

THE WINDS OF CHANGE: SEPSIS AND THE ROLE OF THE RESPIRATORY THERAPIST

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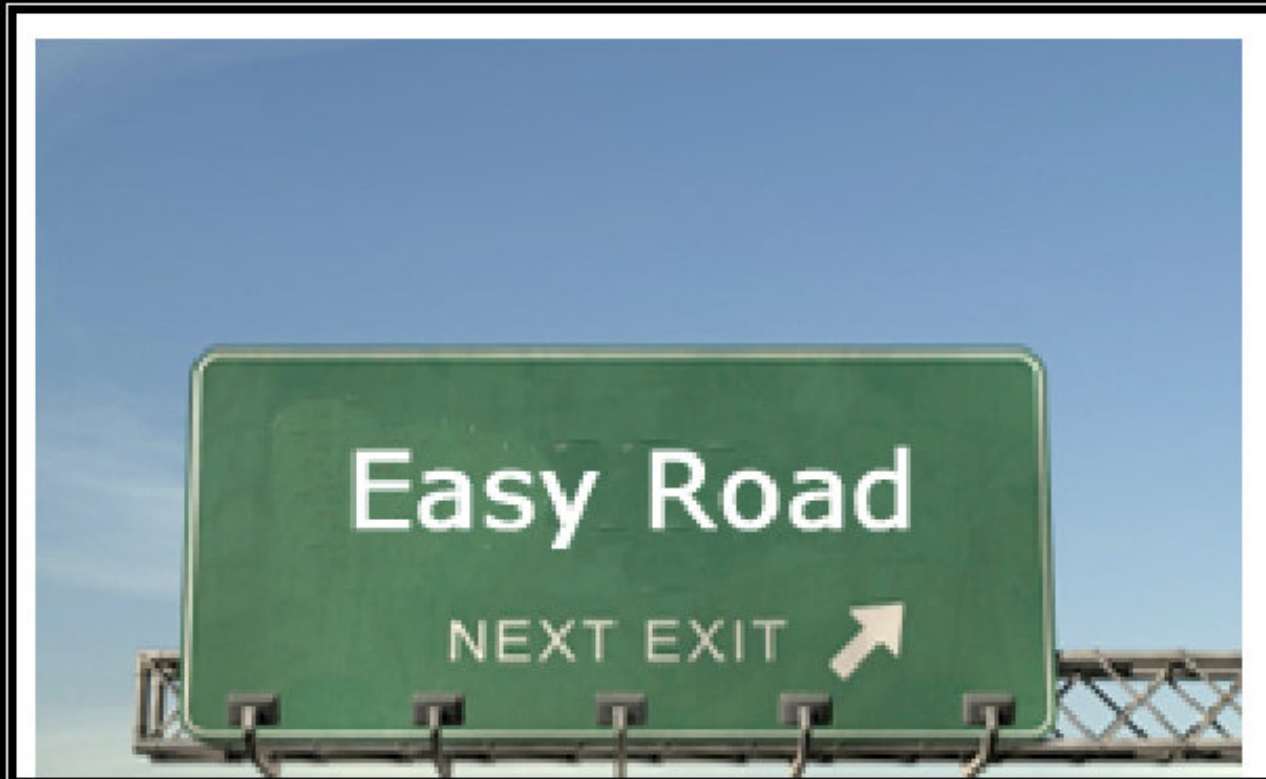
OBJECTIVES

- Understand the causes and management of sepsis.
- Review physiology of sepsis
- Understand the importance of sepsis guidelines
- Discuss the importance of how you can make the most difference in not only the management, but especially the prevention of Sepsis

MULTI-PROFESSIONAL ICU TEAMS DISCIPLINE=CRITICAL CARE

- Intensivists
- Nurses
- Respiratory Therapists
- Pharmacists
- Nutritionists
- Physical and occupational therapists

MANY TIMES IN ICU IN CRISIS



WHY THINK...

WHEN YOU CAN JUST CALL RESPIRATORY



DOCTOR'S ORDERS

IF THEY'RE NOT BASED ON SCIENCE...
THEN THEY ARE STUPID

HISTORY OF SEPSIS

SEPSIS AND THE ANCIENT GREEKS AND ROMANS

- The word “sepsis” derives from the Greek “shjiz” which refers to the “decomposition of animal, or vegetable or organic matter in the presence of bacteria.”
- The first use of “sepsis” in the medical context occurred over 2700 years ago in the poems of Homer. In this use, the term “sepsis” derives directly from the word “sepo”, which means “I rot.”
- The term is also found in the writings of the great physician and philosopher Hippocrates (circa 400 BC) in his Corpus Hippocraticum.
- Hippocrates is well known for the introduction of the concept of dysregulated body humors (the bodily fluids of blood, yellow bile, black bile, and phlegm) as a cause of disease.

HISTORY OF SEPSIS

- Hippocrates viewed sepsis as the dangerous, odiferous, biological decay that could occur in the body.
- It was further believed that this biological decay occurred in the colon and released “dangerous principles” that could cause “auto-intoxication.”
- Hippocrates was one of the first to examine antiseptic properties of potential medicinal compounds including alcohol in wine and vinegar.

EARLY WORK ON THE TRANSMISSION OF INFECTIOUS DISEASE AND THE DISCOVERY OF “ANIMACULES”

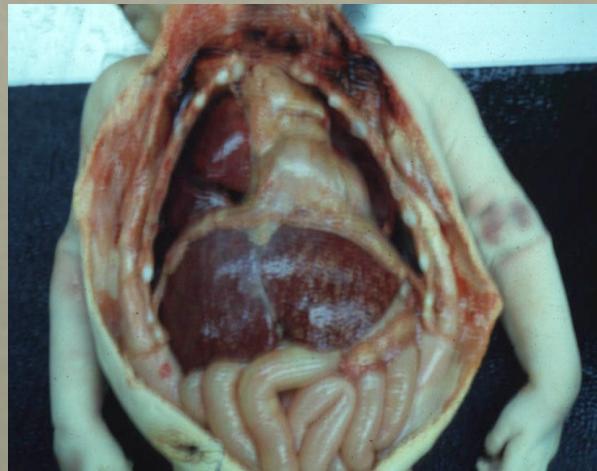
- Marcus Terentius Varro, in “De re rustica libri III” (three books on agriculture circa 100 BC), was the first to articulate the notion of contagion.
- He suggested, “small creatures invisible to the eye, fill the atmosphere, and breathed through the nose cause “dangerous diseases.”
- In the millennia since his insightful analysis, major pandemics of bubonic and pneumonic plague, cholera, smallpox, measles, tuberculosis, syphilis, gonorrhoea and influenza have devastated the human population.

HISTORY OF SEPSIS

- Anthony van Leeuwenhoek (1632–1723) had no scientific background or medical training, yet he was able to build his own compound microscope and made a number of significant discoveries to advance the study of infectious disease.
- Leeuwenhoek's first description and drawings of "animacules" in 1674, including spheres, rods and spirals (ie, cocci, bacilli and spirochetes), paved the way for other scientists to further develop germ theory

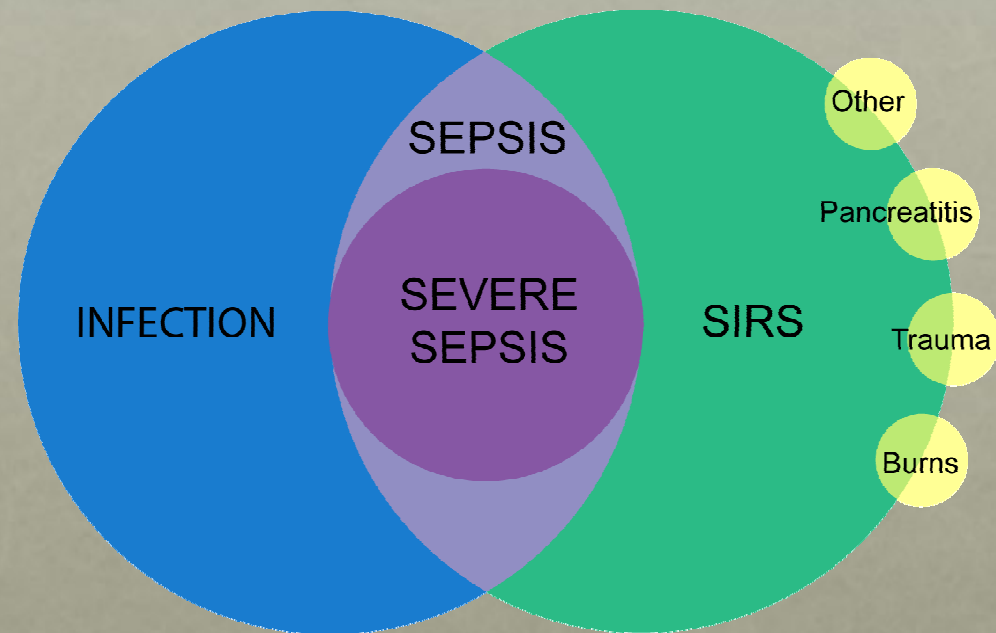
WE HAVE COME A LONG WAY

- Or have we?
- Death is still extremely high for a disease that has been around since the dawn of time



SEPSIS: A COMPLEX DISEASE

- This Venn diagram provides a conceptual framework to view the relationships between various components of sepsis.
- The inflammatory changes of sepsis are tightly linked to disturbed hemostasis.



Adapted from: Bone RC et al. *Chest*. 1992;101:1644-55.
Opal SM et al. *Crit Care Med*. 2000;28:S81-2.

SEPSIS: DIAGNOSIS

- **Sirs**: inflammatory response to wide variety of severe clinical insults, manifested by 2 or more following conditions:
 - Temperature > 38 degrees C. or < 36 degrees C.
 - Heart rate > 90 bpm
 - Respiratory Rate > 20 bpm or PaC02 < 32 mm Hg
 - WBC $> 12,000$ or < 4000 or $> 10\%$ bands
- **Sepsis**: SIRS to documented infection...manifestations are same as SIRS

SEPSIS: DEFINITION

- **Severe Sepsis:** SIRS associated with organ dysfunction, hypoperfusion, or hypotension (acidosis, oliguria, confusion, oxygen dysfunction, etc.)
- **Septic Shock/SIRS Shock :** subset of severe sepsis and defined as induced hypotension despite adequate fluid resuscitation along with perfusion abnormalities: oliguria, acidosis, etc.
- **MODS:** Presence of altered organ function in acutely ill patients....homeostasis cannot be maintained without intervention

PIRO MODEL OF SEPSIS

“TNM-TYPE” FOR POTENTIAL STAGING

- **P**-----Predisposition: Genetics, Chronic illness, Cultural Attitudes
- **I**-----Insult: Infection, Endotoxin, Injury, Ischemia
- **R**-----Response: Physiologic, Specific Mediators, Generic Markers
- **O**-----Organ Dysfunction: Shock, ARDS, etc.

SEPSIS: THE DIFFERENCE BETWEEN MEDICINE AND SURGERY PATIENTS

- Surgical Sepsis vs. Medical Sepsis? **There is a difference!**
- **Medical Sepsis**
 - Present with sepsis
 - Not mechanically ventilated in the beginning

SURGICAL (TRAUMA) SEPSIS

- Already have Cytokine “HIT” from Stress of Trauma or Surgery
- Usually already on Ventilator with Respiratory Weakness if not Failure

SURGICAL SEPSIS

- Possible **Hemodynamic changes** due to 3rd spacing of fluids; invasive hemodynamic monitoring—guiding resuscitation
- Already significant cytokines / inflammation circulating: may be low on the “radar screen” due to prior surgical procedure

CMC EXPERIENCE

POSTER PRESENTATION SCCM 2004

Time from admit to diagnosis: 3 days vs. 8 days

DIC: higher incidence in Medical patients

Bleeding Risk: > 9% vs. 3.5%

SURGICAL SEPSIS

- Sepsis starts later in hospital course — more resistant organisms, etc.
- May already have 1-2 organs “HIT” when sepsis begins (2nd HIT phenomenon)

SURGICAL SEPSIS

INCLUDES TRAUMA PATIENTS

- “smoldering sepsis”—low level vs. profound
- Managed differently: fluids/wounds/etc.
- **Wounds**: another organ dysfunction?

SEPSIS: A COMPLEX DISEASE

- SEPSIS: WHAT IS IT?
 - A disorder of coagulation
- SEPSIS: WHERE DOES IT TAKE PLACE?
 - ENDOTHELIUM:
 - Throughout BODY
 - small ORGAN blood vessels

ENDOTHELIUM:

MOLECULAR LEVEL

- Endothelium is normally anticoagulated by natural APC, etc.
- Sepsis induced decrease in APC allows thrombosis at endothelial level
- Thrombosis allows cell dysfunction and persistent organ perfusion defects

ENDOTHELUM:

