



SEPSIS:

GUIDELINES FOR CURRENT MANAGEMENT

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SEPSIS MANAGEMENT

- **Definitions**
- **Scoring systems**
- **Surviving Sepsis Campaign**
- **Evaluation of evidence**
- **Management guidelines**

SEPSIS MANAGEMENT

SYNDROMES

SIRS

**Systemic
inflammatory
response**

MODS

**Multiple organ
dysfunction**

SEPSIS MANAGEMENT

DEFINITIONS

**Inflammation
(fever, leukocytosis)**

SIRS

SIRS + infection

Sepsis

**Sepsis +
multiorgan dysfunction**

Severe sepsis

**Severe sepsis +
refractory hypotension**

Septic shock

SEPSIS MANAGEMENT

SIRS: CLINICAL CRITERIA

Any two or more:

Body temperature	> 38 or < 36
Heart rate	> 90
Respiratory rate	> 20
Hyperventil. (PaCO ₂)	< 32
WBC	> 12K or < 4K
Immature polys	> 10%

Chest '92

SEPSIS MANAGEMENT

SIRS: CAUSES

Infection

Intestinal endotoxin

Ischemia

Multisystem trauma

Noxious substances

Shock

Thermal injury

Chest '92

SEPSIS MANAGEMENT

MODS

Lungs

Acute respiratory distress synd.

Kidneys

Acute tubular necrosis

Cardiovascular

Hyperdynamic hypotension

CNS

Metabolic encephalopathy

PNS

Polyneuropathy of crit. illness

Coagulation

Disseminated intravasc. coag.

GI tract

Gastroparesis / ileus

Liver

Acute noninfectious hepatitis

Adrenals

Acute adrenal insufficiency

Skeletal muscle

Rhabdomyolysis

SEPSIS MANAGEMENT

CLINICAL SCORING SYSTEMS

APACHE II	Acute Physiology & Chronic Health Evaluation	<i>ICU adm.</i>
MODS	Multiple Organ Dysfunction Score	<i>Daily</i>
GCS	Glasgow Coma Scale	<i>Dynamic</i>

SEPSIS MANAGEMENT

SURVIVING SEPSIS CAMPAIGN

- Multinational expert committee
- Barcelona Declaration (2002)
- International Sepsis Forum (2001)
- 14 year MEDLINE review (1990-03)
- Grading
 - *Evidence*
 - *Recommendations*
- Total consensus in all but 2 recs.

**(steroids, antibiotics)*

Dellinger, CCM '04

SEPSIS MANAGEMENT

GRADING OF EVIDENCE

Level

- I** Large randomized trials
- II** Small randomized trials
- III** Nonrandom., contemp. controls
- IV** Nonrandom., historical controls
- V** Case series; uncontr.; expert opinion

SEPSIS MANAGEMENT

GRADING OF RECOMMENDATIONS

Grade

Support

- A** At least 2 level I investigations
- B** One level I investigation
- C** Level II investigations only
- D** At least 1 level III investigation
- E** Level IV or V evidence

Dellinger, CCM '04

SEPSIS MANAGEMENT

GRADES IN GUIDELINES (n=52)

	<u><i>n</i></u>	<u><i>%</i></u>
A At least 2 level I investigations	5	10
B One level I investigation	11	21
C Level II investigations only	5	10
D At least 1 level III investigation	4	8
E Level IV or V evidence	27	52

Dellinger, CCM '04

SEPSIS MANAGEMENT

- **Definitions**
- **Scoring systems**
- **Surviving Sepsis Campaign**
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SEPSIS MANAGEMENT

INITIAL RESUSCITATION

- **For severe sepsis or hypoperfusion (hypotension or lactic acidosis)**
- **Normotensive: Elevated lactate identifies hypoperfusion**
- **Begin immediately**
- **Do not delay for ICU admission**
- **1st 6 hours: Goals and interventions**

SEPSIS MANAGEMENT

INITIAL RESUSCITATION

- **First 6-hour goals:**
 - ***CVP 8-12***
 - ***MAP \geq 65***
 - ***Urine \geq 0.5 ml/kg/hr***
 - ***O₂ sat (CV or MV) \geq 70%***
- **If O₂ sat < 70% with CVP 8-12:**
 - ***PRBC to Hct \geq 30***
and/or
 - ***Dobutamine (up to 20 ? g/kg/min)***

SEPSIS MANAGEMENT

DIAGNOSIS

- **Cultures before antibiotics**
- **At least two blood cultures**
 - *Percutaneous*
 - *Each vasc access device unless inserted within 48 hrs.*
- **Diagnostic studies**
 - *Unless unstable for transport*
 - *Consider bedside tests (sono)*

SEPSIS MANAGEMENT

ANTIBIOTIC THERAPY

- **Initiation**
- **Regimen**
 - *Empiric*
 - *Specific (focused)*
- **Cessation**

SEPSIS MANAGEMENT

ANTIBIOTIC THERAPY

- **Initiation:** within one hour
- **Empiric regimen**
 - *Initial broad spectrum*
 - *Active ag. likely pathogens*
 - *Penetrate likely site*
 - *Consider local susceptibility patterns*
 - *Hepatic, renal function affect dosing*
- **Cessation** if noninfectious cause

