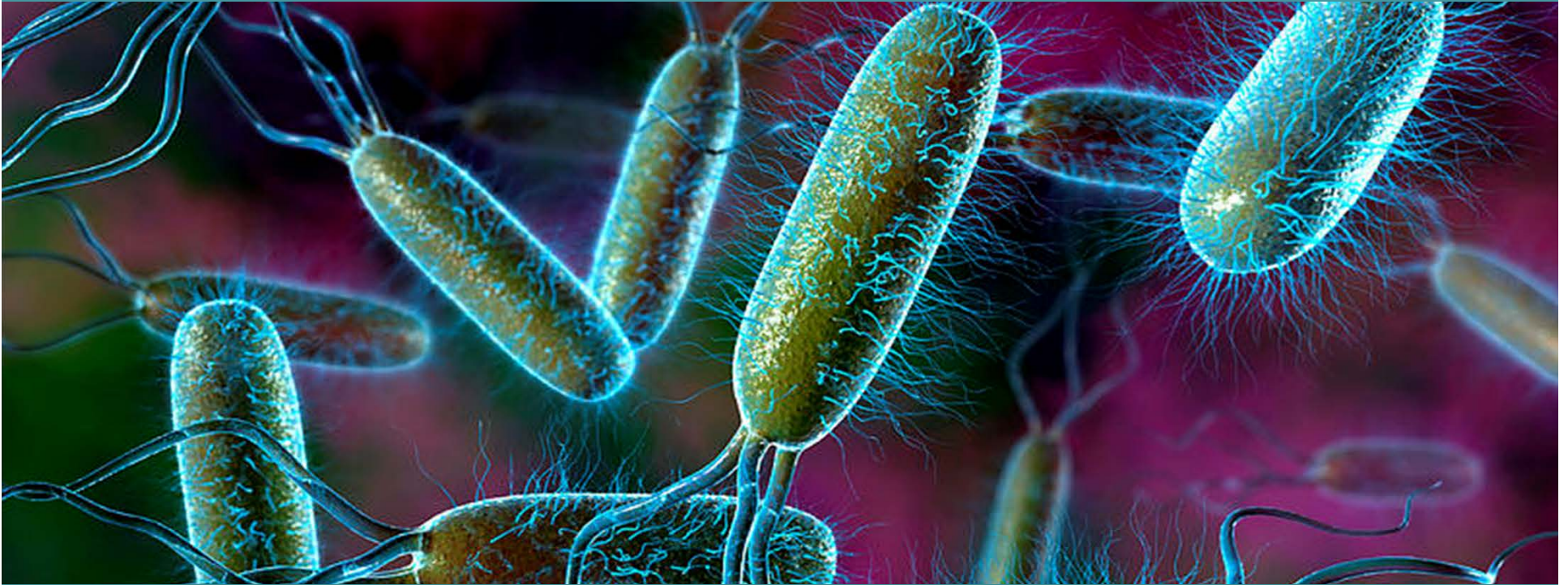


Perioperative Management of Sepsis: A Paradigm Shift



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Outline of Presentation

- Definition of Sepsis**
- Overview of Pathophysiology**
- Initial resuscitation of patients with sepsis undergoing surgical intervention**
- Surviving Sepsis Campaign Guideline**
- Perioperative Issues**
- Conclusion**

The Impact of Sepsis

- Sepsis and septic shock are *major healthcare problem*
- Accounts for as much as 2 5% of intensive care unit (ICU) bed utilization
- Common in elderly, immunocompromised and critically ill patients
- Mortality from septic shock remain high (30-50%)

The Impact on Our OR/ICU ?

■ Generalized Peritonitis

- Bowel perforation
- Bowel obstruction

■ Wound Infections

■ ICU – CAP, HAP, VAP

Definitions

The Third International Consensus Definitions (Sepsis-3)

Sepsis



Life-threatening *organ dysfunction* caused by a **dysregulated** host response to infection

Organ
Dysfunction



Increase in the Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score of 2 points or more



In ED and general ward settings, at least 2 *quickSOFA (qSOFA)*:
RR of 22/min or greater, altered mentation (GCS < 13/15) or SBP of 100 mmHg or less.