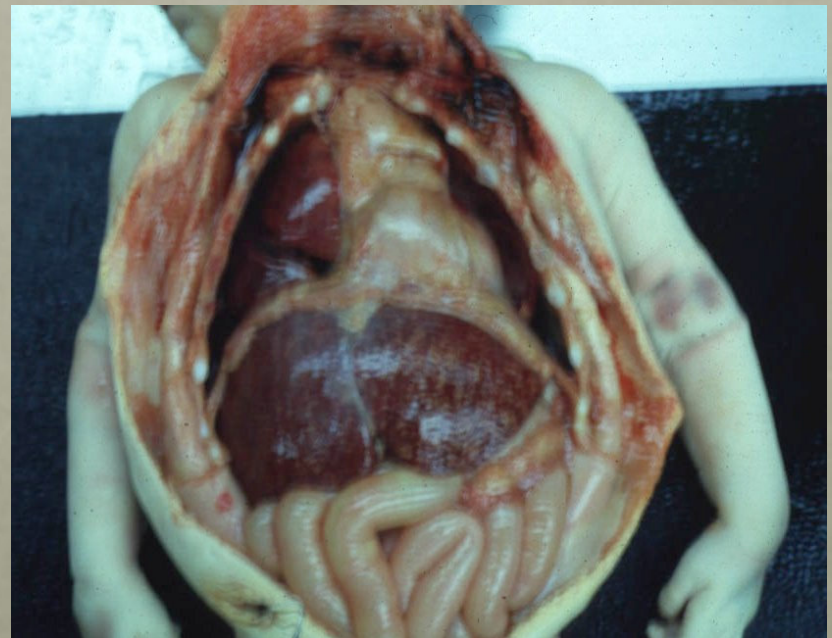
MOLECULAR LEVEL

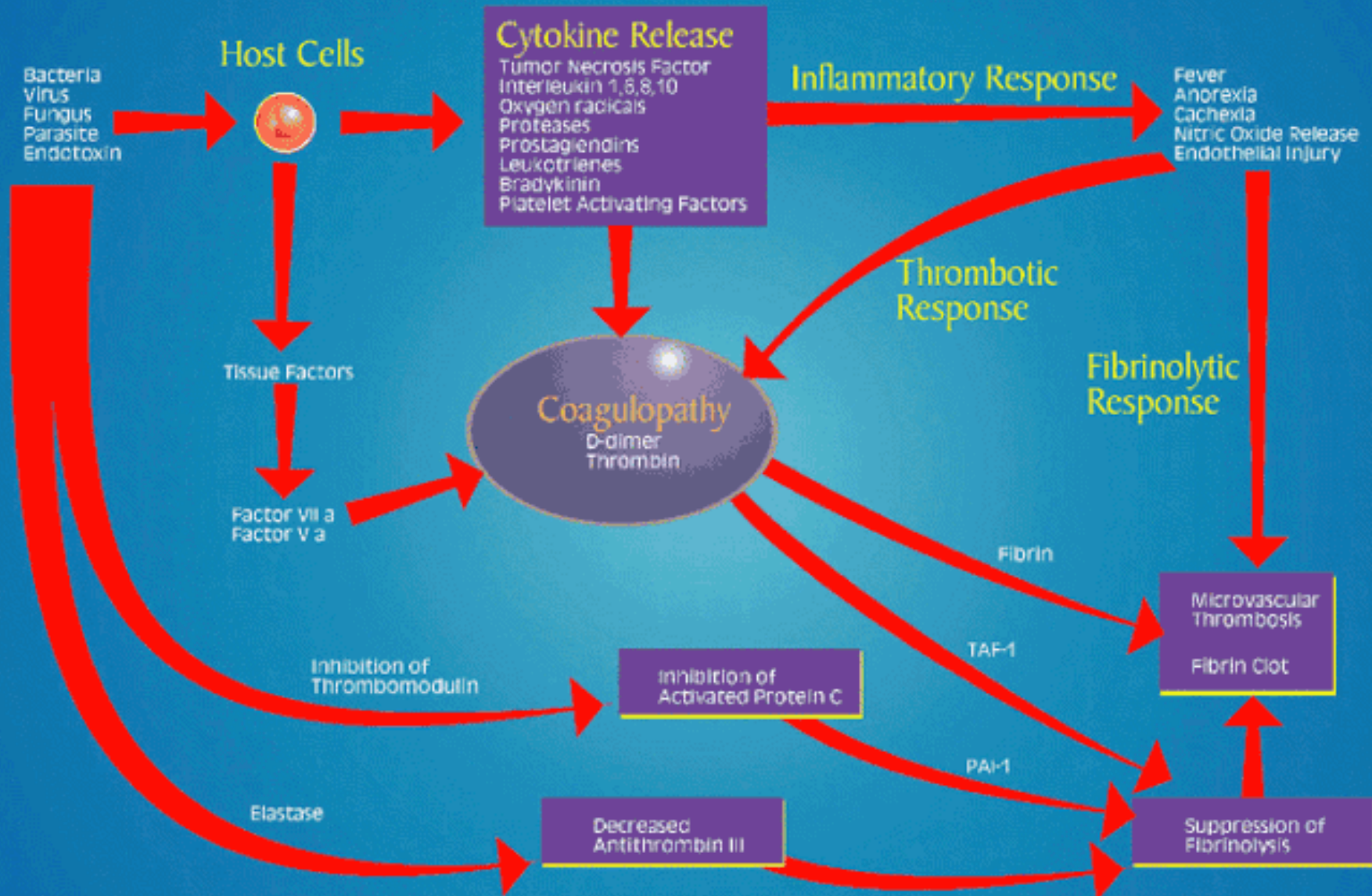
- **Sepsis:**
 - Nuclear factor *kappa*-B
 - Activation occurs early in SIRS, SEPSIS, ALI
- **NF *kappa* B required for transcription of pro-inflammatory mediators**
 - Increases **ICAM**—intracellular adhesion molecule
 - Enzymes: nitric oxide synthase
 - Cytokines IL-1
 - Chemokines IL-8
 - Etc.

SEVERE SEPSIS ENDOTHELIAL DYSFUNCTION

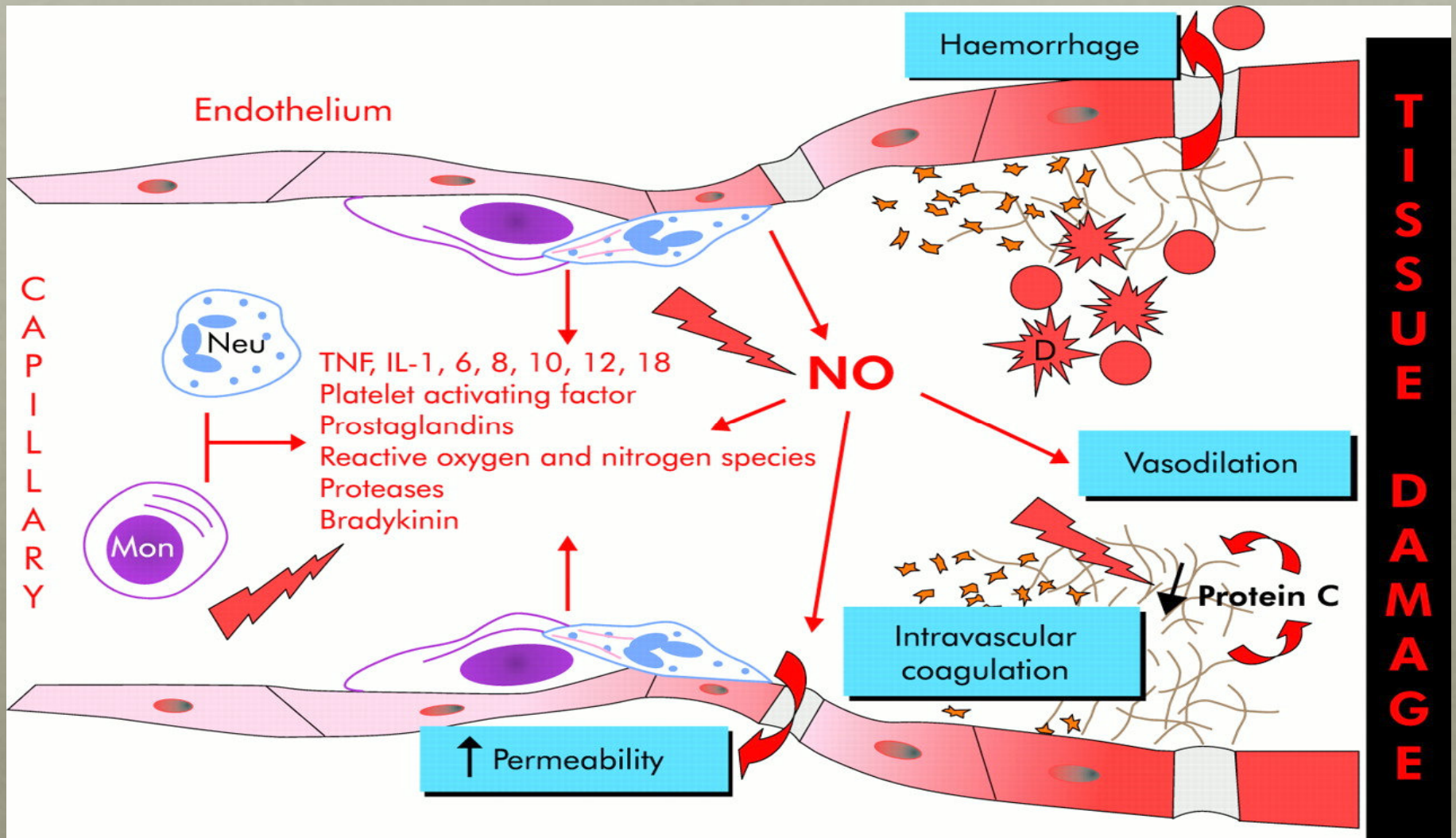


CAN START WITH LINE SEPSIS AND END WITH DEATH

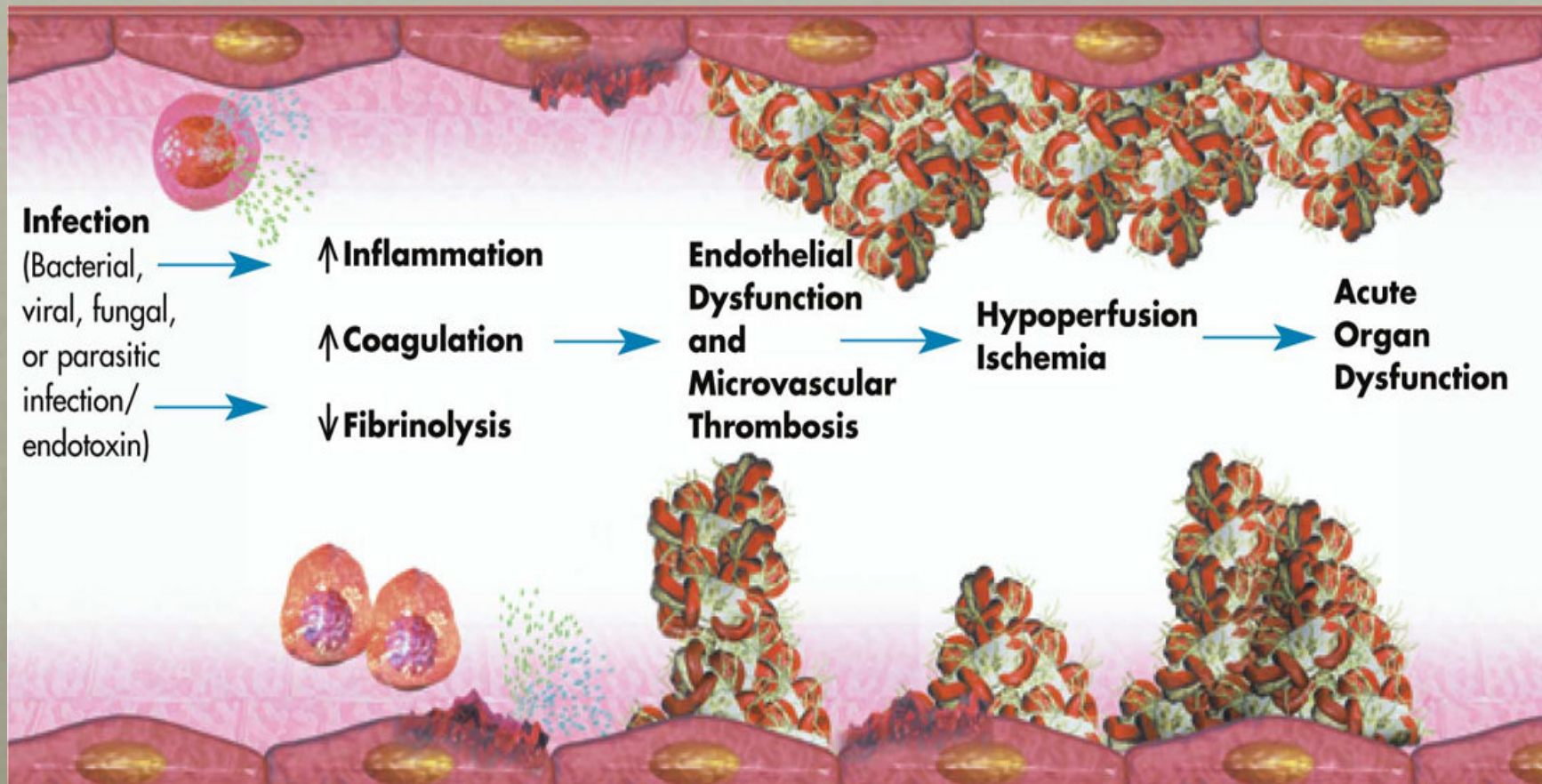




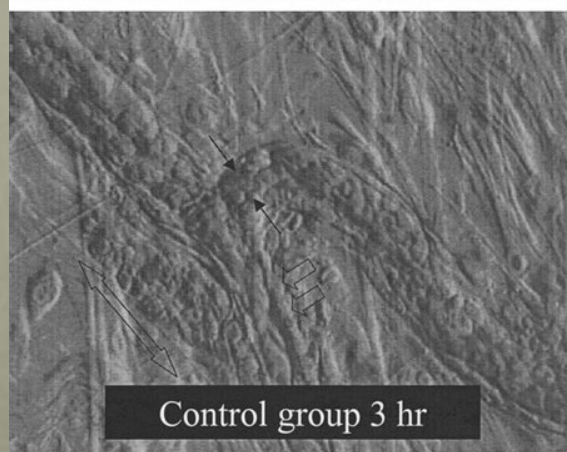
THE ENDOTHELIUM: NOT JUST ANOTHER ORGAN



Pathophysiology of Severe Sepsis

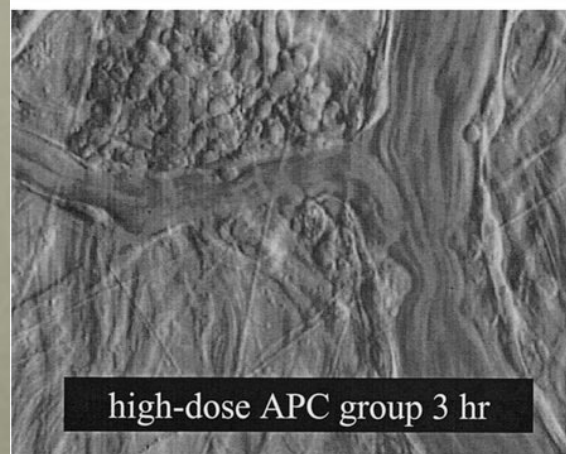
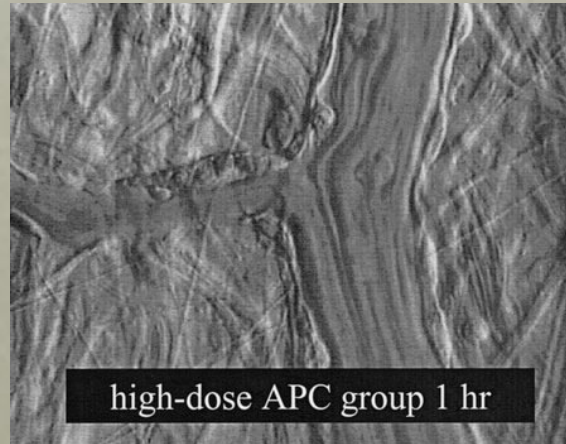


