Sepsis

台中榮總 兒童醫學部

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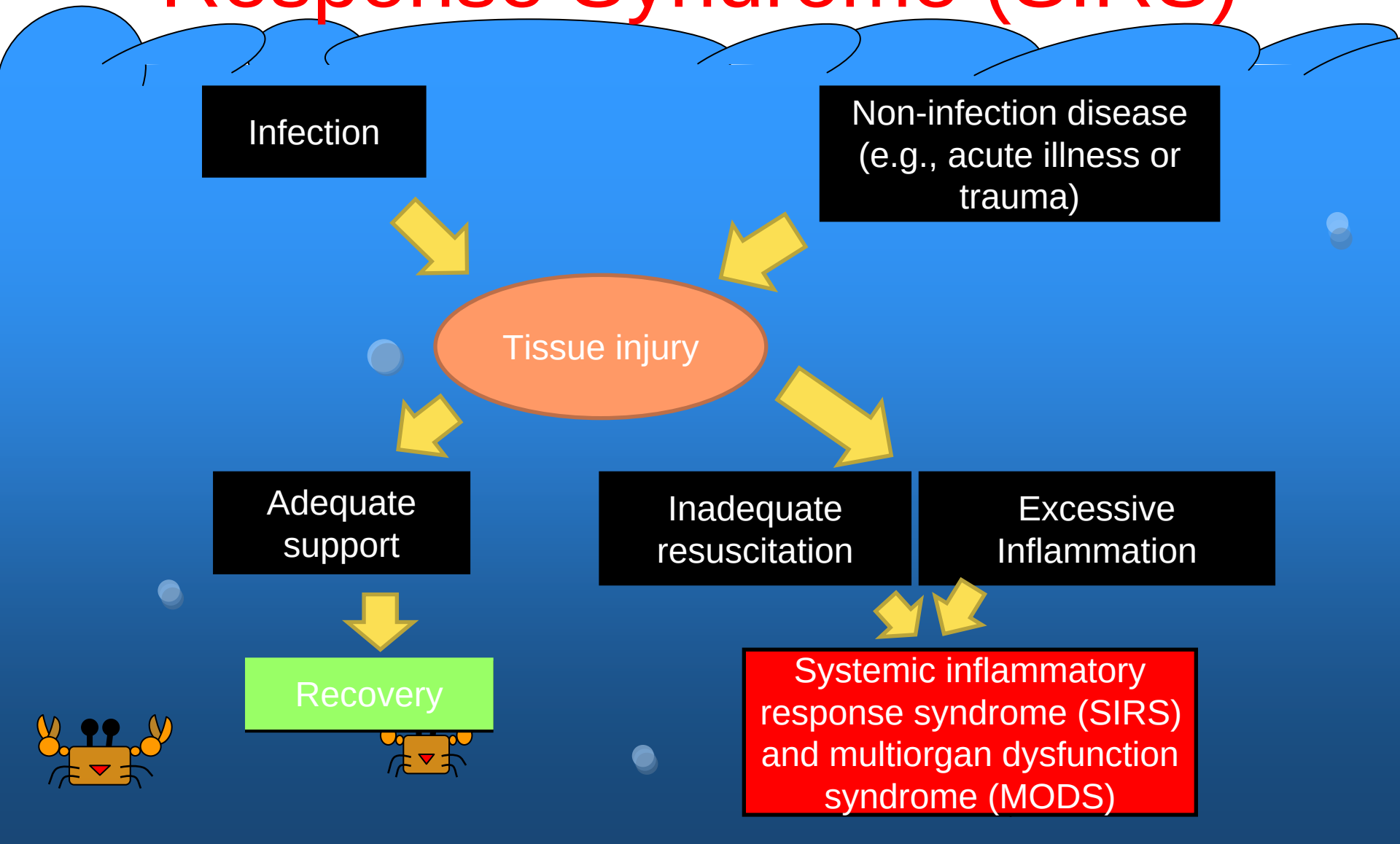
Systemic Inflammatory Response Syndrome (SIRS)

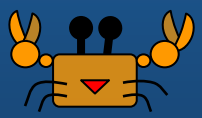
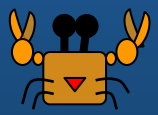
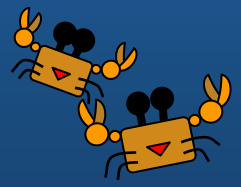


定義

- SIRS: >=2 criteria
  - 發燒 Core Temp > 38.5 or < 36 ℃
  - 心跳加速Unexplained tachycardia or bradycardia < 1 y
  - 喘 Tachypnea or mechanical ventilation for an acute process
  - 白血球降低或上升band form
    - Leukopenia or 10% immature neutrophiles
- Sepsis: 感染相關的SIRS
- Severe sepsis:
  - Cardiac vascular dysfunction
  - ARDS
  - >= 2 organs dysfunctions
- Septic shock:
  - sepsis and cardiovascular organ dysfunction

