TOSOH

SEPSIS

DIAGNOSIS MADE CLEAR THROUGH PRESEPSIN TESTING

Clear and Timely Sepsis Diagnosis for Precise Patient Care • Better diagnostics **for better living**

TOSOH BIOSCIENCE

SEPSIS AROUND THE WORLD

50,000,000
CASES PER YEAR

LIFELONG
CONSEQUENCES FOR SURVIVORS

1 DEATH
EVERY 2.8 SECONDS

1/5
OF WORLDWILDE DEATHS

WE CAN'T SEE WHAT'S KILLING US !

DESPITE BEING A GLOBAL HEALTHCARE PROBLEM THE IMPACT OF SEPSIS IS STILL NOT WIDELY RECOGNISED

→ Sepsis Kills More People Each Year than Cancer

An estimated 47 to 50 million people worldwide are affected by **sepsis** each year. Mortality ranges between 15 and 50% depending on the country. Many survivors suffer from after-effects for the rest of their lives[1].

Despite being a global healthcare problem the impact of sepsis is still not widely recognised.

→ A Multitude of Symptoms that can Quickly Develop

Sepsis is defined as life-threatening organ dysfunction caused by a **dysregulated** host response to infection[2]. It is a very heterogeneous disease. Clinical phenotypes of a septic patient may be like that of sterile, systemic inflammation, making the diagnosis unclear.

Severe symptoms in sepsis can develop quickly. In effect, the body's response to combat infection causes **organ damage and failure**, which in some people may lead to **death within hours** or results in life-long effects.

Key to addressing this global crisis is **early diagnosis of sepsis** and **monitoring** treatment effectively.

1. www.global-sepsis-alliance.org

2. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) JAMA 2016; 315(8):801±10

A look at lab values

Hypoxaemia / Blood pressure / Platelets / Bilirubin / Creatinine / Urine output / Glasgow Coma Scale

PRE SEP SIN

The following lab abnormalities may be seen in sepsis and septic shock. These are indications of inflammation and organ dysfunction and are not meant to diagnose sepsis. Refer to your specific hospital laboratory reference ranges, which may differ slightly.

LAB VALUE NORMAL RANGE	CHANGES IN SEPSIS
Lactate 0.5 — 2.0 mmol/L	> 2.0 mmol/L — Hyperlactataemia > 4.0 mmol/L— Lactic acidosis
Partial pressure of oxygen / fraction of inspired oxygen (PAO_2/FiO_2 > 400)	< 300 (arterial hypoxaemia)
Creatinine (0.7 — 1.3 mg/dL)	increase > 0.5 mg/dL
Total bilirubin (0.3 — 1.2 mg/dL)	> 4 mg/dL
Serum glucose (70 — 105 mg/dL)	> 140 mg/dL (in the absence of diabetes)
White blood cell count (4,000 — 11,000 µL)	> 12,000 µL (leukocytosis) or > 4,000 µL (leukopenia) or normal range with > 10% immature forms
Platelets (150 — 350 x 10^3/µL)	< 100 x10^3 / µL ((Thrombocytopenia)
aPTT (25 — 35 seconds)	> 60 seconds
INR (< 1.5)	> 1.5
Procalcitonin (< 0.15 — 105 ng/mL)	> 2 standard deviations above normal
Plasma C-Reactive Protein (0-10 mg/L)	> 2 standard deviations above normal

DIAGNOSIS CAN BE UNCLEAR. IS THIS SEPSIS?

Sepsis Diagnosis is Confusing, even with Experience.

Patients with sepsis can present in a variety of ways making sepsis complicated to recognise, even for experienced clinicians.

Identifying sepsis has traditionally relied on clinical signs followed by tools such as the SOFA (Sepsis-related Organ Failure Assessment) score. Yet this can be too complicated to put in place in a clinical setting. More recently, a series of laboratory-based tests to measure indicators of inflammation and organ dysfunction have been incorporated into international guidelines.
Some tests have turnaround times of hours or even days, as is the case of blood culture tests.

