內科急重症疾病之介紹

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課程大綱

1. 敗血症
2. 急性腎衰竭
3. 電解質異常

敗血症

前　言

全球敗血症發病率高達 437/100000

占美國住院人數的6%

敗血症(Sepsis) 意指人體針對感染產生一系列反應，導致器官功能失常 (dysfunction) 的一種現象

前　言

器官功能失常未能得到控制，將進一步惡化成多重器官衰竭(multiple organ failure) 或稱多重器官功能失常(multiple organ dysfunction syndrome)。

時至今日，敗血症及其併發症仍於全球造成相當多死亡

定義及診斷標準

嚴重敗血症 (severe sepsis)：因敗血症造成器官功能失常、組織灌流不足或低血壓

敗血性休克 (septic shock) ：因敗血症導致即使在輸液復甦 (resuscitation) 後，仍呈現低血壓 (定義為收縮壓小於 90 mmHg 或是比原先基準收縮壓降低 40mmHg) 合併灌流異常。

定義及診斷標準

2001年共識會議增加

生理 (如: 水腫、高血糖、低血氧)、

實驗室 (如:C 反 應 蛋 白 (C-Reactive protein，CRP)、 前 降 鈣 素 (Procalcitonin)、乳酸)、血行動力學(如:心指數 (Cardiac index)) 指標描述，期待及早診斷

仍維持先前因感染造成的 SIRS，即診斷為敗血症的定義

定義及診斷標準

2016 年修改敗血症的診斷標準

定義為因人體對感染的反應失調 (dysregulated)，導致危及生命的器官功能失常。

器官功能失常定義為 Sepsis- related Organ Failure Assessment (SOFA) score 急性上升兩分以上

SOFA score

心:MAP 與升壓劑

肝:Bilirubin

肺:P/F ratio

腎:Creatinine 與尿量

血:Platelet

神:Coma scale

SOFA score

系統	分數				
	0	1	2	3	4
呼吸 PaO_2/FiO_2，mmHg	≧ 400	< 400	< 300	< 200 並使用呼吸器	< 100 並使用呼吸器
凝血 血小板 $\times 10^3$/uL	≧ 150	<150	<100	< 50	< 20
肝臟 膽紅素，mg/dL	< 1.2	1.2-1.9	2.0-5.9	6.0-11.9	> 12
心血管	平均動脈壓≧ 70 mmHg	平均動脈壓< 70 mmHg	Dopamine < 5（ug/kg/min）或任何 dobutamine	Dopamine5.1-15 或 epinephrine ≦ 0.1 或 norepinephrine ≦ 0.1（ug/kg/min）	Dopamine > 15 或 epinephrine > 0.1 或 norepinephrine > 0.1（ug/kg/min）
中樞神經 昏迷指數	15	13-14	10-12	6-9	<6
腎臟 Creatinine,mg/dL 小便量，mL/day	< 1.2	1.2-1.9	2.0-3.4	3.5-4.9 < 500	> 5.0 < 200

定義及診斷標準

時提出 Quick SOFA (qSOFA) 準 則 (criteria)，即若因感染 (或是疑似因感染) 造成

意識狀態改變

呼吸次數大於每分鐘 22 下

收縮壓小於 100 mmHg

三項指標符合兩項， 也可診斷敗血症。

定義及診斷標準

敗血性休克:定義為，在適當的輸液復甦後，持續低血壓，需血管收縮藥 物 (vasopresssor) 維持平均動脈壓 (mean arterial pressure, MAP) 在 65 mmHg 以上，且血中乳酸大於 2 mmol/L (18 mg/dl)

捨棄“嚴重敗血症”，因敗血症已合併器官功能失常，極可能危及生命，只要診斷敗血症，即為嚴重狀態，不可等閒視之

定義及診斷標準

2021 年 guideline 捨棄 qSOFA，認為其相較於其他指標缺乏敏感度，不建議單獨使用 qSOFA 篩選病人是否為敗血症

1992, 2016 及 2021 年敗血症定義比較

	1992 年	2016	2021
敗血症	因感染 (或是疑似因感染) 造成的 SIRS	因感染造成 SOFA score 急性上升 2 分以上或 qSOFA 三項符合兩項	因感染造成 SOFA score 急性上升 2 分以上 (不建議單獨使用 qSOFA)
嚴重敗血症	因敗血症造成器官功能失常、組織灌流不足或低血壓	無此定義	無此定義
敗血性休克	因敗血症導致即使在輸液復甦後， 仍呈現低血壓合併灌流異常	在適當的輸液復甦後需藥物維持血壓，且血中乳酸上升	在適當的輸液復甦後需藥物維持血壓，且血中乳酸上升

qSOFA & SIRS

	敏感度	特異度
qSOFA	29.7%	96.1%
SIRS	61%	72.1%

一、抗生素

及早給予適當的抗生素能有效降低敗血症 / 敗血性休克死亡率

若高度懷疑敗血症或 敗血性休克，應於一小時內給予抗生素

和 2016 年的建議不同，若總是追求及早給予抗生素，有抗生素濫用的危機。2021 年指引建 議，若敗血症或敗血性休克的可能性不強，應繼續監測臨床變化，若仍有感染疑慮，仍建議使用抗生素

一、抗生素

2016 年指引建議起始的經驗性抗生素抗菌範圍應涵蓋所有可能的致病菌

2021 年指引則建議若 MRSA (methicillin-resistant Staphylococcus aureus) 或 / 以及黴菌感染風險高，應使用相對應抗生素

針對有高風險感染多重抗藥性革蘭氏陰性菌應使用兩種抗生素予以治療

一、抗生素

為了避 免抗藥性產生，在確定致病菌後，應調整抗生素避免濫用

2016 年指引建議七到十天，視個別病情、治療反應、感染部位、致病菌種…等予以增減 使用天數

2021 年指引則建議，相較於長天數，更偏好短天數抗生素療程

搭配前降鈣素 (procalcitonin) 作為停用抗生素的參考，可能有減少抗生素使用天數及降低死亡率好處

二、輸液治療

2016 年指引建議，因敗血症引起的組織灌流不足，於前三小時內至少需給予每公斤理想體重 30ml crystalloid fluid (晶 體 溶 液)

2021 年指引仍維持此建議

對於容易因 大量輸液產生併發症的族群，如末期腎病、心 衰竭、肝硬化 …等病人，治療指引未給予額外建議

二、輸液治療

2016 年指引建議，若血行動力學持續改善，可持續給予輸液

要用何種指標當作評估或治療目標，未多加著墨

2021 年指引則提 到 lactate (乳酸) 或 capillary refill time (微血管 回充時間) 可做為復甦的指引

二、輸液治療

病人無明顯組織灌流不足證據，採取保守輸液策略並不會增加風險

輸液應視同一般藥物，若無明確適應症，則不該貿然給予，避免增加可能的副作用

復甦結束後，要採取何種輸液策略，目前無足夠證據可建議 。

二、輸液治療

	Crystalloid Saline	Balanced crystalloid	Colloid Albumin
特點	鈉及氯濃度高於血漿	除含有鈉、氯離子外，亦含有鉀 鈣、離子	膠體溶液
	可能導致發炎、代謝性酸中毒、 腎動脈收縮、降低 microcirculation (微循環)	相較於 saline，可能較低腎損傷及死亡風險	昂貴 相較於晶體溶液，較能改善生理數值，但死亡率無差異

二、輸液治療

2016 年指引建議，輸液選擇為 balanced crystalloids (平衡晶體溶液)或 saline (生理食鹽水)

若需要大量輸液時，可考慮增加使用 albumin (白蛋白)

避免使用 hydroxyethyl starches (羥乙基澱粉) 因為會增加急性腎損傷及死亡風險

Saline 的氯離子高於人體， 有 引 起 hyperchloremic acidosis (高氯血酸中毒)，進而造成急性腎損傷的疑慮

二、輸液治療

分析發現， 在敗血症，balanced crystalloids 相較於 saline 明顯降低 30 天死亡 率 (balanced crystalloids 組:26.3%，saline 組: 31.2%，p 值 0.01)

2021 年 指 引 建 議 復甦輸液選擇為 balanced crystalloids

心臟加護病房、創傷性腦損傷、creatinine (肌酐酸) 小於 1.5 mg/dl (毫克 / 公合) 等病人族群可能使用 saline 優於 balanced crystalloids

二、輸液治療

敗血性休克可得到 albumin 補充的益 處 。

補充到血中 albumin 濃 度到 30 g/l，平均 7 天給予 1100 毫升濃度 20% albumin

現行健保制度 (僅血中 albumin 濃度 未達 25 g/l 予以給付 albumin 滴注，上限為 50 克 albumin) 有相當大鴻溝

Fresh frozen plasma (新鮮冷凍血漿) 和 albumin 一樣同為自然產生 的 colloid (膠體溶液)。

於敗血症的角色不明確，治療指引未特別提及

三、昇壓藥物

治療指引建議目標 MAP 為 65 mmHg 以 上

仍無法明確得知高血病史的敗血性休克，應設定的血壓目標

敗血性休克合併急性腎損傷血壓目標亦無定論。

三、昇壓藥物

2016 年指引建議 norepinephrine 作為首選升壓藥物。

若仍無法達到目標血壓，建議加入 vasopressin 或 Epinephrine

2021 年 指 引 維 持 norephinephrine 為第一線昇壓藥物的建議

2021 年指引則提到，若無法達到目標血壓，建議予以第二種藥物而非增加 norepinephrine 劑量。建議實務上若 norephinephrine 已達 0.25~0.5 μ g/kg/min，則開始給予vasopressin