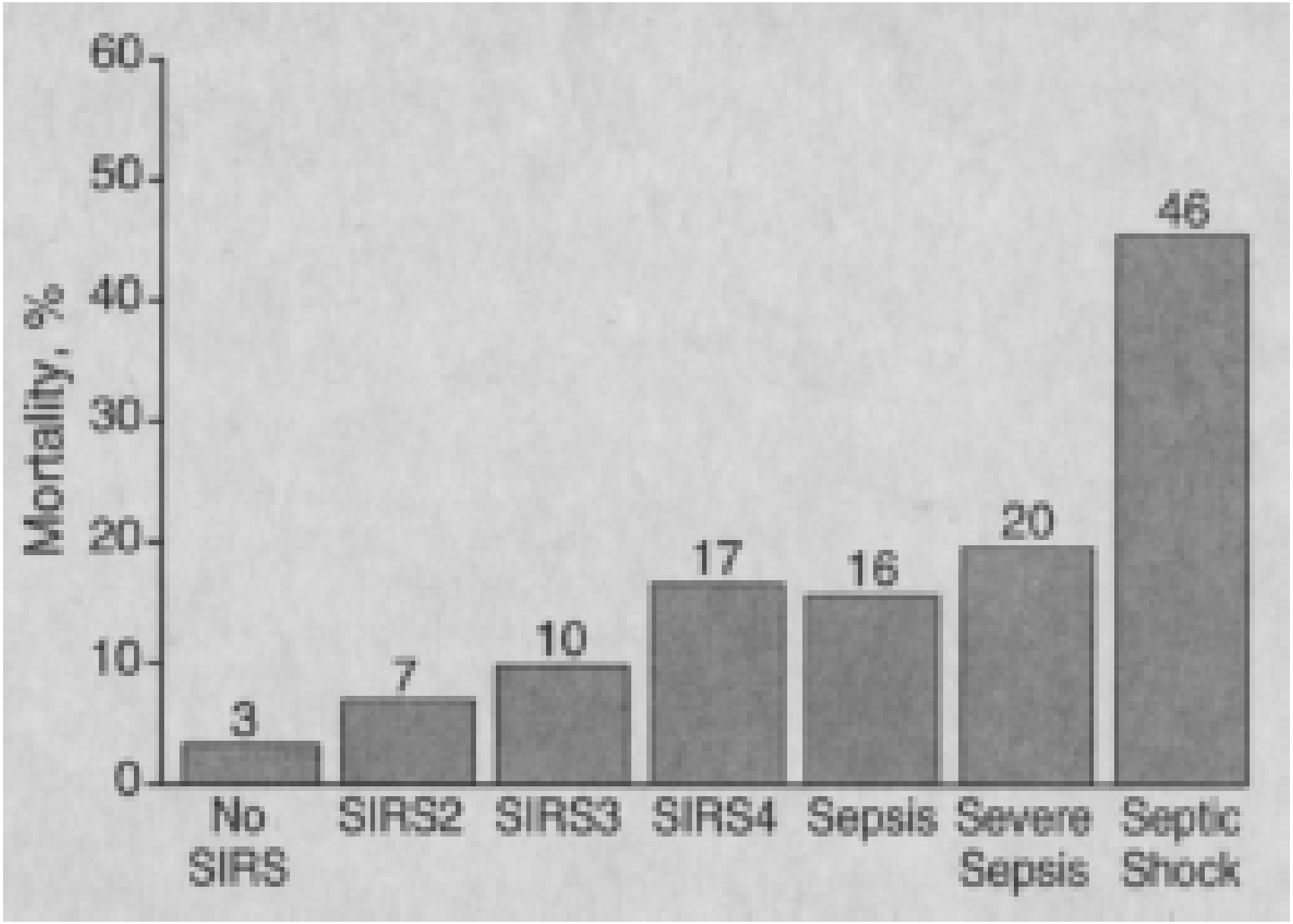
流行病學

- SIRS/sepsis 750,000 American adults, mortality 28~60%
- Children 0.56 cases/1000 person-year
- In-hospital mortality 10%
- Death rate increased with the numbers of organ failure
  - 7% single organ, 53.1% four organ
- Mean length of stay 31 days
- Cost US$ 40,600, annually $1,970,000,000

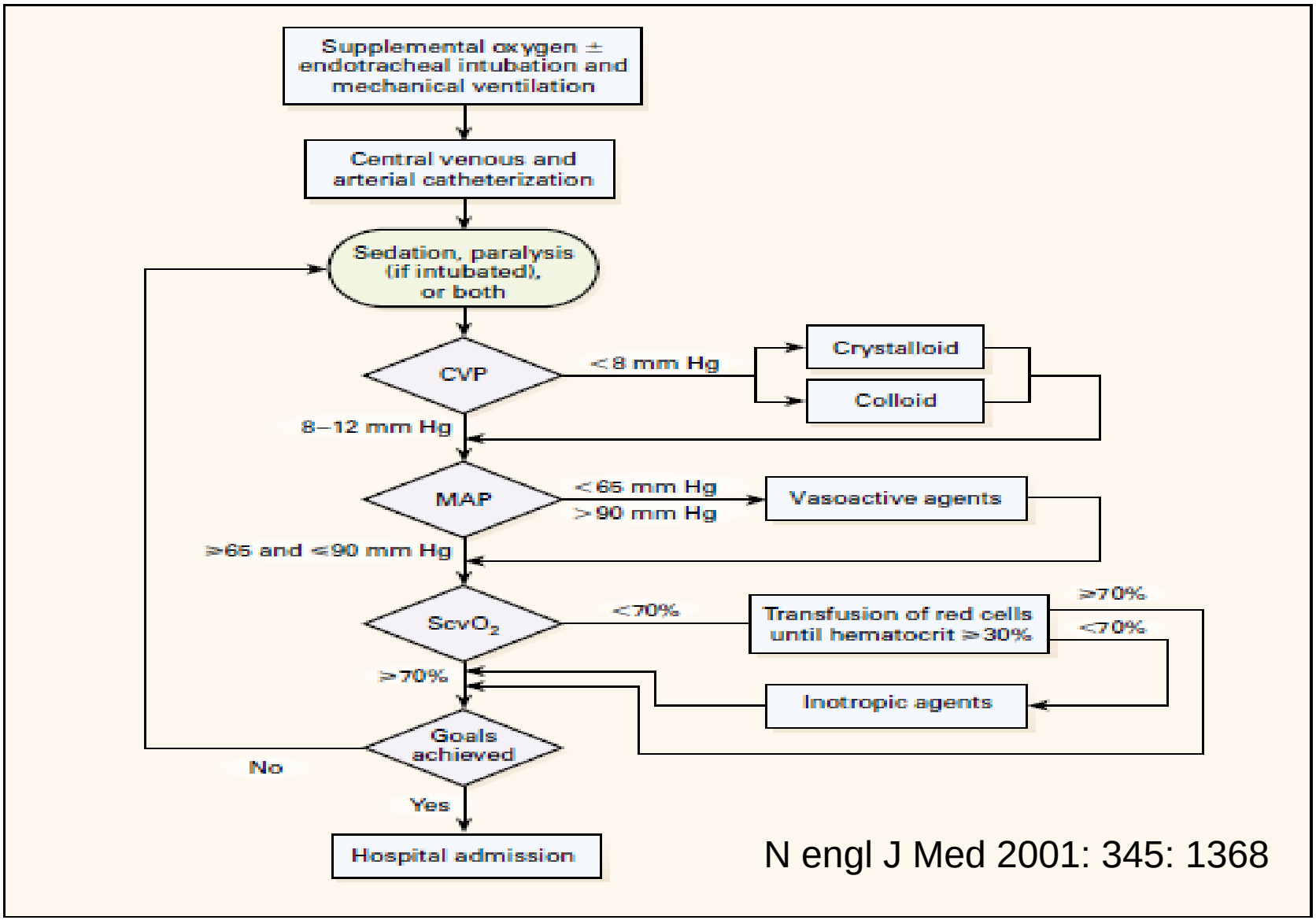
Organ dysfunction

系統	表現
心血管系統	在fluid bolus >= 40 mL/kg in 1 hr仍 低血壓 需使用強心劑 或以下兩個以上： 1. 代謝性酸中毒 2. 乳酸升高兩倍以上 3. 寡尿 4. 微血管回填>=5 sec 5. 中心與周邊體溫差大於3度
呼吸	1. PaO2/FiO2 < 300 2. PaCO2 > 65 mmHg or 20 mmHg above baseline >50% FiO2 to maintain O2Sat > 92%
神經系統	GCS <=11 or change >=3
血液	Plt < 80000 mm3 or decline > 50%, or INR > 2
腎臟	Cr >= 上限兩倍，或兩倍上升
肝臟	Bil. Total > 4 mg/dL （NB例外）or ALT 兩倍上升



