YOU ARE WHAT YOU EAT?!

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DISCLOSERS

NONE

OBJECTIVES

- WHEN AND HOW TO FEED TO IMPACT SEPSIS?
- HOW MUCH NUTRITION IS ENOUGH?
- SUPPLEMENTS AND THEIR ROLE IN SEPSIS MANAGEMENT?
- HOW DOES PREMORBID MEDICATIONS ALTER SEPSIS?

SEPSIS

- 1.7 MILLION INDIVIDUALS PER YEAR
- 250K DEATHS PER YEAR
- 24 BILLION DOLLARS IN COST

GUT HEALTH

- Gastrointestinal microenvironment
  - Single cell layer of epithelia
  - Local immune system
  - Microbiome
- 4 dominant phyla
  - Firmicutes (bad)
  - Bacteroides (good)
  - Actinomycetota
  - Pseudomonadota

GUT HEALTH

- Bacteroides
- Clostridium
- Faecalibacterium
- Eubacterium
- Ruminococcus
- Peptococcus
- Peptostreptococcus
- Bifidobacterium

GUT HEALTH

- Firmicutes : Bacteroides ratio
  - Shifts with aging
  - Associated with metabolic syndromes
    - Type 2 diabetes
    - NAFLD
    - Atherosclerotic vascular disease
  - Low fiber reduces the variety of gut bacteria
  - Carbs/Protein are required for SCFA which in-turn inproves the immune response
    - T cells
    - Enhances the gut integrity

GUT HEALTH

- Bacteroides Fragilis
  - reduces inflammation
- Clostridium
  - Improves T cell development
  - Suppresses autoimmune diseases
- Firmicutus
  - Modulates immune response
  - Promotes a pro-inflammatory state

GUT HEALTH

- Gut failure
- Ileus
  - Absent bowel sounds
  - Abdominal distention
  - Vomiting
  - Decrease GI motility with high residuals
- Diarrhea
- GI bleed (gastric ulcerations)
- If 3 of these symptoms are present on ICU day 1:
  - **3 FOLD INCREASE IN MORTALITY**

GUT HEALTH

- Gut failure
  - Intestinal permeability (vagal nerve stimulation reduces this)
  - Upregulation of apoptosis

  - Alters systemic and local inflammation
  - Changes the microbiome composition

GUT HEALTH

- Dysbiosis
  - Microbial contents
    - Introduction via oropharynx
    - Elimination via fecal material
    - Regulation/proliferation within the GI tract
  - Disruption of the microbiome
    - Antibiotics
    - PPI
    - TPN

