Sepsis: Management

ANUPOL PANITCHOTE, MD.
Division of Critical Care Medicine
Department of Medicine, Khon Kaen University, Thailand

Vital signs

- BT > 38.3 or < 36˚C
- HR > 90 bpm
- RR > 20 /min
- SBP < 90 or MAP < 70 mmHg

Symptoms

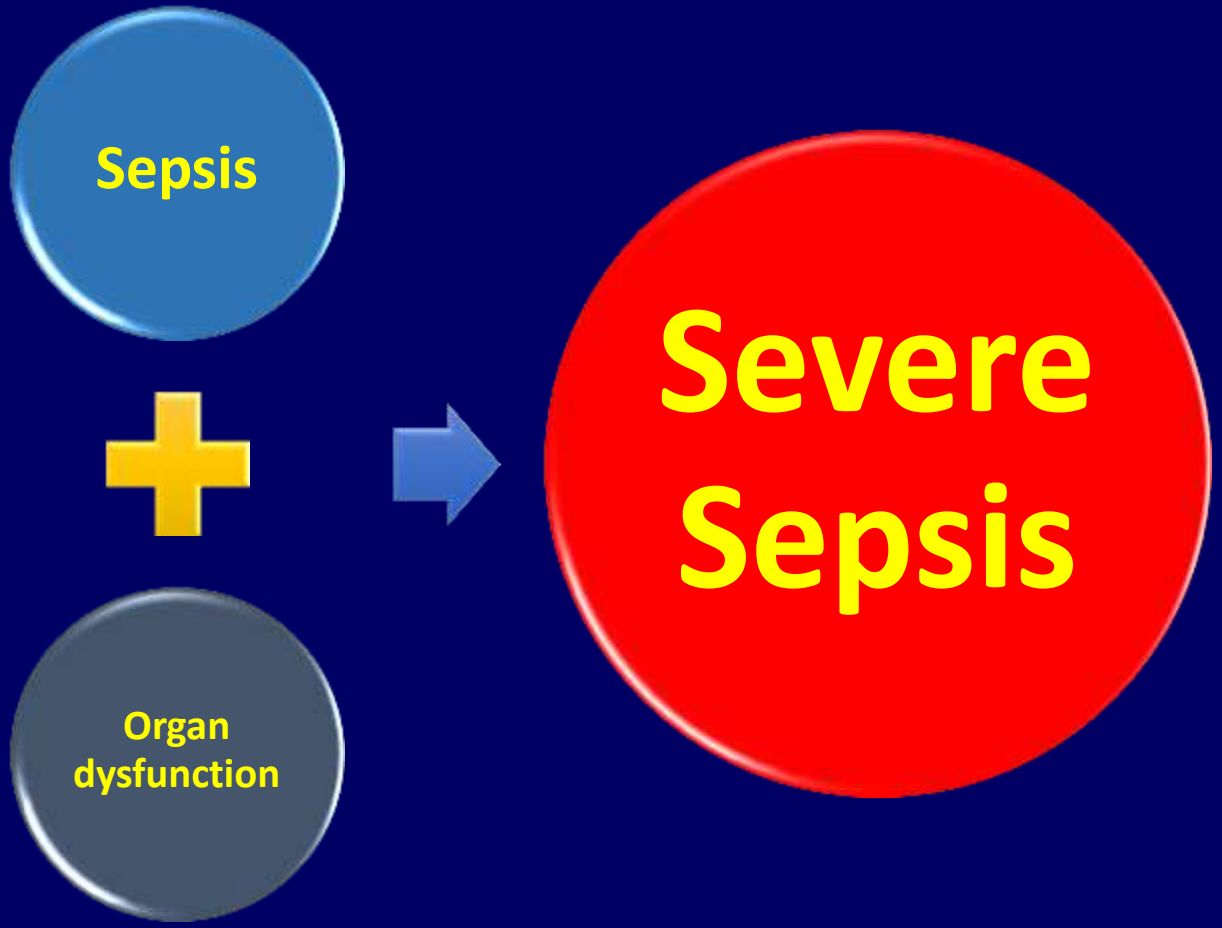
- Altered mental status
- Positive fluid balance
- Hyperglycemia
- Mottling
- Ileus

