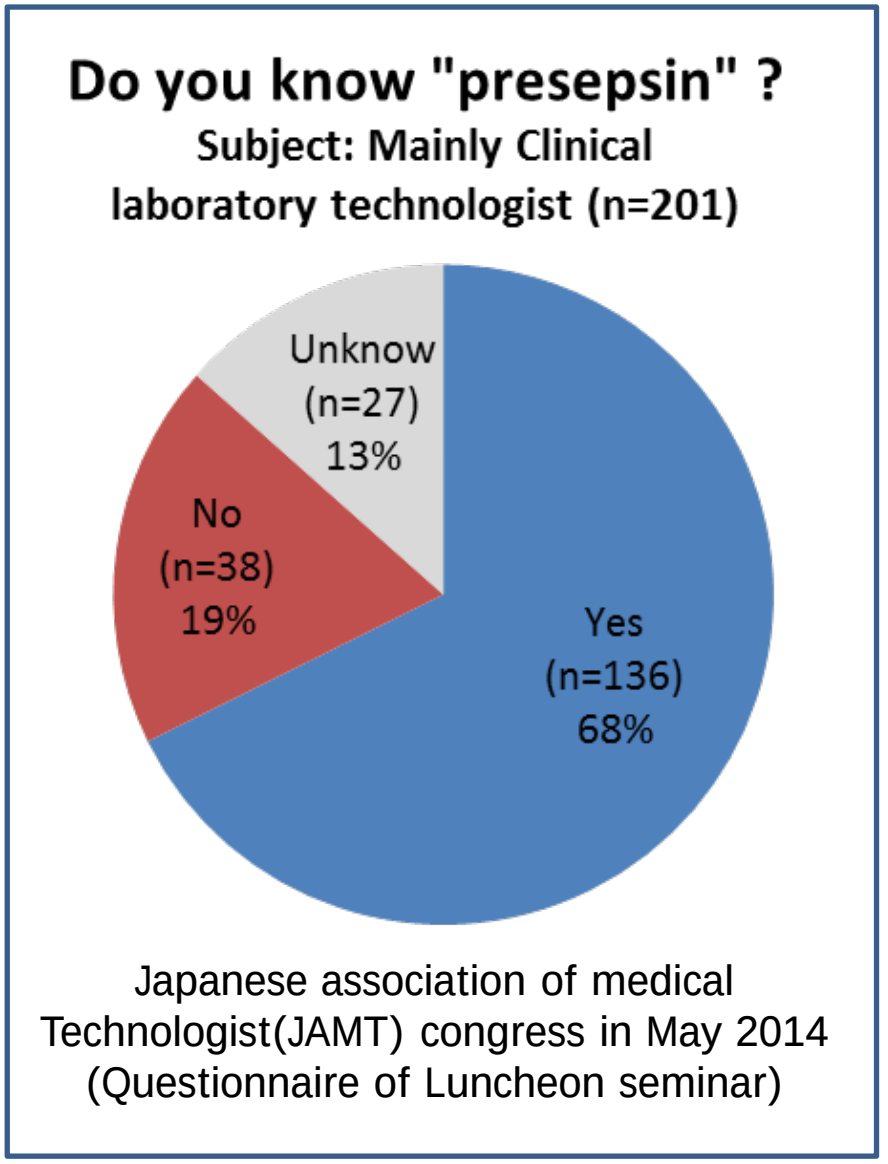
Topics of presepsin in Japan

- Launched in Japan in 2013.
- Covered by reimbursement in Japan in 2014.
- The recognition of “presepsin” is increasing by the sales promotion after launch.
  - Society activity (Presentation & Luncheon seminar)
  - Medical office briefing etc.