JAMA 1995; 273: 117

2008戰勝敗血症，黃金六小時



N engl J Med 2001: 345: 1368

第一小時

1. Monitor ECG, SpO2, NIBP

2. Consider intubation and mechanical ventilation if respiratory failure

3. Artery-line placement & ABP monitor

4. Placement of a CVP catheter (PreSep CVP with ScvO2 is preferred)

5. Obtain smear and related cultures
Obtain 2 or more blood culture
(Previous colonized fungus → fungus culture)

6. Check CBC+DC, INR/PTT, AST, ALT, Bil T/D, Glu, electrolytes, BUN/Cr,CRP or Procalcitonin as needed

7. Check chest x-ray or other image study as needed

8. Check ABG, electrolytes, and lactate

9. Initiate empiric broad spectrum and adequate dose antibiotics therapy

10. Start early goal-directed treatment for shock
Goals: MAP > 65 mmHg, ScvO2>70%
Urine output > 1 ml/kg/h

11. Fluid supplement to target CVP as needed
CVP→ 8-12 mmHg (12-15 mmHg if intubated)
Push NS or colloid 20 ml/kg first, repeated over 60cc/kg as needed

12. If MAP still < 65 mmHg after adequate fluid supplement:
1st line Dopamine 5-20 mcg/kg/min
Dobutamine 2-20 mcg/kg/min (if low cardiac output and elevated systemic vascular resistance states)
2nd line Levophed 0.5-2 mcg/kg/min, or
Epinephrine 0.04-0.2 mcg/kg/min

1-6 hour

1. Ongoing early goal-directed treatment for shock

2. If shock is refractory to vasopressor and inotropic,
may use Solu-Cortef 50 mg/m^2/24hr if at risk for absolute adrenal insufficiency, remember to taper down steroid once the shock is resolved

3. If MAP > 65 mmHg, but ScvO2 < 70%
Consider further fluid supplement as tolerated
PRBC supplement for Hct < 30%

4. If shock persisted, evaluate heart function
Check cardiac echo, PiCCO, PAC, or CCO as needed

5. Control blood sugar < 150 mg/dL

5. Check ABG, electrolytes, and lactate as needed

6-24 hour

1. Ongoing goal-directed treatment for shock
2. Recheck ABG, electrolytes, and lactate as needed
3. Remove source of infection if possible Site:_____ Intervention: _____
4. Protective ventilation strategy If PaO2/FiO2<300, PC mode, VT 6-8 mL/kg, Adequate PEEP, peak airway pressure < 35 cmH2O Head of bed raised to 30 - 45 °
5. RRT for acute renal failure CVVH for hemodynamic unstable patient SLED-f for hemodynamic stable patient
6. Prevent stress ulcer - Zantac 2-4mg/kg/day divided Q6-8H If ulcer history or being bleeding now - Losec 1mg/kg QD
7. Analgesia and sedation as needed
8. At 12-24h, check Modified PRISM III-APS score: _____
9. Control blood sugar

24-48 hour

1. Narrow antibiotics by available report and clinical improvement

2. If clinical condition deteriorated, consult ID doctor

3. Reassess removal of infection source
Site:_____
Intervention: _____

4. RRT for acute renal failure

5. Nutrition support
If enteral feeding is allowed and condition improved (like shock resolved, lactate < 3 mmol/L), start enteral feeding
TPN for NPO patients

6. Analgesia and sedation as needed
Perform daily interruption for continuous sedation

7. Prevent DVT and PE in postpubertal children with severe sepsis
Low risk - choose one of the followings,
(1) heparin loading 2000U then 100 U/h IV t itration to keep aPTT > 50 sec, (2) compressing stocking, or (3) intermittent pneumatic compression device
High risk - combine heparin and mechanical device

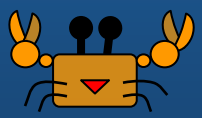
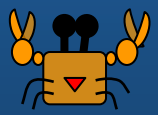
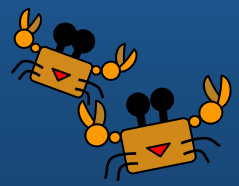
8. Discuss advance care plan with patient & family

9. IVIG may be considered in children with severe sepsis

10. ECMO be limited to refractory pediatric septic shock and/or respiratory failure that cannot be supported by conventional therapies

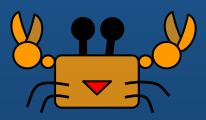
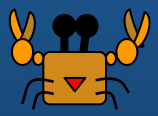
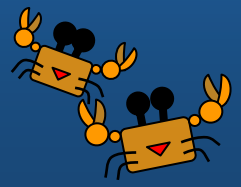
血行力學之支持治療

- 輸液治療：
  - Colloid v.s. crystalloid
  - CVP level
    - 心肺腎不好：8 mmHg
    - 單一器官：10 mmHg
    - 器官正常：12 mmHg
    - 呼吸器：12-15 mmHg