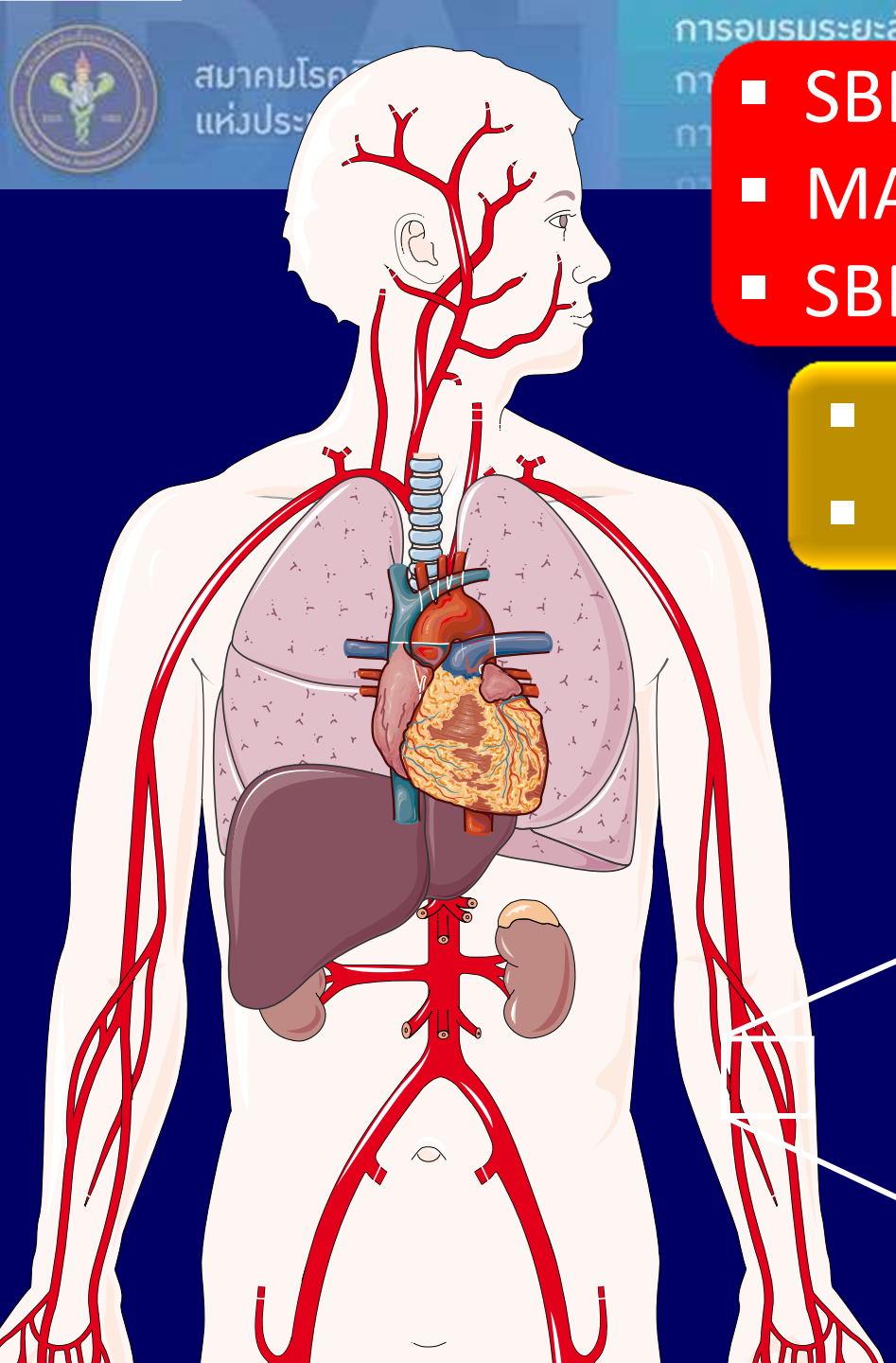
LAB

- WBC > 12000 or < 4000
- Band > 10%
- ↑ CRP
- ↑ procalcitonin
- ↑ Lactate

Systemic manifestation of sepsis

Definition

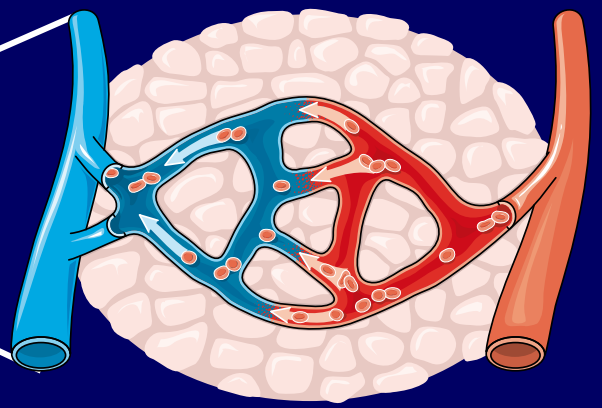




- SBP < 90 mmHg
- MAP < 70 mmHg
- SBP ↓ > 40 mmHg

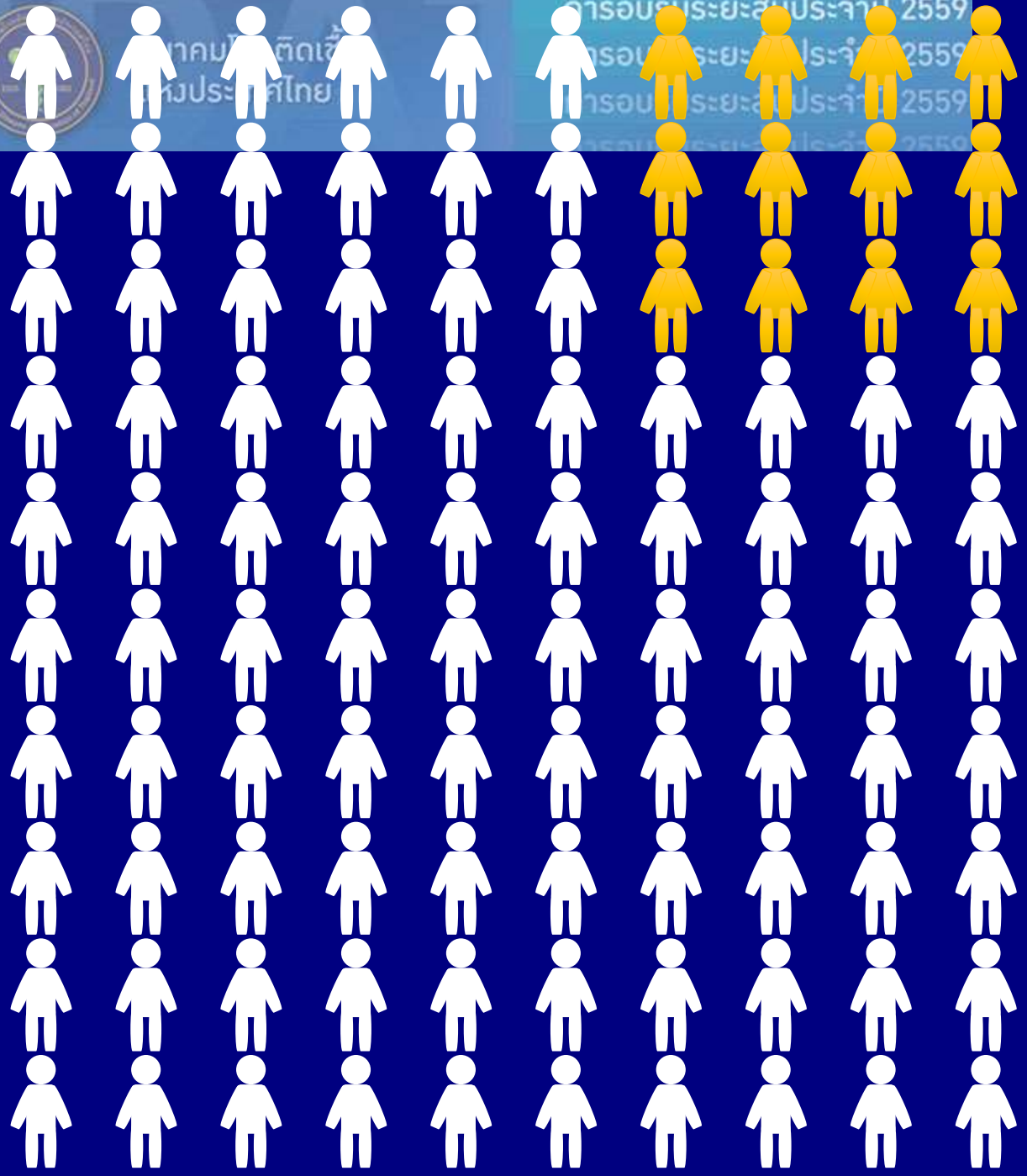
- PaO_2/FiO_2 < 250 (without pneumonia)
- PaO_2/FiO_2 < 200 (with pneumonia)

- Cr > 2 mg/dL
- Urine < 0.5 mL/kg/h x 2 hr.



- TB > 2 mg/dL

- Platelet < 100,000
- INR > 1.5
- Lactate > 2 mmol/L



SIRS negative severe sepsis

Kaukonen K-M, et al. NEJM 2015;372:1629-38.

Who are the SIRS-negative severe sepsis?

- Elderly patients
- ESRD
- Decompensated cirrhosis
- Immunocompromised patients
- Beta-blocker use

Revised definitions (2016)

Sepsis

- Life-threatening organ dysfunction
- Total SOFA score change ≥ 2 points (assume to zero in patients not known).
- Reflects an overall mortality 10%

Septic shock

- Preexisting hypotension requiring vasopressors and lactate > 2 mmol/L (18 mg/dL) despite adequate fluid resuscitation

Singer M, et al. JAMA 2016;315:801-10.

Sepsis screening: quick SOFA

≥ 2/3

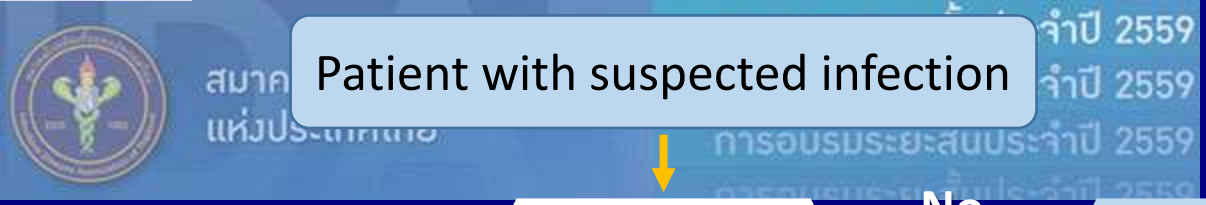
- GCS ≤ 13
- SBP ≤ 100 mmHg
- RR ≥ 22/min

- AUROC 0.81 for general ward
- AUROC 0.66 for ICU

Singer M, et al. JAMA 2016;315:801-10.

SOFA score

Variables	SOFA Score				
	0	1	2	3	4
Respiratory PaO_2/FiO_2, mmHg	≥ 400	< 400	< 300	< 200†	≤ 100†
Coagulation Platelets x $10^3/\mu L$	≥ 150	< 150	< 100	< 50	< 20
Liver Bilirubin, mg/dL	< 1.2	1.2-1.9	2.0-5.9	6.0-11.9	> 12.0
CVS Hypotension	MAP ≥ 70 mmHg	MAP < 70 mmHg	DoP < 5 or DoB (any dose)§	DoP 5.1-15, or Epi ≤ 0.1, or Norepi ≤ 0.1§	DoP > 15, or Epi > 0.1, or Norepi > 0.1§
CNS GCS scale	15	13-14	10-12	6-9	< 6
Renal Cr, mg/dL or urine output, mL/d	< 1.2	1.2-1.9	2.0-3.4	3.5-4.9 or < 500	> 5.0 or < 200



Patient with suspected infection

qSOFA ≥ 2?

No

Sepsis still suspected?

No

Monitor clinical condition; reevaluate for possible sepsis if clinically indicated

Yes

Yes

Assess for evidence of organ dysfunction

SOFA ≥ 2?

No

Monitor clinical condition; reevaluate for possible sepsis if clinically indicated

Yes

Sepsis

Despite adequate fluid resuscitation,
1. Vasopressors required to maintain ≥ 65 mmHg
AND
2. Serum lactate level > 2 mmol/L?