Septic
Shock



Vasopressor requirement to maintain a MAP of ≥ 65 mmHg and serum lactate >2 mmol/L (18mg/dL) in the absence of hypovolemia

Sequential [Sepsis-Related] Organ Failure Assessment Score

System	Score				
	0	1	2	3	4
Respiration					
Pao ₂ /Fio ₂ , mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, ×10 ³ /μL	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular					
	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose) ^b	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1 ^b	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1 ^b
Central nervous system					
Glasgow Coma Scale score ^c	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Vincent JL, Moreno R, Takala J, et al. The SOFA score to describe organ dysfunction/failure
Intensive Care Med. 1996;22(7):707-710.

The Process of Sepsis Definitions by Task Force

Systemic Inflammatory Response Syndrome (SIRS): Two or more of the following:

- Temperature > 38°C or < 36°C
- Heart rate > 90 beats per minute
- Tachypnoea (respiratory rate > 20 breaths.min⁻¹) or hyperventilation (PaCO₂ < 4.25kPa)
- White blood count > 12 x 10⁹.L⁻¹, or < 4 x 10⁹.L⁻¹

1992

Sepsis: Two or more SIRS criteria in response to infection.

Severe sepsis: Sepsis associated with hypotension or organ dysfunction or organ hypoperfusion (e.g. oliguria, altered mental status, lactic acidosis).

Septic shock: Sepsis-induced hypotension (systolic blood pressure < 90mmHg or a reduction ≥ 40mmHg from baseline) despite adequate fluid resuscitation along with signs of hypoperfusion.



2001

International Sepsis Definitions Conference

- General signs and symptoms

- Rigor - Fever (sometimes hypothermia)
- Tachypnea / Respiratory alkalosis
- Positive fluid balance - edema

- General hematologic/Inflammatory reaction

- Increased (sometimes decreased) WBC
- Increased CRP, IL-6 & procalcitonin concentration

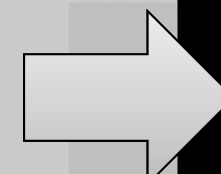
- Signs of organ dysfunction

- Hypoxemia (ALI)
- Altered mental status
- Alteration in renal function

- Hemodynamic alterations

- Arterial hypotension
- Tachycardia
- Increased cardiac output / wide PP / low SVR / high SvO₂
- Altered skin perfusion
- Decreased urine output
- Hyperlactatemia - Increased base deficit

- Hyperglycemia
- Thrombocytopenia, DIC
- Alteration in liver tests (hyperbilirubinemia)
- Intolerance to feeding (altered GI motility)



2016
SEPSIS-3

Mitchell et al(2003) International Sepsis Definitions Conference:
Intensive Care Med 29:530–538.

Why SOFA score ???

SOFA score of 2 or greater identified a 2- to 25-fold increased risk of dying compared with patients with a SOFA score less than 2

SOFA score is not intended to be used as a tool for patient management but as a means to **clinically characterize** a septic patient

SIRS Criteria

The task force wishes to stress that SIRS criteria may still remain useful for the **identification of infection.**

Overview of Pathophysiology

Endotoxin (LPS)