對於 norepinephrine 反應不佳的敗血性休克病人，及早併用其他藥物可能更容易達到目標血壓

三、昇壓藥物

2015 年系統性回顧 (systematic review) 及統合分析 (meta- analysis) 發 現，相 較 於 Dopamine， 用 norepinephrine 治療的病人死亡率較低、血行動力學 較佳、副作用較少

第一線升壓劑使用 vasopressin 或 epinephrine 並無法比 norepinephrine 降低死亡率，考慮到證據等級，兩者使用順 位在norepinephrine 之後

血行動力學改善時升壓藥物 的調降治療指引未明確說明

2019 年回溯性研究發現，相較於先停用 norepinephrine，先停用 vasopressin，後續發生血行動力學不穩定的風險較高

升壓劑跟輸液

敗血症及敗血性休克的治療，通常在輸液復甦後仍無法恢復血壓，才考慮使用升壓藥物

2014 年回溯性研究發現，在外科加護病房發生敗血性休克後前六小時，每延遲一小時開始 norepinephrine 滴注增加 5.3% 死亡率

於敗血性休克前兩小時予以 norepinephrine 滴注比起超過兩小時後才給予 norepinephrine， 二十八天死亡率較低

升壓劑跟輸液

2019 年研究，在輸液復甦中位數800ml時介入0.05 μ g/kg/min norephinephrine，相較標準治療，可得到較好的休克控制，死亡率無差距

1-hour bundle 亦提及，即便在輸液復甦尚未完成，若平均動脈壓無法達到 65 mmHg，應使用藥物維持血壓

為了達成敗血 性休克目標血壓，輸液復甦與升壓劑兩者間的轉換時機，應視病人條件予以調整，不應用單 一策略套用在所有病人。但目前仍未有好的指標可供參考

類固醇

2016 年指引建議，敗血性休克於輸液復甦及升壓劑使用後仍無法穩定血行動力學，予以 hydrocortisone，每天 200mg

2021 年指引未做調整 。

類固醇

統合分析 發現，類固醇可加速休克緩解 、減少升壓 藥物使用 、較低的第七天 SOFA 分數 、減 少加護病房住院天數 、減少住院天數 、減 少呼吸器使用天數

類固醇的使用可望降低 28 天死亡率 或短期死亡率

類固醇常見的副作用包括高血糖、續發性感染、腸胃道出血、瞻妄 (delirium)、腦病變 (encephalopathy)

Sodium bicarbonate (碳酸氫鈉)

因灌流低下導致高乳酸酸血症，除非 pH 小 於 7.15，2016 年指引反對使用 sodium bicarbonate

2018 年研究，於加護病房病人，代謝性酸血症 pH 小於 7.2，予以 sodium bicarbonate 使 pH 升高至 7.3 以上。雖未見死亡率差異

Sodium bicarbonate (碳酸氫鈉)

但於 第 2 至 3 期急性腎損傷次分組中，使用 sodium bicarbonate 可降低死亡率

2021 年指引建議，敗血性休克合併代 謝 性 酸 血 症 (ph 小 於 7.2) 及第 2 至 3 期 急 性 腎損傷，給予 sodium bicarbonate

Vitamin C (維他命 C) 及 thiamine (硫胺)

Vitamin C 降低敗血症引起的器官損傷、於嚴重敗血症病人降低 SOFA score、 C-reative proetein、procalcitonin、血管內皮損傷 、減少嚴重燒傷病人所需復甦液體 。Glucocorticoid 增加細胞攝取 vitamin C，vitamin C可能回復 glucocorticoid receptor 功能 ，兩者間有協同作用

腎臟功能異常病人給予大 vitamin C 可能增加 oxalate (草酸鹽) 於組織沉積及腎臟結石風險

Vitamin C (維他命 C) 及 thiamine (硫胺)

Thiamine 缺乏影響 oxalate 代謝，使 glyoxylate (乙醛酸鹽) 於組織 堆積，尿中排出增加，形成高草酸鹽尿

部分敗血性休克病人缺乏 thiamine，予以補充可降低死亡率

Vitamin C (維他命 C) 及 thiamine (硫胺)

Vitamin C 及 thiamine 不昂貴，相對安全且易於取得。之後，於敗血性休克合併使用這三 種藥物的比例增加 。後續研究發現其可降低加護病房住院天數 、加速休克緩解 、改善 SOFA score。

2021 年指引統整 RCT 結果發現 vitamin C 有降低死亡率傾向 ，但近期的兩篇 RCT 死亡 率較偏向對照組 ，故反對於敗血症及敗血性休克使用維他命 C

Care bundle (組合式照護)

2015 年的觀察性研究發現，針對嚴 重敗血症或敗血性休克，完成 3-hour 及 6-hour bundle (表四) 的病人死亡率較低

3-hour bundle	6-hour bundle
測量乳酸	追蹤乳酸 (如果初次測量 乳酸即偏高)
予以抗生素之前留取血 液培養	若輸液復甦後仍持續低血 壓則給予升壓
靜脈給予廣效性抗生素	若輸液復甦後仍持續低血 壓或初次測量乳酸高於 4 mmol/L 則測量 CVP 及 ScvO2
若乳酸高於 4 mmol/L 或 低血壓，則給予每公斤 體重 30 毫升 crystalloid	

Care bundle (組合式照護)

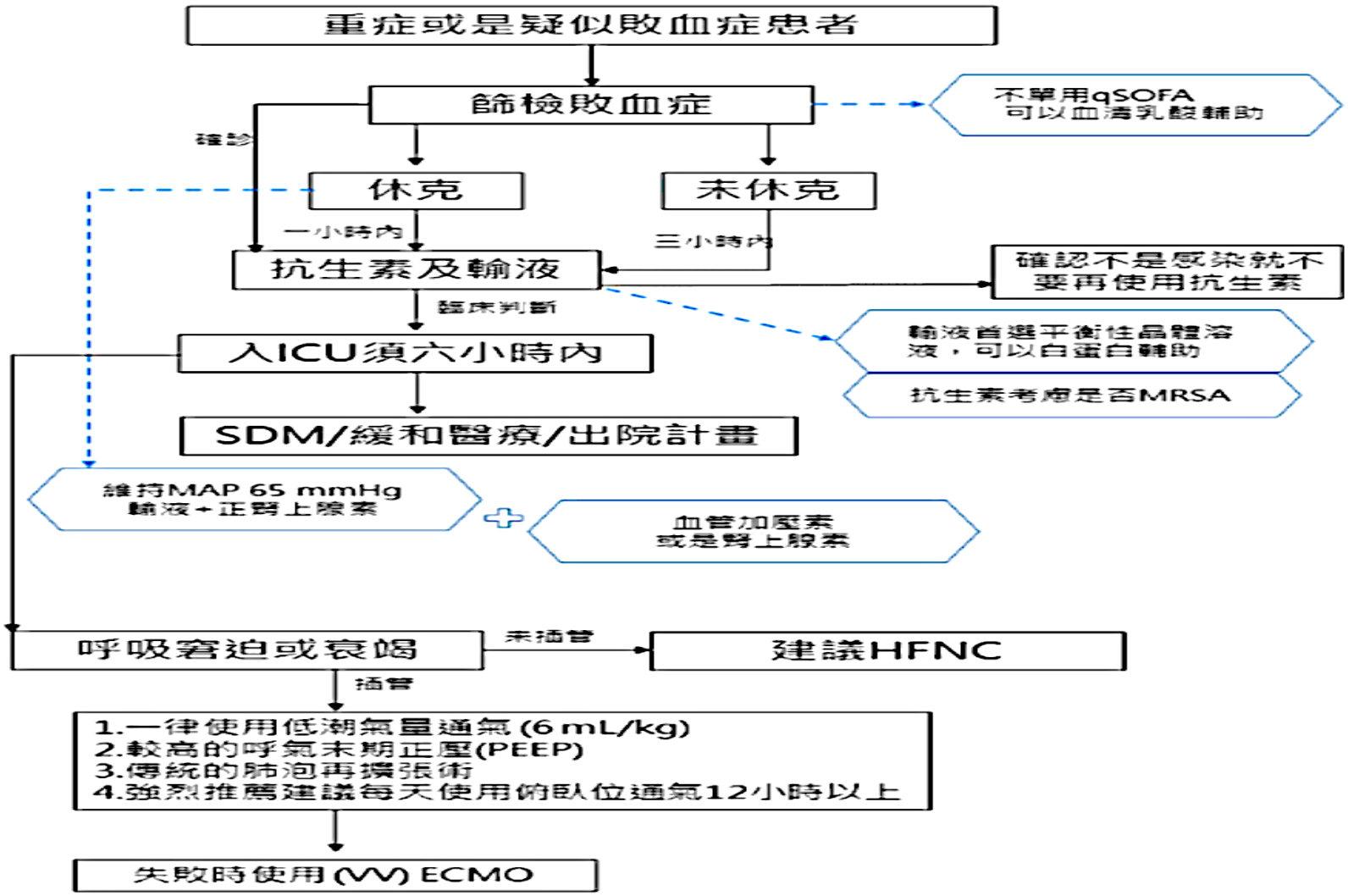
2018 年， 3-hour 及 6-hour bundle 修正為 1-hour bundle

