

Cheng Hsin General Hospital

## ICU的任務- 代謝平衡及復甦 The role of critical care-metabolic resuscitation

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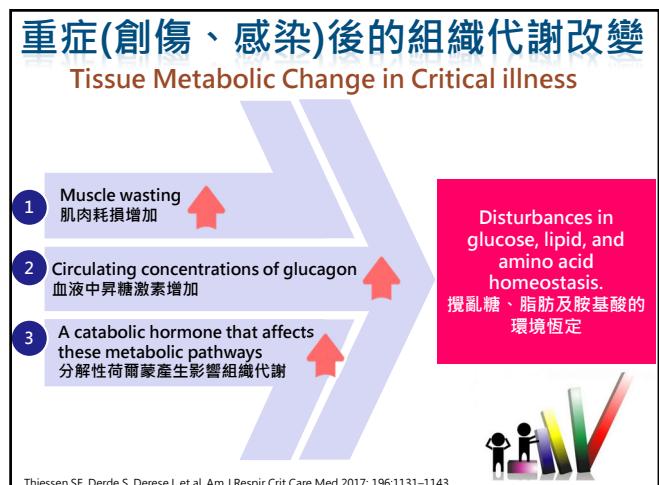
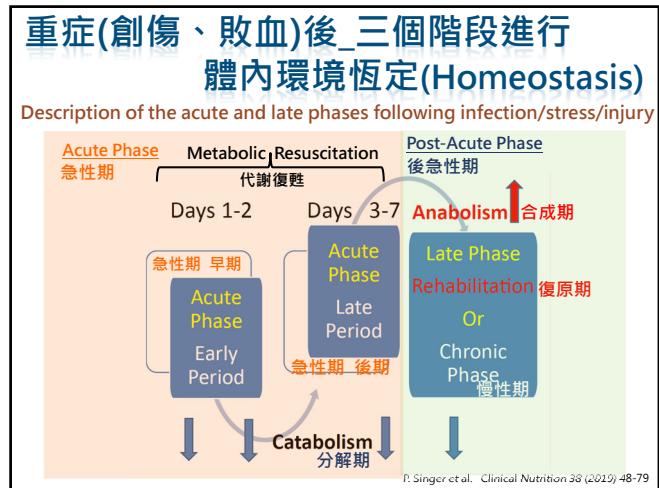
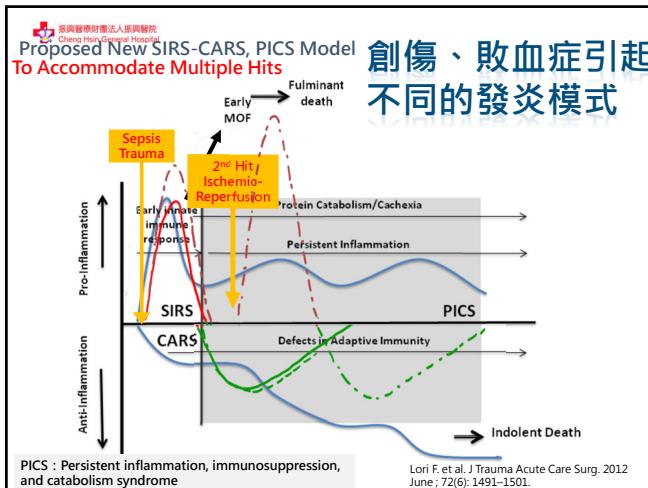
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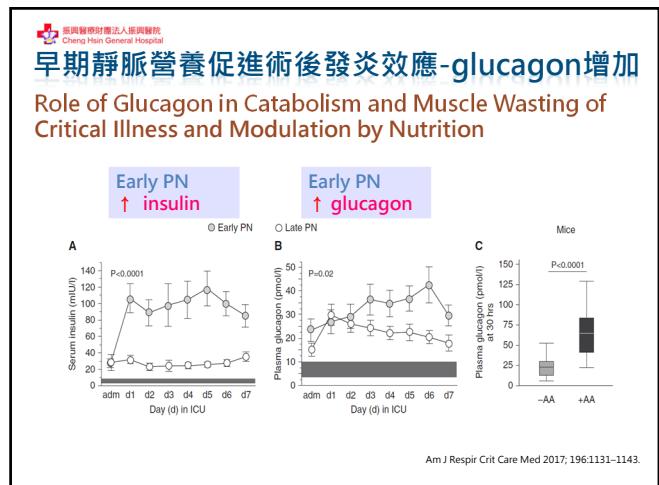
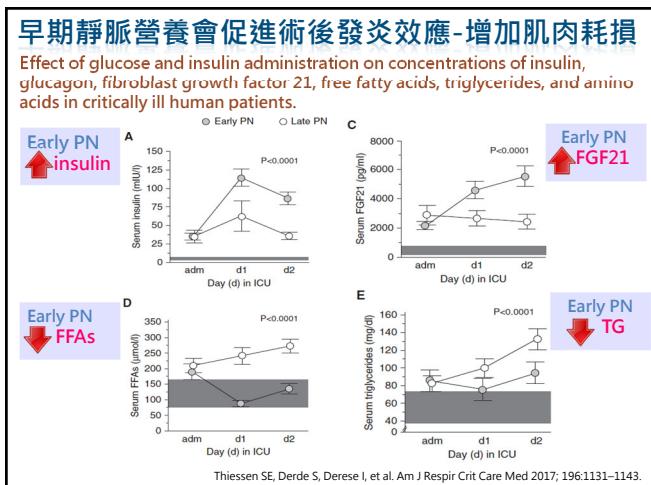
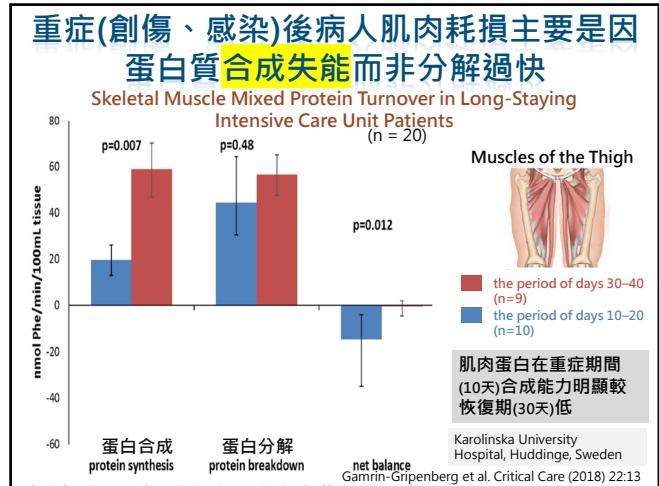
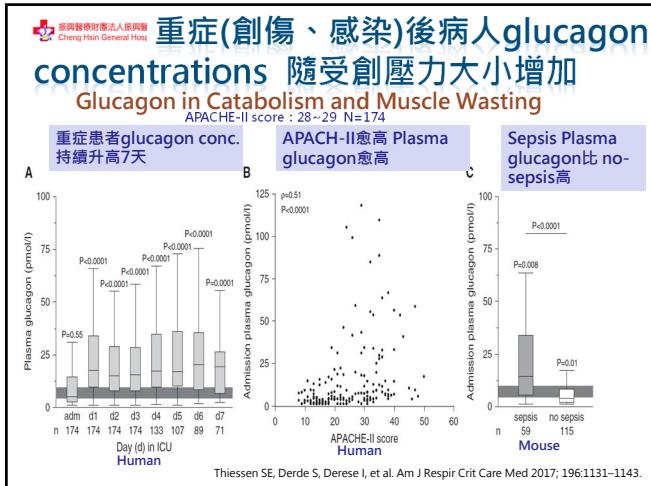
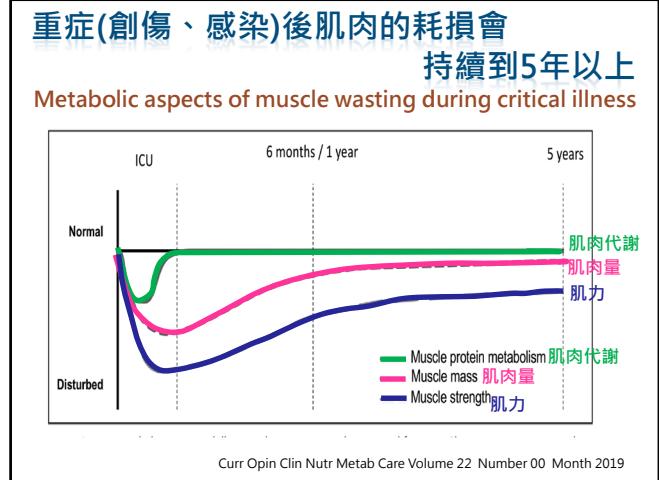
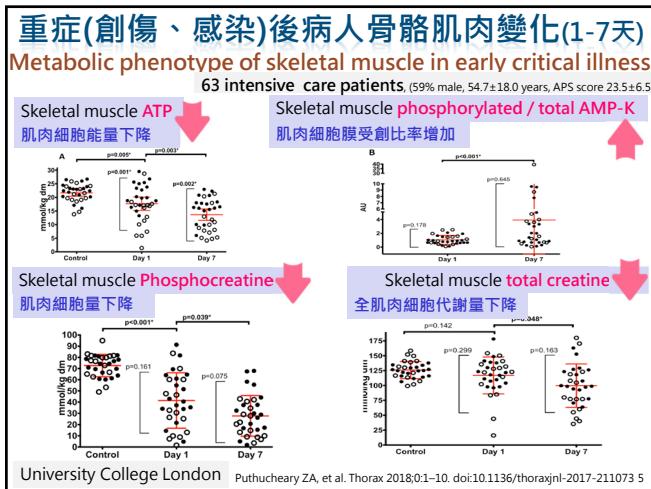
Cheng Hsin General Hospital

