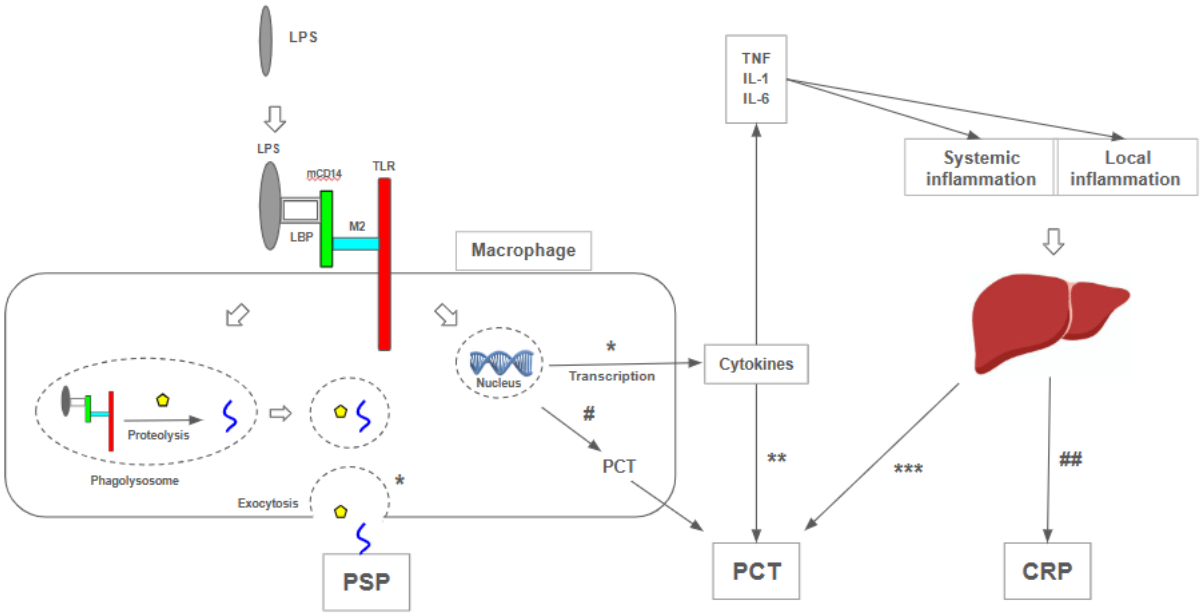
Figure 1. Mechanisms of presepsin, procalcitonin, and C-reactive protein production [72, 120-123].



(*) The molecular complex LPS-LBP-mCD14-M2-TLR is internalized into a phagolysosome; proteolysis and internalization processes release presepsin (PSP), which is released in circulation after exocytosis. CD 14 promotes the expression of genes responsible for the immune response, such as cytokine production[72]. (**) The rise of TNF, IL-1, IL-2, and IL-6 levels increases PCT[120]. (***) the liver is considered to be the most important site of production of PCT during an inflammatory response, especially those induced by bacterial infections[121]. (#) Peripheral blood mononuclear cells express PCT both on mRNA and on protein levels[122]. (##) CRP is an acute-phase protein, and its synthesis is rapidly upregulated, principally in hepatocytes, under the control of cytokines[123]. LPS: lipopolysaccharide, TLR: Toll-like receptor; LBP: Lipoprotein Binding Protein; mCD14: membrane-bound CD14; M2: co-protein of TLR; TNF: tumor necrosis factor; IL-1: interleucin-1; IL-6: interleucin-6; CPR: C-reactive protein; PCT: procalcitonin; PSP: presepsin.

Table 1. Admission levels of presepsin - comparison between sepsis and non sepsis, and suvivor and non survivors. Cutoff values of presepsin in all stages of life.

Age group	Author	Admission medium PSP levels (ng/mL)				Cutoff values (ng/mL)
		Sepsis	Non sepsis	Survivor	Non survivor	
Neonates & Children	Poggi et al. 2015 [107]	1295	562	-	-	885
	Pugni et al. 2015 [79]	-	649	-	-	-
	Montaldo et al. 2016 [80]	598	328	-	-	788*
	Korpelainen et al. 2017 [84]	1432	-	-	-	-
	Bellos et al. 2018 [82]	-	-	-	-	650-850**
	Baraka et al. 2018 [86]	1014	178	-	-	Multiple
	Yoon et al. 2019 [83]	-	-	-	-	650**
	Puspaningtyas et al. 2023 [77]	806.5	717	-	-	761*
Adults	Shozushima et al. 2011 [104]	817.9	190	-	-	399
	Endo et al. 2012 [105]	1579	312	-	-	Multiple
	Giavarina et al. 2015 [87]	55-184	-	-	-	-
	Ali et al. 2016 [114]	1183	472	615,5	1301	Multiple
	Yu et al. 2017 [115]	-	-	1230,5	1269	-
	Claessens et al. 2017 [99]	476	200	-	-	-
	Ikeda et al. 2019 [89]	-	-	3251	1108	-
	Zvyagyn et al. 2019 [88]	-	-	1718	3266	-
	Dragoş et al. 2023 [96]	1039	372	-	-	-
Old adults	Imai et al. 2019 [97]	639.93	866.56	-	-	285
	Ruangsomboon et al. 2020 [98]	746	316	470	795	Multiple

*Best of multiple values; ** Best accuracy values in the metanalysis.

Table 2. Positive and negative aspects of presepsin in all stages of life.

Aspects	Pediatric	Adult	Elderly
Positive	Early elevation, affordable cost, better diagnostic performance (PCT and CRP) and prognostic validity (30-day mortality), monitoring of antibiotic therapy, levels not influenced by gestational age, predictor of clinical evolution in febrile neutropenics	Better prognostic validity (PCT, CRP, ESR), correlation with hospital mortality in sepsis and septic shock, prognostic validity (28-day mortality), correlation with clinical outcomes, stable in different clinical scenarios (cirrhosis, rheumatoid arthritis, febrile neutropenia)	A better predictor of bacteremia in the Emergency Department (PCT, CRP), similar diagnostic accuracy to PCT, similar prognostic accuracy (qSOFA, SIRS)
Negative	Poor predictor of bacterial infection (PCT), non-standardized cutoff points, inaccessible in most scenarios	Poor predictor of bacterial infection (PCT), requires adjustments when kidney function is altered	Diagnostic and prognostic accuracy lower than combination (PCT + CRP + PSP), major renal dysfunction in older adults, specific cutoff point (immunosenescence)

PSP: presepsin; CRP: C-reactive protein; PCT: procalcitonin; ESR: erythrocyte sedimentation rate; qSOFA: quick Sequential Organ Failure Assessment; SIRS: systemic inflammation response syndrome.