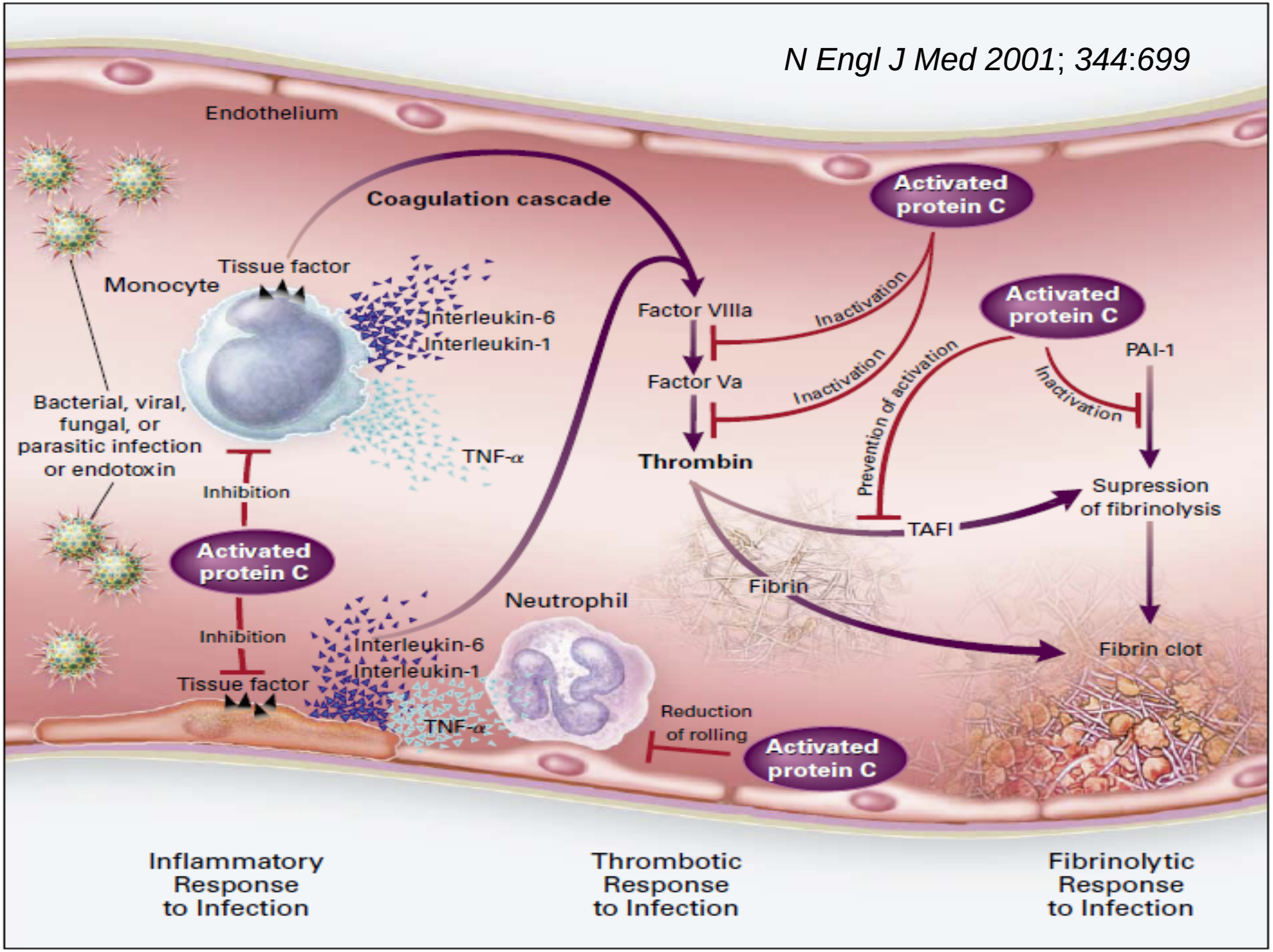




血行力學之支持治療

- 升壓劑
  - MAP > 65 mmHg
  - dopamine, norepinephrine
  - Epinephrine
  - Vasopression (0.03 units/min), not for 1st line
- 避免低劑量dopamine保護腎臟
- 盡快放置arterial line
- Dobutamine提高cardiac output
- 不建議以預設高於正常值的cardiac index治療病人

