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台灣靜脈暨腸道營養醫學會 Taiwan Society for Parenteral and Enteral Nutrition

108年度秋季繼續教育暨學術研討會

2019 Autumn Continuing Education

早產兒暨兒童營養治療

10月5日(六)

時間 13:00-17:00

地點 彰化基督教醫院 福懋大樓B1 國際培訓中心



主辦單位：台灣靜脈暨腸道營養醫學會、彰化基督教醫院營養醫療小組 / 靜脈營養治療小組

協辦單位：彰化基督教醫院體系營養暨膳食部、彰化基督教兒童醫院

時 間	主 題	主 講 人	座 長
13:00-13:30	報 到		
13:30-13:40	致歡迎詞	陳家玉 院長	
13:40-14:30	小兒暨成人腸衰竭合併肝疾病的處置-藝術的論述	Professor Lingtak-Neander Chan	賴鴻緒 醫師 陳家玉 院長
14:30-15:00	Omega-3 長鏈不飽和脂肪酸在極低出生體重早產兒的角色	蕭建洲 醫師	王蒼恩 醫師 鄭金寶 營養師
15:00-15:30	腸道微生物群與疾病的關係	倪衍玄 教授	許自齊 醫師 謝德澄 護理師
15:30-15:50	Coffee Break		
15:50-16:20	重症兒童患者的營養照護	李明聲 醫師	周佳滿 醫師 邱哲琳 營養師
16:20-16:50	維生素D3與兒童健康	李宏昌 醫師	林巧峰 醫師 韓吟宜 醫師
16:50-17:00	綜合討論	倪衍玄 理事長	



T S P E N

/ 專題主講簡介

TSPEN

2019 Autumn Continuing Education





Lingtak-Neander Chan

Vice Chair and Professor, Department of Pharmacy;
Interdisciplinary Faculty, Nutritional Sciences Program,
University of Washington

Education

- PharmD, University of Washington
- Bachelor of Science in Pharmacy, Northeastern University
- Bachelor of Science in Toxicology, Northeastern University

Research Focus

- Nutrient-drug interactions
- Bariatric medicine

Courses Taught

- Pharm 510 : Current Topics in Clinical Nutrition
- Pharm 562 : Pharmacotherapeutics VI
- Pharm 569 : Fluid & Electrolytes & Parenteral Nutrition
- Pharm 570 : Critical Care Pharmacotherapy
- Pharm 571 : Current Topics in Acute Care Pharmacotherapy

Biography

Dr. Chan is a Professor of Pharmacy in the School of Pharmacy, an Interdisciplinary Faculty of the Graduate Program in Nutritional Sciences, and a full faculty of the UW Graduate School. He received BS degrees in toxicology and pharmacy, and a post-baccalaureate PharmD degree, followed by residency training in clinical pharmacy. He was formerly a faculty member of the College of Pharmacy and College of Medicine at the University of Illinois at Chicago. He is board certified in nutrition support pharmacy and an elected fellow of the American College of Nutrition.

His primary research focus is on the absorption kinetics of micronutrients and drugs after bariatric surgery and other GI tract repairs. Other key areas of interest include micronutrient deficiencies, intestinal failure, and general health and nutritional management after bariatric surgery and intestinal surgery. He has extensive practice experience in the critical care setting with expertise in clinical nutrition and obesity.

Dr. Chan is currently serving as a member of the Board of Directors for the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). He is also a member of the Specialty Council in Nutrition Support Pharmacy for the Board of Pharmacy Specialties. He has served as an Associate Editor for the Journal of Parenteral and Enteral Nutrition until 2016.

He is extensively involved in the didactic curriculum of the UW PharmD program, both as an instructor and a coursemaster. He has published book chapters, review articles, original research papers and a number of invited editorials, and has been an invited speaker at numerous scientific and professional conferences throughout the United States, Hong Kong, and Taiwan, and a recipient of numerous grants relating to his area of research. He also mentors many graduate students in the Nutritional Sciences Program at the UW School of Public Health and Community Medicine.