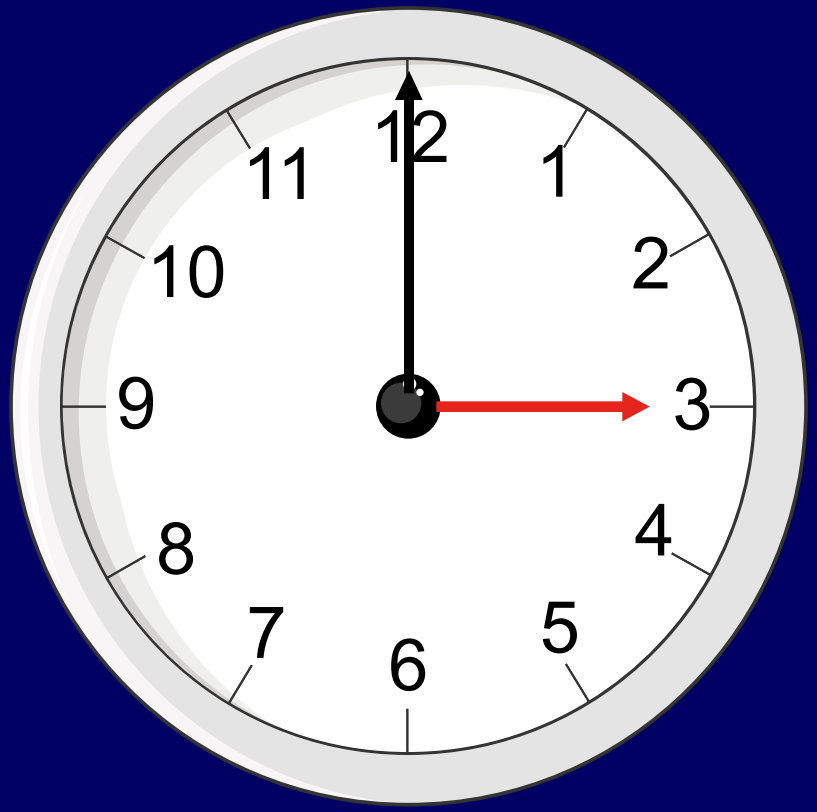
No

Yes

Septic shock

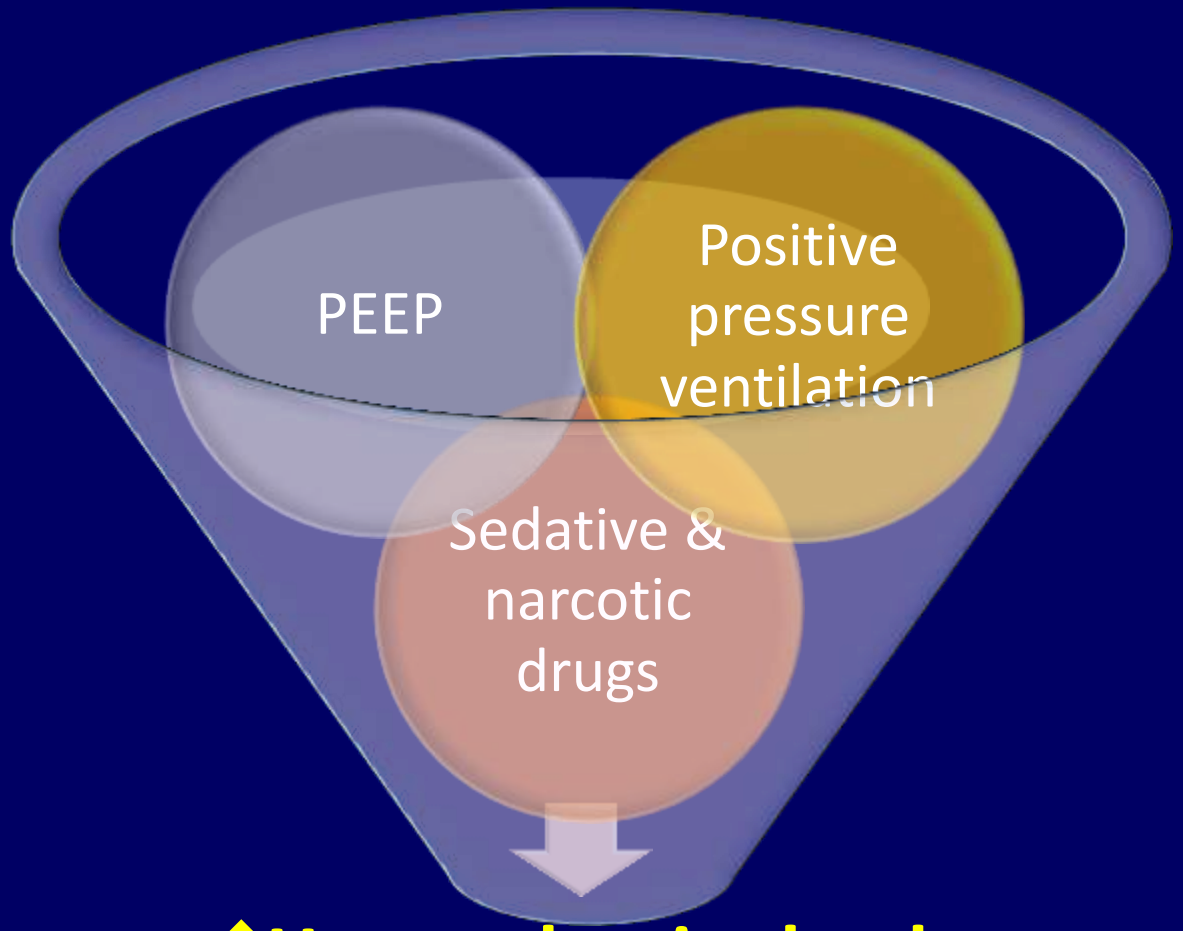
Singer M, et al. JAMA 2016;315:801-10.

Management in first 3 hours



- ✓Airway & breathing
- ✓Hemoculture & site culture
- ✓Antibiotic
- ✓Fluid

(1) Airway and breathing



↑Hypovolemic shock

- RR > 40 /min
- Respiratory muscle fatigue
- Hypoxemia
- Cardiac function impairment
- Severe metabolic acidosis
- Alteration of conscious

(2) Lab investigation

Hemoculture

- 2 specimens
- H/C from central line

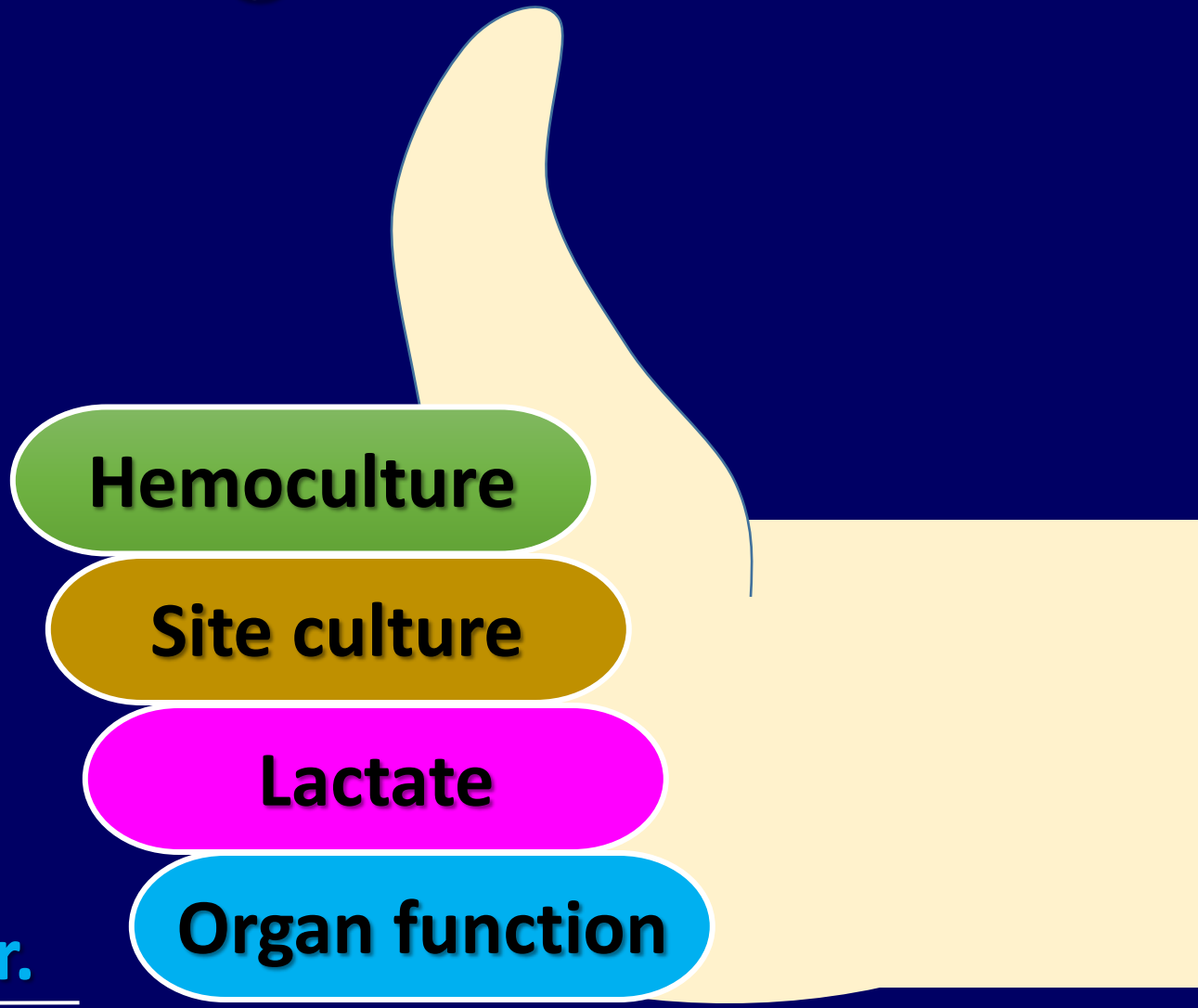
Site culture

- Sputum, urine, CSF, etc.