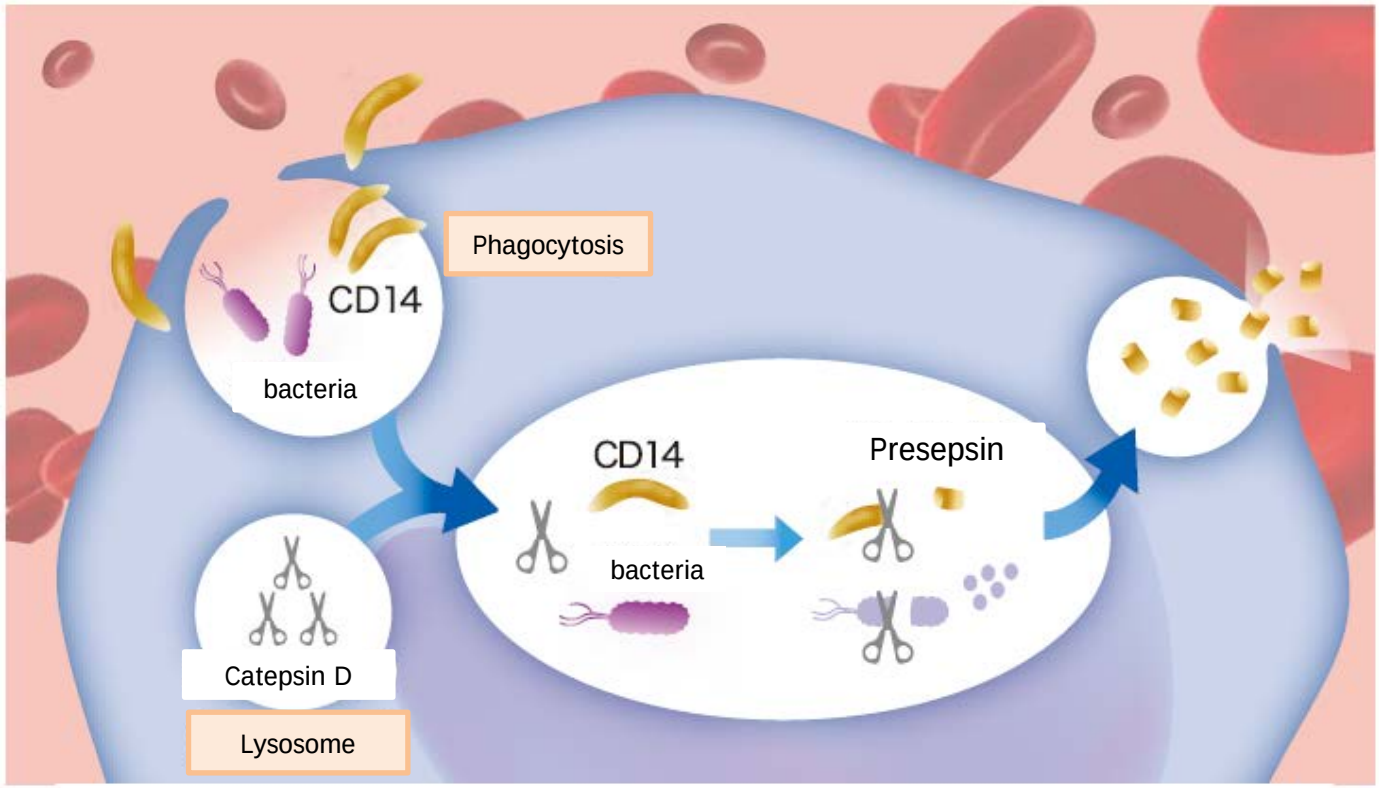
Presepsin and CD14

Presepsin is a 13 kDa N-terminal fragment of CD14 around amino acids 1-64 in which a CD14 molecule is enzymatically digested by cathepsin D.

Type	Amino acid sequence	Molecular weight (kDa)	Reference interval (95th percentile)
Membrane CD14 (mCD14)	1 - 356	55	
Soluble CD14 (sCD14)		43 - 55	< 4.5 μg/mL
Presepsin (sCD14-ST)		13	< 314 pg/mL

Reference : Clinica Chimica Acta 2011; 412(23-24): 2157-61.
IBL IMMUNO-BIOLOGICAL LABORATORIES sCD14 ELISA instructions for use

The production mechanism of presepsin



One of the production mechanisms hypothesis of presepsin is related to bacterial phagocytosis.

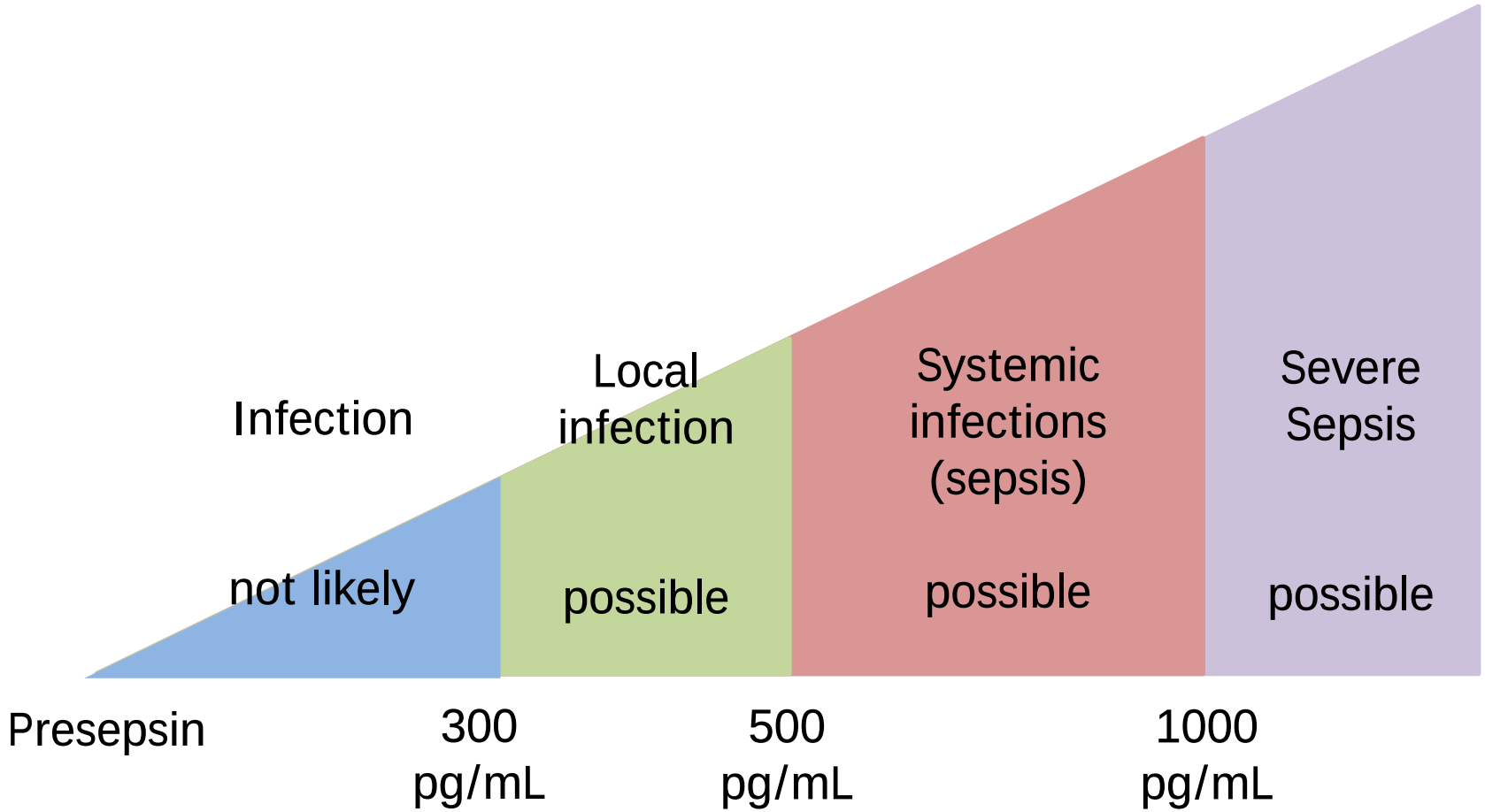
Reference: Endo S. The 60th National Congress of JSLM

