臺灣兒科醫學會第六十屆年會暨第二三八屆學術演講會時間表

民國108年4月20日(星期六)

101A、B 會議室

08:30 **第一單元：新生兒學**
(1~8題)

09:50
09:50 休息
10:00
10:00 **第一單元：新生兒學**
(9~17題)

11:30

12:10 **附加研討會**
主　題：嬰兒腦部發展新進展研討會
主持人：鍾育志校長、楊俊仁理事長
演講者：Prof. Weili Lin

13:30

101C、D 會議室

08:30 **第四單元：過敏免疫風濕病學**
(34~43題)

10:10
10:10 休息
10:20
10:20 **第四單元：過敏免疫風濕病學**
(44~52題)

11:50
12:00 **附加研討會**
主　題：關鍵1000天—益生菌與母乳寡糖對長期健康的影響
主持人：江伯倫理事長
演講者：Dr. Michelle Pietzak

13:30

102 會議室

08:30 **第六單元：心臟血管學**
(75~83題)

10:00
10:00 休息
10:10
10:10 **第六單元：心臟血管學**
(84~92題)

11:40
12:00 **附加研討會**
主　題：多價數與多劑型的兒童與青少年疫苗發展趨勢
主持人：黃玉成教授、李秉穎醫師
演講者：李秉穎醫師、黃玉成教授

13:30

103 會議室

08:30 **第九單元：腎臟學**
(113~120題)

09:50
09:50 休息
10:00
10:00 **第十單元：重症學**
(121~126題)

11:00
11:00 休息
11:10
11:10 **第十一單元：急診學**
(127~129題)

11:40
12:00 **附加研討會**
主　題：精準醫療專題講座：臨床基因檢測於兒科之應用與發展
主持人：蔡立平醫師、陳燕彰醫師
演講者：呂俊毅醫師、林達雄醫師

13:30

101A、B 會議室

13:30 **第二單元：腸胃學、營養學**
(18~23題)

14:30
14:30 休息
14:40
14:40 **第二單元：腸胃學、營養學**
(24~30題)

15:50
15:50 休息
16:00
16:00 **第三單元：肺臟學**
(31~33題)

16:30

101C、D 會議室

13:30 **第四單元：過敏免疫風濕病學**
(53~61題)

15:00
15:00 休息
15:10
15:10 **第五單元：感染學**
(62~68題)

16:20
16:20 休息
16:30
16:30 **第五單元：感染學**
(69~74題)

17:30

102 會議室

13:30 **第七單元：神經精神醫學**
(93~98題)

14:30
14:30 休息
14:40
14:40 **第七單元：神經精神醫學**
(99~105題)

15:50
15:50 休息
16:00
16:00 **第八單元：血液、腫瘤學**
(106~112題)

17:10

103會議室

13:30 **第十二單元：青少年醫學**
(130~131題)

13:50
13:50 **第十三單元：內分泌學**
(132~135題)

14:30
14:30 休息
14:40
14:40 **第十四單元：醫學遺傳學、新陳代謝學**
(136~141題)

15:40
15:40 休息
15:50
15:50 **第十四單元：醫學遺傳學、新陳代謝學**
(142~148題)

17:00

民國108年4月21日(星期日)

101A、B、C、D會議室

08:30 **陳炯霖教授講座獎**
主　題：兒童急性淋巴細胞白血病完全治癒前景
主持人：呂鴻基教授
演講者：裴正康院士

09:30
09:30 **教育演講**
主　題：青少年健康現況及挑戰
主持人：李宏昌常務理事、羅福松醫師
演講者：羅福松醫師、Prof. Susan Sawyer、廖靈瓊理事長

11:50
12:00 **附加研討會**
主　題：從疫苗設計探討預防醫學重要性 VS 國內疫苗政策探討
主持人：黃立民教授、邱政洵教授
演講者：邱南昌醫師、陳志榮醫師、李秉穎醫師

13:30

13:30 **頒獎/會員代表大會**

14:30
14:30 休息
14:40
14:40 **醫學的科學、倫理與法律講座**
主　題：探討藥物仿單核准適應症外的使用
主持人：江伯倫理事長、林奏延教授
演講者：吳怡雪醫師、范振中主持律師

16:40

102 會議室

09:30 **專題演講**
主　題：兒童血液/腫瘤病患常見徵候
主持人：林東樑醫師、彭慶添醫師
演講者：林佩瑾醫師、盧孟佑醫師、王士忠醫師、翁德甫醫師、顏秀如醫師

11:30
12:00 **附加研討會**
主　題：疫苗面面觀
主持人：李秉穎醫師、劉清泉教授、黃立民教授
演講者：黃玉成教授、呂俊毅醫師、陳伯彥醫師

13:30

103會議室

09:30 **特別演講**
主　題：如何優化兒童醫療網
主持人：陳武元常務理事
演講者：石崇良司長、曾光宏醫師

11:30
12:00 **附加研討會**
主　題：兒童健康益生菌的新時代
主持人：楊俊仁理事長、倪衍玄副院長、吳子聰教授
演講者：倪衍玄副院長、吳子聰教授

13:00

地址：臺北國際會議中心 (台北市信義路五段 1 號)

一般演講：口頭報告

第一單元：新生兒學

日期：民國108年4月20日(星期六)
時間：08:30~11:30
地點：101A、B會議室

主持人：

08:30~08:37　1. 20公分的臍帶擠壓對於極度早產兒的死亡與共病症的影響：北台灣單一醫學中心的研究
沈上博、張瑞幸、許瓊心、張弘洋、詹偉添[1]、林佳瑩[1]、彭純芝
馬偕兒童醫院新生兒科

08:37~08:44　2. 比較無侵襲性的方式給予肺表面活性素來治療非常小早產兒的呼吸窘迫徵候群
陳俐如[1]、王杏安[2]、蕭建州[1]、陳曉能[1]、李政翰[1]、陳善銘[2]、蘇本華[2]、陳家玉[1]
彰化基督教兒童醫院新生兒科[1]；中山醫學大學附設醫院小兒部新生兒科[2]

08:44~08:51　3. 極低體重新生兒之經皮水分散失量：一個醫學中心觀察性研究
鐘浩瑋[1]、陳秀玲[1,2]、楊書婷[1]、蘇品淳[1]
高雄醫學大學附設中和紀念醫院小兒部[1]；高雄醫學大學醫學院呼吸治療學系[2]

08:51~08:58　4. 霧化salbutamol在早產兒非寡尿性高血鉀症治療中減少血糖的波動
蘇玄白[1]、陳家玉[2]
台中澄清綜合醫院中港分院[1]；彰化基督教兒童醫院[2]

08:58~09:05　5. 利用NT-proBNP預測早產兒使用Ibuprofen治療開放性動脈導管的反應療效：一項初步研究
林雅藍[1]、洪依利[1]、沈仲敏[1]、謝武勳[1,2]
國泰醫院[1]；國立臺灣大學醫學院[2]

09:05~09:12　6. 輕度新生兒腦室內出血對於極度早產兒長期神經發展預後的影響
賴美吟、周怡君[1]、林光麟[1]、林建志[2]、李建忠、朱世明、林瑞瑩、江明洲
林口長庚紀念醫院兒童內科部新生兒科、兒童神經科[1]、兒童重症加護科[2]

09:12~09:19　7. 針對極低體重早產兒先天性甲狀腺功能不足的篩檢完備嗎?
陳琬瑄、李建忠、徐任甫、朱世明、邱巧凡[1]、林瑞瑩
林口長庚醫學中心兒童內科部新生兒科及兒童內分泌科[1]，長庚大學醫學院

09:19~09:26　8. Cathelicidin通過抑制新生大鼠的NF-κB活性減輕高氧誘導的腸損傷
陳中明[1,2]、周綉珠[3]
台北醫學大學附設醫院小兒部[1]；台北醫學大學醫學院小兒學科[2]、解剖暨細胞生理學科[3]

09:26~09:50　討論

09:50~10:00　休息

主持人：

10:00~10:07　9. 懷孕母鼠Tn免疫通過抑制氧化應激和炎症減輕高氧誘導的新生仔鼠肺損傷
陳中明[1,2]、黃昭蓮[3]、周琇珠[4]
台北醫學大學附設醫院小兒部[1]；台北醫學大學醫學院小兒學科[2]、癌症中心[3]、解剖暨細胞生理學科[4]

10:07~10:14　10. 極低體重早產兒用早期血清生化值來評估發生骨質疏鬆的風險
陳韻寧、曹伯年、周弘傑、顏玎安、陳倩儀
國立台灣大學醫學院附設醫院兒童醫院小兒部

10:14~10:21　11. 以血片技術來檢測母親及嬰幼兒之維生素D營養狀態
陳倩儀、曹伯年、周弘傑、顏玎安、胡務亮、簡穎秀
國立台灣大學醫學院附設醫院兒童醫院小兒部

10:21~10:28　12. 新生兒早發性敗血症15年來的變化
魯怡群、陳映廷、蔡明倫、林湘瑜、邱曉郁、林鴻志
中國醫藥大學兒童醫院新生兒科

10:28~10:35　13. 三個月以下發燒嬰兒之病毒或細菌病原臨床分析探討
吳政宏[1]、唐翊軒[1]、鄭玫枝[1,2,3]、李昱聲[1,3]、曹珮眞[1,2,3]、陳威宇[1,2,3]、宋文舉[1,3]
台北榮民總醫院兒醫部[1]；國立陽明大學急重症醫學研究所[2]；國立陽明大學醫學系小兒學科[3]

10:35~10:42　14. 探討足月單胞新生兒之母體因子與胎兒巨嬰症的關係
陳裕璇[1,3]、唐翊軒[1,3]、卓靜怡[1,3]、葉長青[4]、陳威宇[1,2,3]、曹珮眞[1,3]、李昱聲[1,3]、鄭玫枝[1,2,3]
臺北榮民總醫院兒童醫學部[1]；國立陽明大學急重症醫療研究所[2]；國立陽明大學醫學系小兒科學[3]；臺北榮民總醫院婦女醫學部[4]

10:42~10:49　15. 周產期窒息新生兒經過低溫治療發生急性腎衰竭的危險因子
莫澤儀[1]、江明洲[1]、曾敏華[2]、林瑞瑩[1]、朱世明[1]
林口長庚紀念醫院兒科部新生兒科[1]；林口長庚紀念醫院兒科部腎臟科[2]

10:49~10:56　16. 新生兒氣漏症候群之周產期特徵及預後 — 單一中心回溯研究
陳德論[1]、洪依利[1]、沈仲敏[1]、謝武勳[1,2]
國泰綜合醫院小兒科[1]；國立台灣大學醫學院小兒部[2]

10:56~11:03　17. 學齡前極低出生體重兒之口腔顏面功能評估
陳秀玲[1,2]、張梅珍[3]
高雄醫學大學附設醫院小兒科部[1]；高雄醫學大學醫學院呼吸治療學系[2]；高雄榮民總醫院護理部[3]

11:03~11:30　討論

附加研討會
嬰兒腦部發展新進展研討會

日期：民國108年4月20日(星期六)
時間：12:10~13:30
地點：101A、B會議室

主持人：鍾育志校長、楊俊仁理事長

12:10~12:15　1. 開幕致詞
鍾育志校長
高雄醫學大學

12:15~13:15　2. 大腦連結計畫：嬰幼兒腦結構與功能連結
(BCP & BCP Enrich 研究計畫新進展)
Prof. Weili Lin, PhD
University of North Carolina at Chapel Hill, USA

13:15~13:30　3. 問題討論與結語
楊俊仁理事長
台灣小兒消化醫學會

第二單元：腸胃學、營養學

日期：民國108年4月20日(星期六)
時間：13:30~15:50
地點：101A、B會議室

主持人：

13:30~13:37　18. 葛西手術術後一週之膽紅素數值可預測膽道閉鎖患者的原肝存活
黃琢懿、張美惠、陳慧玲、倪衍玄、許宏遠、吳嘉峯
國立臺灣大學醫學院附設醫院小兒部

13:37~13:44　19. 肝肺症候群於膽道閉鎖孩童的預後及危險因子分析
陳如瑩[1]、張美惠、張凱琪、邱郁淳、陳慧玲、倪衍玄、許宏遠、吳嘉峯
國立台灣大學醫學院附設醫院小兒部

13:44~13:51　20. 潰瘍性腸炎於小兒原發性硬化性膽管炎族群之特性：單一中心研究
簡睦旼[1]、張美惠[1,2]、張凱琪[1,3]、邱郁淳[1,4]、陳慧玲[1]、倪衍玄[1,2]、許宏遠[1]、吳嘉峯[1]
國立台灣大學醫學院附設醫院兒童醫院小兒部[1]；國立台灣大學醫學院附設醫院肝炎研究中心[2]、急診部[3]、教學部[4]

13:51~13:58　21. 兒童諾羅病毒胃腸炎中之病毒體排出與病毒感染、臨床特異性之關聯性研究
林招慶[1]、陳世彥[1]、方旭彬[1]、邱政洵[2]
衛生福利部雙和醫院(委託臺北醫學大學興建經營)兒科部[1]；長庚醫療財團法人林口長庚醫院兒科部[2]

13:58~14:05　22. yqiC基因對沙門氏菌全轉錄體之調控以及YqiC蛋白與沙門氏菌在定植人類腸道上皮細胞時之交互作用
范閎皓[1,2]、黃志宏[3]、張珮茹[1,2]、孫維聲[1,2]、方旭彬[1,2]
臺北醫學大學部立雙和醫院小兒部小兒消化科[1]；臺北醫學大學醫學院醫學系小兒學科[2]；國立台北科技大學生化與生醫工程研究所[3]

14:05~14:12　23. 以次世代定序發現之多基因組合偵測非傷寒沙門氏菌對安比西林抗生素之抗藥性
方旭彬[1,2]、張偉嶠[3]、周宛萱[3]、王克銓[1,2]
臺北醫學大學部立雙和醫院小兒部小兒消化科[1]；臺北醫學大學醫學院醫學系小兒學科[2]；臺北醫學大學藥學院臨床藥物基因體學暨蛋白質體學碩士學位學程[3]

14:12~14:30　討論

14:30~14:40　　休息

主持人：

14:40~14:47　　24. 急性區段性壞死性腸炎在孩童身上的表現及治療：一個醫學中心22年的經驗
郭恬伶、劉明發、林明益、宋增銓、林妊慧
新光吳火獅紀念醫院小兒科

14:47~14:54　　25. 早期廣泛性抗生素對極低體重早產兒腸道菌叢的影響
游雅婷[1]、張弘洋[1]、江謝正雄[2]、李宏昌[1]、何宇軒[3]、蔡昆男[3]、劉珈延[3]、楊俊仁[1]、陳偉燾[1]、江椿彬[1]
馬偕兒童醫院兒科部[1]；馬偕紀念醫院醫學研究部[2]；台達電子工業股份有限公司台達研究院[3]

14:54~15:01　　26. 實驗鼠中飲食缺乏維生素D對調節Toll-like受體及腸道微生物的影響
劉雅之、李宏昌、江謝正雄、楊俊仁、陳偉燾、江椿彬
馬偕兒童醫院兒童腸胃科

15:01~15:08　　27. 探討益生菌及益生源對於小鼠腸道菌叢的影響
莊曜鴻、陳建彰、陳琨傑[1]、葉宏瑀、趙舜卿、賴明瑋
林口長庚紀念醫院兒童胃腸科、兒童健康研究部[1]

15:08~15:15　　28. 高鹽飲食對食物過敏之影響 — 小鼠實驗
黃治綱[1]、劉喆瑩[1, 2]、李士寬[1, 3]、黃清峯[1]
臺北榮民總醫院兒童醫學部兒童胃腸科[1]；臺北醫學大學-北醫・萬芳醫院-小兒科[2]；財團法人天主教永和耕莘醫院小兒科[3]

15:15~15:22　　29. 核磁共振膽胰道攝影術在膽汁滯留早產兒身上診斷膽道閉鎖的角色
陳緯哲[1]、楊燿榮[1]、賴馥蘋[1]、羅筱淯[1]、蔡依珊[2]
國立成功大學醫學院附設醫院小兒部[1]、放射診斷部[2]

15:22~15:29　　30. 細菌培養之藥物敏感性測試報告做爲兒童胃幽門桿菌治療依據，有較好的除菌率及較好之成本效益
洪綺彣[1,2]、賴馥蘋[2]、陳志成[3]、楊燿榮[2]
高雄榮民總醫院[1]；國立成功大學醫學院附設醫院[2]；臺灣恆春基督教醫院[3]

15:29~15:50　　討論

15:50~16:00　　休息

第三單元：肺臟學

日期：民國108年4月20日(星期六)
時間：16:00~16:30
地點：101A、B會議室

主持人：

16:00~16:07　31. 阿奇黴素可減少小兒重症心血管手術的患者的呼吸器相關肺炎
黃永豐[1,2,3]、劉伯彥[2]、潘俊彥[4]
國防醫學院三軍總醫院小兒科[1]；高雄榮民總醫院兒童醫學部[2]；唯兒諾兒科[3]，杭州；高雄榮民總醫院心臟血管外科[4]

16:07~16:14　32. 喉谿部囊腫併軟喉症於幼兒之正確診斷與有效治療：使用軟式氣管鏡輔以非侵入性通氣術
宋文舉[1,2]、林建亨[1]、唐翊軒[2]、曹珮眞[2]、李昱聲[2]
臺中中國醫藥大學兒童醫院[1]；臺北榮民總醫院兒童醫學部[2]

16:14~16:21　33. 早產兒至晚期嬰幼兒時期之肺功能演進的決定因子
邱俊哲[1]、賴申豪[1,3]、廖穗綾[2,3]、江明洲[1]、朱世明[1]、徐任甫[1]、姚宗杰[1,3]、蔡明翰[2,3]、黃璟隆[1,3]
林口長庚醫院兒童內科部[1]；基隆長庚醫院小兒科[2]；基隆長庚醫院PATCH研究團隊[3]

16:21~16:30　討論

第四單元：過敏免疫風濕病學

日期：民國108年4月20日(星期六)
時間：08:30~15:00
地點：101C、D會議室

主持人：

08:30~08:37　34. 接骨點炎相關型兒童特發性關節炎的臨床分析和治療預後
施養眞[1]、楊曜旭、江伯倫
國立台灣大學醫學院附設醫院小兒部；臺北市立聯合醫院和平婦幼院區小兒科[1]

08:37~08:44　35. 以關節超音波測量健康亞洲學齡兒童的關節軟骨厚度
高純淳、黃璟隆、林思偕、葉國偉、陳力振、歐良修、李文益、姚宗杰、吳昭儀
林口長庚醫院兒童過敏氣喘風濕科

08:44~08:51　36. 單次注射人類臍帶間質幹細胞對小鼠急性和慢性結腸炎的治療作用
張裕隆[1,2,7]、羅惠郁[3,4,7]、鄭舜平[3,7]、張國廷[7]、李秀芳[2]、李昇平[1]、謝明發[2]、詹金淦[5,6,7]
行政院衛生福利部桃園醫院泌尿科[1]、復健科[3]、小兒科[6]、轉譯醫學中心[7]；中原大學生物醫學工程學系[2]、化學系[4]；銘傳大學生物科技學系[5]

08:51~08:58　37. 通過優化的短期低氧缺乏，高效增強人類UCMSCs對PBMCs的免疫調節作用
呂秉澤[1]、羅惠郁[2,3,7]、鄭舜平[2,7]、黃璟隆[4]、張國廷[7]、黃建勳[5]、詹金淦[1,6,7]
行政院衛生福利部桃園醫院復健科[2]、婦產科[5]、小兒科[1]、轉譯醫學中心[7]；中原大學化學系[3]；長庚醫院兒童過敏氣喘風濕科[4]；銘傳大學生物科技學系[6]

08:58~09:05　38. 臍帶間質幹細胞產生的胞外囊泡對單核球往M2表型分化的影響
楊蓴榕[1,2,3,4]、林佳學[3,4]、何世璿[3,4]、陳治平[3,4]、楊崑德[2,3,4]
大同大學生物工程系[1]；國立陽明大學臨床醫學研究所[2]；馬偕紀念醫院[3]；馬偕兒童醫院[4]

09:05~09:12　39. 兩種不同胞外囊泡微小RNA對 DLD-1癌細胞和顆粒細胞遷移作用之研究
簡銘輝[1,2,3]、林佳學[1,2]、楊蓴榕[3,4]、陳治平[5]、楊崑德[1,2,4]
馬偕兒童醫院[1]；馬偕醫學院生醫所[2]；大同大學生物工程學系[3]；國立陽明大學臨醫所[4]；馬偕紀念醫院婦產科、醫研部[5]

09:12~09:19　40. 臍帶間質幹細胞胞囊免疫因子及其對T細胞分化調節的作用原理
林佳學[1,2]、沈婕如[1,2]、何世璿[1,2]、陳治平[3]、楊崑德[1,2,4]
馬偕兒童醫院[1]；馬偕醫學院生醫所[2]；馬偕紀念醫院婦產科和醫研部[3]；國立陽明大學臨醫所[4]

09:19~09:26　41. 臍帶間質幹細胞胞囊對多環芳香碳氫化物抑制肌母細胞生長的恢復與作用機轉
沈婕如[1,2]、林佳學[1,2]、何世璿[1,2]、陳治平[4]、楊崑德[1,2,3]
馬偕兒童醫院[1]；馬偕醫學院生醫所[2]；馬偕紀念醫院婦產科、醫研部[3]；國立陽明大學臨醫所[4]

09:26~09:33　42. 父親抽菸影響新生兒免疫基因甲基化和臍帶血內的免疫分化指標變化
楊崑德[1,2,3]、林佳學[1,2]、何世璿[1,2]、陳治平[4]
馬偕兒童醫院[1]；馬偕醫學院生醫所[2]；國立陽明大學臨醫所[3]；馬偕紀念醫院婦產科、醫研部[4]

09:33~09:40　43. 接種後持續水痘感染主要和RAG1 Hot-Spot基因突變相關，而非IL7RA基因突變[Thr66Ile]；與後續華裔族群RAG1突變之分析
李宛芳[1]、李文益[1,2]、陳世翔[2,3]、張嘉琳[4]、黃璟隆[1,2]、林思偕[1]、葉國偉[1]、陳力振[1]、歐良修[1]、姚宗杰[1]、吳昭儀[1]
林口長庚紀念醫院兒童過敏氣喘風濕科[1]；先天性免疫缺損病照護暨研究中心[2]；林口長庚紀念醫院兒童血液腫瘤科[3]；國家衛生研究院分子與基因組醫學研究所[4]；林口長庚紀念醫院病理科[5]

09:40~10:10　討論

10:10~10:20　休息

主持人：

10:20~10:27　44. 似先天免疫缺損“警示表徵”的孩童蘭格罕細胞組織球增生症
林宣辰[1]、李文益[1]、陳世翔[2]、楊兆平[2]、黃璟隆[1]、葉國偉[1]、陳力振[1]、歐良修[1]、姚宗杰[1]、江東和[2]
林口長庚醫院兒童過敏氣喘風濕科[1]、兒童血液腫瘤科[2]

10:27~10:34　45. 生酮飲食及高脂高糖飲食對狼瘡性腎炎小鼠模型的影響
吳昭儀[1]、楊皇煜[2,3]、葉國偉[1]、李文益[1]、姚宗杰[2,3]、歐良修[2,3]、陳力振[1]、林思偕[1]、鹿虹亦[1]、黃璟隆[2,3]
林口長庚醫院兒童過敏氣喘風濕科[1]、腎臟內科[2]；林口長庚醫院[3]