SEPSIS MANAGEMENT

FOCUSED ANTIBIOTIC REGIMEN

- Reassess after 48 – 72 hrs
- Cultures guide therapy
- Narrow spectrum agent
 - *Resistance, toxicity, costs*
- Course: 7 – 10 days
- Monotherapy, not combination
 - **Possible exception: Pseudomonas*
 - *Definite exception: Neutropenia*

SEPSIS MANAGEMENT

NOSOCOMIAL SEPTICEMIA

<u>Organism</u>	<u>%</u>	<u>Source</u>
Gram neg. enterics	38	Pneumonia
Coag. neg. staph	18	Vasc. catheters
<i>Staph aureus</i>	11	Pneumonia
Enterococci	10	Pneumonia
Streptococci	7	Unknown
Anaerobes	5	Pneumonia
<i>Candida</i> species	5	Vasc. catheters
Other	6	Mult. sources

Pittet, JAMA '94

SEPSIS MANAGEMENT

SOURCE CONTROL

- **Search for treatable focus**
- **Multidisciplinary approach**
- **Interventions:**
Consider risks / benefits
- **Intervene early after resuscitation**
- **Vascular access devices:**
 - ***Common sources of bacteremia***
 - ***If potential source: Establish alternate access, remove early***

SEPSIS MANAGEMENT

CATHETER SEPTICEMIA

<u>Organism</u>	<u>%</u>	
<i>S. epi.</i>	27	<u>Guidewire exchange</u>
<i>S. aureus</i>	26	Suspected infection
<i>Candida</i>	17	Aseptic placement
<i>Klebs.</i>	11	
<i>Serratia</i>	5	<u>New site</u>
<i>Pseud.</i>	3	Infected site (red, pus)
Other	8	Infected tip (> 15 cfu)

13 prosp. studies
S.Clin.N.Am 1988

Marino, The ICU Book

SEPSIS MANAGEMENT

SOURCE CONTROL

Technique

Examples

Drainage

Intra-abd. abscess; empyema;
septic arthritis; pyelo; cholangitis

Debridement

Necrotizing fasciitis; pancreatic
necrosis/abscess; mediastinitis

Device removal

Infected vascular catheter;
urinary catheter; ET tube; IUD

Definitive control

Sigmoid resection (diverticulitis);
cholecystectomy; amputation for
clostridial myonecrosis

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FLUID THERAPY

- **Colloid or crystalloid**
 - ***Crystal:*** ↑ volumes, edema; ↓ cost
- **Fluid challenge**
 - ***Crystal:*** 500 – 1000 mL
 - ***Colloid:*** 300 – 500 mL
 - ***Infuse over 30 min***
 - ***Repeat based on response, tolerance***

SEPSIS MANAGEMENT

VASOPRESSORS

- Indication: ↓ BP, perfusion despite fluids
- Route: through central line
- Agent: norepinephrine or dopamine
- No low-dose dopa for renal protection
- Arterial catheter for monitoring
- Refractory shock: vasopressin .01-.04 u/m