## Are we creating survivors...or victims in critical care?

Duke Health profile for Paul E. Witzelmeyer, MD, showing his expertise in metabolic resuscitation and critical care.

Curr Opin Crit Care. 2016;22(4):279-84.





## 重症創傷病人早期全靜脈營養死亡率高 Energy Supplement is not Necessary in Early Post-operative Period

**Mortality Rate Between Received TPN vs. No-TPN in the SICU**

	Death/TPN Patients (%)	Death/No-TPN Patients (%)	p ( $\chi^2$ )
Total deaths	47/461 (10.2)	395/2,484 (15.9)	0.58
Deaths >24 h	47/461 (10.2)	307/2,396 (12.8)	0.12
Deaths >48 h	47/461 (10.2)	171/2,260 (7.6)	0.058
Deaths >72 h	47/461 (10.2)	119/2,208 (5.4)	0.001
Deaths >96 h	46/460 (10.0)	85/2,174 (3.9)	<0.001
Deaths >120 h	46/460 (10.0)	69/2,158 (3.2)	<0.001
Deaths >144 h	45/459 (9.8)	61/2,150 (2.8)	<0.001
Deaths >168 h	44/458 (9.6)	48/2,137 (2.2)	<0.001

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*J Trauma. 2007;63:1215–1222.*

## 敗血症患者早期接受物理治療可保護肌肉流失 Impact of Very Early Physical Therapy During Septic Shock on Skeletal Muscle: A Randomized Controlled Trial

**Control Group**  
underwent a daily physiotherapy session through manual passive/active limbs mobilization (5/7 d).

**Intervention Group**  
**Two physiotherapy sessions per day (7/7 d)** including 30 minutes (1 hr/d) of continuous passive/active leg chair/bed cycling followed by manual passive/active limbs mobilization

Fiber Type	Control Group (n = 9), Mean ± SD		Intervention Group (n = 8), Mean ± SD		p <sup>b</sup>
	Day 1	Day 7	Day 1	Day 7	
All fibers types ( $\mu\text{m}^2$ )	3,603 ± 1,284	2,629 ± 1,174 <sup>a</sup>	3,448 ± 1,993	3,770 ± 1,473	0.01
Type I fibers ( $\mu\text{m}^2$ )	4,236 ± 1,379	3,135 ± 1,103 <sup>a</sup>	4,250 ± 1,977	4,678 ± 1,189	0.02
Type-IIa fibers ( $\mu\text{m}^2$ )	3,949 ± 1,447	2,744 ± 1,260 <sup>a</sup>	2,574 ± 856	2,920 ± 745	0.003
Type-IIb fibers ( $\mu\text{m}^2$ )	2,624 ± 1,243	2,006 ± 1,286 <sup>a</sup>	2,082 ± 1,083	2,576 ± 948	0.04

<sup>a</sup> Day1 VS. Day7 <0.05

Hickmann CE, Castanares-Zapatero D, Deldicque L, et al. Crit Care Med 2018; 46:1436–1443.