10:34～10:41　46. 紅斑性狼瘡病童罹患骨頭缺血性壞死的流行病學與危險因子分析
張瑞文[1]、蔡昕霖[2]、陸振翮[1]
臺北榮民總醫院兒童醫學部[1]、兒童外科[2]

10:41～10:48　47. 台灣兒童紅斑性狼瘡血中VitD3的濃度與疾病活性之間的關係
鄭堪弘、蔡明瑾、傅令嫻
台中榮民總醫院兒童醫學部

10:48～10:55　48. 母乳中維生素D含量，血清25-羥基維生素D濃度與嬰兒異位性皮膚炎疾病嚴重程度的相關性分析
黃筠涵[1,2]、李志鴻[2]、王麗潔[2]、林璧鳳[3]、江伯倫[2]
台北醫學大學-市立萬芳醫院兒科部[1]；國立台灣大學醫學院附設醫院小兒部[2]；國立台灣大學生化科技學系[3]

10:55～11:02　49. 巨噬細胞極化與動脈硬化損傷在幼年型系統性紅斑性狼瘡病人上的關聯性
李則逸、吳怡樺、林宜君、郭明慧、王玲、蘇昱日
高雄長庚紀念醫院兒童心臟內科

11:02～11:09　50. 川崎症冠狀動脈擴張與年齡之關係
林怡汝、郭和昌、張鈴偲、顏嘉惠
高雄長庚紀念醫院川崎中心、兒童內科部、長庚大學

11:09～11:16　51. FCGR2B甲基化在川崎症不同階段的變化
張鈴偲[1,2]、郭和昌[1,2]
高雄長庚醫院兒童內科部川崎中心[1]；長庚大學[2]

11:16～11:23　52. 尋麻疹與過敏性休克的關係
楊樹文[1,2,3]、黃景揚、陳皇希[1]、魏正宗[1,4]
中山醫學大學醫學研究所[1]；秀傳紀念醫院小兒部[2]；美和科技大學[3]；中山醫學大學免疫風濕科[4]

11:23～11:50　討論

附加研討會
關鍵1000天—益生菌與母乳寡糖對長期健康的影響

日期：民國108年4月20日(星期六)
時間：12:00~13:30
地點：101C、D會議室

主持人：江伯倫理事長

12:00~12:10　1. 開幕致詞
江伯倫理事長
臺灣兒科醫學會

12:10~13:10　2. 關鍵1000天—益生菌與母乳寡糖對長期健康的影響
Dr. Michelle Pietzak
Assistant Professor of Clinical Pediatrics at the University of Southern California in Los Angeles

13:10~13:30　3. 問題討論與結語
江伯倫理事長
臺灣兒科醫學會

主持人：

13:30~13:37　53. 重組微角塵蟎Der m2蛋白的功能與誘發動物氣喘模式的角色
羅佩君[1]、曾碧緣[2]、李育慈[3]、柯俊良[3]、劉玉凡[4]、鄔碧瑜[1]、潘蕙嫻[1]、顧明修[1]、孫海倫[1]、呂克桓[1,3]
中山醫學大學附設醫院兒童部[1]；中山醫學大學附設醫院檢驗科[2]；中山醫學大學醫學研究所[3]；中山醫學大學生物醫學系[4]

13:37~13:44　54. 氧化壓力標記與過敏性指標以及孩童時期過敏性疾病間的關係
朱宇薇[1]、葉國偉[2]、黃璟隆[2]、蘇冠文[3]、蔡明翰[3]、花曼津[3]、廖穗綾[3]、賴申豪[2]、陳力振[2]、邱志勇[2]
長庚大學醫學院醫學系[1]；長庚醫療財團法人林口長庚紀念醫院兒童內科部[2]；長庚醫療財團法人基隆長庚紀念醫院小兒科[3]

13:44~13:51　55. 血清牛奶特異性抗體IgE/IgG4比值與牛奶蛋白過敏臨床表現之相關性研究
康竣閔[1,2]、朱冠驊[3]、俞欣慧[1]、李志鴻[1]、王麗潔[1]、林于粲[1]、楊曜旭[1,2]、江伯倫[1,3]
國立台灣大學醫學院附設醫院兒童醫院小兒部[1]；國立台灣大學醫學院附設醫院新竹分院小兒部[2]；國立台灣大學醫學院附設醫院[3]

13:51~13:58　56. 過敏原特異性IgE對臨床食物過敏症狀兒童的診斷價值
李儒、林靜微、李欣蓉[1]、陳威毓、陳柏嵩、陳志安、王志堯
國立成功大學醫學院附設醫院小兒過敏免疫科；財團法人天主教聖馬爾定醫院[1]

13:58~14:05　57. 克拉氏蛋白質調控經由嗜中性球過氧化物生成與花生四烯酸代謝路徑的發炎反應
陳力振[1]、陸虹亦[1]、郭敏玲[2]、葉國偉[1]、李文益[1]、黃嘯谷[3]、黃璟隆[1]
長庚醫院兒童過敏氣喘風濕科[1]；長庚大學微生物免疫研究所[2]；國家衛生研究院環境衛生暨職業醫學組[3]

14:05~14:12　58. 長效乙二型受體刺激劑對於人類呼吸道上皮細胞分泌之IL-25之影響
洪志興[1,2,3]、郭昶宏[4]、林宜靜[1,2,5]
高雄醫學大學附設醫院小兒部[1]；高雄醫學大學小兒學科[2]；高雄市立小港醫院小兒科[3]；大郭診所[4]；高雄醫學大學附設醫院檢驗部[5]

14:12~14:19　59. 白三烯素受體刺激劑對於人類呼吸道上皮細胞分泌之IL-25之影響
洪志興[1,2,3]、林宜靜[1,4]、郭昶宏[5]
高雄醫學大學附設醫院小兒部[1]；高雄醫學大學小兒學科[2]；高雄市立小港醫院小兒科[3]；高雄醫學大學附設醫院檢驗部[4]；大郭診所[5]

14:19~14:26　60. 西元2004年至2018年南台灣小學學童氣喘盛行率之趨勢
陳威毓、林靜微、陳柏嵩、李儒、陳志安、王志堯
國立成功大學醫學院附設醫院小兒部

14:26~14:33　61. 一歲前急性細支氣管炎的周產期危險因素
陳柏嵩、陳威毓、于鴻仁[1]、林靜微、李儒、陳志安、王志堯
國立成功大學醫學院附設醫院小兒過敏免疫科；高雄長庚紀念醫院小兒過敏氣喘科[1]

14:33~15:00　討論

15:00~15:10　休息

第五單元：感染學

日期：民國108年4月20日(星期六)
時間：15:10~17:30
地點：101C、D會議室

主持人：

15:10~15:17　62. 北台灣兒童皰疹性齒齦炎的臨床表徵
黃琛爲、謝繼賢、林明儒、黃玉成
林口長庚紀念醫院兒童內科部

15:17~15:24　63. 紫錐花及丹蔘萃取物抗病毒組合物之抗病毒作用及機轉
張鑾英[1]、陳裕星[2]、程愛淩[1]、呂俊毅[1]、黃立民[1]
國立臺灣大學醫學院小兒科[1]；行政院農業委員會台中區農業改良場[2]

15:24~15:31　64. 北台灣兒童的高度抗藥性非傷寒沙門氏菌感染分析
陳米琪[1]、張鄔榮[1]、陳苡靜[1]、李欣潔[2]、楊欣萍[2]、余敏嘉[2]、邱政洵[1,2,3]
林口長庚紀念醫院兒童內科部[1]、分子感染症研究中心[2]；長庚大學醫學院臨床醫學研究所[3]

15:31~15:38　65. 台灣中部一家醫學中心多重抗藥性沙門氏菌感染的出現，2015-2018
林曉娟[1,2]、田霓[3,4]、林秀姍[3]、邱乾順[5]、許玉龍[1]、衛琇玫[1]、謝宗學[1]、賴奐丞[1]、黃高彬[1,2]
中國醫藥大學兒童醫院兒童感染科[1]；中國醫藥大學醫學系[2]；中國醫藥大學附設醫院檢驗醫學部[3]；中國醫藥大學醫學院醫學檢驗生物技術學系[4]；衛生福利部疾病管制署食媒疾病研究中心[5]

15:38~15:45　66. 2008至2016年南台灣兒童非傷寒性沙門氏菌血症之回溯性分析
林芳如、龔尹翔、陳志和、黃懿娟、郭光哲
高雄長庚醫院兒科部

15:45~15:52　67. Minocycline在腸病毒71型感染的作用
廖郁婷[1]、王世敏[1,2,3]、劉清泉[1,2]、陳舜華[1,4]
國立成功大學傳染性疾病與訊息研究中心[1]；國立成功大學醫學院附設醫院小兒部[2]、急診部[3]；國立成功大學醫學院微生物與免疫學研究所[4]

15:52~15:59　68. PCV13世代中耳炎、鼻竇炎、中耳積液與健康兒童肺炎鏈球菌鼻咽部帶菌血清型差異
陳志和[1,2]、徐美華[4]、郭光哲[1]、邱政洵[2,3,4]
高雄長庚醫院兒童內科部[1]；長庚大學臨床醫學研究所[2]；林口長庚醫院兒童內科部[3]；長庚醫院分子感染症研究中心[4]

15:59~16:20　討論

16:20~16:30　休息

主持人：

16:30~16:37　69. 兒童中耳炎與心理壓力之關係
陳凱威[1]、黃瑽寧[1]、周麗端[2]、聶西平[2]、傅仁煇[3]、張鑑如[2]
馬偕兒童醫院兒科部小兒感染科[1]；國立台灣師範大學人類發展與家庭學系[2]；林口長庚紀念醫院新生兒科[3]

16:37~16:44　70. 二氧化矽孔洞結構上的奈米銀粒子(AgNP)對抗藥性金黃色葡萄球菌(MRSA)的殺菌能力
林昭仁[1,2]、顏宏偉[2]、石啓仁[3]、楊瑞成[4]、王士忠[5]、陳家玉[5]
彰化基督教兒童醫院兒童感染科[1]；東海大學化學工程與材料工程學系[2]；高雄醫學大學香粧品學系[3]；高雄醫學大學小兒科[4]；彰化基督教兒童醫院[5]

16:44~16:51　71. 兒童泌尿道感染致病菌與尿液ph值之關聯性研究
賴奐丞[1]、林曉娟[1]、顏廷聿[1]、衛琇玫[1]、許玉龍[1]、姜秀穎[2]、張仕妮[2]、郭錦輯[2,3]、黃高彬[1]
中國醫藥大學兒童醫院兒童感染科[1]；中國醫藥大學附設醫院大數據中心[2]；中國醫藥大學附設醫院腎臟醫學中心[3]

16:51~16:58　72. 伊科病毒第十一型與克沙奇病毒第五型在台灣兒童所造成之疾病特色與表現
陳苡靜、陳志榮、林奏延、黃玉成、邱政洵、謝育嘉、郭貞孍、黃冠穎
林口長庚紀念醫院兒童感染科

16:58~17:05　73. 伊科病毒11型感染於南台灣一醫學中心
蔡瑋峻、王世敏、沈靜芬、何宗憲、劉清泉
國立成功大學醫學院附設醫院小兒部

17:05~17:12　74. 南臺灣兒童乙型鏈球菌感染：自新生兒到青少年
郭正彥[1]、蔡瑋峻、沈靜芬、何宗憲、王世敏、劉清泉
國立成功大學醫學院附設醫院小兒部 [1]

17:12~17:30　討論

第六單元：心臟血管學

日期：民國108年4月20日(星期六)
時間：08:30~11:40
地點：102會議室

主持人：

08:30~08:37　75. 吉里巴斯學童風濕性心臟病篩檢：期中結果
葉樹人、林穎予、游昌憲[1]、鄭崑山[2]、趙彥均、陳福昌[2]、洪偉力、林珊妙、陳銘仁
馬偕兒童醫院兒童心臟科；馬偕紀念醫院台東分院小兒科[1]；馬偕紀念醫院新竹分院小兒科[2]

08:37~08:44　76. 以二維心臟超音波定義正常胎兒心臟結構之參考值
田智瑋、池宛玲[1]、Eric C. Lussier[1]、葉樹人[2,3]、林珊妙[2,3]、周昱青[1]、黃思萍[1]、張東曜[1]、陳銘仁[2,3,4]
台兒診所[1]；馬偕紀念醫院小兒科[2]；馬偕醫學院[3]；馬偕醫護管理專科學校[4]

08:44～08:51　77. 法洛氏四重症術後病患之右心室出口型態、肺動脈瓣環直徑、與雙側肺動脈不均等對患者之不良預後指標的影響
沈宛臻、陳俊安[1]、陳世杰[2]、曾文毅[3]、吳美環[1]、盧俊維[1]、林銘泰[1]、邱舜南[1]、王主科[1]
天主教輔仁大學附設醫院兒童醫學部；國立台灣大學醫學院附設醫院兒童醫院小兒部[1]；國立台灣大學醫學院附設醫院影像醫學部[2]；國立台灣大學醫學院光電生物醫學研究中心[3]

08:51～08:58　78. 肺動脈壓是預測Fontan手術預後最重要的因子：單一醫學中心之經驗
林杏佳[1,2]、吳美環[2]、王主科[2]、林銘泰[2]、陳俊安[2]、盧俊維[2]、陳益祥[3]、黃書健[3]、邱舜南[2]
國立台灣大學醫學院附設醫院雲林分院小兒部[1]；國立台灣大學醫學院附設醫院兒童醫院小兒部[2]；國立台灣大學醫學院附設醫院外科部[3]

08:58～09:05　79. 兒童心因性心跳停止生存者的基因檢測
邱舜南[1]、吳美環[1]、莊志明[1]、曾偉杰[1]、陳文彬[2]
國立台灣大學醫學院附設醫院[1]；國立台灣大學醫學院附設醫院藥理所[2]

09:05～09:12　80. 經心導管關閉膜周邊型心室中隔缺損：單一醫學中心的臨床經驗
李昱昕、徐新貿、儲聖知[2]、劉顥筌、張育生[1]、黃茂盛、蘇文鈐、鍾宏濤
長庚紀念醫院林口分院兒童內科部、心臟外科[1]；國軍桃園總醫院小兒科[2]

09:12～09:19　81. 經心導管利用安普拉茲第二型血管塞治療膜邊型心室中膈缺損的初步經驗
傅雲慶、徐宗正
中國醫藥大學兒童醫院兒童心臟科

09:19～09:26　82. 兩種不同品牌靜脈注射免疫球蛋白球對川崎病患者的臨床療效
吳焜烺[1]、林銘泰[2]、張玉君[3]
彰化基督教兒童醫院兒童心臟科[1]；國立台灣大學醫學院附設醫院兒童心臟科[2]；彰化基督教醫院研究教學與流病中心[3]

09:26～09:33　83. 頑固型川崎病的最適治療—免疫球蛋白併用類固醇與否的前瞻性隨機研究
張正成[1]、呂俊毅[2]、紀鑫[3]、林銘泰[2]、47 RAST研究群[4]
中國醫藥大學兒童醫院[1]；國立台灣大學醫學院附設醫院兒童醫院[2]；馬偕兒童醫院[3]；中華民國心臟病兒童基金會[4]

09:33～10:00　討論

10:00～10:10　休息

主持人：

10:10~10:17　84. 研究脈衝療法對川崎病動脈瘤之成效
戴以信、謝凱生、郭和昌
長庚醫療財團法人高雄長庚紀念醫院川崎病中心

10:17~10:24　85. 降低DNA甲基轉移酶的表達並與川崎病中的冠狀動脈病變形成有關
黃瀛賢、郭和昌
高雄長庚醫院兒童內科部川崎病研究中心

10:24~10:31　86. Mir-182-5p增加川崎症併有冠狀動脈病灶的體外白血球浸潤
翁根本、簡光仁、陳昱潔、陳俊宇、林竹川、蔡國旺、謝凱生
高雄榮民總醫院兒醫部[1]、教研部[2]；台北醫學大學兒科學系[3]

10:31~10:38　87. 研究嗜酸性球在川崎病患之動態變化與冠狀動脈病變之關連性
戴以信[1]、盧怡婷[2]、黃瀛賢[2]、郭明慧[2]、張鈴偲[2]、謝凱生[3]、郭和昌[2]
中國醫藥大學兒童醫院[1]；高雄長庚紀念醫院川崎病中心[2]；台北醫學大學[3]

10:38~10:45　88. 細胞凋亡與青少年肥胖引起之心室舒張功能異常相關
楊明浚[1,,2]、劉賢冠[1]、蘇有村[1,2]、蔡璟忠[1,2]、吳俊仁[1]
義大醫院兒童醫學部[1]；義守大學醫學院[2]

10:45~10:52　89. 腺病毒感染和後續得川崎症與冠狀動脈併發症風險相關性探討：世代研究
陳俊宇[2]、劉萬雄[2]、陳昱潔[1]、簡光仁[1]、林竹川[1]、謝凱生[3]、魏正宗[4]、翁根本[1]
高雄榮民總醫院兒醫部[1]；奇美醫院兒醫部[2]；台北醫學大學兒科學系[3]；中山醫學大學醫學研究所[4]

10:52~10:59　90. 體重小於1800克且存有開放性動脈導管之早產兒，接受傳統手術及心導管治療前後之血液動力學的比較：南台灣30例早產兒病例回溯性分析
郭正彥、朱映慈、魏昱仁、張毓珊、謝旻玲、林永傑、甘宗旦、林毓志、王玠能、吳俊明
國立成功大學醫學院附設醫院

10:59~11:06　91. 臍靜脈於新生兒介入性治療之應用
朱映慈、林永傑、魏昱仁、謝旻玲、王玠能、吳俊明
國立成功大學附設醫院小兒科

11:06~11:13　92. 母親服用H1抗組織胺藥可能引發其哺乳嬰兒抽搐及QTc延長
沈慶村、王麗君、陳勇全、王南焜、洪焜隆、侯家瑋
國泰綜合醫院

11:13~11:40　討論

附加研討會
多價數與多劑型的兒童與青少年疫苗發展趨勢

日期：民國108年4月20日(星期六)
時間：12:00~13:30
地點：102會議室

主持人：黃玉成教授、李秉穎醫師

12:00~12:30　1. 兩性HPV相關疾病發展趨勢及預防
李秉穎醫師
國立臺灣大學醫學院附設醫院兒童醫院兒童感染科

12:30~12:40　2. Q&A 討論

12:40~13:20　3. 如何呈現眞實世界中疫苗的保護效果？以輪狀病毒疫苗爲例
黃玉成教授
林口長庚紀念醫院兒童內科部兒童感染科

13:20~13:30　4. Q&A 討論

第七單元：神經精神醫學

日期：民國108年4月20日(星期六)
時間：13:30~15:50
地點：102會議室

主持人：

13:30~13:37　93. 自嗜作用失調是造成MELAS症候群的病理機轉_以iPS細胞模型的研究
林達雄[1,2]、何啓生[1]、洪碧蓮[3]、徐美欣[3]、蔣明富[4,5]
馬偕紀念醫院[1]；馬偕醫學院[2]；高雄長庚紀念醫院兒童神經科及長庚醫學大學[3]；馬偕紀念醫院神經外科部[4]；台北醫學大學[5]

13:37~13:44　94. 放射治療對兒童腦瘤治療效果與長期追蹤
李逢卿、胡智棻、陳錫洲、許庭榕[1]
三軍總醫院小兒科部；台北榮民總醫院兒童醫學部[1]

13:44~13:51　95. 兒童睡眠疾病的分析—兒童睡眠特別門診的兩年經驗
張明瑜[1,3]、林光麟[1]、黃玉書[2,3]
林口長庚兒童醫院兒童神經科[1]、兒童青少年精神醫學科[2]、兒童睡眠中心[3]

13:51~13:58　96. 新生兒時期發現之Multiple subependymal pseudocysts與後續注意力不足過動症及自閉症譜系發生之關聯性
張璽、曾頌惠[1]、李儒卿[2]、蔡明蘭
臺北醫學大學附設醫院小兒科部、復健科[1]、精神科[2]

13:58~14:05　97. 嬰幼兒時期巨細胞感染可能增加之後癲癇及自閉症之風險
林建亨[1]、洪宣羽[2]、林瑋德[2]、周宜卿[2]
中國醫藥大學兒童醫院胸腔科[1]、神經科[2]

14:05~14:12　98. 以陀螺儀及加速度計輔助注意力不集中併過動症之診斷
林龍昌、歐陽振森[1]、江景泰[3]、吳榮慶[2]、楊瑞成
高雄醫學大學附設醫院小兒部；義守大學資訊工程系[1]、電機系[2]；國立屏東大學電通系[3]

14:12~14:30　討論

14:30~14:40　休息

主持人：

14:40~14:47　99. 癲控達有效及無效之頑固性癲癇病人特性分析
郭政諺[1,2]、林光麟[2,3]、周怡君[2,3]、王煇雅[2,3]、洪伯誠[2,3]、周明亮[2,3]、林建志[2,3]、謝孟穎[2,3]、張明瑜[2,3]、王薏珊[2,3]
林口長庚紀念醫院兒童內科部[1]、兒童神經內科部[2]；長庚大學醫學院[3]

14:47~14:54　100. 探討一群患有具病源體診斷的中樞神經系統感染兒童其癲癇和神經發展預後：一項爲期12年的觀察性研究
洪宣羽[1]、周宜卿[1,2]、林瑋德[3,4]、蔡輔仁[4,5]、蔡長海[1]
中國醫藥大學兒童醫院兒童神經科[1]；中國醫藥大學醫學院整合醫學研究所[2]；中國醫藥大學學士後中醫學院[3]；中國醫藥大學附設醫院醫學遺傳學部[4]；中國醫藥大學中醫藥學院[5]；亞洲大學[6]

14:54~15:01　101. 醫源性外顯子定序檢查在兒童嚴重癲癇合併神經發展障礙病人的應用
李英齊[1,2*]、楊建洲[3]、李宣佑[3]、Victor Zhang[4]、Lee-Jun C. Wong[4]
中山醫學大學附設醫院小兒科、小兒神經科[1]；中山醫學大學醫學系[2]；基因實驗與生物科學系，中山醫學大學[3]；分子與人類遺傳科，貝勒醫學院，德州，美國[4]

15:01~15:08　102. 嬰兒時期發燒合併低腦脊髓葡萄糖之嬰兒其發展預後及帶有SLC2A1變異之比率
余文豪[1]、陳俐文[1]、王新台[2]、杜伊芳[1]、吳博銘[1]、黃朝慶[1]
國立成功大學附設醫院小兒科[1]；國立成功大學老人所[2]

15:08~15:15　103. 肢帶型肌失養症在台灣
梁文貞[1,4,5]、王建華[1,6]、王晨華[1]、Xia Tien[7,8]、陳婉姿[2]、甘慈閔[1]、Narihiro Minami[9,10,11]、Ichizo Nishino[10,11]、Lee-Jun C. Wong[7,8]、鐘育志[1,3,4,5]
高雄醫學大學附設醫院小兒科[1]、病理科[2]、檢驗醫學科[3]；高雄醫學大學醫學院 醫學系小兒學科[4]、臨床醫學研究所[5]；高雄市立小港醫院小兒科[6]；貝勒基因，美國[7]；分子及人類基因部，貝勒醫學院，美國[8]；檢驗醫學部，國立精神神經醫療研究中心醫院，日本[9]；神經肌肉研究部，神經研究所，國立精神神經醫療研究中心，日本[10]；基因醫學發展部，醫學基因中心，國立精神神經醫療研究中心，日本[11]