小兒暨成人腸衰竭合併肝疾病的處置 – 藝術的論述

Management of Intestinal Failure Associated Liver Disease (IFALD) in Children and Adults: State of the Art

Lingtak-Neander Chan, PharmD, BCNSP Professor of Pharmacy Interdisciplinary Faculty in Nutritional Sciences University of Washington, Seattle, USA

Summary Abstract

The objectives of this presentation include:

- 1) to review the presentation of IFALD;
- 2) to discuss the role of intestinal microbiota and inflammation in the pathophysiology of IFALD;
- 3) to analyze the current scientific and clinical data on how different components of injectable lipid emulsions (ILE) contribute to the progression and reversal of IFALD;
- 4) to explore the future clinical research agenda to further the understand the therapeutic potential of different ILE in preventing IFALD.

Intestinal failure-associated liver disease (IFALD) is a form of hepatobiliary dysfunction associated with the presence of intestinal failure. Depending on the stage of disease at the time of diagnosis, IFALD may progress to end-stage liver disease, or can be stabilized or reversed with promotion of intestinal adaptation. Although the use of parenteral nutrition (PN), especially over a long period of time, is a well-known factor in the development of IFALD, primary parenchymal liver pathology (e.g. viral or autoimmune hepatitis), other hepatotoxic factors (e.g. alcohol/medication) or biliary obstruction may also contribute to disease presentation and progression.

The intestinal microbiota secrete factors that modulate intestinal permeability, the mucus layer, epithelial cell function, innate and adaptive immunity, intestinal motility, and neurotransmission. Recent research suggests that in the presence of intestinal failure, and especially IFALD, the density of different microbial colonies and their diversity are significantly affected. For example, in patients with IFALD presenting with steatosis, actinobacteria colony is 1.5 to 6 times higher than that in patients without evidence of hepatic disease.

It has also been noted that the shift in microbiota diversity and richness, such as *E. coli*, promotes intrahepatic inflammation by increasing hepatic exposure of lipopolysaccharides (LPS), thus contributing to IFALD. These observations and theories support the use of anti-inflammatory strategy in reducing the severity or preventing the progression of IFALD.

Injectable lipid emulsions (ILE) is an important energy source for patients receiving PN. Its glucose sparing effect has been shown to decrease the risk of cholestasis and jaundice associated with PN. However, chronic use ILE-containing PN regimen can still contribute to PN-associated liver disease (PNALD). Recent research has further identified the specific components in the lipid formulation that have major impact on cholestasis and the progression of hepatic injuries. These components include w3 fatty acid and the ratio between w3:w6 fatty acids, the presence of vitamin E, especially higher amount of alpha-tocopherol, the inclusion of medium-chain triglycerides (MCT) oil, and the avoidance of soy-based phytosterols. Phytosterols have a more direct effect on the enterohepatic regulation of bile acid synthesis and reabsorption, whereas modulation of the inflammatory cascade appears to be one of the mechanisms associated with w3 fatty, alpha-tocopherol, and MCT oil.

Suggested References

1. Dao DT, Anez-Bustillos L, Finkelstein AM, et al. Trends of INR and Fecal Excretion of Vitamin K During Cholestasis Reversal: Implications in the Treatment of Neonates With Intestinal Failure-Associated Liver Disease. *JPEN J Parenter Enteral Nutr.* 2019 Jul 7. doi: 10.1002/jpen.1677. [Epub ahead of print]
2. Fell GL, Cho BS, Dao DT, et al. Fish oil protects the liver from parenteral nutrition-induced injury via GPR120-mediated PPAR γ signaling. *Prostaglandins Leukot Essent Fatty Acids.* 2019 Apr;143:8-14.
3. Baker MA, Cho BS, Anez-Bustillos L, et al. Fish oil-based injectable lipid emulsions containing medium-chain triglycerides or added α -tocopherol offer anti-inflammatory benefits in a murine model of parenteral nutrition-induced liver injury. *Am J Clin Nutr.* 2019 Apr 1;109(4):1038-1050. :
4. Nandivada P, Fell GL, Gura KM, Puder M. Lipid emulsions in the treatment and prevention of parenteral nutrition-associated liver disease in infants and children. *Am J Clin Nutr.* 2016 Feb;103(2):629S-34S.
5. Korpela K, Mutanen A, Salonen A, et al. Intestinal Microbiota Signatures Associated With Histological Liver Steatosis in Pediatric-Onset Intestinal Failure. *JPEN J Parenter Enteral Nutr.* 2017Feb;41(2):238-248.
6. Lavallee CM, MacPherson JAR, Zhou M, et al. Lipid Emulsion Formulation of Parenteral Nutrition Affects Intestinal Microbiota and Host Responses in Neonatal Piglets. *JPEN J Parenter Enteral Nutr.* 2017 Nov;41(8):1301-1309.
7. Lee WS, Sokol RJ. Intestinal Microbiota, Lipids, and the Pathogenesis of Intestinal Failure-Associated Liver Disease. *J Pediatr.* 2015 Sep;167(3):519-26.