Organ function

- CBC, Coagulogram
- BUN, Cr, electrolyte
- LFT

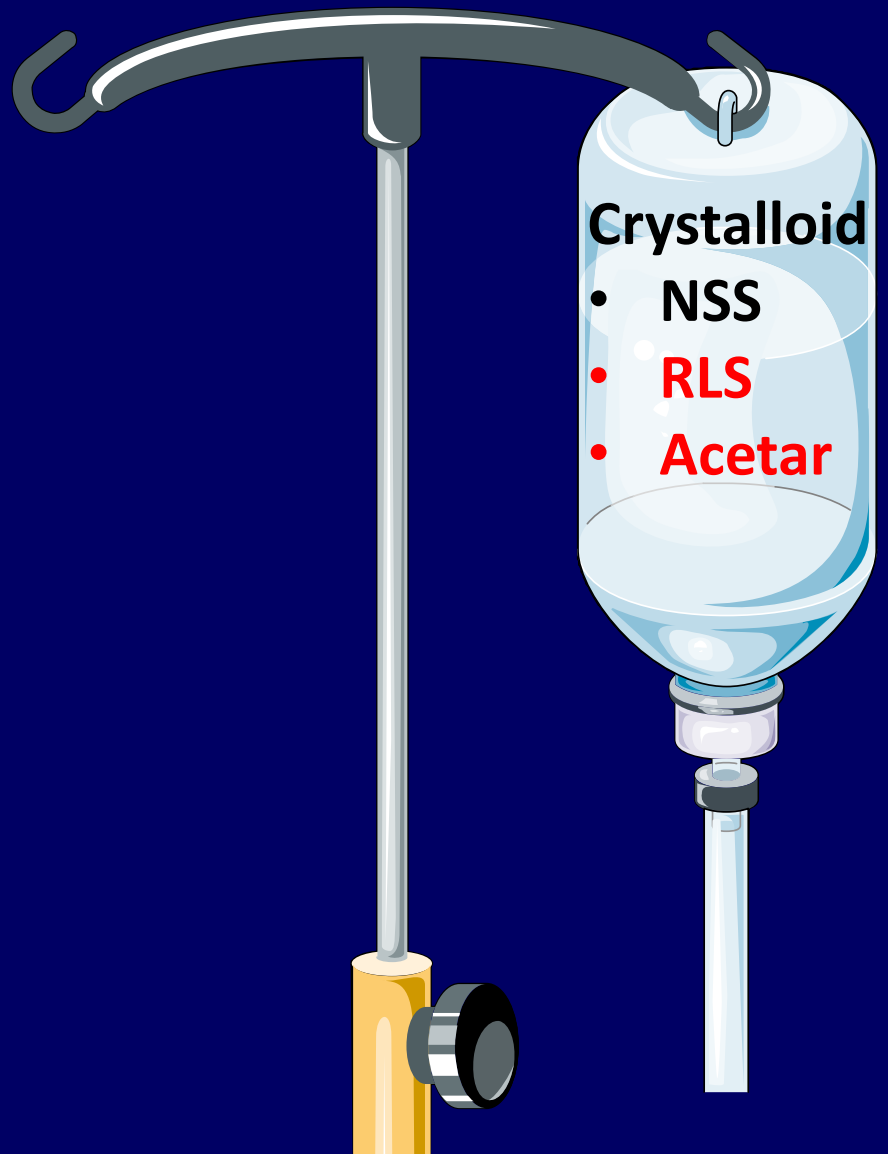
Lactate every 6 hr.



(3) Antimicrobial

Empirical antibiotic 1 HR.

(4) Fluid

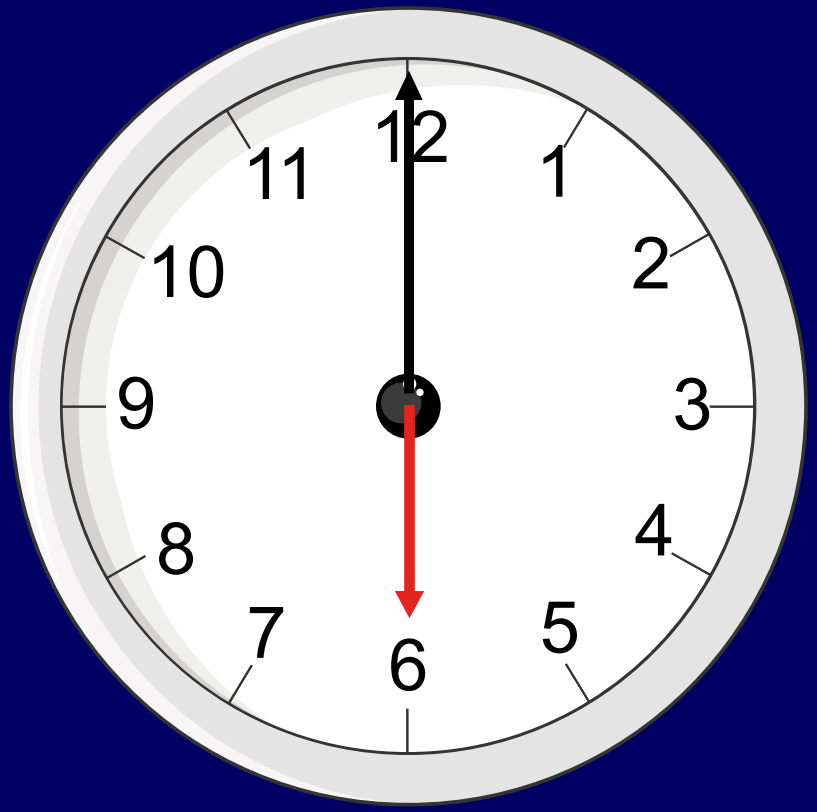


- ✓**500-1000 mL in 30 min**
- ✓At least **30 mL/kg**
- ✓NSS increased risk of hypercholremic metabolic acidosis and AKI
- ✓Use albumin solution in patient with crystalloid non-responsive
- ✗ Don’t use HES

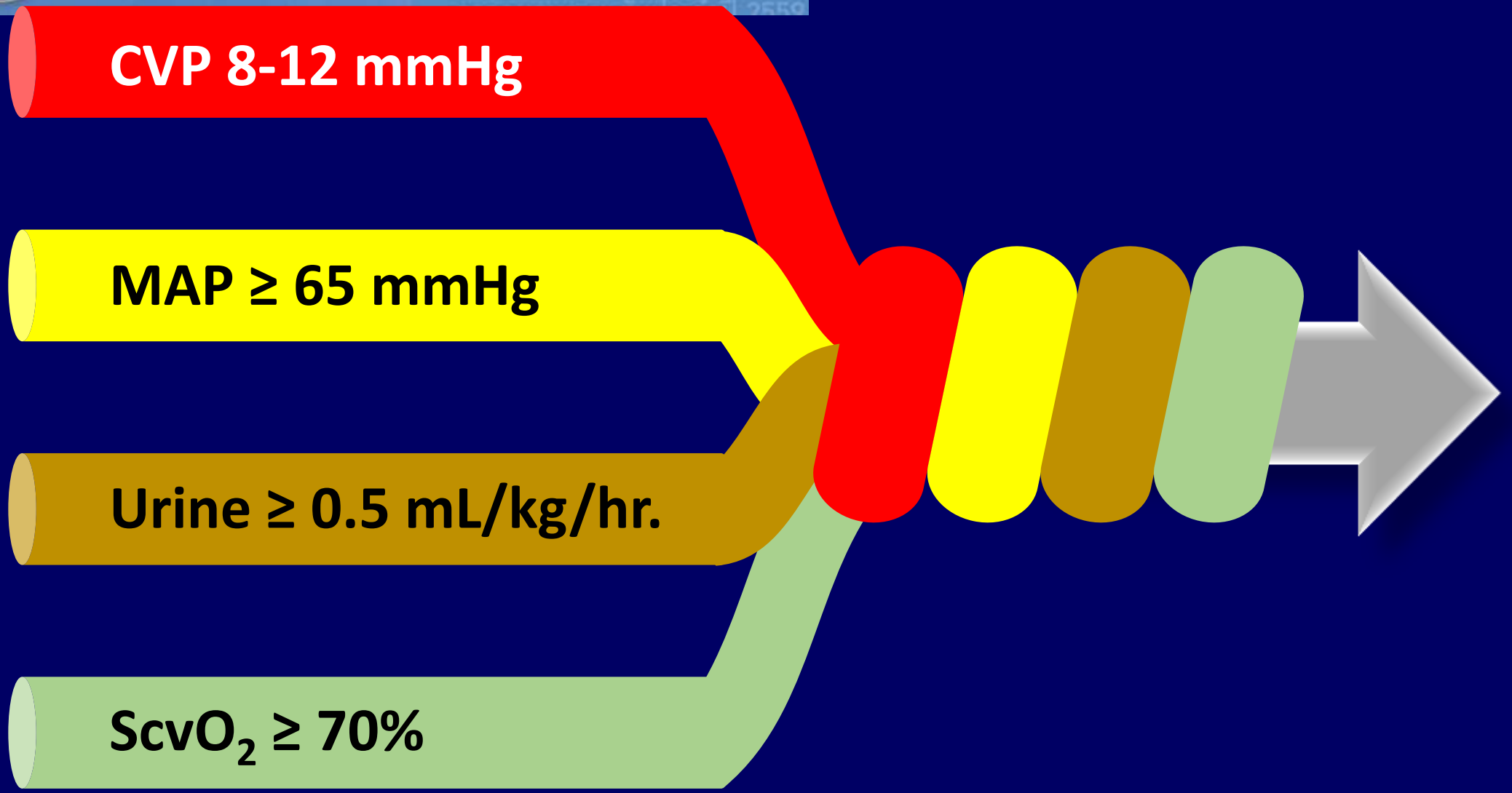
Chloride-restrictive strategy was associated with a significant **decrease** in the incidence of **AKI** and **use of RRT**

Yunos NM, et al. JAMA 2012;308:1566-72.