LBP on CD 14
Macrophage, Endothelial

Intracellular Signal Transduction via TLR

Complex Endothelial-Leucocyte Interaction

Increased TF and PAI

O₂ radical, Cytokine, Complement, Lipid mediators

Procoagulant

Capillary Leak, Vasodilatation

Microvascular occlusion

CVS instability

MODF

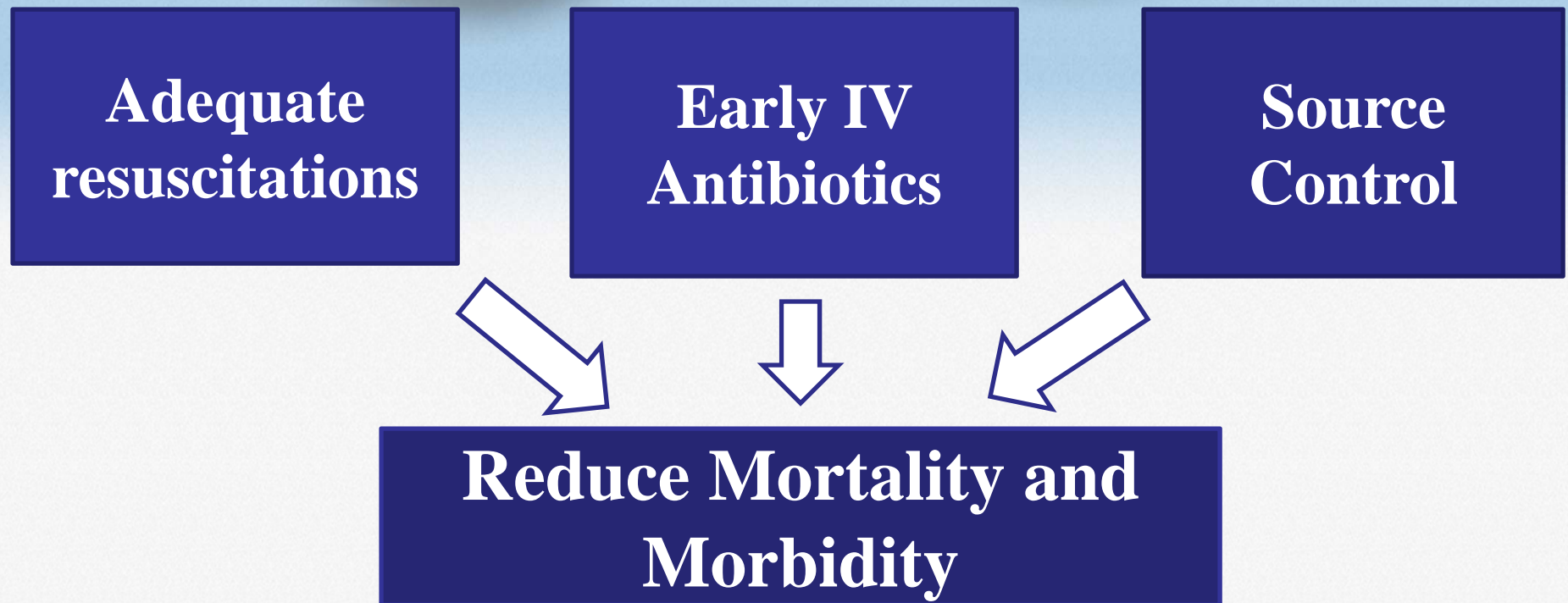
Proinflammatory Vs
Anti-inflammatory

Dysregulated Immune Response

Perioperative Management of Sepsis

- ❑ **Early recognition** and treatment of sepsis is important.
- ❑ Not all septic patients have self-evident septic focus
- ❑ Initial assessment followed by secondary assessment
 - a. State of IV *Volume status*
 - b. The need and *Adequacy of resuscitation*
 - c. Severity of *Organs dysfuctions*
 - d. Presence of *Comorbid conditions*

Early haemodynamic optimization can reduce mortality



Martijn P et al (2005) Meta-analysis of hemodynamic optimization: relationship to methodological quality: *Critical Care* 2005, 9:R771-R779

Initial Assessment and Management

A brief history taking with limited examination (eSOFA)

Airway

- Recovery position, oro/ or nasopharyngeal airway
- Appropriate Oxygen therapy ★
- Early intubation

Breathing

- Signs of respiratory failure
- Head up position
- Assisted by Ambu bag/Waters to and fro
- NIV Vs Intubation and Mechanical Ventilation

Circulation

- Rapid assessment (HR, BP, Capillary refill etc)
- Fluid resuscitation – 20-30 ml/kg

Fluid Resuscitation

How much ?



Types



How Fast?

When to stop?



How Much ???

At least 30 ml/kg

Study ID	OR (95% CI)	Events, EGDT	Events, control	% Weight
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How Fast ???

Within first 3 hours

ARISE Investigators (2014)	0.98 (0.76, 1.26)	147/792	150/796	30.71
ProMISe Investigators (2015)	1.02 (0.80, 1.30)	184/623	181/620	32.23
Overall (I-squared = 56.7%, p = 0.055)	1.01 (0.88, 1.16)	495/2134	582/2601	100.00

.3

1

3

Favours EGDT

Favours control

Fluid of Choices ????