1 HOUR AND 3 HOURS AFTER SEPTIC INSULT IN RAT MODEL— VISCERAL NOT TONGUE

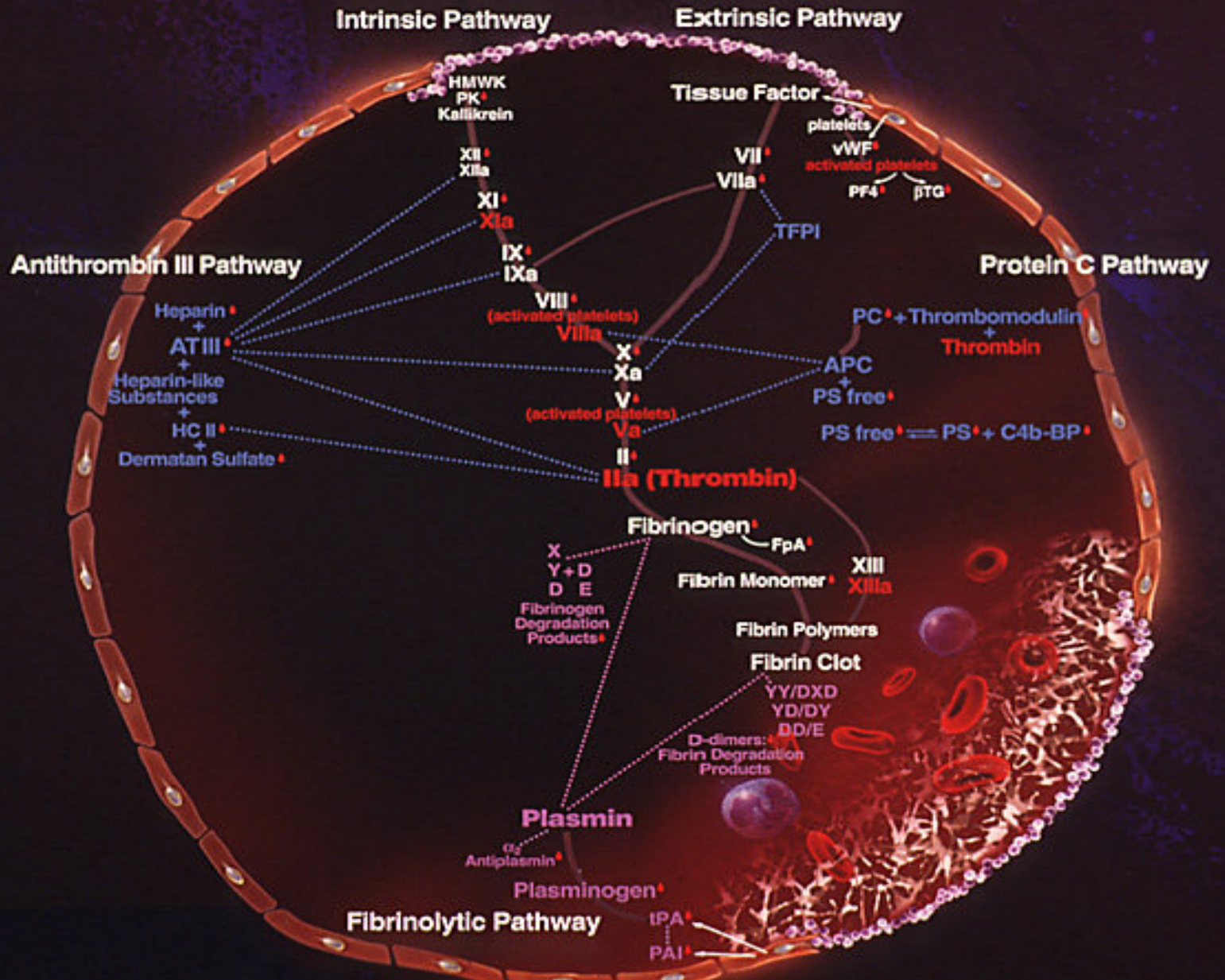


CHANGES IN MICROCIRCULATION WITH APC TREATED ANIMALS

LEUKOCYTE ADHESION WAS SUPPRESSED AT 1 AND 3 HOURS



Coagulation Cascade



BIOCHEMICAL MARKERS OF SEPSIS

RESEARCH AND FUTURE USE

- **Interleukin-6:** elevated in sepsis/ correlates with severity. Higher in infected patients with SIRS
- **C-reactive Protein:** acute phase reactant. Increased after exposure to IL's. diagnostic marker for inflammation.

BIOCHEMICAL MARKERS OF SEPSIS

- **Procalcitonin**: derived from preprohormone preprocalcitonin. Have better predictive value for sepsis than IL-6 or C-reactive protein. Associated with severity of infection and organ dysfunction. Significant amount of research using this as a marker of antibiotic use.....
- **High Mobility Group-B1**: macrophage derived proinflammatory cytokine. Acts through NF-kB mediated mechanism. Participates in activation endothelium in sepsis. Increased in patients dying of severe sepsis!

HEMODYNAMIC MONITORING IN THE PATIENT WITH SEVERE SEPSIS

- Adequacy of tissue perfusion
 - Vital sign trends
 - BP alone is not adequate
 - Surrogate measurements for tissue perfusion
 - Urine output
 - Serum lactate
 - Capillary refill

WHAT IS EARLY DYSFUNCTION?

CLINICAL / LABORATORY TOOLS TO IDENTIFY ORGAN DYSFUNCTION

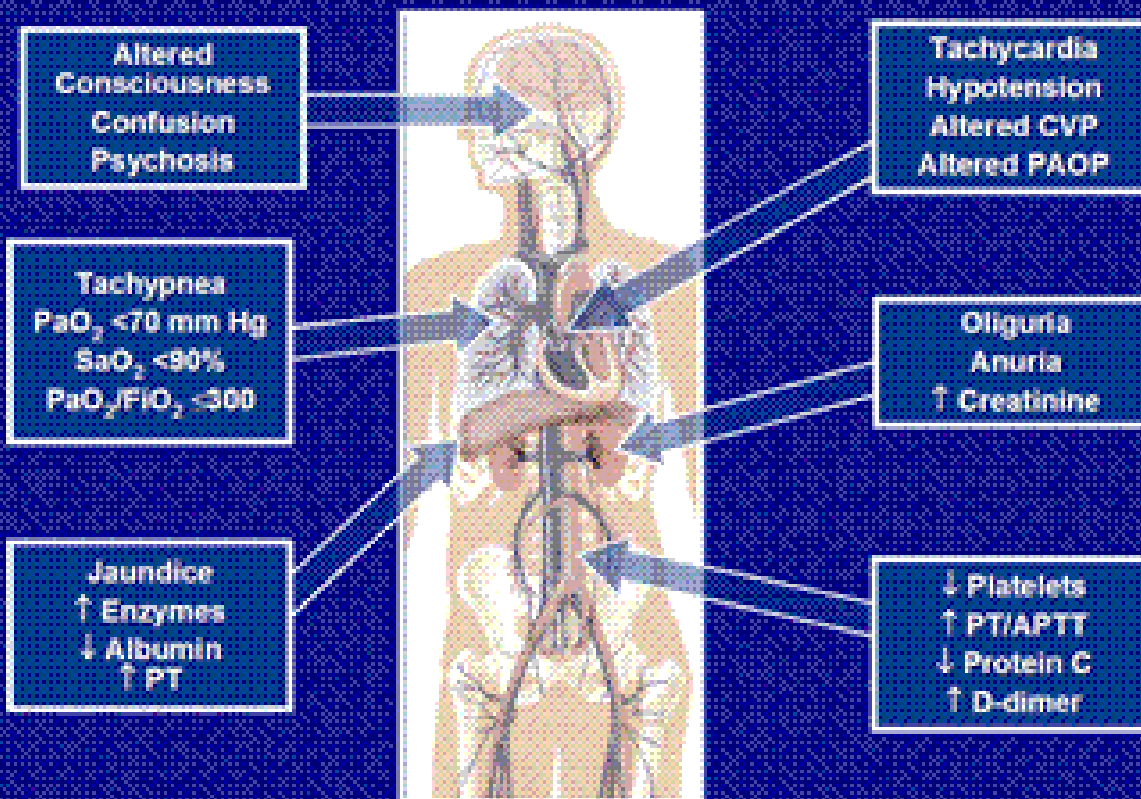
- **Respiratory:** PaO₂ < 70 mmHg (minimal settings), SaO₂ < 90%, PaO₂/FIO₂ < 300
- **Renal:** Increased creatinine, not just anuria
- **Hepatic:** low albumin, increased bilirubin. Not just jaundice
- **Cardiac:** signs of hypoperfusion, not just septic shock
- **Neuro:** altered consciousness (difficult in ventilated patients)
- **Endocrine:** hyperglycemia, low albumin, low cortisol

ORGAN FAILURE

- Average risk of death increases 15% - 20% with failure of each additional organ
- Median – 2 organ failure with associated mortality rate of 30% - 40%
- Changes in renal, neurological and hematologic best correlate to increased mortality

MICRO-VASCULAR CLOTTING

Identifying Acute Organ Dysfunction as a Marker of Severe Sepsis



SEPSIS

- **More than 750,000 cases of sepsis or septic shock in the United States each year**

(3.0 cases/1000 population)

- **215,000 deaths each year (9.3% of all deaths)**
- **Estimated annual increase 1.5% per year**
 - 934,000 in 2010
 - 1,110,000 in 2020
- **Estimated annual cost \$16.7 billion**

SEPSIS PROGNOSIS

- The prognosis in most patients is good, except in those with intra-abdominal or pelvic abscesses due to organ perforation.
- The underlying physiologic condition of the host is the primary determinant of outcome.
- A systematic review by Winters et al suggested that, beyond the standard 28-day in-hospital mortality endpoint, ongoing mortality rates in patients with sepsis remain elevated up to 2 years and beyond. In addition, survivors consistently demonstrate impaired quality of life.

Best Evidence] Winters BD, Eberlein M, Leung J, Needham DM, Pronovost PJ, Sevransky JE. Long-term mortality and quality of life in sepsis: a systematic review. *Crit Care Med.* May 2010;38(5):1276-83.

HOW SHOULD WE APPROACH SEPSIS?

- **Recognize Early**
 - Signs / Organ failure
 - Document!
- **Team Approach**
 - MD, Nursing, PharmD., RespTherapy
 - Sepsis “SWAT TEAM” (Code Sepsis Teams)
- **Organized Management**
 - Guidelines, Standardization
- **Process Improvement**

TEAM APPROACH

- **Organized – 24/7**
 - All patients with infection
 - SIRS
- **Guidelines – ICU management**
 - Early Goal Directed Therapy / resuscitation
 - Antibiotics / antifungals
 - Glucose
 - Blood Transfusion
 - ALI / Ventilator

SURVIVING SEPSIS CAMPAIGN

GUIDELINES FOR MANAGEMENT OF SEVERE SEPSIS AND
SEPTIC SHOCK

CRITICAL CARE MEDICINE 2004/2008

SURVIVING SEPSIS CAMPAIGN-SCCM

HTTP://WWW.SURVIVINGSEPSIS.ORG

GUIDELINES FOR MANAGEMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

Surviving Sepsis Campaign is a voluntary, non-profit organization that provides evidence-based clinical practice guidelines for the management of severe sepsis and septic shock. The guidelines are based on the best available evidence and are intended to be used as a reference for clinical practice. The guidelines are not intended to be used as a substitute for clinical judgment or to replace the role of the clinician. The guidelines are intended to be used as a reference for clinical practice and to provide a framework for the development of local protocols and procedures. The guidelines are intended to be used as a reference for clinical practice and to provide a framework for the development of local protocols and procedures.

Example of recommendations and goals (not written as bullet points) and rationale (written as bullet points):
- **Recommendation:** "Fluid resuscitation should be initiated in patients with severe sepsis and septic shock." (Class I)
- **Goal:** "To improve survival and reduce organ dysfunction." (Class I)
- **Rationale:** "Fluid resuscitation improves survival and reduces organ dysfunction in patients with severe sepsis and septic shock." (Class I)



These guidelines have been endorsed by:
- American College of Chest Physicians
- American College of Surgeons
- American Society of Anesthesiologists
- American Society of Intensive Care Medicine
- American Society of Nephrology
- American Society of Parenteral Science and Technology
- American Society of Perioperative Nurses
- American Society of Trauma Surgeons
- American Society of Transplantation
- American Society of Translational Research
- American Society of Translational Research
- American Society of Translational Research

Initial resuscitation bundle (1 hour):
- Give 30 mL/kg of crystalloid fluids for fluid resuscitation in patients with hypotension or hypoperfusion (Class I)
- Measure lactate (Class I)
- Obtain a blood culture before starting antibiotics (Class I)
- Obtain a prothrombin time (PT) and international normalized ratio (INR) (Class I)
- Obtain a urine output measurement (Class I)

Resuscitation bundle (6 hours):
- If lactate remains elevated, initiate a second 30 mL/kg bolus of crystalloid fluids (Class I)
- If hypotension persists, initiate vasopressor therapy to maintain a mean arterial pressure (MAP) of at least 65 mmHg (Class I)
- If hypoperfusion persists, initiate additional fluid resuscitation (Class I)

Antibiotic therapy:
- Administer antibiotics within 1 hour of recognition of severe sepsis or septic shock (Class I)
- Obtain a blood culture before starting antibiotics (Class I)
- Administer antibiotics based on local antibiogram (Class I)

Source control:
- Identify and control the source of infection (Class I)
- Perform source control within 6 hours of recognition of severe sepsis or septic shock (Class I)

Fluid management:
- Use dynamic parameters to guide fluid resuscitation (Class I)
- Avoid fluid overload (Class I)

Shock therapy:
- Consider vasopressor therapy to maintain a MAP of at least 65 mmHg (Class I)
- Consider inotropic therapy to improve cardiac output (Class I)

Renal replacement therapy:
- Consider renal replacement therapy in patients with acute kidney injury (AKI) (Class I)

Transfusion:
- Transfuse red blood cells to maintain a hemoglobin of at least 7 g/dL (Class I)

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SURVIVING SEPSIS CAMPAIGN

- An international (11 CC organizations) effort to increase the awareness and improve outcome in severe sepsis.
 - Increase, awareness, understanding and knowledge
 - Change perceptions and behaviors
 - Increase the pace of change in patterns of care
 - Influence public policy
 - Define standards of care in severe sepsis
 - Reduce mortality associated with sepsis by 25% in 5 years

EARLY!!!!!!!!!!!!

