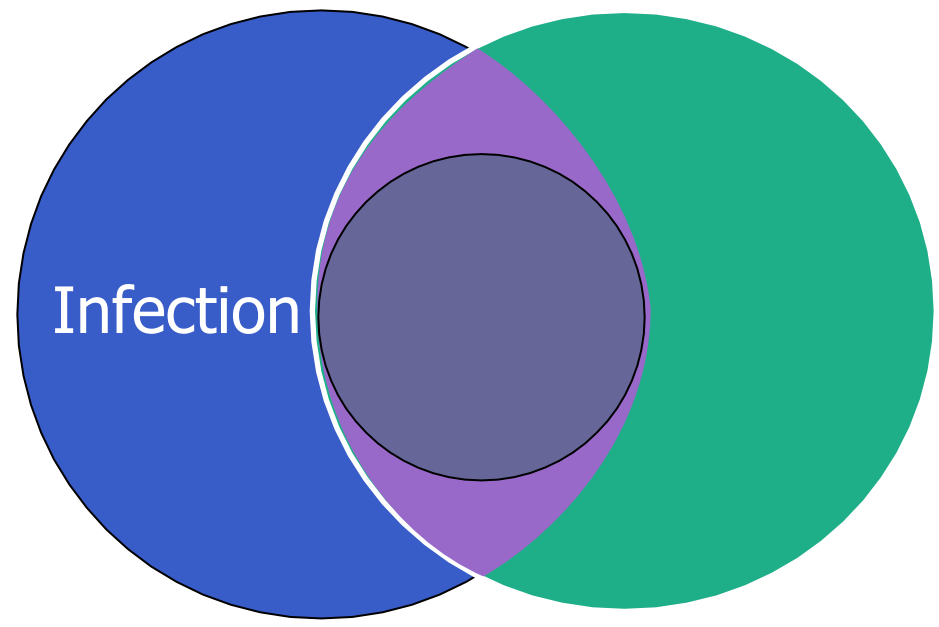
Systemic Inflammatory Response Syndrome,MODS,Sepsis

Infection

Presence of organisms in a closed space or location

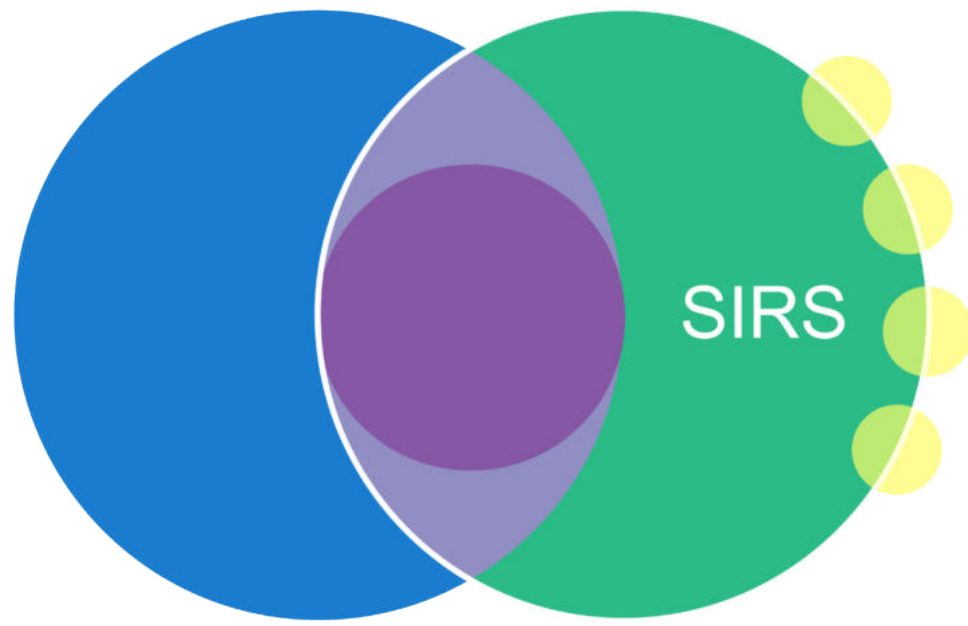
where not normally found



SIRS: Systemic Inflammatory Response Syndrome

A clinical response arising from a nonspecific insult manifested by ≥2 of the following:

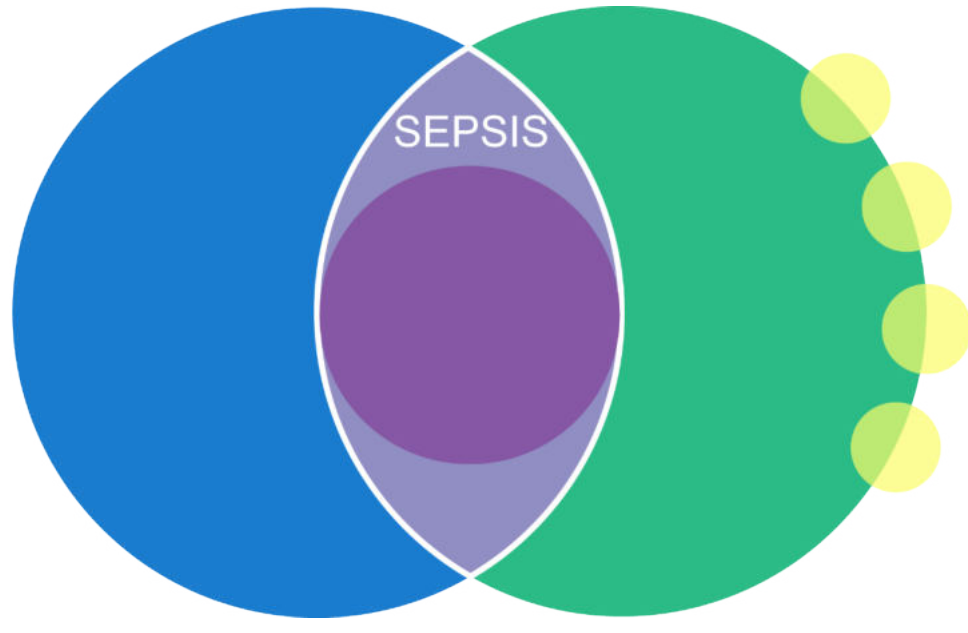
- Temperature: ≥38°C or ≤36°C
- HR: ≥90 beats/min
- Respirations: ≥20/min
- WBC count: ≥12,000/mL or ≤4,000/mL or >10% immature neutrophils