15:15~15:22　104. 兒童不寧腿症候群~病例系列報告
黃正憲[1,2]、張欣平[2,3]、洪品晞[2]
臺北市立聯合醫院陽明院區小兒科[1]；臺北市立聯合醫院陽明院區睡眠中心[2]；臺北市立聯合醫院陽明院區耳鼻喉科[3]

15:22~15:29　105. STIM1突變之Stormorken症候群：臺灣第一例
王晨華、梁文貞、曾育昇、林珮瑾、楊瑞成、鐘育志
高雄醫學大學附設中和紀念醫院小兒部

15:29~15:50　討論

15:50~16:00　休息

第八單元：血液、腫瘤學

日期：民國108年4月20日(星期六)
時間：16:00~17:10
地點：102會議室

主持人：

16:00~16:07　106. NUT中線上皮癌(NMC)：臨床表現與分子病理
劉彥麟[1,2,5]、高郁茜[2,10]、謝宗翰[1,3]、李欣倫[1,2,7]、謝立群[1,8]、張家堯[1,2,5]、曾頌惠[1,2,9]、黃玄贏[11]、James S. Miser[1,2,4]、黃棣棟[1,6]
臺北醫學大學兒童腦瘤照護團隊[1]、肉瘤及肌肉骨骼腫瘤團隊[2]、聯合人體生物資料庫[3]、醫學科技學院[4]；臺北醫學大學附設醫院小兒部[5]、神經外科[6]、放射腫瘤科[7]、影像醫學部[8]、復健科[9]；衛生福利部雙和醫院(委託臺北醫學大學興建經營)病理科[10]；高雄長庚紀念醫院解剖病理科[11]

16:07~16:14　107. 兒童急性淋巴性白血病引導期治療間G-CSF預防使用之經驗
葉庭吉、劉希哲、侯人尹、黃鼎煥
馬偕兒童醫院小兒血液腫瘤科

16:14~16:21　108. 兒童惡性睪丸腫瘤：單一機構的12年經驗
江東和[1]、陳世翔[1]、楊兆平[1]、曾振淦[2]、賴勁堯[3]、薛純[4]
長庚大學，林口長庚紀念醫院兒童醫學中心，兒童血液腫瘤科[1]、放射腫瘤科[2]、兒童外科[3]、解剖病理科[4]

16:21~16:28　109. 兒童蘭格罕氏組織細胞增生症的臨床特徵與治療成果：單一機構之經驗
陳世翔[1]、楊兆平[1]、洪悠紀[1]、江東和[1]、張從彥[1]、吳杰才[2]、張嘉獻[3]、薛純[4]
林口長庚紀念醫院兒童血液腫瘤科[1]、兒童神經外科[2]、兒童骨科[3]、病理科[4]

16:28~16:35　110. 高風險伊汶氏肉瘤病患接受高劑量化學藥物治療併自體幹細胞移植：單一機構治療經驗
李致穎、顏秀如、洪君儀、余廷彥、邱宗傑[1]
台北榮民總醫院兒童醫學部、輸血醫學科[1]；國立陽明大學醫學院

16:35~16:42　111. Denosumab對兒童癌症存活者之骨密度低下治療的效果與安全性：初步經驗報告
黃鼎煥[1]、劉希哲[2]、侯人尹[2]、葉庭吉[2]
新竹馬偕醫院小兒血液腫瘤科[1]；馬偕兒童醫院血液腫瘤科[2]

16:42~16:49　112. 順鉑引起之腎毒性早於耳毒性？一個斑馬魚動物模式
洪君儀[1,2]、吳巧羚[2]、鄒宜伶[2]、鄭劍廷[2]、洪君琳[3]、林豐益[2]
臺北榮民總醫院兒童醫學部血液腫瘤科；國立陽明大學醫學系[1]；國立台灣師範大學生命科學系[2]；台北醫學大學醫學系解剖學暨細胞生物學科[3]

16:49~17:10　討論

第九單元：腎臟學

日期：民國108年4月20日(星期六)
時間：08:30~09:50
地點：103會議室

主持人：

08:30~08:37　113. 由腹膜透析引流液分離人類腹膜間皮細胞之細胞凋亡與相關機轉
王馨慧[1,2,3]、林清淵[4,5]
臺北榮民總醫院兒童醫學部[1]；陽明大學醫學院小兒學科[2]、急重症醫學研究所[3]；中國醫藥大學醫學院[4]；中國醫藥大學兒童醫院[5]

08:37~08:44　114. 應用尿液代謝質體學分析兒童夜間遺尿
周易宣[1]、王大民[2]、邱志勇[1]、邱益煊[3]、余美靜[1,4]
林口長庚紀念醫院兒童內科部[1]、兒童泌尿科[2]；高雄榮民總醫院兒童內科部[3]；林口長庚紀念醫院兒童腎臟科[4]

08:44～08:51　115. 以低劑量Afinitor治療結節性硬化症血管平滑肌脂肪瘤的成效—48個月追蹤結果
張佩祺[1]、許績男[1]、魏長菁[2]、蔡政道[1,3]
中山醫學大學附設醫院兒童部[1]；中國醫藥大學兒童醫院腎臟科[2]；馬偕兒童醫院腎臟科[3]

08:51～08:58　116. 無肛症病童合併膀胱輸尿管迴流的危險因子分析
吳重緯[1]、魏長菁[1,2]、林清淵[1,2]
中國醫藥大學兒童醫院[1]；中國醫藥大學醫學院[2]

08:58～09:05　117. 尿中微蛋白量做爲診斷川崎氏症的次要標準
馮瑩芝[1]、方乃文[1]、邱益煊[1]、陳昱潔[1]、簡光仁[1]、林竹川[1]、謝凱生[2]、翁根本[1]
高雄榮民總醫院兒醫部[1]；台北醫學大學兒科學系[2]

09:05～09:12　118. 以基因改造小鼠(神農鼠)模式建立高靈敏且高專一性的腎毒性檢測平台
邱元佑[1]、蔣思澈[2]
國立成功大學附設醫院小兒部小兒腎臟科[1]；國家實驗動物中心[2]

09:12～09:19　119. 白藜蘆醇藉由調控腸道菌群和氧化壓力，避免產前L-NAME治療加上產後高脂肪飲食所造成的計畫性高血壓
陳宏恩[1]、林育如[2]、林宜君[1]、于鴻仁[1]、沈俊明[1]、蔡慶璋[2]、黃立同[1,3]、田祐霖[1]
高雄長庚紀念醫院兒童內科部[1]、婦產部[2]；長庚大學中醫系[3]

09:19～09:26　120. 針對腸道微生物代謝產物三甲胺-N-氧化物和短鏈脂肪酸預防母親高果糖飲食誘導的程序化高血壓產生
田祐霖[1]、許茜甯[2]、張簡國平[3]、侯智耀[4]
高雄長庚紀念醫院兒童內科部[1]、藥劑部[2]；正修科技大學超微量研究科技中心[3]；高雄科技大學水產食品科學系[4]

09:26～09:50　討論

09:50～10:00　休息

第十單元：重症學

日期：民國108年4月20日(星期六)
時間：10:00~11:00
地點：103會議室

主持人：

10:00~10:07　121. 社區型肺炎和院內感染肺炎可能導致需要兒童加護病房照顧的危險因子
戴睿宏、曾偉杰、顏玎安、吳恩婷、呂立、王景甲
國立台灣大學醫學院附設醫院兒童醫院

10:07~10:14　122. 在兒科加護病房急性呼吸窘迫病童Filmarray呼吸道檢驗的臨床意義
陳姿均[1,2]、張智卿[3]、林以晨[1,2]、林建志[2,3]、夏紹軒[2,3]
長庚大學醫學系[1]；林口長庚醫院兒童加護科[2]；林口長庚醫院呼吸治療科[3]

10:14~10:21　123. 兒科加護病房在急性呼吸衰竭使用高流量鼻導管的經驗
林以晨[1,2]、張智卿[3]、陳姿均[1,2]、林建志[2,3]、夏紹軒[2,3]
長庚大學醫學系[1]；林口長庚醫院兒童加護科[2]；林口長庚醫院呼吸治療科[3]

10:21~10:28　124. 兒童腸病毒A71型重症感染之尿液兒茶酚胺研究：與兒童敗血性休克比較
劉瑋莉[1]、陳書農[2]、詹聖霖[2]、林明志[2]、陳伯彥[3]、黃芳亮[3]、李秀芬[4]
大林慈濟醫院小兒科[1]；臺中榮民總醫院兒童醫學中心兒童心臟科[2]、兒童感染科[3]、兒童神經科[4]

10:28~10:35　125. 兒童嗜血症候群死亡預後因子探討
陳琮硯[1,2]、林盈瑞[1]、徐美欣[1]、郭玄章[1]、沈俊明[1]、楊生湳[2]
高雄長庚紀念醫院兒童內科部[1]；義大醫院兒童醫學部[2]

10:35~10:42　126. 在新生兒使用葉克膜：一個醫學中心的經驗分析
鄭明洲、林盈瑞、郭玄章、徐美欣
高雄長庚紀念醫院兒童加護科

10:42~11:00　討論

11:00~11:10　休息

第十一單元：急診學

日期：民國108年4月20日(星期六)
時間：11:10~11:40
地點：103會議室

主持人：

11:10~11:17　127. X光片氣管比值在預測兒童急診哮吼病童結果之角色
楊文傑、陳俊佑、吳漢屏
中國醫藥大學兒童醫院兒童急診科

11:17~11:24　128. 院外急產感染風險及預後研究
張佳容[1]、張龍[2]、紀鑫[2]、詹偉添[3]、邱南昌[2]
馬偕兒童醫院小兒科部、兒童急診科[1]、兒童感染科[2]、新生兒科[3]

11:24~11:31　129. 兒童急診病童腦炎之回顧性研究
張雅惠[1]、胡美華[2]、吳昌騰[2]、李嶸[2]、夏紹軒[3]、王煇雄[4]、林光麟[4]、洪伯誠[4]、周明亮[4]、周怡君[4]
林口長庚醫院兒童內科[1]、兒童一般醫學科[2]、兒童加護科[3]、兒童神經科[4]

11:31~11:40　討論

第十二單元：青少年醫學

日期：民國108年4月20日(星期六)
時間：13:30~13:50
地點：103會議室

主持人：

13:30~13:37　130. 青少年發展資產與長期生理與心理社會健康影響：台灣世代研究分析
蔡孟哲[1]、吳美彤[2]、游怡芳[3]、莊佳蓉[3]、謝薏苹[4]、林宜靜[5]、林宗瑩[2]
國立成功大學醫學院附設醫院小兒科[1]；香港理工科技大學醫療及社會科學院康復治療科學系[2]；國立成功大學醫學院公共衛生學科暨研究所[3]；北達科他大學護理及專業學院社會工作學系[4]；國立臺北教育大學幼兒與家庭教育學系[5]

13:37~13:44　131. 透過Photovoice了解男性高風險青少年的生活經歷
蕭予德[1]、陳曉盈[2]、Mellissa Withers[1]
南加州大學醫學院[1]；財團法人基督教更生團契附設花蓮縣私立信望愛少年學園[2]

13:44~13:50　討論

第十三單元：內分泌學

日期：民國108年4月20日(星期六)
時間：13:50~14:30
地點：103會議室

主持人：

13:50~13:57　132. 口服維生素D補充對於以純母乳哺育新生兒的影響
林昭旭[1,6]、宋聿翔[1]、李松澤[1]、鄭弼文[1]、翁順隆[2]、張幸治[2]、丁瑋信[3]、李宏昌[4]、張弘洋[5]、林志生[6]
新竹馬偕紀念醫院小兒科部[1]、婦產科部[2]；馬偕兒童醫院兒童內分泌科[3]、兒童胃腸科[4]、新生兒科[5]；交通大學生物科技學系[6]

13:57~14:04　133. 顱咽管瘤患兒的臨床和內分泌表現：台灣一醫學中心報告
黃敬之、羅福松、邱巧凡
林口長庚紀念醫院兒童內分泌暨遺傳科

14:04~14:11　134. 顱內生殖細胞腫瘤患兒的臨床和內分泌表現：台灣一家醫學中心報告
張馨元、羅福松
林口長庚醫院兒童內分泌暨遺傳科

14:11~14:18　135. 當AI人工智慧成爲醫院中的臨床診斷幫手：以AI骨齡評估系統爲例
蔡輔仁[1]、廖英凱[2]、鄭奇洚[3]、黃宗祺[2,4]
中國醫藥大學附設醫院基因醫學部[1]；中國醫藥大學附設醫院醫研部人工智慧醫學診斷中心[2]；中國醫藥大學附設醫院醫學研究部[3]；亞洲大學生物資訊與醫學工程學系[4]

14:18~14:30　討論

14:30~14:40　休息

第十四單元：醫學遺傳學、新陳代謝學

日期：民國108年4月20日(星期六)
時間：14:40~17:00
地點：103會議室

主持人：

14:40~14:47　136. 台灣黏多醣症第三型患者的心臟特徵
林翔宇[1,2,3,4]、林炫沛[1,2,3,5]、陳銘仁[1,3,4]、莊志光[2]、林珊妙[1,3,4]、洪崇烈[2,3,6]、牛道明[7]、張通銘[8]
馬偕紀念醫院小兒科部[1]及醫學研究部[2]；馬偕醫學院醫學系[3]；馬偕醫護管理專科學校[4]；國立台北護理健康大學嬰幼兒保育系[5]；馬偕紀念醫院心臟內科[6]；台北榮民總醫院兒童醫學部[7]；彰化基督教兒童醫院小兒神經科[8]

14:47～14:54　137. 以尿液葡萄胺聚糖的檢測進行黏多醣症高風險族群的篩檢計畫
林翔宇[1,2,3,4]、林炫沛[1,2,3,5]、莊志光[2]、羅允廷[6]、李忠霖[7]、張家穎[7]、邱寶琴[8]、張通銘[9]、蔡文暉[10]、牛道明[11]
馬偕紀念醫院小兒科部[1]及醫學研究部[2]；馬偕醫學院醫學系[3]；馬偕醫護管理專科學校[4]；國立台北護理健康大學嬰幼兒保育系[5]；馬偕紀念醫院檢驗醫學部[6]；新竹馬偕紀念醫院小兒科[7]；高雄榮民總醫院兒童醫學部[8]；彰化基督教兒童醫院小兒神經科[9]；台南奇美醫學中心小兒科部[10]；台北榮民總醫院兒童醫學部[11]

14:54～15:01　138. 全外顯子定序作爲兒科罕見或困難個案的診斷平台
謝秀盈[1]、莊淑樺[1]、蔡文心[1]、王緒斌[1]、洪碧蓮[2]、余俊賢[1]、李致任[1]、楊佳鳳[3]、賴明聰[4]、蔡立平[1]
台北慈濟醫院兒科部[1]；高雄長庚紀念醫院兒童內科部[2]；台北榮民總醫院兒童醫學部[3]；華聯生物科技[4]

15:01～15:08　139. 疑似膠原蛋白病變的基因缺損探究
李妮鍾[1]、簡穎秀[1]、林宜霖[1]、林如立[2]、李振豪[3]、陳乃琦[1]、洪妙子[1]、胡務亮[1]
國立台灣大學醫學院附設醫院小兒部、基因醫學部[1]；林口長庚醫院兒童內科部[2]；義大醫院兒童醫學部[3]

15:08～15:15　140. 以iPS細胞模型重現MELAS症候群的病理機轉
林達雄[1,2]、何啓生[1]、洪碧蓮[3]、徐美欣[3]、蔣明富[4,5]
馬偕紀念醫院[1]；馬偕醫學院[2]；高雄長庚紀念醫院兒童神經科及長庚醫學大學[3]；馬偕紀念醫院神經外科部[4]；台北醫學大學[5]

15:15～15:22　141. 新生兒型龐貝氏症呼吸道異常：一大型研究
楊佳鳳[1]、何慧貞[2]、高淑敏[3]、牛道明[1]、宋文舉[1]
台北榮民總醫院兒童醫學部[1]；醫療財團法人病理發展基金會台北病理中心[2]；財團法人中華民國衛生保健基金會[3]

15:22～15:40　討論

15:40～15:50　休息

主持人：

15:50～15:57　142. 高雪氏症新生兒篩檢之台灣經驗
王亭皓[1]、陳菁兒[1]、高淑敏[4]、何慧貞[3]、李致穎[1]、顏秀如[1]、王仲興[2]、蔡輔仁[4]、林瑋德[4]、牛道明[1]、楊佳鳳[1]
台北榮總兒童醫學部[1]；中國醫藥學大學兒童醫學部[2]；醫療財團法人病理發展基金會台北病理中心[3]；財團法人中華民國衛生保健基金會[4]

15:57~16:04　143. 亞洲高好發率的法布瑞氏症IVS4基因突變的遺傳起源研究
許庭榕[1]、梁恭豪[2]、盧永修[1]、張勝凱[1]、楊佳鳳[1]、牛道明[1]
台北榮民總醫院兒童醫學部[1]、醫學研究部[2]

16:04~16:11　144. 台灣成人成骨不全症患者股骨骨折的盛行率及治療分析，以一醫學中心72位患者爲例
李忠霖[1]、林翔宇[2,3,4,5]、林炫沛[2,3,4,6]、劉士嘉[7]
新竹馬偕紀念醫院小兒部[1]；台北馬偕紀念醫院小兒部[2]；馬偕紀念醫院醫學研究部[3]；馬偕醫學院醫學系[4]；馬偕醫護管理專科學校[5]；國立台北護理健康大學嬰幼兒保育學系[6]；台北馬偕紀念醫院骨科部[7]

16:11~16:18　145. 矮或不矮：家族性矮小症之易感基因研究
林應如[1,2]、鄭奇洚[1,3]、王仲興[4]、謝瓊如[3]、梁文敏[3]、蔡立平[5]、陳建勳[2,6]、鄔哲源[2,6]、李明達[2,7]、蔡輔仁[1,2,8]
中國醫藥大學附設醫院醫學研究部遺傳中心[1]；中國醫藥大學中醫學院中醫學系[2]；中國醫藥大學公衛學院生物統計研究所[3]；中國醫藥大學附設兒童醫院[4]；台北慈濟醫院兒科部[5]；中央研究院生物醫學研究所[6]；美國Geisinger健康系統基因體醫學研究所[7]；亞洲大學生物科技學系[8]

16:18~16:25　146. 初經相關基因變異在原發性中樞型性早熟女童的關聯分析
林瑋德[1,4]、林應如[1,5]、鄭奇洚[1]、王仲興[3]、蔡輔仁*[1,2,3,5]
中國醫藥大學附設醫院醫學研究部[1]、基因醫學部[2]；中國醫藥大學兒童醫院遺傳及內分泌新陳代謝科[3]；中國醫藥大學學士後中醫學系[4]、中醫學系[5]

16:25~16:32　147. 比較基因組雜交晶片診斷第四及第五號染色體缺失症候群並探討其臨床症狀及預後分析
陳冠容[1]、吳信儒[1]、趙美琴[1]、陳曉能[2]、張通銘[3]、馬國欽[4]、陳明[4]
彰化基督教兒童醫院兒童遺傳科[1]、新生兒科[2]、兒童神經科[3]；彰化基督教醫院基因醫學部[4]

16:32~16:39　148. 羧化全酶合成酶缺乏症：一個新突變和一個非典型臨床表現案例報告，以及文獻回顧
吳信儒[1]、陳冠容[1]、趙美琴[1]、吳怡磊[2]、蕭惠彬[3]、蕭宛綾[3]
彰化基督教醫院兒童遺傳科[1]、兒童內分泌科[2]；高雄醫學大學附設中和紀念醫院兒童部[3]

16:39~17:00　討論

陳炯霖教授講座獎

日　期：民國108年4月21日(星期日)
時　間：08:30~09:30
地　點：101A、B、C、D會議室

主持人：呂鴻基教授

08:30~09:20　1. 兒童急性淋巴細胞白血病完全治癒前景
裴正康院士
St. Jude Children's Research Hospital, Memphis, TN, USA

09:20~09:30　2. 綜合討論

教育演講：
青少年醫學論壇

日　期：民國108年4月21日(星期日)
時　間：09:30~11:50
地　點：101A、B、C、D會議室

主持人：李宏昌常務理事、羅福松醫師

09:30~09:40　1. 致詞
王英偉署長
衛生福利部國民健康署

09:40~10:00　2. 台灣青少年醫學現況
羅福松醫師
林口長庚紀念醫院

10:00~10:50　3. Current Global Opportunities and Challenges in Adolescent Health
Susan Sawyer
Professor, Royal Children's Hospital and The University of Melbourne, Australia
President, International Association for Adolescent Health

10:50~11:30　4. 青春的美麗與哀愁：小兒科醫師在飲食障礙症的角色
廖璽璜理事長
杏璞身心健康關懷協會

11:30~11:50　5. 綜合討論

附加研討會
從疫苗設計探討預防醫學重要性
VS 國內疫苗政策探討

日期：民國108年4月21日(星期日)
時間：12:00~13:30
地點：101A、B、C、D會議室

主持人：黃立民教授、邱政洵教授

12:00~12:10　1. 開幕致詞
黃立民教授
國立臺灣大學醫學院附設醫院兒童醫院

12:10~12:40　2. 獨創的輪狀病毒疫苗設計在廣泛預防新興輪狀病毒的重要性
邱南昌醫師
馬偕兒童醫院

12:40~13:00　3. 國中女生公費施打HPV疫苗政策探討
陳志榮醫師
林口長庚紀念醫院

13:00~13:25　4. 兒童感染症醫學會Guideline update：百日咳的預防與治療指引
李秉穎醫師
國立臺灣大學醫學院附設醫院兒童醫院

13:25~13:30　5. 問題討論與結語
邱政洵教授
林口長庚紀念醫院

頒獎/會員代表大會

日　期：民國108年4月21日(星期日)
時　間：13:30~14:30
地　點：101A、B、C、D會議室

14:30~14:40　　休息

醫學的科學、倫理與法律講座：探討藥物仿單核准適應症外的使用

日　期：民國108年4月21日(星期日)
時　間：14:40~16:40
地　點：101A、B、C、D會議室

主持人：江伯倫理事長、林奏延教授

14:40~15:30　　1. 小兒科仿單核准適應症外藥物的使用
吳怡萱醫師
林口長庚紀念醫院兒童內科部

15:30~15:40　　2. 討論

15:40~16:30　　3. 仿單核准適應症外藥物使用的法律問題
范振中主持律師
明永大揚聯合法律事務所

16:30~16:40　　4. 討論

專題演講：
兒童血液/腫瘤病患常見徵候

日　期：民國108年4月21日(星期日)
時　間：09:30~11:30
地　點：102會議室

主持人：林東燦醫師、彭慶添醫師

09:30~09:55　1. 兒童臉色蒼白怎麼辦？— 缺鐵性貧血
林佩瑾醫師
高雄醫學大學附設醫院小兒血液腫瘤科

09:55~10:20　2. 兒童臉色蒼白怎麼辦？— 海洋性貧血
盧孟佑醫師
台大兒童醫院小兒血液腫瘤科

10:20~10:45　3. 淋巴結腫大怎麼辦？
王士忠醫師
彰化基督教兒童醫院兒童血液腫瘤科

10:45~11:10　4. 常有瘀青或常流鼻血怎麼辦？
翁德甫醫師
中國醫藥大學兒童醫院兒童血液腫瘤科

11:10~11:30　5. 兒童癌症九大警徵
顏秀如醫師
臺北榮民總醫院兒童醫學部血液腫瘤科

3

附加研討會
疫苗面面觀

日期：民國108年4月21日(星期日)
時間：12:00~13:30
地點：102會議室

主持人：黃玉成教授、呂俊毅醫師、陳伯彥醫師

12:00~12:05　1. 開幕致詞
李秉穎醫師
國立臺灣大學醫學院附設醫院兒童醫院

12:05~12:30　2. 四價流感疫苗的臨床效益
黃玉成教授
林口長庚紀念醫院兒童內科部兒童感染科

12:30~12:55　3. 疫苗接種率及群體免疫
呂俊毅醫師
國立臺灣大學醫學院附設醫院兒童醫院

12:55~13:20　4. 疫苗政策的執行考量
陳伯彥醫師
台中榮民總醫院

13:20~13:30　5. 問題討論與結語
黃立民教授
國立臺灣大學醫學院附設醫院兒童醫院

特別演講：
如何優化兒童醫療網

日　期：民國108年4月21日(星期日)
時　間：09:30~11:30
地　點：103會議室

主持人：江伯倫理事長、陳武元常務理事

09:30~09:50　1. 致詞
衛生福利部長官
(邀請中)