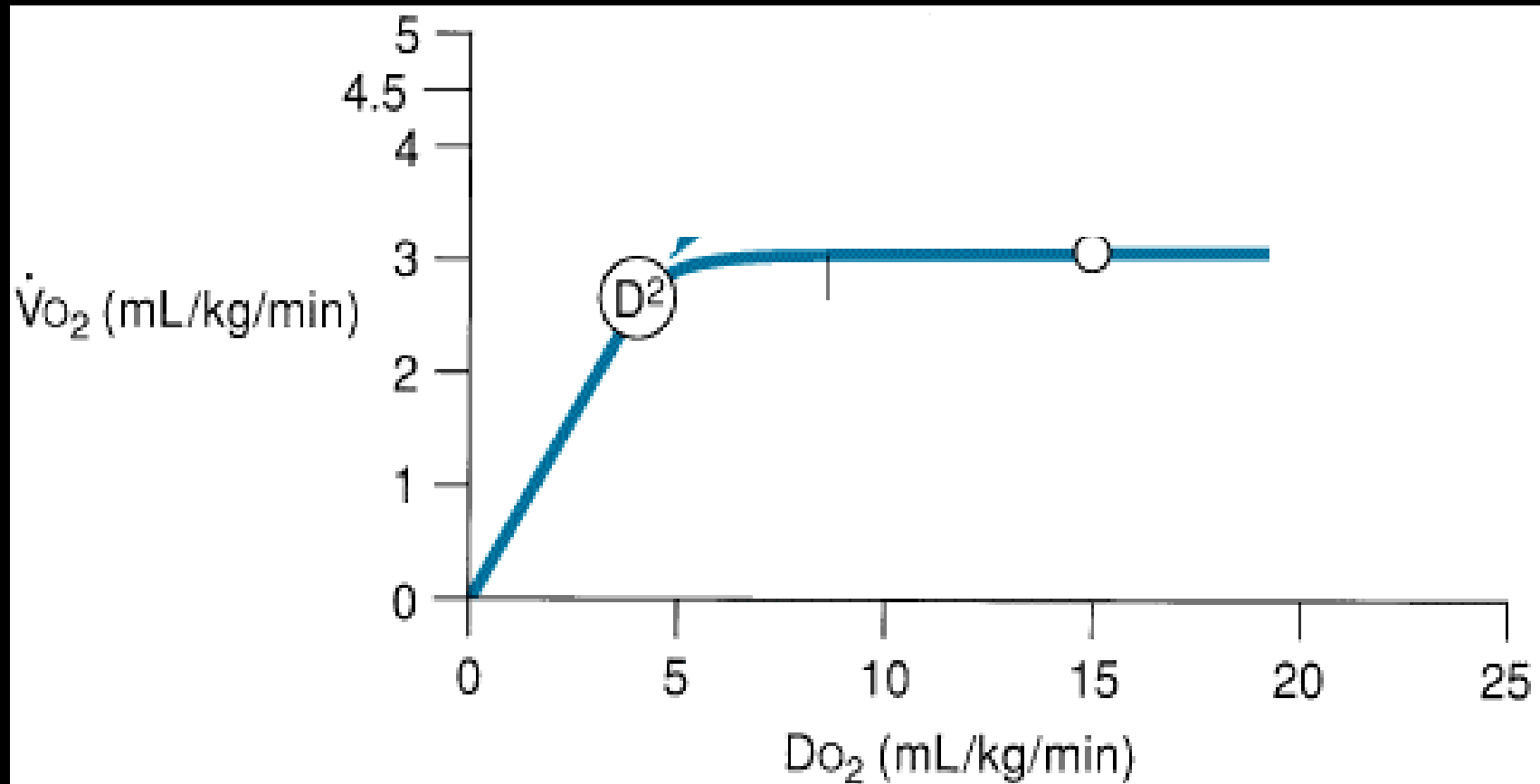
SEPSIS MANAGEMENT

INOTROPIC THERAPY

- **Indication: Low CO despite fluids**
- **Agent: Dobutamine**
- **Low BP: combine with vasopressors**
- **Goals:**
 - *Arbitrary elevated level not advised (A)*
 - *Adequate oxygen delivery*
 - *Avoid flow-dependence*

SEPSIS MANAGEMENT

O₂ EXTRACTION - DELIVERY

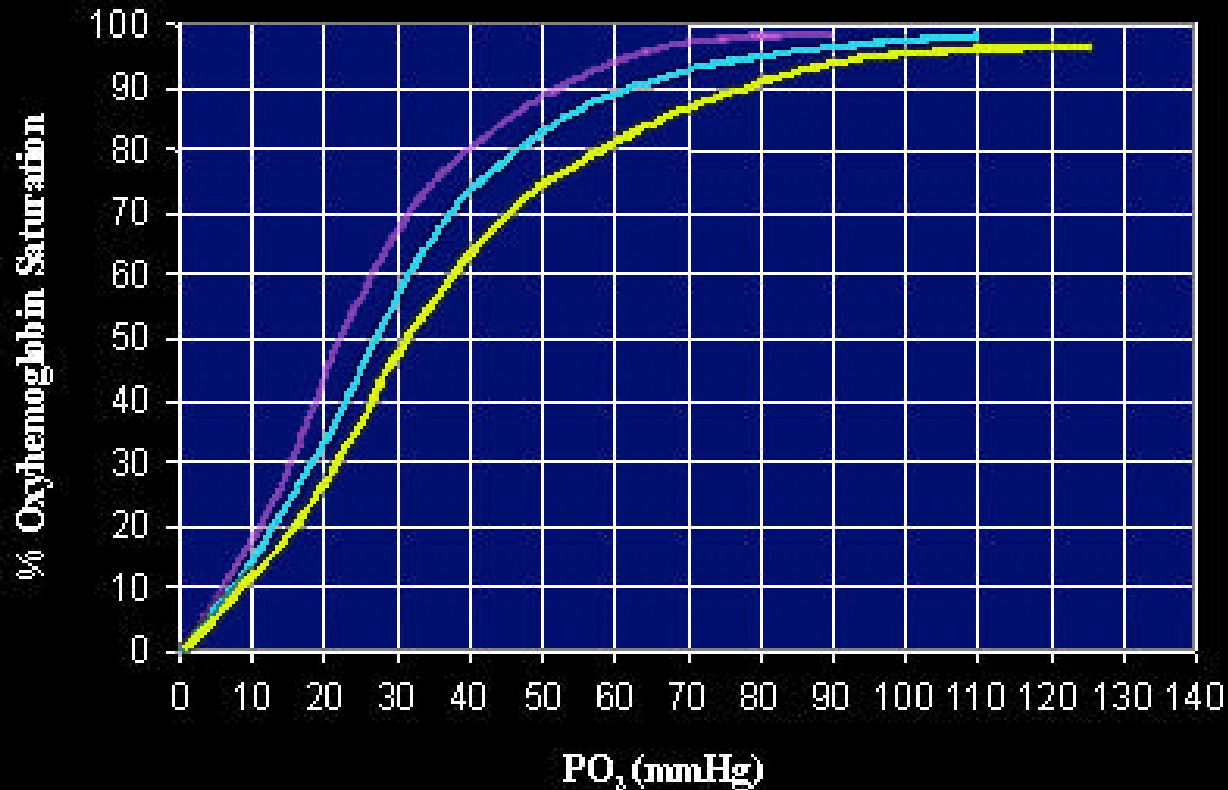


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ARTERIAL OXYGEN CONTENT

$$\begin{aligned} \text{CaO}_2 &= (1.34 \times \text{Hb} \times \text{SaO}_2) \\ &\quad + (0.003 \times \text{PaO}_2) \\ &= 1.34 \times 15 \times 0.98 \\ &= 19.7 \text{ mL/100 ml} \end{aligned}$$