Sepsis: More Than Just Inflammation

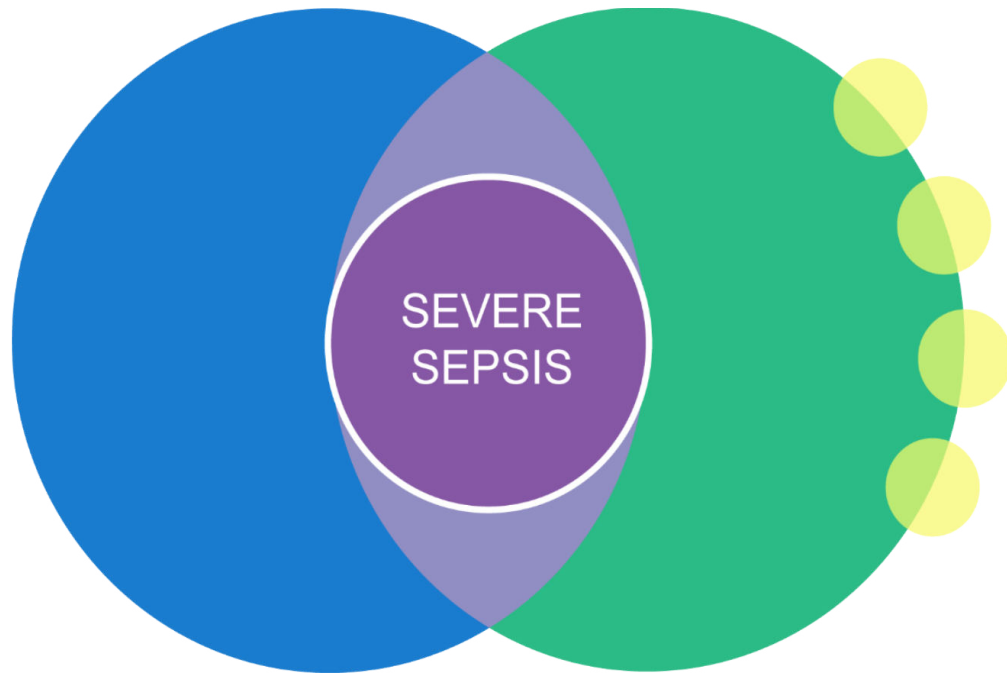
Sepsis:

- Known or suspected infection
- SIRS criteria

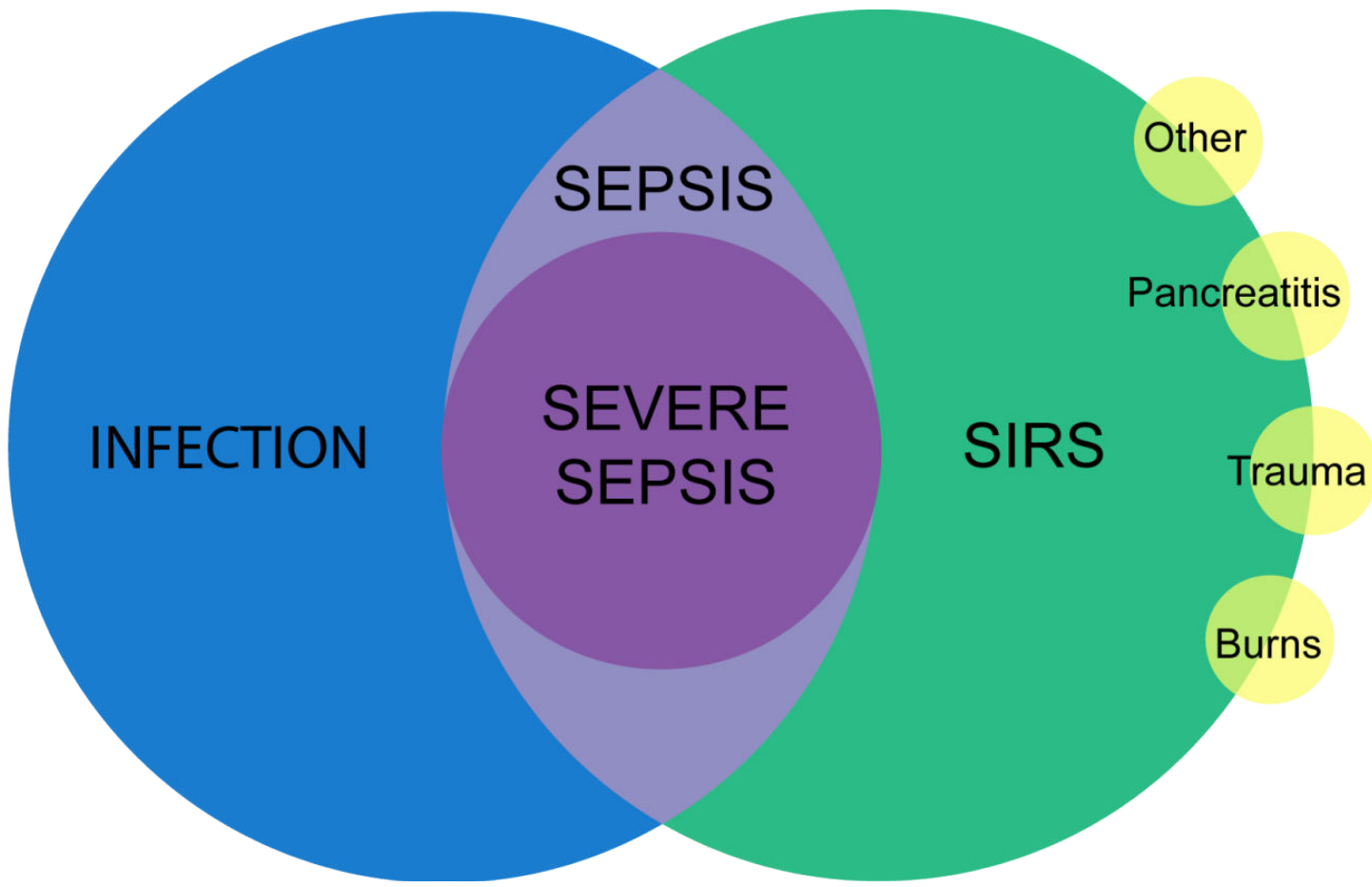


Severe Sepsis: Acute Organ Dysfunction

- Severe Sepsis =
  Sepsis with signs of ***acute*** organ dysfunction in any of the following systems:
  - Cardiovascular (septic shock)
  - Renal
  - Respiratory
  - Hepatic
  - Hemostasis
  - CNS
  - Unexplained metabolic acidosis