1-hour bundle
測量乳酸。若測得數值大於 2 mmol/L，則需繼續追蹤
予以抗生素之前留取血液培養
給予廣效性抗生素
於低血壓或是乳酸大於 4 mmol/L 的病人開始快速給予 每公斤體重 30 毫升 crystalloid
若病人在予以輸液復甦過程中或輸液復甦後低血壓， 給予升壓劑使平均動脈壓大於等於於 65 mmHg

Care bundle (組合式照護)

2021 年指引並未對 care bundle 多加著墨

臨床上使用亦需小心可能的副作用， 如為了早期給予抗生素導致過度使用、輸液復甦造成的 fluid overload (過載)


重症或是疑似敗血症患者
篩檢敗血症
不單用qSOFA
可以血清乳酸輔助
確診
休克
未休克
一小時內
三小時內
抗生素及輸液
確認不是感染就不要再使用抗生素
臨床判斷
入ICU須六小時內
輸液首選平衡性晶體溶液，可以白蛋白輔助
抗生素考慮是否MRSA
SDM/緩和醫療/出院計畫
維持MAP 65 mmHg
輸液+正腎上腺素
血管加壓素
或是腎上腺素
呼吸窘迫或衰竭
未插管
建議HFNC
插管
1.一律使用低潮氣量通氣 (6 mL/kg)
2.較高的呼氣末期正壓(PEEP)
3.傳統的肺泡再擴張術
4.強烈推薦建議每天使用俯臥位通氣12小時以上
失敗時使用 (V-V) ECMO

急性腎衰竭

Epidemiology of Acute Kidney Injury in the Intensive Care Unit

Acute kidney injury (AKI) is common and associated with substantial morbidity, mortality, and medical costs.

AKI is currently defined by KDIGO (Kidney Disease: Improving Global Outcomes) criteria and is divided into 3 stages based on increases in serum creatinine level or decreases in urine output.

Q 1

Common Causes of AKI in the ICU

Case 1: *A 68-year-old woman with a history of hypertension presents to the emergency department with fever, nausea, vomiting, and confusion. Vital signs include temperature, 39.3° C; heart rate, 98 beats/min; blood pressure (BP), 130/59 mm Hg; respiratory rate, 26 breaths/min; and arterial oxygen saturation (Sao_2), 92% while breathing room air. Examination is notable for disorientation and right-sided costovertebral angle tenderness. Laboratory test results are notable for white blood cell count of 22 ×10^3/μL; serum creatinine level, 2.3 (baseline, 0.7) mg/dL, and >50 white blood cells/high-power field on urine microscopy. Imaging includes noncontrast computed tomography of the abdomen and pelvis with right perinephric stranding but no stones or hydronephrosis bilaterally. Blood and urine cultures are obtained, ceftriaxone therapy is initiated, and she is admitted to the ICU.*

Question 1: Which of the following statements about this patient's AKI is most correct?

(a) The patient's AKI is likely due to ischemic acute tubular necrosis as a result of decreased blood flow.

(b) Her AKI is unlikely to be attributable to sepsis because she does not meet the current consensus definition of sepsis.

(c) Her AKI is unlikely to be attributable to sepsis given her normal BP.

(d) The patient's AKI puts her at increased risk for secondary infections during her hospitalization.

(e) Given her stage 3 AKI in the setting of sepsis, she would likely benefit from pre-emptive RRT before the development of an urgent indication.

For the answer to the question, see the following text.

Sepsis Definition

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) defines sepsis as “life threatening organ dysfunction caused by a dysregulated host response to infection,” with organ dysfunction defined as an increase in Sequential Organ Failure Assessment (SOFA) score ≥ 2 points.

A screening tool, the quick SOFA, can be used in which sepsis is suggested by the presence of 2 of 3 features: (1) respiratory rate ≥ 22 breaths/min, (2) altered mental status, and (3) systolic BP ≤ 100 mm Hg. Thus, for Question 1, answer (b) is incorrect

Epidemiology

Increasing data suggest that AKI is a risk factor for subsequent sepsis or secondary infections.

The relationship between AKI and sepsis is therefore now thought to be bidirectional; thus, the best answer to Question 1 is (d).

Pathophysiology of SA-AKI

SA-AKI can occur in the absence of hypotension (the reason that answer (c) is incorrect for Question 1). More recent data point to microvascular dysfunction, inflammation, oxidative stress, and endothelial dysfunction as contributors to SA-AKI.

One unifying theory is that SA-AKI is an adaptive energy-conserving response of tubular endothelial cells .

Pathophysiology of SA-AKI

it is important to note that SA-AKI pathophysiology is unique and should not be considered simply a subtype of ischemic injury (thus, answer (a) is incorrect for Question 1).

Q 2

Case 2: *A 62-year-old woman is seen in the clinic with cough, fever, and hypoxemia. A nasopharyngeal swab comes back positive for influenza A, and she is initiated on oseltamivir treatment. She is seen in the emergency department 24 hours later and is admitted to the ICU with high-grade fever, multifocal opacities on chest x-ray, and respiratory failure requiring intubation. Blood cultures and bronchoscopy with bronchoalveolar lavage are performed and methicillin-resistant Staphylococcus aureus is isolated from both. Despite an initial 2-L (30 mL/kg) bolus of crystalloid and appropriate antibiotic treatment, the patient develops progressive hypotension. A central venous catheter is placed through the right internal jugular vein, after which the patient's mean arterial pressure (MAP) is 45 mm Hg, central venous pressure (CVP) is 11 mm Hg, and central venous oxygen saturation ($ScVo_2$) is 89%. Arterial lactate level is 10.2 mmol/L, and urine output is 10 mL/h.*

Question 2: Which of the following statements is correct about the next step in management?

(a) The next best option is to initiate norepinephrine treatment and perform a passive leg raise to assess whether she is likely to respond to additional fluids.

(b) The next best option is to initiate dopamine treatment.

(c) The next best option is to continue to administer intravenous fluids until CVP is ≥12 cm H_2O.

(d) Because of the dangers associated with volume overload, the patient should not have been treated with a 30-mL/kg fluid bolus and should receive no further fluids.

(e) Because $ScVo_2$ is >70%, oxygen delivery to her tissues is adequate and therefore no additional treatment is warranted.

For the answer to the question, see the following text.

Q 3

AKI and Respiratory Failure

Case 3: *A 64-year-old man is admitted with cough, fever, and hypoxemia. Soon thereafter, he develops respiratory distress and requires endotracheal intubation. Chest x-ray shows diffuse bilateral pulmonary opacities. Blood gas reveals Pa_{O_2} of 130 mm Hg on 100% fraction of inspired oxygen (FiO_2). Bedside echocardiography shows normal left ventricular systolic function. A nasopharyngeal swab comes back positive for influenza A.*

Question 3: Which of the following statements is correct about management of this patient's fluid balance?

(a) There are no data to guide fluid management in patients with ARDS.

(b) Fluid removal (with diuretics or ultrafiltration) should only be attempted in patients with ARDS and impaired cardiac function.

(c) Conservative fluid management (less fluid, more diuretics) in patients with ARDS results in decreased mortality.

(d) Conservative fluid management in patients with ARDS results in more ventilator- and ICU-free days.

(e) Conservative fluid management in patients with ARDS is associated with increased risk for dialysis-requiring AKI.

For the answer to the question, see the following text.

Q 4

Palliative Care Nephrology in the ICU

Case 4: *A 70-year-old man is admitted with respiratory failure due to community-acquired pneumonia. Blood cultures are positive for pneumococcus. He is started on appropriate antibiotic therapy and requires intubation. Shortly afterward, he is initiated on norepinephrine and vasopressin therapy due to worsening hypotension despite intravenous fluids. Over the next 72 hours, the patient's creatinine level increases from 1.0 to 4.4 mg/dL, and urine output decreases to 0 to 5 mL/h. A family meeting is planned to discuss the initiation of CRRT.*

Question 4: Which off the following is most correct?

(a) Palliative care (PC) consultation would be inappropriate because he has AKI rather than chronic kidney disease.

(b) A goals-of-care discussion is not indicated because most patients with AKI and respiratory failure survive.