SEPSIS MANAGEMENT



**OXYHEMOGLOBIN
DISSOCIATION CURVE**

SEPSIS MANAGEMENT

OXYGEN DELIVERY

$$\begin{aligned} \text{DO}_2 &= Q \times \text{CaO}_2 \\ &= Q \times (1.34 \times \text{Hb} \times \text{SaO}_2) \times 10 \\ &= 5 \times 19.7 \times 10 \\ &= 985 \text{ mL/min} \\ &= 520 - 570 \text{ mL/min/m}^2 \end{aligned}$$

SEPSIS MANAGEMENT

OXYGEN EXTRACTION

$$\begin{aligned} \mathbf{VO_2} &= \mathbf{Q \times 13.4 \times Hb \times (SaO_2 - SvO_2)} \\ &= \mathbf{5 \times 13.4 \times 15 \times (0.98 - 0.73)} \\ &= \mathbf{229 \text{ ml/min}} \\ &= \mathbf{110 - 160 \text{ mL/min/m}^2} \end{aligned}$$

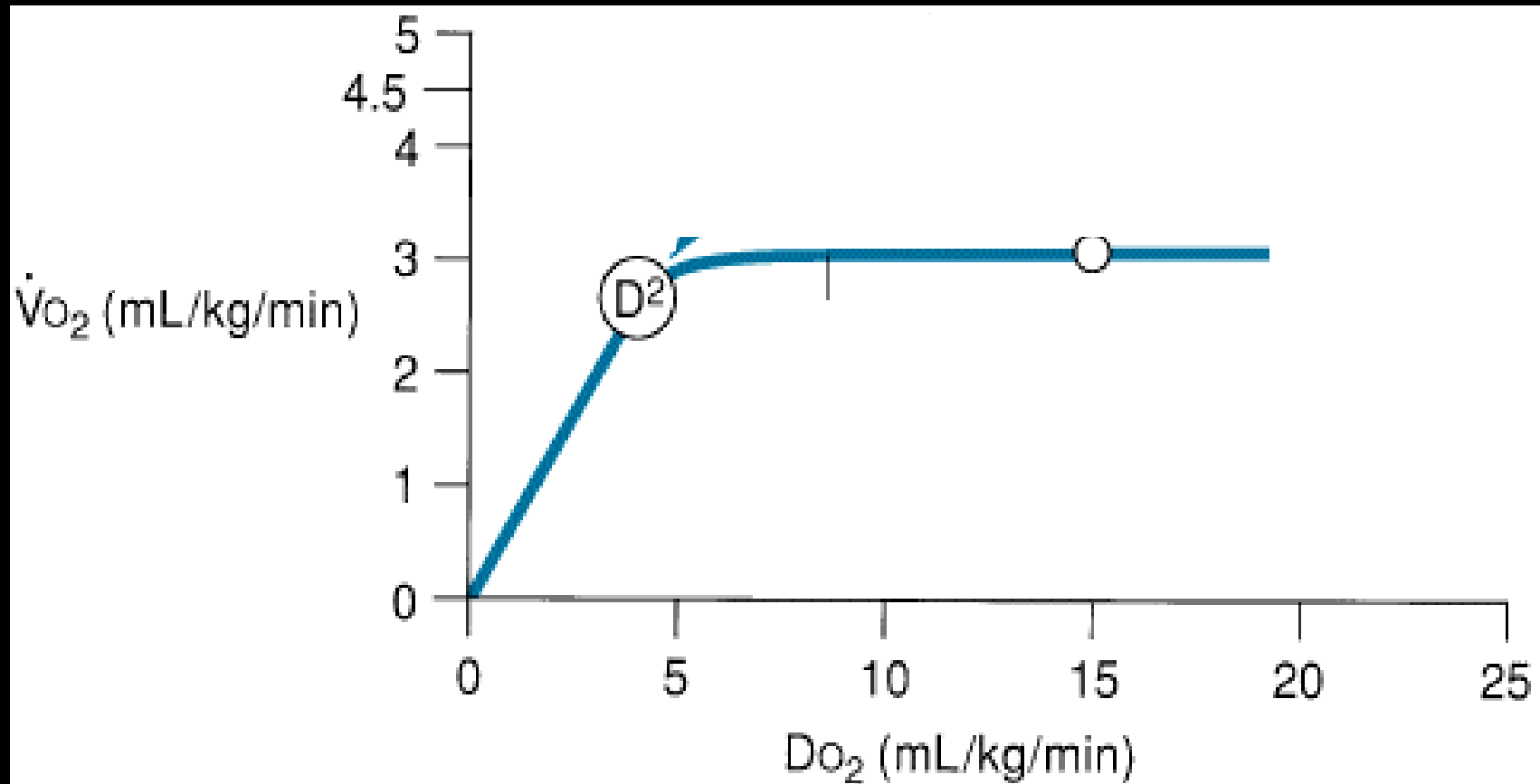
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OXYGEN EXTRACTION RATIO

$$\begin{aligned} \text{O}_2\text{ER} &= \text{VO}_2 / \text{DO}_2 \\ &= 110 / 520 \\ &= 0.2 - 0.3 \end{aligned}$$