N Engl J Med 2001; 344:699



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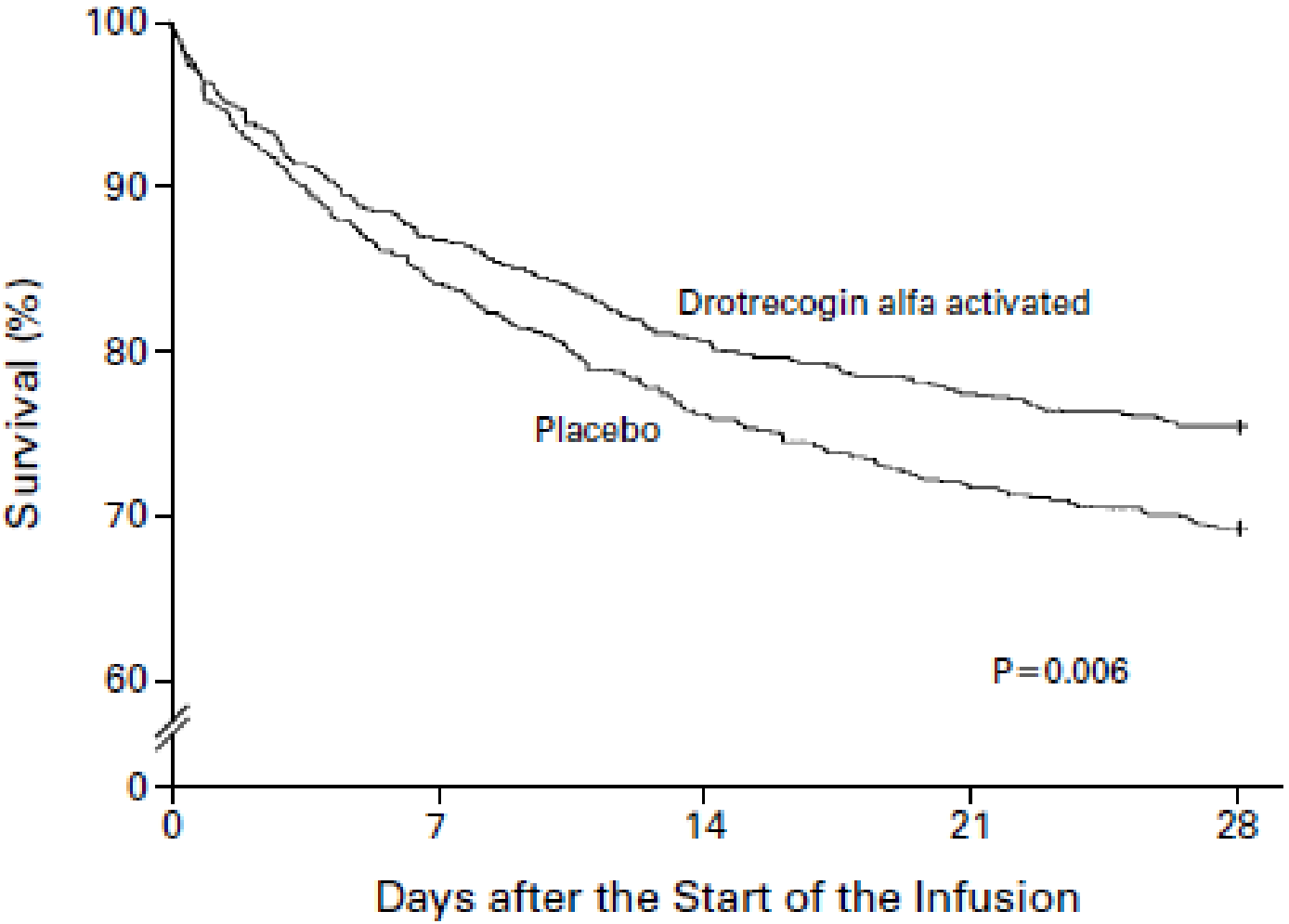
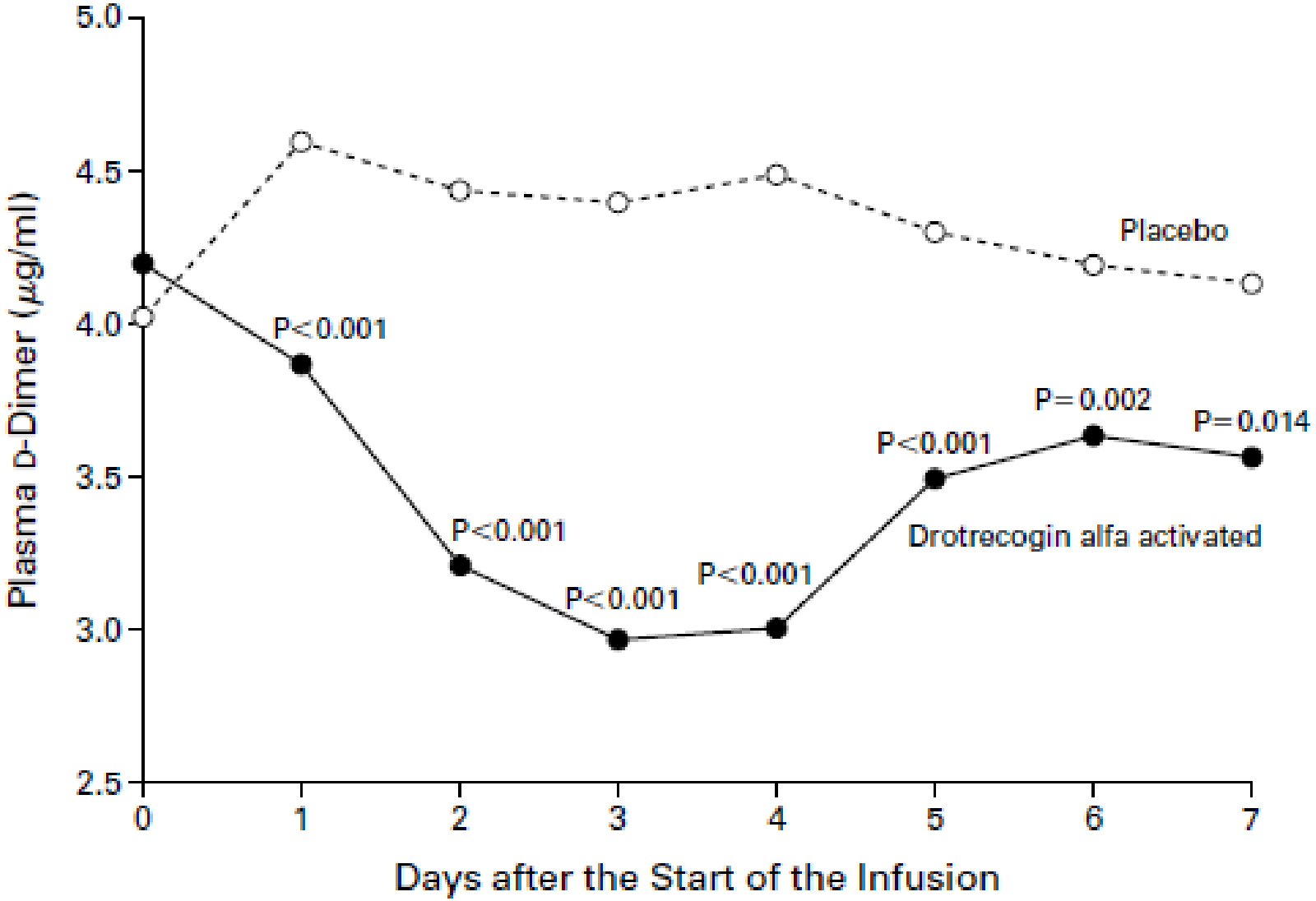


No. at Risk					
Drotrecogin alfa activated	850	737	684	657	640
Placebo	840	705	639	602	581

N Engl J Med 2001; *344*:699



1. 限重度敗血症病患且同時符合下列條件者

（1） 十八歲以上之成人且因敗血症導致急性的第一個主要器官衰竭並入住加護病房十二至四十八小時的病患。

（2） 病患經感染症專科醫師會診，懷疑（suspected）或確認有感染症發生。

（3） 除了本次敗血症之外，病患必須有良好之存活預後（存活預期大於六個月）。

（4） 病患至少需符合下列四項標準中的三項：

I. 體溫≧ 38℃或 ≦36°℃。

II. 心跳≧90 次/分鐘。

III. 呼吸速率≧20 次/分鐘 或血中二氧化碳濃度（$PaCO_2$）≦32 mmHg或使用呼吸器患者。

IV. 白血球數目≧12,000/mm^3或≦ 4,000/mm^3 或未成熟的嗜中性白血球數 >10%。

（5） 病患至少需符合下列急性器官衰竭（指發作小於等於四十八小時）二項以上：

I. 心血管：於給予適當之輸液急救、維持適當之血管內容積、或已使用升壓素的狀態下，收縮壓仍<=90 mm Hg，或平均動脈壓<=70 mm Hg 並持續一小時以上。

II. 腎臟：於給予適當之輸液急救、連續四小時之排尿量<0.5 ml/kg/hr。

III. 呼吸：PaO_2/FiO_2 <= 250，或當有肺炎時，PaO_2/FiO_2 <=200。

IV. 血液：血小板數<80,000/mm^3，或血小板數於三日內下降百分之五十。

V. 代謝性酸中毒：pH 值<=7.3，或血漿乳酸濃度高於正常值上限一・五倍以上，合併鹼基不足（basedeficit）>=5 mEq/L。

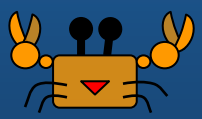
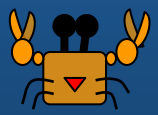
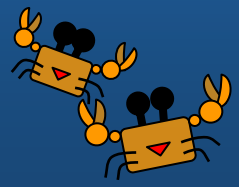
（6） APACHE II score 大於等於二十五分且小於五十三分。