Presepsin compared to other markers

Feature	Presepsin	PCT	CRP
Molecular Weight	13 kDa	13 kDa	120 kDa
Expression Organ	Granulocyte, etc	Systemic organs (Lung, liver, kidney, fat cells, muscle, etc)	Liver
Expression Stimulus	Bacteria, etc	Bacterial infection, cytokines, LPS, etc	Cytokine （IL-6）
Response time after onset	< 2 hours	2 - 3 hours	6 hours
Half-life in Blood	0.5 - 1.0 hours	20 - 24 hours	4 - 6 hours
Disease with high levels	Sepsis, systemic infection, Chronic kidney disease	Systemic infection, sepsis, severe trauma, severe burns, etc	Inflammatory response

Features presepsin: “production mechanism” & ”response time after onset”
(Presepsin expression is depend on infection compared to other markers)

Recommended cutoff values for presepsin in Japan



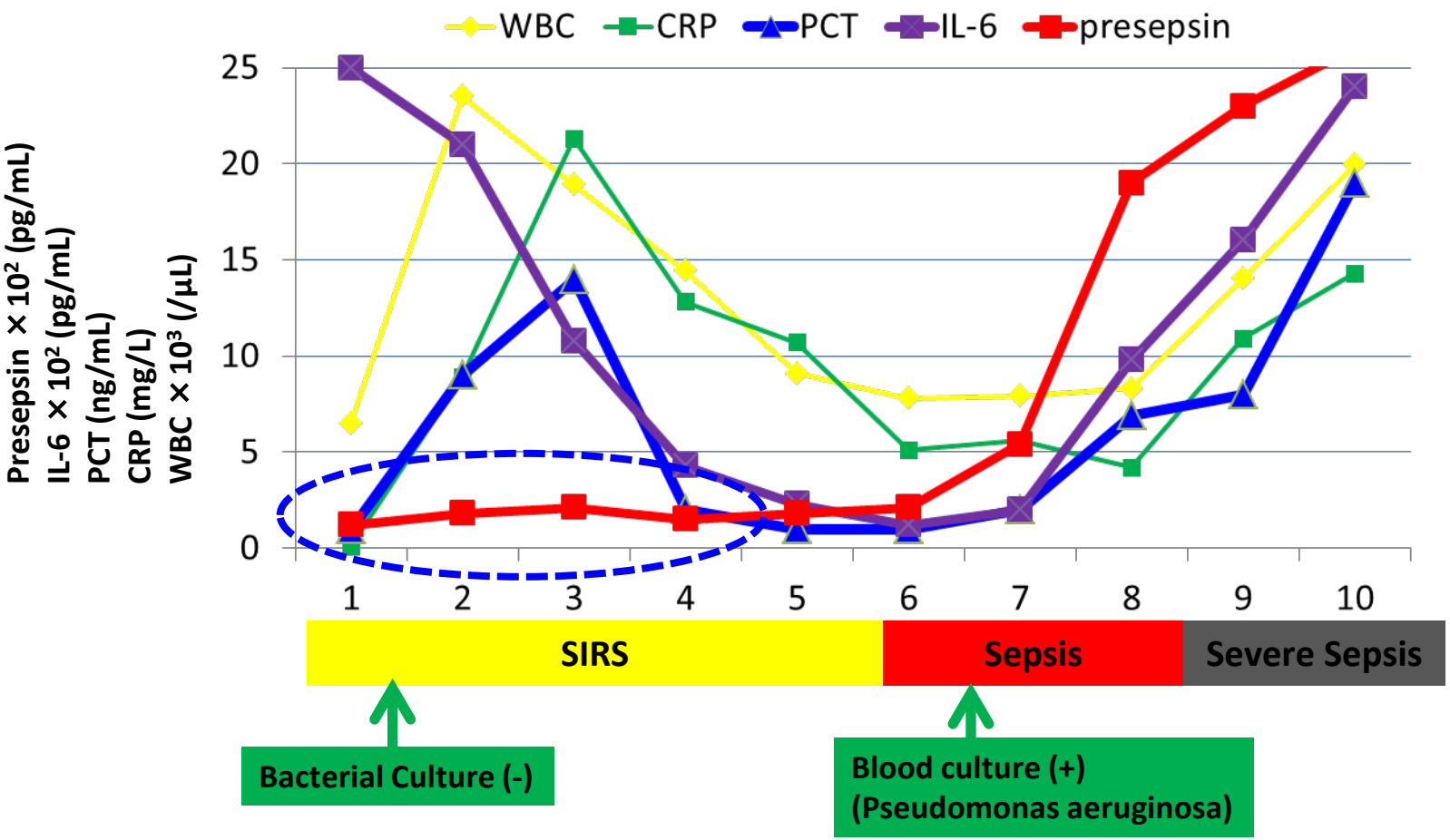
Characteristics of presepsin

Characteristics of presepsin are following in based on the previous results in Japan.