09:50~10:50　2. 如何優化兒童醫療網
衛生福利部醫事司長官
(邀請中)

10:50~11:05　3. 基層診所對優化兒童醫療的回應與建議
曾光宏醫師
聖光小兒科診所

11:05~11:30　4. 綜合討論

附加研討會
兒童健康益生菌的新時代

日期：民國108年4月21日(星期日)
時間：12:00~13:00
地點：103會議室

主持人：楊俊仁理事長、倪衍玄副院長、吳子聰教授

12:00~12:10　1. 開幕致詞
楊俊仁理事長
台灣小兒消化醫學會

12:10~12:40　2. 腸道微生物與兒童疾病－綜論
倪衍玄副院長
國立臺灣大學醫學院

12:40~13:10　3. 益生菌在兒童疾病作用機轉之新知－LGG&BB-12
吳子聰教授
臺北榮民總醫院

13:10~13:25　4. 問題討論
倪衍玄副院長
國立臺灣大學醫學院

13:10~13:30　5. 結語
吳子聰教授
臺北榮民總醫院

一般演講：口頭報告

1 The Effects of 20cm Cut-Cord Milking on Mortality and Morbidity of Very Premature Infants: A Single-Center Study in Northern Taiwan

20公分的臍帶擠壓對於極度早產兒的死亡與共病症的影響：北台灣單一醫學中心的研究

Shang-Po Shen, Jui-Hsing Chang, Chyong-Hsin Hsu, Hung-Yang Chang, Wai-Tim Jim, Chia-Ying Lin, Chun-Chih Peng
Division of Neonatology, MacKay Children's Hospital
沈上博、張瑞幸、許瓊心、張弘洋、詹偉添[1]、林佳瑩[1]、彭純芝
馬偕兒童醫院新生兒科

Background: To evaluate the impact of 20 cm cut-cord milking on short-term outcomes of very premature infants.
Methods: A prospective randomized controlled trial was held in a medical center in northern Taiwan. Inborn very preterm infants (less than 30 weeks of gestational age) were randomly assigned to 20 cm cut-cord milking (CCM) and immediate cord clamping (ICC) groups. In both groups, the umbilical cord was clamped at the point at least 20 cm distal to the infant immediately after birth. For the CCM group, infant received at least 20cm cut-cord milking during immediate postnatal resuscitation. For the ICC group, the cord was clamped near the umbilicus and cut without milking. The primary outcomes were primary hematological parameters. The secondary outcomes were the mortality and morbidities of the preterm infants. Subgroup analyses for 23 0/7 to 26 6/7 weeks of gestational age and 27 0/7 to 29 6/7 weeks of gestational age were also performed.
Results: A total of 76 infants were enrolled (CCM group: ICC group = 37: 39). The mean gestation ages did not differ between the 2 groups (27.2±1.8 weeks vs 26.5±1.7 weeks, p=0.389). There were also no significant differences in birth weight between these 2 groups (987±269 gm vs 1023±313, p=0.601). The primary hemoglobin levels (14.8± 1.4 vs. 14.7± 1.6 g/dl, p= 0.842) and hematocrit values (45.2± 4.0 vs. 44.5± 5.2 %, p= 0.535) were not significantly different between CCM and ICC groups. There were also no significant differences between two groups on the aspects of mortality (13.5% vs 2.6%, p=0.076) and common morbidities of preterm infants such as bronchopulmonary dysplasia, intraventricular hemorrhage, periventricular leukomalacia, necrotizing enterocolitis, and retinopathy of prematurity. The subgroup analyses also failed to show significant differences on both primary outcomes and secondary outcomes.
Conclusions: A 20 cm cut-cord milking could not improve the primary hematological parameters and short-term outcomes of very premature infants. The applicability of cut-cord milking in very preterm infants needs further evaluation.

2 Minimally Invasive Surfactant Therapy for the Treatment of Very Low Birth Weight Infants with Respiratory Distress Syndrome

比較無侵襲性的方式給予肺表面活性素來治療非常小早產兒的呼吸窘迫徵候群

Lih-Ju Chen[1], Xing-An Wan[2], Chien-Chou Hsiao[1], Hsiao-Neng Chen[1], Cheng-Han Lee[1], Shan-Ming Chen[2], Pen-Hua Su[2], Jia-Yuh Chen[1]
Division of Neonatology, Department of Pediatrics, Changhua Christian Children's Hospital[1]; Division of Neonatology, Department of Pediatrics, Chung Shan Medical University Hospital[2]
陳俐如[1]、王杏安[2]、蕭建州[1]、陳曉能[1]、李政翰[1]、陳善銘[2]、蘇本華[2]、陳家玉[1]
彰化基督教兒童醫院新生兒科[1]；中山醫學大學附設醫院小兒部新生兒科[2]

Background: Minimally invasive surfactant therapy (MIST) is a new strategy to give surfactant without intubation. The aims of this study were to assess the efficacy, feasibility and safety of using this new method (MIST) to give surfactant for very low birth weight (VLBW) infants with respiratory distress syndrome (RDS).
Methods: A total of 53 VLBW infants (birth weight < 1500 grams), who were born before 32 gestational weeks with spontaneously breathing and respiratory distress were divided into two groups. All these 53 VLBW infants were diagnosed as RDS and needed surfactant replacement therapy. Group A (n=29) were intubated and received surfactant replacement therapy via endotracheal tube. Group B (n=24) received surfactant replacement therapy via tracheal catheterization using a semirigid vascular catheter without intubation.
Results: Our data showed that group B (MIST group) had significantly lower rate ($P < 0.05$) of composite outcome of death or bronchopulmonary dysplasia (BPD), duration of intermittent positive pressure ventilation (IPPV), medical treatment of patent ductus arteriosus (PDA), surgical ligation of PDA than group A (surfactant replacement therapy via endotracheal tube).
Conclusions: MIST is feasible, safe and may reduce the composite outcome of death or BPD for VLBW infants with RDS requiring surfactant replacement therapy.

3 Transepidermal Water Loss in Very Low Birth Weight Infants: An Single-center Observational Study

極低體重新生兒之經皮水分散失量：一個醫學中心觀察性研究

Hao-Wei Chung[1], Hsiu-Lin Chen[1,2], Shu-Ting Yang[1], Pin-Chun Su[1]
Department of Pediatrics, Kaohsiung Medical University Hospital[1], Kaohsiung, Taiwan; Department of Respiratory Therapy, College of Medicine, Kaohsiung Medical University[2], Kaohsiung, Taiwan
鐘浩瑋[1]、陳秀玲[1,2]、楊書婷[1]、蘇品淳[1]
高雄醫學大學附設中和紀念醫院小兒部[1]；高雄醫學大學醫學院呼吸治療學系[2]

Background: The skin is the biggest and dynamic-complex organ of human body. It majorly provides a barrier and connection between the body's viscera and the external environment. Underdeveloped epidermis has important consequences of preterm infant. The immature skin stratum corneum is accompanied by a relatively high proportion of body surface area resulting in high transepidermal water loss (TEWL).
Methods: A prospective, observation study was conducted from February 2018 to December 2018 at NICU of Kaohsiung medical university hospital, Taiwan.38 infants born under 1500 gram were enrolled in the study after parent consent had been obtained. TEWL was measured by VapoMeter at the volar aspect of the forearm and forehead of enrolled infants on postnatal day 1, day 3, day 5, day 7, day 14, day 21 and day 30 (VapoMeter; Delfin Technologies). For preparation for measurements, the neonates was on supine position with unclothing measuring site in incubator and the humidity was lowered to 50% with body temperature monitor.
Results: The mean ± standard deviation of GA and BW in 38 enrolled VLBW infants were 29 ± 2 weeks and 1120 ± 262 g, respectively. The mean TEWL of forearm was higher than that of forehead, and TEWL was decreasing gradually with increasing postnatal age on postnatal day 1 to day 7. The mean TEWL of forehead and forearm in the entire cohort were 18.1±4.2 / 20.6±5.0, 15.1±4.4 / 18.3±5.0, 13.8±3.0/17.2±5.0, 13.4±2.9/16.1±3.7, 12.8±3.5/14.7±4.2, 12.8±4.0/13.5±3.9 ,12.4±4.2/12.9±4.1(g/m2/h) on postnatal day 1, day 3, day 5, day 7, day 14, day 21 and day 30. Comparing the TEWL between infants born at GA≦28 6/7 and GA ＞ 28 6/7, TEWL on both measured site were higher in GA≦28 6/7 group since day 1 to day 7($p < 0.05$). After the postnatal day 7, there is no significance difference between two groups for both sites.
Conclusions: Very low birth weight infants have higher TEWL during their first week of life and their forearms have higher TEWL than foreheads. After the postnatal day 7 to day 30, the change of TEWL became stabilized and both forearms and foreheads have similar TEWL in very low weight infants.

4 Nebulized Salbutamol Diminish the Blood Glucose Fluctuation in the Treatment of Non-oliguric Hyperkalemia of Premature Infants

霧化salbutamol在早產兒非寡尿性高血鉀症治療中減少血糖的波動

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Background: Hyperkalemia is a risky and potentially life-threatening condition in pre-term infants. Glucose-insulin infusion has been considered a major therapeutic way for non-oliguric hyperkalemia but affects the stability of blood sugar level. We aimed to evaluate the effectiveness of salbutamol nebulization compared to glucose-insulin infusion for the treatment of non-oliguric hyperkalemia in premature infants.
Methods: Forty premature infants (gestation age ≤36 weeks) with non-oliguric hyperkalemia (central serum potassium level greater than 6.0 mmol/L) within 72 h of birth were enrolled in this study. These infants were randomly assigned into two groups. One group received a regular insulin bolus with glucose infusion (Group A; n = 20), and the other received salbutamol (Ventolin) by nebulization (Group B; n = 20). Potassium level, blood sugar, heart rate, and blood pressure were recorded for each group before treatment and at 3, 12, 24, 48, and 72 h post-treatment.
Results: The serum potassium levels were reduced after treatment in both groups. No significant changes in heart rate or blood pressure were observed in either group. The fluctuation in glucose levels was gentler in the salbutamol treated group than in the glucose-insulin infusion group.
Conclusions: Salbutamol nebulization is not only as effective as glucose-insulin infusion for treating non-oliguric hyperkalemia in premature infants but can avoid potential side effects such as vigorous blood glucose fluctuations.

5 N-terminal Pro-B-type Natriuretic Peptide Levels Predict Ibuprofen Treatment Response for Patent Ductus Arteriosus in Preterm Neonates: a Preliminary Study

利用NT-proBNP預測早產兒使用Ibuprofen治療開放性動脈導管的反應療效：一項初步研究

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Background: N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a cardiac natriuretic hormone released by cardiomyocites in response to volume loading, pressure loading and increased ventricular stress. Hemodynamically significant patent ductus arteriosus (hsPDA) could lead to increased work of breathing, poor body weight gain and

even heart failure. Early effective treatment for hsPDA was encouraged. This study was aimed to assess whether NT-proBNP predicts ibuprofen responsiveness in premature neonates with hemodynamic significant PDA.
Methods: Preterm neonates receiving ibuprofen for hsPDA were enrolled. Oral or intravenous Ibuprofen was administered for a 3 days course with an initial daily dose of 10mg/kg and two following doses of 5mg/kg. All neonates underwent paired pro-BNP measurements at the first day before the administration of ibuprofen and the 3rd day before the final dose. All neonates underwent echocardiography before and after completed ibuprofen treatment.
Results: Six premature neonates (male/female= 5/1) were retrospectively recruited for analysis. The mean gestational age was 28.5 ±3.39weeks (26~35 weeks), and the mean birth body weight was 1231±788 g (540 g~2755 g). The median NT-proBNP level was 7347 pg/mL before treatments and was higher compared to those of after treatment (4277 pg/mL). PDA was closed after ibuprofen usage in 4 neonates. In the ibuprofen responsive group, 3 of them had decreased NT-proBNP level more than 50%. On the contrary, the remaining neonate with increased NT-proBNP level developed severe oliguria and elevated creatinine level after 2 doses of Ibuprofen. In the two patients without response to ibuprofen, the NT-proBNP level did not have obvious decrements after ibuprofen usage.
Conclusions: NT-proBNP level decreased more than 50% after ibuprofen treatment may predict good response in premature neonates with hsPDA. However, the side effect of ibuprofen may interfere with the predictability of NT-proBNP level. Further study with larger numbers is warranted.

6 The Impact of Low Grade Germinal Matrix-Intraventricular Hemorrhage on Neurodevelopmental Outcomes of Extremely Low Birth Weight Preterm Infants

輕度新生兒腦室內出血對於極度早產兒長期神經發展預後的影響

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Background: Germinal matrix-intraventricular hemorrhage (GM-IVH) is a common but serious problem in preterm infants. Poor neurodevelopmental outcomes in preterm neonates with high grade IVH were well studied, however, the effect of low grade GM-IVH on long term neurodevelopmental outcomes remained inconclusive. We aimed to clarify the impact of low grade GM-IVH on future neurodevelopmental impairment (NDI) among ELBW infants.
Methods: This retrospective cohort study enrolled ELBW infants admitted to our NICU during Jan 2012 and Dec 2016, with a grade I or II GM-IVH detected by ultrasound. Infants with grade III or IV IVH, congenital anomalies, cerebral malformations, focal infarction were excluded. Relevant clinical parameters were collected. The primary outcome was the NDI at corrected age 2 years-old. Secondary outcomes included mortality rate and length of hospital stay. NDI was evaluated using the BSID-III for motor, cognition and language assessment.
Results: During this period, 475 ELBW infants were admitted and 446 infants received at least one cUS exam for IVH screening. The mean GA and birth weight were 26±2 wks and 779±145 gms (mean). The overall incidence of GM-IVH was 34.7%. 113 (23.6%) preterm infants had either grade I or II IVH. After exclusion, 378 infants were included with 271 infants in control group (no IVH) and 107 in low grade GM-IVH group. The primary outcomes revealed no significant differences of BSID-III scores between 2 groups regarding motor (low grade IVH group vs non-IVH group, 89.2±15.4 vs 90.3±14.4; meanSD; p=0.64), cognitive (88.6±12.9 vs 91.5±15.1; p=0.23) and language (87.4±13.1 vs 89.7±14.5; p=0.34) domains at 24 month's corrected age. The secondary outcomes analysis suggested significantly prolonged hospital stay (106.1±60 vs 94.8±43; p=0.41) of low grade GM-IVH group without increase in all-cause mortality.
Conclusions: The incidence of low grade GM-IVH was 23.6% among ELBW infants. Although infants with low grade GM-IVH did not have significantly lower BSID scores at corrected age 2-years-old, a trend for higher percentage of NDI was observed. In addition, significantly longer period of hospital stay was observed in low grade GM-IVH group without increase in mortality.

7 Screening of Congenital Hypothyroidism in VLBW Preterm Infants

針對極低體重早產兒先天性甲狀腺功能不足的篩檢完備嗎?

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Background: Congenital hypothyroidism (CH) is among the most preventable causes of growth failure and mental retardation, both of which VLBW infants are at high risks to encounter due to the nature of their diseases. Because of the immaturity of hypothalamic-pituitary-thyroid axis, VLBW infants with hypothyroidism may show a delayed postnatal rise in thyroid stimulating hormone (TSH). Therefore, screening strategy for full term infants might not be suitable for premature infants who are at even higher risks for thyroid insufficiency.
Methods: Currently, blood samples are collected within 72

hours after birth for test of TSH concentration in all newborn infants. In preterm infants, a second test is performed when the infant reaches 37 wks. post-menstrual age and weighs over 2200 gms. A confirmation test of TSH and Free T4 is required when the screening TSH is abnormal (＞10 mU/L). We retrospective review medical records of all VLBW (BW＜1500gms.) inborn infants admitted to our NICU during 1.1.2015~12.31.2017 and identified those who survived and diagnosed with CH or received thyroxine supplementation. All CH screening results, and time of blood sampling were recorded.

Results: There were 10 infants who met the treatment criteria of CH following AAP guidelines for VLBW infants. The prevalence rate of CH was 1.5 in 100 of our surviving VLBW infants (10 in 665). Six out of the 10 patients had TSH concentration below cut off value (10 mcU/mL) on day 3 of life and missed the first screening for CH. The median gestational age and birth weight of these infants was 25 (24-30) weeks and 708 (480-1030) gms., respectively. The diagnosis of CH was made on a median of 7 (0.5-13) weeks postnatal age. Conversely, the other four patients who was diagnosed with CH from initial TSH screening were less immature (median GA 31 weeks, and median BW 1122 gms.)

Conclusions: The prevalence rate of CH is high in VLBW infants. Current screening protocol might miss a majority of those infants who are at the highest risks to suffer from thyroid insufficiency.

8 Cathelicidin Attenuates Hyperoxia-Induced Intestinal Injury through Inhibition of NF-κB Activity in Newborn Rats

Cathelicidin通過抑制新生大鼠的NF-κB活性減輕高氧誘導的腸損傷

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Background: Preclinical studies have demonstrated that neonatal hyperoxia injures the distal small intestine and activates nuclear factor-κB (NF-κB). Cathelicidin inhibits NF-κB activity and ameliorates lipopolysaccharide-induced intestinal barrier disruption in rats.

Methods: Sprague–Dawley rat pups were reared in either room air (RA) or hyperoxia (85% O2) and were randomly treated with low-dose cathelicidin (4 mg/kg, LDC) and high-dose cathelicidin (HDC, 8 mg/kg) in 0.05 mL of normal saline (NS) administered intraperitoneally on postnatal days 1–6. The following six groups were obtained: RA + NS, RA + LDC, RA + HDC, O2 + NS, O2 + LDC, and O2 + HDC. The animals were sacrificed and the kidneys were removed for Western blot and histological analyses on postnatal days 7.

Results: The hyperoxia-reared rats exhibited significantly lower body weights, higher intestinal injury scores, lower occludin and ZO-1 expression, higher intestinal permeability and bacterial translocation, and higher inducible IκB kinase inhibitor (IKKi) and NF-κB expression than the RA-reared rats. Cathelicidin significantly reduced the detrimental effects of hyperoxia. The decrease in intestinal injury was accompanied by a decrease in IKKi and NF-κB expression.

Conclusions: Cathelicidin attenuated hyperoxia-induced intestinal injury in the newborn rats, likely through NF-κB activity inhibition.

9 Maternal Tn Immunization Attenuates Hyperoxia-Induced Lung Injury in Neonatal Rats Through Suppression of Oxidative Stress and Inflammation

懷孕母鼠Tn免疫通過抑制氧化應激和炎症減輕高氧誘導的新生仔鼠肺損傷

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Background: Hyperoxia therapy is often required to treat rat newborns with respiratory disorders. Prolonged hyperoxia exposure increases oxidative stress and arrests alveolar development in newborn rats. Tn immunization increases the serum anti-Tn antibody titers and attenuates hyperoxia-induced lung injury in adult mice. We hypothesized that maternal Tn immunizations would attenuate hyperoxia-induced lung injury through the suppression of oxidative stress in neonatal rats.

Methods: Female Sprague–Dawley rats (6 weeks old) were intraperitoneally immunized five times with Tn (50 μg/dose) or carrier protein at biweekly intervals on 8, 6, 4, 2, and 0 weeks before the day of delivery. The pups were reared in room air (RA) or 2 weeks of 85% O2, creating the four study groups: carrier protein + RA, Tn vaccine + RA, carrier protein + O2, and Tn vaccine + O2. The lungs were excised for oxidative stress, cytokine, vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF) expression, and histological analysis on postnatal day 14. Blood was withdrawn from dams and rat pups to check anti-Tn antibody using western blot.

Results: Neonatal hyperoxia exposure reduced the body weight, increased 8-hydroxy-2′-deoxyguanosine (8-OHdG) expression and lung cytokine (interleukin-4), increased mean linear intercept (MLI) values, and decreased vascular density and VEGF and PDGF-B expressions. By contrast, Tn immunization increased maternal and neonatal serum anti-Tn antibody titers on postnatal day 14, reduced MLI, and increased vascular density and VEGF and PDGF-B expressions to normoxic levels. Furthermore, the alleviation of lung injury was accompanied by a reduction in lung cytokine and 8-OHdG expression.

Conclusions: Maternal Tn immunization attenuates hyperoxia-induced lung injury in neonatal rats through the suppression of oxidative stress and inflammation.

10 The Early Serum Biochemical Marker for Evaluating the Risk of Metabolic Bone Disease in Extremely Low Birth Weight Infants

極低體重早產兒用早期血清生化值來評估發生骨質疏鬆的風險

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Background: Parenteral nutrition (PN) is important source for nutrition in preterm infants who could not tolerate enteral feeding but the precipitations of solution limited the intake of calcium and phosphorus. Those who had prolonged PN should be aware of the development of metabolic bone disease. The purpose of this study was to explore the early marker of metabolic bone disease by analyzing the serial change of serum biochemical in extremely low birth weight (ELBW).
Methods: We retrospectively collected data on ELBW delivered in our hospital. Inclusion criteria were: premature infants ＜30 weeks gestation, BW ＜1000 g. Infants were excluded who with insufficient data to analyze and those who had major congenital anomalies. The trend of serum calcium, phosphorus and alkaline phosphate level were compared in ELBW with or without prolonged PN exposure (＞14 days).
Results: Totally 28 preterm infants are included, 14 of them was in the group of prolonged PN. The overall median birth weight was 734 g (range, 350 to 965), and the median gestational age was 26 weeks (range, 22 to 30). On average, the prescriptions of Ca and PO4 are, respectively, 22.5±10.7 mg/kg/d and 24.5 ±5.8 mg/kg/d for extremely low birth weight infants who kept nil per os (NPO) within first weeks of life. Lower serum phosphorus (mg/dL) level was noted in the prolonged PN group on day 14 (5.25±1.34 vs 3.71±1.3, $p < 0.005$), 28 (5.99±1 vs 3.36±0.9, $p < 0.005$), and 42 (6.1±0.7 vs 3.76±1.3, $p < 0.005$). Higher levels of alkaline phosphatase(U/L) was only found two months after birth in the group of prolonged PN(321±87 vs 631±287, $p < 0.005$). There is no significant difference in serum calcium level between two groups in all time point.
Conclusions: The preliminary data showed that ELBW preterm infants who put on NPO for more than 14 days had early hypophosphatemia. Thus, it is important to increase PO4 amounts in PN for preterm infants. Adequate calcium and phosphorus administration through PN is a challenge. Previous studies that recommended the use of organic Ca and PO4 salts could be mixed without precipitation. Further larger follow-up study is needed.