蕭 建 洲
Chien-Chou Hsiao



現 職

彰化基督教兒童醫院新生兒科主任

學 歷

- 高雄醫學院醫學系畢業
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主 要 經 歷

- 美國哥倫比亞大學附設紐約兒童醫院研究員
- 彰化基督教兒童醫院兒科部部長
- 教育部定助理教授
- 高雄醫學大學醫學系兼任助理教授

Omega-3長鏈不飽和脂肪酸在 極低出生體重早產兒的角色

The Role of Omega-3 Long Chain Unsaturated Fatty Acid in Very Low Birth Weight Premature Children

早產兒的腦部和其他器官中之長鏈多不飽和脂肪酸 (LCPUFA) 的濃度明顯低於足月嬰兒，因為他們提早出生，錯過了懷孕晚期二十二碳六烯酸(DHA)和花生四烯酸(AA)大量從母體傳輸到胎兒的主要時期。LCPUFAs與健康成長，大腦發育，免疫和過敏反應以及營養相關的慢性疾病等都發揮著至關重要的作用。而且已知LCPUFA可在不同階段調節發炎反應和免疫細胞功能，包括細胞膜特性，吞噬作用和生物活性物質如細胞激素的產生。最常見的全靜脈營養(TPN)配方是含有大豆油脂的脂肪乳劑(LE)，富含n-6長鏈多不飽和脂肪酸和植物甾醇，但有肝臟毒性和促炎細胞激素的產生如腫瘤壞死因子(TNF- α)和白細胞介素(IL-6)。

許多證據強烈支持發炎反應和氧化壓力是導致全靜脈營養相關膽汁淤積和支氣管肺發育不良(BPD)的主要致病原因。對這種不良反應的擔憂導致了另一種新型脂肪乳劑的發展，其中大豆衍生的脂質被來自魚油的n-3長鏈不飽和脂肪酸(EPA和DHA)部分取代。在成人患者的一些研究發現，含有魚油的脂肪乳劑可以增加血漿中EPA和DHA的濃度，並增加白細胞中白三烯B5的產生。此外，最近的研究發現，接受含有中鏈甘油三酯(MCTs)和n-3長鏈不飽和脂肪酸之脂肪乳劑的新生兒的氧化壓力和炎症反應都顯著降低，對於早產兒的併發症有顯著的影響。



倪 衍 玄
Yen-Hsuan Ni

現 職

- 台灣大學醫學院院長 (2019-迄今)
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- 臨床醫學研究所合聘教授 (2017-迄今)

學 歷

- 台灣大學醫學院臨床醫學研究所博士
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主 要 經 歷

- 台灣大學醫學院副院長暨共同教育及教師培訓中心主任 (2013-2019)
- 台灣大學醫學系主任 (2018-2019)
- 台大醫院肝炎研究中心主任 (2015-2019)
- 台大醫院基因醫學部主任 (2012-2015)
- 台大醫院教學部主任 (2011-2012)

腸道微生物群與疾病的關係

Relationship Between Gut Microbiota and Disease

成人腸道中含有各種共生菌，每公克糞便約有 10^{14} 細菌。胎兒在子宮內每天吞進的是無菌羊水，因此它的腸道是無菌的狀態。有趣的是剛出生嬰兒如何獲得其菌叢？而其腸道菌又如何轉變成像大人一樣型態？嬰幼兒腸道菌種、數量的演進與很多因素有關，例如生產方式、餵食方式、住院設置或母親健康狀況、種族、以及生活環境。傳統研究腸內菌是靠培養法，其敏感度有很大的變異性，完全決定於培養方式(如培養液的選擇)與環境因素。較新的研究方法是以DNA為基礎，針對細菌共有的16S rDNA序列，探測其為何種細菌。透過PCR擴增整個細菌群落的16S rDNA，可接著用次世代序列分析(NGS)以分析PCR所擴增的複雜細菌群落。此方法可排除培養法的培養液偏好缺點，且可提升腸內菌偵測、鑑別與定量的準確性。目前使用NGS分析腸道菌叢的方法有長足的進步，對於細菌的種類，甚至其在人體內提供的種種代謝途徑，都能略窺其堂奧，目前的資料顯示，由新生兒到三歲之間與成人腸道菌叢存在著相當差異，三歲以後的菌叢型態已經接近成人。重點是三歲以前腸道菌叢的型態是否會影響人後來一生健康的變化？相關的研究目前方興未艾。