Accurate management of antibiotics

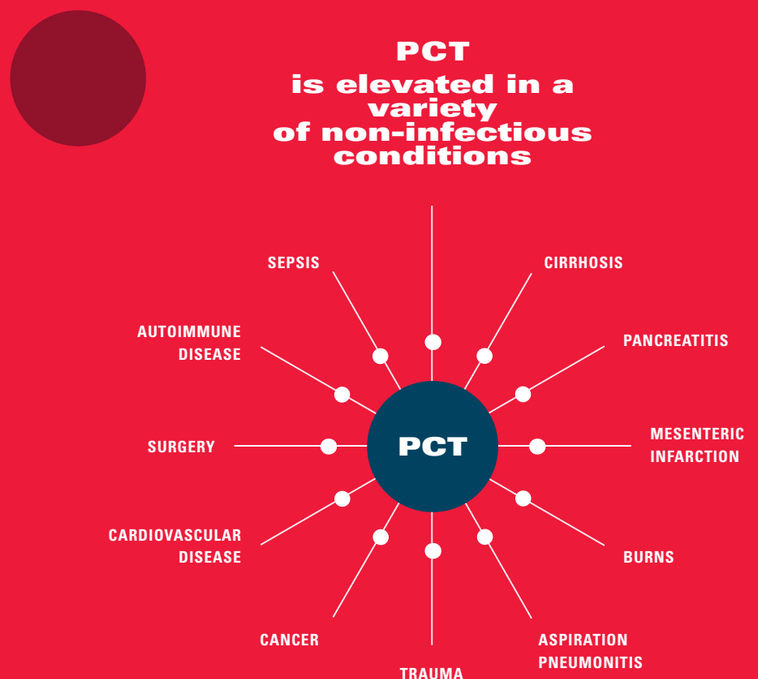
Recent treatment guidelines emphasise the need for sepsis patients to be treated with antibiotics within an hour. **Delays in initiating antimicrobial treatment are correlated with a progressive increase in mortality**[3].

However, with the alarming rise in antimicrobial resistance and the emergence of multi-resistant bacteria in recent years, **prophylactic** antimicrobial treatment is **problematic. Misuse of antimicrobials in patients where they are not needed only contributes to resistance.**

Recent treatment guidelines emphasise the need for sepsis patients to be treated with antibiotics within an hour.

3. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006;34(6): 1589–1596.

SOME BIOMARKERS PROVIDE NO CLEAR ANSWER



IF PCT IS SO EFFECTIVE, WHY SO MANY DEATHS?

Procalcitonin (PCT) is one of the biomarkers that has been widely used in recent years to diagnose sepsis. The PCT level reflects the pathological status of sepsis well, but:

- PCT is elevated in a variety of non-infectious conditions, such as cirrhosis, pancreatitis, mesenteric infarction, burns, and aspiration pneumonitis [4, 6].
- Its diagnostic and predictive value declines in patients with severe sepsis and localised infections (e.g., endocarditis, emphysema) [4,7, 8].

→ *Sepsis diagnosis is ambiguous*

OTHER BIOMARKERS ARE NOT SPECIFIC TO SEPSIS EITHER

C-Reactive Protein is another biomarker used that is not sufficiently specific for diagnosing sepsis. It can also be elevated during inflammatory non-infectious states, such as trauma, burns, cancer, cardiovascular disease, surgery, and autoimmune disease[9]. The same is true of lactate and Interleukin-6.
None of these is recommended as a sepsis marker.

→ *Sepsis diagnosis is uncertain*

SO, IS IT POSSIBLE TO FOCUS JUST ON SEPSIS?

Like a beacon, is there a biomarker that:

- Can be quantitatively and rapidly measured,
- Highlights non-infectious and infectious inflammation,
- Reveals the severity of the disease and guides physicians to making the most appropriate medical decisions ?

→ *Yes.
It is possible to have a precise diagnosis of sepsis and an overall view of its status.*

4. Meisner, M. Update on procalcitonin measurements. Ann. Lab. Med. 2014, 34, 263–273. [CrossRef] [PubMed] / 5. Christ-Crain, M.; Muller, B. Procalcitonin in bacterial infections Hype, hope, more or less? Swiss Med. Wkly. 2005, 135, 451–460. [PubMed] / 6. El-Solh, A.A.; Vora, H.; Knight, P.R., 3rd; Porhomayon, J. Diagnostic use of serum procalcitonin levels in pulmonary aspiration syndromes. Crit. Care Med. 2011, 39, 1251 – 1256. [CrossRef] / 7. Tang, B.M.; Eslick, G.D.; Craig, J.C.; McLean, A.S. Accuracy of procalcitonin for sepsis diagnosis in critically ill patients: Systematic review and meta-analysis. Lancet Infect. Dis2007, 7, 210–217. [CrossRef] / 8. Gilbert, D.N. Procalcitonin and pulmonary aspiration: Another possible interpretation. Crit. Care Med. 2011, 39, 2019–2020. [CrossRef] / 9. Morley, D.; Torres, A.; Cilloniz, C.; Martin-Loeches, I. Predictors of treatment failure and clinical stability in patients with community acquired pneumonia. Ann. Transl. Med. 2017, 5, 443.