## Summary I

The role of critical care- metabolic resuscitation

- 重症造成的代謝生理變化，形成不同型態的發炎模式。
- 重症患者的組織細胞代謝改變主要在肌肉，而內分泌 (glucagon) 主要主導其代謝變化。
- 重症病人的肌肉耗損主要是蛋白質的合成失能，而非分解過快。
- 重症病人早期靜脈營養促發發炎反應，增加glucagon，增加肌肉耗損。
- 患者的肌肉復原即早物理治療介入，可促進重症患者的肌肉復原。

## 創傷患者兩階段發炎反應現象 Hypothetical Biphasic Immuno-Inflammatory Response to a Traumatic Insult

**HYPER INFLAMMATION**  
Excess inflammatory eicosanoids, cytokines, ROS, adhesion molecules; NFκB activation

**Hypo**  
~12-48 hrs

**IMMUNO SUPPRESSION**  
Excess anti-inflammatory cytokines; suppressed HLA expression & antigen presentation; suppressed T cell function

British Journal of Nutrition (2007), 98, Suppl. 1, S133–S139

## 低卡路里高蛋白的發炎代謝需求 Tailoring Nutrition Therapy for Critical Illness

**Proposal for targeted nutrition delivery in critical illness**

**Kcal/kg/day**

**Protein (g/kg/d)**

**Activity/rehab increases**

*Curr Opin Crit Care. 2016;22(4):279-84.*

## 重症初期自我降低免疫反應 Early down-regulation of the pro-inflammatory potential of monocytes is correlated to organ dysfunction in patients after severe multiple injury: a cohort study

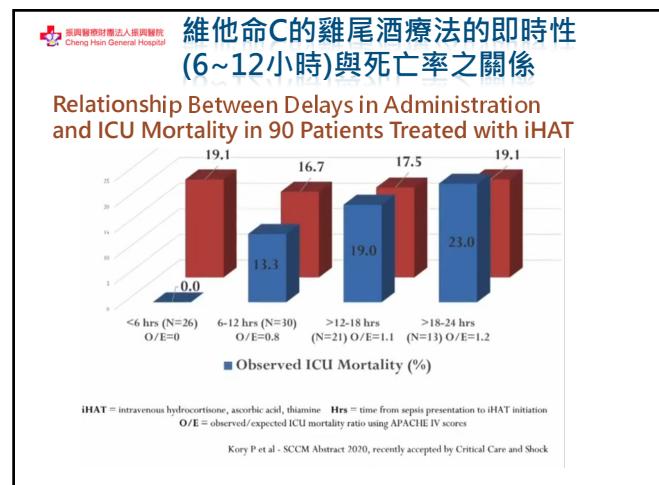
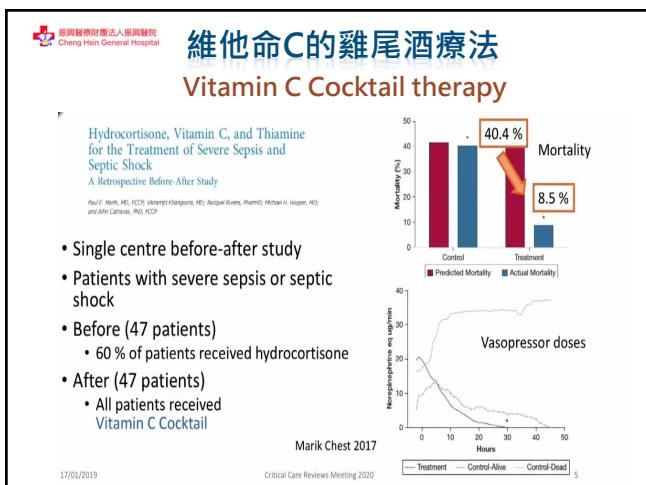
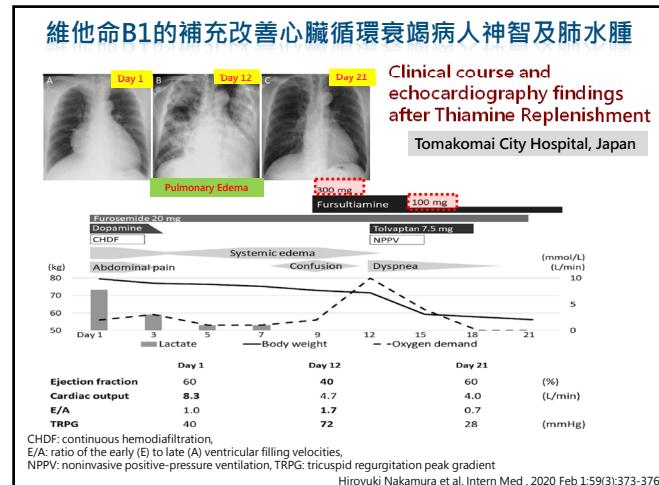
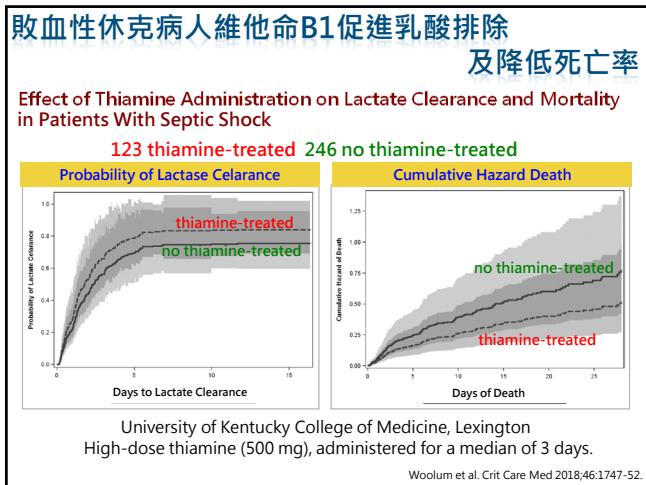
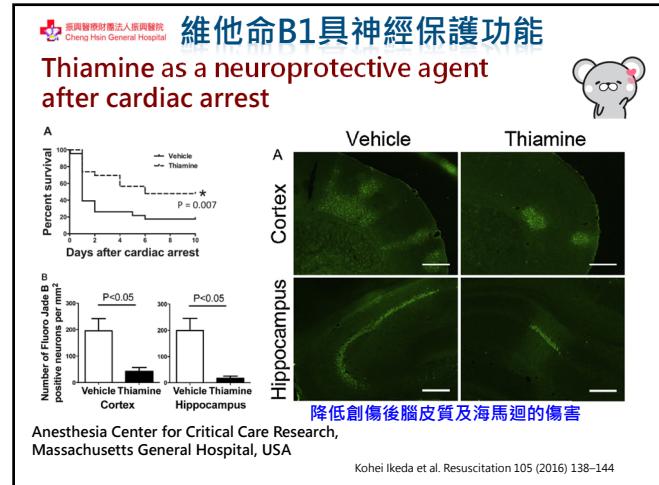
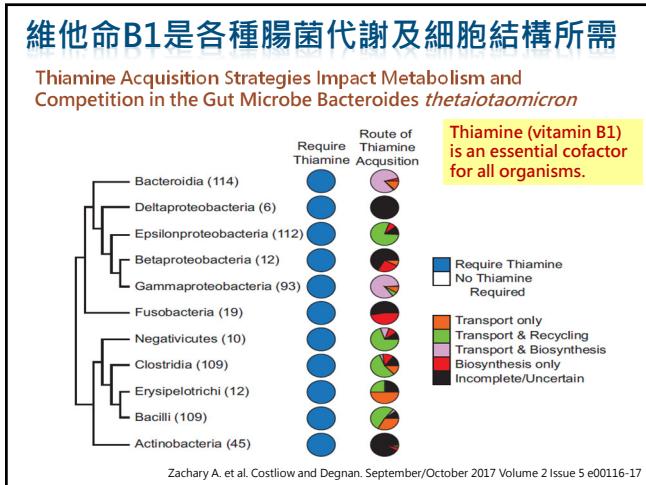
Chlodwig Kirchhoff<sup>1</sup>, Peter Biberthaler<sup>2</sup>, Wolf E Mutschler<sup>2</sup>, Eugen Faist<sup>3</sup>, Marianne Jochum<sup>4</sup> and Siegfried Zedler<sup>3</sup>