- Presepsin rises early compared to other biomarkers (IL-6, PCT and CRP) after the onset of sepsis
- Presepsin is not affected by severe trauma, surgical invasive procedures, or severe burn
- Presepsin is useful for monitoring of septic patient

Time course of presepsin levels in patients with severe burn

Reference: Takahashi G. The 40th Annual meeting of JSICM 2013

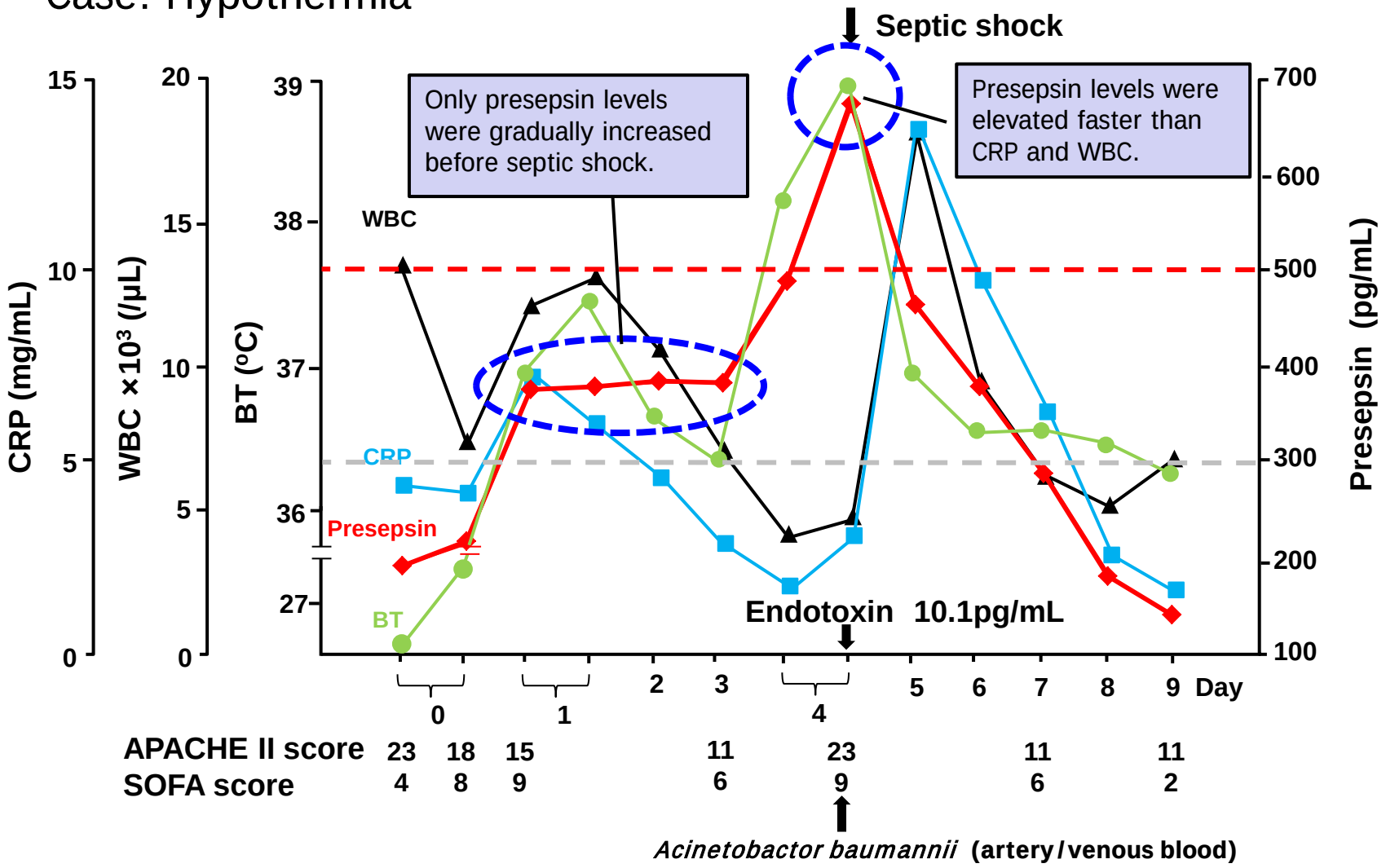


Presepsin wasn't affected to severe burn in comparison with PCT, IL-6 and CRP.