Crystalloids Vs Colloids

Crystalloids as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement

Balanced Salt Solution Vs 0.9% Normal Saline

Either is acceptable
Close monitoring of serum Cl⁻ to avoid hyperchloraemic metabolic acidosis

Suggest using Albumin in addition to crystalloids for initial resuscitation and subsequent intravascular volume replacement

Xu et al. *Critical Care* 2014, **18**:702
<http://ccforum.com/content/18/6/702>



RESEARCH

Open Access

Comparison of the effects of albumin and crystalloid on mortality in adult patients with severe sepsis and septic shock: a meta-analysis of randomized clinical trials

Jing-Yuan Xu, Qi-Hong Chen, Jian-Feng Xie, Chun Pan, Song-Qiao Liu, Li-Wei Huang, Cong-Shan Yang, Ling Liu, Ying-Zi Huang, Feng-Mei Guo, Yi Yang and Hai-Bo Qiu*

A trend toward reduced 90-day mortality was observed in severe sepsis patients resuscitated with albumin compared with crystalloid and saline

Role of Synthetic Colloids

Recommend **Against** using Hydroxyethyl Starches (HES) for intravascular volume replacement

BMJ

BMJ 2013;346:f839 doi: 10.1136/bmj.f839 (Published 15 February 2013)

Page 1 of 12

Hydroxyethyl starch 130/0.38-0.45 versus crystalloid or albumin in patients with sepsis: systematic review with meta-analysis and trial sequential analysis

 OPEN ACCESS

Nicolai Haase *physician*¹, Anders Perner *professor*¹, Louise Inkeri Hennings *physician*¹, Martin Siegemund *professor*², Bo Lauridsen *physician*¹, Mik Wetterslev *medical student*¹, Jørn Wetterslev *chief physician*³

HES 130/0.38-0.45 increased the use of RRT, RBC transfusion and resulted in more serious adverse events

Role of Synthetic Colloids (Gelatins)

Gelatin use in critically ill adult patients did not increase mortality or acute kidney injury compared to albumin or crystalloid

SSC suggest using **Crystalloids over Gelatins** when resuscitating patients with sepsis or septic shock

gelatin-containing plasma expanders vs crystalloids and albumin ☆☆☆

Claudia Moeller^{a, 1}, Carolin Fleischmann^{a, b, 1}, Daniel Thomas-Rueddel^{a, b}, Vlasislav Vlasakov^a, Bram Rochweg^c, Philip Theurer^a, Luciano Gattinoni^d, Konrad Reinhart^{a, b},  , Christiane S. Hartog^{a, b}

What are GOALS for EGDT???

2012

MAP > 65 mmHg

Urine Output
>0.5 ml/kg/hr

Capillary Refill <
2 sec

CVP 8-12 mmHg

ScvO₂ > 70%

Serum Lactate < 4
mmol/L

Dynamic over static variables

CVP and ScvO₂ : Not reliable
and fail to show improve
outcome

MAP 65 Vs 85 mmHg : No
difference outcome

Serum lactate guided
resuscitation : Significant
reductin in Mortality

VASOACTIVE MEDICATIONS

- Norepinephrine as the first-choice vasopressor
- Adding Epinephrine (20-50 mcg/min)/Vasopressin (upto 0.03 U/min)
- Dopamine only in selected cases (risk of arrhythmia)
- Dobutamine for hypoperfusion with fluid & vasopressor agents
- Phenylephrine : Still controversial !!!

Dose of Norepinephrine

The mean dose of norepinephrine ranges from 0.2 to 1.3 mcg/kg/min with a maximum dosage of 3.3 mcg/kg/min

When to consider adding another vasopressor ????

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

FEBRUARY 28, 2008

VOL. 358 NO. 9

Potential benefit in the population requiring
 $\geq 15 \mu\text{g}/\text{min}$ of norepinephrine

and Dieter Ayers, M.Sc., for the VASST Investigators*

Corticosteroids

Against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability

When to Start and How much ??