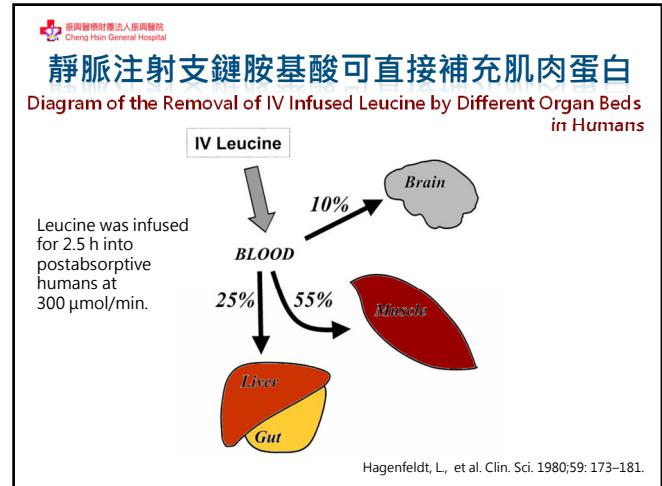
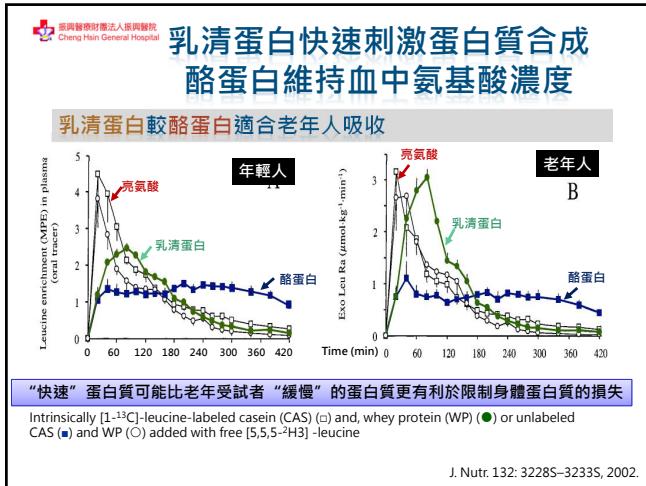
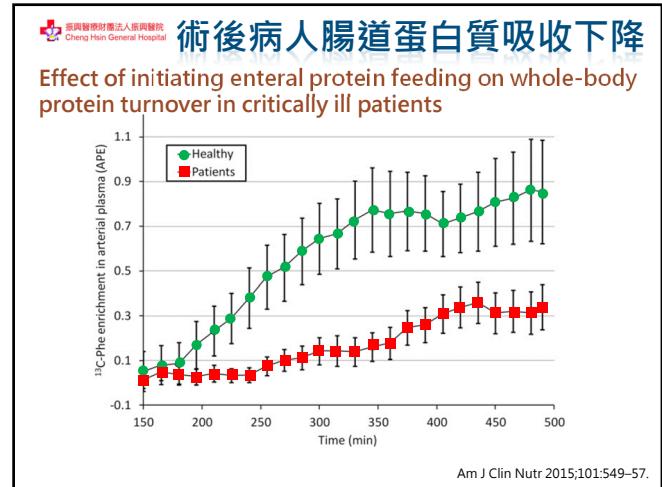
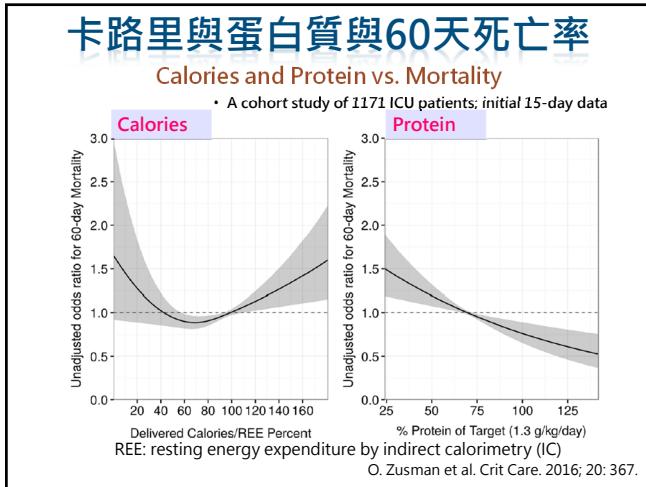
An immediate hyperactivation of circulating monocytes is rapidly followed by a substantial paralysis of cell function

(a) TNF $\alpha$   
(b) IL-1 $\beta$   
(c) IL-6  
(d) IL-8

Severe multiple injury results in a rapid decline of intracellular cytokine synthesis by monocytes within the first 24 hours after trauma