Management in 3-6 hours



- ✓Hemodynamic goal
- ✓Vasopressors
- ✓Microcirculation monitoring



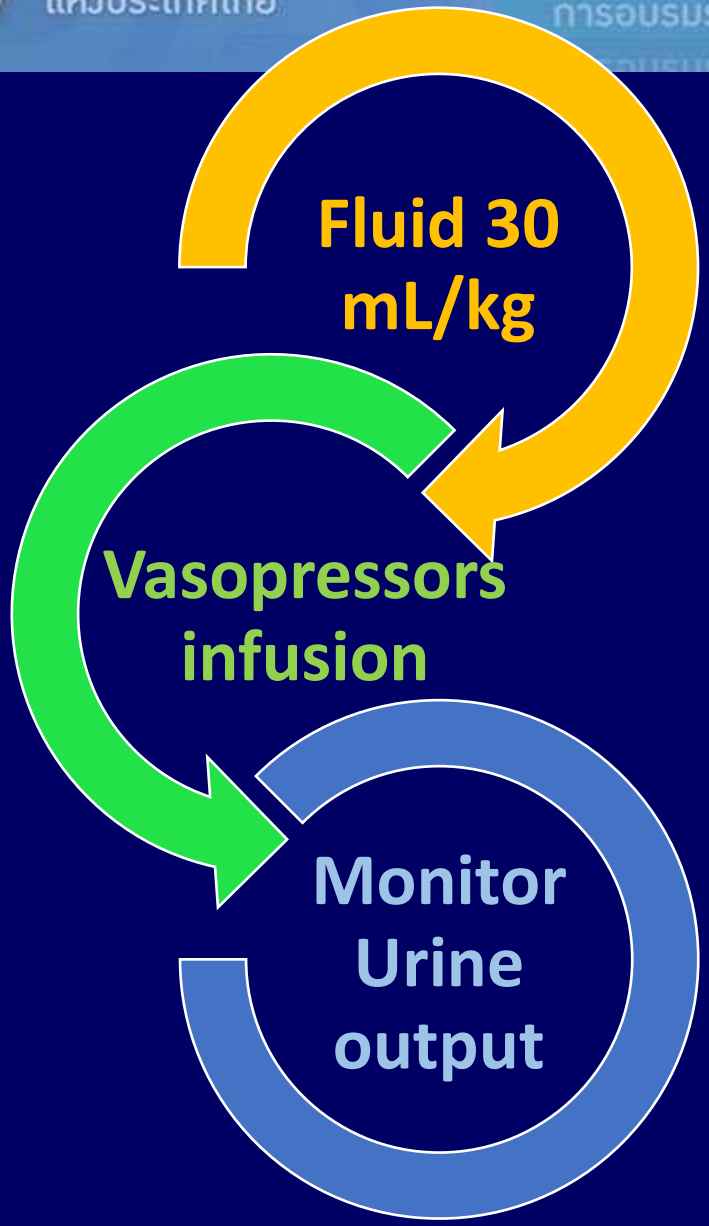
How to adequate fluid resuscitation?

- ✓Static parameter: CVP
- ✓Dynamic parameter: PPV, PLR

รพ.ชุมชน

รพ.จังหวัด

รพ.ศูนย์

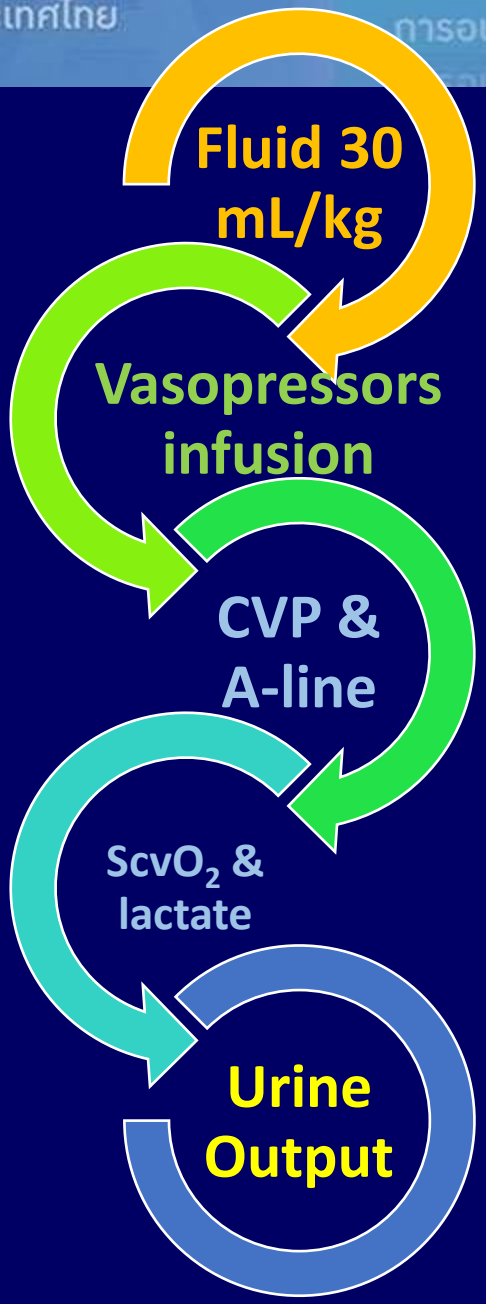


Primary Care

- ✗ CVP
- ✗ A-line
- ✗ CO

When will refer?

- ✓ Acute respiratory failure
- ✓ Oliguria
- ✓ Vasopressor non-responsive



Secondary Care

- ✗ A-line
- ✗ CO

When will refer?

- ✓ AKI III required CRRT

Fluid responsiveness

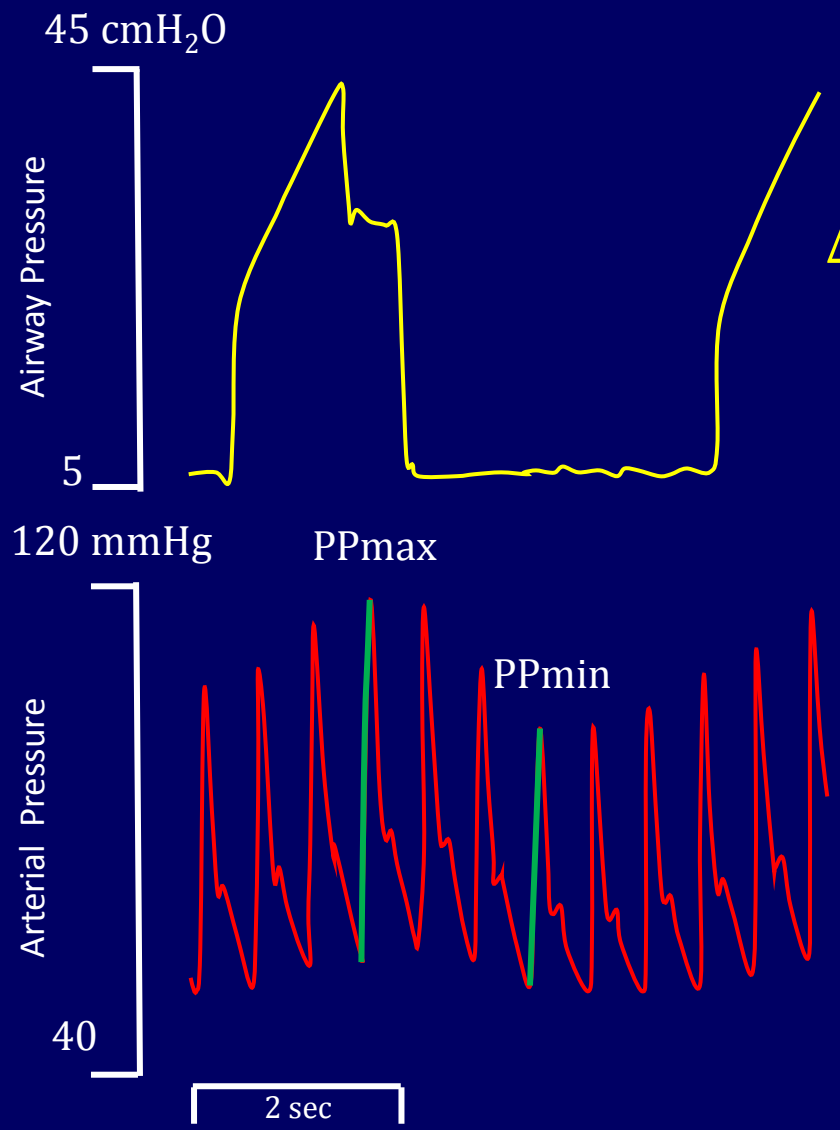
500 mL over 10-15 min

↑ CO 10-15%

Fluid challenge

- **Rate of infusion (over 30 min)**
  - Crystalloid 500-1000 mL
  - Colloid 300-500 mL
- **Goal: reversal of perfusion failure**
  - Hypotension, oliguria, tachycardia
- **Safety limit**
  - CVP 15 mmHg

Pulse pressure variation



$$\Delta PP\ (\%) = 100 \times \frac{(PP_{max} - PP_{min})}{(PP_{max} + PP_{min})/2}$$