- Only if Adequate fluid therapy and vasopressor fail to achieve target MAP
- IV hydrocortisone at a dose of 200 mg per day
- Use continuous flow



Blood Products

RBC transfusion only when hemoglobin concentration decreases to **< 7.0 g/dL** in adults in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, or acute hemorrhage

Against the use of **erythropoietin** for treatment of anaemia associated with sepsis

A Randomized Trial of Protocol-Based Care for Early Septic Shock



Blood Products cont:

Against the use of fresh frozen plasma to correct clotting abnormalities in the absence of bleeding or planned invasive procedures

Prophylactic platelet transfusion when counts are $< 10,000 /\text{mm}^3$ ($10 \times 10^9/\text{L}$) in the absence of apparent bleeding and when counts are $< 20,000/\text{mm}^3$ ($20 \times 10^9/\text{L}$) if the patient has a significant risk of bleeding

Higher platelet counts ($\geq 50,000/\text{mm}^3$ [$50 \times 10^9/\text{L}$]) are advised for active bleeding, surgery, or invasive procedures

Giancarlo et al (2009) Italian Society of Transfusion Medicine and Immunohaematology (SIMTI) Working Party: *Blood Transfus* 2009; 7: 132-150

SSC Guidelines Against

Use of IV immunoglobulins

Use of blood purification techniques (CPFA, Hemoadsorption etc)

Use of Antithrombin

No recommendation regarding the use of thrombomodulin or heparin

Blood Culture

Appropriate routine microbiologic cultures (including blood) be obtained before starting antimicrobial therapy

Appropriate routine microbiologic cultures always include at least two sets of blood cultures (aerobic and anaerobic)

Antibiotic Therapy

Administration of IV antimicrobials should be initiated **as soon as possible** after recognition and within one hour

Empiric therapy with one or more antimicrobials for patients presenting with sepsis or septic shock. **Daily Assessment** for pathogens

Antibiotic **de-escalation** should be done within first few days depending on clinical improvements and/or evidence of infection resolution

Antibiotic Therapy

Antimicrobial treatment duration of **7 to 10 days** is adequate for most serious infections

Longer Duration : Only for poor clinical resolution

Recommend **against** sustained systemic anti-microbial prophylaxis in patients with **severe inflammatory states of noninfectious origin** (e.g., severe pancreatitis, burn injury)

BICARBONATE THERAPY

Against the use of sodium bicarbonate therapy to improve hemodynamics or to reduce vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with **pH \geq 7.15**

Sepsis Bundles

WITHIN 3 HOURS

1. Measure *lactate* level
2. Obtain *blood cultures*
3. I.V broad spectrum *antibiotics*
4. I.V *30ml/kg crystalloid* for hypotension or lactate $\geq 4\text{mmol/L}$

WITHIN 6 HOURS

1. Apply *vasopressors* (MAP $\geq 65\text{mmHg}$)
2. *Re-assess* volume status and tissue perfusion
3. *Re-measure lactate*

**Initial Assessment and Resuscitation should be followed
Secondary Assessment**

Preoperative Assessment

Detailed History & Examination + Airway Assessment

Investigations

- Full blood count /BUN/ Creatinine/Electrolyte/Coagulation profile/Blood Glucose
- CXR /EKG
- Imaging studies – May be helpful for decision of *source control procedure*

Diagnosis and the clinical course



Timing and Degree of Surgery

!!! Immediate goal !!!

Aequate source control with the least physiological embarrassment

Communication with Surgical Team is critically important

Preoperative Preparation

- Optimize patient using SSC guidelines (Bundles)**
 - Heamodynamic stability**
 - Correction of coagulopathy**
 - Aspiration prophylaxis**
 - Blood glucose control (≤ 180 mg%)**
- Prepare for Post-operative plan (ICU or HDU)**
- Explain the possible risks and outcome after anesthesia and surgery with patients and family**

Choice of Anesthetic Technique

**Severity of Sepsis
(esp CVS stability)**

Neuraxial Anesthesia

- Relative contraindication
- Exaggerated physiological response
- Coagulopathy
- Epidural abscess, epidural haematoma

**Nature and extent
of surgical
procedure**

General Anesthesia

- CVS instability
- Need for RSI
- Easily desaturate
- Can provide high FiO₂
- Lungs protective ventilation

**Expertise of
anesthesiologist on
specific technique**

Pheripheral nerve block

- Can avoid systemic effects of IV or inhalational agents
- CVS stability
- Pharmacokinetic of LA on acidic environment

Intraoperative Management

Before Induction

- Emergency medications/ anesthetic machine/ airway and resuscitation equipment
- Prepare for i.v lines (16 – 14 G)