- Education surrounds early diagnosis
- Early antibiotic treatment
- Early and aggressive fluid resuscitation
- Early DVT and ulcer treatment prophylaxis
- Early administration of Xigris
- **STANDARDIZE!**

SURVIVING SEPSIS CAMPAIGN GUIDELINES

“(Sepsis) Similar to an acute myocardial ischemic attack and an acute brain attack, the speed and appropriateness of therapy administered in the initial hours after the syndrome develops likely influence outcome”

Dellinger

SURVIVING SEPSIS CAMPAIGN

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SURVIVING SEPSIS CAMPAIGN

- Phase I: Initiated October 2002 with the Barcelona Declaration to improve survival in severe sepsis
- Phase II: A group of critical care and infectious disease experts in the diagnosis and management of infection and sepsis, representing 11 organizations, produced these guidelines for the bedside clinician.
 - No industry input
- Phase III: Targets to implement a core set of the following recommendations in hospitals where change in behavior and clinical impact can be measured

Table 1. Grading system

Grading of recommendations

- A. Supported by at least two level I investigations
- B. Supported by one level I investigation
- C. Supported by level II investigations only
- D. Supported by at least one level III investigation
- E. Supported by level IV or V evidence

Grading of evidence

- I. Large, randomized trials with clear-cut results; low risk of false-positive (alpha) and/or false-negative (beta) error
 - II. Small, randomized trials with uncertain results; moderate-to-high risk of false-positive (alpha) and/or false-negative (beta) error
 - III. Nonrandomized, contemporaneous controls
 - IV. Nonrandomized, historical controls and expert opinion
 - V. Case series, uncontrolled studies, and expert opinion
-

Table 1. Grading system

From: Dellinger: Crit Care Med, Volume 32(3), March 2004, 858-873

INITIAL RESUSCITATION

- Goal of 1st 6 hours to resuscitate sepsis induced hypoperfusion (Early Goal-directed Therapy)
 - CVP 8-12 mm Hg (12-15 if mechanically ventilated)
 - MAP \geq 65 mm Hg
 - UOP \geq 0.5 ml/kg/hour
 - Central venous or mixed venous oxygenation saturation \geq 70%
 - Institute for Healthcare Improvement's 6 hour and 24 hour sepsis bundles!

INITIAL RESUSCITATION

- During 1st 6 hours:
 - If adequate CVP obtained,
 - and central venous or mixed venous oxygenation saturation $\geq 70\%$
 - Then transfuse pRBC's to achieve HCT $\geq 30\%$
 - and/or administer dobutamine infusion

B

DIAGNOSIS

- **Appropriate cultures**
 - At least 2 blood cultures
 - 1 percutaneous and one each vascular access device (unless inserted < 48 hrs ago)
- **Appropriate diagnostic studies promptly if patient stable**

D

E

ANTIBIOTIC THERAPY

- Started within 1st hour of recognition of sepsis, after appropriate cultures **E**
- Establishing a supply of premixed antibiotics in ER or Critical Care unit for such urgent situations is an appropriate strategy to increase likelihood of prompt administration **D**
- Broad enough to cover all likely pathogens
 - Inappropriate antibiotic choice associated with adverse outcome **D**

McCabe et al. Arch Intern Med 1962;110:92-100

Kreger et al. Am J Med 1980;62:344-55

Leibvici et al. J Intern Med 1998;244:379-86

Ibrahim et al. Chest 2000;118:146-55

ANTIBIOTIC THERAPY

- Reassess after 48-72 hours on the basis of clinical and microbiologic data with aim of using a narrow spectrum antibiotic to:
 - Prevent development of resistance
 - Reduce toxicity
 - Reduce cost

- Stop antibiotics if clinical syndrome determined to be non-infectious

E

E

SOURCE CONTROL

- As soon as possible after initial resuscitation
 - Drain abscess
 - Debride necrotic tissue
 - Remove potentially infected devices
 - Removal and replacement of vascular access devices should be a priority – even if tunneled or surgically implanted

E

FLUID THERAPY

- May use colloids or crystalloids
 - No evidence to support one over another

C

- Fluid challenge in suspected hypovolemia
 - 500-1000 ml crystalloid or
 - 300-500 ml colloid
 - Give over 30 minutes

E

VASOPRESSORS

- When appropriate fluid challenge fails to restore adequate BP and organ perfusion vasopressors should be started E
- First choice of vasopressor should be norepinephrine or dopamine D
 - Epi – potential tachycardia, affects splanchnic circulation
 - Phenyephine - least likely to ↑ HR, decreases stroke volume
 - DA - particularly useful with compromised systolic function, causes more tachycardia than norepi, may be more arrhythmogenic

MECHANICAL VENTILATION OF SEPSIS-INDUCED ACUTE LUNG INJURY (ALI)/ARDS

- High tidal volumes that are coupled with high plateau pressures should be avoided in ALI/ARDS
 - Low tidal volume - 6 ml/kg of predicted body weight
 - Maintain end-inspiratory pressure < 30 cm H₂O
 - Largest trial using volume and pressure limited strategy showed a 9% reduction in all cause mortality

Amato et al. N Engl J Med 1998;338:347-54

Stewart et al. N Engl J Med 1998;338:355-61

Brochard et al. AM J Respir Crit Care Med 1998;158:1831-38

Brower et al. Crit Care Med 1999;27:1492-98

Eichacker et al. AM J Respir Crit Care Med 2002;166:1510-14

The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000;342:1301-8

B

MECHANICAL VENTILATION OF SEPSIS-INDUCED ACUTE LUNG INJURY (ALI)/ARDS

- **Permissive hypercapnia can be tolerated if required to minimize plateau pressures and tidal volumes**
 - Contraindicated in patients with increased ICP
 - Limited to patients with pre existing metabolic acidosis

C

- **Weaning protocols should be in place**
 - Reduce duration of mechanical ventilation
 - Sedation Vacations!!!

A

Hickling et al. Crit Care Med 1994;22:1568-78

Bidani et al. JAMA 272:957-62

The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000;342:1301-8

Esteban et al. Am J Respir Crit Care 1999;159:512-8

Ely et al. N Engl J Med 1996;335:1864-9

Esteban et al. Am J Respir Crit Care Med 1997;156:459-65

MECHANICAL VENTILATION OF SEPSIS-INDUCED ACUTE LUNG INJURY (ALI)/ARDS

- A minimum amount of PEEP should be set to prevent lung collapse at end-expiration
 - Setting PEEP based on severity of oxygenation deficit and guided by the FIO_2 required to maintain adequate oxygenation is one acceptable approach
 - Titrate PEEP according to bedside monitoring of thoracopulmonary compliance
- Unless contraindicated, mechanically ventilated patients should be in semirecumbant position with HOB at 45°

C

MECHANICAL VENTILATION OF SEPSIS-INDUCED ACUTE LUNG INJURY (ALI)/ARDS

- In facilities with experience, prone positioning should be considered (more on this tomorrow)
 - A majority of patients with ALI/ARDS have improved oxygenation in the prone position
 - May only benefit patients with the most severe hypoxemia
 - Prone positioning may associated with life-threatening complications

Stocker et al. Chest 1997;111:1008-17

Lamm et al. Crit Care Med 1994;150:184-93

Jolliet et al. Crit Care Med 1998;26:1977-85

Gattinoni et al. N Engl J Med 2001;345:568-73

Chatte et al. Am J Respir Crit Care Med 1997;155:473-8

SEDATION, ANALGESIA AND NEUROMUSCULAR BLOCKADE IN SEPSIS

- Sedation protocols when sedation is required
 - Sedation goal measured by a standardized subjective sedation scale
- Daily interruption or lightening of continuous sedation with awakening and retitration if needed

B

B

Kollef et al. Chest 1998;114:541-8

Kress et al. N Engl J Med 2000;342:1471-7

Brook et al. Crit Care Med 1999;27:2609-15

SEDATION, ANALGESIA AND NEUROMUSCULAR BLOCKADE IN SEPSIS

- Neuromuscular blockade should be avoided if possible
 - Risk of prolonged neuromuscular blockade following discontinuation
 - If needed beyond 1st few hours of mechanical ventilation either
 - Bolus intermittantly as needed
 - Continuous infusion with train of four to monitor depth of blockade

VASOPRESSORS

- All Patients on vasopressors should have an arterial catheter as soon as practical E

- Low dose dopamine should not be used for renal protection B
 - No difference in primary outcomes
 - Peak serum CR, UOP, Hemodialysis, time to renal recovery
 - No difference in secondary outcomes
 - Survival to ICU or hospital discharge, length of ICU or hospital stay, arrhythmias

Bellarmo et al. Australian and New Zealand Intensive Care Society (ANZICS)
Clinical Trials Group. Lancet 2000;356:2139-43
Kellum J, Decker J. Crit Care Med 2001;29:1526-31

VASOPRESSORS

- Consider **low dose vasopressin** for refractory shock despite adequate fluid and high dose vasopressors
 - Not recommended as a replacement for Norepinephrine or Dopamine
 - 0.01-0.04 units/min
 - Doses > 0.04 associated with myocardial ischemia, significant ↓ C.O. and Cardiac arrest
 - Do not use if cardiac index < 2L/min/m²

INOTROPIC THERAPY

- Dobutamine may be used to increase C.O. in pts w/low C.O. despite adequate fluid resuscitation E
 - Dobutamine is 1st choice inotrope

- Increasing cardiac index to achieve an arbitrarily predefined elevated level is not recommended A

Gattinoni et al. N Engl J Med 1995;333:1025-32

Hayes et al. N Engl J Med 1994;330:1717-22

STEROIDS

- Corticosteroids equivalent to 200-300 mg/day of hydrocortisone for 7 days in patients requiring vasopressors C
 - 1 multi-center RCT showed significant shock reversal and a reduction in mortality rate
 - 2 additional smaller RCTs showed significant effect on shock reversal
- Steroids should not be used in the treatment of sepsis without shock E

Annane et al. JAMA 2002;288:862-71

Breigel et al. Crit Care Med 1999;27:723-32

Bollaert et al. Crit Care Med 1998;26:645-50

STEROIDS

- Doses > 300 mg/day should not be used for the purpose of treating septic shock A
 - 2 randomized prospective clinical trials and 2 meta-analysis conclude high-dose corticosteroids to be ineffective or harmful

- Some experts would suggest:
 - ACTH stimulation test could be used to identify responders but steroids should not be held pending results E
 - Decrease dosage after resolution of septic shock
 - Taper steroids at the end of therapy
 - Add 50 micrograms fludrocortisone QID

Bone et al. N Engl J Med 1987;317:635-8.

Cronin et al. Crit Care Med 1995;23:1430-39.

The V.A. Systemic Sepsis Cooperative Group: N Engl J Med 1987;317:659-65.

Bernard et al. N Engl J Med 2001;344:699-709.

RECOMBINANT HUMAN ACTIVATED PROTEIN C

- **Recommended in patient's w/high risk of death**
 - APACHE II score > 25
 - Sepsis-induced multiple organ failure
 - Sepsis-induced ARDS
 - Best determined by bedside clinical evaluation and judgement
- **Unless**
 - Absolute contraindication related to bleeding
 - Relative contraindication that outweighs potential benefit

B

ABSOLUTE CONTRAINDICATIONS

- Active internal bleeding
- Recent (within 3 months) hemorrhagic stroke
- Recent (within 2 months) intracranial or intraspinal surgery or severe head trauma
- Trauma with an increased risk of life-threatening bleeding
- Presence of an epidural catheter
- Intracranial neoplasm or mass lesion or evidence of cerebral herniation
- FDA Clinical review

WARNINGS

- Concurrent therapeutic heparin (> 15 units/kg/hr)
- Platelet count < 30,000 x 10⁹/L, even if the platelet count is increased after transfusions
- Prothrombin time -INR>3.0
- Recent (within 6 weeks) gastrointestinal bleeding
- Recent (within 3 days) thrombolytic therapy
- Recent administration (within 7 days) of oral anticoagulants or glycoprotein IIb/IIIa inhibitors
- Recent administration (within 7 days) of aspirin >650 mg per day or other platelet inhibitors
- Recent (within 3 months) ischemic stroke (see CONTRAINDICATIONS)
- Intracranial arteriovenous malformation or aneurysm
- Known bleeding diathesis
- Chronic severe hepatic disease
- Any other condition in which bleeding constitutes a significant hazard or would be particularly difficult to manage because of its location.
- FDA Clinical review

RECOMBINANT HUMAN ACTIVATED PROTEIN C

- Once a patient has been identified as at high risk of death, treatment with rhAPC should begin as soon as possible
 - Given the uncertainty of risk assessment and the potential for rapid deterioration
 - The inflammatory response in severe sepsis is integrally linked to procoagulation and endothelial activation
 - rhAPC is an endogenous anticoagulant with anti-inflammatory properties

BLOOD PRODUCT ADMINISTRATION

- Transfuse only for Hgb < 7.0 g/dL, except:
 - CAD
 - Acute hemorrhage
 - Initial resuscitation recommendations **B**
- Erythropoietin not recommended as a specific treatment for sepsis related anemia **B**
- **Thromboelastograph (TEG)**

Transfusions Requirements in Critical Care Trial
Corwin et al. Crit Care med 1999; 27:2346-50
Corwin et al. JAMA 2002;288:2827-35

BLOOD PRODUCT ADMINISTRATION

- **Antithrombin is not recommended**
 - No improvement in 28 day outcome
 - Increased risk of bleeding when administered with heparin

B

- **Platelet transfusions**
 - $< 5000/\text{mm}^3$ regardless of apparent bleeding
 - $5000-30,000/\text{mm}^3$ and significant risk for bleeding
 - $\geq 50,000$ typically required for surgery or invasive procedures

E

GLUCOSE CONTROL

- **Maintain Blood Glucose \leq 150 mg/dL**

D

- **Glycemic control should include a nutrition protocol with preferential use of the enteral route**

E

Van den Berghe et al. N Engl J Med 2001;345:1359-67

Finney et al. JAMA 2003;290:47-57

Van den Berghe et al. Crit Care Med 2003;31:359-66

Klein et al. Am J Clin Nutr 1997;66:683-706

RENAL REPLACEMENT/BICARBONATE THERAPY

- **In Acute Renal Failure**
 - In hemodynamically stable patients continuous venovenous hemofiltration and intermittent hemodialysis are considered equivalent
 - In hemodynamically unstable patients continuous hemofiltration offers easier management of fluid balance

B

- **NaHCO₂ not recommended for PH ≥ 7.15**

C

Mehta et al. *Kidney Int* 2001;60:1154-63

Kellum et al. *Intensive Care Med* 2002;28:29-37

Cooper et al. *Ann Intern Med* 1990;112:492-8

Mathieu et al. *Crit Care Med* 1991;19:1352-6

DVT PROPHYLAXIS

- Low-dose unfractionated heparin or low-molecular weight heparin
- Mechanical prophylactic device if heparin contraindicated
- Use a combination in high-risk patients **A**
 - Severe sepsis
 - History of DVT

Cade et al. Crit Care Med 1982;10:448-50

Belch et al. Scott Med J 1981;26:115-17

Samama et al. N Engl J Med 1999;341:793-800

STRESS ULCER PROPHYLAXIS

- Should be given to all patients with severe sepsis
 - H2 receptor inhibitors more efficacious than sucralfate
 - PPI's not directly compared to H2 receptors
 - PPI's equivalent increase in gastric PH

A

Borrero et al. Am J Med 1985;79:62-4
Bresalier et al. Am J Med 1987;83:110-6
Cook et al. N Engl J Med 1998;338:791-7
Stoohert et al. Ann Surg 1980;192:169-74

CONSIDERATION FOR LIMITATION OF SUPPORT

- Advance care planning including the communication of likely outcomes and realistic goals of treatment should be discussed with patients and families
- Decisions for less aggressive support may be in the patient's best interest