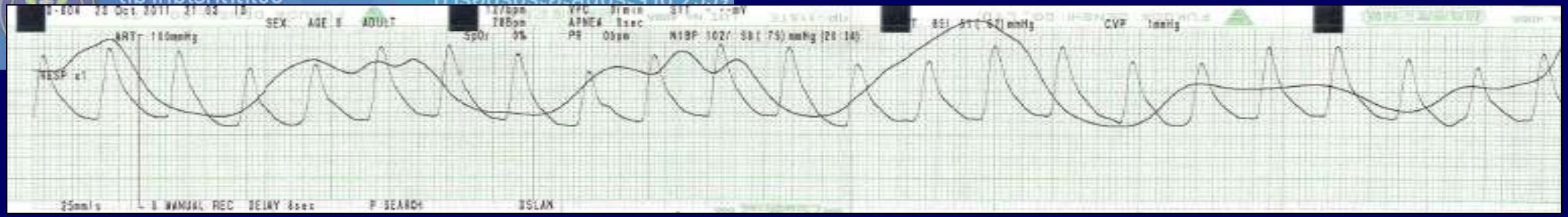
Defined as responder

- Threshold > 13%
- Sensitivity 94%
- Specificity 96%

Limitation of PPV/SVV

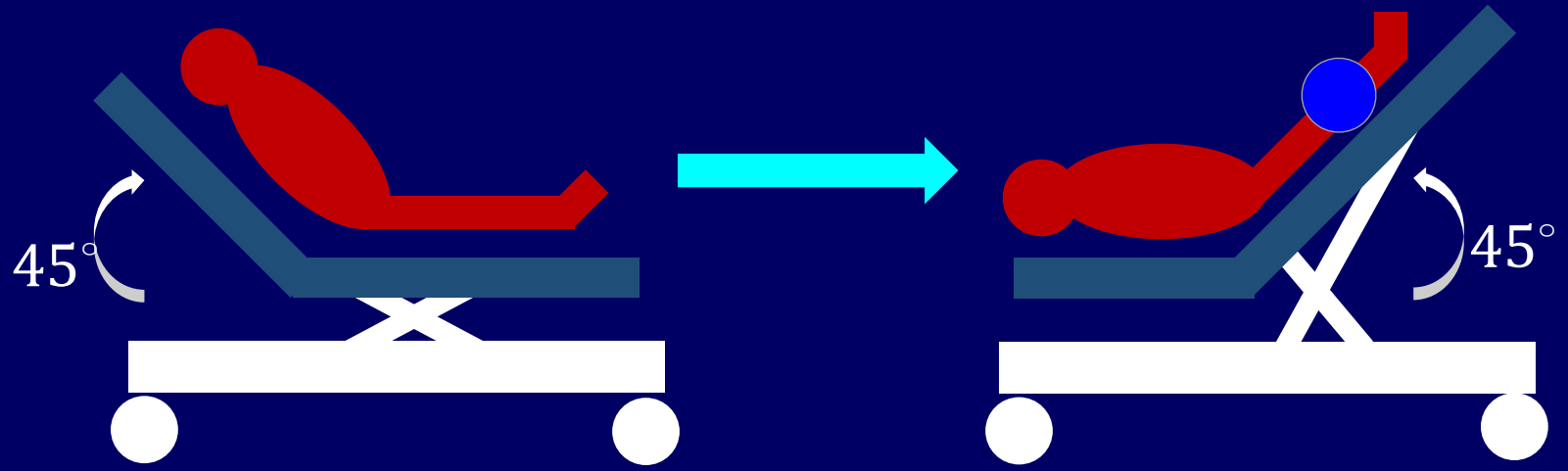
- **Spontaneous breathing (FN)**
- **Cardiac arrhythmias (FP)**
- **Low V_T < 8 mL/kg (FN)**
- **Tachypnea: HR/RR < 3.6 (FN)**
- **Low C_{rs} : < 30 mL/cmH_2O (independent with V_T)**
- High IAP (FP)
- Acute cor pulmonale (FP)
- Open chest surgery

การอบรมระยะสั้นประจำปี 2559

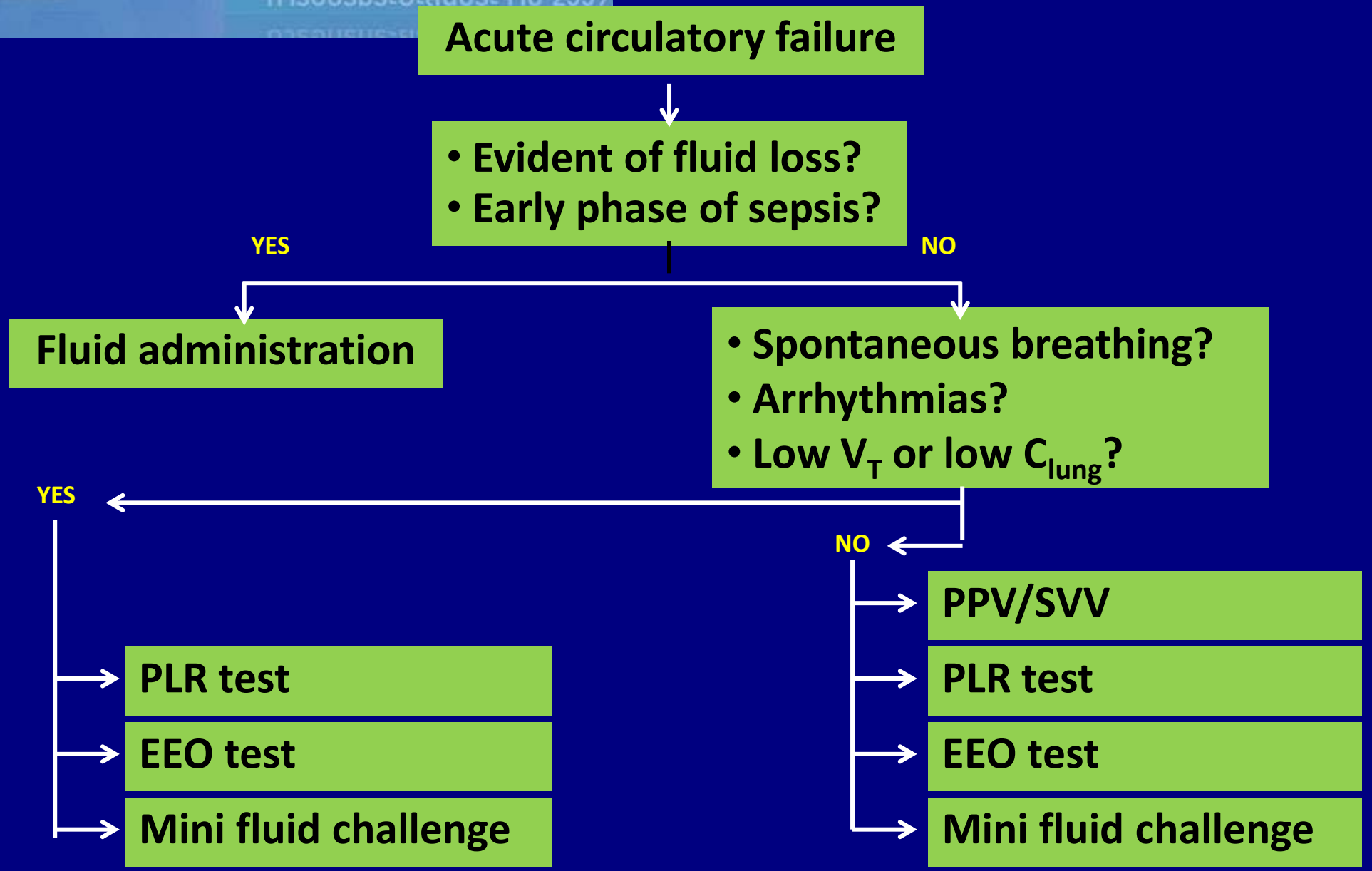


Fluid resuscitation

Passive leg rising test (PLR)



- Self volume challenge 300 ml
- Real time hemodynamic measurement (CO, A-line)
  - 30-90 sec
  - Aortic blood flow > 10%
  - Cardiac output > 10%
  - Pulse pressure increased ≥ 12% (low sensitivity)



EEO = End-expiratory occlusion test

Monnet X et al. In Annual update in intensive care and emergency medicine 2013.

Four phases in treatment of shock

	Salvage	Optimization	Stabilization	De-escalation
Principles	Life saving	Organ rescue	Organ support	Organ recovery
Goals	Correct shock	Maintain tissue perfusion	Zero or negative fluid balance	Mobilize fluid accumulation
Time	Min	Hours	Days	Days to weeks
Phenotype	Severe shock	Unstable	Stable	Recovering
Fluid therapy	Rapid boluses	Titrate fluid Fluid challenges	Minimal maintenance	Oral intake avoid IV

Monitoring of fluid optimization

Minimum	Salvage	Optimization	Stabilization	De-escalation
BP, HR	→	→	→	→
Capillary refill/ pulse volume	→	→	→	→
Lactate / ABG	→	→	→	→
Altered mental status	→			
Urine output		→	→	→
Fluid balance		→	→	→

Monitoring of fluid optimization

Additional monitoring	Salvage	Optimization	Stabilization	De-escalation
Echocardiography	→	→	- - -	- - -
CVP	- - -	→	- - -	- - -
$ScvO_2$		→	- - -	- - -
Cardiac ouput		→	- - -	- - -
Signs of fluid responsiveness		→		
Fluid challenge		→		

Vasopressors

- MAP ≥ 65 mmHg.
- Using vasopressor early in patients with **very low DBP.**
- **Norepinephrine** as the first-choice
- **Epinephrine** (added or substituted)
  - Increased blood lactate
  - Prevent use lactate clearance to guide resuscitation

How to choose target MAP (65-70 VS 80-85)?