11 The Application of Dried Blood Spots for the Assessment of Maternal and Neonatal Vitamin D Status

以血片技術來檢測母親及嬰幼兒之維生素D營養狀態

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Background: The health impact of vitamin D deficiency is especially important during pregnancy and infancy, but the epidemiological data is lacking in Taiwan. The difficulty in obtaining adequate blood sample is the major resistance in determining neonatal vitamin D status. The purpose of this study is to develop a novel screening test by dried blood spots (DBS) and the accuracy is compared with the standard serum test in infants and their mothers.
Methods: This is a cross-sectional study of the infants who is under 1 year of age and their mother from June 2017 to June 2018. After informed consent was signed, around 2.5 cc blood was collected from artery or vein. The blood sample was first to fill five DBS in a card, and then serum was collected from the rest blood sample after appropriate centrifuged. DBS were analyzed with LC/MS/MS assay, and the serum 25OHD levels (ng/ml) was measured by LIAISON® (DiaSorin, Inc, Stillwater, MN, USA).
Results: Totally 117 DBS samples were available for analysis and compared to serum sample, 31 from newborn, 41 from infants and 45 from mothers. 25OHD concentrations in DBS and serum were highly correlated (Pearson r=0.8246, 95% CI 0.7563 to 0.8752, $P < 0.0001$). In the 46 deficient cases (serum 25OHD level ＜12 ng/mL), 10 of them had DBS level ＞12 ng/ml, but only 1 had DBS level ＞20ng/ml. In the 78 inadequate cases (serum 25OHD level ＜20 ng/mL), 15 of them had DBS level ＞20 ng/ml, but only 1 had DBS level ＞30ng/ml.
Conclusions: Using DBS to measure 25OHD level is a valid and practical method for screening vitamin D deficiency. Further larger study is warranted.

12 Changes in Neonatal Early-onset Sepsis during 15 Years

新生兒早發性敗血症15年來的變化

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Background: This study aimed to summarize the change of common pathogens and associated drug resistance and outcome of early onset neonatal sepsis (EOS) during 15 years
Methods: Pathogens of blood and cerebrospinal fluid culture, drug sensitivity results and outcome of EOS cases treated from January 2004 to Dec 2018 in a single level III neonatal intensive care unit were retrospectively analyzed.
Results: Totally, there of 40 pathogenic bacteria were

detected from these 135 EOS cases; 103 cases were full term infants 32 cases were preterm infants , 14 cases were very low birth weight infants. 31 cases were E-COLI, 33 cases were GBS, 3 cases were enterococcus fecalis were the common pathogen of EOS. Invasive GBS infection often presented with respiratory distress with mortality 4/33=12.1% was decrease after 2013 when university GBS screen was proceeded. E-COLI was common in very preterm infants with high mortality 8/31=25.8%. 4/33=12.1% of GBS complicated with meningitis, E-COLI with meningitis set 2/31=6.4% In EOS, the ampicillin sensitivity rate of E- coli was decrease from % to 3/9=33.3% 3/8=37.5% 1/14=7.1%; the cephalosporin sensitivity rate of E- coli was decrease from 6/9=66.7% 6/8=75% 7/14=50%; the gentamycin sensitivity rate of E-coli was from 6/9=66.7% 7/8=87.5% 7/14=50% every 5 years. No drug resistant in GBS was noted for the t 15 years.

Conclusions: Though the prevalence of EOS was relative low, E-coli has high mortality in very preterm infants, invasive GBS infection was decrease after 2013, it could develop sometime even with negative GBS screen and born via caesarian section. Since the resistant rate of E- coli of ampicillin and cephalosporin, clinician should aggressive in the antibiotics selection in very preterm infants or even early termination if there was a sign of clinical chorioamnionitis according to the survival rate of their own unit.

13 Analysis of Clinic Features of Viral or Bacterial Pathogens in Febrile Young Infants within Three-month-old of Life

三個月以下發燒嬰兒之病毒或細菌病原臨床分析探討

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Background: Febrile infants, who are in their first 90 days with rectal temperature of 38℃ or greater, tend to had serious bacterial infection (SBI) such as bacteremia, urinary tract infection, meningitis, and pneumonia compared to their older counterparts. However, the managements depend on pathogens identified in febrile infants and the clinical features in these patients with different pathogens were still unclear. Thus it important to identify the clinical features and laboratory data linked to the different type of pathogen, bacteria or virus in febrile infants (age ≦ 90 days).

Methods: A retrospective one-hospital-based cohort study was conducted by reviewing hospitalized patient data for all infants born at age of ≦ 90 days and ever with rectal temperature of 38℃ or greater in a tertiary medical center from May 2018 to November 2018. The pathogens were identified by direct culture, throat and rectal viral culture or respiratory viral panel polymerase-chain reaction. The clinical characteristics were compared in patients with viral or bacterial pathogens.

Results: A total of 30 febrile infants hospitalized into our neonatal care unit within 90 days of life, among whom 10 (33.3%) and 15 (50%) infants were identified with viral pathogens and bacterial pathogens respectively. Three infants had bacteremia and five infants with evidence of enterovirus infection. Patients with bacteremia had higher body temperature (39.5℃ vs 38.6℃, $p < 0.001$), CRP level (11.4 vs 1.7 mg/dl, $p < 0.001$), and absolute white blood count (13750 vs 5935 cumm/uL, p=0.01) compared to patients without bacteremia. According to conditional multivariable logistic regression analysis, low-grade fever (＜38.5℃) (OR 8.8, 95% CI 1.0-77.8) and mild elevated ALT level (＞20 U/L) (OR 24.0, 95% CI 2.0-287.9) are associated with infants with viral pathogens. On the other hand, elevated CRP level (＞2 mg/dl) (OR 12.3, 95% CI 1.3-118.4) is linked to bacterial pathogens.

Conclusions: Febrile infants with low-grade fever or mild elevated ALT level may tend to have viral pathogens but elevated CRP level may indicate bacterial pathogens. Further studies will be required for subtype pathogens analysis.

14 Relationship between Maternal Factors and Fetal Macrosomia in Full-term Singleton Births

探討足月單胞新生兒之母體因子與胎兒巨嬰症的關係

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Background: Fetal growth is highly related to maternal conditions. Fetal or neonatal macrosomia with birth body weights (BBW) ≥ 4,000 g have high risk of birth injury. Maternal body size, maternal sizes, gestational weight gain (GWG) and gestational diabetes mellitus (GDM) are known to have association with birth sizes of newborn infants. Although there is suggestion on the ideal maternal GWG and prevention of maternal overweight, the current relationship between neonatal outcome and maternal conditions require further investigation.

Methods: We retrospectively reviewed maternal and their newborn infants' birth data from January 2013 to June 2016.The inclusion criteria were singleton with gestational age(GA)＞= 37 weeks. Any case with a lack of maternal 6-month GWG (6mGWG) was excluded. Maternal body

weights (BWs), body heights (BHs), body mass index (BMI), 6mGWG, and disease history were recorded. Infants' data included birth body weight (BBW), birth BH, GA, delivery mode, placenta weight, blood loss, and apgar scores. Logistic regression was used to calculate odds ratios (ORs) of associated factors for fetal macrosomia (BBW≥ 4,000 g).
Results: A total of 4262 full-term infants were enrolled, and the mean birth weight were 3156+-383g (range: 1606 to 4910 g), including 77 (1.8%) cases with BBW 4000 g, and 154 (3.6%) infants with BBW ＜ 2500 g. The maternal BW were 67.6+-10.1kg (range: 21 to 122 kg), 6-mGWG were12.3+-4.2 kg (range: -4 to 45 kg) , and BMI were 26.2+-3.6. The infants BBW showed positive correlation to maternal BW, BH, 6mGWG, GA, placenta weight, and maternal delivery blood loss ($p < 0.05$). The 3rd quartile of maternal 6-month GWG was 15 kg. The ORs for infants' BBW 4000 g was 3.1 [95% CI: 1.9-5.0] with maternal 6mGWG＞=15kg, 6.3 [95%CI: 3.4-11.6] with maternal diabetes, and 4.1[95%CI: 2.8-6.1] with maternal BMI＞=30. There no significant correlation in the infants BBW or maternal BW, BMI, 6mGWG with the requirement of cesarean section ($p > 0.05$).
Conclusions: Newborn infants' BBW are positively correlated to maternal body size and 6mGWG. The presence of maternal GDM, 6mGWG＞=15kg, and maternal BMI＞=30 are significantly related to fetal macrosomia in full-term singleton births.

15 Associated Risk Factors of Acute Kidney Injury in Asphyxiated Newborns Treated with Therapeutic Hypothermia

周產期窒息新生兒經過低溫治療發生急性腎衰竭的危險因子

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Background: Asphyxia results in redistribution of cardiac output thus acute kidney injury (AKI) is a common consequence following perinatal asphyxia. Studies have reported variable incidence of AKI in asphyxiated newborns using different diagnostic criteria but an apparent observation is that AKI is associated with a poorer outcome. Early recognition of AKI is vital to implement therapies aimed at preventing or treating anticipated complications. Our study aims to identify incidence and predictors of AKI in asphyxiated newborns treated with therapeutic hypothermia (TH).
Methods: Newborns admitted with a diagnosis of perinatal asphyxia and completed 72 hours of TH between the period of January 2011 and May 2018 were enrolled. Demographic data, resuscitation details, laboratory results and use of medications were collected and compared between newborns with AKI and those without. The diagnosis of AKI was made using the neonatal modified KDIGO criteria which is based on an absolute rise of serum creatinine from a previous trough.
Results: A total of 66 newborns were included in our study. 33% (22) were found to have AKI. Demographic data including birth weight, gender, Apgar scores at 1 minute and 5 minutes did not differ significantly among the two groups. The AKI-group had a lower gestational age (p=0.006), lower hemoglobin and hematocrit levels (p=0.012 and 0.038 respectively), higher lactate level before and after TH (p=0.013 and 0.03 respectively) and higher troponin-I level after TH ($p < 0.001$). After logistic regression analysis, elevated troponin-I after TH was independently associated with risk of AKI (OR:1.697, 95%CI:1.067-2.699, p=0.025).
Conclusions: The incidence of AKI among asphyxiated newborns who received therapeutic hypothermia is 33%. A persistently elevated troponin-I level after therapeutic hypothermia is independently associated with an increased risk of AKI in asphyxiated newborns.

16 Perinatal Characteristics and Neonatal Outcomes in Neonates with Air-leak Syndrome: A Single Institute Experience

新生兒氣漏症候群之周產期特徵及預後 一 單一中心回溯研究

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Background: Air leak syndrome is not uncommon in neonates and may impose the baby to mechanical ventilation and/or invasive procedures, such as thoracocentesis and chest tube insertion. This study was aimed to identify the perinatal risk factors, management and the outcomes in neonates with air leak syndrome.
Methods: We retrospectively enrolled neonates admitted in neonatal intensive care unit from Jan. 1 to Dec. 31, 2018, with the diagnosis of air leak syndrome including pneumothorax, pneumomediastinum, pneumopericardium, pneumoperitoneum, subcutaneous emphysema, and pulmonary interstitial emphysema. The diagnosis of air leak was confirmed by an independent radiologist and a neonatologist. The maternal and perinatal characteristics, clinical courses and management were reviewed and analyzed.
Results: 27 neonates (male: female= 19:8) were recruited with the diagnosis of air-leak syndrome. The mean gestation age was 37.3±2.21 weeks and the mean birth body weight was 2983±544gm. 4 neonates were preterm and one of them developed pneumothorax after surfactant therapy for respiratory distress syndrome. In the remaining 23 full term neonates, 2 neonates (8.6%) had ever received bag-mask ventilation immediately after delivery and another 2 neonates (8.6%) had a history of meconium-stained amniotic fluids. 7 (30.4%) were diagnosed with congenital

pneumonia. 22 neonates (95.7%) had pneumothorax and the majority occurred over the right side (22/23). 6 of the 22 neonates with pneumothorax had combined with pneumomediastinum. The full term neonates with combined pneumothorax and pneumomediastinum had significant longer mechanical ventilation duration and CPAP usage duration compared with those with only pneumothorax. Air leak improved spontaneously after conservative treatment in 78.3% full term neonates. Only 5 neonates needed thoracocentesis or chest tube insertion.
Conclusions: Spontaneous pneumothorax was not unusual in full term neonates. Combined pneumothorax and pneumomediastinum in full term neonates usually need longer duration of mechanical ventilation and nasal CPAP usage. Most of the full term neonates with air leak syndrome resolved after conservative treatment.

17 Orofacial Function in Preschool Children Born with Very Low Birth Weight
學齡前極低出生體重兒之口腔顏面功能評估

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Background: Orofacial functions, such as nutrition, breathing, speech and facial expression are essential for daily life. Children born prematurely or those with neurological disorders often exhibit orofacial dysfunction. The purpose of this study was to evaluate the condition of orofacial function in preschool children born with very low birth weight.
Methods: A cross-sectional study was conducted involving 56 children (25 boys and 31 girls), aged 3-5 years old, and born with very low birth weight (VLBW, birth weight less than 1500 g). The Nordic Orofacial Test-Screening (NOT-S), children's chew and swallow assessment and questionnaire were used to survey orofacial, swallowing and chewing function in this study. NOT-S protocol contains 12 orofacial function domains with maximum score of 12 points. The scores of NOT-S higher than 4 points indicate orofacial dysfunction. The prenatal and neonatal information during neonatal intensive care unit were obtained from their mothers and medical records.
Results: The mean total NOT-S score was 1.25 (± 1.1; range: 0-4) which was within normal range among enrolled children. Univariate analysis revealed age, gender, gestational age at birth, birth weight, and condition of small for gestational age did not affect NOT-S scores, swallowing and chewing function. Multivariate multiple regression analysis was further analyzed and the results revealed there was no effect of the duration of intubation, gastric tube placement, and days of stay in neonatal intensive care unit on NOT-S scores and the swallowing and chewing function.
Conclusions: The present study indicates that NOT-S score was within normal range in preschool children born with very low birth weight. Although we speculated there might be higher percentage of orofacial dysfunction in preschool children born with very low birth weight because of intensive care during infancy, our study showed there was no effect of medical intervention during infancy including intubation, and gastric tube placement on NOT-S scores and the swallowing and chewing function in them.

18 Bilirubin Level 1 Week after Hepatoportoenterostomy Predicts Native Liver Survival in Biliary Atresia
葛西手術術後一週之膽紅素數值可預測膽道閉鎖患者的原肝存活

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Background: The predictor of hepatoportoenterostomy (HPE) outcome in BA patients had been widely discussed. We aimed to determine a very early predictive biomarker after HPE for the prediction of native liver survival in biliary atresia (BA) patients.
Methods: A retrospective chart review was conducted of BA patients who underwent HPE in the National Taiwan University Hospital between August 2000 and April 2018. The laboratory data, including total bilirubin (T-bil), direct bilirubin, and gamma-glutamyl transferase, at 1 week after HPE were analyzed. The predictors of jaundice-free survival within 3 months of HPE and native liver survival were investigated.
Results: A total of 81 BA patients who received HPE were recruited. Receiver operating characteristic curve analysis showed that a post-HPE 1-week T-bil level ≤ 4.85 mg/dL predicted jaundice-free after HPE (P=0.038). BA patients with a post-HPE 1-week T-bil ≤ 4.85 mg/dL and age at HPE ≤ 60 days were more likely to be jaundice-free within 3 months of HPE (odds ratio = 4.19 and 4.58; P=0.006 and 0.008, respectively). Kaplan-Meier plot analysis and the log-rank test showed that the likelihood of native liver survival and jaundice-free native liver survival was significantly higher in BA subjects with a post-HPE 1-week T-bil ≤ 4.85 mg/dL than the other subjects (P=0.019 and 0.015, respectively).
Conclusions: The serum post-HPE 1-week T-bil level may predict the long-term outcome in BA patients. A post-HPE 1-week T-bil ≤ 4.85 mg/dL correlated with native liver survival and jaundice-free native liver survival in BA patients.

19 The Prevalence of Clinical Impact of Hepatopulmonary Syndrome in Biliary Atresia Children

肝肺症候群於膽道閉鎖孩童的預後及危險因子分析

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Background: The clinical impact of hepatopulmonary syndrome (HPS) occurrence in biliary atresia (BA) children remains unclear in large. Liver transplantation is considered to be the definitive treatment of HPS. We aimed to investigate the prevalence of HPS in BA children and also elucidate the impact of HPS on native-liver and overall survival of BA children.
Methods: This retrospective study enrolled 193 consecutive BA patients followed in National Taiwan University Hospital during Dec-1996 until Jun-2018. Clinical data including gender, age of Kasai operation, jaundice-free within 3 months of Kasai operation, the occurrence of HPS et al. were collected through medical records. Long-term clinical outcomes were also included in the analysis.
Results: During the mean follow-up period of 10 years, HPS was noticed in 8/193 (4.15%) patients. The average diagnostic age of HPS was 10 years of age. There are 4 patients (50%) had Child-Pugh C status at the time of diagnosis. There are 6 (75%) patients receiving liver transplantation. The native-liver survival rate is significantly lower in HPS patients (n=8) than other BA children without HPS (n=185) (0% vs. 35.13%, p=0.05, Fisher's exact test). The overall survival rate of HPS patients is also significantly lower than BA children without HPS (12.5% vs. 90%, $p < 0.001$, Fisher's exact test). The overall mortality rate is significant higher in HPS patients in the survival analysis(Hazard ratio=7.02, 95% CI=2.92-16.89, $p < 0.001$).
Conclusions: The prevalence of HPS in BA children is 4% in the mean time of 10 years follow-up period in our institution. The occurrence of HPS in BA children is an ominous sign which indicate significant lower native-liver and overall survival rate than BA children without HPS.

20 The Characteristics of Ulcerative Colitis of Paediatric Primary Sclerosing Cholangitis: A Single-Centre Study

潰瘍性腸炎於小兒原發性硬化性膽管炎族群之特性：單一中心研究

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Background: Primary sclerosing cholangitis (PSC), a cholestatic liver disease, is often associated with ulcerative colitis (UC). We aimed to elucidate the difference in clinical characters between UC and PSC-UC children in this study.
Methods: We retrospectively recruited UC children with and without PSC between 2006 and 2017 in a tertiary center in Taiwan. The clinical data including gender, the age of diagnosis, the extent of the disease, UC-related surgery, clinical and endoscopic severity scores, medications and laboratory data were analyzed
Results: We identified 5 PSC-UC children (PSC-UC group), and another 26 children with UC alone (non-PSC UC group) in our institution during the study period. UC Endoscopic Index of Severity (6.00 vs. 9.00, P = 0.007) and Mayo score (4.00 vs. 8.00, P = 0.010) were significantly lower in PSC-UC group as compared with non-PSC UC group. PSC-UC group had higher aminotransferase and total bilirubin level than non-PSC UC group. The prevalence of immunosuppressants usage is significantly higher in PSC-UC than non-PSC UC group during their course (100% vs. 42.3%, P = 0.04), but no difference in the prevalence in the use of steroid, mesalamine, or biologics. However, more PSC-UC patients continue the use of steroid (80% vs. 14.5%, P = 0.010). In the 5 PSC-UC patients, 3 patients were compatible with definite autoimmune sclerosing cholangitis (ASC), 1 with probable ASC. Two of the definite ASC patients also compatible with IgG4-related disease.
Conclusions: Paediatric PSC-UC patients had less severe UC activity in terms of clinical activity index and endoscopic severity index but are more likely to continue the use of steroid and immunosuppressants for the control of liver disease

21 Virological and Clinical Characteristics Associated with Viral Shedding of Norovirus in Children's Gastroenteritis

兒童諾羅病毒胃腸炎中之病毒體排出與病毒感染、臨床特異性之關聯性研究

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Background: Norovirus (NoV) is an emerging enteric pathogen and being recognized as a global health burden as leading viral cause of outbreaks of gastroenteritis worldwide. The rapid transmission of NoV via person-to-person contact makes infection control difficult. Our study is to establish the standardization of viral load in NoV acute gastroenteritis to investigate and correlate

clinical features, disease characteristics, viral shedding and transmissibility.
Methods: Fecal specimens from recruited children in Chang-Gung Children's Hospital under diagnosis of NoV gastroenteritis examined by RT-PCR and their clinical features of hospitalization were characterized. NoV real time RT-PCR assay with viral copy numbers ((log)/g feces) calculation as viral load were performed. Fisher exact test was used to determine differences between clinical features.
Results: The viral load increasing varied from the 3rd day to the 8th day forming an unsmooth plateau feature without peaking. After the 8th day, the viral load declined and sheded at the 15th day after illness onset. In regards to correlate viral load with clinical manifestations, we found there is a longer shedding period in patients in 17 febrile patients (16.3 days after disease onset) than in 21 afebrile ones (12.7 days after disease onset) (P=0.03) also a significantly longer shedding period of patients infected by GII.4 Sydney strain (17.6 days after illness onset) then by non- GII.4 Sydney (12.3 days after disease onset) strain NoV (P ＜0.01).
Conclusions: In conclusion, the copy numbers based method viral load evaluation provide a more specific and precise way for assessment NoV detection, viral shedding, transmissibility, and even clinical correlation.

22 Regulation of yqiC on the Global Transcriptome of Salmonella and Interaction of YqiC with Salmonella Colonization in Human Intestinal Cells

yqiC基因對沙門氏菌全轉錄體之調控以及YqiC蛋白與沙門氏菌在定植人類腸道上皮細胞時之交互作用

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Background: We discovered a virulence gene yqiC of Salmonella Typhimurium (S. Typhimurium) that is required for in colonization/invasion in human cells. How yqiC regulates the other genes and YqiC affects bacteria colonization is unknown.
Methods: First, S. Typhimurium yqiC-deleted mutant (ΔyqiC) and its wild-type strain SL1344 infected confluent Caco-2 cells for 2 hours (MOI=50, n=3). Bacterial RNAs were isolated for NGS RNA-sequencing (RNA-seq) and their global transcriptomes were compared. Second, Caco-2 cells were treated with YqiC generated from yqiC and non-YqiC media for 90 min (MOI=5, n=4) before 90-min treatment of SL1344 (exclusion assay), 90-min co-incubation with SL1344 with and without further 90-min incubation (competition assay), and after the 90-min treatment of SL1344 with (displacement assay). Finally, SL1344 colonizing in Caco-2 cells were quantified and compared between YqiC and non-YqiC groups.
Results: First, RNA-seq identified 117 significantly upregulated and 291 significantly downregulated genes (ΔyqiC/SL1344 ratio＞log2 and ＜-log2 fold-change, p＜0.005). Emapplot of GO analysis showed that yqiC in involved in Salmonella pathogenesis, pilus assembly, fimbiral usher porin activity, response to antibiotic, and transaminase activity. Cnetplot of GO analysis showed that yqiC regulates ion-sulfur cluster assembly, iron ion binding, molybdenum ion binding, molybdopterin cofactor binding, and de novo inosine monophosphate biosynthetic process. KEGG analysis showed that specific genes are involved in well-known pathogenesis and metabolism, including Salmonella bacterial invasion into epithelial cells, the phosphotransferase system, the two-component system, the alanine/aspartate/glutamate metabolism, glycolysis/gluconeogenesis, and carbon metabolism. Second, YqiC significantly excludes and displaces S. Typhimurium from Caco-2 cells (p=0.041 and p=0.019, respectively), but did not competitively inhibit colonization of S. Typhimurium in Caco-2 cells in 3 YqiC assays.
Conclusions: We discovered the unreported genes remarkably regulated by yqiC and YqiC excludes and displaces S. Typhimurium from Caco-2 cells. The results provide useful clues for developing strategies against salmonellosis.