Useful for early diagnosis of sepsis

Case: Hypothermia

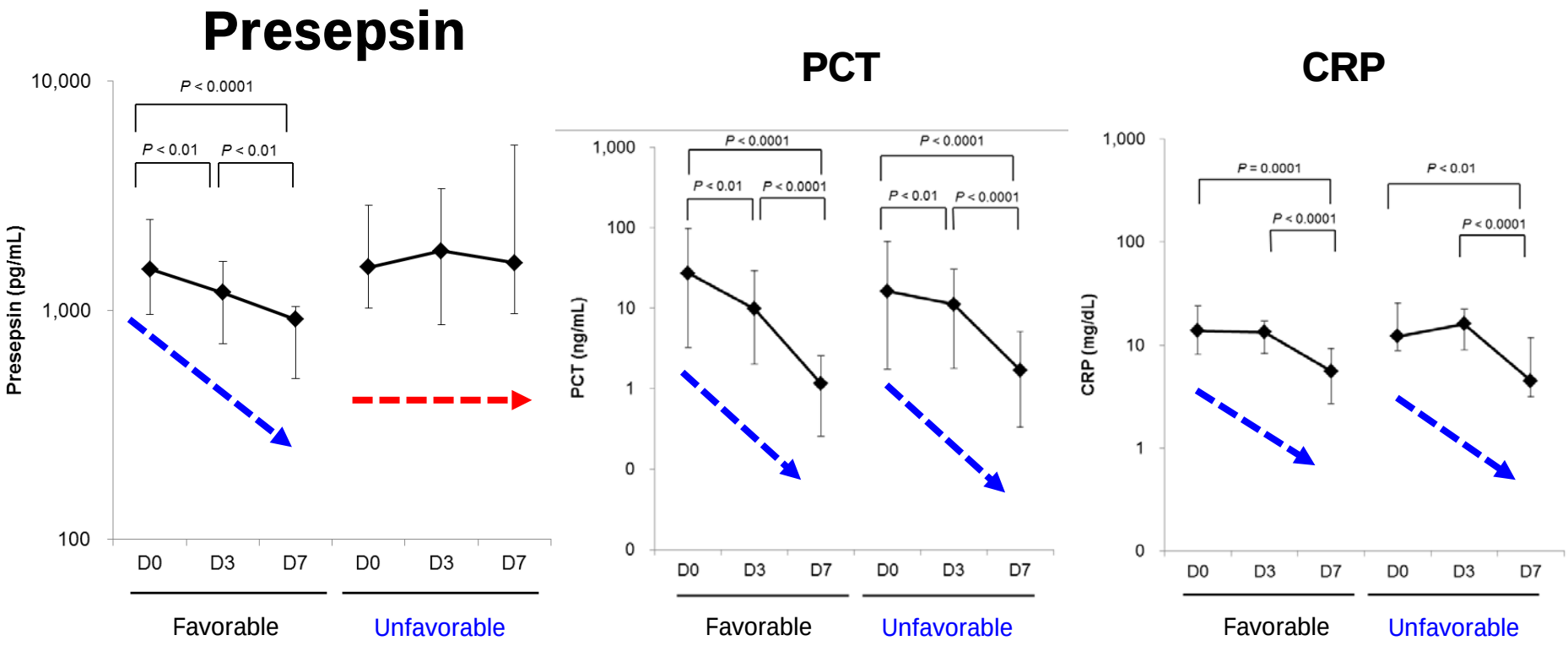
Reference: Endo S. The 60th National Congress of JSLM



Presepsin reflected the clinical condition of critically ill patient.

Useful for monitoring of septic patients

The transition of each marker for patients with severe sepsis, classified on the basis of severity scores (SOFA score): Favorable prognosis group (n = 27) and Unfavorable prognosis group (n = 26)