Sepsis: A Complex Disease

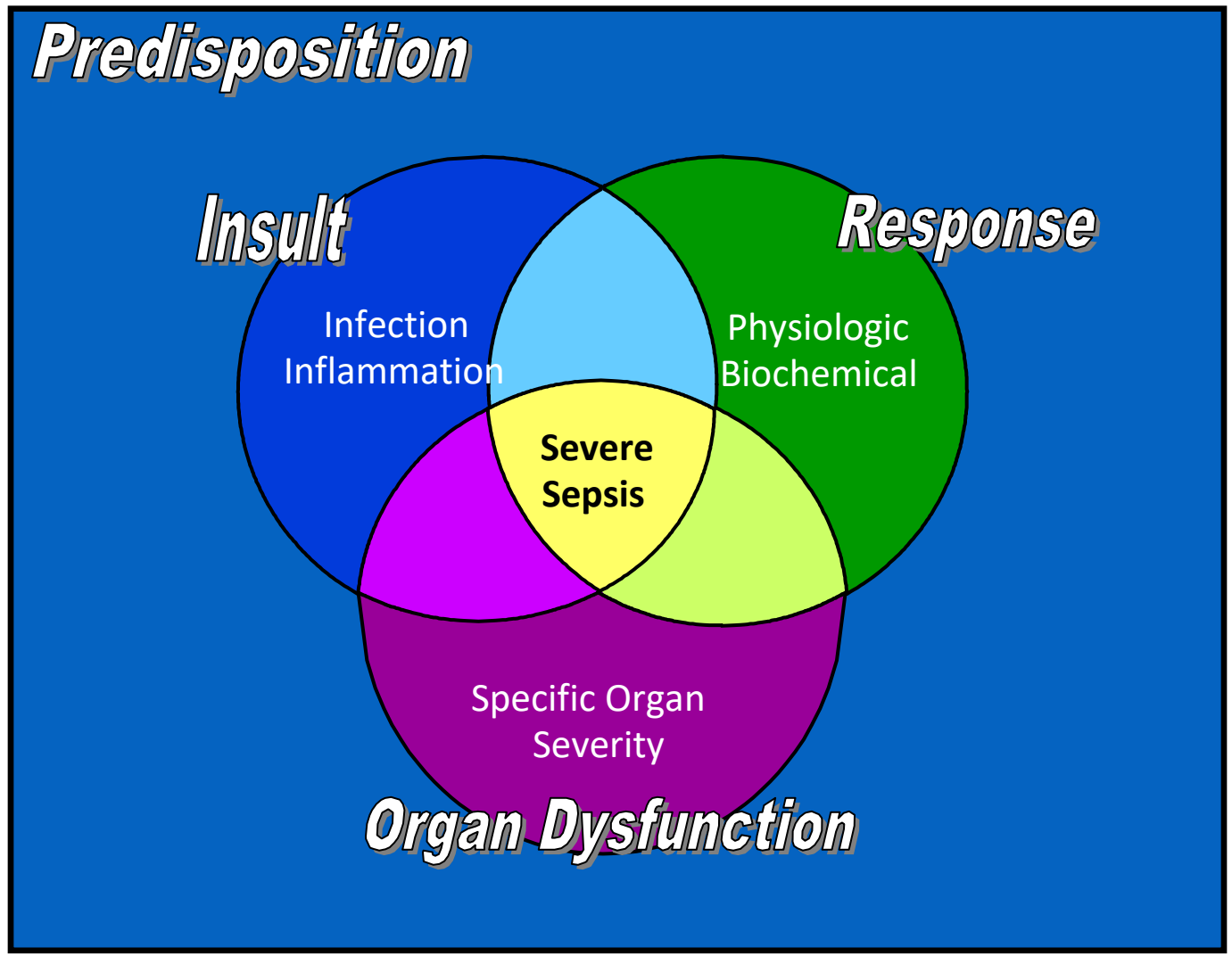


Septic Shock:

Sepsis induced with hypotension despite adequate resuscitation along with the presence of perfusion abnormalities which may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status

Multiple Organ Dysfunction Syndrome (MODS):

Presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention



Predisposition

- Pre-existing disease
  - Cardiac, Pulmonary, Renal
  - HIV
- Age (extremes of age)
- Gender (males)
- Genetics
  - TNF polymorphisms (TNF promoter high secretor genotype)

Response

Physiology

- Heart rate
- Respiration
- Fever
- Blood pressure
- Cardiac output
- WBC
- Hyperglycemia