23 Detection of Ampicillin Resistance in Nontyphoidal Salmonella Using a Multigene Panel Identified by Next-Generation Sequencing

以次世代定序發現之多基因組合偵測非傷寒沙門氏菌對安比西林抗生素之抗藥性

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Background: Antibiotic resistance of nontyphoidal Salmonella (NTS) is a serious problem worldwide. The ampicillin (AMP) resistance rates of NTS were high in Taiwan. The currently used Clinical and Laboratory Standards Institute (CLSI) bacterial cultures for detecting NTS and its antibiotic resistance are time-consuming with low detection rates. Therefore, a rapid, accurate, and affordable diagnostic tool for detection of Salmonella antibiotic resistance is warranted.
Methods: First, 19 NTS isolates (8 AMP-resistant and 11 AMP-susceptible) were collected in TMU-SHH. We

isolated bacterial DNAs for next-generation sequencing (NGS) using the illumina® MiSeq sequencer. We analyzed to examine antibiotic resistance genes or mutations in the genome of Salmonella spp. and others reported in the PubMed, ARG-ANNOT, CARD, and ResFinder. Next, the identified AMP resistance genes were tested by PCR in a total of 49 NTS isolates in TMU-SHH. The rates and statistics of detecting AMP resistance by individual or any combination of these genes in the multigene panel were analyzed.

Results: Our pilot study in the 19 NTS isolates, we discovered either one or more genes of the 4-gene panel (blaTEM-1B, blaCMY-2, blaCARB2, and ampC) universally present in the 8 AMP-resistant isolates but none of them present in the 11 AMP-susceptible isolates, with the correct prediction rates of 100% (19/19) and the false negative rate of 0% (0/19). When the 4-gene panel was applied to the 49 NTS isolates, the detection rate for AMP resistance was as high as 91.8% (45/49) whereas the false positive rate was 4.1% (2/49) and the false negative rate was 4.1% (2/49). Meanwhile, the sensitivity remained as high as 89% and their specificity was 90% in the 4-gene panel.

Conclusions: Our NGS-identified 4-gene panel exhibited a high detection rate of AMP resistance in NTS isolates from TMU-SHH. Validation of the 4-gene panel in more NTS isolates from different geographical regions is performed to obtain a minimized multigene number for accuracy. If successful, the multigene panel can be integrated into a feasible platform to develop a practical rapid accurate diagnostic tool for AMP resistance in NTS.

24 The Clinical Features and Management of Acute Segmental Necrotizing Enteritis in Children: a 22-year, Single Tertiary Medical Center Experience

急性區段性壞死性腸炎在孩童身上的表現及治療：一個醫學中心22年的經驗

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Background: In the past years, we have identified a small group of children whom presented with symptoms of acute upper intestinal obstruction, such as severe abdominal pain and vomiting. This group of patients were later diagnosed with acute segmental necrotizing enteritis (ASNE). We have reviewed the clinical features and the management of ASNE in the past 22 years.

Methods: From year 1996 to 2018, a total of 53 children (< 18 years) diagnosed as ASNE were collected. Patients' demographics, clinical features, laboratory data, abdominal ultrasound images and treatment were collected and analyzed.

Results: In this study, 38 (72%) children were diagnosed between 2 to 6 years old. More than two thirds of patients had abdominal pain with duration 3 to 7 days before diagnosis. The majority (93.3%) of pain located at epigastric and periumbilical area. 18 had vomiting and only 4 presented with bilious vomitus. For children with laboratory data, 26 of 51 (51.0%) had leukocytosis (defined as WBC > 10000/ul) and 13 of 35 (37.1%) had elevated CRP (defined as CRP > 0.5 mg/dl). Those with serum blood urea nitrogen and creatinine checked showed normal. 4 out of 35 children had hyponatremia. Under ultrasound examination, the swollen intestines were detected at left upper quadrant (27 cases), left lower quadrant (13 cases), right lower quadrant (11 cases) and other locations (4 cases), with wall thickness 0.3 to 0.6 cm in 46 cases. 49 children received steroid treatment and all of the symptoms resolved within 5 days. Four of them had recurrent symptoms happened 3 days, 21 days, 3 months, 5 months and 1 year after the steroid treatment, respectively.

Conclusions: The diagnosis of ASNE can be speculated with acute epigastric or peri-umbilical abdominal pain for 3-6 days along with the affected segment of swollen intestines of wall thickness ≥ 3mm seen on abdominal ultrasound. Of those who were diagnosed with ASNE and treated with steroid, the symptoms resolved within 5 days, showing steroid is an effective medical management for ASNE.

25 The Impact of Early Empiric Antibiotics Use on Gut Microbiota in Very Low Birth Weight Preterm Infants

早期廣泛性抗生素對極低體重早產兒腸道菌叢的影響

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Background: Development of the preterm infant gut microbiome is interrupted or altered in preterm infants by various factors. Antibiotics are frequently prescribed to preterm infants and are known to disrupt microbial balance. Our objective was to determine the impact of different empiric antibiotics use in the first week of life on microbial colonization and diversity in very low birth weight (VLBW) preterm infants.

Methods: Breast fed VLBW infants were divided into two groups, including those who received 3 d of combination treatment of ampicillin and gentamicin (AG group), and those received 7 d of ampicillin and cefotaxime (AC group). Infants with any antibiotics use after age of 7d and infants on exclusive formula feeding were excluded. Stool samples were collected at age of 7d, 14d, and 30d. The 16s ribosomal DNA community profiling was used to compare the microbiota between two groups.

Results: Twenty-four infants were enrolled in our study (AG group =10, AC group =14). The gestation age and birth weight were 30.0± 2.5 weeks and 1286± 190 gm in the AG group versus 28.9± 2.5 weeks and 1099± 280 gm in the AC group, respectively. Infants of AC group had significantly

increased abundance of Enterococcus in the 7th day of life compared to those of AG group (12.3% vs 0.6%, P = .0321). The proportion of Entercoccus increased over time (12.3%, 10.0%, 23.5% in the 7d, 14d, 30d sample, respectively) in the AC group. There was a trend of Bifidobacterium growth over time (5.8%, 14.1%, 31.6% in the 7d, 14d, 30d samples, respectively) in the AG group, but this phenomenon was reversed in the AC group (17.6%, 8.1%, 9.7% in the 7d, 14d, 30d samples, respectively). The evenness was lowest in the 7d sample of AC group comparing to the14d and 30 d samples (p= .041). The diversity within group had no significant difference between two groups in each time period samples.

Conclusions: Different antibiotic treatments affect the early development of gut microbiota in VLBW preterm infants. A combination of ampicillin and cefotaxime resulted in an overgrowth of Enterococcus and a decreased in evenness. The clinical relevance of these findings is to be elucidated in further studies.

26 Effects of Vitamin D Deficient Diet on Modulating Toll-like Receptors and Intestinal Microbiota in a Mice Model

實驗鼠中飲食缺乏維生素D對調節Toll-like受體及腸道微生物的影響

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Background: Vitamin D (VD) is an important modulator of the immune system and previous studies showed VD insufficiency or deficiency was strongly correlated with gut integrity and immune response. Intestinal microbiota imbalance or abnormality had been found to drive toll-like receptors (TLRs) signaling, cause Th17 up-regulation and disrupt Treg cells, and could induce rheumatoid arthritis. There are many factors, including diet, which can affect gut microbiota composition. Previous report demonstrated mice fed high-fat and VD deficient diet were found increased amount of pathogen (Helicobacter hepaticus) in the ileum but the amount of symbiotic bacteria (Akkermansia muciniphila) decreased. In this study, we try to establish an animal model in raising mice fed VD deficient or sufficient diet and to investigate the effects of VD deficient diet on modulating TLRs and intestinal microbiota.

Methods: Male C57BL/6 mice were administered either vitamin VD-deficient (VDD, 0 IU/per mouse) or VD-sufficient (VDS, 37.8 IU/per mouse) special diets for 7 weeks. After sacrificed, jejunum specimens were collected for TLRs analysis by Q-PCR. DNA was extracted from fecal samples, amplified by PCR using conserved bacterial primer sets and subjected to next generation sequencing. Intestinal microbiota of different groups were compared using principal coordinate analysis (PCoA).

Results: In our animal model, we found mice fed VDS diet had indeed higher serum level of VD (＞60ng/ml). TLR1 and TLR2 mRNA expressions were significantly up-regulated in VDD group than in VDS group ($p < 0.05$). There was no difference in TLR4 and TLR6 mRNA expressions between the two groups. Based on PCoA plots analysis in family, genus and species-levels, we demonstrated obvious difference in intestinal microbiota diversity between VDD and VDS groups.

Conclusions: In this study, we successfully established an animal model in raising mice fed VD deficient or sufficient diet. Up-regulation of TLR1 and TLR2 mRNA expressions in VDD mice was suggested to modulate intestinal microbiota both in abundance and diversity. Further study to investigate the specific bacterial strains involved is under processing.

27 Effect of Probiotics and Prebiotics on Gut Microbiota in the Infant and Younger Mice

探討益生菌及益生源對於小鼠腸道菌叢的影響

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Background: Probiotics and prebiotics are beneficial to the health and immune modulation. To determine the long term observation of intestinal ecosystem through the "children" period, we set the mice model fed with probiotics, prebiotics, and synbiotics. The aim of our study seeks to determine if prebiotics and probiotics modulate the gut microbiota during the weaning period of the mice.

Methods: BALB/c ByJ mice were fed either with L. acidophilus weekly since 2-week old [probiotics group] or fed with sterile drinking water containing 15% fructo-oligosaccharide (FOS) daily [prebiotics group] or both [synbiotics group]. Fecal samples were collected every two weeks during the experimental course. Total fecal specimens were analyzed by next generation sequencing. Individual microbial diversity and composition were analyzed via PCR and sequencing will be performed using a modified version adapted for the Illumina HiSeq2000/ MiSeq.

Results: A comparison of the taxonomic data revealed that the mice in prebiotics group exhibited relatively high abundances of Proteobacteria, Verrucomicrobia and Tenericutes at the phylum level and a relative underrepresentation of Bacteroidetes and Firmicutes. The phylum Firmicutes is more abundant in probiotics group, and the phylum Bacteroidetes is more abundant in control group. Using the LEfSe method, we found that Clostridia and Clostridiales sequences were significantly enriched in the mice of probiotics group, and Proteobacteria, Enterobacteriales, Enterobacteriaceae were enriched in prebiotics group. In analysis of alpha diversity, the Shannon index increased in the fecal specimen of probiotics group, which compared to prebiotics group. In analysis of non-metric multidimensional scaling, it is different in the

fecal specimens of probiotics, prebiotics, and synbiotics groups.
Conclusions: Our results suggest that pre-colonization with probiotics since early life is beneficial in modulating the gut microbiota. Dietary FOS can enhance intestinal microflora when the mice inoculation with probiotics. The long term observation in the above mice model provides some primary information about gut microbiota, which will be helpful to explore the human research.

28 Effect of High Salt Diet on Food Allergy in Mice
高鹽飲食對食物過敏之影響 ─ 小鼠實驗

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Background: The prevalence of food allergies appears to be increasing. High salt intake has been proven as a risk factor for multiple sclerosis which is an autoimmune disease. The effect of high salt intake on food allergy has not been elucidated.
Methods: Two groups of BALB/c mice (n=10) were enrolled in this study. Group 1 mice were fed with high salt chow containing 4% NaCl and water containing 1% NaCl. Control mice (group 2) received traditional rodent diet containing 1.07% NaCl and distill water. Chow and water were intake for two months ad libitum. All the mice were sensitized with food allergen ovalbumin (OVA). Serum specific IgG, IgG1 antibody responses and cytokine profiles of spleen cells were investigated.
Results: Mice with high salt diet induced higher level of anti-OVA antibody than the mice in the control group (61.4 + 30.7 & 39.2 + 8.3 units, respectively). In the meanwhile, mice fed with high salt diet had higher serum OVA specific IgG1 antibody than the mice fed with traditional chow (122.9 + 54.4 & 86.8 + 46.2 units, respectively). Compared with the controls, those receiving high salt diet showed higher production of type 2 T helper cell related cytokine, interleukin-4 (167.3 + 105.6 and 18.8 + 16 pg/ml, respectively), but little of regulatory cytokine, interleukin-10 (82.4 + 41.8 and 159.9 + 71.4 pg/ml, respectively). There were no differences in serum sodium and chloride concentration between these two groups.
Conclusions: Mice fed with high salt diet may induce higher allergic antibody production to food allergen and systemic Th2 cytokine. It may induce by lower productive of regulatory cytokine.

29 The Role of Magnetic Resonance Cholangiopancreatography on Diagnosis of Biliary Atresia in Preterm Infants with Cholestasis
核磁共振膽胰道攝影術在膽汁滯留早產兒身上診斷膽道閉鎖的角色

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Background: Early diagnosis of biliary atresia (BA) is of great clinical importance because timely surgical intervention can restore bile flow and prevent worsening of liver disease. The reported incidence of BA in Taiwan shows that the disease has higher prevalence in preterm infants than in term infants. Magnetic Resonance cholangiopancreatography (MRCP) is an useful and non-invasive examination for biliary atresia in term infants. In this study, we aimed to evaluate the accuracy of MRCP for diagnosing BA in preterm infants with cholestasis.
Methods: This study enrolled infants aged less than 5 months received MRCP examination for cholestasis in the National Cheng Kung University Hospital in 2009-2018. The information of patients' gestational age, age, sex, body weight, laboratory data, drug and TPN history were retrospectively obtained. All patients received laboratory study and abdominal echo prior MRCP. One pediatrics radiologist reviewed the MRCP images. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of MRCP for diagnosing BA based on surgical prove or a 3-month follow-up were assessed. The accuracy were compared between preterm infants and term infants.
Results: A total of 51 infants with cholestasis received MRCP in 2009-2018. One case was excluded due to MRCP failure, remaining 24 preterm infants and 26 term infants. The mean age was 1.9 months old. The female-to-male ratio was 0.92. In preterm infants, the sensitivity was 100% (4/4), specificity was 80% (16/20), PPV was 50% (4/8), and NPV was 100% (16/16). In term infants, the sensitivity was 75% (9/12), specificity was 93% (13/14), PPV was 90% (9/10), and NPV was 81% (13/16). Low sensitivity and NPV in term infants was due to 2 biliary atresia cases were obscured by choledochal cyst.
Conclusions: MRCP has favorite sensitivity and NPV on diagnosis of BA in preterm infants with cholestasis. However, diagnosis of choledochal cyst by MRCP in term infants with cholestasis needs to be aware of a combination with BA.

30 The Culture-based Strategy Yields Higher Eradication Rate and Lower Costs than Test-to-treat Strategy in Treating Pediatric H. pylori Infection

細菌培養之藥物敏感性測試報告做為兒童胃幽門桿菌治療依據，有較好的除菌率及較好之成本效益

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Background: Helicobacter pylori (H. pylori) infection is one of the major causes of peptic ulcers and gastric cancer. The ESPGHAN/NASPGHAN guidelines in 2016 suggested that eradication regimens for H. pylori should be tailored according to its susceptibility. However, the benefits have not been fully investigated. In this study, we tried to compare the essential costs of the culture-based strategy and test-to-treat strategy in treating pediatric H. pylori infection in Taiwan.
Methods: We enrolled 94 children aged less than 18 years who received esophagogastroduodenoscopy in two medical centers in southern Taiwan from 1998 to 2018. They were divided into two groups according to eradication strategy. Patients with culture-positive and MICs test were allocated into group 1, the others with culture-negative or without culture were group 2. We retrospectively collected their demographic data and eradication rate. Moreover, we calculated the total essential costs of treating a hypothetical cohort of 1000 pediatric H. pylori patients.
Results: The eradication rate in the first treatment was 88.7% and 75.6% in the culture-based strategy and test-to-treat strategy, respectively. There was no significant difference in age, sex, and endoscopic diagnosis between two strategies. The total costs were inversely to the percentage of choosing culture-based strategy. For every 10% increase of culture-based strategy, the total cost was reduced by $NT 43,000 in 1000 patients. The total costs were also inversely to the successful rates of either culture-based or test-to-treat strategy. For every 10% increase of successful rate, the total cost was reduced by $NT 270,000 in culture-based strategy; and reduced by $NT 210,000 in test-to-treat strategy.
Conclusions: The culture-based strategy had higher eradication rate than test-to-treat strategy. More percentage of choosing culture-based strategy and higher eradication rates in either culture-based or test-to-treat strategy all help reduce the total costs of treating pediatric H. pylori patients.

31 Azithromycin Reduce Ventilator Associated Pneumonia in Critical Pediatric Cardiovascular Surgery Patients

阿奇黴素可減少小兒重症心血管手術的患者的呼吸器相關肺炎

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Background: Ventilator associated pneumonia (VAP) is a frequent cause of nosocomial infection (NI) after cardiac surgery in pediatric patients, and results in a significantly longer stay in the intensive care unit. VAP caused by potentially drug-resistant bacteria. Azithromycin has been shown to retard Pseudomonas aeruginosa biofilm formation. Staphylococcus epidermidis and Staphylococcus aureus are the most frequent causes of nosocomial infections and infections on indwelling medical devices, which characteristically involve biofilms This study was to determine whether an anti-biofilm antibiotic (azithromycin) reduced NI and VAP for patients undergoing critical pediatric cardiac surgery.
Methods: We enrolled 207 patients (<20 years) who underwent cardiovascular surgery for congenital heart disease. Data on postoperative courses were compared between children with and without intravenous azithromycin treatment. We administered perioperative conventional antimicrobial prophylaxis (cefazolin and gentamicin) for 3 days, with (AZI group) and without (previous group) intravenous azithromycin for 3 days. Furthermore, 78 patients from the medical record retrieval system of Kaohsiung Veterans General Hospital, Kaohsiung from 2012 to 2015 were recorded (NOW group).
Results: The previous group had higher rates of VAP infection, longer periods of ventilator dependence and length of post-operative stay in hospital than AZI Group. There was a significantly higher rate of NI in the previous group compared to the AZI group ($P < 0.05$). We also found the same trend with higher rate of VAP and NI in NOW group compared with AZI group.
Conclusions: The previous group had higher rates of VAP infection, longer periods of ventilator dependence and length of post-operative stay in hospital than AZI Group. There was a significantly higher rate of VAP & NI in the previous group compared to AZI group. We also found the same trend with higher rate of VAP & NI in NOW group compared to AZI group.

32 Accurate Diagnosis and Successful Therapy of Vallecular Cyst Coexisted with Laryngomalacia in Infants by Flexible Bronchoscopy with Non-invasive Ventilation

喉谿部囊腫併軟喉症於幼兒之正確診斷與有效治療：使用軟式氣管鏡輔以非侵入性通氣術

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Background: Traditionally, vallecular cyst (VC) with laryngomalacia (LM) is diagnosed by flexible bronchoscopy (FB), and then treated by rigid bronchoscopy (RB) with endotracheal intubation under general anesthesia. This study is designed to evaluate and compare clinical variables between these two techniques in the treatment of VC with LM in infants.
Methods: A retrospective study of consecutive infants who were diagnosed and managed in our hospital within 12-years period, 2007 to 2018. During FB, infants were routinely support with a non-invasive ventilation, pharyngeal oxygen with optional nose-closure and abdomen compression, under intravenous procedural sedation without any artificial airway. Clinical variables and outcomes were analyzed and reported.
Results: 18 infants with VC coexisted moderate to severe LM were enrolled. At admission, the mean age was 3.0±0.6 months and the mean body weight was 4.6±1.3 kg. These diagnosis were all successfully made in their first FB inspection which was within 2 days of admission. Among them, 12 CT scans had been performed for image research. Before definite therapy, 15 infants were respiratory supported with nasal prongs CPAP. After complete studies, all the VC and LM were managed with laser therapy, de-roofing of VC and plasty of LM, via FB in the same session. The operation (VC and LM) time was 14±1.7 minutes. Two infants needed the additional second laser therapy during the follow up FB, four days after the first therapy. There were no any significant oxygen desaturation (< 90%) or bradycardia (< 100/m) throughout both diagnostic and therapeutic FB. After laser therapy, all infants were supported with NP-MIV and no infant had been tracheal intubation. The total hospital period was 7.2±0.8 days. Infants were discharged without any respiratory support. All infants were followed for 3 months and clinically showed much improvement in feeding, respiration and body weight gain.
Conclusions: FB with this NIV support not only allows for accurate diagnosis but also offer effective therapeutic management of the VC with LM in infants. This technique may be more practical, convenient and cost-effective alternate than the traditional RB.

33 Determinants of Lung Function Evolution till Late Infancy among Infants Born Preterm

早產兒至晚期嬰幼兒時期之肺功能演進的決定因子

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Background: To investigate the evolution of lung function of preterm-born infants with and without bronchopulmonary dysplasia (BPD), and to analyze which perinatal characteristics was associated parameters of lung functions in the later infancy.
Methods: This study was part of an on-going larger, prospective, population-base prospective birth cohort study called the Prediction of Allergies in Taiwanese Children (PATCH) initiated since 2013. Longitudinal lung function assessments, including tidal breath analysis, lung mechanics, tidal and raised-volume forced expiratory flow, were performed at about 6, 12, and 18 months of corrected age in infants born at less than 36 weeks' gestational age. Perinatal features were further analyzed to ascertain the determinants of lung function parameters.
Results: Total 121 preterm infants (61 without BPD and 60 with BPD) were included into this study. Although all preterm infants expressed decreased lung function in the early infancy (6 months of age); however, after adjusted with body length, only infants with BPD had poor performance. Furthermore, lung function of infants with mild-moderate BPD showed catch-up gradually, but that of severe BPD persisted generally poor performance, especially in forced expiratory flow, till later age (18 months age). In analysis of perinatal characteristics, z-score of body length was the main determinant of tidal volume, lung mechanics and tidal forced expiratory flow in early infancy. Postnatal respiratory morbidity majorly determined lung function in the later life, especially in tidal volume and forced expiratory flow.
Conclusions: Persistently poor performance and absence of catch-up in lung function are obvious in preterm with BPD at 18 months of age. Postnatal respiratory morbidity largely determines the expression of lung function, especially forced expiratory flow, in the later infancy.