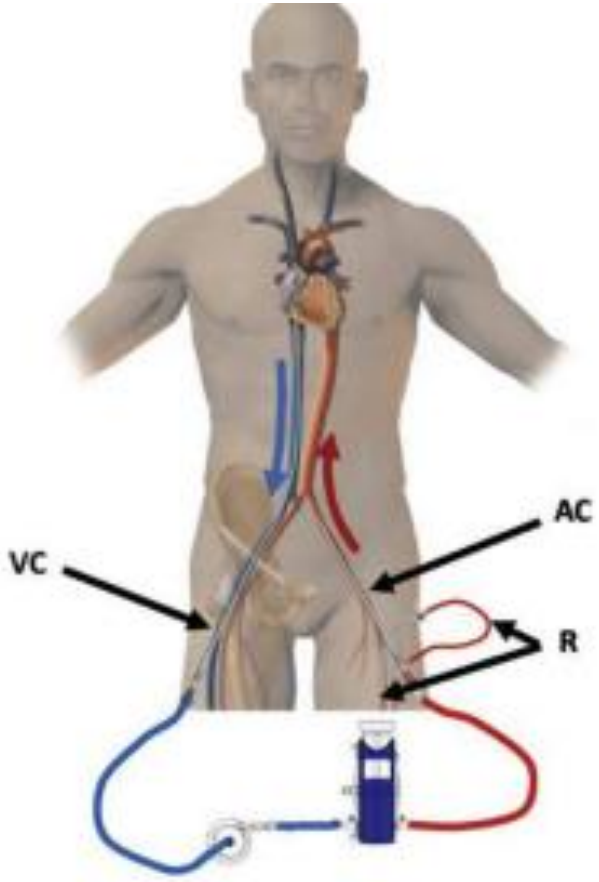
(c) If the patient is started on RRT and survives the hospitalization, his quality of life (QoL) at 60 days is likely to return to his prehospitalization baseline.

(d) CRRT should not be offered even if desired by the family because it would constitute futile care in this case.

(e) A time-limited trial of CRRT should be pursued in this case if CRRT is desired by the family.

For the answer to the question, see the following text.

Q 5



如左圖所示,ECMO 的接法為何種？

A: V-V mode

B: A-A mode

C: A-V mode

Table 1. Risk Stratification Is Important to Determine Which Patients Are at High Risk for Progression to AKI, Which Can Allow for Closer Monitoring and Earlier Intervention

Risk Stratification Tool	Clinical Utility	Key Readings
Clinical risk prediction scores	Used to give greater context to a patient's clinical situation; eg, analogous to cardiac angina, "renal angina" is a concept intended to identify patients at high risk for AKI. Risk factors (eg, advanced age, hypertension, DM, CKD) and exposures (eg, volume depletion, nephrotoxins, sepsis) are combined with symptoms (eg, reduced urine output, volume overload, creatinine elevation). Malhotra et al developed a risk score based on acute and chronic factors to predict AKI development in ICU patients. Understanding a patient's baseline risk (pretest probability) allows for better interpretation of biomarker data and furosemide stress test results.	Chawla et al (*Crit Care* 2015; https://doi.org/10.1186/s13054-015-0779-y) Malhotra et al (*NDT* 2017; https://doi.org/10.1093/ndt/gfx026)
Computer algorithms	Machine learning algorithms have been used to identify patients at high risk for AKI or for requiring RRT. These complicated models can predict AKI with greater precision than risk prediction scores and can be used in real time to screen for AKI in the ICU and have been shown to detect AKI up to 6 h earlier than laboratory markers (Automated Continuous Acute Kidney Injury Prediction and Surveillance: A Random Forest Model, Chiofolo et al, *Mayo Clin Proc* 2019)	Koyner et al (*Crit Care* 2018; https://doi.org/10.1097/CCM.0000000000003123)
Furosemide stress test	Like a cardiac stress test, this functional test is meant to further stratify patients at intermediate risk of AKI progression. The patient is given IV furosemide at 1.0 mg/kg (if furosemide-naive) or 1.5 mg/kg (if previously exposed). Urine output < 200 mL over the next 2 h has 87% sensitivity and 84% specificity to predict progression to stage 3 AKI.	Koyner et al (*JASN* 2015; https://doi.org/10.1681/ASN.2014060535)

AKI Biomarker	Source	Function	Clinical Utility
[TIMP-2] × [IGFBP-7]	Urine	21- and 29-kDa proteins, respectively, involved in G_1 cell cycle arrest	Best at AKI prediction in the ICU setting out of 340 candidates evaluated in the Discovery Trial; FDA approved for marketing in 2014
NGAL	Urine or serum	25-kDa protein that binds to iron-siderophore complexes and has a bacteriostatic function via the sequestering of iron during infection	Systemic levels are elevated in sepsis and severe inflammation, so clinical use is limited in the adult ICU setting
Cystatin C	Urine or serum	13-kDa protein in the family of cysteine protease inhibitors, produced in all nucleated cells	In serum, marker of GFR similar to creatinine; in urine, because it is normally absorbed and fully degraded in the proximal tubule, urinary cystatin C is a marker of tubular dysfunction
KIM-1	Urine	Transmembrane protein thought to participate in both kidney injury and healing processes	FDA approved for detection of drug-induced AKI in preclinical studies; unreliable in the setting of inflammation
IL-18	Urine	Cytokine that regulates innate and adaptive immunity	Has not been well evaluated in the adult ICU setting

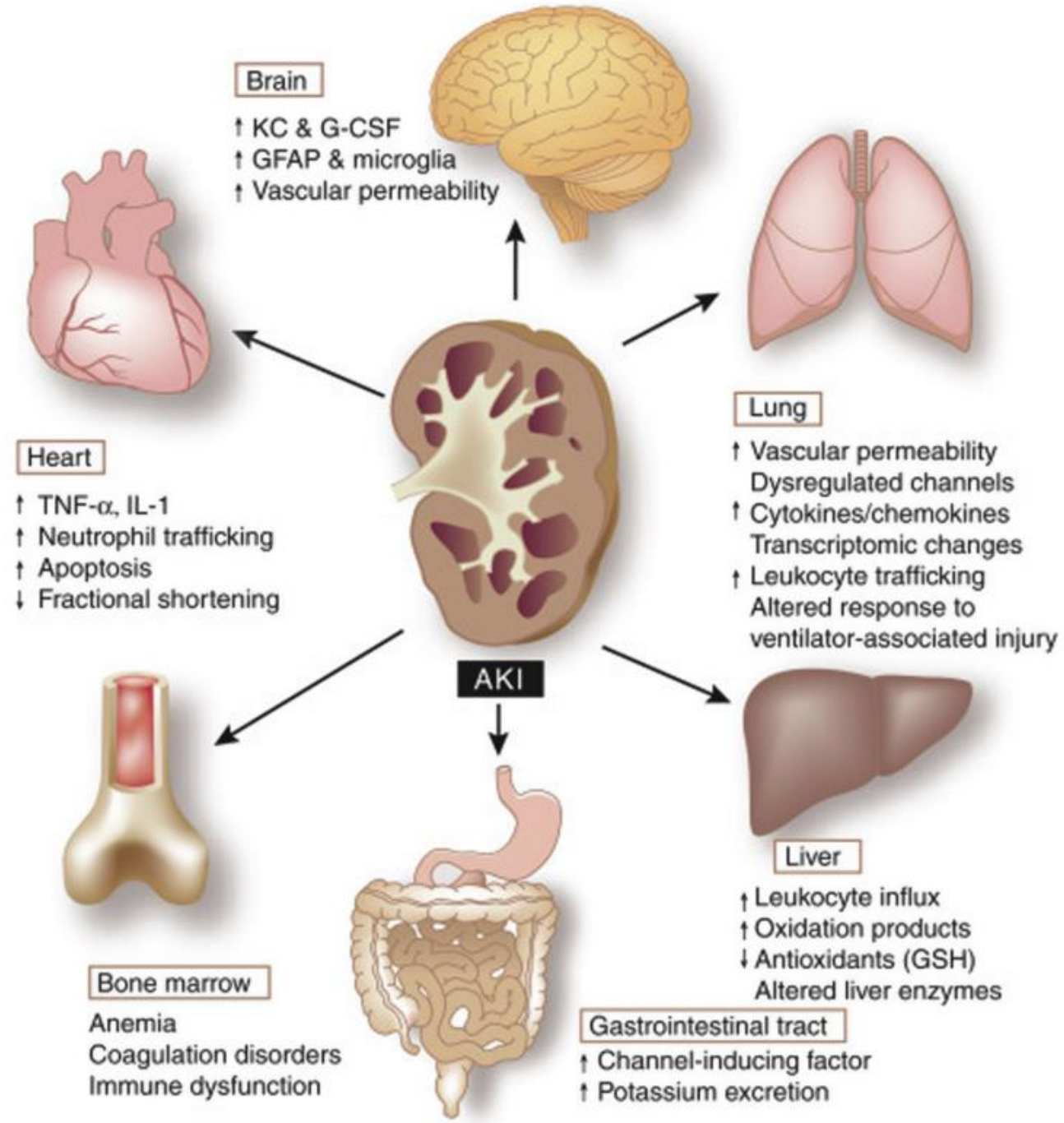

Brain
↑ KC & G-CSF
↑ GFAP & microglia
↑ Vascular permeability
Heart
↑ TNF-α, IL-1
↑ Neutrophil trafficking
↑ Apoptosis
↓ Fractional shortening
Lung
↑ Vascular permeability
Dysregulated channels
↑ Cytokines/chemokines
Transcriptomic changes
↑ Leukocyte trafficking
Altered response to
ventilator-associated injury
AKI
Liver
↑ Leukocyte influx
↑ Oxidation products
↓ Antioxidants (GSH)
Altered liver enzymes
Bone marrow
Anemia
Coagulation disorders
Immune dysfunction
Gastrointestinal tract
↑ Channel-inducing factor
↑ Potassium excretion