OPTIMISE CARE THANKS TO A COMPREHENSIVE ASSESSMENT

Optimised Care Thanks to a Comprehensive Assessment

Sepsis testing and diagnosis is a two-phase process.

Phase 1: Test and assess patients immediately for emergency intervention and entry into sepsis treatment protocols.

Phase 2: Accurately identify the source of infection and related adjustments in clinical care.

Current diagnostic testing practices focus primarily on Phase 2, yet Phase 1 is the most critical. Presepsin makes Phase 1 simple, fast and easy.

Early Diagnosis

Presepsin is a specific and sensitive biomarker for sepsis and is a valuable tool for the very early diagnosis of Sepsis. Presepsin rises earlier than other biomarkers and does not show unspecific increases.

Prognosis Risk Stratification

Presepsin exceeds the prognostic power of other sepsis biomarkers and is specifically useful when combined with clinical risk scores.

Monitoring

The time course of Presepsin can be used for monitoring: a decline demonstrates response to therapy and predicts a favourable outcome.

TIMELY, CLEAR AND SPECIFIC

A NEW LIGHT IN THE DIAGNOSIS OF SEPSIS

2002

Presepsin discovered as a blood biomarker in patients with sepsis in Japan.

2004

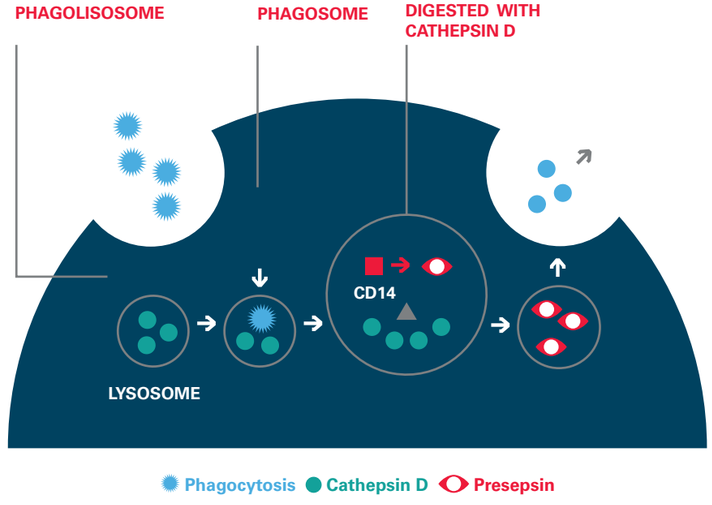
Discovery of presepsin's value in diagnosis and evaluation of sepsis.

2015

Confirmation of presepsin's diagnostic accuracy in sepsis by meta-analysis.

➔ Present at the earliest stages of infection, before visible clinical symptoms, the quantity of presepsin in the blood can be accurately measured in minutes, giving clinicians actionable information on :

- Sepsis diagnosis and prognosis
- Risk stratification
- Disease progression
- The efficiency of treatment throughout the infection



40 KDa glycoprotein cleavage N-terminal fragment of CD14, released into circulation after activation of a pro-inflammatory signal cascade on contact with infectious agents[10].

Presepsin can be detected by biochemical methods and is considered a new biomarker of infection.

10. Wright SD, Ramos RA, Tobias PS, Ulevitch RJ, Mathison JC. CD14, a receptor for complexes of lipopolysaccharide (LPS) and LPS binding protein. Science. 1990; 249(4975):1431±3. https://doi.org/10. 1126/science.1698311 PMID: 1698311.

PRESEPSIN & AIA-360

SEPSIS DIAGNOSIS MADE SIMPLE

➔ Bench-Top, Emergency Testing

Tosoh's AIA-360® can be placed in satellite labs close to the ICU and Emergency Department, and is always ready to run, streamlining testing.