34 Clinical Characteristics, Treatment and Outcomes of Enthesitis-Related Arthritis

接骨點炎相關型兒童特發性關節炎的臨床分析和治療預後

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Background: Juvenile idiopathic arthritis (JIA) has been categorized into seven different subtypes according to International League of Associations for Rheumatology system (ILAR) criteria. Enthesitis-related arthritis (ERA) has represented the largest subtype in Taiwanese cohort study. The aim was to compare the clinical characteristics, treatment and outcomes in patients with ERA in National Taiwan University Hospital (NTUH) to those in patients with other subtypes of JIA. Further to determine genetic markers, patient characteristics, and risk factors help to predict the development of active and non-active treatment outcomes in ERA.
Methods: Retrospective chart review of all patients with JIA referred to a pediatric rheumatology center in NTUH between 1990 and 2018 were identified according to ILAR criteria. The outcome assessments were based on Wallace criteria to categorize patient into active and non-active (inactive, remission on medication and remission off medication) group. A subset of samples were further tested by DNA sequencing for identification of HLA-B27 subtypes.
Results: One hundred and eighty three patients were included for 8 years mean follow up duration. ERA was the single largest category of JIA (39.89%), psoriasis and undifferentiated were both the least common (0.55%). ERA was male predominant (86% vs 54% in other subtypes), late onset age (11.1±3.2 yrs vs 8.1±4.7 yrs), majority with HLA-B27 positive (92% vs 6%), sacroiliac join/lumbosacral involvement (16% vs none) and anterior uveitis (10% vs none). ERA and extensive oligoarthritis are less likely to achieve non-active treatment response compare to persistent oligoarthritis with P value of significant (0.036 and 0.027). Among risk factors contribute to poorer treatment response in ERA have shown that any clinical signs of sacroiliitis with P value of significant (0.0057).
Conclusions: ERA has represented the most common subtype of JIA in Taiwanese cohort study and has poorer treatment responses when compare to other JIA subtypes. To identify risk factors that contribute poorer ERA treatment response can help more aggressive treatment strategy and improve treatment outcome of ERA.

35 Ultrasound Measurement of Joint Cartilage Thickness in Healthy Asian School-aged Children

以關節超音波測量健康亞洲學齡兒童的關節軟骨厚度

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Background: Degeneration of the osteocartilaginous structures due to synovial inflammatory process is a feature of juvenile idiopathic arthritis (JIA). While anthropometry difference has been reported between Asian and Caucasian, Asian specific age- and gender-related normal standard reference values should be established before ultrasound (US) measurement of cartilage thickness (Cth) becomes standard procedure in the clinic.
Methods: A cross-sectional study was performed in 100 healthy Asian children (including 48 girls and 52 boys, age between 5 to 12 years-old). Bilateral knees, ankles, wrists, second metacarpophalangeals (MCPs) and proximal interphalangeals (PIPs) were measured using US. Children's body weight and body height were also recorded for later adjustment.
Results: We observed no difference in the Cth between right and left knees, ankles and wrists but MCPs and PIPs. Cartilage thickness in the large joints such as ankles and knees differed between sexes ($p < 0.001$), and the boys had thicker cartilage than those of the girls. Cartilage thickness decreases with increasing age after weight, height and BMI adjustment. A formula for calculating sex-specific cartilage thickness at different ages in childhood is suggested.
Conclusions: Cartilage thickness measurement with US in small joints may be biased. A standard reference of Cth for Asians in the knee, ankle and wrist joints between age 5- to 12 have been proposed.

36 Therapeutic Effects of a Single Injection of Human Umbilical Mesenchymal Stem Cells on Acute and Chronic Colitis in Mice

單次注射人類臍帶間質幹細胞對小鼠急性和慢性結腸炎的治療作用

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Background: Multiple injections of bone marrow mesenchymal stem cells (BMMSCs) have been used for treatment of chronic colitis in mice. We aimed to report the therapeutic effects of a single injection of human umbilical cord mesenchymal stem cells (hUCMSCs) on acute and chronic colitis.
Methods: Male C57BL/6JNarl mice were divided into control, phosphate-buffered saline (PBS), and hUCMSCs treated groups, respectively. Acute and chronic colitis were induced in the mice (except controls) using 3% dextran sulfate sodium (DSS). The mice in the hUCMSCs group underwent a single injection of hUCMSCs. The disease activity index (DAI), colon length, histology, colon inflammation score, in vivo stem cells images, and blood cytokine levels were recorded.
Results: The DAI was significantly higher in the hUCMSCs group than in the control group and lower than in the PBS group on all days. The colon length was significantly longer and the colon inflammation score was significantly lower in the hUCMSCs group than in the PBS group on days 8 and 25. IL17A, Gro-α, MIP-1α, MIP-2, and eotaxin were significantly lower in the hUCMSCs group than in the PBS group on days 8 and 25.
Conclusions: Single-injection hUCMSCs improved DSS–induced acute colitis and decreased progression of acute colitis to chronic colitis.

37 Supper High Enhancement of Immunomodulation Effect of Human UCMSCs on PBMCs by Optimized Short-Term Low Hypoxia

通過優化的短期低氧缺乏，高效增強人類UCMSCs對PBMCs的免疫調節作用

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Background: Mesenchymal stem cells (MSCs) are widely used in research and clinical use. Because they are easily obtained, proliferate rapidly, and are immunosuppressive, umbilical cord MSCs (UCMSCs) are ideal candidates for cell-based therapies. MSCs develop in low oxygen tension environmental niches, varying from 1% to 7% O2 in bone marrow and rarely exceeding 5% in the umbilical cord, raising concerns regarding hypoxic conditions.
Methods: UCMSCs grown in hypoxic conditions constituted the study group while UCMSCs grown in normoxic conditions constituted the control group. The peripheral blood mononuclear cell (PBMC) suppression assay and carboxyfluorescein succinimidyl ester (CFSE) assay were used to assess the immunosuppressive effects of the cells. Gene expression was evaluated using DNA microarrays. Enzyme-linked immunosorbent assays were used to determine cytokine levels.
Results: UCMSCs grown in both normoxic and hypoxic conditions significantly inhibited PBMC proliferation of UCMSCs grown in 1% hypoxia for 4-6 hr significantly inhibited PBMC proliferation better than UCMSCs grown in normoxia for 4-6 hr. UCMSC exosomes showed a significant dose-dependent inhibitory effect on PBMC proliferation. After 4-6 hr of 1% hypoxia pulse therapy, UCMSCs secreted more IL-6, H-GCSF, TNF-α, PGE2, exosomes that suppressed PBMC proliferation, more IL-10, TGF-β, exosomes that enhanced T reg cells than UCMSCs under normoxic conditions.
Conclusions: Short-term 1% hypoxia pulse therapy prompted powerful UCMSC inhibition of PBMC proliferation. UCMSCs are appealing for the treatment of diseases associated with aberrant immune responses because of their immunosuppressive effects and cell expansion capacity. Thus, UCMSCs are ideal candidates for clinical cell-based therapies.

38 Influence of Extracellular Vesicles Derived from Umbilical Cord Mesenchymal Stem Cells(ucMSC-EVs) on Monocyte Differentiation toward M2 Phenotype

臍帶間質幹細胞產生的胞外囊泡對單核球往M2表型分化的影響

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Background: Monocytes are a type of innate immunity cells whose functional alterations had been linked to many diseases including liver cirrhosis, helminth infection, sepsis, atherosclerosis and tumor metastasis (International Journal of Biological Sciences. 2014;10(5):520-529.). Umbilical cord mesenchymal stem cells (ucMSCs) have biological activities and have the ability to differentiate into bone, muscle or neuron. ucMSCs are well known to possess anti-inflammatory property in addition to regenerative effects (American Journal of Translational Research.2018; 10(1):212-223.). Recently, it has been reported that extracellular vesicles derived from ucMSC (ucMSC-EVs)

play a pivotal role on the therapeutic effects of MSCs (Stem Cells 2017 ;35(4):851-858.). We postulate that ucMSC-EVs have the property to modulate monoyte differentiation. We aim to investigate whether ucMSC-EVs have the ability to induce monoyte differentiation toward M2 phenotype.
Methods: Employing HL-60 myeloid cell line, we used vitamin D (100nM) for 4 days to induce HL-60 cells to differentiate into monocyte cell showing positive CD14 and CD11b expression. Monocytic cells were treated with 10% volume (120 ug/ml) of ucMSC-EVs and stimulated by lipopolysaccharide (LPS) (10ng/ml) for 24hr to see the monocytic cell differentiation between M1 and M2 phenotype by flow cytometry analysis.
Results: Vitamin D (100 nM) induced HL-60 cell expression of CD14 and CD11b after 4 days of incubation, indicating monocytic differentiation. Preincubation of monocytic cells with ucMSC-EVs one hour before the LPS (10ng/ml) stimulation for M1 polarization for 24 hours demonstrated that the vitamin D induction of monocyte polarization under LPS stimulation revealed CD80+ CD86+ expression (6.98%) and CD80+ expression 15.09%. The treatment of ucMSC-EVs suppressed the CD80+ expression from 15.09% to 1.53%, indicating switch of M1 to M2 differentiation.
Conclusions: This study demonstrates that ucMSC-EVs mediated monocytic cell differentiation from M1 to M2 phenotype, which will be further validated by cytokine production and signal transduction in the presentation.

39 MicroRNAs Profile of Extracellular Vesicles (EVs) Derived from Umbilical Cord Mesenchymal Stem Cells Different from EVs from DLD-1 Cancer Cells Involved in Migration of DLD-1 Cells and Granulocytes

兩種不同胞外囊泡微小RNA對 DLD-1癌細胞和顆粒細胞遷移作用之研究

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Background: Extracellular vesicles (EVs), including microvesicles and exosomes are released to facilitate intercellular communication in diverse cellular processes. Endocytic EVs could affect the response of cancer therapy depend on microRNAs and proteins of cargos by EVs. We investigated effects of EVs derived from umbilical cord mesenshymal stem cells (ucMSC) called M-EV and those from DLD-1 cancer cells (D-EV) on the colon cancer and granulocytes migration.
Methods: EVs harvested from ucMSCs and DLD-1 were used in this study. Different EVs microRNAs and proteomic landscapes are identified by RNA-seq and LC-MS/MS. Next, we validated the expression levels of ten microRNAs between M-EV and D-EV by RT-qPCR. The in vitro effects of two different EVs on colon cancer cell (DLD-1) or granulocytes migration were evaluated by transwell assay. Cells at 2.5 x 10^4 cells/well in 100 ul serum free medium were incubated with or without MEV (2.2 x 10^10 vesicles, 12 ug/well) and DEV (12 ug/well) for 24 hrs; microRNA-loaded EVs were also prepared by incorporation of miRNA10a antagomir (2ug/120ug), called EV-miRNA10a, to test the role of miRNA10a on DLD-1 and granulocytes migration.
Results: The results showed that MEV and DEV had reverse profiles of miRNAs; MEV and DEV had an opposite effect on promotion of DLD-1 cell migration ($p < 0.05$). MEV incorporated with miR10a antagomir, markedly inhibited the colorectal cancer cell migration ($P < 0.05$). Comparisons among different MEV and DEV with and without miRNA10a antagomir found that incorporation of miRNA10a antagomir (called EV-miRNA10a) showed significantly different on the DLD-1 tumor cell migration. MEV and MEV-miR10a down-regulated DLD-1 cell migration, but DEV enhanced DLD-1 cell migration. The signal transduction responsible for the enhancement or downregulation of DLD-1 cells would be explained by immunoblotting.
Conclusions: Different EVs had potential benefit or drawback on the inhibition of cancer cell migration depending on its lineage and miRNA profile. Clarification of the EVs with and without incorporation of certain miRNA antagomir might provide strategies for the inhibition of cancer cell migration and metastasis.

40 Different Formulations of Extracellular Vesicles Derived from Umbilical Cord Mesenchymal Stem Cells Modulate T Cell Differentiation toward Treg Expression

臍帶間質幹細胞胞囊免疫因子及其對T細胞分化調節的作用原理

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Background: Extracellular vesicles (EVs) including exosomes and microvesicles are cell-derived membrane vesicles, carrying messengers for cell-cell communications. EVs contain many components, mainly miRNAs and proteins, for cell-cell interactions and signaling transduction for immune regulation. We postulate and investigate that different mediators of extracellular vesicles derived from umbilical cord mesenchymal stem cells modulate T cell differentiation toward Treg expression.
Methods: Peripheral blood mononuclear cells at 2x 10^5 cells/well at 300 ul were incubated with or without anti-CD3 (10ug/well) and anti-CD28 (2 ug/well) antibodies

for 4 days; different extracellular vesciles (EVs): ucMSC-naive-EV, byro-EV (prepared from preconditional treatment of bryostatin (10 nM) for 24 hours), asp-EV (prepared from preconditional treatment of aspirin (250 ug/ml) for 24 hours) was added into the well at 2.2 ~ 7.1 x 10^11 vesicles in the presence of anti-CD3 and anti-CD28 on day 2 and day 3. Flow cytometry was used to assess the CXCR3 expression presenting Th1, the CCR4 expression presenting Th2, CD25 expression presenting Treg, and CCR6 expression presenting Th17 differentiation. The transcription factors of T cell differentiation: T-bet, Gata-3, FoxP3 and RORrT expression presenting Th1, Th2, Treg and Th17 were analyzed by RT-PCR assays.

Results: The EVs from usMSCs contained higher levels of FGF2, and chemokine factors: IL-8, MCP-1 and MCP-3, and IL-6 and IL-15 as well. Administration of different formulation of EVs on day 2 and day 3 showed varied effects on the T helper cell differentiation on surface markers expression. The treatment of ucMSC-naive-EVs significantly enhanced CD25 and CCR4 expression ($P < 0.05$), indicating ucMSC-naive-EV treatment induced Treg and Th2 differentiation. On the other hand, ucMSC-naive-EVs (EV) significantly enhanced transcription factors of FoxP3 and RORrT expression, but asp-EVs enhanced FoxP3 expression and suppressed RORrT expression.

Conclusions: This study postulates and proves that ucMSC-EVs in different formulations could significantly enhance or suppress the effect on T cell differentiation implicated in immune regulation.

41 Extracellular Vesicles (EVs) Derived from Umbilical Cord Mesenchymal Stem Cells Rescue Polycyclic Aromatic Hydrocarbon (PAH) Suppression of C2C12 Myoblast Cell Growth and Mechanism

臍帶間質幹細胞胞囊對多環芳香碳氫化物抑制肌母細胞生長的恢復與作用機轉

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Background: Polycyclic aromatic hycrocarbon (PAH) are released by overheating of lipids or plastic materials. PAH is highly toxic to human cells. Extracellular vesicles (EVs) are cell-derived membrane vesicles, and represent an endogenous mechanism for intercellular communication. Any cell can release different types of EVs, and the released EVs can be up-taken by recipient cells, and thereby resulted in delivering the contents of EVs for suppression of inflammatory reactions. We postulate and investigate that EVs derived from umbilical cord mesenshymal stem cells (EVs-ucMSCs) could rescue PAH-suppressed myoblast C2C12 cell growth.

Methods: The ucMSC culture between passages 3 and 10 in low glucose DMEM was subject to isolation of EVs from the ucMSCs. The contents of cytokines and growth factors were measured by a milliplex bead-array, and the myoblast cell growth was assessed in C2C12 myoblast cell growth. The rescuing mechanism of PAH (0.5 uM) suppression of C2C12 cell growth by ucMSC-EVs was assessed by Western blot analysis.

Results: The cells were proved mesenchymal stem cells as flow cytometric analyses of CD29, CD44 and CD73 positive but negative for CD34 marker. The EVs were confirmed to be vesicles around 50-150 nm under electromicroscopy and expressed tetraspanins: CD81 and CD63 markers of EVs in flow cytometric analysis. The data indicated that compared with supernatants, EVs-ucMSCs containing higher growth factors (such as FGF2 and PlGF) significantly ($p < 0.05$). In contrast, EVs containing significantly less amount of cytokines such as GM-CSF, IL-6, IFNa2, IL-8 and IL-4 than culture supernatants, significantly suppressed PMA-induced expression of oxygen free radicals. EVs-ucMSCs enhanced C2C12 cell growth in a dose dependent pattern ($P<0.05$), and rescued PAH-suppression of C2C12 growth ($p<0.05$).

Conclusions: EVs-ucMSCs contain higher growth factors (such as FGF2 and PLGF) significantly ($p < 0.05$), associated with promotion of myoblast cell growth, and inhibition of PMA-induced oxygen free radicals. Moreover, EVs-ucMSCs significantly rescue PAH-suppression of C2C12 growth. This may be implicated in the rescue for regeneration of muscle weakness in aging frailty.

42 Influence of Paternal Tobacco Smoke on CG Methylation of Immune Genes and Immune Differentiation Markers in Umbilical Cord Blood

父親抽菸影響新生兒免疫基因甲基化和臍帶血內的免疫分化指標變化

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Background: Little is known about effects of paternal tobacco smoke (PTS) on the offspring's asthma and its epigenetic programming and immune differentiation in umbilical cord blood. We investigate whether prenatal exposure of PTS was associated with the offspring's asthma correlated to epigenetic CG methylation of potential tobacco-related immune genes and immune differentiation markers in umbilical cord blood.

Methods: In a birth cohort study, we completed the follow up of 1348 infants at 18 months of age and 756 children at 6 years of age. The exposure rates of PTS and maternal tobacco smoke (MTS) exposure were respectively 23.0% and 0.2%. This cohort is therefore suitable for studying effects of prenatal PTS exposure on the offspring's asthma.

Prenatal exposure of PTS, cord blood DNA methylation, infant infection, cord blood T cell polarization in mRNA and cytokine profiles and childhood allergic diseases were analyzed.

Results: Infants with exposure of PTS had a significantly higher rate of upper respiratory tract infections (URIs) at age of 18 months (p=0.007), and a significantly higher risk of asthma by age of 6 than those without (p=0.026). The LMO2_P794 and IL10_P325 CG methylation levels detected were individually associated with prenatal PTS exposure (p=0.005 and p=0.033, respectively), and the LMO2_P794 methylation content was associated with physician-diagnosed asthma (p=0.019). The LMO2_P794 and GSTM1_P266 CG methylation levels at age 0 were significantly correlated to those at age of 6. Newborns with PTS had higher MCP-1 but lower IFNr and IL-4 levels, and higher T-bet, RORrT and FoxP3 but lower GATA-3 expression.

Conclusions: Prenatal exposure of PTS can program epigenetic CG methylation of LMO2, GSTM1 and IL-10, which is retained into childhood and associated with development of asthma. The PTS is associated with altered T cell polarization in cord blood related to transcription factors and cytokines expression. Clarifying the prenatal epigenetic program of PTS for childhood asthma may provide a novel regimen to prevent childhood asthma.

43 The Hot-Spot Mutation of T Insertion in the RAG1 Gene rather than the Missense [Thr66Ile] Variation in the IL7RA Gene Causing Persistent Varicella Infection after Vaccination and Comparative Analysis of RAG1 Mutations in Patients of Chinese Descent

接種後持續水痘感染主要和RAG1 Hot-Spot基因突變相關，而非IL7RA基因突變[Thr66Ile]；與後續華裔族群RAG1突變之分析

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Background: Mutations of Recombination-activating gene 1 (RAG1) cause autosomicrecessive severe combined immunodeficiency (SCID) and typically show severely reduced T-cell and B-cell but a normal NK-cell as T-B-NK+SCID phenotype. However, expanding CD8 cells during varicella infection disturbed in-time genetic identification.

Methods: A 1-year-6 month girl developed facial varicella vesicles after vaccination and accompanying chronic cough over 4 months. Her lymphopenia and hypogammaglobuliemia referred to the SCID phenotype. Lymphocyte subsets, proliferation and candidate genetic approach based on Medline search were analyzed.

Results: With CD4 and CD 19 lymphopneia but normal CD8, candidate gene approach revealed the normal variant homozygous [Thr66Ile] IL7RA substitute and the hot-spot pathogenic c. 3198-3199 ins T (L1025F fsX39) in the RAG1 gene. Overall in Chinese-descent RAG1 mutations, their phenotypes were SCID (9 patients), Omenn syndrome (OS) (9), Atypical SCID (2) but without CID-G/AI. All had recurrent sinupulmonary infections and chronic diarrhea except one recognized by newborn SCID screening and successful in HSCT. Autoimmune-related disorders encompassed erythroderma (11), lymphoadenopathy (10), hepatosplenomegaly (9), autoimmune hemolytic anemia (4), and idiopathic thrombocytopenia purpura (1). All died of infection-related complications except for three, two receiving HSCT and the third in the HSCT list. Different from two with this hot-spot mutation presenting as SCID and OS, our patient with atypical SCID possibly related to increased CD8 cells and lack of anti-cytokine antibodies and antoimmunity. Unfortunately, she succumbed of varicella- and influenza-related necrotizing pneumonia complicating pneumothorax and pneumomediastinum.

Conclusions: Prompt HSCT should be encouraged in Chinese-descent patients with RAG1 mutations to improve survival prognosis.

44 Mimicking Warning Signs of Primary Immunodeficiency Diseases (PID) in Children with Langerhans Cell Histiocytosis (LCH)

似先天免疫缺損"警示表徵"的孩童蘭格罕細胞組織球增生症

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Background: Recurrent or/and refractory infections could be a herald sign in PID. However, mimicking refractory infections could also be present in patients with Langerhans cell histiocytosis (LCH).

Methods: Because of a referred case with recurrent and refractory facial cutaneous virus infections in suspicion of PID whose diagnosis finally turns to LCH after speculating

her bone lesion in X-ray, we wonder whether such mimicking ten warning signs in PID occurred in children with LCH. We retrospectively reviewed all LCH children in the department of pediatric hematology in our institute since January 2001 to date. A complete medical review of sex, ages, symptoms, treatment course and outcome was recorded and compared.

Results: There were all 39 reported patients. Three additional cases had recurrent and refractory ear discharge even though aggressive antibiotics for otitis media mimicking PID-warning signs in the otolaryngologic and infection Clinics. Severe atopic dermatitis complicated by refractory cellulites in inguinal regions was mentioned. After unremarkable immunologic evaluations, local biopsy revealed LCH. These four cases presenting mimicking-PID warning signs were all classified as multisystem LCH and all recurrent but without risk organs involvement. Overall, the diagnosis-age ranged between 1 month-old (mo) to 161 mo (with a median of 24.5 mo). Eighteen patients (46.2%) were multisystem. The lag-time was significantly shorter in single-system group compared to those with multisystem (median 1.0 mo vs. 2.5 mo; $P < 0.003$). The diagnosis-age in patients involving risk organs was significantly younger than those without (median 8 mo vs. 43 mo; $P < 0.004$). No any significant existed in the diagnosed-age, lag time, classification and risk organs involvement between remission group and recurrent group.

Conclusions: With mimicking PID-warning signs, these four LCH patients in our study were all recurrent but similar diagnosed-age, lag-time, classification and prognosis compare to the others.

45 The Impact of Ketogenic Diet and High-Fat-High-Glucose Diet in Pristane Induced Lupus-Like Nephritis Murine Model

生酮飲食及高脂高糖飲食對狼瘡性腎炎小鼠模型的影響

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Background: Dietary components and metabolites can largely affect our physiological functions including the immune system. An interest in the anti-inflammatory property of ketogenic diet (KD) has recently come to attention. It not only alters the balance between Th17 and Treg cells, its metabolite, beta-hydroxybutyrate was known to block NLRP3 inflammasome-mediated inflammation. High-fat-high-glucose diet (HFGD), on the other hand, was known for a proinflammatory property. Aim to understand the immune modulatory effect of KD and HFGD in cases with systemic lupus erythematous, a chronic systemic inflammatory disease with glomerulonephritis, pristane induce lupus like nephritis murine model was used.