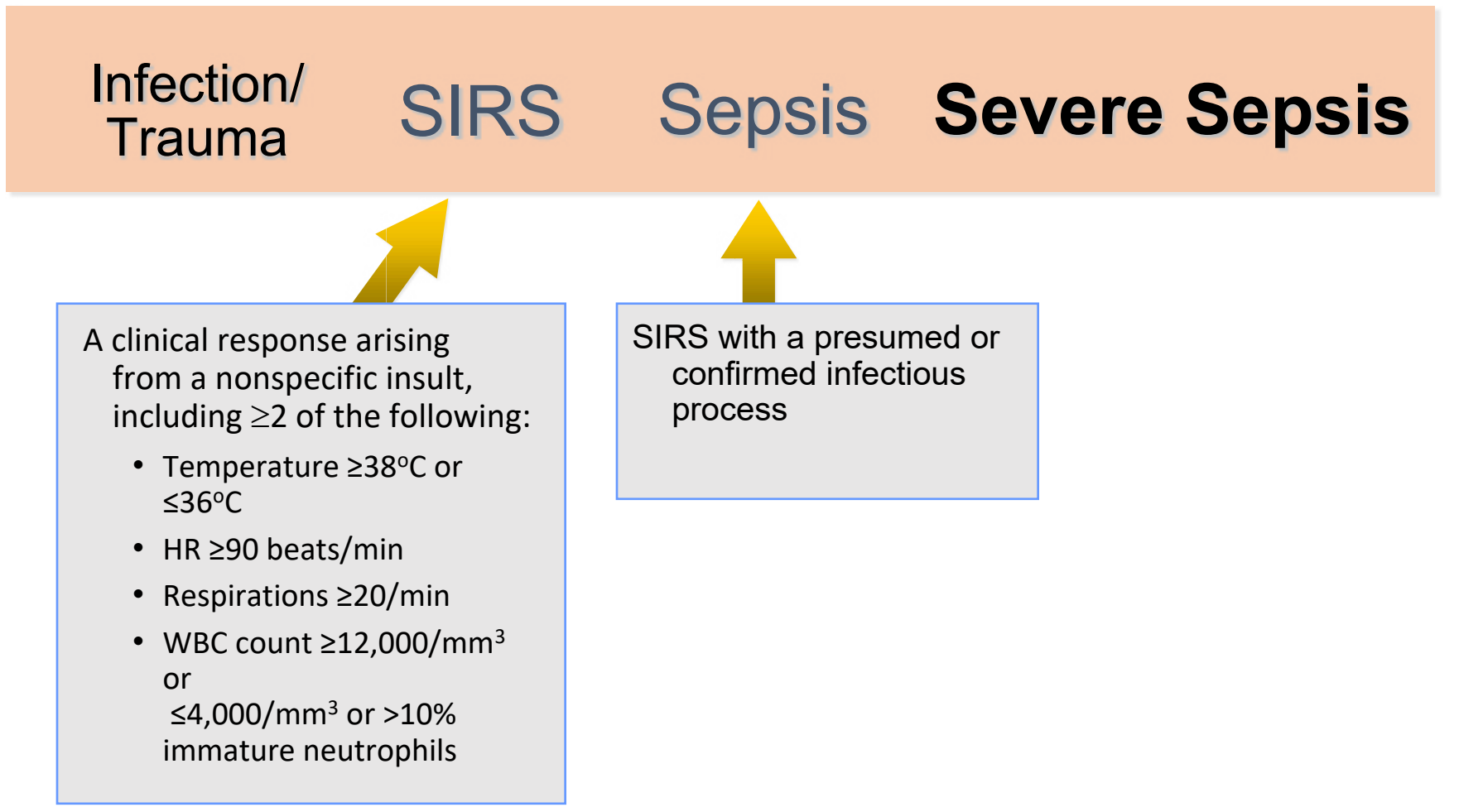
Markers of Inflammation

- TNF
- IL-1
- IL-6
- Procalcitonin
- PAF

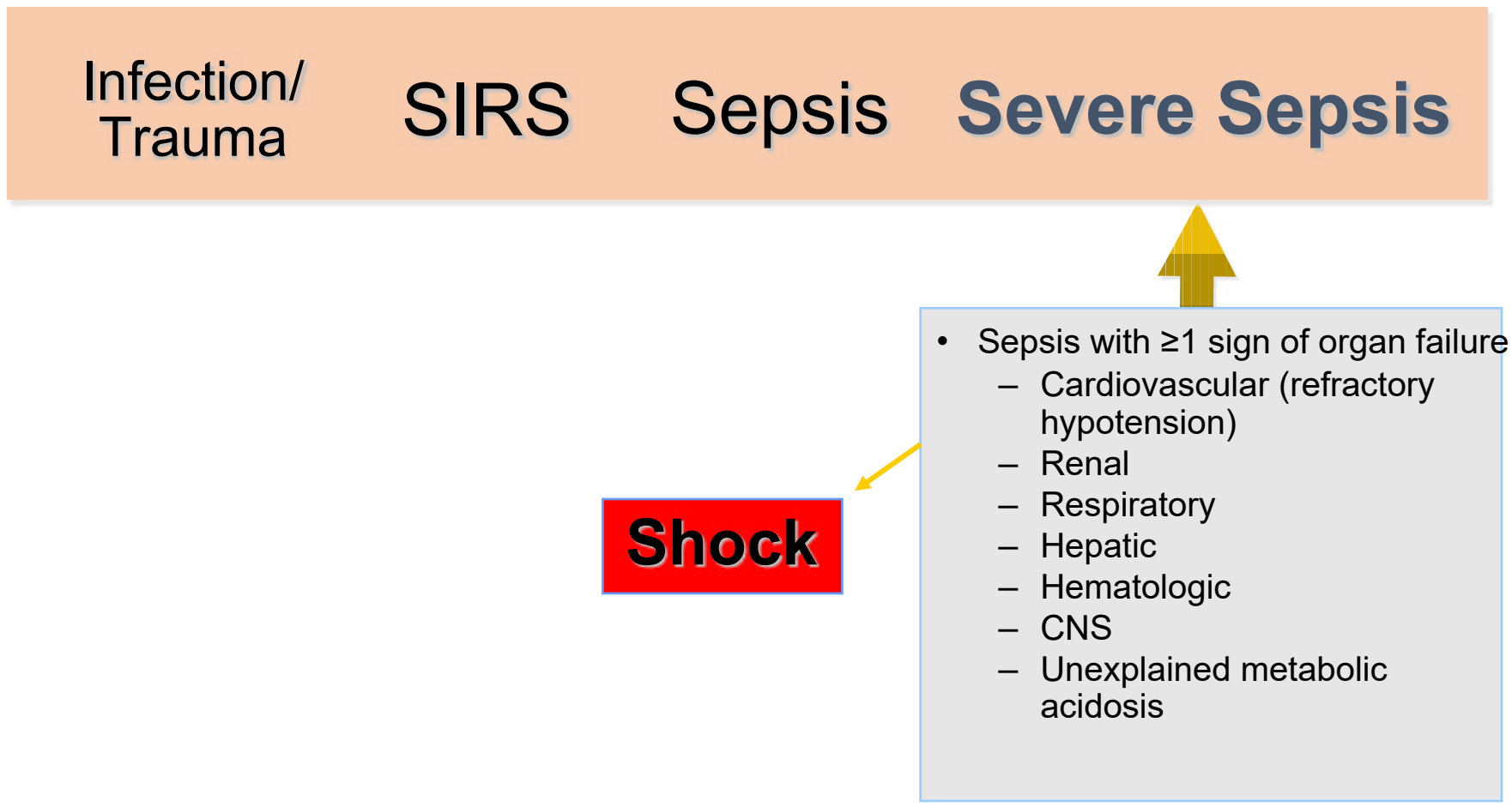
Organ Dysfunction

• Lungs	➢ Adult Respiratory Distress Syndrome
• Kidneys	➢ Acute Tubular Necrosis
• CVS	➢ Shock
• CNS	➢ Metabolic encephalopathy
• PNS	➢ Critical Illness Polyneuropathy
• Coagulation	➢ Disseminated Intravascular Coagulopathy
• GI	➢ Gastroparesis and ileus
• Liver	➢ Cholestasis
• Endocrine	➢ Adrenal insufficiency
• Skeletal Muscle	➢ Rhabdomyolysis