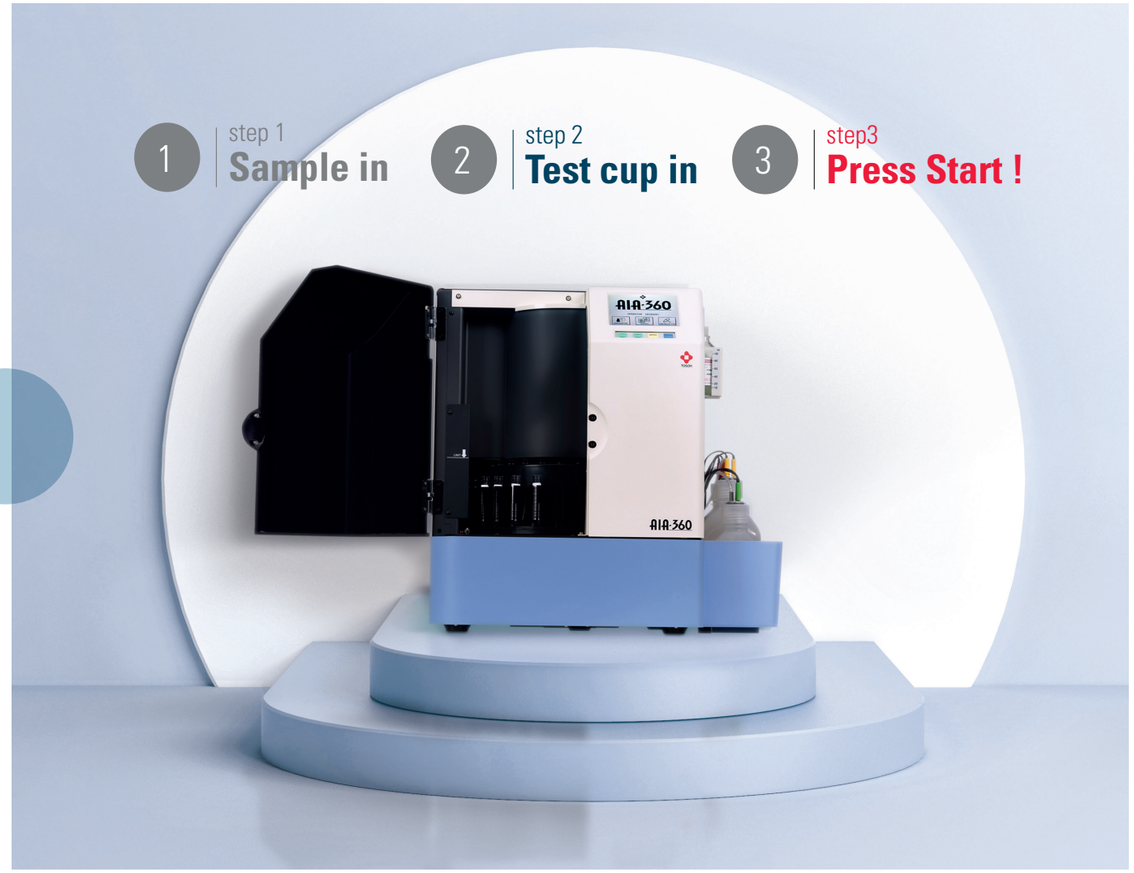
- **Results in 15 minutes**
- **Better triage and risk stratification**
- **Optimise use of antimicrobials**
- **Monitor treatment effectively**
- **Improved patient outcomes**

TOSOH BIOTIN-FREE TESTS

➔ Reliable and High Quality Test Performance

The AIA-360® is an efficient, easy to use and compact analyser, all in one.

- **The one cup, one test system reduces costs**
- **Handles primary samples**
- **Simple: only 3 steps**
- **Rapidly delivers useful clinical information**
- **Limited maintenance needed**



AIA-360 | CAN RUN ANYWHERE | SET UP IN 5 MINUTES | 1 AIA-PACK = 1 TEST

The presepsin assay also runs on Tosoh's high throughput AIA system.

AIA-900

AIA-2000

PRESEPSIN HELPS YOU MAKE A CLEAR DIAGNOSIS OF SEPSIS AND PATIENT RISK

TOSOH

1.
Presepsin is an early and specific biomarker for sepsis.

2.
Timely results help you to manage patient's risk and monitor treatment effectively.

3.
The benchtop AIA-360 is easy to use and always ready to run, ideal for emergency testing.

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