表一、Drotrecogin alfa 禁用於下列情況[17]

1. 進行性內出血。
2. 顱內病變，腫瘤或大腦疝氣。
3. 目前使用 heparin 治療，且劑量高於 15 IU/kg/hr。
4. 已知易出血體質，不包括敗血症引起之急性凝血病變。
5. 慢性重度肝臟疾病（晚期肝硬化，食道或胃靜脈曲張，或 INR（國際標準凝血時間比）> 2.0 之慢性肝臟疾病 ）。
6. 血小板數小於 30 K/μL，即使輸血後血小板數回升。
7. 容易出血的高危險群：
   （1）任何大手術（需全身或脊髓麻醉的手術），於術後 12 小時內立即輸注本劑；或任何術後。
   （2）病人具出血現象；或於輸注本劑期間，即將或預期進行手術的病人。
   （3）頭部重度創傷需住院治療或顱內或脊髓手術的病史，或近三個月內曾發生出血性中風，或具顱內動靜脈血管變形、腦動脈瘤、中樞神經系統大型損傷的病史；病人接受硬膜外插管，或預期將於輸注本劑期間，接受硬腦膜外插管。
   （4）先天性易出血體質。
   （5）近六週內曾發生胃腸道出血，且除非進行手術治療，必須以藥物控制病情。
   （6）創傷伴隨高度出血危險。
8. 禁用於已知對 drotrecogin alfa、此藥品的任何賦形劑或牛凝血酶（製程中微量殘留）過敏者。

呼吸照護

- Low tidal volume, limited peak and plateau pressure
  - Tidal volume 6 mL/kg
  - Peak pressure < 35 mmH2O
  - Plateau pressure < 30 mmHg
- Permissive CO2 retention
- PEEP
- Prone position
- Head up 30-45 degress
- Pul. Artery catheterization not recommended
- Limited fluid therapy

Ventilator Strategy for ARDS

- 6 mL/kg with PIP < 30 cmH_2O compared with 12 mL/kg PIP < 50 cmH_2O
  - 22% reduction in mortality
  - Increased ventilator free day during the first 28 hospital days
  - Adult patients

    (ARDS Network, NEJM 2000, 342: 1307-8)
- Permissive hypercapnia
  - CO_2 allowed to rise
  - Maintain pH > 7.2 with buffered solution

Parameter	protocol
Mode	Volume assist-control
Tidal Volume	≤6 mL/kg predicted body weight
Plateau pressure	≤30 cm H2O
Frequency	6–35 breaths/min, titrated for pH 7.30–7.45
IE ratio	1:1 to 1:3
Oxygenation Goal	PaO_2 55–80 mm Hg, or SaO_2 88–95%
FiO2/PEEP (cmH2O) combination allowed	0.3/5, 0.4/5, 0.4/8, 0.5/8, 0.5/10, 0.6/10, 0.7/10, 0.7/12, 0.7/14, 0.8/14, 0.9/14, 0.9/16, 0.9/18, 1.0/18, 1.0/20, 1.0/22, 1.0/24
Weaning	By pressure support, required when FIO2/PEEP ≤ 0.4/8

(ARDS Network, NEJM 2000, 342: 1307-8)

ARDS Net

E. ARDSNET Ventilator Management (96)

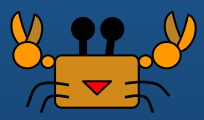
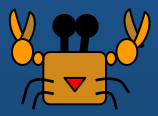
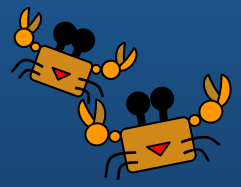
- Assist control mode – volume ventilation
- Reduce tidal volume to 6 mL/kg lean body weight
- Keep inspiratory plateau pressure (Pplat) $\leq$ 30 cm H_2O
  - Reduce TV as low as 4 mL/kg predicted body weight to limit Pplat
- Maintain SaO_2/SpO_2 88–95%
- Anticipated PEEP settings at various FIO_2 requirements

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

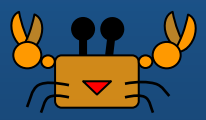
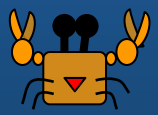
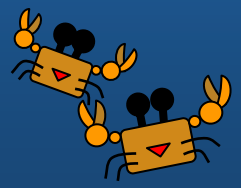
- Male – 50 + 2.3 (height (inches) – 60) or 50 + 0.91 (height (cm) – 152.4)
- Female – 45.5 + 2.3 (height (inches) – 60) or 45.5 + 0.91 (height (cm) – 152.4)

TV, tidal volume; *SaO_2*, arterial oxygen saturation; *SpO_2*, pulse oximetry oxyhemoglobin saturation; *PEEP*, positive end-expiratory pressure

輸血的原則

- 無心肌缺氧，組織血液灌流不足，嚴重低血氧，急性出血，缺氧性心臟病，乳酸血症，PRBC keep 7-9 g/dL
- FFP不該被常規使用，10-15 mL/kg
- Plt < 5000/mm3, 5000-30000 若有出血風險，手術前 > 50,000

感染的Issue

Diagnosis

- Obtain appropriate cultures before starting antibiotics provided this does not significantly delay antimicrobial administration. (1C)
  - Obtain two or more blood cultures (BCs)
  - One or more BCs should be percutaneous
  - One BC from each vascular access device in place > 48 h
  - Culture other sites as clinically indicated
- Perform imaging studies promptly in order to confirm and sample any source of infection; if safe to do so. (1C)