GUT HEALTH

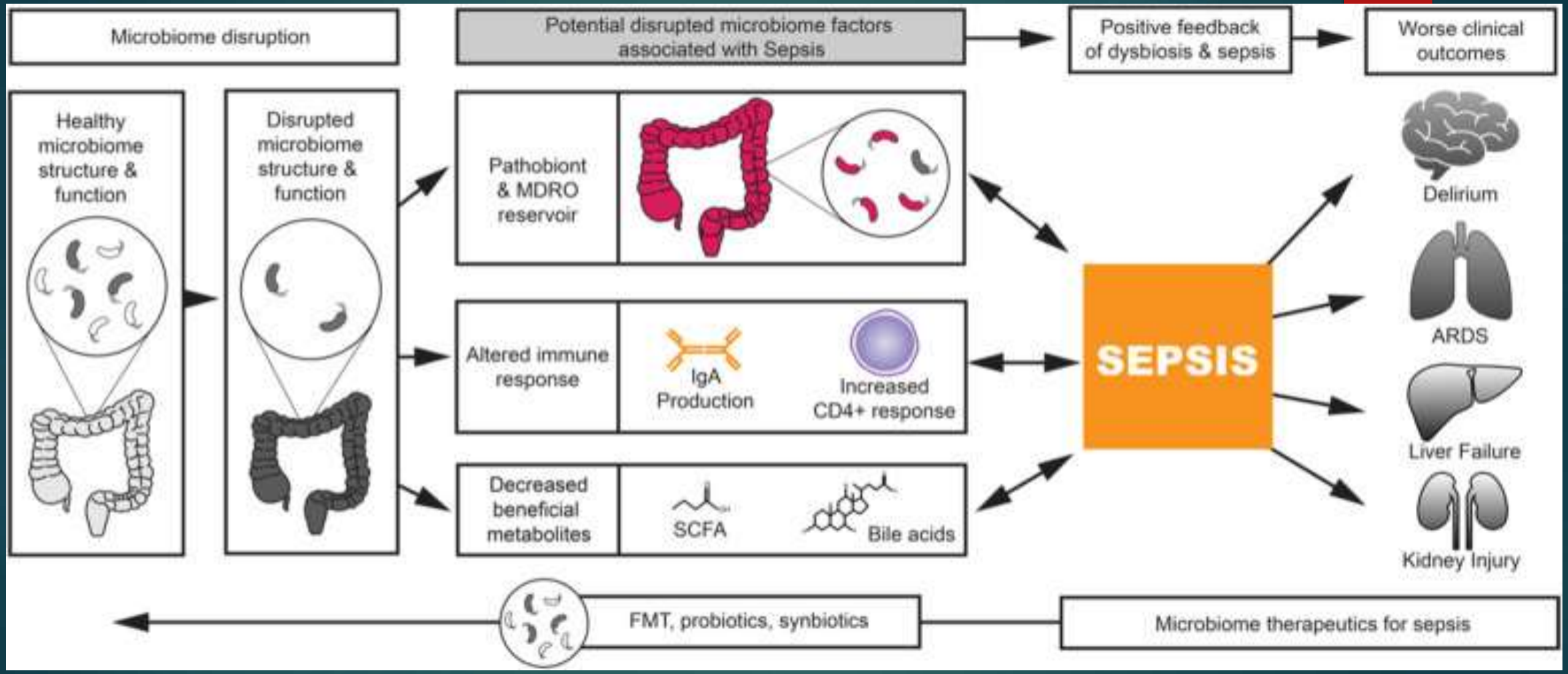
- Dysbiosis becomes pathobiome
  - Loss of microbial diversity
  - Dominance of pathogenic microorganisms
  - Alterations leading to a more virulent organism

- Phosphate depletion
  - TPN use
  - Liver disease
  - Malabsorption/malnutrition

GUT HEALTH

- Gut microbia disruptions are associated with:
  - Asthma
  - Epilepsy
  - Sepsis
  - C. Difficile

- Prime the immune system
  - T-cell
  - Humoral system - IgA


Microbiome disruption
Potential disrupted microbiome factors associated with Sepsis
Positive feedback of dysbiosis & sepsis
Worse clinical outcomes
Healthy microbiome structure & function
Disrupted microbiome structure & function
Pathobiont & MDRO reservoir
Altered immune response
IgA Production
Increased CD4+ response
Decreased beneficial metabolites
SCFA
Bile acids
SEPSIS
Delirium
ARDS
Liver Failure
Kidney Injury
FMT, probiotics, synbiotics
Microbiome therapeutics for sepsis


BUFFET
ALL YOU CAN EAT

NUTRITION

- WHERE AND WHEN TO START?
  - Route
  - Dose
  - Timing

ROUTE

- Enteral nutrition has several advantages
  - Maintains gut health and integrity
  - Modulates the inflammatory state
  - Reduces systemic infection
  - Reduces organ failure
  - Reduces hospital LOS

ROUTE

- Calories provided and associated outcomes
  - > 70% - increase in mortality (1-7days)
  - > 110% - overfeeding
    - Increase mortality and infections
    - Increase glucose levels
    - Increase lipids and fat mass
    - Increase CO2
    - Decrease lean muscle and muscle function

Zusman at el

DOSE

- CALORIES REQUIRED
  - Indirect caloric vs calculated (no difference)
  - Calories - 10 kcal/kg – 30 kcal/kg ideal body weight
    - 10-18 kcal/kg < 7 days and 18-30 kcal/kg > 7 days
  - Protein –0.8 g/kg early < 4 days
    - 1.2 g/kg – 2 g/kg > 4 days
  - Not measuring gastric residual volume is recommended (< 500 is acceptable)