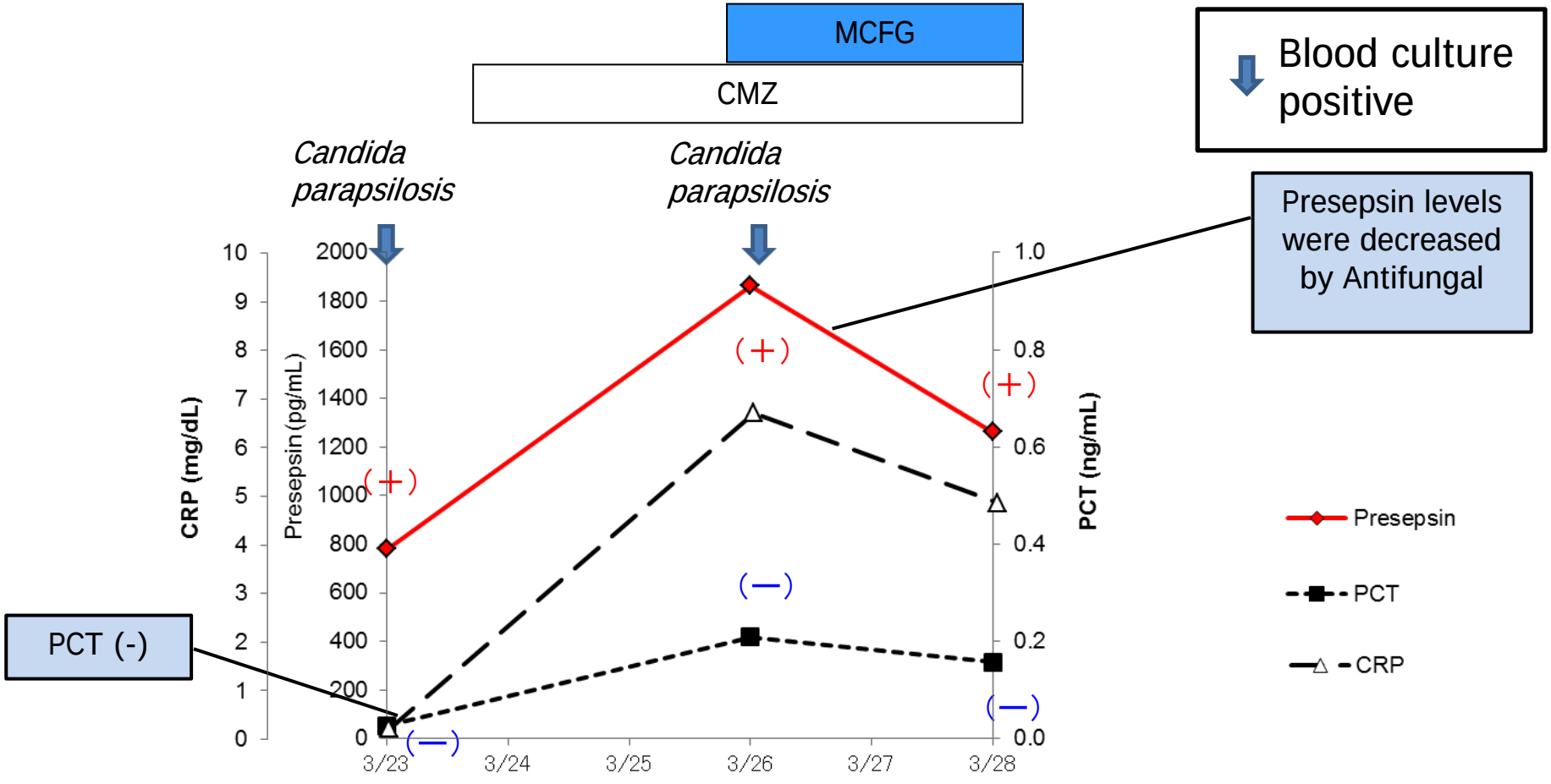


Reference: S. Endo et al. J Infect Chemother. 2013

Presepsin reflected the clinical condition (therapeutic effect) of septic patients.