腸道是人體最大的免疫器官。它接受無數的細菌從口腔中隨著食物進入，有些細菌會被排出、有些則被腸道細胞所認識而產生耐受性。細菌如何與腸道免疫器官互動以調節全身免疫反應？這是當前難解但卻是非常重要的問題。事實上除了年齡的因素外，疾病狀態與健康狀態之菌叢亦頗有不同，克隆氏症及肥胖都是很好的例子。我們的研究已經找到某些細菌在腸道內早期定殖，與嬰兒時期過敏疾病息息相關。嬰幼兒時期使用抗生素，造成腸道菌相失衡，與後來肥胖甚至於代謝性疾病有關的證據，也越來越多。而這一部分的腸道菌叢功能與疾病的產生及正常生理功能的維持其實息息相關。事實上目前已漸漸發現，不同菌種可以產生相同的生理或病理作用，所以即使因為種族或環境不同，有不同的菌株，但是人類大體生理功能是一致的。至於所謂益生菌，定義是對人體有益的細菌，但是詳細到底如何，未來希望藉由與腸道菌叢分析資料的對應，可以知道嬰幼兒腸內菌的建立與各種情境之關係；亦可藉以了解嬰幼兒發生疾病時，其腸內菌在疾病前、中、後之型態改變，從而建立益生菌的新定義。甚至有望經由腸內菌的調節來預防或治療疾病的發生。



李 明 聲
Ming-Sheng Li



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- 彰化基督教兒童醫院兒童胸腔重症科主治醫師
- 兒童加護病房主任

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- 高雄醫學大學醫學系學士
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主 要 經 歷

彰化基督教醫院 (2003-2019)

重症兒童患者的營養照護

Nutritional Care for Critically Ill Children

1. Patients and nutritional problems in PICU.
2. Common consideration of major nutrients of EN in pediatric ICU.
3. Common consideration of PN in pediatric ICU.
4. Nutritional guidelines in the Pediatric Critically Ill Patient: American Society for Parenteral and Enteral Nutrition.
5. Use of a stepwise algorithmic approach to advance EN in children admitted to the PICU.
6. Different formula according to patient age and etiology.
7. Measuring GRV as a marker of EN intolerance in the PICU population.
8. Timing of EN and PN, nutrition goal in the PICU population.
9. Critically ill infants and children have an variable basal metabolic rate and intensive protein catabolism.
10. Watch for refeeding syndrome.



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主 要 經 歷

- | | |
|---------------|-----------------------------------|
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| • 馬偕紀念醫院 | 小兒胃腸科主任 (1997-2007) |
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維生素D3與兒童健康

Vitamin D3 and Child Health

The primary role of vitamin D is the regulation of bone mineral homeostasis; however, its importance in the regulation of the immune system has emerged in the last 30 years.

Rickets is a childhood vitamin D insufficiency and may develop only several months after delivery. Besides fetal bone, the development of fetal lung and neonatal immune conditions such as asthma may relate in part to maternal vitamin D levels.

Evidence grew of the role of vitamin D in the regulation of the immune system. The recent studies have emphasized that vitamin D play an important role in disease prevention in children, not only rickets and DM, but also respiratory infection and asthma. Because the awareness of the importance of vitamin D , the AAP published a new statement in November 2008 that a daily intake of vitamin D of 400 IU/day for all infants and children beginning in the first few days of life is recommended to prevent vitamin D deficiency.

Studies in both human and animal models add strength to the hypothesis that the unrecognized epidemic of vitamin D deficiency worldwide is a contributing factor of many chronic debilitating diseases. Greater awareness of the insidious consequences of vitamin D deficiency is needed.