*Critical Care 2009, 13:R88*



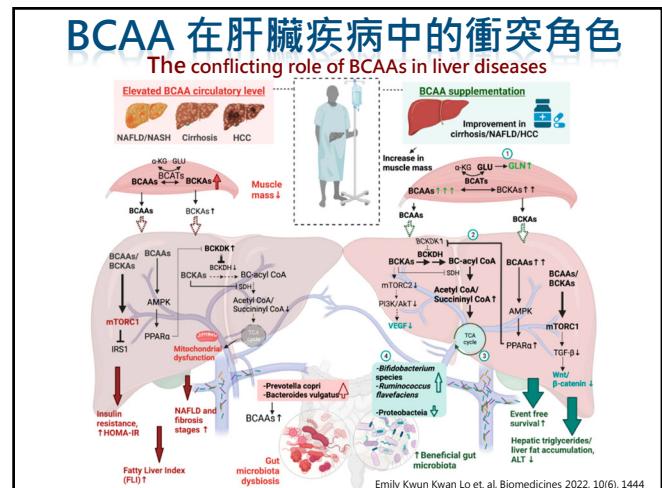


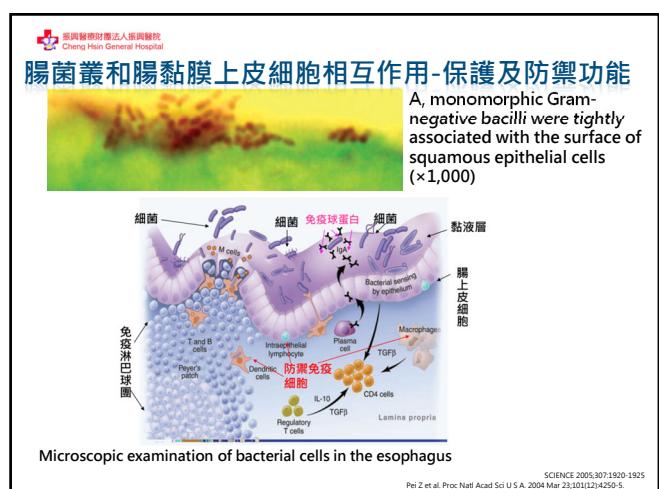
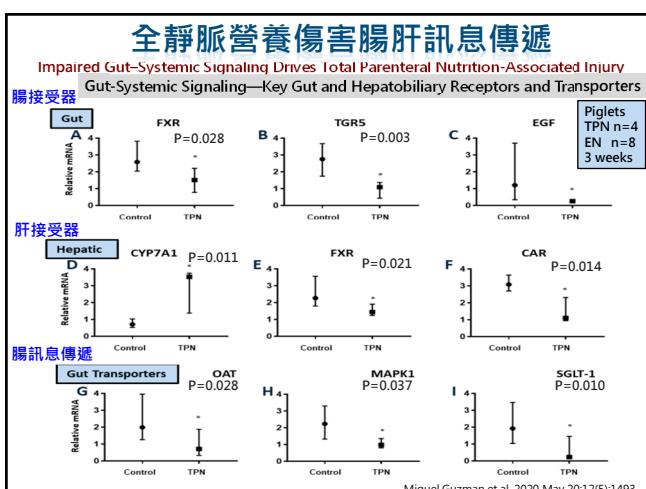
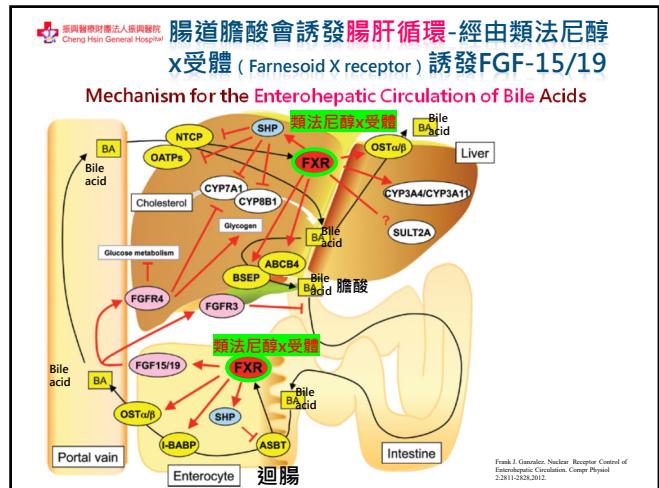
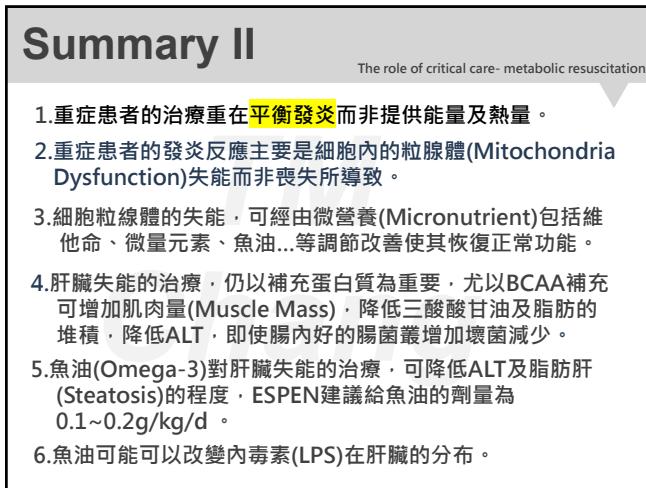
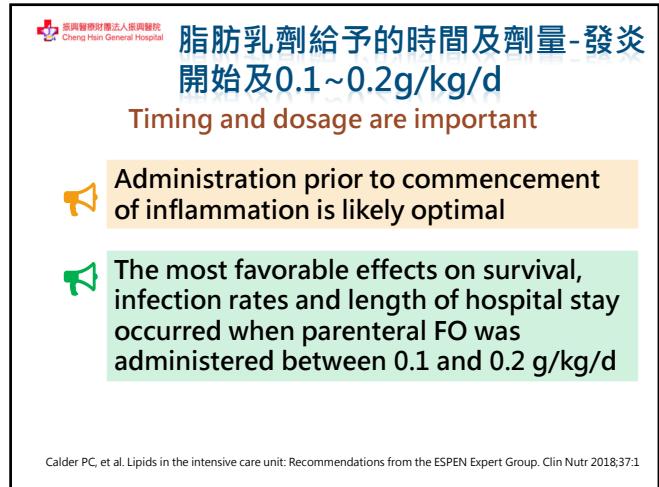
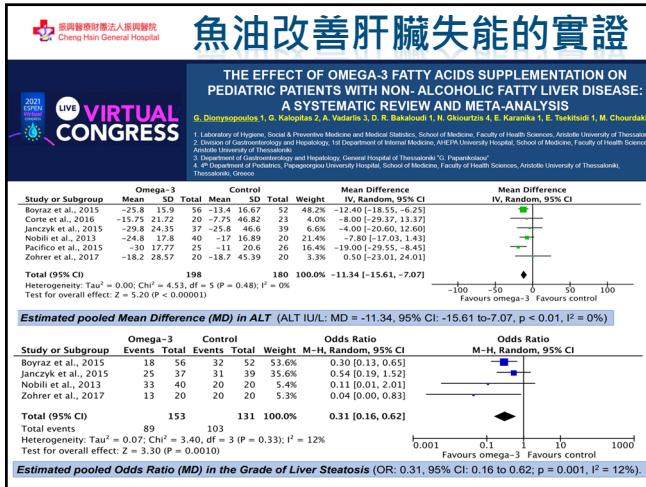
### BCAA治療肝臟疾病成效