Useful for monitoring of sepsis with fungi infection

Case: CV catheter infection in patient with esophageal cancer

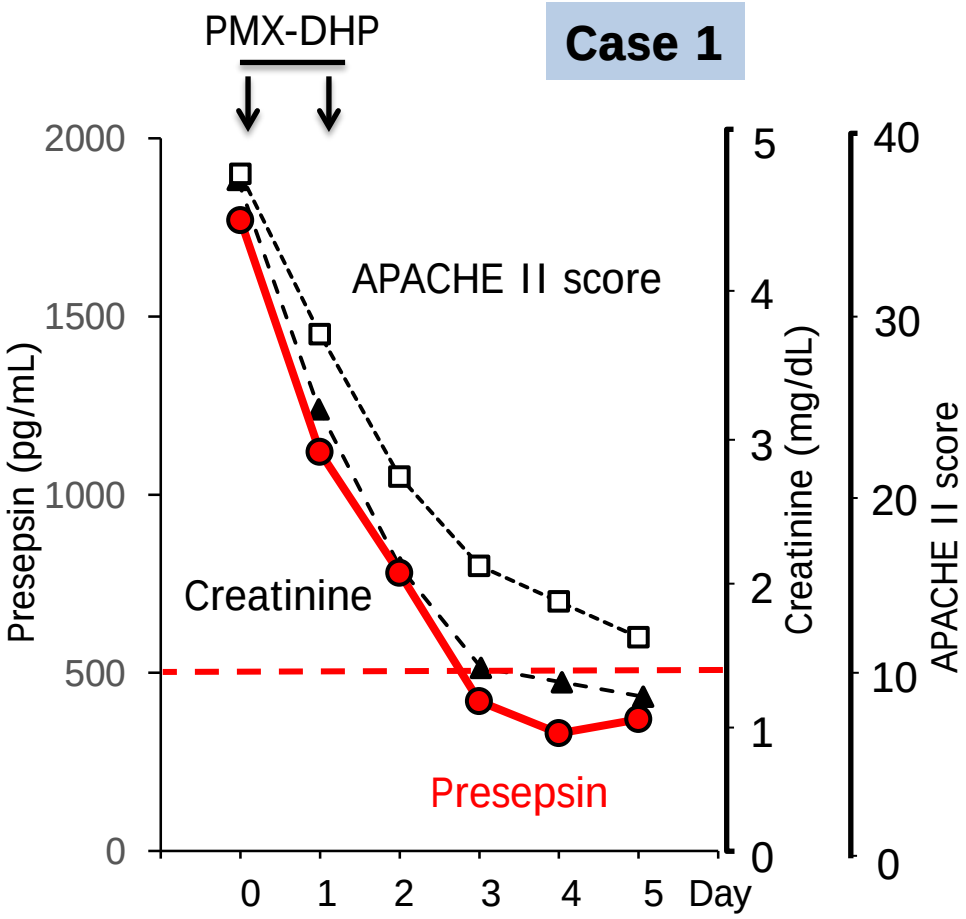


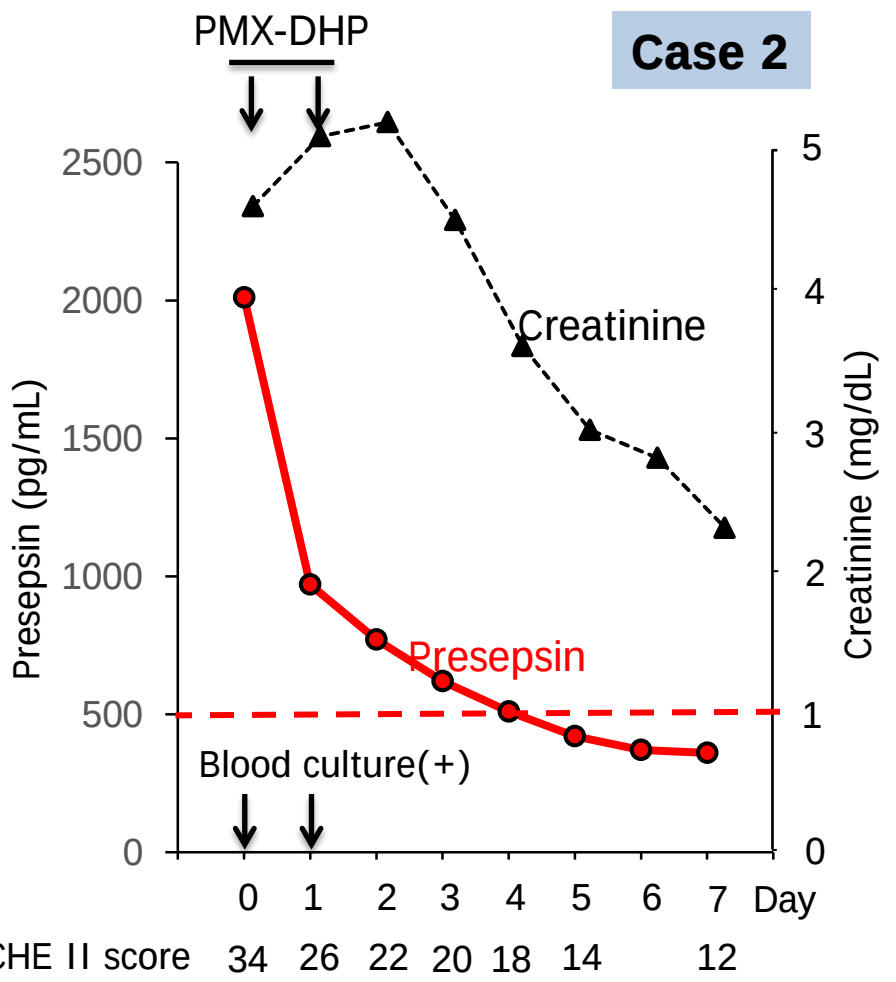
Reference: Yasuo Fukui et al. Sepsis 2013 poster

Presepsin might reflect the clinical condition of septic patient with fungal infection.

Comparison between presepsin and creatinine in colon perforation patients with septic shock

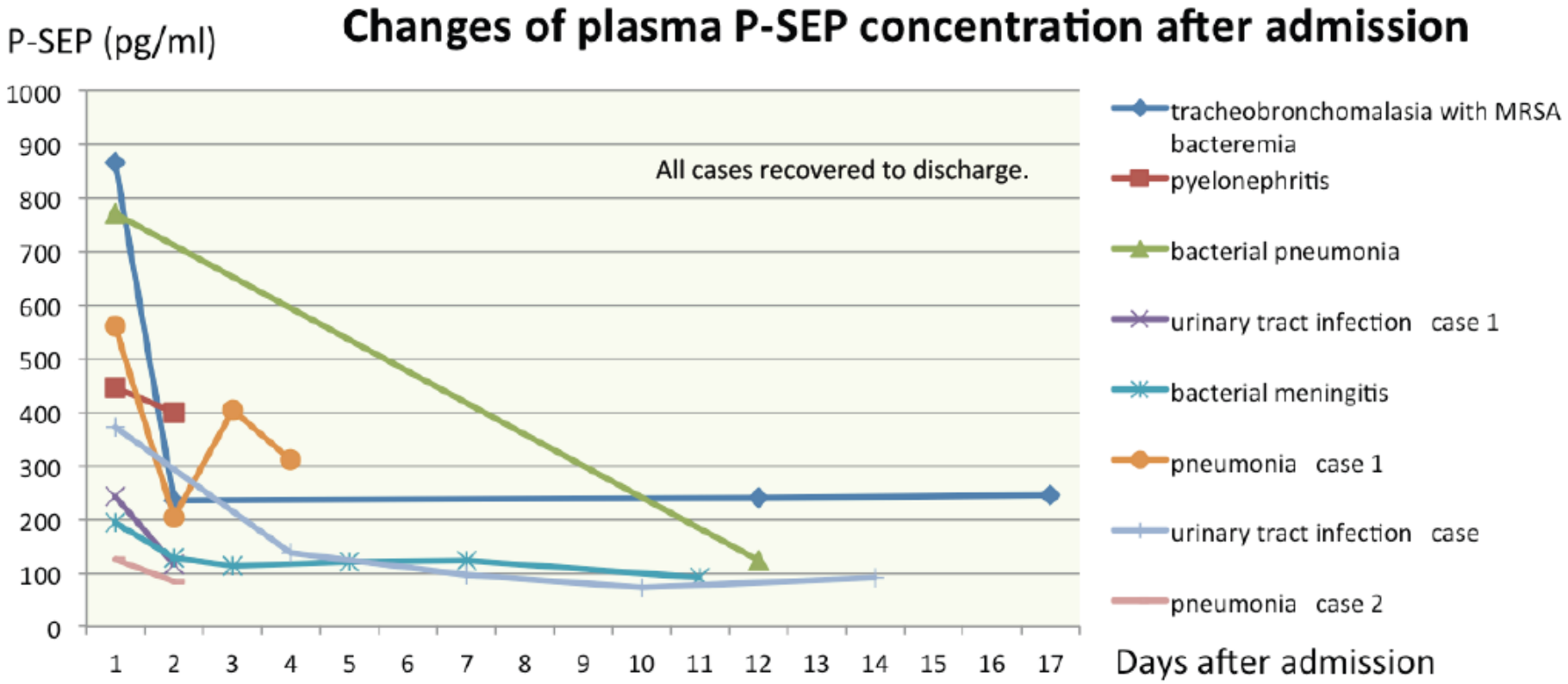
Reference: Endo S. The 18th JAMM Kyushu district meeting