SEPSIS MANAGEMENT

O₂ EXTRACTION - DELIVERY



SEPSIS MANAGEMENT

STEROIDS

- **Indication: septic shock requiring pressors despite adequate fluids**
- **Agent: Hydrocortisone IV**
 - *200-300 mg/day*
 - *3 or 4 divided doses*
 - *7-day course*
- *** Consider: ACTH stimulation test**
 - *ACTH 250 µg IV*
 - *Measure cortisol 30-60 min*
 - *Responder: increase ≥ 9 µg/dl*

SEPSIS MANAGEMENT

STEROIDS FOR SEPTIC SHOCK

- Consider taper at end of therapy
- Consider fludrocortisone (50 ? g PO qid)
- Hydrocortisone > 300 mg/day not indicated **(A)**
- No shock: steroids not indicated
- Maintenance or stress dose steroids: no contraindication

SEPSIS MANAGEMENT

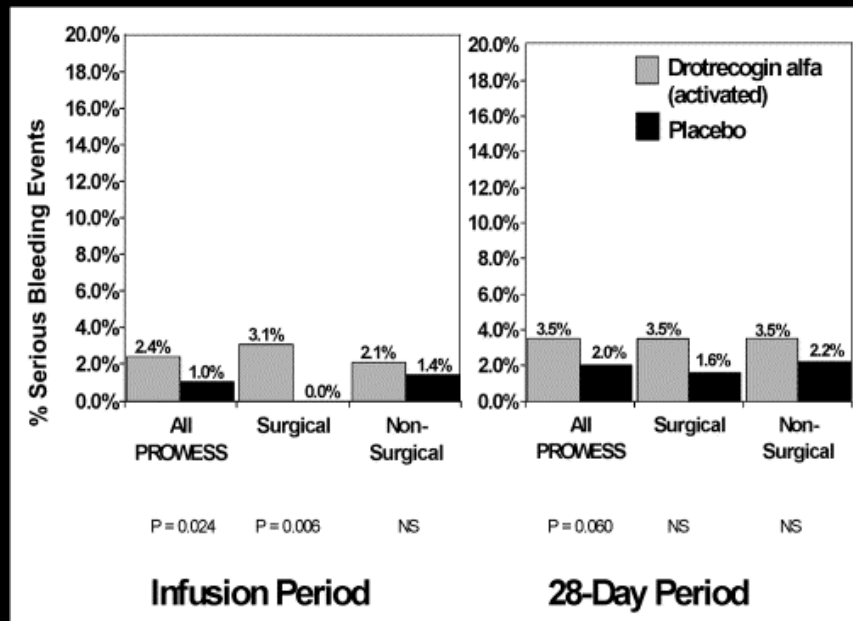
RECOMBINANT HUMAN ACTIVATED PROTEIN C (rhAPC)

- Endog. anticoagulant, anti-inflammatory
- Rationale: coagulation, endothelial activation in septic inflam. response
- Improved survival (Bernard, NEJM 2001)
- Recommended:
 - *APACHE II \geq 25*
 - *Sepsis-induced MOF, shock, or ARDS*
 - *No contraindications*

SEPSIS MANAGEMENT

rhAPC IN SURGICAL PATIENTS

- 28% of 850 PROWESS patients
- Mortality risk reduction:
 - *All surgical pts.: 3.2%*
 - *Intra-abdominal procedures: 9.1%*
- Bleeding:



*Barie,
Am J Surg 04*

SEPSIS MANAGEMENT

rhAPC: CONTRAINDICATIONS

- Active internal bleeding
- Recent (3 mos) hemorrhagic stroke
- Recent (2 mos):
 - *Intracranial operation*
 - *Intraspinal operation*
 - *Severe head trauma*
- Trauma with increased bleeding risk
- Epidural catheter
- Intracranial neoplasm, mass, herniation

SEPSIS MANAGEMENT

BLOOD PRODUCTS

- **PRBC** for Hgb < 7 g/dl
- Erythropoietin not indicated
- **FFP**: bleeding, invasive procedures
- Antithrombin not indicated
- **Platelet** transfusion:
 - *Counts < 5000*
 - *5-30,000 w significant risk of bleeding*
 - *≥ 50,000 for surgery / invasive proced.*

