Learning Outcomes

- Analyze the mediators (cytokines) responsible for cellular and clinical changes during the inflammatory response.
- Correlate the clinical significance of immunoparalysis to trauma, sepsis and open heart surgery.
- Evaluate strategies used to manage patients with immunoparalysis.
recovery from critical illness requires proper immunologic balance between pro- and anti-inflammatory forces.

Persistence of a marked compensatory anti-inflammatory innate immune response following an insult such as sepsis, surgery, or trauma is termed **immunoparalysis**.
Innate - Noncellular Elements

<table>
<thead>
<tr>
<th>Cytokines</th>
<th>Immunoglobulins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemokines</td>
<td>Cytokines</td>
</tr>
<tr>
<td>Complement</td>
<td>Chemokines</td>
</tr>
</tbody>
</table>

Adaptive - Noncellular Elements

- Complement
  - activated by:
    - antigen/antibody complex
    - tissue injury
    - tissue ischemia
    - coagulation

- Complement
  - activated by:
    - cell debris
    - kinins
    - endotoxin
    - bacterial cell debris

lrmmiller@msn.com
Complement
- opsonization
- mediator release
  - histamine
  - leukotrienes

Coagulation
- activated by:
  - Intrinsic pathway
  - Extrinsic pathway

Coagulation excessive intravascular coagulation leads to:
- vascular damage
- tissue ischemia
Fibrinolysis
- Hemorrhage leads to:
  - decreased O₂ delivery
  - tissue ischemia

Triggers to IIR
- infection
- hypoperfusion
- hypoxemia
- injury

Etiology
- ARDS
- Sepsis
- DIC
- ATN
- Shock
Activation of the Immune Response

Critical Care Immunology

• Pathophysiology
  • role of initial insult in promoting INFECTION
  • Immunosuppression
    • downregulation
    • blood products
  • stress response
  • hypercatabolism

Critical Care Immunology

• Pathophysiology
  • Transluminal migration
  • SIRS
  • nosocomial pneumonia
Critical Care Immunology

**Pathophysiology**
- tissue ischemia and reperfusion
- xanthine oxidase $\rightarrow$ O$_2$ free radicals (ROS) $\rightarrow$ tissue injury

**Mortality rates**
- One organ = 1%
- Two organs = 11%
- Three organs = 50%
- Four organs = 75%

**Nurse’s Role in Treatment**
- early identification
- assessing system failure
- minimizing complications
SIRS Criteria (2 or more)

- Temperature > 38 °C or < 36 °C
- Heart rate > 90 beats
- RR > 20 or paCO₂ < 32
- WBC > 12,000 or < 4,000 or > 10% bands

Definitions

- SIRS
- SIRS + Infection = Sepsis
- Sepsis + Acute Organ Dysfunction or hypoperfusion = Severe Sepsis
- Severe Sepsis + CV failure = Septic Shock

Most common sites of origin

- Urinary tract
- GI system
- Respiratory tract
- Skin & wounds

lrmmiller@msn.com
Critical Care Immunology

**Predisposing Factors**
- extremes in age
- granulocytopenia
- prior antibiotic use
- severe burn, trauma, surgery
- functional asplenia
- pre-existing autoimmune disease

**Predisposing Factors**
- immunosuppression
- malnutrition & TPN
- alcohol & drug abuse
- prolonged ICU stay

**Assessing Acute Immune Inflammatory Response**
- Procalcitonin (PCT) 0.12 – 0.26 ng/mL
- C – reactive protein (CRP) 0 – 5 mg/L
- IL – 6 0 – 28 pg/mL

**1st Three Hours**

Resuscitation =
1. Measure lactate level
2. Cultures prior to antibiotics
3. Administer antibiotics
4. Administer 30 mL/kg crystalloid for hypotension or lactate > 4 mmol/L

**1st Six Hours (IC)**

Resuscitation =
1. Vasopressors to maintain a mean (MAP) ≥ 65 mm Hg
2. Persistent hypotension
   a. measure CVP
   b. measure $S_cVO_2$
3. Re-measure lactate if initial lactate was elevated
   CVP ≥ 8, $S_cVO_2$ ≥ 70%, and normalization of lactate

**1st Six Hours**

- Delays in management of the SIR result in higher mortality rates and increased utilization of hospital resources
Identification of High Risk Patient

- single lactate > 4.0 or more at initial presentation
- failure to clear lactate levels during the 1st 6 hours is associated with increased morbidity and mortality
• **Management of IIR**
  - Initial Resuscitation
  - Endpoints
    - CVP 8 to 12 mm Hg
    - MAP > 65 mm Hg
    - UO > 0.5 mL/kg/hr
    - SvO₂ > 70%

• **Management of IIR**
  - Early antimicrobial therapy
    - Empiric antibiotics within 4 to 8 hours of hospital presentation
  - Surviving Sepsis Campaign recommends antibiotics within 1 hour (1B)
Volume Therapy (1B)
- repletion of intravascular volume
- rapid, 30 mL/kg boluses of either crystalloid or colloid
- CVP 8 – 12 mm Hg