Table 2. Summary of Common Causes of AKI in the ICU Setting

Cause	Definition	Epidemiology	Pathophysiology	Management
Sepsis	KDIGO AKI in the setting of "life threatening organ dysfunction caused by a dysregulated host response to infection"; SOFA score increase ≥ 2 points or qSOFA ≥ 2	Most common cause of AKI (accounts for 50% of AKI cases in the ICU); incidence is 10%-20% of septic patients overall, 50%-70% in septic shock	No longer thought to be primarily ischemic/hypotensive in nature; key factors are: (1) Microvascular dysfunction (2) Endothelial dysfunction (3) Inflammation (4) Oxidative stress	Early fluid resuscitation
Cardiac surgery	No consensus definition, but KDIGO criteria are becoming standard	Second most common cause of AKI in the ICU; incidence ranges from 5%-42% depending on AKI definition used	Multifactorial; extracorporeal circulation and hemolysis are unique contributors to CSA-AKI	PrevAKI trial showed adhering to KDIGO guideline reduced AKI rates by 30% in a high-risk population
Acute liver failure	(1) Hepatic encephalopathy of any severity, (2) INR ≥ 1.5 (3) Onset of illness < 26 wk (4) No evidence of cirrhosis	50% of ALF cases due to acetaminophen toxicity; 70% develop AKI, 30%-70% require RRT	(1) Renal hypoperfusion from decreased MAP and increased renal vasoconstriction (2) Direct tubular toxicity from offending agent (acetaminophen most commonly)	"Early" RRT; expedited liver transplant
Intra-abdominal HTN	IAH defined as IAP > 12 mm Hg; ACS defined as IAP > 20 mm Hg associated with new organ dysfunction	Interestingly, IAH—likely via renal venous congestion—has been associated with both HRS and CRS; AKI rate may be as high as 40%	Decreased perfusion mediated by elevations in renal vein pressure and renal parenchymal pressure (rather than by decreased cardiac output or ureteral compression)	(1) Decompressive laparotomy (2) Adequate sedation and analgesia to control abdominal muscle tone

Hepatorenal syndrome	(1) Presence of cirrhosis & ascites (2) Scr increase ≥ 0.3 mg/dL (3) No improvement in Scr after 48 h of diuretic withdrawal & volume expansion with albumin (4) Absence of shock (5) No nephrotoxic drugs (6) Absence of proteinuria, hematuria, or US findings	HRS type 1 has a 2-wk mortality of 80%; HRS type 2 has a median survival of 6 mo; in patients awaiting liver transplant, rate of HRS is nearly 50%	Primarily due to intense renal vasoconstriction without structural kidney damage	(1) Midodrine and octreotide (2) Terlipressin (outside the US) (3) TIPS (4) Liver transplant
Malignancy	KDIGO-defined AKI in the setting of malignancy	18% in first y following cancer diagnosis; mortality in AKI-RRT is 66%-88%	Cancer-specific causes include: (1) Nephrotoxic chemotherapy (2) Cast nephropathy (3) Lymphomatous infiltration (4) Hepatic sinusoidal obstruction syndrome (5) TMA	(1) Discontinue offending agent if possible (2) Treatment of underlying condition (3) RRT
Cardiorenal syndrome	Type 1: Acute cardiac dysfunction leading to decreased kidney function; Type 3: Acute worsening of kidney function causing cardiac dysfunction; Type 5: Systemic conditions causing simultaneous dysfunction of the heart and kidney	45%-65% of patients with HF with reduced ejection fraction will develop concomitant kidney disease	Type 1: Kidney arterial underfilling and increased venous congestion due to systolic dysfunction; Type 3: Incompletely understood; Type 5: Sepsis is the most common example in the ICU	Diuresis; stepped pharmacologic therapy is superior to ultrafiltration for the preservation of kidney function

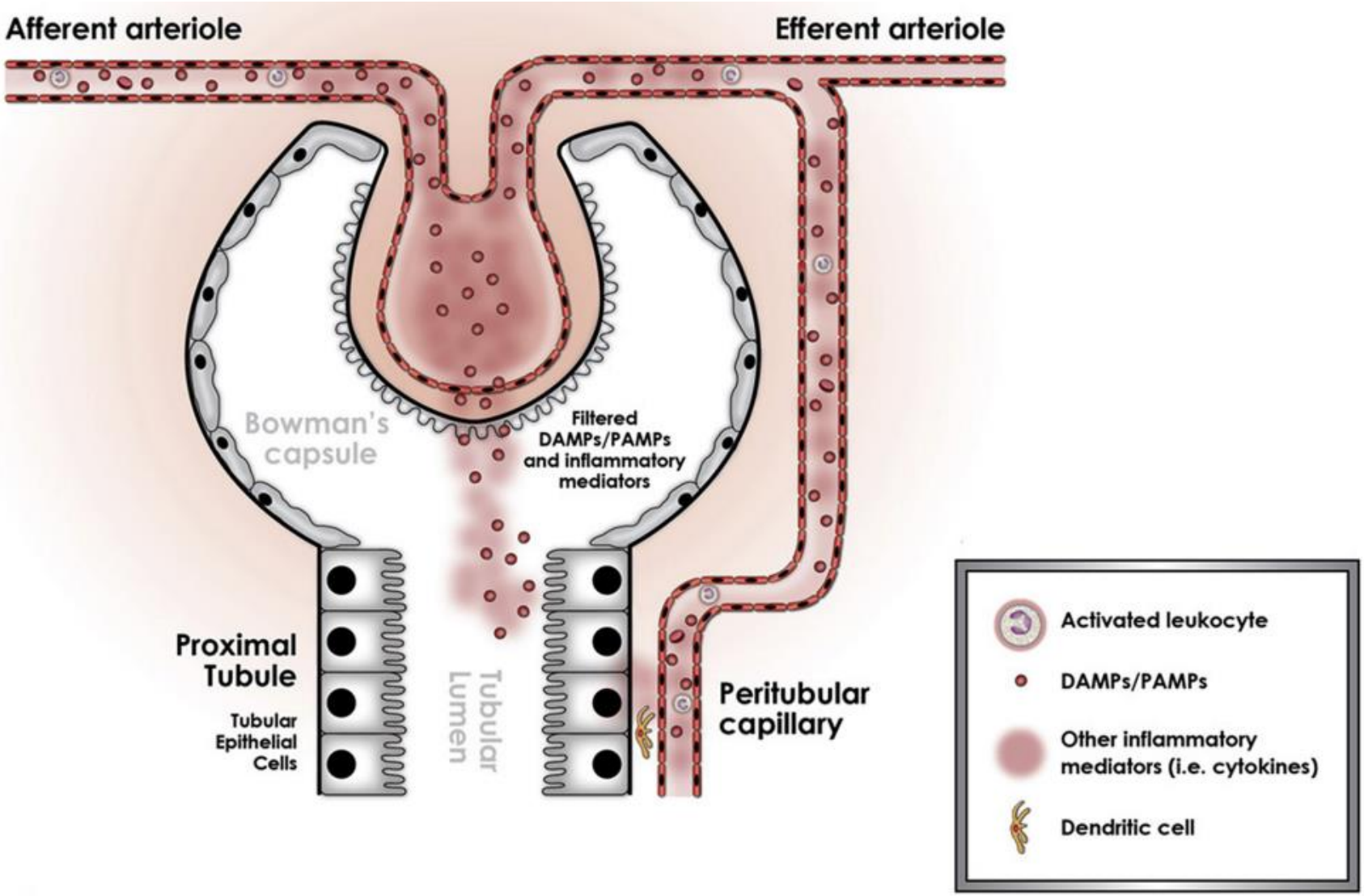

Afferent arteriole
Efferent arteriole
Bowman's capsule
Filtered DAMPs/PAMPs and inflammatory mediators
Proximal Tubule
Tubular Epithelial Cells
Tubular Lumen
Peritubular capillary
Activated leukocyte
DAMPs/PAMPs
Other inflammatory mediators (i.e. cytokines)
Dendritic cell