TIMING

- Early vs Late < 48 hrs (1-4 d) vs > 4-7 d
  - Early is superior
  - Avoid while pressors are still escalating
  - Avoid parenteral nutrition for up to 7 -10 days
  - Reduce mortality
  - Reduce infectious morbidity
  - Reduce hospital LOS
  - Reduction in pneumonia

THIAMINE

- 35% of septic patients have a thiamine deficiency
- If deficient and supplemented:
  - Reduced mortality
- Low cost, low risk
- 200 mg/day for 7 days

THIAMINE

- "Metabolic Resuscitation"
  - Thiamine 200 mg every 12 hrs
  - Vitamin C 1500 mg every 6 hrs
  - Hydrocortisone 50 mg every 6 hrs

- Ongoing research
  - Renal protection
  - Neuroprotection post arrest

Marik et al

THIAMINE

- Patient selection
  - Lactic acid is slow to clear despite resuscitation
  - Alcoholic
  - Chronic diuretic use
  - Malnutrition
  - Diabetics
  - ESRD
  - Bariatric surgery

VITAMIN D

- Vitamin D < 12 ng/ml is critically low
  - D3 supplementation improves hospital survival
  - 50k-100 IU/day for 5 days

Warnkross et al

ACID SUPPRESSION

- Proton Pump Inhibitors (PPI) VS Histamine 2 receptor blocker (H2B)
  - PPI
    - Increase in-hospital mortality (6%)
    - Increase GI bleeding (6 times)
    - Increase nosocomial pneumonia (1.32 times)
    - Increase C. Difficile infections
    - Increase cardiovascular risk
    - Increase overt bleeding
    - Increase thrombocytopenia

BETA BLOCKERS

- Are all beta blockers created equal?
  - Atenolol, Metoprolol, Bisoprolol (Selective)
    - Attenuation /modulation of the immune system through PD-L1 expression
    - Down regulation of the receptors on T-cells that are upregulated by LPS
    - Reduces free radical production (ROS)

    - **REDUCTION IN THE DEVELOPMENT OF SEPSIS**
    - **REDUCTION IN SEPSIS MORTALITY**
    - **IMPROVE CARDIAC RHYTHMS**
    - **IMPROVE ACID-BASE STATUS**

Tank et al

BETA BLOCKERS

- Sepsis
  - Increase in catecholamines
  - Increases resting energy expenditure (REE)
  - Increases protein catabolism
  - Increases blood glucose levels