Volume Therapy (2C)
- 4% albumin or NS
- found no significant difference in mortality between the group
- Hetastarch (1C)

Vasoactive Agents
- Norepinephrine 2 – 20 µg/min (1B)
- Epinephrine (2B)
- Vasopressin 0.01 – 0.04 units/min – (VASST study) (UG)
- Dopamine 5 – 20 µg/kg/min (2C)
- Phenylephrine 40 – 300 µg/min (1C)
Vasoactive Agents
- Adverse consequences
  - splanchnic hypoperfusion
  - excess tachycardia
  - coronary ischemia

ARDS
- Conservative fluid (1C)
- Protocols for sedation & weaning (1A)
- Avoid neuromuscular blockers (1C) unless P/F < 150 (2C)

RBC Replacement
- If ScvO₂ remains < 70% after optimization of preload, afterload and arterial O₂ saturation
  - increase Hct to 30%
  - optimal erythrocyte transfusion
  - fresh vs. stored blood
Inotropic Therapy

- Sepsis may be accompanied by myocardial suppression in 10 – 15% of patients
- Dobutamine titrated at 2.5 µg/kg/min every 20 – 30 minutes to ScvO₂ of 70%
- Milrinone (long half – life and accumulates in renal failure)

Decreasing O₂ consumption

- Intubation, sedation, analgesia
- Control fever

Steroid Therapy

- If on vasopressors, draw random cortisol level; if < 25 mcg/mL give corticosteroids
- If not on vasopressor, draw baseline random cortisol level, do cort stim test; get levels @ 30 & 60 min – if difference is < 9 ⇒ give steroids
Protective Lung Strategies
- Plateau pressure < -30 cm/H₂O
- 6mL/kg vs. 12 mL/kg
  ✓ 9.9% absolute 28 – day mortality in low TV group

Tight Glycemic Control (1A)
- 100 – 150 mg/dL
  ✓ 8.0% reduction in mortality

High – volume Hemofiltration (2B)
- removal of inflammatory cytokines
Other

- DVT prophylaxis (1B)
- Stress ulcer prophylaxis (1B)
- Oral or enteral feedings within 48 hours (2C)

Case Study
- 23 year old female admitted to outpatient clinic
  - 40°C
  - chills
  - fatigue
  - coughing up brown sputum x 5 days
### BP
- 110/70/82

### T
- 37.9°C

### R
- 30

### HR
- 84

- rales and decreased breath sounds over the left base

### Laboratory data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>7.6 g/dL</td>
</tr>
<tr>
<td>WBC</td>
<td>16,900/mm³</td>
</tr>
<tr>
<td>Platelets</td>
<td>41,000/mm³</td>
</tr>
<tr>
<td>CRP</td>
<td>300 mg/dL</td>
</tr>
<tr>
<td>ESR</td>
<td>146 mm/h.</td>
</tr>
</tbody>
</table>

### Laboratory data

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</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>0.7 mg/dL</td>
</tr>
<tr>
<td>AST</td>
<td>59 IU/mL</td>
</tr>
<tr>
<td>ALT</td>
<td>22 IU/mL</td>
</tr>
<tr>
<td>LDH</td>
<td>364 IU/L</td>
</tr>
<tr>
<td>Glucose</td>
<td>280 g/dL</td>
</tr>
</tbody>
</table>
Laboratory data

- Albumin: 2.2 g/dL
- d-dimer: 0.667 µg/mL
- Procalcitonin: 64.05 ng/mL

Microscopic hematuria

Blood, urine, and sputum cultures sent

Bilateral lower lobe pulmonary infiltration and right-sided pleural effusion on PA chest X-ray

cefotaxime and moxifloxacin, IV started as initial empiric therapy for suspected community-acquired sepsis.

lrmmiller@msn.com
In addition, supportive therapy
- fresh frozen plasma
- red cells
- albumin
- isotonic fluids
- oxygen, 40%

Blood cultures grew gram-positive coccus defined as S. pneumoniae

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paO₂ / SaO₂  85 / .95
pH  7.42
paCO₂ / HCO₃  38 /25
FiO₂ / P/F ratio  .40 / 212.5

Supplemental oxygen x ambulatory, intubation and mechanical ventilation

Central venous pressure catheter and continuous arterial pressure monitoring

Sedation, paralysis (Fentanyl), or both

CVP  8-12 mm Hg
B: SBP  105-110 mm Hg
MAP  >85 mm Hg or >65 mm Hg

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CVP, Central Venous Pressure
MAP, Mean Arterial Pressure
SaO₂, Central Venous Ox Saturation

Sepsis
Infection
Catecholamines
Inotropic Agents
CVP, Central Venous Pressure
MAP, Mean Arterial Pressure
SaO₂, Central Venous Ox Saturation

Goal Achieved

Hospital Admission
Antinuclear antibody (ANA) was positive at a titer of 1/1,000.
Anti-double-stranded DNA was positive at 984 IU/mL.
Diagnosed with SLE.