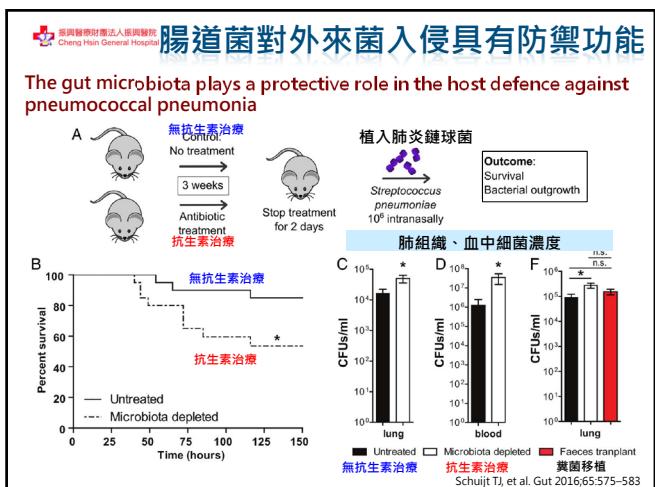
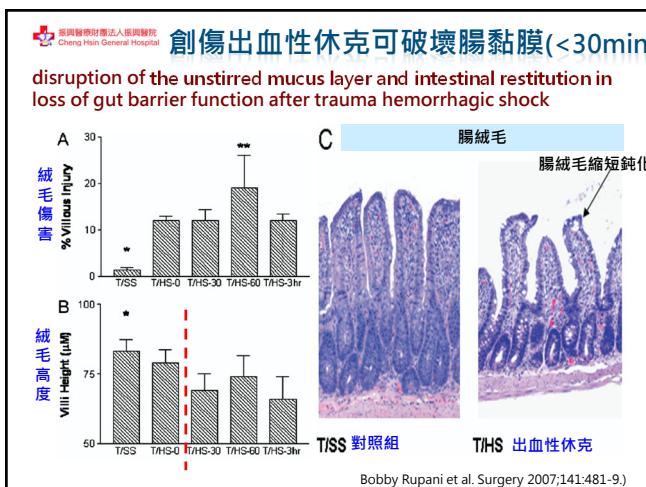
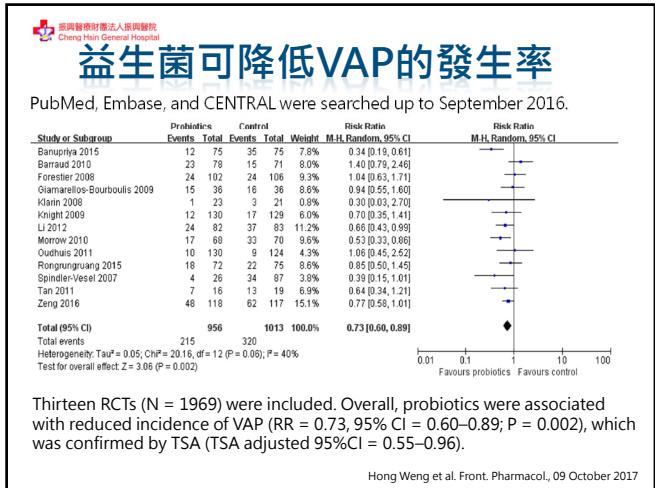
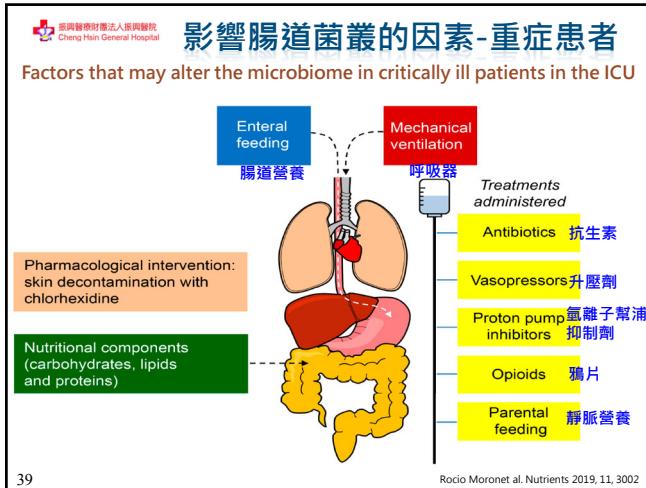
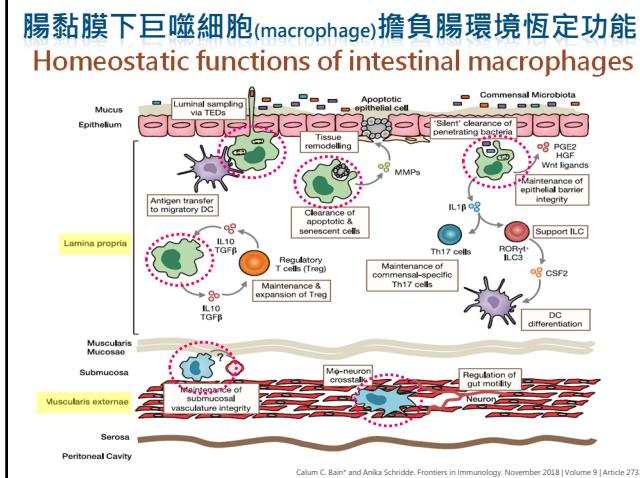
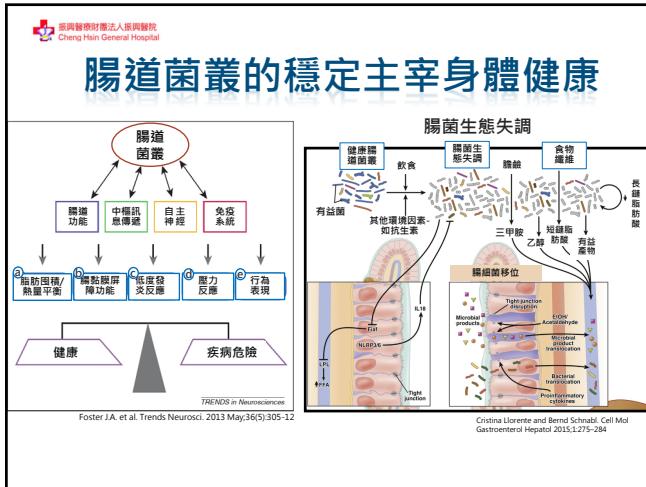
**Clinical trials and ongoing clinical studies utilizing BCAA to treat liver disease.**