Figure 2. (A) Sepsis results in the release of damage- (DAMPs) and pathogen-associated molecular patterns (PAMPs), which are filtered at the glomeruli. (B) These "danger signals" can lead to significant microcirculatory dysfunction, which is manifest by heterogeneity of flow. A number of capillaries begin to exhibit sluggish flow, which may lead to amplification of the danger signals in these areas and lead to increased oxidative stress. Also, expression of tumor necrosis factor (TNF) receptors in the S2 segment tubular cells has inspired the proposal that secretion of TNF-α by S1 cells may signal distal segments in a paracrine fashion. There is some evidence that this paracrine signal may also include mediators of cell cycle arrest, namely tissue inhibitor of metalloproteinase 2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP-7). (C) Paracrine stimulation from S1 segment tubular epithelial cells triggers an "oxidative outburst" in the S2 and S3 segment tubular epithelial cells. This oxidative outburst may affect mitochondrial function by uncoupling respiration, thereby causing energetic imbalance, production of radical oxygen and nitrogen species (ROS/RNS), and loss of mitochondrial membrane potential. Apoptosis may be avoided through reduced energy utilization, mitophagy, and cell-cycle arrest. Finally, downregulated apical ionic transport leads to chloride accumulation which triggers tubuloglomerular feedback (TGF) and subsequent constriction of the afferent arteriole, leading to decreased glomerular filtration rate. Abbreviations: AMP, adenosine monophosphate; ATP, adenosine triphosphate; ICAM, intercellular adhesion molecule; NHE1, sodium-hydrogen antiporter 1; VCAM, vascular cell adhesion molecule. Figure panels adapted from Gomez et al (A unified theory of sepsis-induced acute kidney injury: inflammation, microcirculatory dysfunction, bioenergetics, and the tubular cell adaptation to injury. *Shock*. 2014;41(1):3-11) with permission of Wolters Kluwer Health, Inc; original images

Table 3. Comparison of Randomized-Controlled Studies Evaluating the Timing of RRT Initiation

	AKIKI (n = 619)	ELAIN (n = 231)	IDEAL ICU (n = 488)	STARRT AKI (target n = 2,866)
Study site	Multicenter (France)	Single surgical ICU (Germany)	Multicenter (France)	Multicenter (international)
Inclusion criteria	KDIGO stage 3 AKI and on ventilator (85%) or pressors (85%) (with septic shock in 56%)	(1) KDIGO stage 2 AKI, (2) plasma NGAL > 150 ng/mL, and (3) severe sepsis, pressors, fluid overload despite diuretics, and/or nonrenal SOFA > 2	RIFLE-F AKI in early septic shock (100% on pressors)	KDIGO stage 2 AKI
Significant exclusion criteria	Severe AHRF ($Fio_2 \geq 50\%$)	—	Pulmonary edema despite diuretics	—
Early RRT	Within 6 h of stage 3 AKI	Within 8 h of stage 2 AKI	Within 12 h of stage 3 AKI	Within 12 h of randomization
Indications for RRT in delayed arm	SUN > 112 mg/dL, K > 6 mmol/L, pH < 7.15, severe pulmonary edema, oliguria > 72 h	Stage 3 AKI or SUN > 100 mg/dL, K > 6 mmol/L, organ edema, urine output < 200 mL/d	At 48 h unless recovery or K > 6.5 mmol/L, pH < 7.15, or pulmonary edema	K ≥ 6.0 mmol/L, pH ≤ 7.20, bicarbonate ≤ 12 mmol/L, $Pao_2/Fio_2 \leq 200$, persistent AKI > 72 h
Receipt of RRT (early vs late)	98% vs 51%	100% vs 91%	97% vs 62%	Awaiting results
Spontaneous recovery (in late-start group)	49%	9%	38%	
RRT modality	55% IHD, 45% CRRT	100% CVVHDF	55% CRRT, 45% IHD	
60-d mortality (early vs late)	48.5% vs 49.7% ($P = 0.79$)	38.4% vs 50.4% ($P = 0.07$)	—	
90-d mortality (early vs late)	—	39.3% vs 54.7% ($P = 0.03$)	58% vs 54% ($P = 0.38$)	
ICU LOS in survivors	13 d in both groups (NS)	19 vs 22 days (NS)	12 d in both groups (NS)	
MV (early vs late)	7 vs 6 d free of MV (NS)	125 vs 181 h ($P = 0.002$)	2 vs 3 d free of MV (NS)	

Table 4. Typical Hemodynamics in Various Shock States and Their Differential Diagnosis

	CVP or Preload	CO	SVR	Examples
Distributive	↓	↑	↓↓	• Septic • Neurogenic • Anaphylaxis • Adrenal insufficiency
Hypovolemic or hemorrhagic	↓↓	↓	↑	• Hemorrhagic • Other volume depletion (diarrhea, vomiting, overdiuresis, inadequate intake)
Cardiogenic	↑	↓↓	↑	• Acute myocardial infarction • Heart failure • Valvular disease • Post cardiopulmonary bypass • Arrhythmia
Obstructive	NA	↓↓	↑	• Massive pulmonary embolism • Tamponade • Tension pneumothorax • Mechanical ventilation with excess PEEP

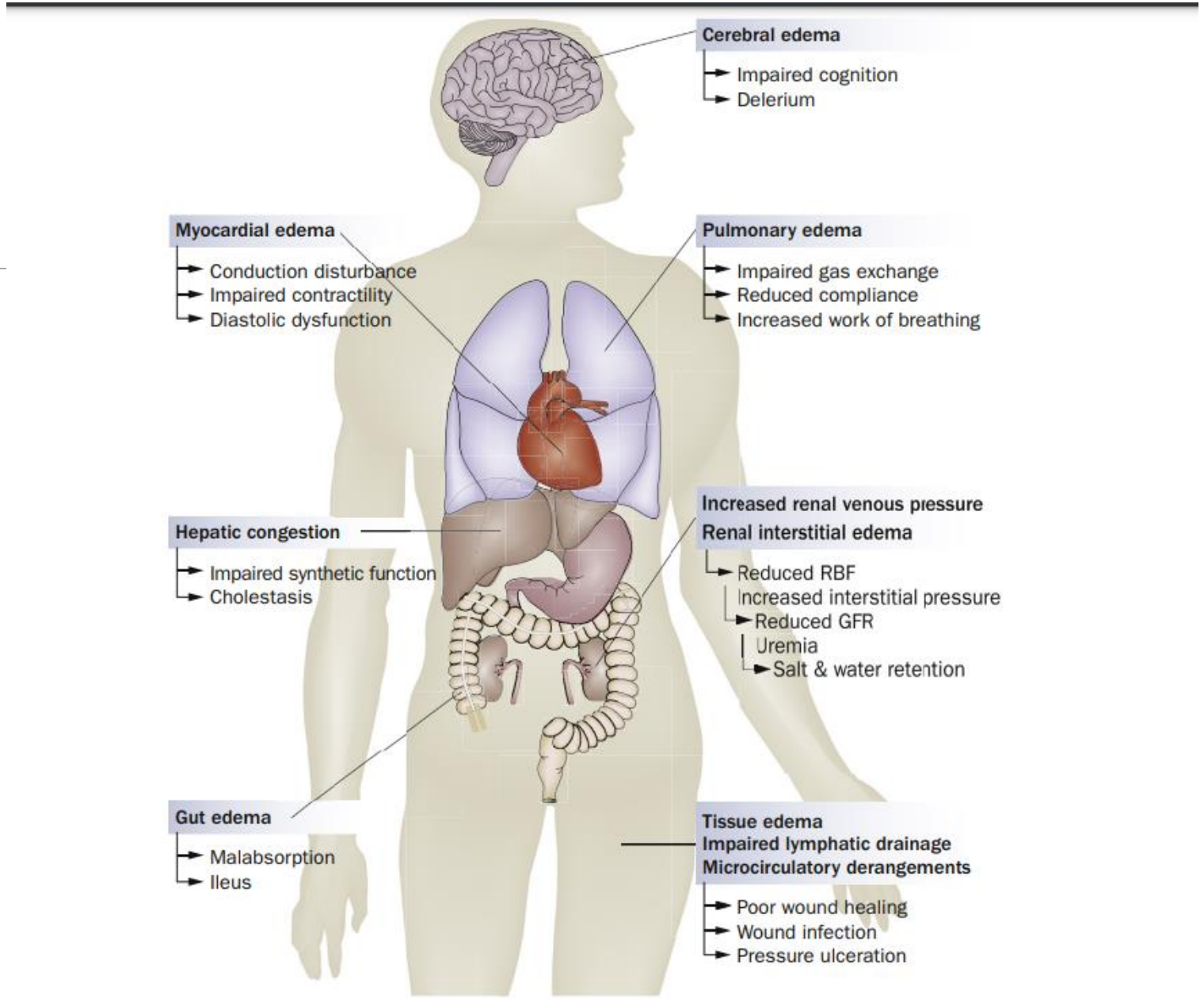


Figure 4. Pathologic sequelae of fluid overload in organ systems. Abbreviations: GFR, glomerular filtration rate; RBF, renal blood flow. Reproduced from Prowle et al (Fluid balance and acute kidney injury. *Nat Rev Nephrol*. 2010;6(2):107-15) with permission of Springer Nature; original image © 2010 Macmillan Publishers Limited.