E

TREATING SEPSIS

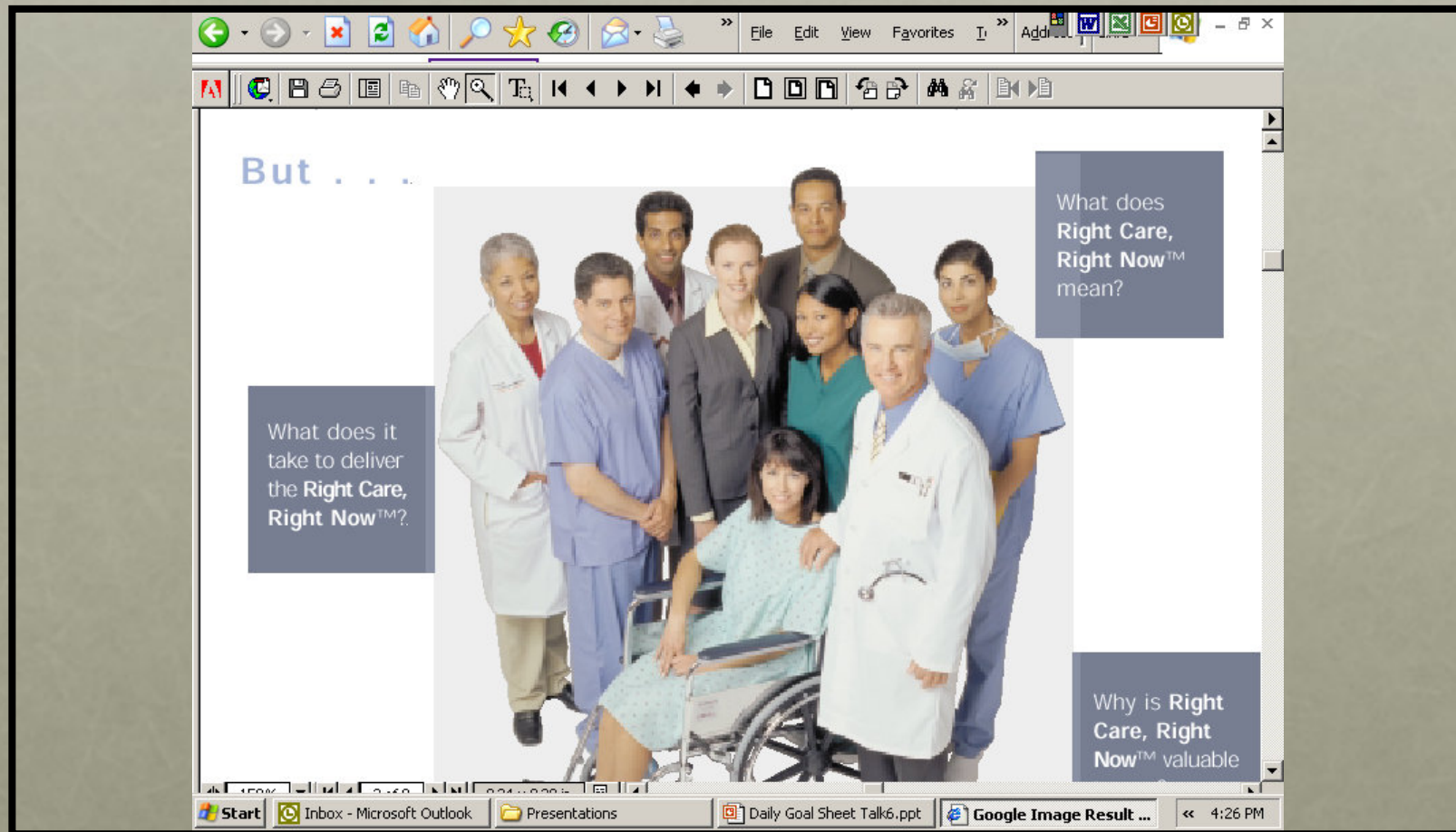
- Use the Guidelines
- Be a part of the development of the guidelines at your hospital system
- **EDUCATE Everyone on their use!!!**

OLD AND NEW THERAPY

NEW IDEAS FROM OLD THERAPY

- PREVENTION!!!
- Source control
- Better Diagnostic Modalities and Less invasive drainage techniques
- Tighter glucose control
- Choice/timing/type/appropriate use of antibiotics
- Early goal directed therapy
- EPO/Factor 7/Blood conservation techniques to decrease blood transfusions
- New Ventilator management strategies:
 - Reduce Ventilator Induced Injury
 - High Frequency Oscillatory Ventilation
- Activated Protein-C (XIGRIS)

SCCM 2005 CATCHPHRASE: “RIGHT CARE, RIGHT NOW”



THE 1999 INSTITUTE OF MEDICINE REPORT *“TO ERR IS HUMAN: BUILDING A SAFER HEALTH SYSTEM”*

- **44-98K** hospital mortalities each year are 2° to *medical errors*

- Medical Errors would be the **8th** leading cause of death!!

- Loss of trust
- Loss of life
- Loss of morale
- Loss of \$\$\$

Cause of death (Based on the International Classification of Diseases, Tenth Revision, 1992)	Rank ¹	Deaths
All causes	2,102,589
Diseases of heart(I00-I09,I11,I13,I20-I51)	1	606,876
Malignant neoplasms(C00-C97)	2	482,481
Cerebrovascular diseases(I60-I69)	3	139,719
Chronic lower respiratory diseases(J40-J47)	4	115,395
Accidents (unintentional injuries)(V01-X59,Y85-Y86)	5	90,866
Diabetes mellitus(E10-E14)	6	58,459
Influenza and pneumonia(J10-J18)	7	58,346
Alzheimer's disease(G30)	8	55,058
Nephritis, nephrotic syndrome and nephrosis(N00-N07,N17-N19,N25-N27)	9	32,615
Intentional self-harm (suicide)(*U03,X60-X84,Y87.0)	10	28,731
Septicemia(A40-A41)	11	27,110
Chronic liver disease and cirrhosis(K70,K73-K74)	12	23,809

The 'cycle of inaction' must be broken

Kohn, IOM Report 1999

MISTAKES OF COMMISSION

- Study combining self-reports and direct observations found 1.7 errors per patient per day in the ICU
- Healthcare errors called “a national problem of epidemic proportions”

Vincent, BMJ '98

Quality Interagency
Coordination Task Force, 2000

INFAMOUS MISTAKES OF COMMISSION



Jessica Santillan was give an ABO-incompatible heart-lung transplant



Surgical instruments washed in hydraulic fluid (rather than detergent)

THE OPRAH WINFREY SHOW (10/03): “OUTRAGEOUS MEDICAL MISTAKES”



Linda McDougal underwent unnecessary double mastectomies after her breast biopsies were mislabeled by the pathologist



While in his last year of medical school, Paul Barach was asked to perform procedure he'd never done before. His mentor was called away, and the young student made a mistake that led to complications that cost a woman her life. "I shouldn't have been doing that procedure, certainly not by myself."

Mistakes of Commission:

100,000 LIVES CAMPAIGN

Diagnosis: Mistakes. Cure: Higher standards.

Program may help cut hospitals' death rate

BY LINDA A. JOHNSON
Associated Press

For 13 straight months at Newark Beth Israel Medical Center, not one patient on a ventilator has developed pneumonia.

Not impressed? You should be.

Typically, there is a case of pneumonia every week among ventilator patients at busy ICUs, and up to 40 percent of these patients die.

The Newark, N.J., hospital is among hundreds nationwide that are drastically curbing in-

house infections. Stung by repeated reports that hospitals make preventable mistakes that kill tens of thousands of patients each year, hospitals are ratcheting up efforts to improve care.

"There are people walking around their communities that wouldn't have seen their daughter's graduation, that wouldn't have seen their next birthday" but for these efforts, said Dr. Thomas Rainey, chairman of the ICU care project at the Institute for Healthcare Improvement.

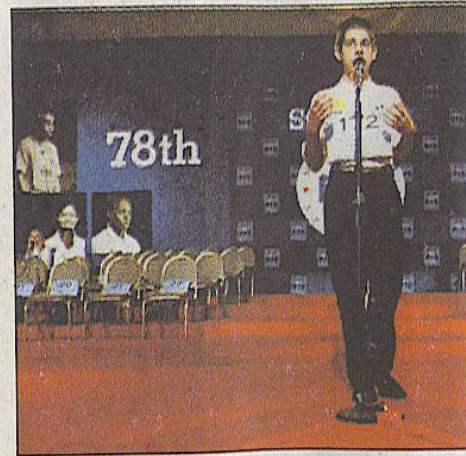
The not-for-profit Cambridge, Mass.-based institute, which was

SEE HOSPITALS | 12A

LIST INSIDE

12A | Carolina participants

BEE ENDS



CHUCK KENNEDY - K

Marshall Winchester, 13, of Mineral Springs co-national spelling bee Thursday in Washington, last year of eligibility, tied for fifth.

Jury may get case today

16A | Prosecution, defense give starkly different portrayals of pop star Michael Jackson in closing arguments



Deadly day in Iraq

5A | At least 38 people die in a series of car bombs and ambushes across the country

More

High: 7.
afterno
Areas 0

MISTAKES OF OMISSION

The Quality of Adult Healthcare Today:

- The average patient only receives ~50% of the therapies they should

MISTAKES OF OMISSION

	% NOT Receiving Rx	Preventable Deaths
Pronovost, JAMA '02	76%	135K
Bernard, NEJM '01	89%	10K
Annane, JAMA '02	50%	5K
Van den Berghe, NEJM '01	75%	12K
ARDSNet, NEJM '00	70%	5K
	~167K Total Lives Lost	

Pronovost, Journal of Crit Care '04

BAD PEOPLE OR BAD SYSTEMS?

“Bad systems, not bad people, lead to the majority of errors and injuries...”

Safety Improvement: Fix the system, not the workers

Leape, JAMA 2005

IN NEED OF BETTER COMMUNICATION

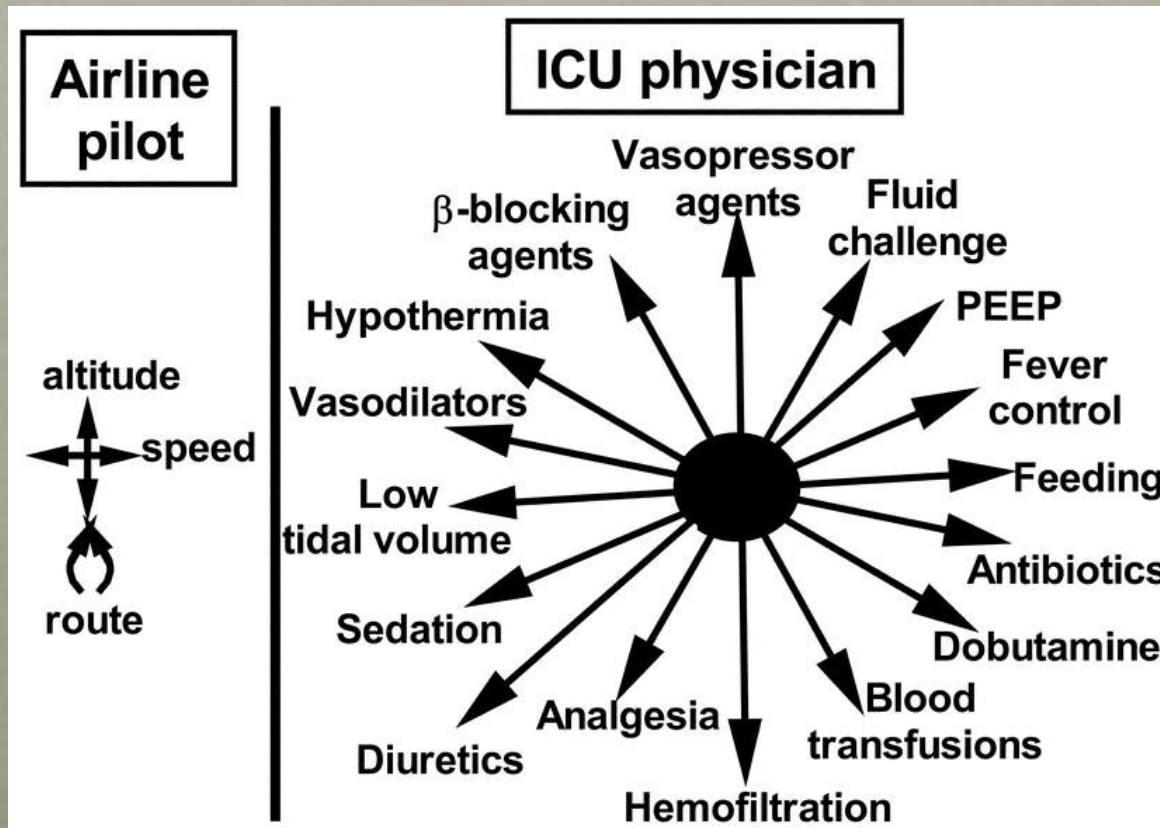


DAILY GOAL SHEET -- BUNDLES

- What is a ‘Bundle’??
 - “Group of interventions related to a disease that when instituted together give better outcomes than when done individually”
- Rules:
 - Each component is scientifically solid
 - Use of each component is a Yes/No
 - Bundle is for a frequently occurring issue

DAILY GOAL SHEET – REDUNDANCY

The ICU patient is *complicated and dynamic*.