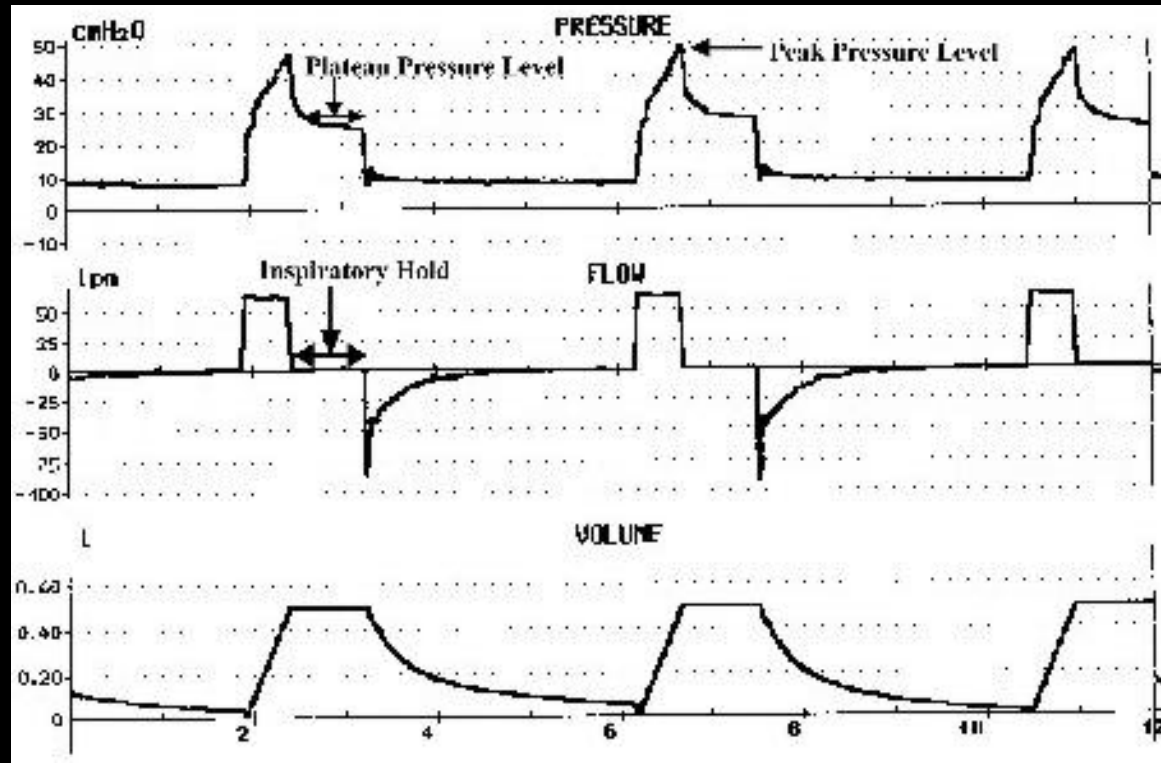
SEPSIS MANAGEMENT

ALI / ARDS: MECHANICAL VENT.

- **Reduced tidal volumes (6 mL/kg)**
- **Plateau pressure < 30 cm H₂O**
- **Permissive hypercapnia acceptable**
- **PEEP to prevent end-expir. collapse**
- **Consider prone positioning**
- **Elevate HOB 45° (prevents pneumonia)**
- **Use weaning protocol**

SEPSIS MANAGEMENT

PLATEAU PRESSURE



- P_{plat} : small airways pressure in PPV
- Cause of ventilator-induced lung injury

SEPSIS MANAGEMENT

WEANING CRITERIA

- **Arousable**
- **Stable hemodynamics off pressors**
- **No new potentially-serious conditions**
- **Low vent., PEEP requirements**
- **F_iO₂ deliverable by mask or prongs**
- **Spontaneous breathing trial (A)
(CPAP or T-piece)**

SEPSIS MANAGEMENT

SPECIFIC WEANING CRITERIA

<u>Parameter</u>	<u>Nl. adult range</u>	<u>Wean. threshold</u>
PaO ₂ / FiO ₂	> 400	200
Tidal volume	5-7 mL/kg	5 mL / kg
Resp. rate	14-18 / min	< 40 / min
Vital capacity	65-75 mL / kg	10 mL / kg
Min. ventilation	5-7 L / min	< 10 L / min

Greater predictive value

Max. insp. press.	>-90 cm H ₂ O (F) >-120 cm H ₂ O (M)	- 25 cm H ₂ O
Rate / tidal vol.	< 50 / min / L	< 100 / min / L