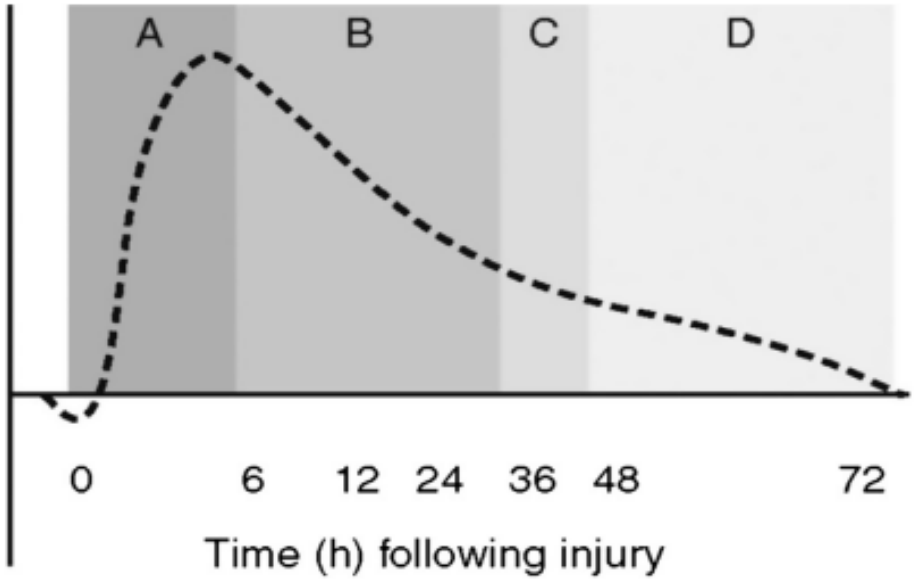


Figure 5. Changing fluid resuscitation strategies parallel the phases of critical illness and the immune response to sepsis or another injury. Phase A (0-6 hours): initial aggressive volume resuscitation (eg, 30 mL/kg of intravenous crystalloid), also known as the ebb phase of critical illness. Phase B (6-36 hours): decelerating fluid resuscitation; fluid is often still required to compensate for extravascular sequestration, but fluids should only be provided as needed to maintain organ perfusion in a targeted manner, with frequent reassessment of fluid responsiveness. Phase C (36-48 hours): equilibrium phase; fluid administration is stopped. Phase D (beyond 48 hours): mobilization, deresuscitation, or flow phase; fluids are withheld to allow for spontaneous diuresis or, in those who fail to autodiurese, pharmacologic diuresis or ultrafiltration can be provided to achieve euvolemia. The time at which a given patient transitions phases may vary and multiple insults can substantially disrupt this sequence. Reproduced from Godin et al (Clinical approach to the patient with AKI and sepsis. *Semin Nephrol.* 2015 Jan;35(1):12-22) with permission of Elsevier; original image © 2015 Elsevier Inc.

First - Na

90% extracellular

Major determinant of extracellular osmolality

Very important for CNS

Large rapid changes can be life threatening

Small changes are harmless but warn of other processes

Check electrolytes!

Hyponatremia - causes

Decreased Na – increased loses, AI, CSW, diuretics, osmotic loses (DKA)

Increased Na – free water retention exceeds Na retention, CHF, cirrhosis, nephrotic syndrome, renal failure

Normal Na - SIADH

Which of the following drugs is NOT associated with SIADH

A. Vincristine
B. Haldol
C. Azithromycin
D. Ecstasy
E. SSRI

C. Azithromycin

Hyponatremia: Symptoms & Treatment

Cellular swelling and cerebral edema

Lethargy, N/V, cramps, confusions

Seizures and coma <120 (acute)

Chronically CNS cells compensate – rapid correction - osmotic demyelination

Treatment – 1st stop herniation/seizures

5-6 ml/kg 3% will raise Na 5mEq/L

Chronic or acute with CNS sx – 0.5mEq/L/h

Acute with no CNS sx – 0.7-1mEq/L/h

MUST follow levels!

How many mEq of Na are in a L of 3% Saline

A. 513

B. 462

C. 300

D. A lot

E. Too much math

Answer A. Normal saline is 0.9% 154mEq/L. Divide by 9. Add to 154 to get “1% saline”. Multiple by 3. Other options include google. Note “normal saline” is actually not.

Hypernatremia: Causes

Decreased Na – free water loses > Na loses, diarrhea, iatrogenic from insufficient free water, diuresis

Normal Na – DI

Increased Na – usually iatrogenic – 3% in TBI, $NaHCO_3$ during resuscitation, improperly prepared infant formula

Hypernatremia: Symptoms & Treatment

Increased osmolality, most issues in CNS

Irritability, spasticity, N/V, seizures, coma and of course death

Decreased brain cell volume – tearing of vessels, subcortical or subdural bleeds, vascular congestion, CVT, demyelination

Accumulation of idiogenic osm in CNS cells occurs with time

Rapid correction – brain edema

Correct over 48 h no faster than 1 mEq/L/H

Now, K^+

Mostly intracellular

Hypokalemia is common, rarely fatal

Hyperkalemia is uncommon and very bad

Mostly K is managed by kidneys and GI tract

Also affected by acid-base balance, insulin, catecholamines, Mg and aldosterone

Kidneys secrete K during alkalosis and resorb it during acidosis

Cells exchange K^+ for H^+ when acidosis is caused by excess H^+ therefore….

Hypokalemia: causes, symptoms & treatment

Beta-agonists, hyperaldosteronism, elevated renin, diuretics, osmotic diuresis, GI loses, malnutrition, re-feeding, geophagia, Barium poisoning, Barter syndrome, RTA, drugs…

Symptoms – flattened T-waves, ST depression, U-waves, arrhythmias, weakness, ileus

Hyperkalemia: Causes, symptoms & Treatment

Causes – redistribution, administration error, blood products, rhabdo, hemolysis, renal failure, TLS, metabolic acidosis, AI

EKG – peaked T-waves, decreased P and R wave, widened QRS, bradycardia, classic sine wave blending P and QRS complex

EKG can progress over minutes, CPA, V-fib/tach can happen at any point in this progress

< 6.5 remove K^{+} +/- kayexalate and monitor

>6.5 or EKG changes, Ca^{+2} , insulin/glucose, sodium bicarb, albuterol, dialysis, loop/thiazides diuretics

You are NF senior. A pt has a K^+ of 7.5 with EKG changes. What is the 1st thing you should do?

A. Order calcium
B. Order insulin/glucose
C. Order sodium bicarb
D. Call rapid response
E. Call code blue
F. Call PICU attending

Answer: Discuss. Real life is not multiple choice….

Same patient has pulseless v-tach, the first thing you should do?

A. CPR
B. Defibrillate
C. Calcium
D. Sodium bicarb
E. Insulin
F. Call a code blue

Answer: start (or make sure someone else starts) CPR. Everything else should happen simultaneously, again really life not multiple choice.

通用流程

A: 呼吸道 (airway)

氣管插管

B: 呼吸 (breathing)

確認氣管插管

評估氧氣

評估通氣

通用流程

C: 循環 (circulation)