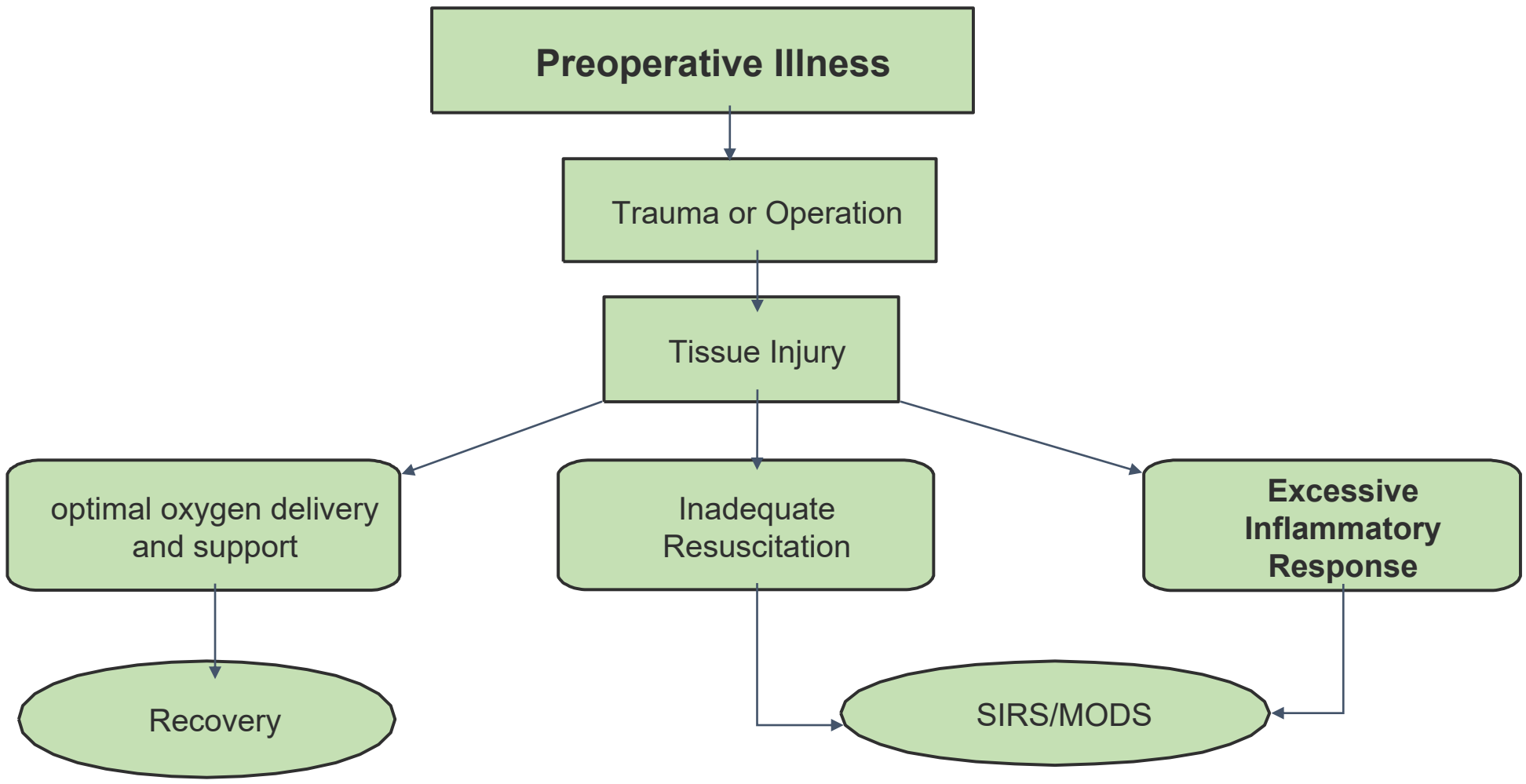
Sepsis: Defining a Disease Continuum



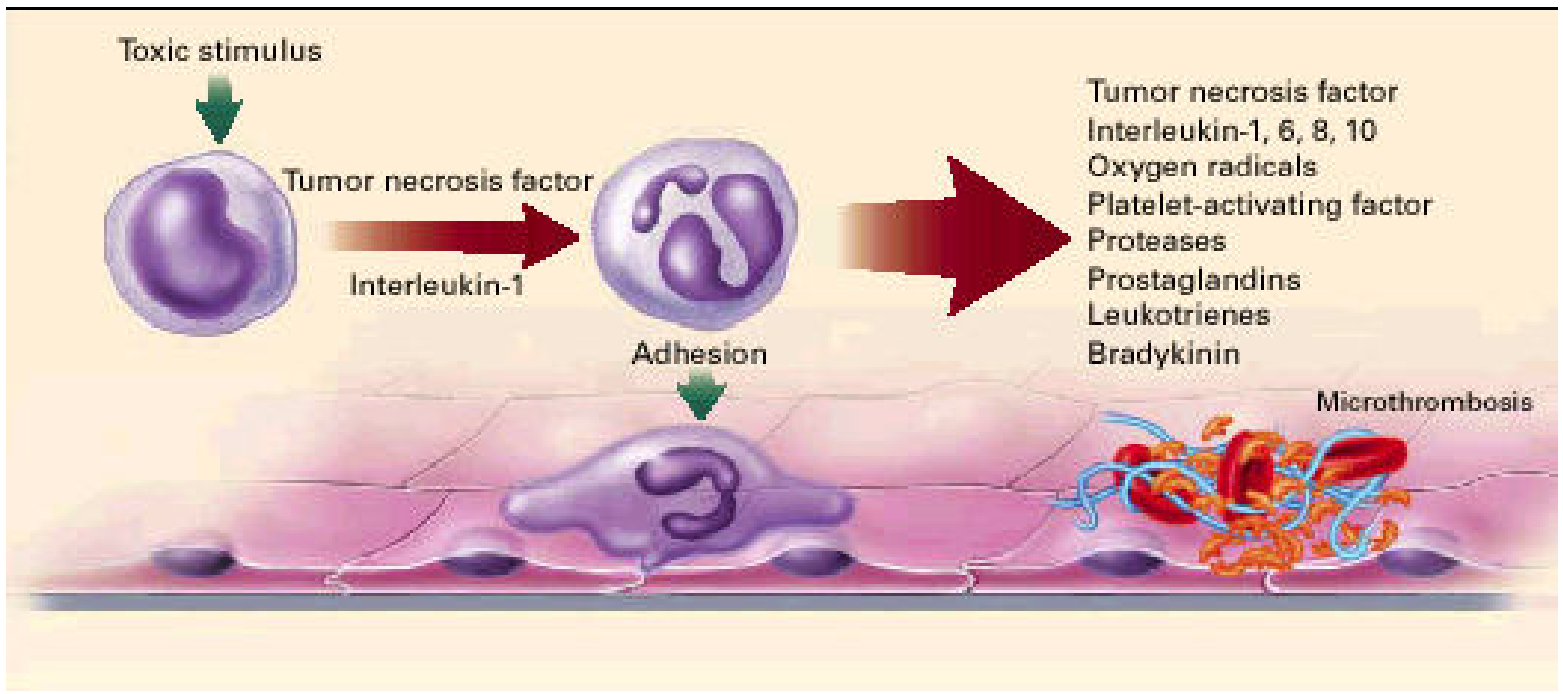
Sepsis: Defining a Disease Continuum



Pathogenesis of SIRS/MODS