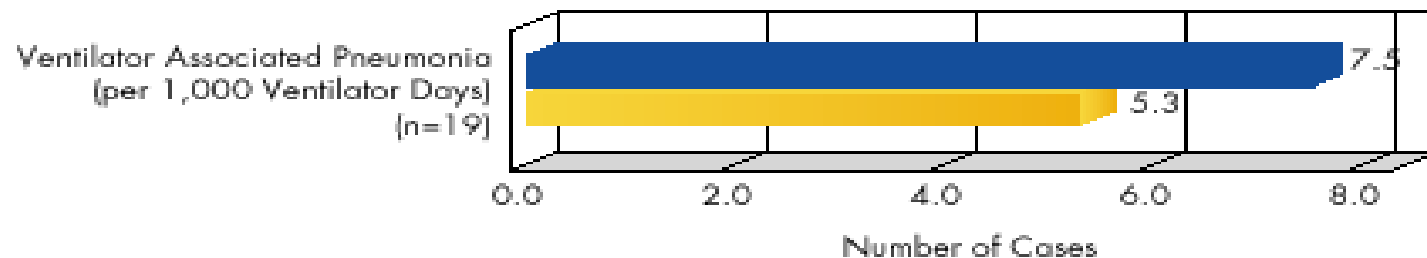
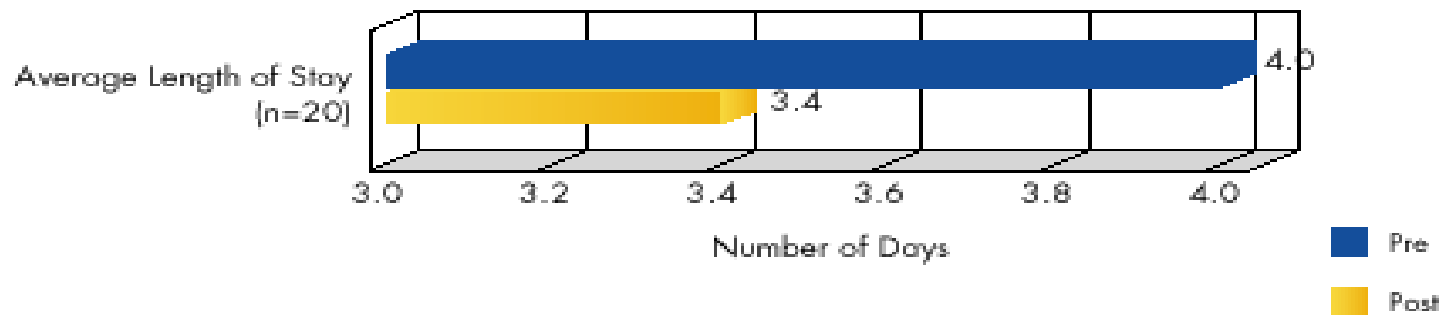


DAILY GOAL SHEET -- BUNDLES

- **Ventilator Bundle (John Hopkins):**

- Head of Bed > 30° Drakulovic, Lancet 1999
- GI Prophylaxis Cook, NEJM 1998
- DVT Prophylaxis Attia, Arch Int Med 2001
- [Glc] Control Van den Berghe, NEJM '01
- Sedation Holidays Kress, NEJM 2000
- Vent Weaning Ely, NEJM 2003

DAILY GOAL SHEETS – BUNDLES



Daily Goal Sheets – Bundles

Advances in Medicine: New methods curb hospital infections

Hospitals using simple steps, like stronger skin disinfectant, to save lives, lower health care costs.

By Linda A. Johnson

Associated Press

Trenton, N.J. — For 13 straight months at Newark Beth Israel Medical Center, not one patient on a ventilator has developed pneumonia.

Not impressed? You should be.

Typically there is a case of pneumonia every week among ventilator patients at busy ICUs, and up to 40 percent of these patients die.



Ginaloy Loa, a nurse at Newark Beth Israel Medical Center in New Jersey, checks supplies into a crash cart, used when patients are given catheters. The center is using simple steps to lower infection rates.

Associated Press, 6/14/05

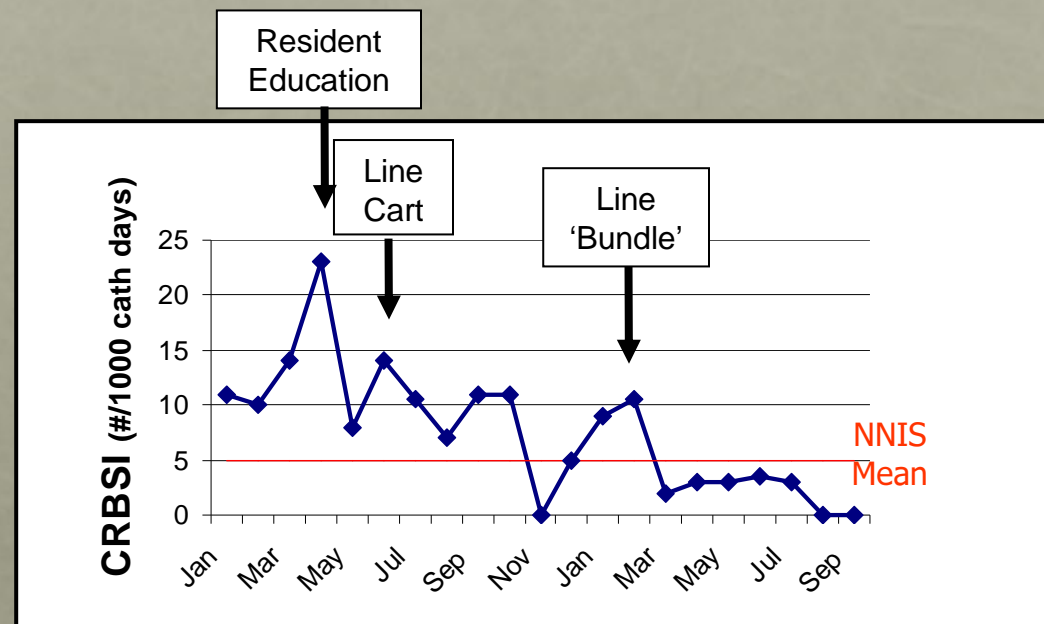
DAILY GOAL SHEET -- BUNDLES

- **Central Line Insertion Bundle (Checklist)**

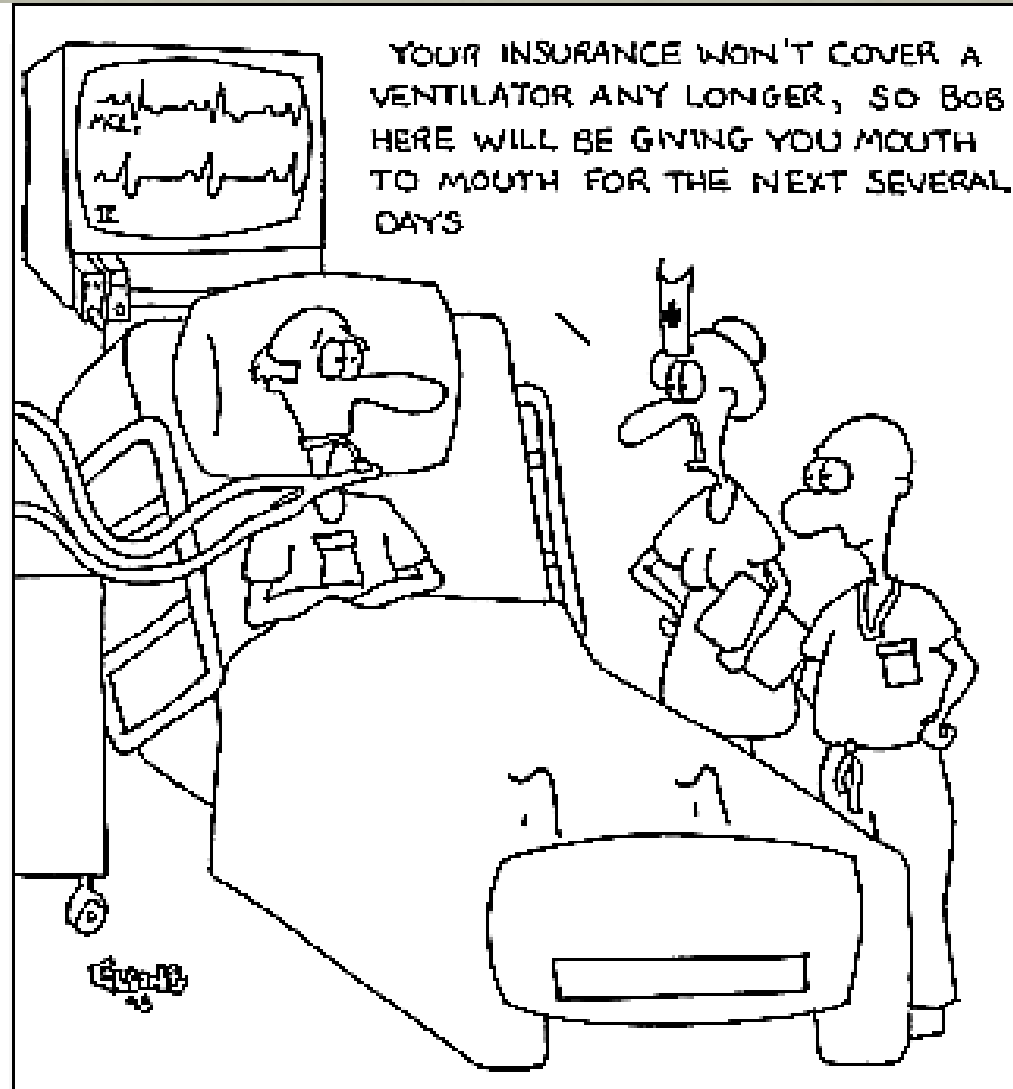
- Full Barrier Precautions
- Chlorhexidine Skin Prep
- Avoid Femoral Lines
- Use of Ultrasound

- **Sepsis Bundles**

- MUST Protocol
- ABC's of sepsis



ALTERNATIVE VENT BUNDLE



WHAT DOES A DAILY GOAL SHEET LOOK LIKE??

Whatever you want it to...

ICU PATIENT DAILY GOAL SHEET

Date _____

M.R. # _____

Today's Goals (multidisciplinary)

1. Ventilator Goal _____

2. Vasopressor Goal _____

3. Sedation Goal _____

4. Procedures/Tests Planned: _____

Other Goals/Plans: _____



Is the patient stable enough for a lower level of care? _____

	AM			If no, provide interventions	PM		
	No	Yes	NA		No	Yes	NA
HOB > 30 degrees							
DVT Prophylaxis							
PUD Prophylaxis							
Glucose < 130							
Daily Interruption of Sedation							
Nutritional Support Initiated and at goal							
Appropriate Level of Sedation							
Appropriate Level of Pain Control							
Appropriate Bed Rotation							
Ventilator Weaning Initiated							
Central Catheters/Drainage Tubes Necessary							
Bowels Regular							
Volume Status Appropriate							
Able to Change to PO/ Restart Home Meds							
Family Updated							

DAILY GOAL SHEET -- BUNDLES

- **Bottom Line:**

- Bundling Order Sets can ensure standard-of-care practices for every patient
- Bundling Order Sets can improve outcomes
- Incorporating Bundles into a Daily Checklist or Goal Sheet may help Bundle Compliance

MECHANICAL VENTILATION

- **Conventional Mech Ventilation**
 - High PEEP / Low PEEP
 - FI02 – oxygen toxicity
 - Stimulates Alveolar neutrophil activation
 - Increases cytokine release
 - Increases ALI
- **Low volume ventilation (6 cc/Kg)**
 - Reduces morbidity and mortality

DAILY GOAL SHEET -- COMMUNICATION

- Written words bring *accountability*:
 - RN has daily plan at the bedside constantly
 - RT has outline of expectations for the day
 - “Multidisciplinary” components involved
 - Nutritionist
 - Therapists
 - Social Work/Case Manager, ...
- Gives Family information for the day

WHAT ELSE CAN WE DO IN THE ICU?

EVIDENCE BASE FOR NEWER MODES OF MECHANICAL VENTILATION: OVERVIEW

- Background for evidence base levels
- Dual modes of ventilation
- Adaptive Support ventilation (ASV)
- Proportional Assist Ventilation (PAV)
- Airway Pressure Release Ventilation (APRV)

EVIDENCE BASE FOR NEWER MODES OF MECHANICAL VENTILATION: *BACKGROUND*

- Evidence-based medicine:
“...the integration of individual clinical expertise with the best available research evidence from systematic research and the patient’s values and expectations.”
D. R. Hess, RC, 2004;49:7, 730-741.

GET INVOLVED IN DISASTER MANAGEMENT

Where to Begin with Pandemic Planning
Should Hospitals Begin to Stockpile
Essential Medical Supplies Now?

- This could lead to immediate shortages throughout the world
- If we do not increase our inventory we could find ourselves short of essential supplies and drugs


Adobe Acrobat Professional - [vent_guidelines[1].pdf]

File Edit View Document Comments Tools Advanced Window Help

Create PDF Comment & Markup Send for Review Secure Sign Forms

Select 75% Help

**Guidelines for Acquisition
of Ventilators to Meet Demands
for Pandemic Flu and Mass Casualty Incidents**



American Association for Respiratory Care
May 25, 2006
AACRC, 9425 N. MacArthur Blvd., Irving TX 75063
972-243-2272 * info@aacrc.org

1 of 12

Start Hospit... Po... No... No... Ne... Mai... Pa... Ad... 10:56 AM



Flu Ward 2007 ???

HOW TO STOP SEPSIS IN ITS TRACKS?

HOW TO STOP SEPSIS IN ITS TRACKS?

PREVENTION!!!!

RESPIRATORY THERAPISTS=FRONT LINES

PROACTIVE SPUTUM REMOVAL



RRT

YOUR SPUTUM IS OUR BREAD AND BUTTER

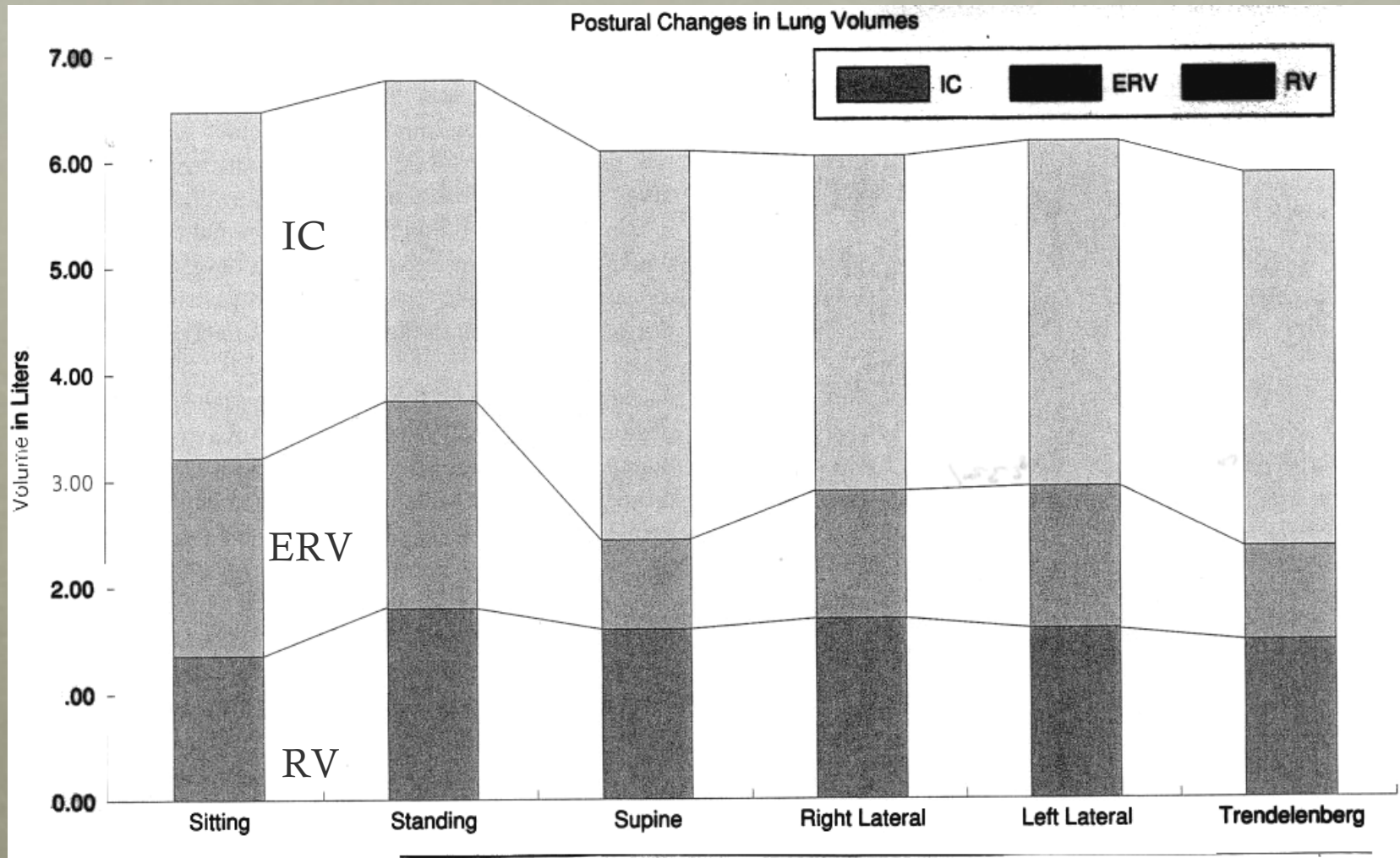
TEAM COMMUNICATION

- Communicate changes to sputum
 - Nurses do not have as much time since EMR
 - RT's are a part of the multiprofessional team
 - Should direct care—EBM guideline development
- Suggest ways to eliminate sputum and ventilation problems

