

The Apoptotic Pathway As A Therapeutic Target in Sepsis

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SEPSIS

- Sepsis adalah suatu sindroma klinik yang terjadi oleh karena adanya respon tubuh yang berlebihan terhadap rangsangan produk mikroorganisme.
- Ditandai dengan fever, tachycardia, tachypnea, hypotension dan organ dysfunction berhubungan dengan gangguan sirkulasi darah.

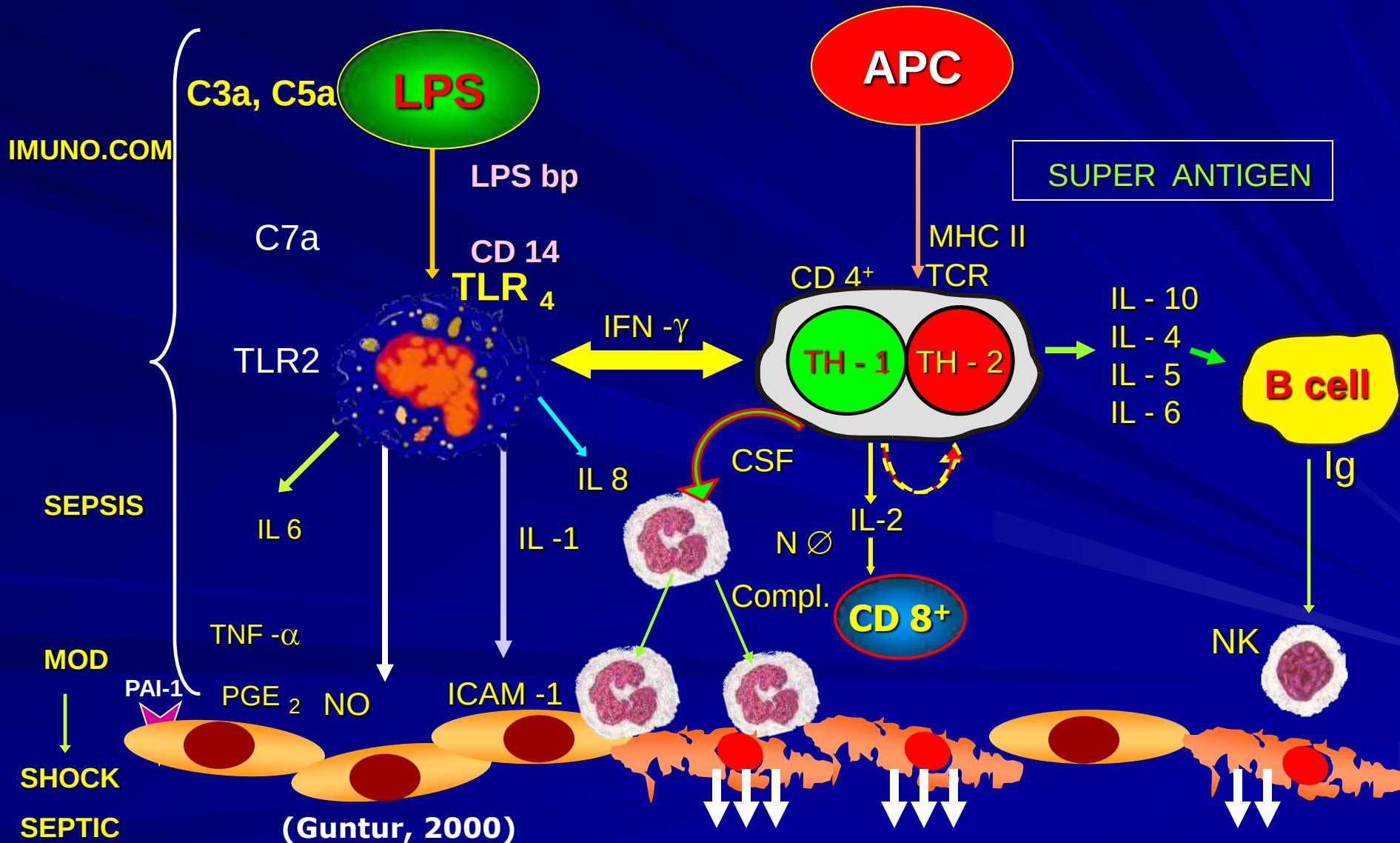
DERAJAT SEPSIS

1. **SIRS**, ditandai dengan ≥ 2 gejala sbb:
 - a. **Hyperthermi / Hypothermi** ($> 38,3^{\circ}\text{C}$ / $< 35,6^{\circ}\text{C}$)
 - b. **Tachypneu** (resp > 20 / mnt)
 - c. **Tachycardi** (pulse > 100 / mnt)
 - d. **Leukocytosis** $> 12000/\text{mm}$ atau **Leukopenia** $< 4000/\text{mm}$
 - e. **10% > cell imature**
2. **SEPSIS**
Infeksi disertai SIRS
3. **SEPSIS BERAT**
Sepsis yg disertai MODS/MOF, Hipotensi, oligouri bahkan anuri.
4. **Sepsis dengan hipotensi**
Sepsis dengan hipotensi (tek. sistolik < 90 mmHg atau penurunan tek. Sistolik > 40 mmHg).
5. **Syok Septik**
Syok septik adalah subset dari sepsis berat, yang didefinisikan sebagai hipotensi yang diinduksi sepsis dan menetap kendati telah mendapat resusitasi cairan, dan disertai hipoperfusi jaringan.

Definition of Sepsis and Related Conditions (1892,1992); Proposed PIRO Classification Scheme for Sepsis (Adapted From 2003 Consensus Paper)

DEFINITION : WILLIAM OSLER, 1892	DEFINITION : CONSENSUS, 1992	PROPOSED SCHEME : CONSENSUS, 2003