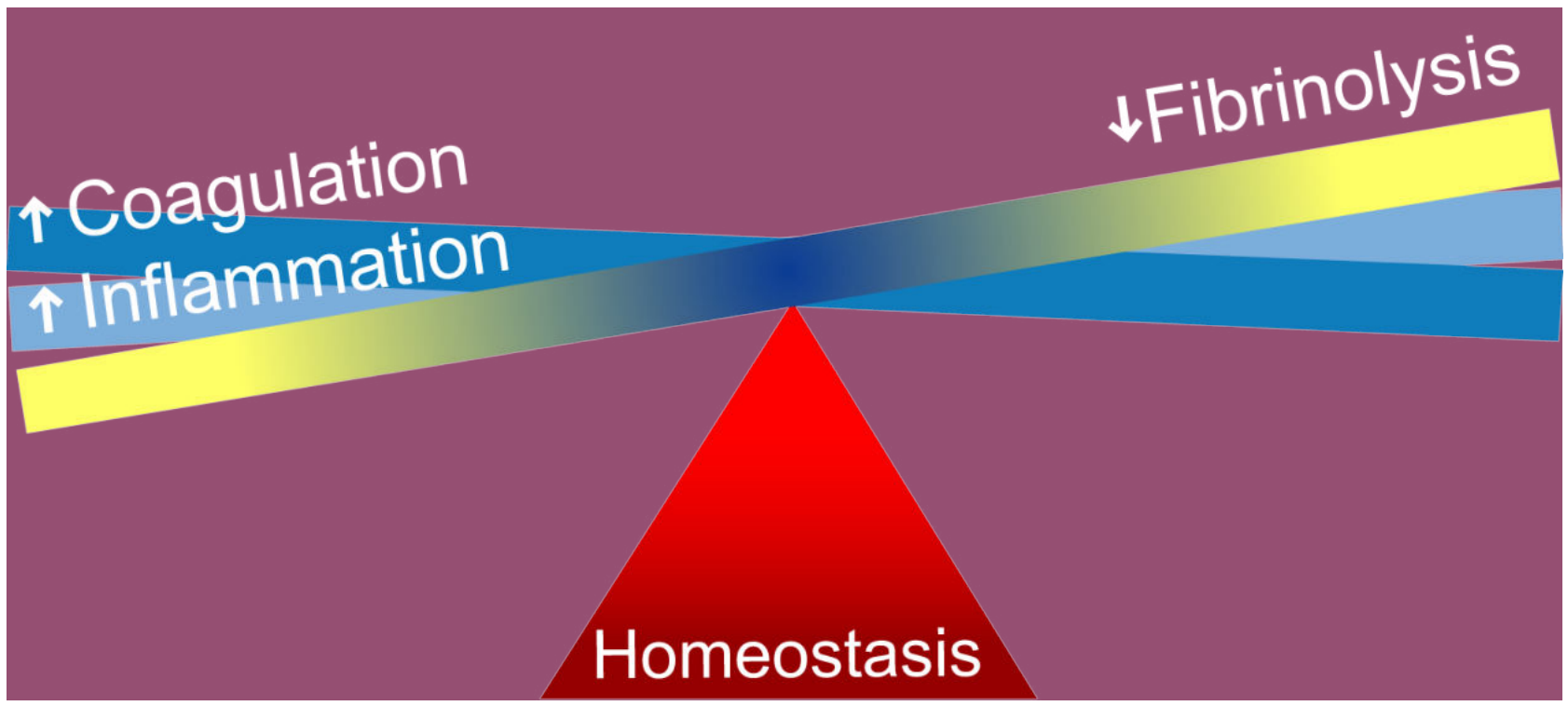


Initiation of Inflammatory Response



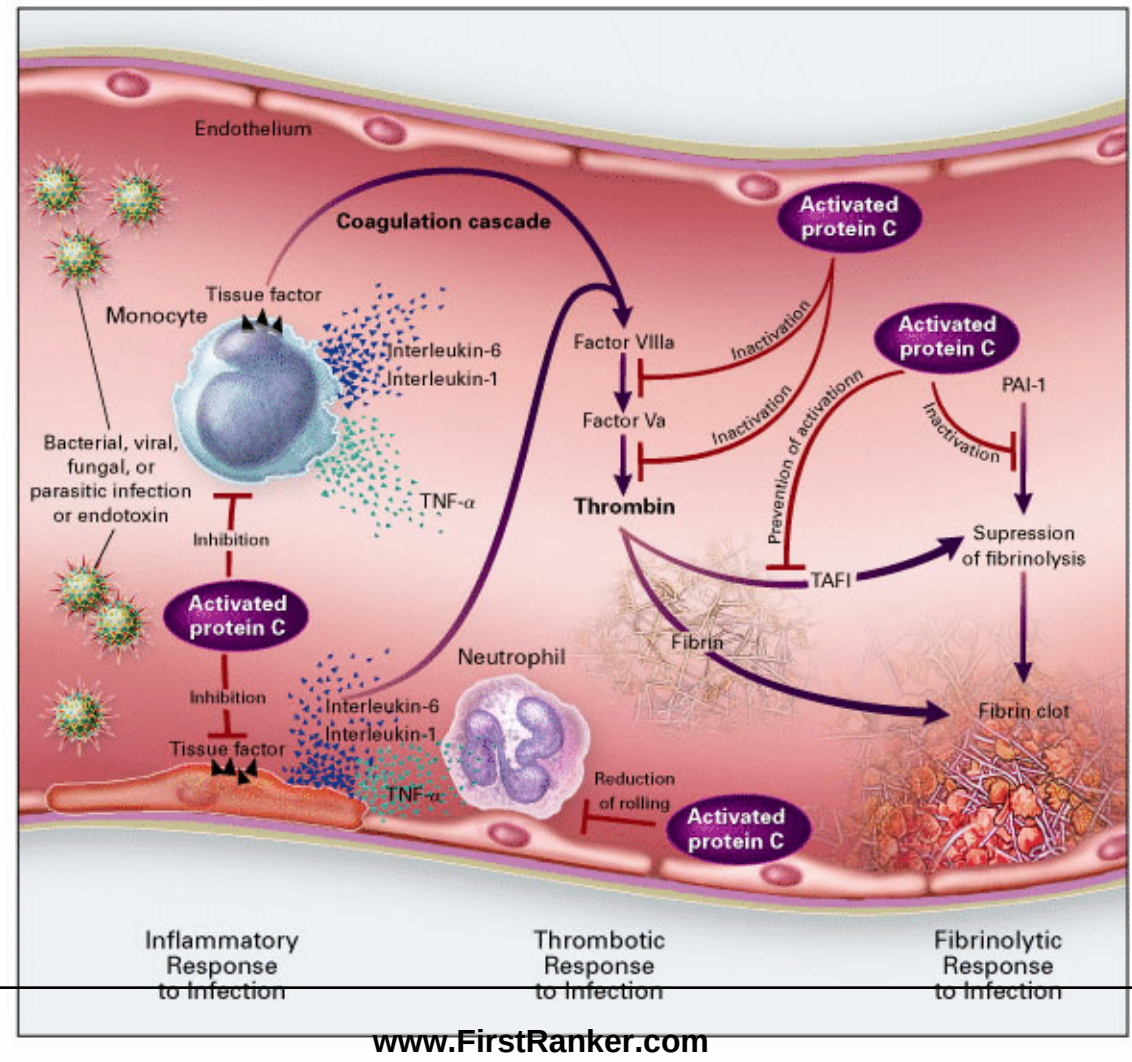
From Wheeler & Bernard, NEJM 1999

Homeostasis is unbalanced in Severe Sepsis