EVIDENCED BASED REVIEWS AGREE

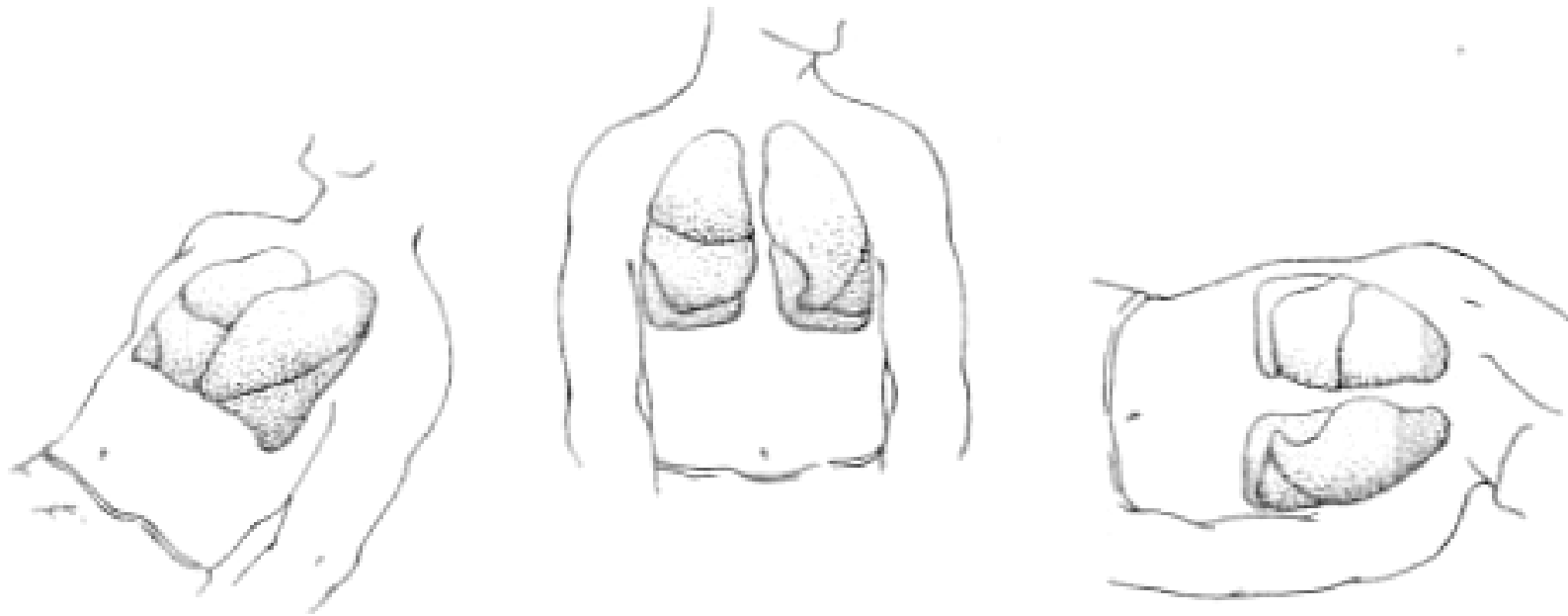
- Standard physical therapy resulted in a significantly greater sputum expectoration than no treatment (effect size of 0.61 SD units, $p < 0.0001$).
- The combination of standard therapy with exercise with associated with a statistically significant increase in FEV1 over STD alone (effect size of 0.48 SD units, $p = 0.04$).
- No other differences between physical therapy modalities were found.

Position Effects Lung Volumes



Position Effects

Ventilation: Perfusion



Position Effects

Ventilation: Perfusion

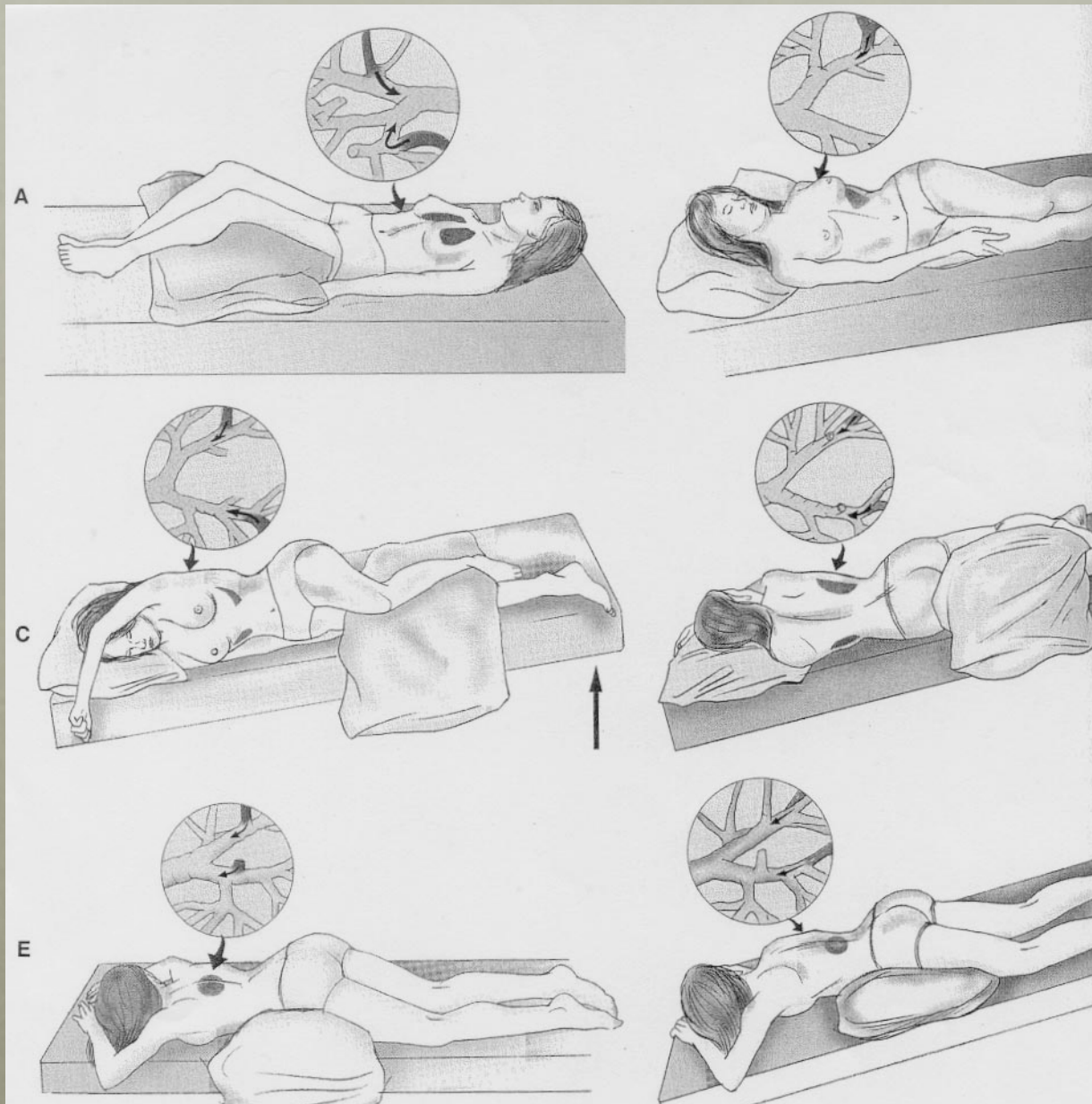


POSTURAL DRAINAGE

- Gold standard of bronchial hygiene when each position is drained 5 - 20 minutes
 - 11 positions requires >55 minutes
 - One hour session – concentration on 3 – 4 positions
- Percussion and vibration
 - No demonstrated benefit without positioning
- Everything works as well as PD except vibration and percussion alone – which doesn't work
- The time required for PD is prohibitive

STANDARD PHYSICAL THERAPY
RESULTED IN SIGNIFICANTLY
GREATER EXPECTORATION THAN NO
TREATMENT ($P < 0.0001$).

CPT WITH EXERCISE WAS
ASSOCIATED WITH AN INCREASED IN
FEV1 OVER CPT ALONE ($P = 0.04$).



HIGH FREQUENCY CHEST WALL COMPRESSION

ELECTROMED, INC.