Time course of presepsin in septic patients wasn't necessarily correlated with creatinine.

Useful for monitoring of antibiotics in pediatric patients



Reference: Kimura S. et al, IFCC 2014 poster

Generally, concentration of P-SEP quickly decreased after successful treatment of febrile disease with antibiotics.

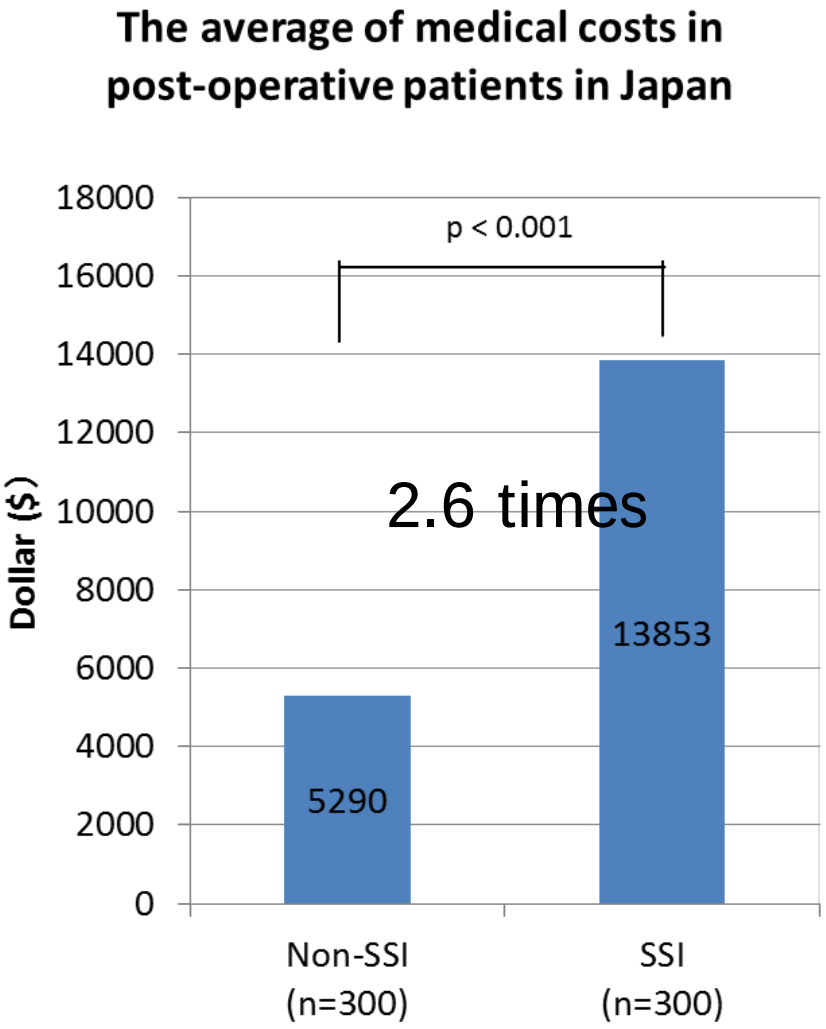
The past and future of clinical evaluation in Japan

- **Clinical studies finished** (Total 5 publications)
  - Analytical performance of assay
  - The usefulness for diagnosis of sepsis
  - The usefulness for monitoring of sepsis patients
  - The usefulness for prediction of the severity of sepsis induced DIC

- **On going clinical studies** (Total > 20 evaluators)
  - General evaluation of sepsis
  - Focused evaluation: kidney, febrile neutropenia, monitoring of antibiotics, surgery, pediatric, DIC, autoimmune, etc.

Future outlook of presepsin

- Decreasing of nosocomial infection (Surgical site infection (SSI), etc)
  - ➢ Early diagnosis of sepsis
- Decreasing economical costs of infectious treatment
  - ➢ The monitoring of optimal infectious treatment



Reference: J. Jpn. Soc. Surg. Infect. 2010: 7(3): 185-190

Summary

- The production mechanism of presepsin is different from PCT and CRP

- Features of presepsin
  - Presepsin rises early compared to other biomarkers (IL-6, PCT and CRP) after the onset of sepsis
  - Presepsin is not affected by severe trauma, surgical invasive procedures, or severe burn
  - Presepsin is useful for monitoring of septic patient

- Presepsin could be clinically useful for
  - Early diagnosis of sepsis
  - Assessment of the disease severity and monitoring of septic patients

Thank you for your attention