Antibiotic therapy

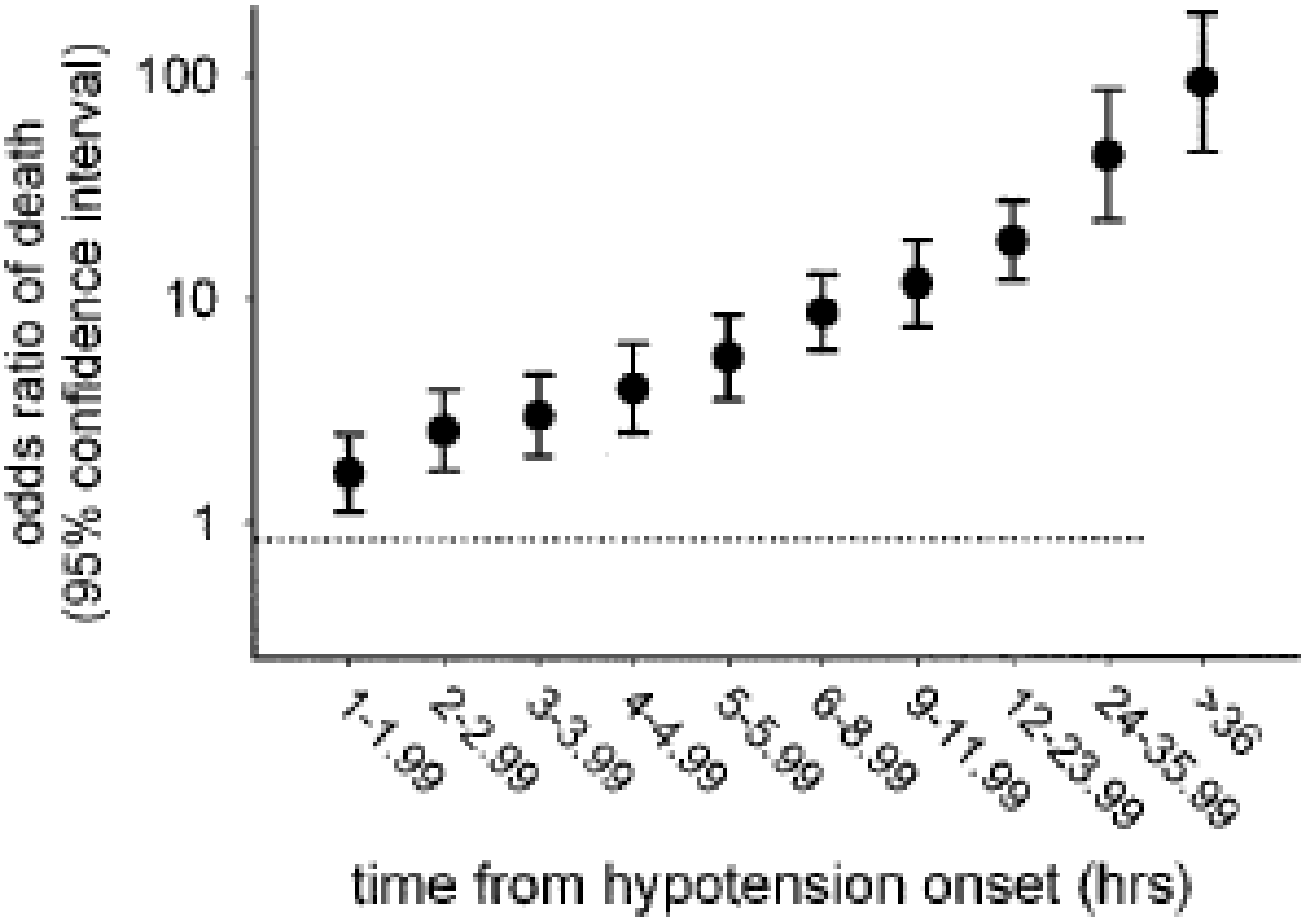
- Begin intravenous antibiotics as early as possible, and always within the first hour of recognizing severe sepsis (1D) and septic shock (1B).
- Broad-spectrum: one or more agents active against likely bacterial/fungal pathogens and with good penetration into presumed source.(1B)
- Reassess antimicrobial regimen daily to optimise efficacy, prevent resistance, avoid toxicity & minimise costs. (1C)
  - Consider combination therapy in Pseudomonas infections. (2D)
  - Consider combination empiric therapy in neutropenic patients. (2D)
  - Combination therapy no more than 3–5 days and deescalation following susceptibilities. (2D)
- Duration of therapy typically limited to 7–10 days; longer if response slow, undrainable foci of infection, or immunologic deficiencies. (1D)
- Stop antimicrobial therapy if cause is found to be non-infectious. (1D)

Source identification and control

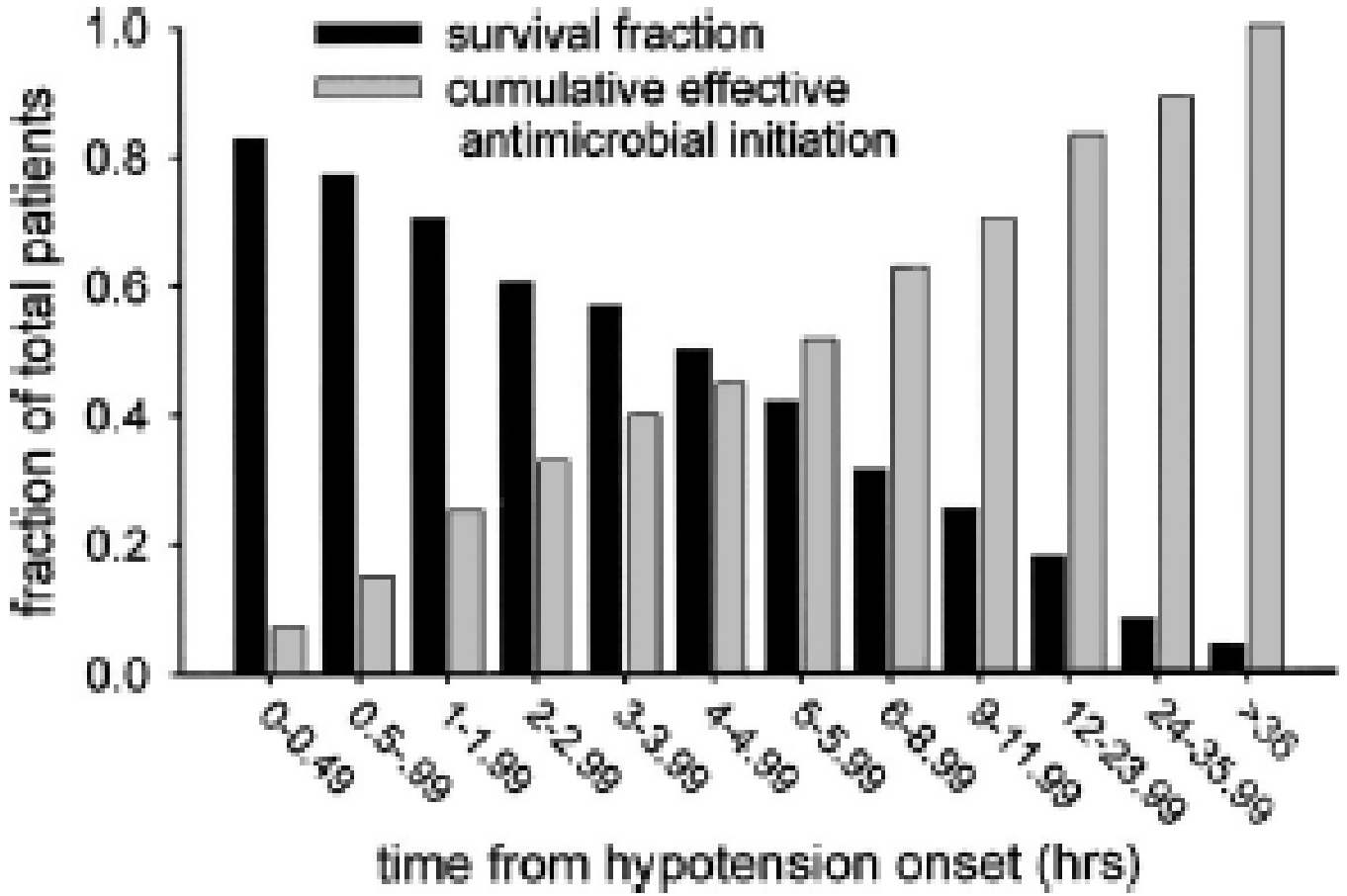
- A specific anatomic site of infection should be established as rapidly as possible (1C) and within first 6 hrs of presentation (1D).
- Formally evaluate patient for a focus of infection amenable to source control measures (eg: abscess drainage, tissue debridement). (1C)
- Implement source control measures as soon as possible following successful initial resuscitation. (1C)