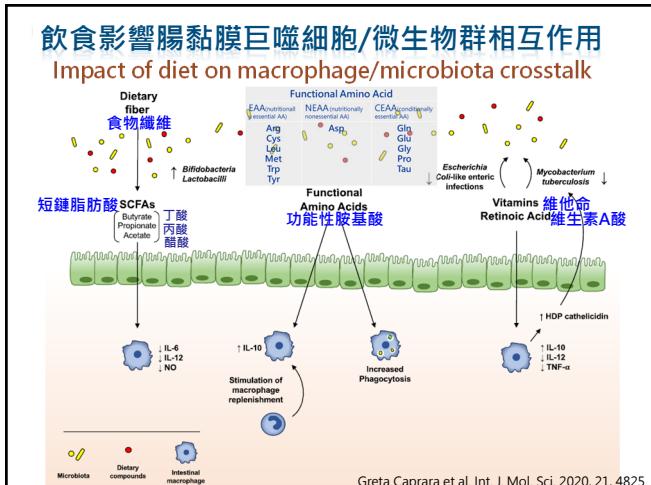
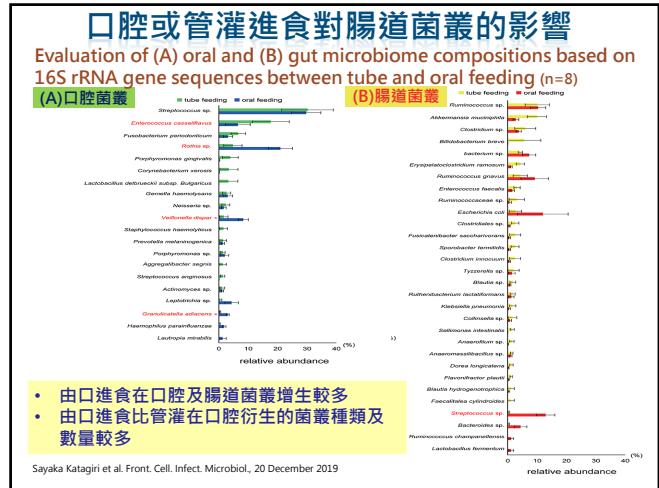
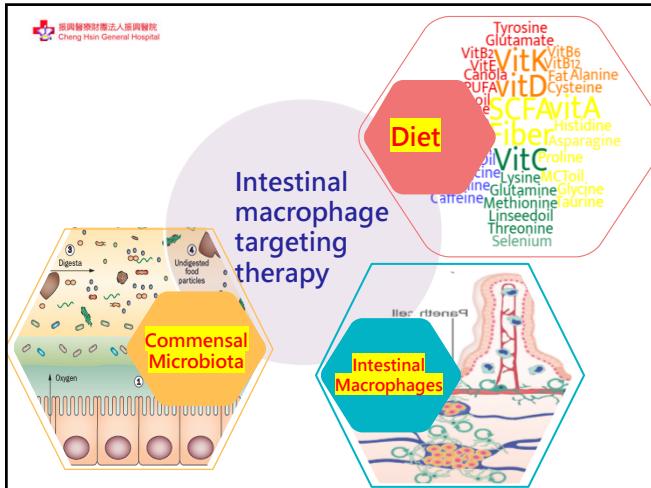
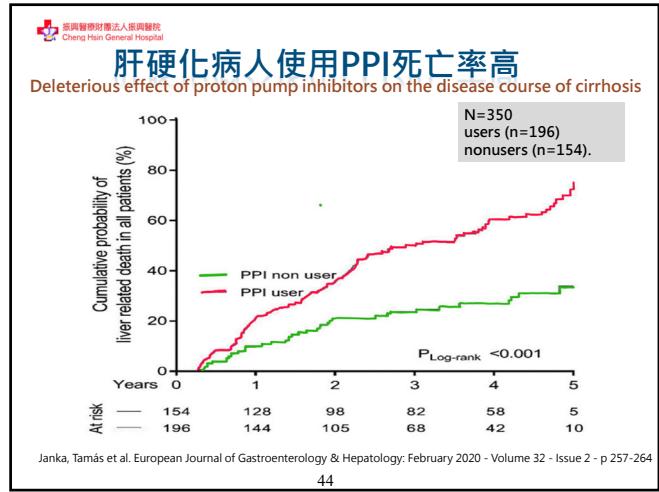
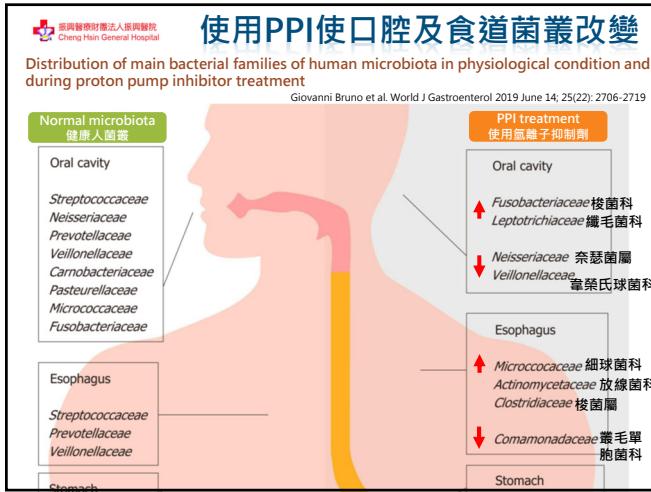
Type of Studies*	Interventions	Patients/Control	Sample Size	Duration	Outcome & Outcome Measures	
Nutrients 2020; 12,429	Multicenter RCT	VAL, LEU, ILE	Advanced liver cirrhosis	232	6 months	- MELD, CP score, Cumulative cirrhosis-related overall survival
Gastroenterology 2003; 124,170	Double-blinded RCT	VAL, LEU, ILE	Advanced cirrhosis	174	12 months	- CP score
Gastroenterol. Jpn. 1989; 24,62	N/A	VAL, LEU, ILE /AAA	Cirrhosis	104	>6 months	- Total bilirubin level
Dig Dis 2011; 29,326	N/A	VAL, LEU, ILE	Cirrhosis	211	≥6 months	- Delayed coagulation including hepatic failure and gastrointestinal bleeding
Gastroenterol. 2020; 11, e0222	Single-blinded RCT	AXA1663 (Leuc Val)	Child-Pugh A and B Cirrhosis	16	15 days	- HCC occurrence
Am J Gastroenterol 2021; 116,2399	Single-blinded, Multicenter RCT	AXA1125 (VAL, LEU, ILE, ARG, GLN)	Patients with NAFLD with and without T2D	102	16 weeks	- Liver Frailty Index
Nutrition 2018; 33, 20	RCT	VAL, LEU, ILE	HCC	51	12 months	- ALT, Kt/B
					- Intrahepatic recurrence rate	
					- Event-free survival	
					Ongoing clinical studies	
Triple-blinded RCT, Phase II	AXA1125 (VA, LEU, ILE, ARG, GLN)	NASH with fibrosis	273	48 weeks	Improvement in steatosis and resolution of NASH/fibrosis	
	RCT	VAL, LEU, ILE	Cirrhosis	60	3 months	Muscle mass, insulin-resistant