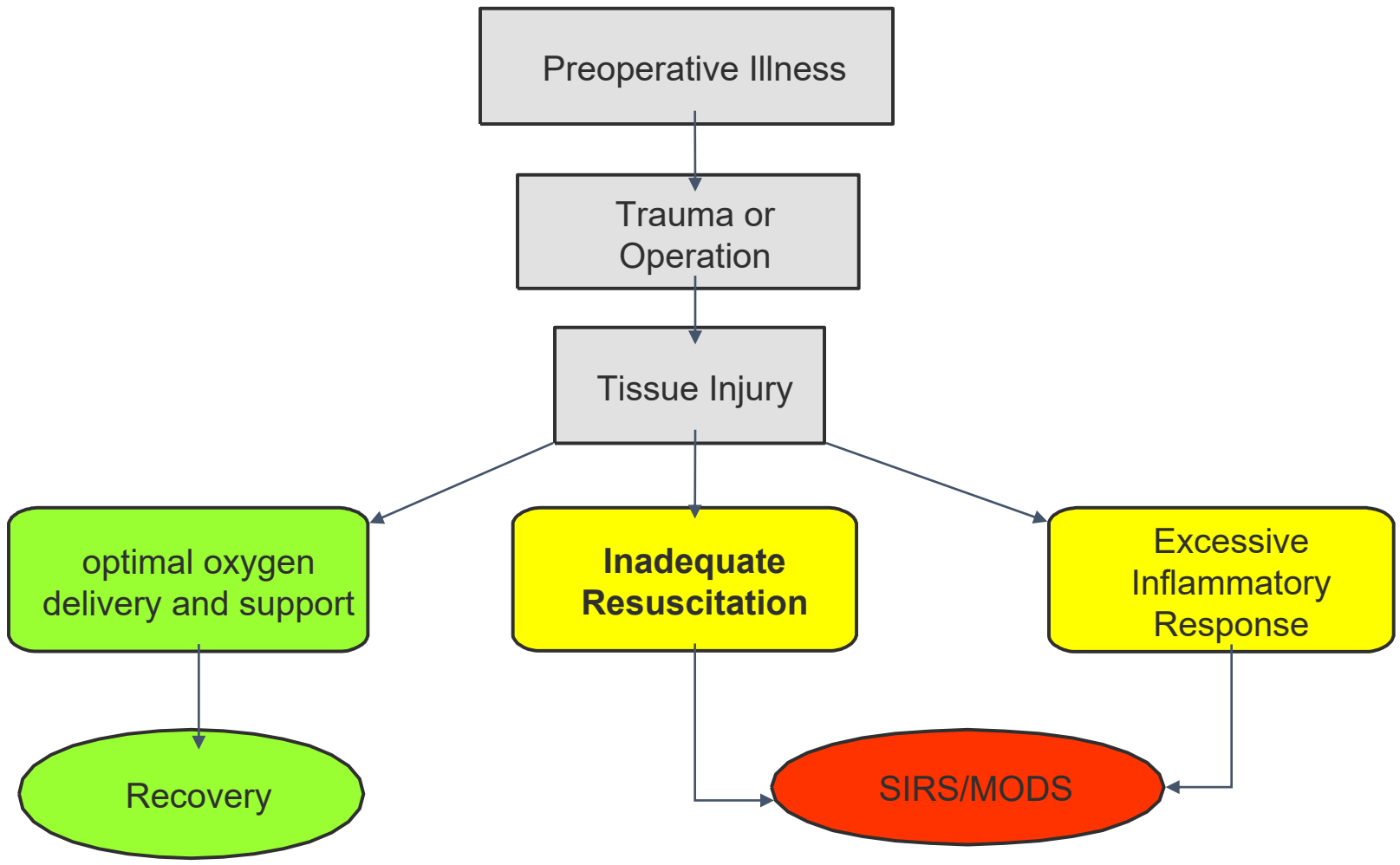
Carvalho AC, Freeman NJ. *J Crit Illness.* 1994;9:51-75; Kidokoro A et al. *Shock.* 1996;5:223-8; Vervloet MG et al. *Semin Thromb Hemost.* 1998;24:33-44.