SmartVest® Airway Clearance System

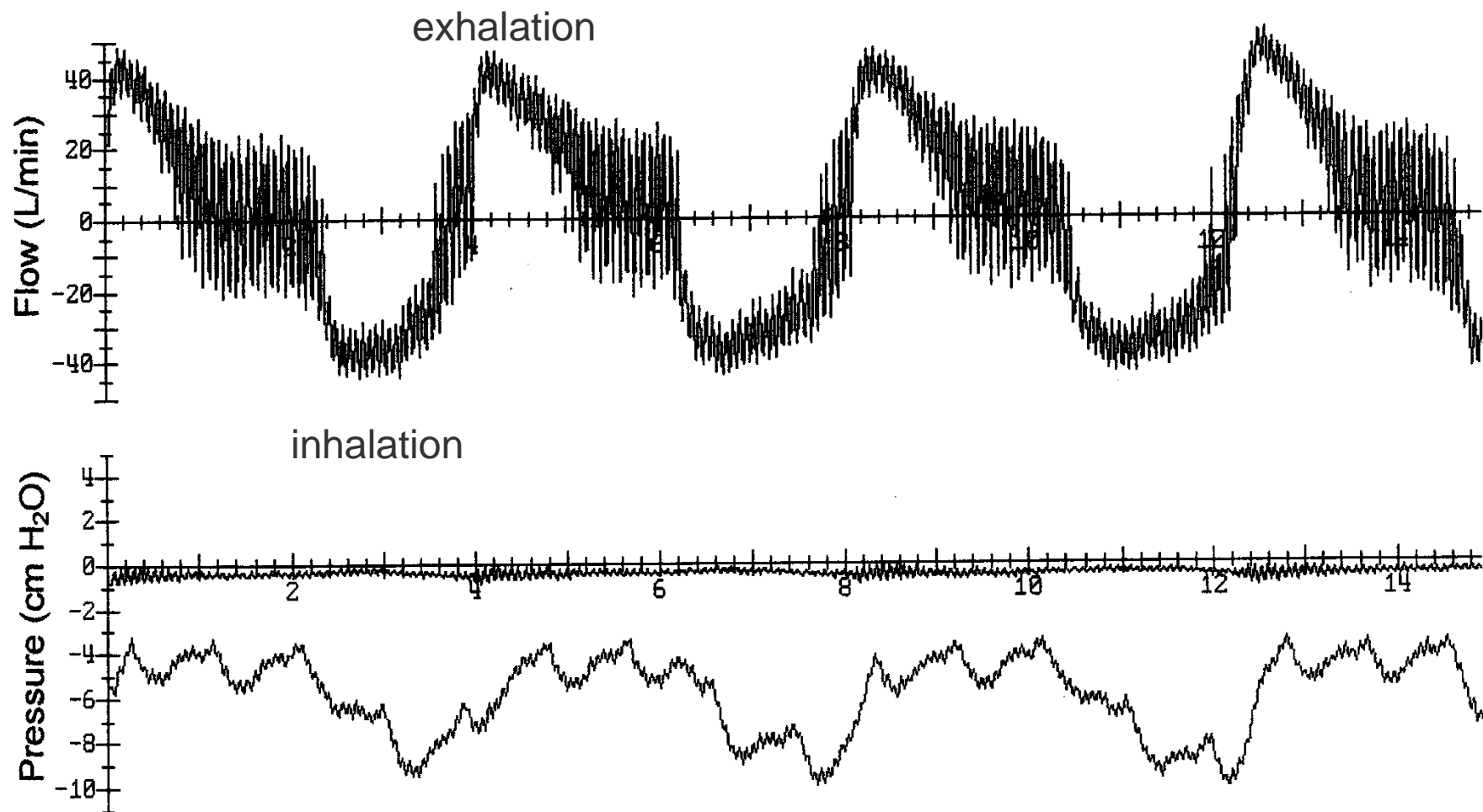


RespirTech®

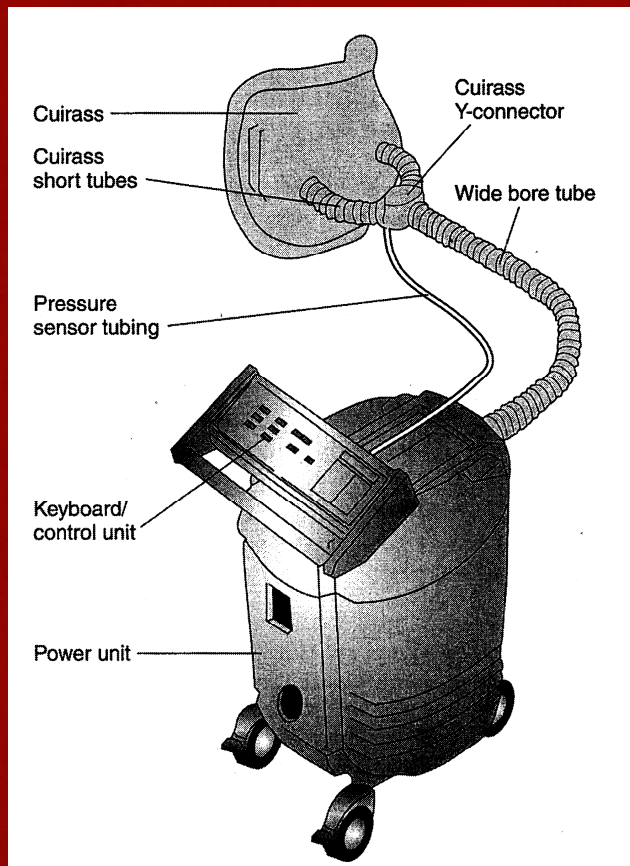
the
inCourage™
system



HIGH FREQUENCY CHEST WALL COMPRESSION

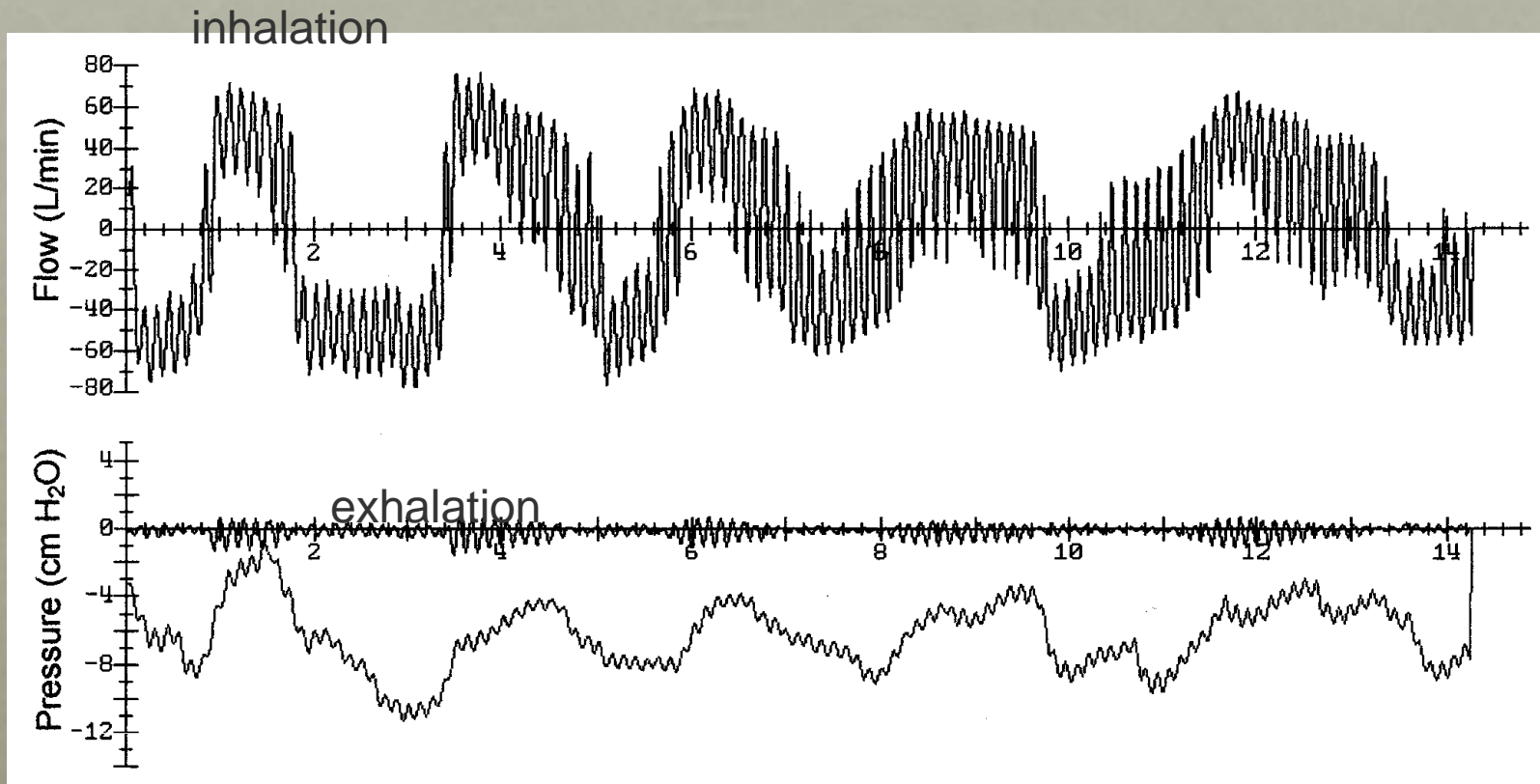


HIGH FREQUENCY CHEST WALL OSCILLATION



- Hayek 1993
- Cuirass based
- Positive and negative P_{TR}
- Controllable end exp pressure
- 1-17 Hz
- 1:6 to 6:1 I:E ratio control
- Most versatile device
- Can be used as ventilator

HIGH FREQUENCY CHEST WALL OSCILLATION –



MECHANISMS OF ACTION

- Air-liquid shear forces: multiple “mini coughs”
- Scherer model (factors increasing mucus transport)
 - Faster rate
 - Expiratory flow > inspiratory flow
 - Inspiratory time > expiratory time
 - Equal flows and times = zero transport

OTHER SEPSIS/RT ITEMS

- Intubation with etomidate
- Cognitive impairment after sepsis
- Isolation and prevention of Sepsis

ETOMIDATE

- **Short-Acting Hypnotic Okay for Rapid Intubation in Patients With Suspected Sepsis**
- **Etomidate may cause adrenal suppression with just 1 dose**
- **Randomized controlled trial of Etomidate and Midazolam, no difference in LOS/Mortality/Morbidity**
- **September 24, 2011**

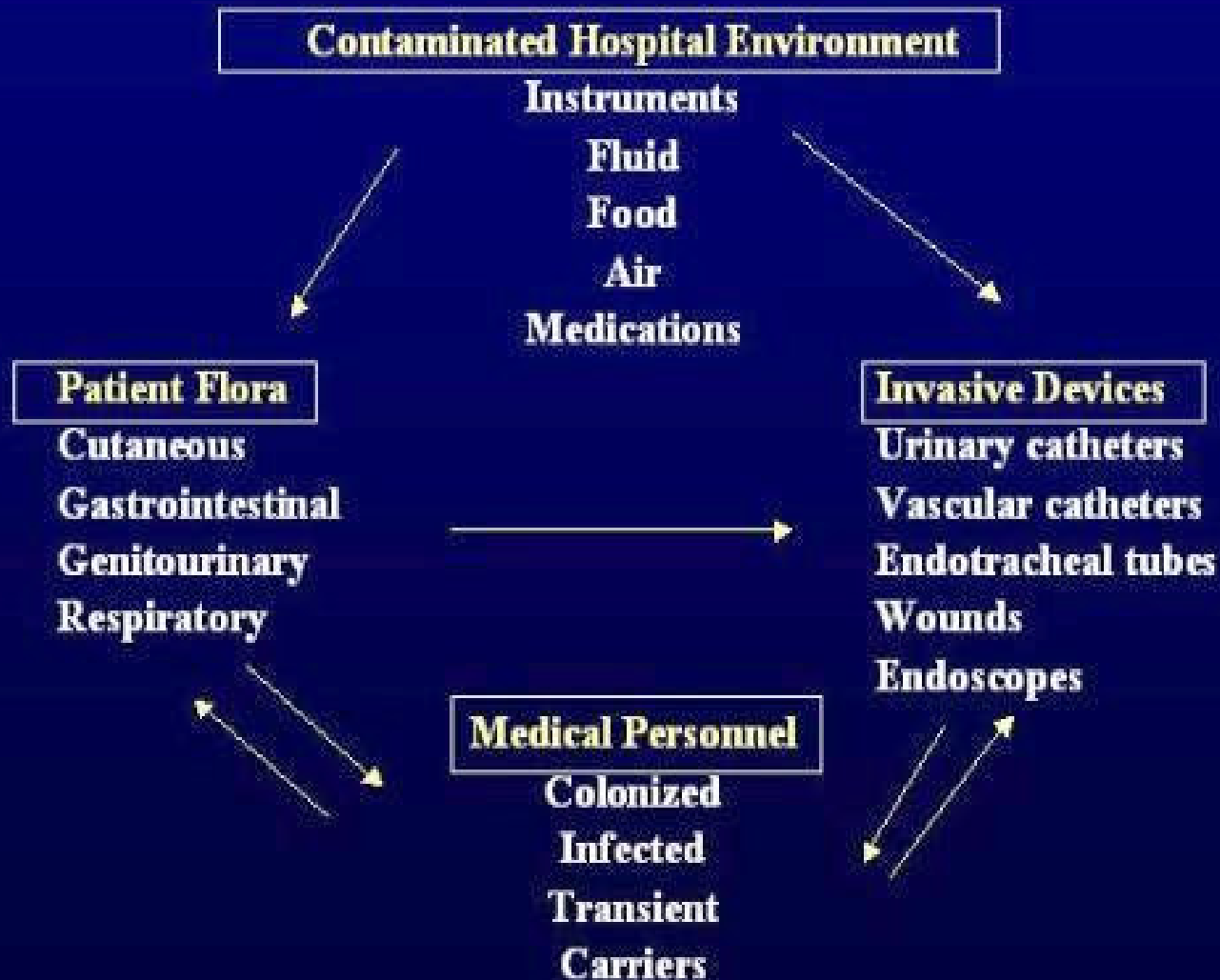
COGNITIVE IMPAIRMENT

- **Cognitive and Functional Decline Often Follow Severe Sepsis**
- Older adults who survive an episode of severe sepsis may be left with substantial and enduring cognitive impairment and functional disability
- Following severe sepsis hospitalization, but not nonsepsis general hospitalization, there was a significant increase in the odds of developing both cognitive and physical dysfunction that persisted throughout the 8-year follow-up period

MORE PREVENTION

- Government regulations:
 - Line sepsis
 - VAP
 - UTIs
 - Decubiti
- Pay for Performance/Outcomes
- Be proactive! Use Isolation devices
- Empower your staff to stop violators

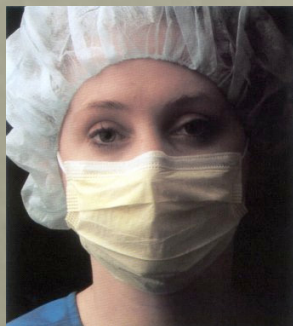
Sources of Hospital-Acquired Infections





Isolation

Well dang





UCSF Medical Center
UCSF Benioff Children's Hospital



DROPLET ISOLATION PRECAUTIONS

Visitors ~ See Nurse before entering



Clean Hands ~ Surgical Mask ~ Eye Protection



N-95 for High Hazard Procedures (See other side)

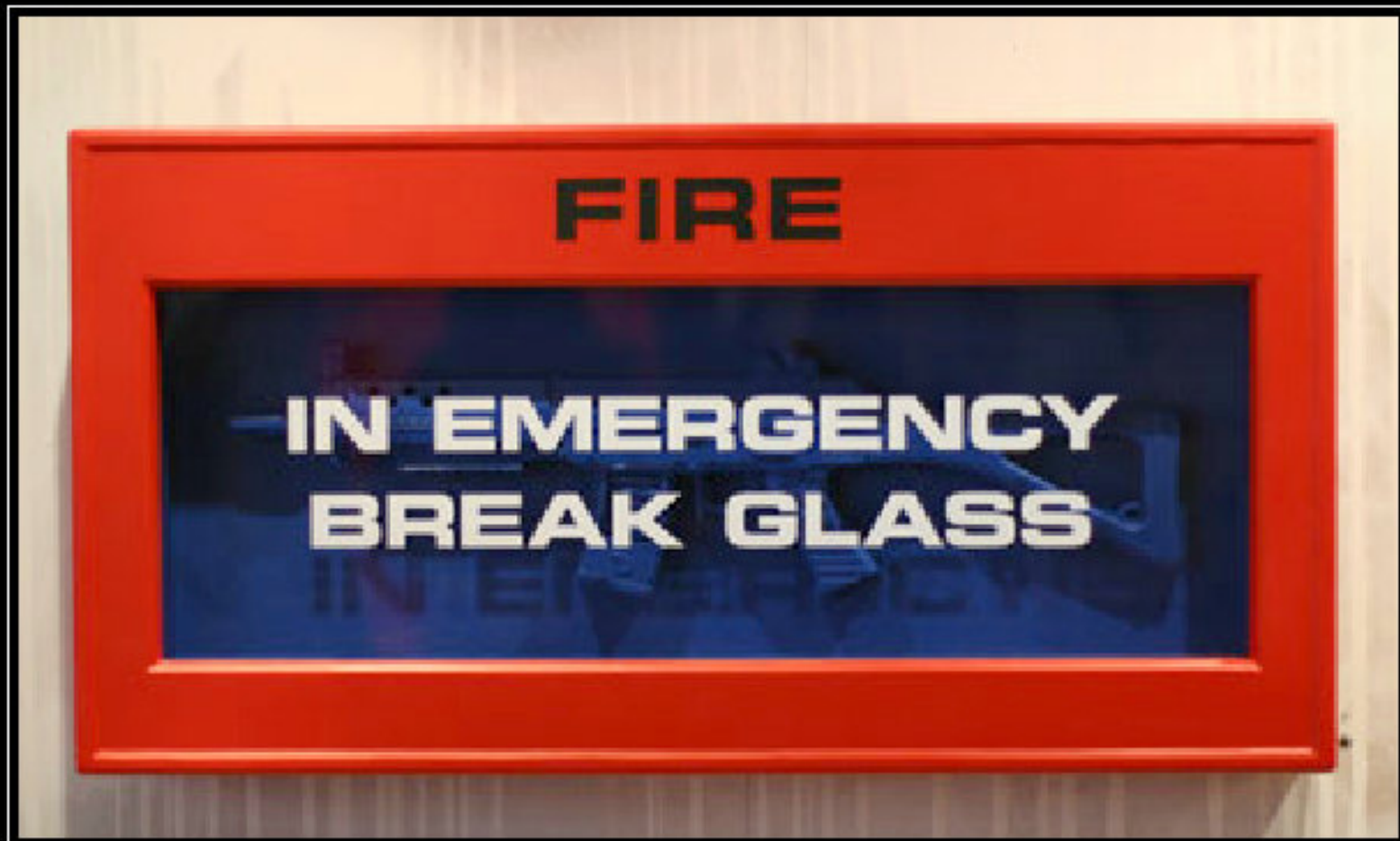
HOW SHOULD WE APPROACH SEPSIS?

- Recognize Early
 - SIRS / Organ failure
 - Document!
- Team Approach
 - MD, Nursing, PharmD., RespTherapy
 - Sepsis “SWAT TEAM”
- Organized Management
 - Guidelines, Standardization
- Process Improvement
- Prevention



IGNORANCE

IT IS IMPOSSIBLE FOR A MAN TO LEARN
WHAT HE THINKS HE ALREADY KNOWS



CRITICAL MOMENT

IN CASE OF EMERGENCY CALL RESPIRATORY
OTHERWISE WE'RE JUST A BUNCH OF USELESS DUMMIES

QUESTIONS????

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sticumd@gmail.com