Emily Kwun Kwan Lo et. al, Biomedicines 2022, 10(6), 1444









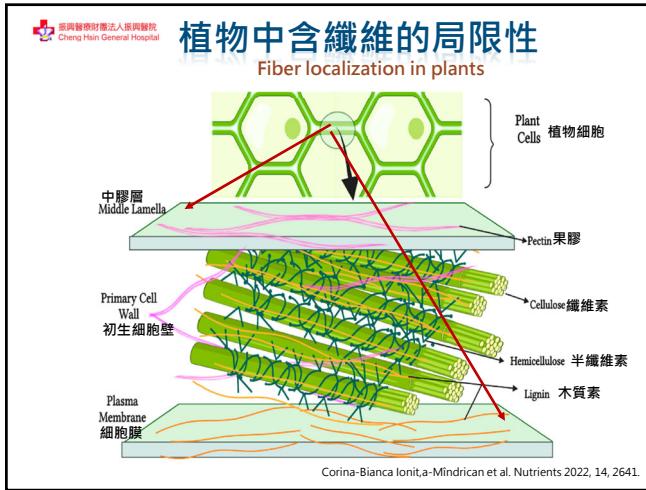
**膳食纖維依溶於水的狀態分為兩類**

two forms of dietary fiber based on their capacity to dissolve in water

- 1. soluble fibers 水溶性纖維 (80~100%可發酵)**  
包括果膠 (Pectin)、洋車前子 (Psyllium) 和β-葡聚醣 (Beta-glucan) 等  
a) 在腸道中形成膠體溶液 in the presence of water, form colloidal solutions in the intestine  
b) 延緩營養素的消化和吸收 slow down digestion and absorption of nutrients  
c) 延長飽足感和降低食慾, 例如降低食物昇糖指數 provides a prolonged feeling of satiety and a decrease in appetite, such as and a reduction in food glycemic index)
- 1. insoluble fibers 非水溶性纖維 (50%可發酵)**  
包括木質素 (Lignin) 和纖維素 (Cellulose) 等  
a) 可完整通過消化系統的纖維 those that pass primarily intact through the digestive system  
b) 加速腸道蠕動 accelerating intestinal transit  
c) 在身體的解毒過程中發揮重要作用 playing an important role in the body's detoxification process

★發酵纖維會被益生菌分解，提供他們能量，進而維持腸道菌叢的平衡

Corina-Bianca Ionita-Mindrigan et al. Nutrients 2022, 14, 2641.



**老年人使用菊糖纖維可改變糞便菌叢**  
Effects of Lactose or Inulin Administration on Fecal Flora in Elderly Patients

35 female with a mean age of 76.4 y (range: 68-89 y)

Fecal variable	Lactose (n = 15)			Inulin (n = 10)		
	Before administration	20 g/d	40 g/d	Before administration	20 g/d	40 g/d
Total counts	9.3 ± 0.7 <sup>†</sup>	9.7 ± 0.8	9.7 ± 0.7	9.2 ± 0.3	9.5 ± 0.7	9.3 ± 0.8
Bifidobacteria 雙歧桿菌	8.2 ± 0.7 [100] <sup>‡</sup>	8.6 ± 0.9 [93.3]	8.5 ± 0.9 [100]	7.9 ± 0.4 [90]	8.8 ± 0.8 <sup>†</sup> [92 ± 0.5]	9.0 ± 0.4 [90]
Bacteroides	9.0 ± 1.1 [100]	9.3 ± 0.9 [100]	9.5 ± 0.7 [100]	9.0 ± 0.3 [100]	9.2 ± 0.8 [100]	8.6 ± 0.9 [90]
Clostridia	6.4 ± 1.2 [86.7]	6.0 ± 0.8 [73.3]	5.6 ± 0.8 <sup>†</sup> [90.9]	6.3 ± 1.4 [100]	6.2 ± 1.2 [100]	6.4 ± 1.2 [90]
Lactobacilli	7.9 ± 0.9 [100]	7.1 ± 1.1 <sup>†</sup> [93.3]	7.0 ± 1.0 <sup>†</sup> [81.8]	7.6 ± 0.7 [80]	7.5 ± 1.2 [80]	7.2 ± 0.8 [90]
Enterococci 粪腸球菌	7.1 ± 1.1 [100]	8.0 ± 0.6 <sup>†</sup> [100]	8.1 ± 1.2 <sup>†</sup> [100]	7.3 ± 1.2 [100]	7.1 ± 1.2 [100]	6.3 ± 0.6 <sup>†</sup> [90]
Enterobacteria	7.1 ± 1.6 [86.7]	6.8 ± 1.6 [86.7]	6.4 ± 1.2 [100]	7.0 ± 1.1 [100]	6.8 ± 0.9 [90]	6.1 ± 1.5 [60]
H <sub>2</sub> S-forming bacteria	6.9 ± 1.7 [100]	6.4 ± 1.7 [100]	6.2 ± 1.5 [90.9]	6.9 ± 1.2 [100]	6.9 ± 1.1 [100]	7.0 ± 1.2 [100]
Percentage of dry matter (%)	32.3 ± 6.3	28.4 ± 6.4 <sup>‡</sup>	27.3 ± 5.5 <sup>†</sup>	33.8 ± 5.1	27.4 ± 5.1 <sup>†</sup>	31.5 ± 2.3

<sup>†</sup> Bacterial counts expressed as  $\bar{x} \pm SD$  log<sub>10</sub>/g dry feces. Counts of organism based exclusively on positive cultures.  
<sup>‡</sup> Frequency of occurrence in brackets.  
<sup>†,‡</sup> Significantly different from before administration: <sup>†</sup> $P < 0.05$ , <sup>‡</sup> $P < 0.01$ .

Cheng Hsin General Hospital

## Conclusion

The role of critical care- metabolic resuscitation

1. 腸黏膜的免疫力控制腸道菌叢的細菌平衡，食物中的營養素，會影響腸菌叢及腸黏膜上的巨噬細胞，控制腸黏膜的免疫力。
2. 各種不同的營養素，如維生素、纖維及維他命，可提供腸菌的營養而產生不同的生理及免疫反應。
3. 對於肝臟的失能，不僅限於脂肪肝、肝炎及肝硬化，重症患者也會因肝臟蛋白質製造異常，或酸鹼不平衡所引起的代謝失能。
4. 對於肝臟的失能，需透過腸肝循環的維護才能降低其損傷。
5. 要維護腸肝循環，需健全腸的生理功能。而腸功能健全必須依賴腸菌叢穩定。腸菌叢穩定需有健康正確的腸道營養。