Coagulation and Fibrinolysis

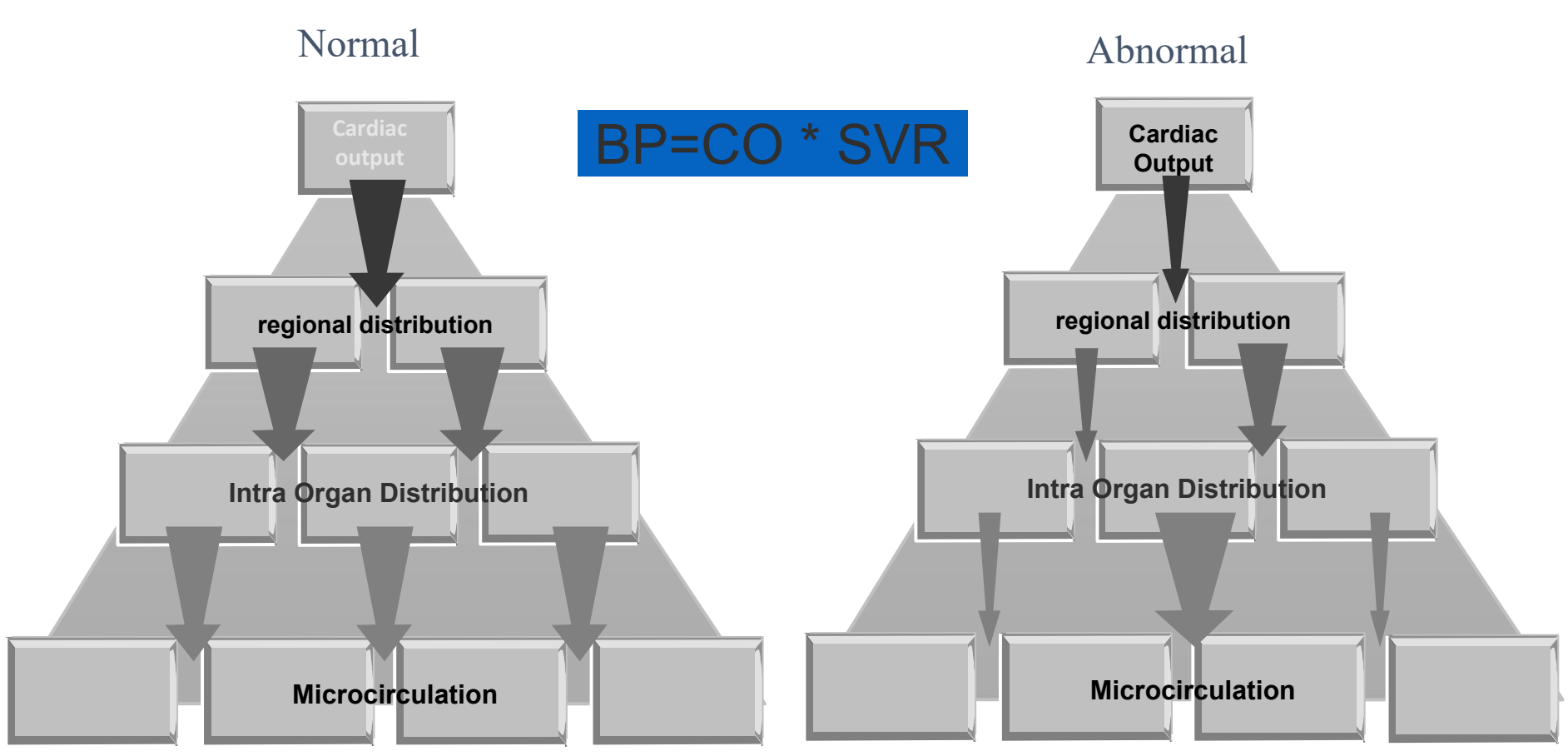


Bernard, GR. NEJM 2001;344;10:699-709

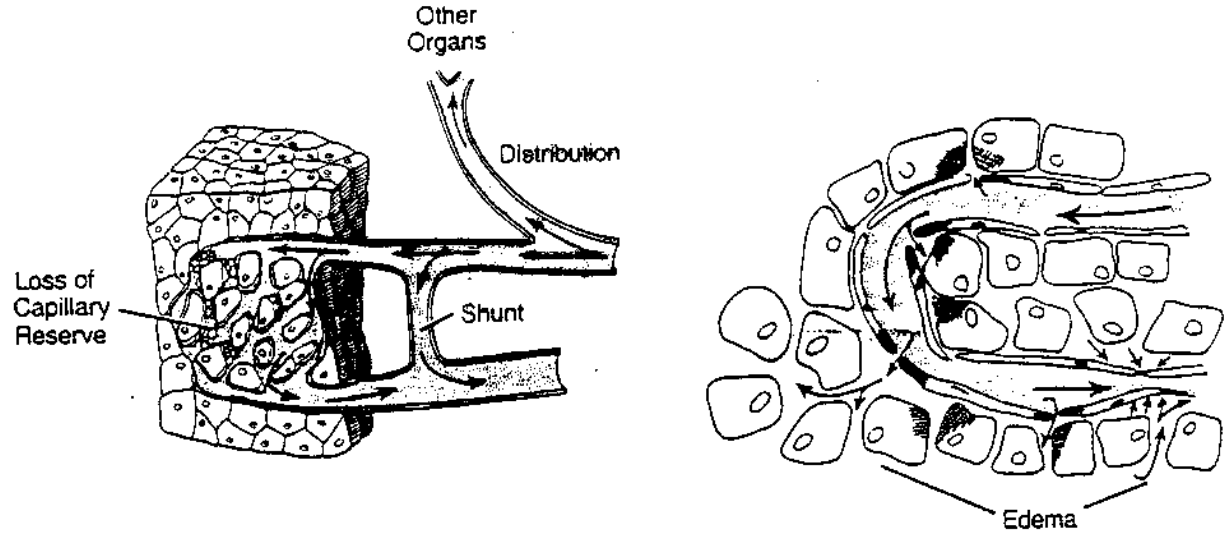
Pathogenesis of SIRS/MODS



Regulation of oxygen delivery

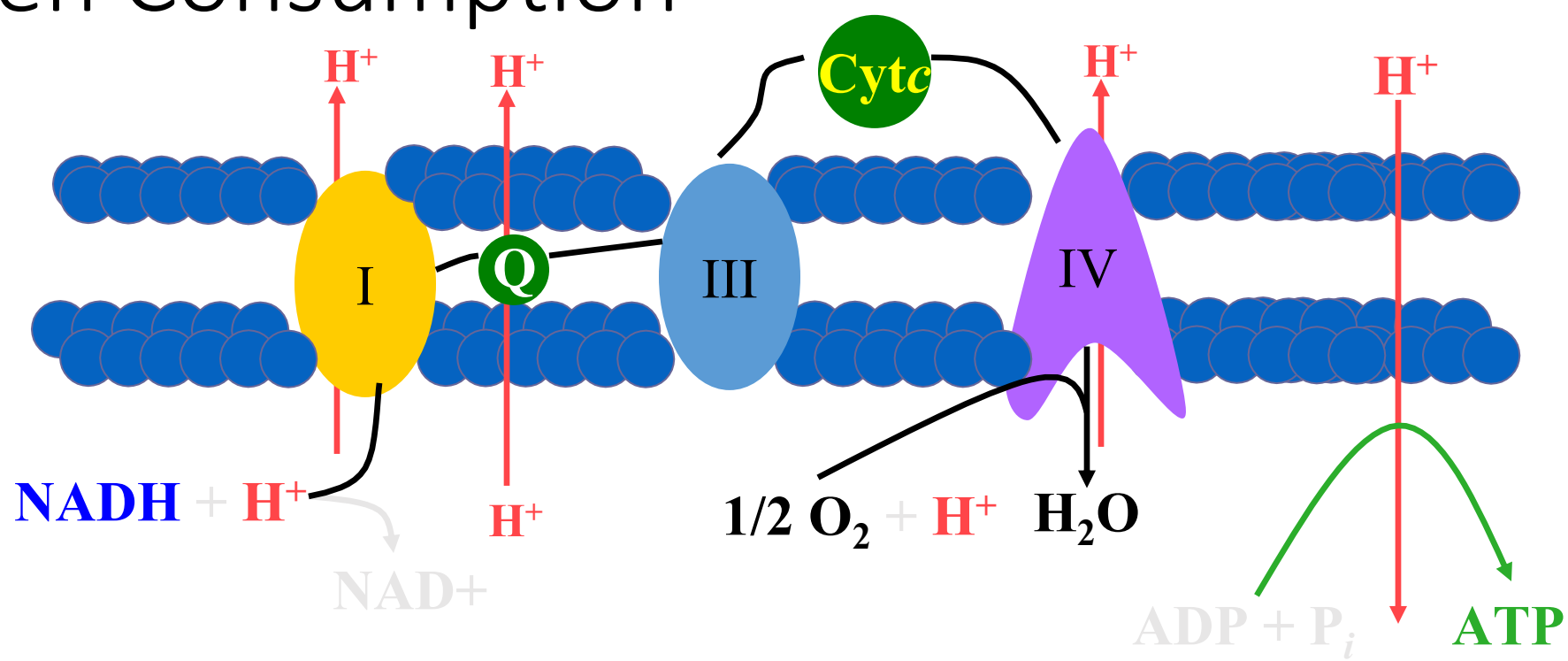


Oxygen Delivery



- Delivery: Demand mismatch
- Diffusion limitation (edema)

Oxygen Consumption



- Pyruvate Dehydrogenase (PDH) activity decreased
  - Decreased delivery of Acetyl CoA to TCA cycle
- Mitochondrial dysfunction

Severe Sepsis: The Final Common Pathway

Endothelial Dysfunction and Microvascular Thrombosis

▼

Hypoperfusion/Ischemia

▼

Acute Organ Dysfunction (Severe Sepsis)

▼

Death

Diagnosis (Rapid Response Team)

1. Screen patients with SIRS clinically for organ hypoperfusion
2. Obtain plasma lactate, blood cultures, and other appropriate studies.
3. Initiate appropriate antibiotics within 1 hour
4. Transfer patients with severe sepsis to ICU

Resuscitation (SIRS plus hypotension or plasma lactate > 4mmol/L)

1. Place central venous or pulmonary artery catheter
2. Institute Early Goal Directed Therapy Protocol with targets:
   a. CVP 8-12 mmHg, utilizing volume expansion
   b. MAP > 65 mmHg, utilizing pressors
   c. SvO_2 > 70%, utilizing dobutamine and transfusions
3. Achieve targets within 6 hours

Septic Shock Management (ICU)

1. Empiric hydrocortisone after ACTH stimulation test
2. APACHE II score and evaluation for rhAPC
3. Glucose control protocol with target BS < 150 mg/dl
4. Ventilator management protocol TV < 6 cc/kg, EIPP < 30 cm H2O

Components:

- Early Recognition
- Early Goal-Directed Therapy
  - Monitoring
  - Resuscitation
  - Pressor / Inotropic Support
  - Steroid Replacement
  - Recombinant Activated Protein C
  - Source Control
  - Glycemic Control
  - Nutritional Support
- Adjuncts:
  - Stress Ulcer Prophylaxis, DVT Prophylaxis, Transfusion, Sedation, Analgesia, Organ Replacement