Monitoring

- EKG, SpO₂, NIBP, EtCO₂, Temperature, Urine Output
- Other monitoring (IBP, CVP, ScVO₂, lactate, CO monitoring, TEE only if available)

Induction

- RSI is the usual technique of choice
- Preoxygenation with 100% O₂
- *Step-wise* process, *Small* doses of i.v agents, *Titrated* to clinical response
- The CARE how anesthetic agents are administered

Choosing an Induction Agent

Etomidate (0.2 to 0.3 mg/kg)

- Rapid onset and short DOA
- CVS stability
- Issue of *Adrenal insufficiency*
- Current literature doesn't support absolute mortality effect

Midazolam (0.1-0.3 mg/kg)

- Rapid onset, short DOA
- Directly relax laryngeal muscle
- Decrease in BP (approx 10%)
- Reflex increase in HR
- Cardiac index is well maintained

Ketamine

- I.V 1-2 mg/kg
- Rapid onset and short DOA
- Increase in HR, BP, SVR
- Increase in myocardial O₂ demand
- Maintain airway reflexes and increase secretion
- Useful for septic shock

Choosing an Induction Agent

Continue...

Propofol (1.5 – 2 mg/kg)

- Rapid onset, short DOA
- Inhibit airway reflexes
- Reduce BP, SVR (30% from base line)
- Impaired baroreceptor reflex
- Inhibitory effect on Neutrophil
- Do not affect by renal dysfunction

Thiopentone (3-5mg/kg)

- Rapid onset
- Short DOA
- Decrease SVR, Increase HR
- Direct Myocardial depression
- Immunosuppressive action
- Inhibition of granulocyte recruitment and phagocytosis

Marie Mullen(2012) Induction Agents for Endotracheal Intubation in Severe Sepsis and Septic Shock: Sepsis - *An Ongoing and Significant Challenge* : InTech Publish ;P 391-410

Role of Opioids

- Can enable to reduce dose of I.V agents.
- Can avoid decrease in SVR
- DOA may be increased by impaired *hepatic and renal function*
- Fentanyl/Alfentanil/Remifentanil : NO MORPHINE
- *Bradycardia* (Most are already tachycardiac)

Muscle Relaxants

- DNMBBA can be used for RSI (*hyperkalaemia*)
- For maintenance, cis-atracurium or atracurium has *organ independent metabolism.*
- Vecuronium is devoid of CVS insults (biliary and renal metabolism)

Perioperative Issues

Fluid

- Continue EGDT
- Accessed by by CVP, Capillary refill, *Urine Output* etc.
- Global O₂ Delivery : Serum lactate < 2 mmol/L and ScvO₂ >70%

Blood Components

- Keep Hb% 7-9 g/dl
- FFP and Platelet concentrate depending on amount of blood loss and presence of coagulopathy

Others

- Keep Normothermia
- Blood glucose level < 180 mg/dL
- Proper Timing of I.V Antibiotic

Mechanical Ventilation

Target

- SpO₂ >90% with pH >7.2 (permissive hypercapnia: PaCO₂ < 10 kPa)

FiO₂

- Adjusted with target SpO₂ (usually within 0.5-0.6)

Tidal Volume

- 6-8 ml/kg

Plateau pressures

- 30cmH₂O

Other

- Recruitment manoeuvres

PC-IRV

- Failed oxygenation with lungs protective ventilation strategy

Postoperative Management

- The ***Rate of blood loss*** should be minimal
- Decision to extubate depend on
 - Severity of Sepsis (Hemodynamic Instability)
 - Presence of comorbid diseases
 - Extensiveness of surgical procedures
- Monitoring should be continued at PACU / Pain Control
- Safe transfer of the patient to the ICU/HDU is essential
- A focused hand-over report is helpful for the ICU colleagues
- **Pre-resuscitation measurements** should be used to calculate the ICU APACHE score

Conclusion

A major healthcare issue with a high mortality

Definitions has been changed recently

Fluid resuscitation with vasopressors to optimize CVS parameter is critically important