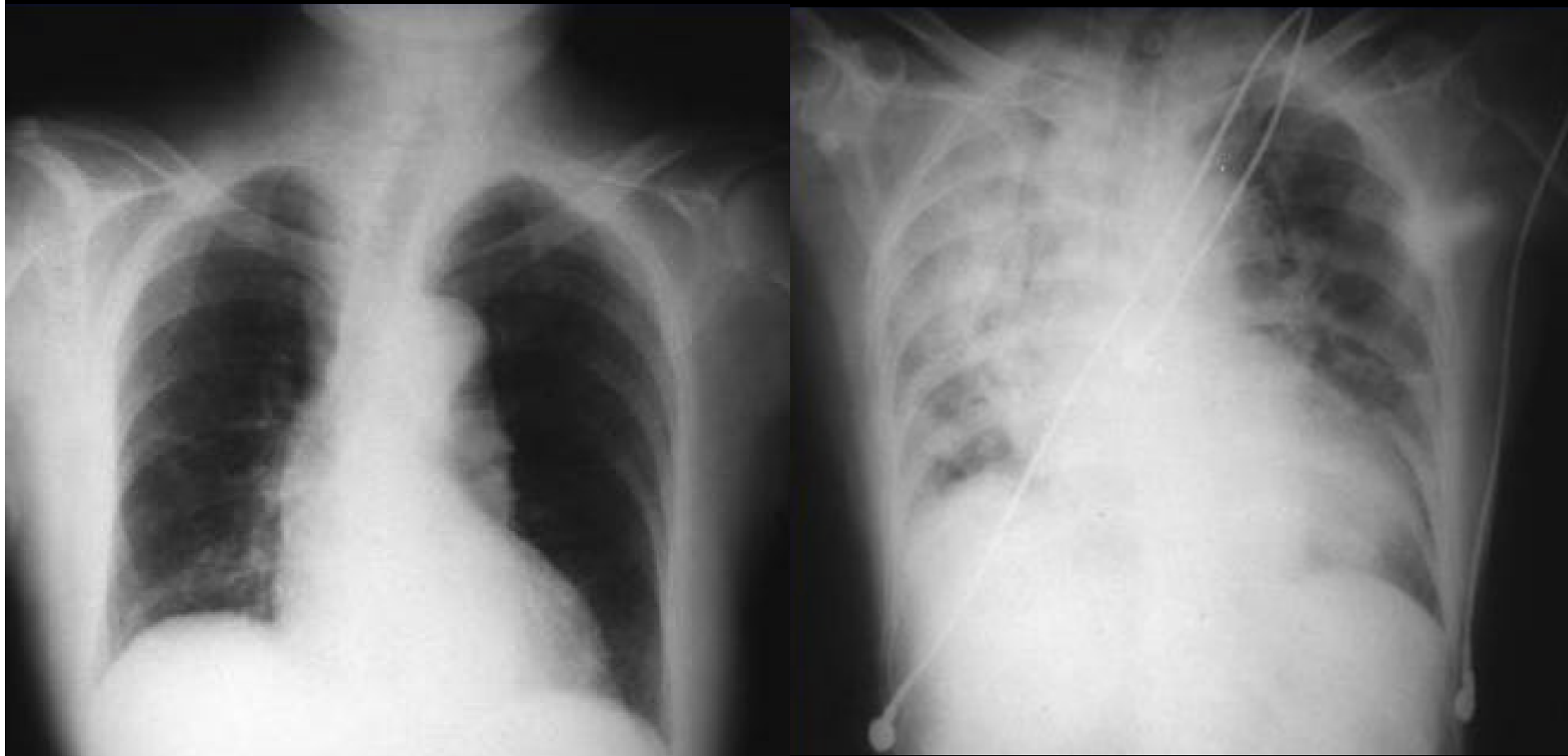
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CLINICAL CRITERIA FOR ARDS

<u>Parameter</u>	<u>ARDS</u>
Onset	Acute
Clinical setting	Predisposing condition
Gas exchange	$\text{PaO}_2 / \text{FiO}_2 < 200$ regardless of PEEP level
Chest x-ray	Bilateral infiltrates
Wedge pressure	≤ 18 mm Hg

SEPSIS MANAGEMENT

ARDS



SEPSIS MANAGEMENT

ARDS WEANING TRIAL

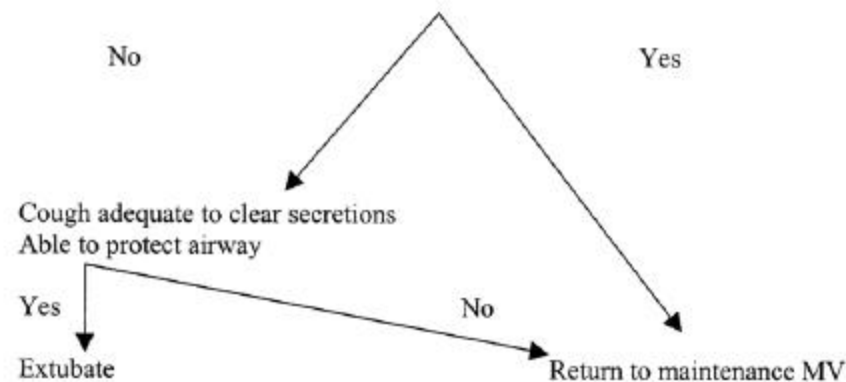
Original illness resolving; no new illness
Off vasopressors and continuous sedatives
Cough during suctioning
 $\text{PaO}_2/\text{FIO}_2 > 200$ mm Hg
 $\text{PEEP} \leq 5$ cm H₂O
Minute ventilation < 15 L/min
 F/TV ratio ≤ 105 during 2-min spontaneous breathing trial



Spontaneous breathing trial^a (30–120 mins)

Respiratory rate > 35 /min
Oxygen saturation < 90
Pulse > 140 /min or change $\geq 20\%$
SBP > 180 mm Hg or < 90 mm Hg
Agitation, diaphoresis, or anxiety
 F/TV ratio > 105

Note: Achieving any of these criteria for a sustained period at any time during the trial represents a weaning failure and the need to return to maintenance MV.



SEPSIS MANAGEMENT

ARDSNET PROTOCOL

- Assist control mode—volume ventilation
- Reduce tidal volume to 6 mL/kg predicted body weight
- Keep Pplat <30 cm H₂O
—Reduce Tv as low as 4 mL/kg predicted body weight* to limit Pplat
- Maintain SaO₂/SpO₂ 88–95%
- Anticipated PEEP settings at various FIO₂ requirements

FIO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	20–24

*Predicted Body Weight Calculation

- Male— $50 + 2.3 [\text{height (inches)} - 60]$ or $50 + 0.91 [\text{height (cm)} - 152.4]$
- Female— $45.5 + 2.3 [\text{height (inches)} - 60]$ or $45.5 + 0.91 [\text{height (cm)} - 152.4]$

Tv, tidal volume; SaO₂, arterial oxygen saturation; PEEP, positive end-expiratory pressure.