- ✓ **Equivalent** in mortality rate
- ✓ Higher target BP increased rate of AF
- ✓ Higher target BP in chronic HT patients had **lower rate of AKI and RRT**

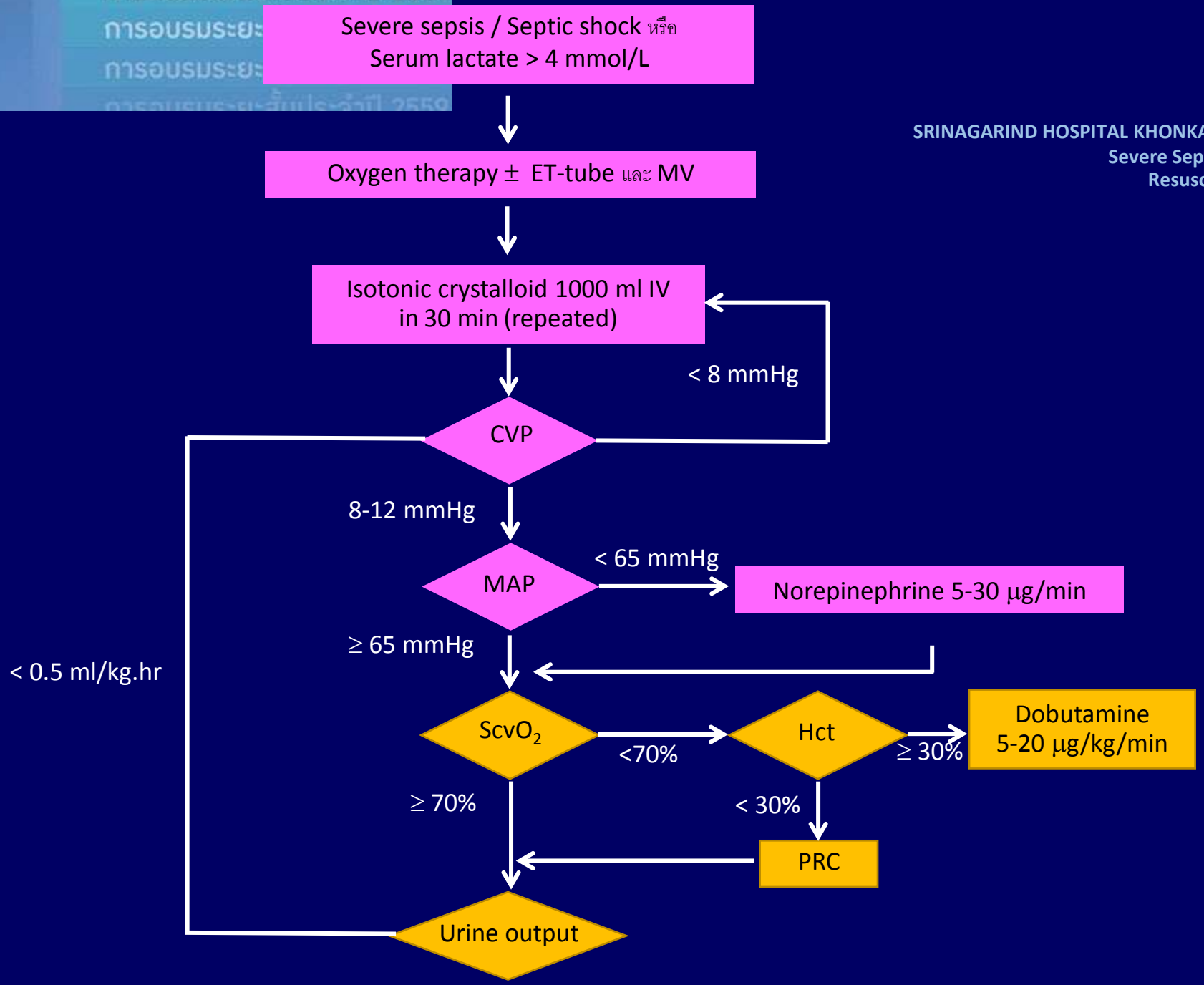
Asfar P, et al. NEJM 2014; 370:1583-93.

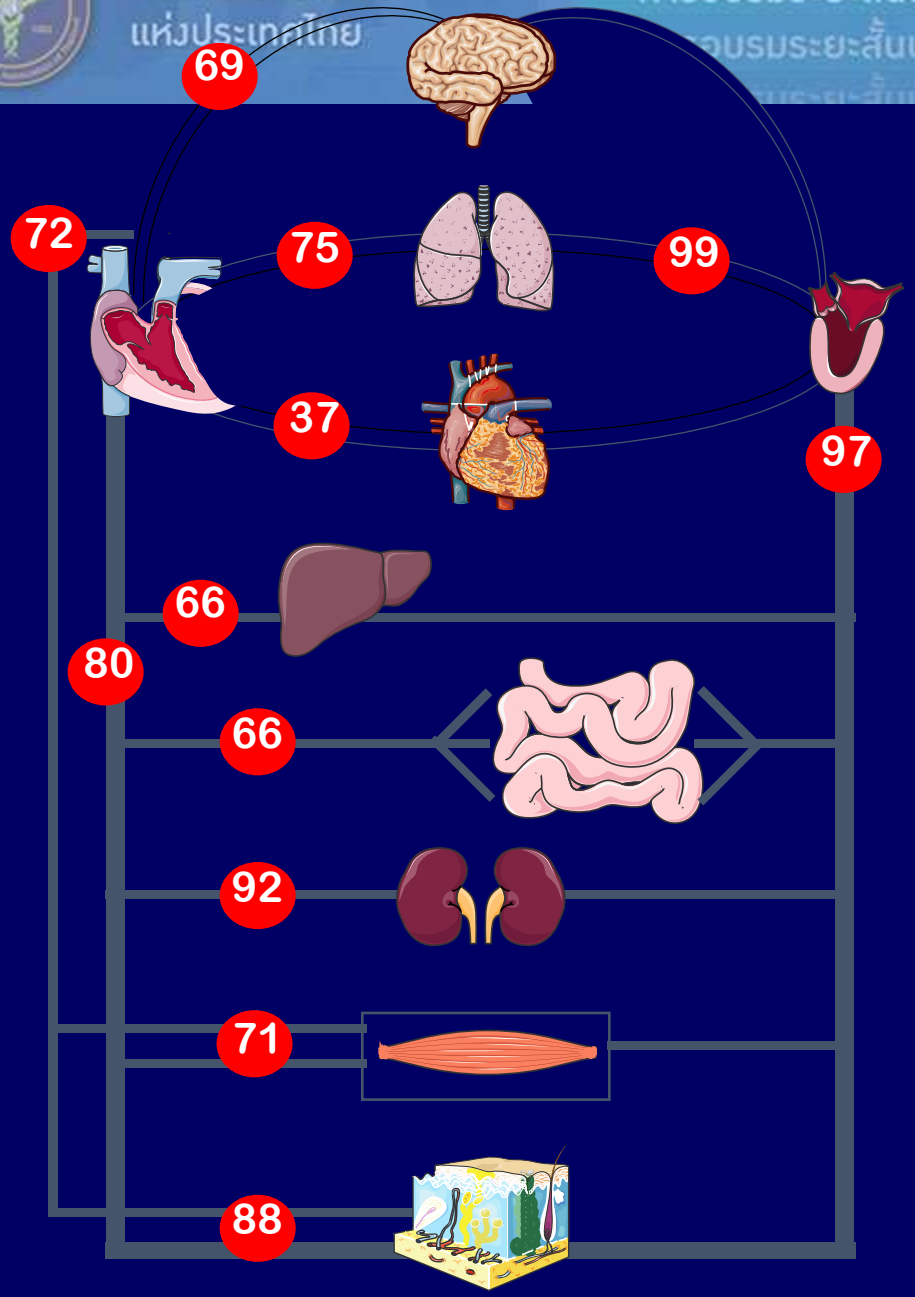
Corticosteroid

- **Vasopressor unresponsive** septic shock
- Continuous infusion hydrocortisone **200 mg/d**
- Improved shock reversal
- Not use ACTH stimulation test
- Cortisol level in patient suspected absolute adrenal insufficiency
- **Taper steroid** when vasopressors are no longer required

How to assessment the adequacy of circulation?