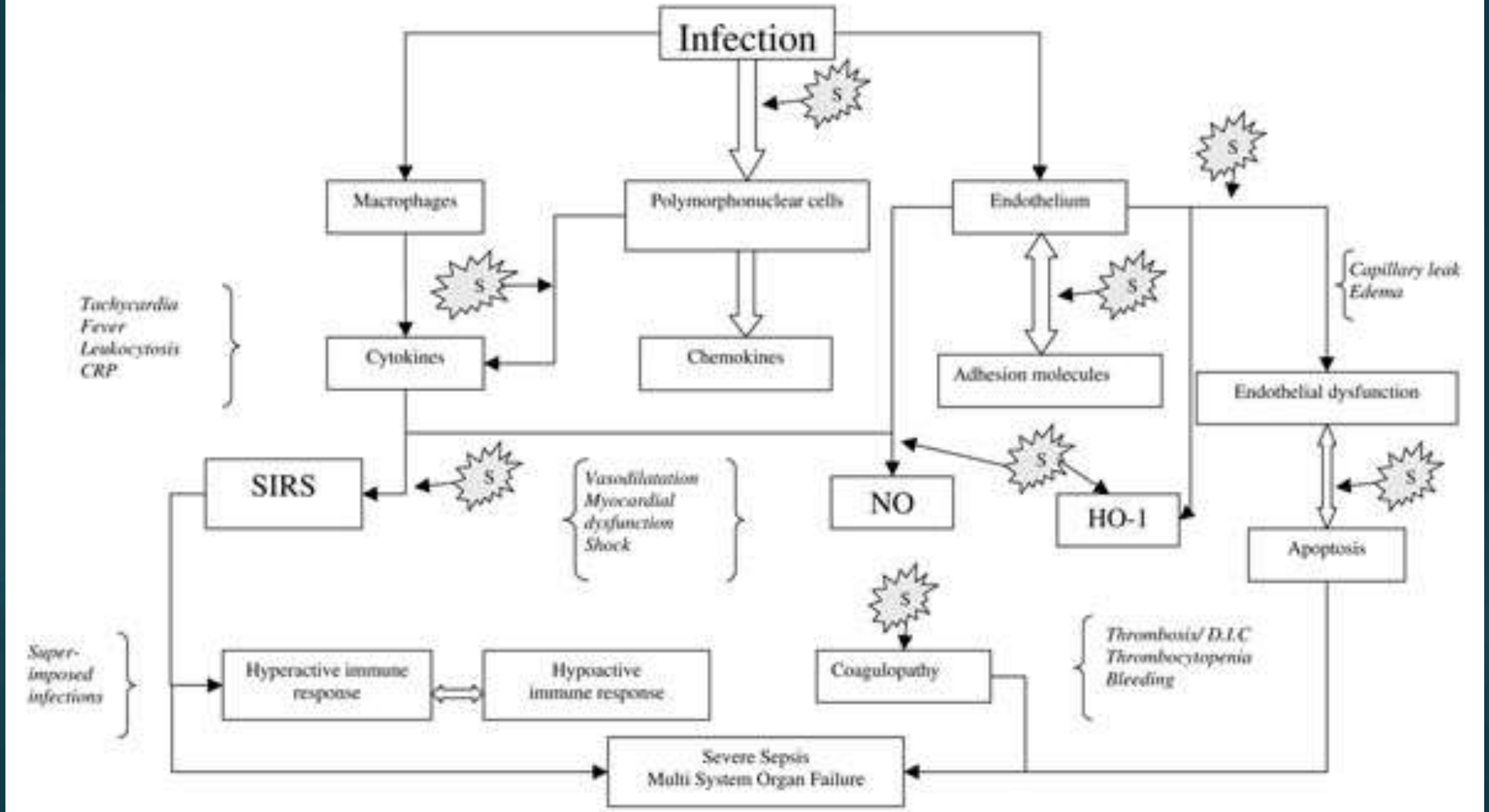
- **SELECTIVE BETA BLOCKERS MODULATE THESE DELETERIOUS EFFECTS**

Macchia et al

STATINS

- Pleotropic effects
  - Anti-inflammatory
  - Anti-oxidant (reduction in ROS)
  - Immunomodulatory
  - Anti-apoptotic
  - Anti-thrombotic

Blanco-Colio LM et al


Infection
S
Macrophages
Polymorphonuclear cells
Endothelium
S
S
S
Tachycardia
Fever
Leukocytosis
CRP
Cytokines
Chemokines
Adhesion molecules
Capillary leak
Edema
Endothelial dysfunction
SIRS
S
S
Vasodilatation
Myocardial
dysfunction
Shock
NO
HO-1
S
Apoptosis
S
Super-
imposed
infections
Hyperactive immune
response
Hypoactive
immune response
Coagulopathy
Thrombosis/ D.I.C
Thrombocytopenia
Bleeding
Severe Sepsis
Multi System Organ Failure

STATINS

- How do statins impact sepsis
  - Reduce 30 day ICU mortality – 8%
  - Reduce ICU LOS – 6%
  - Reduce 30 hospital LOS – 14%

STATINS

- Are all statins created equal?
  - Hydrophilic/synthetic vs Lipophilic/fungal

Statin	Derivation	Property
Atorvastatin	Synthetic	Lipophilic
Fluvastatin	Synthetic	Lipophilic
Lovastatin	Fungal	Lipophilic
Pitavastatin	Synthetic	Lipophilic
Pravastatin	Fungal	Hydrophilic
Rosuvastatin	Synthetic	Hydrophilic
Simvastatin	Fungal	Lipophilic

STATINS

- Hazard of death with statin use
  - 13% reduction
  - Both 30 day and 90 day

- Synthetic / Hydrophilic > Fungal / lipophilic

Liang et al

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