Timely intervention to complete sepsis bundles can improve outcome

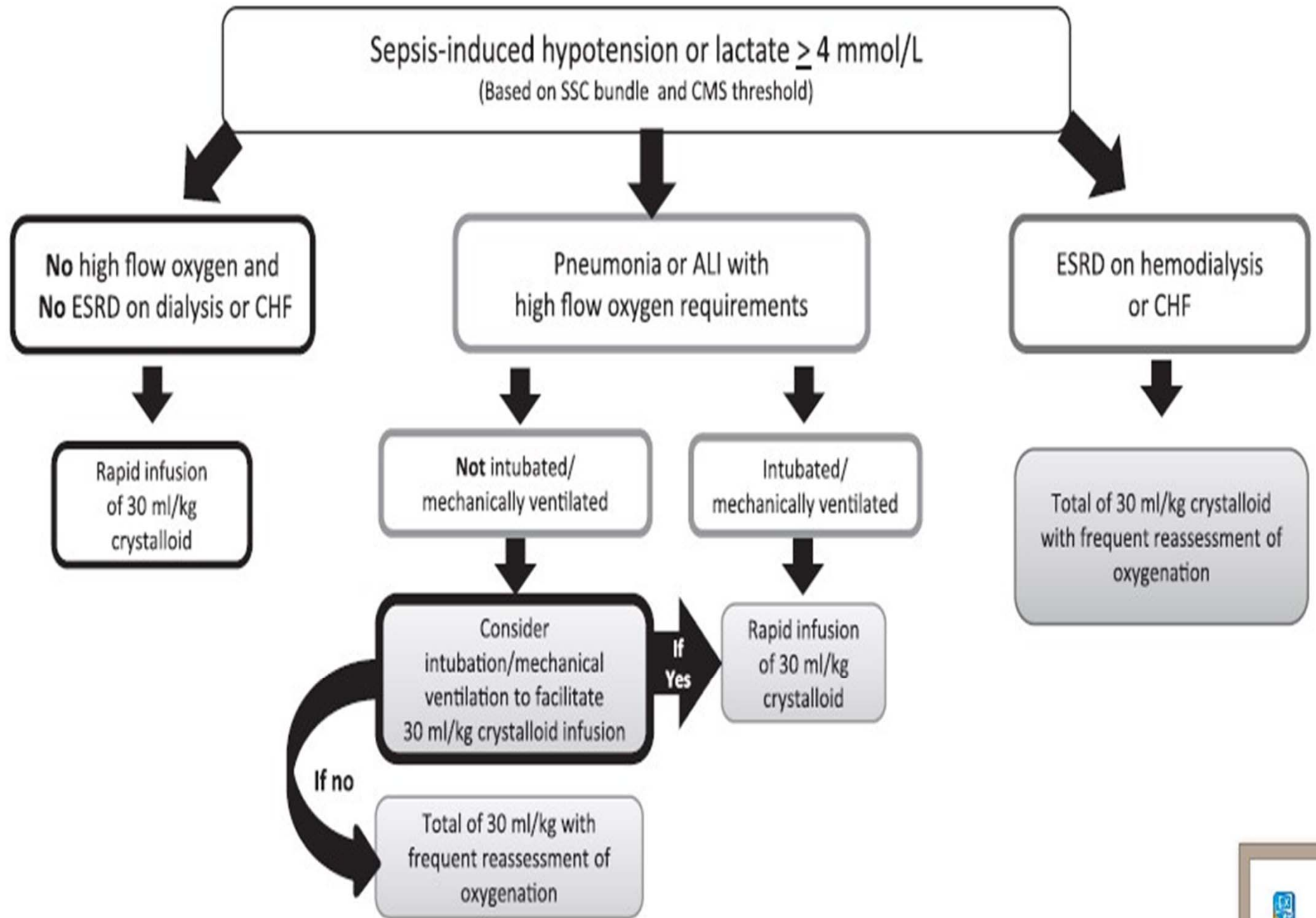
Conclusion

I.V Antibiotic should be started ASAP & Continued intraoperatively if required

Decision for source control with appropriate surgical intervention always depend on sincere communication between surgical and anaesthesia teams

If intubation is decided in ER, always consider appropriate anaesthetic agents depending on pharmacodynamic/kinetics in relation to sepsis

Application of Fluid Resuscitation in Adult Septic Shock



Thank You for Attention