- ✓ MAP
- ✓ Urine output
- ✓ $ScvO_2$
- ✓ Lactate clearance
- ✓ pCO_2 gap





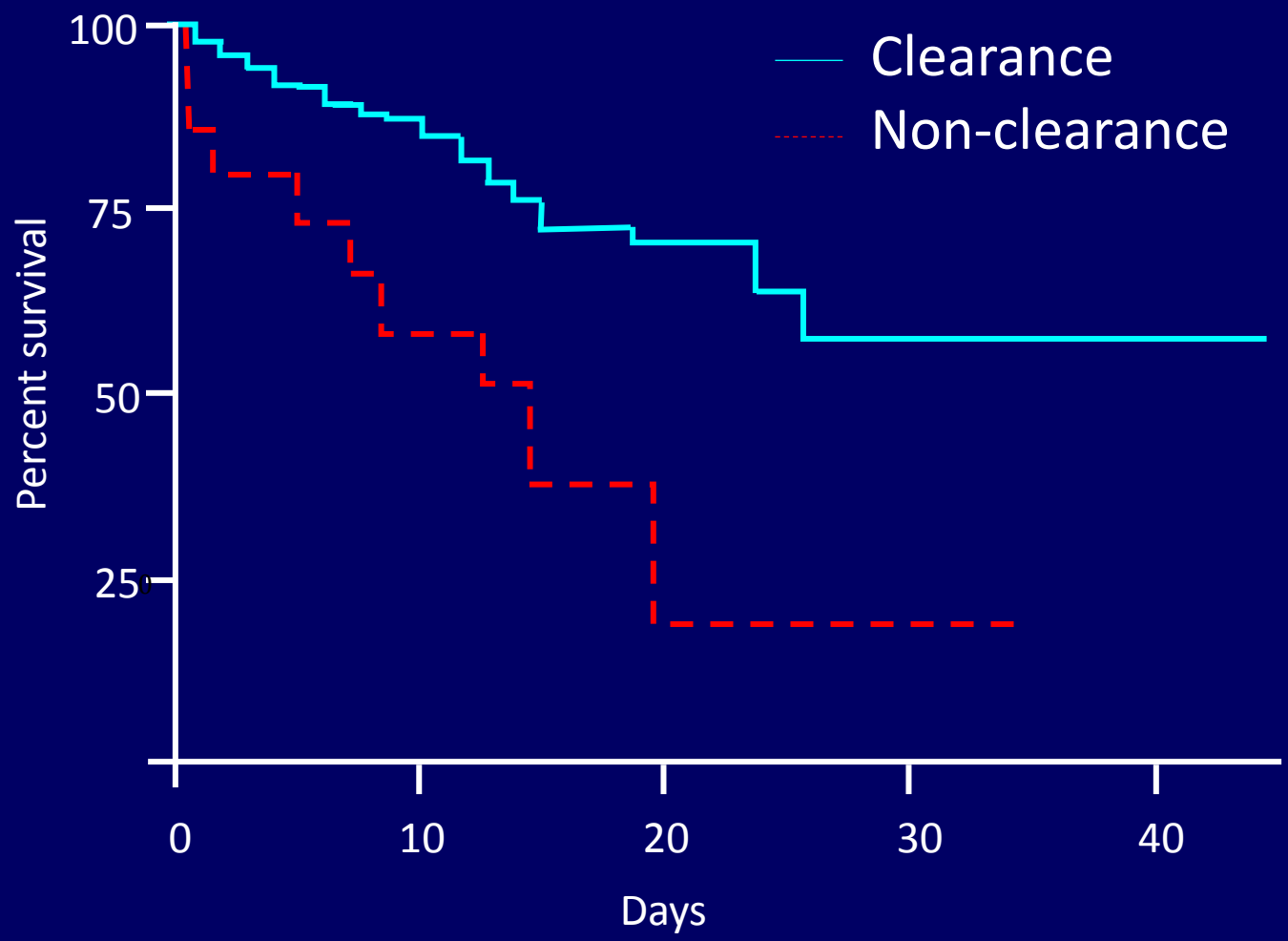
$ScVO_2 \geq 70\%$

- Dobutamine
- Blood transfusion

Lactate

- Insensitive marker of tissue dysoxia
- Normal value < 2 mmol/l
- Lactate clearance indicate adequacy of resuscitation

MULTICENTER STUDY OF EARLY LACTATE CLEARANCE AS A DETERMINANT OF SURVIVAL IN PATIENTS WITH PRESUMED SEPSIS



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 1, 2014 VOL. 370 NO. 18

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

The ProCESS Investigators*

Goal-Directed Resuscitation for Patients with Early Septic Shock

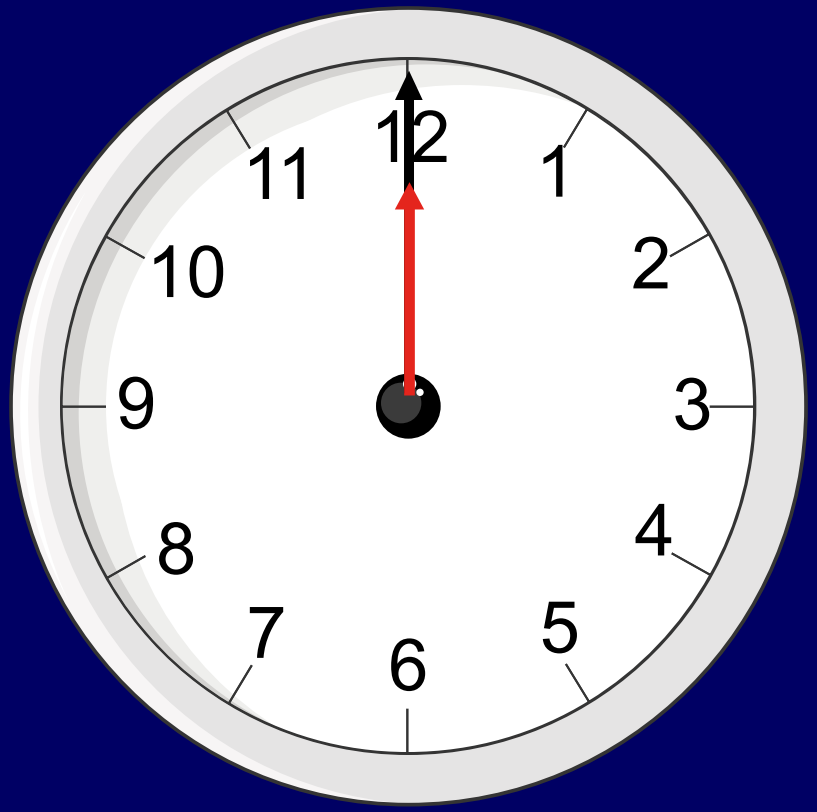
The ARISE Investigators and the ANZICS Clinical Trials Group*

Trial of Early, Goal-Directed Resuscitation for Septic Shock

Goal directed resuscitation VS Usual care

NO difference
in mortality rate

Management in 6-72 hours



- ✓Source control
- ✓Nutrition support
- ✓Sedation and analgesia
- ✓Transfusion of blood product
- ✓Renal replacement therapy
- ✓DVT prophylaxis
- ✓VAP prevention
- ✓Setting goal of care

Nutrition support

- EN within 24-48 hr.
- Hypocaloric feeding
- NPO in unstable hemodynamic
- Trophic feeding in hemodynamic improvement

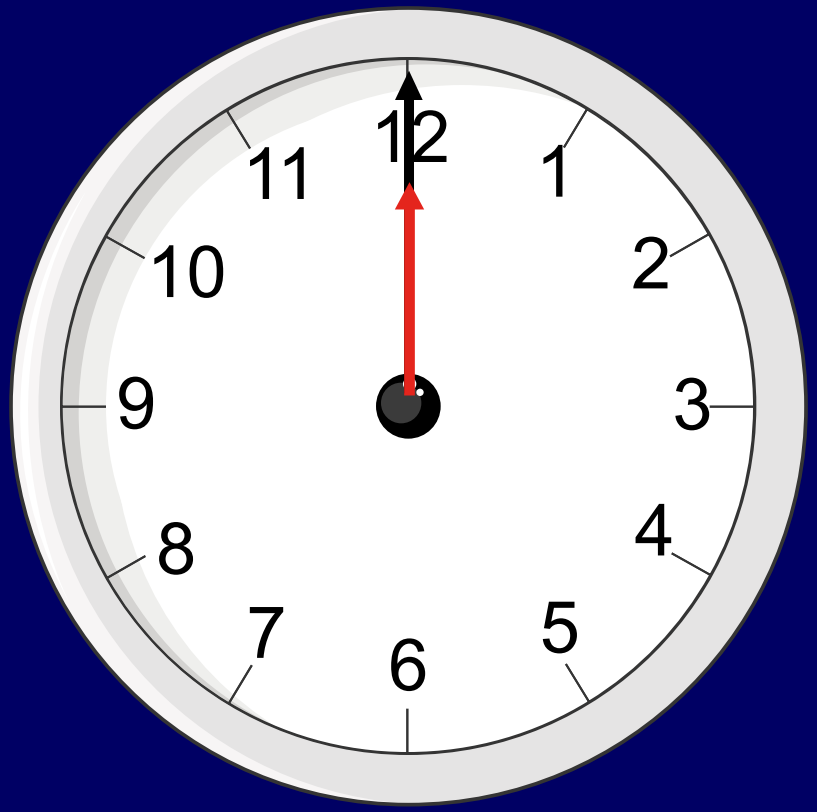
Sedation and analgesia

- Minimal sedation
- Light sedation level
- NMBA in early ARDS (PaO_2/FiO_2 < 150 mmHg)

Blood product

- PRC: Hb < 7 g/dL
- FFP: bleeding, high risk procedure
- Platelet: ≤ 10,000
  - ≤ 20,000: High risk bleeding
  - ≤ 50,000: Bleeding, invasive procedure

Management after 72 hours



- ✓De-escalation antibiotics
- ✓Weaning
- ✓Early mobilization

Early exercise and mobilization

Elements for save lives in septic shock

1. Early **recognition** in sepsis
2. Early administration of **antibiotics**
3. Early adequate **volume** resuscitation
4. Clinical assessment of the **adequacy of circulation**

CONCLUSION