SEPSIS MANAGEMENT

SEDATION PROTOCOLS

- **Required in critical illness**
- **Sedation goals**
 - ***Set end-points***
 - ***Measured by standard subjective scales***
- **Bolus or continuous infusion**
- **Daily awakening / retitration**
- **Reduce vent. duration, LOS, trach rate**

SEPSIS MANAGEMENT

NEUROMUSCULAR BLOCKERS

- **Avoid if possible**
- **Bolus or continuous infusion**
- **Train of four monitoring**
- **Risk: prolonged muscle weakness**

SEPSIS MANAGEMENT

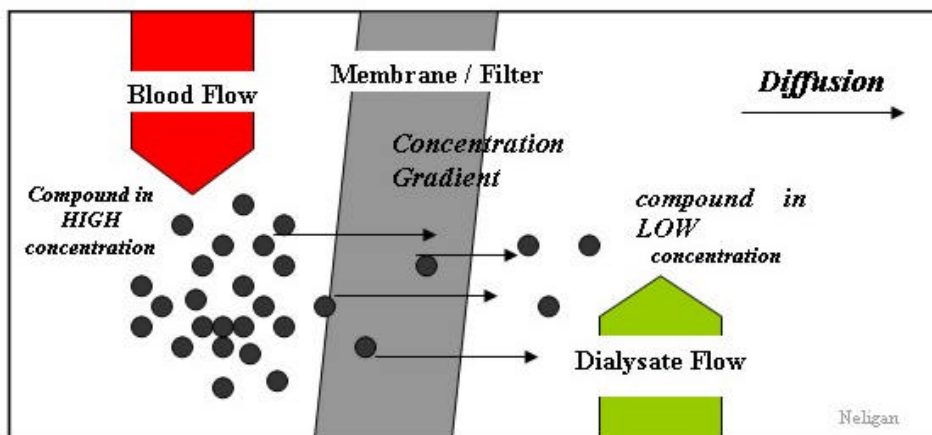
GLUCOSE CONTROL

- **Maintain blood glucose < 150 mg/dL**
- **Continuous insulin / glucose**
- **Glucose monitoring**
 - *Initiation: q 30-60 min*
 - *Maintenance: q 4 hr*
- **Enteral nutrition preferred**

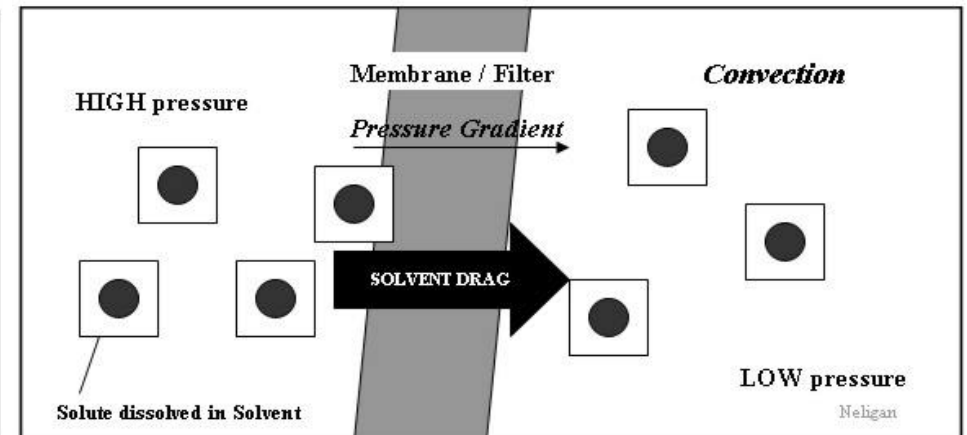
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RENAL REPLACEMENT

- Hemodialysis, continuous venovenous hemofiltration (CVVH) equivalent
- Unstable hemodynamics: CVVH



Dialysis



Ultrafiltration

SEPSIS MANAGEMENT

BICARBONATE THERAPY

- **Not recommended for treatment of hypoperfusion-induced lactic acidemia with pH \geq 7.15**

SEPSIS MANAGEMENT

DVT PROPHYLAXIS

- **Recommended for severe sepsis (A)**
- **Agent: Low-dose unfractionated heparin or LMWH**
- **Compression stockings if heparin contraindicated**
- **Very high risk (DVT hx): combination**

SEPSIS MANAGEMENT

STRESS ULCER PROPHYLAXIS

- Recommended for severe sepsis **(A)**
- H₂ receptor antagonists preferred
- H₂ RA better than sucralfate
- PPI: equivalent gastric pH effects
but not assessed vs. H₂ RI

SEPSIS MANAGEMENT

LIMITATION OF SUPPORT

- **Advance care planning advised**
- **Discussion with patient and family**
 - *Likely outcomes*
 - *Realistic goals of treatment*
- **Consider patient's best interest:**
 - *Less aggressive therapy*
 - *Withdrawal of support*

SEPSIS MANAGEMENT

SUMMARY

- **Practice guidelines**
- **Evidence-based**
- **Source control**
- **Physiologic basis**