1. Septicaemia (a) Fermentation fever Fever, wound infection Temp 103 -104 F (b) Saepremia Septic intoxication, 24h Temp 103 – 104 F " Quick pulse" (c) Progressive septicaemia Septic intoxication 24-72h Organisms in blood Fever, pulse > 120 bpm Delirium, apathy 2. Pyaemia Disseminated abscesses Organisms in blood Small vessel necrosis Recurring chills, fever " Constitutional symptoms"	Systemic Inflammatory Response (SIRS) 2 or more of following : Temp > 38 C or < 36 C Heart Rate > 90 bpm RR > 20 or PaCO2 < 32 WBC >12K, < 4K or > 10% bandemia Sepsis : Sepsis + Infection Severe Sepsis : Sepsis with organ dysfunction, hypoperfusion, or hypotension Septic shock : sepsis with hypotension despite fluid resuscitation Multiple Organ Dysfunction syndrome : Altered organ function in an acutely ill patient; intervention required for homeostasis	Predisposition : Underlying illness Genetics Pathogen-host interaction Insult Infection : Cultute pathogen Source control LPS, virulence factors Response : SIRS, shock, CRP, IL-6, TNF--'5f, protein C level Organ dysfunction : No, failing organs or Composite score <u>apoptosis</u>, cyopathic hypoxia, cell stress

IMUNOPATOGENESIS



Role of Response Immune in Sepsis

Proinflammatory Response

IL-1, IL-6, TNF- α

Anti-inflammatory Response

IL-10, IL-4, IL-1ra

MARS

Mixed Antagonist Response Syndrome

Hyperinflammatory Status

SIRS

Systemic Inflammatory Response Syndrome

Cardiovascular compromise (shock)
Apoptosis - Necrosis
Organ dysfunction (MODS/MOF)

Anti-inflammatory Status

CARS

Compensatory Anti-inflammatory Response Syndrome

Suppression of the Immune
System