建立靜脈注射

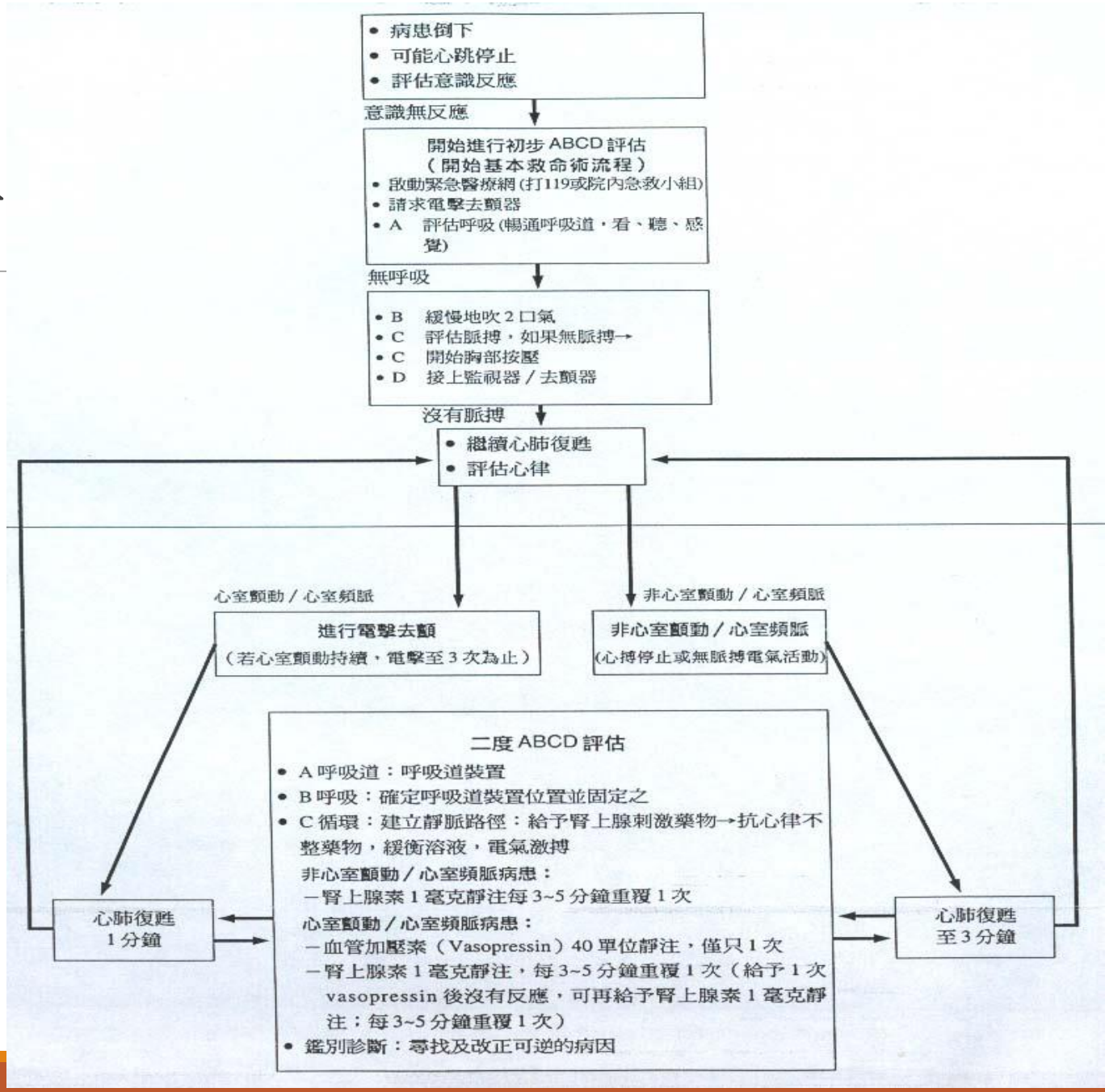
急救藥物

- VF/VT: Vasopression OR Epinephrine
- Non-VF/VT: Epinephrine

D: 電擊去顫 (defibrillation)

Drug-Shock-Drug-Shock

通用流程


病患倒下
可能心跳停止
評估意識反應
意識無反應
開始進行初步 ABCD 評估
（開始基本救命術流程）
啟動緊急醫療網 (打119或院內急救小組)
請求電擊去顫器
A 評估呼吸 (暢通呼吸道，看、聽、感覺)
無呼吸
B 緩慢地吹 2 口氣
C 評估脈搏，如果無脈搏→
C 開始胸部按壓
D 接上監視器 / 去顫器
沒有脈搏
繼續心肺復甦
評估心律
心室顫動 / 心室頻脈
非心室顫動 / 心室頻脈
進行電擊去顫
（若心室顫動持續，電擊至 3 次為止）
非心室顫動 / 心室頻脈
(心搏停止或無脈搏電氣活動)
二度 ABCD 評估
A 呼吸道：呼吸道裝置
B 呼吸：確定呼吸道裝置位置並固定之
C 循環：建立靜脈路徑：給予腎上腺刺激藥物→抗心律不整藥物，緩衝溶液，電氣激搏
非心室顫動 / 心室頻脈病患：
－腎上腺素 1 毫克靜注每 3~5 分鐘重覆 1 次
心室顫動 / 心室頻脈病患：
－血管加壓素（Vasopressin）40 單位靜注，僅只 1 次
－腎上腺素 1 毫克靜注，每 3~5 分鐘重覆 1 次（給予 1 次 vasopressin 後沒有反應，可再給予腎上腺素 1 毫克靜注；每 3~5 分鐘重覆 1 次）
鑑別診斷：尋找及改正可逆的病因
心肺復甦 1 分鐘
心肺復甦至 3 分鐘

Special Resuscitation

HYPOTHERMIA（低體溫）

定義

低體溫：中心體溫＜35℃

一般水銀溫計：35~42℃

特殊感測器：鼓膜、直腸、食道

Severity：

- Mild：34~36℃
- Moderate：30-34℃
- Severe：＜30℃（86℉）

處理流程

一般之處置

檢查神智， ABC（須檢查30~45秒）

有脈搏者：

- 按照低體溫嚴重度給予回饋

無脈搏者：

- CPR/電擊去顫（VT/VF）
- 體溫＞30℃方可靜脈給藥或繼續電擊

一般之處置

除去濕衣物

以乾棉被保溫

維持水平姿勢以免產生坐立性低血壓

避免大動作以免產生VF

監控中心體溫（耳/肛溫）

監控心律（needle electrode）

回溫

Mild（34-36℃）
- 被動回溫與主動體外回溫

Moderate（30~34℃）
- 被動回溫與主動體外軀幹回溫（避免afterdrop）

Severe（＜30℃）
- 主動體內回溫
- 院外做主動體內回溫仍屬爭議

主動體內回溫

溫熱之靜脈輸液（43℃）150-200cc/h

溫熱潮溫之氧氣（42~46℃）

腹膜灌洗（KCL-free,每次2L）

胸腔灌洗（chest tubes×2）

食道回溫管回溫

Goal:＞35℃

無呼吸，無脈搏：開始CPR

VT/VF：電擊去顫（200-300-360J）

插入氣管內管

以溫熱潮濕之氧氣換氣（42~46℃）

靜脈注射

給予溫熱之靜脈輸液（43℃）150-200cc/h

主動體內回溫至＞30℃方向靜脈給藥或繼續電擊

Key Points

Not dead until warm and dead（32℃）

ETT, NG, CVP, PCWP, TVP皆可引發VF

低溫之心臟對藥物，節律器之刺激，或電擊都可能無效

相關：溺水，藥物過量，酒精中毒，外傷

Bretylium：對低體溫產生之VF可能有效

Thiamine 100mg：惡病質者，酒癮者

Special Resuscitation

NEAR-DROWING（溺水）

定義

Drowing 溺斃

Near-drowing 溺水

溺水之BLS：從水中救出

個人安全最重要

使用運輸工具

- 船隻
- 救生筏
- 衝浪板
- 救生圈

病患保持水平姿勢

溺水之BLS：急救呼吸

淺水急救
- 確定個人安全後盡快給予口對口人工呼吸

深水急救
- 潛水員通氣管之使用

頸部外傷
- Neutral position
- Jaw thrust/ chin lift without head tilt

毛地黃中毒：誘因

Hypokalemia

Hypomagnesemia

Drug interaction

Hypoxemia

Hypothyroidism

Renal insufficiency

Volume depletion

Loss of muscle mass

考題模擬

高血鉀不會出現於下列何種疾病或情況？

(A) 擠壓症候群 (crush syndrome)

(B) 毛地黃中毒 (digitalis intoxication)

(C) 代謝性酸血症 (metabolic acidosis)

(D) 庫欣氏症候群 (Cushing’s syndrome)

49 歲男性，健檢發現飯前血糖 132 mg / dL、腎絲球過濾率 90 mL / min / 1.73 m ²、無蛋白尿， 其餘檢查皆正常。下列敘述何者最適當？

(A) 無慢性腎臟疾病，維持規律生活型態及避免使用腎毒性藥物即可

(B) 慢性腎臟疾病第一期，加強血糖控制與相關危險因子之衛教

(C) 慢性腎臟疾病第二期，轉由「全民健康保險慢性腎臟病品質支付服務」進行收案

(D) 慢性腎臟疾病第三期，轉診照會腎臟專科醫師

30 歲糖尿病人，主訴漸進性呼吸急促，合併有噁心、肚子不舒服、食慾下降。身體診察 出現深而快的呼吸 38 次 / 分、心跳 140次 / 分、體溫及血壓均正常、呼吸音兩側對稱清晰、 血糖 550 mg / dL 且血清酮體呈陽性。下列敘述何者較不正確？

(A) 若血液中鉀離子濃度為 4.0 mEq / L，治療應同時補充鉀離子

(B) 血液的滲透壓下降至 240 mOsm / kg，因受血糖排擠所致

(C) 血液氣體分析呈現代謝性酸中毒合併呼吸代償的現象

(D) 血液中鈉離子濃度降至 122 mEq / L，可能為假性低血鈉

造成高陰離子間隙之代謝性酸中毒 (high anion - gap metabolic acidosis) 的常見原因，下列何者錯誤？

(A) lactic acidosis

(B) diabetic ketoacidosis

(C) renal tubular acidosis

(D) uremia

體內電解質失衡的處置，下列何者最不適當？

(A) 低血鈉 (hyponatremia) 第一線治療應使用靜脈輸注生理食鹽水
(B) 高血鉀 (hyperkalemia) 應先檢視心電圖是否有相關電氣生理變化

(C) 高血鈣 (hypercalcemia) 治療應給予足夠水份，並依副甲狀腺素指標作鑑別診斷

(D) 矯正低血鈉 (hyponatremia) 時，血清鈉濃度每日上升不應快於 10-12 mEq / L