Exception: infected pancreatic necrosis, where surgical intervention best delayed. (2B)

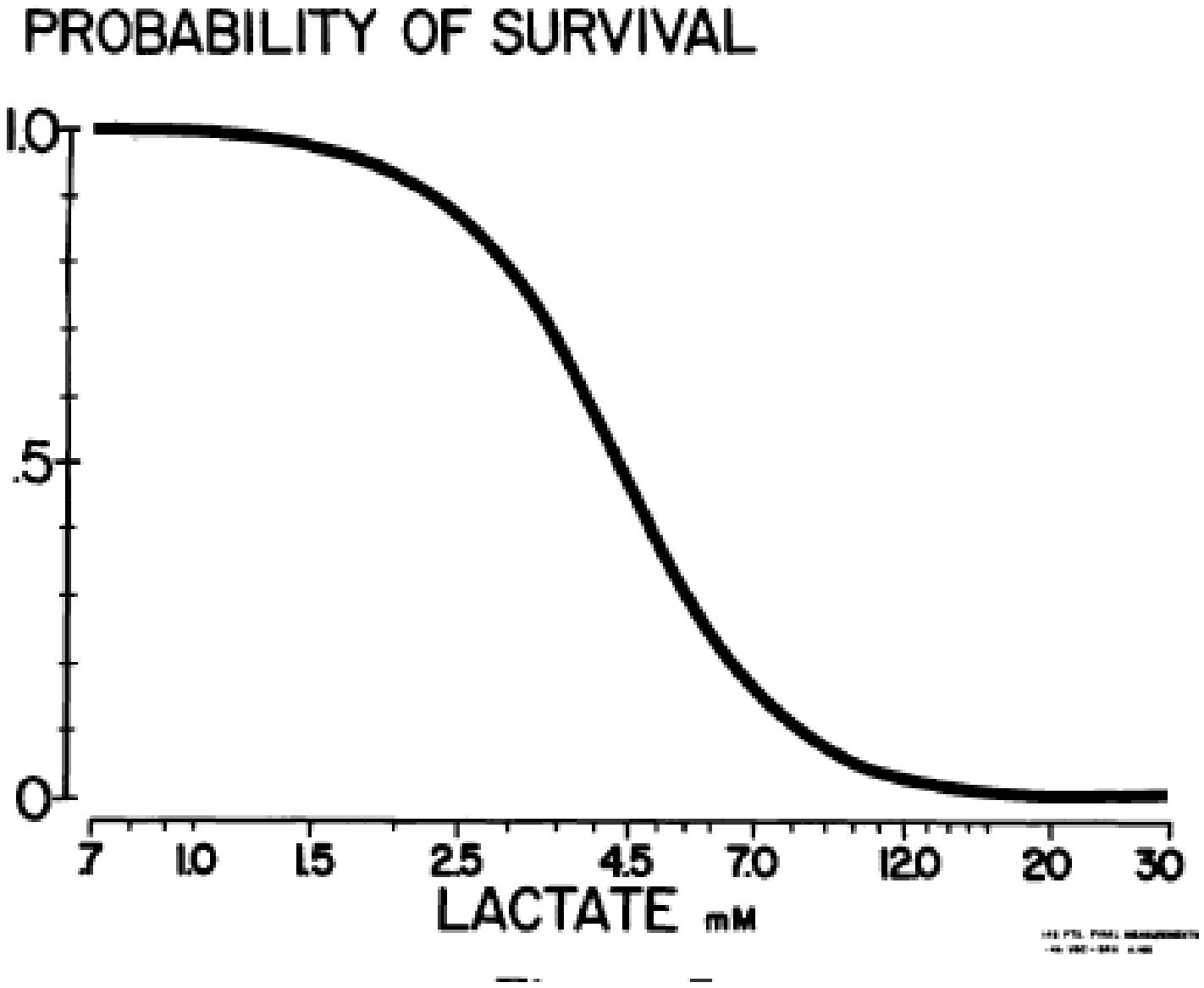
- Choose source control measure with maximum efficacy and minimal physiologic upset. (1D)
- Remove intravascular access devices if potentially infected. (1C)



Crit Care Med 2006; 34: 1589



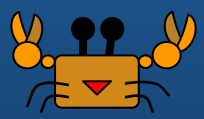
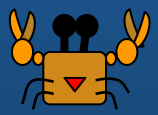
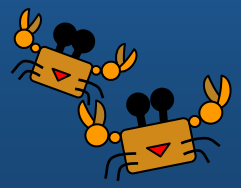
Crit Care Med 2006; 34: 1589



Circulation 1970; 41: 989

類固醇使用的時機

- Children with catecholamine resistance and suspected or proven adrenal insufficiency

Special consideration in children