Methods: Pristane induced lupus nephritis mice were divided in to groups fed with regular chow (CD), KD and HFGD along with healthy controls. The diets were kept for 6 months with regular body weight and urine protein monitoring. Serum samples were collected for metabolic evaluation and immune survey bimonthly. The mice were sacrificed 6 months after diet change. Kidneys, lymph nodes, spleen, blood and guts were collected for evaluation.

Results: KD and HFGD were both well tolerated by experimental mice. Two months after diet change, higher level of beta-hydroxybutyrate and triglyceride but lower sugar level was noted in mice fed on KD when compared to those fed on CD and HFGD (all $p<0.05$). Mice fed on KD and HFGD have a much lower RBC and platelet count than those fed on CD in the experimental mice group (both $p<0.05$). Although global lymphocyte counts were much lower in those pristine treated mice, Th17 lymphocytes were significantly higher in the blood as well as kidneys among those fed on HFGD (all $p<0.05$). This is compatible with their high serum concentration of anti-dsDNA, anti-nRNP and anti-Sm and the rapid progressing proteinuria. Renal, hepatic and intestinal histopathology was still under analysis at present.

Conclusions: In conclusion, food plays a critical role in immune modification. Despite the reported anti-inflammatory effect of KD, it does not mitigate lupus nephritis progression. HFGD formula, however, accelerated the autoimmune phenotype for cases with lupus like glomerulonephritis.

46 Epidemiology and Risk Factors for Avascular Necrosis in Children with Systemic Lupus Erythematosus: a Population-Based Cohort Study

紅斑性狼瘡病童罹患骨頭缺血性壞死的流行病學與危險因子分析

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Background: The childhood onset of systemic lupus erythematosus (SLE) accounts for approximately 20% of all patients with lupus. Childhood-onset SLE is associated with greater disease activity at presentation, more aggressive course, and high rates of organ damage. The prolonged use of corticosteroids in childhood SLE contributes to increased morbidity, including avascular necrosis (AVN). To date, only a small number of studies about AVN in childhood SLE have been published, most of which have included relatively small cohorts.

Methods: We conducted this retrospective study to examine the frequency and risk factors for developing AVN in patients with childhood SLE using claims data from the Taiwan National Health Insurance Research Database (NHIRD). Cox regression analysis was used to assess the hazard ratios (HRs) and 95% confidence intervals (CIs) for

the development of AVN (ICD-9 codes 733.4x).
Results: A total of 1523 cases of childhood SLE were identified from January 1, 2005 to December 31, 2013.The female to male ratio was 6.2:1. A total of 39/1523 patients (2.6%) developed symptomatic AVN during a mean follow-up of 4.5±2.6 years. AVN most commonly affected the hips (87.2% of the patients). The patients with AVN received cyclophosphamide more often and had a higher frequency of lupus nephritis. On the other hand, significantly fewer patients with AVN received hydroxychloroquine prior to the onset of AVN. In univariate analysis, only a mean daily prednisone dose of 7.5 mg/day to 100 mg/day and the use of hydroxychloroquine were predictive and protective factors for the development of AVN, respectively. In multivariate analysis, mean daily doses of prednisone of 7.5 mg/day to 30 mg and 30 mg to 100 mg/day remained as significant risk factors for AVN. In addition, AVN was inversely related to the use of hydroxychloroquine
Conclusions: AVN occurred in 2.6% of the children with SLE in the course of follow up. High daily doses of prednisolone were associated with a significant risk of AVN, whereas the use of hydroxychloroquine conferred an advantage. Recognizing the risk factors and diagnosing AVN in the early stages remain the most effective ways of preventing AVN caused by corticosteroid treatment. .

47 The Correlation between VitD3 Levels and the Disease Activity of Childhood-onset Systemic Lupus Erythematosus (cSLE) in Taiwan

台灣兒童紅斑性狼瘡血中VitD3的濃度與疾病活性之間的關係

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Background: There are growing evidences linking the levels of vitamin D (25-OH) [VitD3] to an increased risk of many diseases such as diabetes, cardiovascular diseases, autoimmune diseases and different forms of cancer. Because of photosensitivity, hypovitaminosis D is more prevalent among children with SLE as compared to the general population. However, there remains controversial evidence as to whether vitamin D deficiency increases cSLE disease activity and vice versa. Therefore, we launch this study to assess the VitD3 levels in cSLE.
Methods: From Sep.to Dec 2018, we recruited 31 cSLE patients from Pediatric OPD in our hospital. All 31 patients fulfilled the diagnosis criteria from ACA 1997 and SLICC 2012. We checked their SLEDAI, laboratory SLE activities, drug usage and VitD3 level. VitD3 analysis was done using the commercial kit, Elecsys® Vitamin D total. The method for quantitative determination of VitD3 is a direct, competitive electrochemiluminescence immunoassay.
Results: A total of 31 patients were enrolled in the study. The mean age was 18±6.0 years old (range: 4-30 years) and mean SLE duration was 5.4±4.0 years(range: 0.17-12.17 years). Females accounted for 80.6% of the study population (n=25). The serum VitD3 concentration was 19.7±7.9 ng/ml. The mean SLEDAI-2K score at VitD3 measurement was 6.2±5.0 points (range: 0-20 points). We found higher VitD3 level in those had SLEDAI less than 5 points (22.9±7.7 vs 16.3±6.7points,p=0.008). Dividing patients by systemic corticosteroids (SCS) usage, those took no SCS had higher VitD3 level (29.8±9.8 vs 19.8±7.9ng/ml, p=0.0004) than those took SCS. However, the no SCS group has lower SLEDAI (2±2.45 vs 7± 5.03points, p=0.02), and higher C3 level (107±21 vs 83±25mg/dL, p=0.0087). Otherwise, the VitD3 levels showed no difference by grouping patients by gender, or age. There was moderate negative correlation between VitD3 level and SLEDAI (rs=-0.55, p=0.001), but no correlation between VitD3 versus C3, C4, Anti-dsDNA level.
Conclusions: VitD3 deficiency is common in patients with cSLE. Serum VitD3 level negatively correlates to SLEDAI. It can be partially explained by less usage of SCS in this study.

48 Analysis of the Relation between Vitamin D Contents of Mothers' Breast Milk, 25-hydroxyvitamin D Levels in Serum, and Disease Severity of Infants with Atopic Dermatitis

母乳中維生素D含量，血清25-羥基維生素D濃度與嬰兒異位性皮膚炎疾病嚴重程度的相關性分析

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Background: Atopic dermatitis (AD) is a chronic allergic skin disease with a typical symptom of pruritic skin rash and relapsing disease course. Recent study had found vitamin D deficiency to be strongly associated with childhood AD, and serum 25-hydroxyvitamin D [25(OH)D] levels to be inversely correlated with disease severity. However, the results are still unclear in infants with AD. We conducted a prospective study to determine the contents of Vitamin D in the breast milk and the serum levels of 25(OH)D from infants with AD and healthy controls.
Methods: We enrolled 44 infants in our study, of which 23 infants was diagnosed AD (AD group) and 21 of them was healthy infants (control group). We also collected breast milk at 5~6 months postpartum and analyzed Vitamin D contents inbreast milk form mothers of these 44 infants. We collected another 33 infants, including 17 infants with AD and 16 healthy infants, and analyzed the serum level of 25 (OH)D from these 33 infants.
Results: In the breast milk study, we found that vitamin D levels in the breast milk for control group (n = 21) was significantly higher than those for AD group (n = 23) (P = 0.02). In the serum study, we demonstrated that AD group (n = 17) had significantly lower serum 25(OH)D levels than

those in control group (n = 16) (P = 0.001) and that AD severity of these 17 infants as indicated by SCORAD showed inverse correlation with their serum 25(OH)D levels (r = -0.38, P = 0.18).
Conclusions: AD infants have lower vitamin D level in their mothers' breast milk. Compared with healthy controls, the serum 25(OH)D level was lower in the AD infants. The low serum level of 25(OH)D inversely correlated to their AD severity. We suggest that vitamin D and their active component 25(OH)D might play a critical role in the pathogenesis of AD and vitamin D supplementation might be helpful to treat AD.

49 Association of Macrophage Polarization and Impaired Arterial Stiffness in Juvenile Systemic Lupus Erythematosus

巨噬細胞極化與動脈硬化損傷在幼年型系統性紅斑性狼瘡病人上的關聯性

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Background: Systemic lupus erythematosus (SLE) is a common autoimmune disease worldwide. It is reported to have in high incidence of myocardial infarction and accelerated atherosclerosis with high morbidity and mortality in Western world. Endothelial dysfunction is a key process in the initiation and progression of coronary artery disease (CAD). Unfortunately, traditional CV risks cannot fully explain the pathogenesis of lupus endothelial dysfunction and CAD events. Due to the involvement of macrophage polarization consisting of classic M1 and alternative M2 in the different stages of atherosclerosis, it seems imperative to clarify the role of specific macrophage polarization and its regulation on endothelial cell function in SLE to early prevent and to customize therapeutic strategy for SLE patients at risk of CAD.
Methods: In this study, we collected blood samples from 60 patients of SLE of varying severity, studied their endothelial function by flow-mediated dilatation (FMD), and examined their vascular stiffness by vascular ultrasound.
Results: As the result, the plasma levels of interleukin (IL)-12 p40 were positively correlated to FMD at diastole but negatively correlated to the intima-media thickness (IMT) of left common carotid artery. In addition, macrophage inflammatory protein-1b, IL-10, IL-13 and IL-1 receptor a all negatively correlatively to IMT of left common carotid artery. EC function was associated with SLE disease activity index. Meanwhile, the levels of complement 3 and 4 were positively but antinuclear antibody was negatively associated with inflammatory protein-10, macrophage chemoattractant protein, tumor necrosis factor-α and IL-10.
Conclusions: In conclusion, it seems no specific macrophage polarization correlated to the endothelial function in SLE. However, the association of the plasma profile and endothelial function probably unscored the correlation of FMD and macrophage polarization in SLE.

50 Children Age and Coronary Artery Abnormalities in Kawasaki Disease

川崎症冠狀動脈擴張與年齡之關係

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Background: Coronary artery aneurysms are more severe in infants than in older children with Kawasaki disease (KD) was reported recently. We aimed to evaluate the relationship between age and severity of coronary artery abnormalities in KD in Taiwan.
Methods: We reviewed a total 478 patients diagnosed with Kawasaki disease retrospectively and compared coronary artery dilation in different age (included 3 months-old, 6 months-old, 1 year-old and 2 years-old) in recent 10 years in Kaohsiung Chang Gung Memorial Hospital.
Results: Of these patients during the study period, 365 patients had complete medical record of coronary survey by echocardiography. There were no statistically significant differences in regarding the coronary artery lesion (CAL) between different ages in cut-off by 3 months, 6 months, 1 years, 2 years, 3 years, 4 years, 5 years and 6 years in age (all $p > 0.05$). However, a higher incidence of coronary artery lesion was found in younger age children (6 month-old vs. 1 year-old vs. 2 year-old: 41.7% vs. 37.5% vs. 36.3%) but not reach a significant difference ($p > 0.05$). Anemia, hypoalbuminemia, CRP, lymphocyte count, Segmental/Lymphocyte ratio, Sodium showed significant difference with CAL formation ($p < 0.05$). After multiple logistic regressions, lymphocyte and albumin showed significant difference with CAL formation. (95% CI: 0.35-0.93, p=0.026)
Conclusions: Previous studies have indicated that Infants with KD have more severe coronary artery dilation compared with older children. Our results showed that there were no statistically significant differences in CAL formation between different ages but albumin and lymphocyte. Our findings implicate that CAL lesion should be monitored in any age.

51 FCGR2B Methylation Change in Difference Stage in Kawasaki Disease

FCGR2B甲基化在川崎症不同階段的變化

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Background: Kawasaki disease is a systemic vasculitis of unknown etiology that primarily affects children less than 5 years of age. The Fc gamma receptors (FCGR) family

contains multiple activating receptors, and a single inhibitory, FCGR2B. We investigated the dynamic methylation changes of FCGR2B levels in different stages as well as clinical treatment outcome in KD.
Methods: A total of 114 participants were enrolled in this study including fever controls (n=40, 2.29 ± 2.66 year-old), and KD patients (n=74, 1.79 ± 1.3 year-old). Whole blood cell (WBC) was collected before intravenous immunoglobulin (IVIG) treatment (KD1), 3 weeks after IVIG treatment (KD3), 6 months after IVIG (KD4) and 1 year after IVIG treatment (KD5), and 74 KD patients enrolled with all stage samples. After extracting WBC DNA from every stage, we converted it to methylation analysis using EZ-Methylation-LightningTM Kit, and then analyze the data after pyrosequencing.
Results: We found that there is no significant difference in FCGR2B methylation expression between fever control and KD1 (p=0.59). However, it is higher expression in KD3 compared to fever control and KD1 (both $p < 0.0001$) and then decreased after IVIG treated for one year (KD5). To rule out the possibility effect of age on methylation, we checked Pearson correlation between age and methylation level and showed negative correlation. Higher methylation percentage of FCGR2B in KD5 was found in this result than KD1, indicating increase of methylation levels in KD in spite of age. FCGR2B methylation level in KD1, KD3, KD4 and KD5 showed no significant with CAL (N=18) formation and non-CAL (N=56) ($p > 0.05$). On the other hand, patients with IVIG-resistance (N=14) showed significant hypomethylation in KD1 (P= 0.0007) but not significant different in KD3 (P= 0.06) and KD5 (P=0.99).
Conclusions: This is the first study to report the dynamic change of FCGR2B methylation and showed hypermethylation after IVIG treatment. Hypomethylation of FCGR2B is associated with IVIG resistance but not CAL formation

52 Impact of Urticaria on Anaphylaxis: A Nationwide Population-based Retrospective Cohort Study in Taiwan
尋麻疹與過敏性休克的關係

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Background: The clinical features of urticaria and anaphylaxis are similar, and they share common causal immune-mediated pathways. We aimed to investigate the risk of anaphylaxis among patients with urticaria.
Methods: A 12-year population- based retrospective cohort study was conducted. Investigated subjects were identified from the Taiwan National Health Insurance Research Database by the International Classification of Disease, Ninth Revision, Clinical Modification. We included 126 031 subjects with newly diagnosed urticaria and 252 062 matched controlsbetween 2000 and 2013. Risk of anaphylaxis among patients with urticaria was calculated by calculating adjusted hazards ratios (HR) after matching for confounding comorbidities.
Results: Urticaria was more common in women than it was in men (58% vs 42%), with a peak onset age of 20 – 40 years. The number of comorbidities including asthma, allergic rhinitis, herpes zoster, hepatitis B and C, rheumatoid arthritis and gout were higher in patients with urticaria than that in age- and sex-matched controls. The crude HR for anaphylaxis among urticaria subjects was 2.883 (95% confidence interval [CI], 2.787 – 2.982; $P < 0.001$). After adjustment for potential confounders which have been proposed to increase the risk of anaphylaxis, patients with urticaria were found to be at a significantly high risk of anaphylaxis with an adjusted HR of 2.529 (95% CI, 2.442 – 2.619; $P < 0.001$).
Conclusions: Incidence rate of anaphylaxis is significantly high in patients with urticaria in Taiwan.

53 Role and Function of Recombinant Der m2 Protein in Asthma Animal Model
重組微角塵蟎Der m2蛋白的功能與誘發動物氣喘模式的角色

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Background: Asthma, a heterogeneous inflammatory disorder of the airway,is a major public health issue. T helper 2 cells(Th2) responses are usually contributed to high levels of allergen-specific immunoglobulin E(IgE) and eosinophilia airway inflammation. Recently, several findings demonstrated that asthma/allergy may causes by living environment. The house dust mites(HDMs) are one of the most important allergens that have been identified in the household environment. HDMs could induce airway inflammation through activation of innate and adaptive immunity and lead to asthma. Well known allergens of HDMs, including Dermatophagoidespteronyssinus(Der p), Dermatophagoidesfarinae(Der f), Blomiatropicalis(Blo t)are important allergens in the Taiwan's asthma research field.
Methods: We were conducted clinical tests on 462 allergic children (2-16 years old) in central Taiwan and found that more than 80% of them were sensitizing to various HDMs. The major allergens were respectively: Der p: 89.0%; Der f:87.0%; Blo t:77.0%and Dermaphagoides microceras: 84.5%. According to the result, not only Der pand Der f, but

also Derm was an important allergen in Taiwan. Der m draft genome bynext generation sequencing(NGS) technology that putativegene structures Der m1 to Der m33 with amino acid sequence homology. The Der m 2is considered to be an important allergen and we investigated the Der m 2-sensitization asthma animal model and cell experiment in THP-1 and BEAS-2B cells in our study.
Results: Der m 2 could sensitization successful in animal. The AHR was high compared with normal group ($p < 0.027$), Der m 2-specific IgE ($p < 0.033$) and Th2 cytokines (such as IL-4 ($p < 0.019$); IL-5 ($p < 0.045$) and IL-13 ($p < 0.011$))were highest express than normal group. Moreover,in cell experiment, used recombinant truncated Der m 2 stimulated in THP-1 and BEAS-2B cells after treated with 200 nM PMA that Der m 2 could induce high IL-6 and CXCL1. The recombinant truncated Der m 2 protein is active.
Conclusions: In our study found that Der m 2 really an allergen in animal and cells model. Therefore, to clarify the majority Der m dust mite allergens and whether the HDMs was one or various intopic allergic/asthma patients is necessary and important.

54 Associations between Oxidative Stress Markers, Allergic Indices and Childhood Atopic Diseases

氧化壓力標記與過敏性指標以及孩童時期過敏性疾病間的關係

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Background: The association between oxidative stress and atopic diseases is uncertain. Although many risk factors for atopic diseases have been identified, a comprehensive investigation of the relationship between oxidative stress markers and allergic indices related to atopic diseases is currently lacking.
Methods: Children aged 7 from a birth cohort in the Prediction of Allergies in Taiwanese Children (PATCH) study were enrolled. Plasma levels of glutathione peroxidase (GPx) and total anti-oxidant capacity (TAC) were quantified using an automatic chemical analyser. Plasma levels of myeloperoxidase (MPO) and urinary levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG) were determined using enzyme-linked immunosorbent assay (ELISA) kits. Allergen-specific IgE levels against food and aeroallergens, FeNO levels, and pulmonary function tests were also measured and obtained.
Results: A total of 132 children who completed a 7-year follow-up were recruited in this study. The activity of GPx and levels of MPO were inversely correlated to food (shrimp and crab) and house dust mite sensitization respectively. Furthermore, the 8-OHdG levels were strongly negatively correlated with FeNO levels ($p < 0.01$). Moreover, a significant positive correlation was found between TAC levels and pre-and post-bronchodilator FVC % and FEV1 % predicted ($p < 0.05$). There were no associations of all oxidative stress markers for the risk of atopic diseases. However, GPx-related crab sensitization and 8-OHdG related FeNO levels were significantly associated with increased risk of allergic rhinitis, while MPO-related mite sensitization and TAC-related pulmonary function parameters were strongly associated with increased risk of asthma ($p < 0.01$).
Conclusions: Oxidative stress appears to have no association with atopic diseases but is correlated with allergic indices relating to increased risk of atopic diseases. Oxidative stress potentially plays a role in the modulation of allergic responses for atopic diseases.

55 Clinical Correlation of Cow Milk Protein Allergy with Serum IgE/IgG4 Ratios

血清牛奶特異性抗體IgE/IgG4比值與牛奶蛋白過敏臨床表現之相關性研究

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Background: Milk protein allergy is an important issue for young children. Antigen-specific serum antibody testing is currently the most prevalent method in Taiwan for identifying specific food allergy. IgE, the most widely used antibody marker in antigen-specific serum test, indicates the possible allergic reaction on exposure to food allergen. On the other hand, antigen-specific IgG4 serves as a protective role and is deemed as a marker of oral tolerance. We proposed that IgE/IgG4 ratio can deliver a better correlation to clinical symptoms than using individual marker alone.
Methods: We collected sera from whom diagnosed or in suspicion of milk-protein allergy after informed consent from November, 2017 till present. The diagnosis of milk protein allergy is based on clinical presentations. The sera were analyzed for antigen-specific IgE and IgG4 levels of cow milk-protein and its components: α-lactalbumin (α-LA), β-lactoglobulin (β-Lg) and casein using purchased kits. The IgE/IgG4 ratio, as well as IgE and IgG4 level for individual components were obtained and statistically analyzed.
Results: We collected 20 blood samples. 11 of them from milk-allergic patients and 9 from non-allergic. Among them, 13 were milk-specific or component-specific IgE sensitized

(10 allergic + 3 non-allergic) and the other 7 (1 allergic + 6 non-allergic) were not. The mean IgE level of milk protein and the three component proteins between allergic and non-allergic groups were all significantly different statistically. The difference is even more significant in the case of IgE/IgG4 (p-values: milk: 0.003; α-LA: 0.001; β-Lg: 0.004; casein: 0.000). Whereas IgG4 level alone failed to show statistical difference. Among patients who were positive for serum IgE sensitization, 3 of them were non-allergic, and all of them had IgE/IgG4 ratios which was significantly lower than those with symptoms. The IgE/IgG4 ratio that discriminates symptomatic from asymptomatic group was around 0.01 to 0.1.
Conclusions: IgE/IgG4 ratio may give a more precise clinical correlation of milk protein allergy than IgE level alone. It may be a better clinical indicator than current serum antigen-specific IgE testing.

56 The Diagnostic Value of In Vitro Food Allergen-specific IgE in Children with Clinical History of Food-induced Allergic Symptoms

過敏原特異性IgE對臨床食物過敏症狀兒童的診斷價值

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Background: Food allergy become common in children and adults in recent years. Clinical history with positive skin prick tests or food-specific IgE help us to make diagnosis precisely. Comparing to skin prick test, food-specific IgE is a more safe and rapid test in out-patient department. Our goal is to evaluate how reliable of food-specific IgE in the diagnostic of food allergy.
Methods: We collected total 16 patients (mean age ? gender ratio ?), who presented clinical food allergy history, by questionnaire and medical records from 2013-2018. Blood sample was sent for further evaluation of allergen-specific IgE (BioIC). We divided these patients into four groups (egg, milk, peanut and shellfish) of food allergy and analyzed the positive predictive value and negative predictive value.
Results: For these patients, we found that the best positive predictive value (PPV) were milk (PPV=0.8, NPV= 0.82) and peanuts (PPV= 0.80; NPV=0.82) and negative predictive value (NPV) was shellfish (PPV= 0.33; NPV= 0.92), followed by egg allergy (PPV= 0.56; NPV=0.86).
Conclusions: For food-specific IgE, positive findings of milk and peanut allergens sensitization seemed more comparable to clinical history. On the other hand, negative finding of shellfish allergen has higher chance to exclude shellfish allergy. However, due to low numbers of patients, more case data is needed for further confirmation.

57 The Anti-inflammatory Effect of Clara Cell 10-kd Protein (CC10) on Neutrophil Superoxide Generation and Arachidonic Acid Metabolism

克拉氏蛋白質調控經由嗜中性球過氧化物生成與花生四烯酸代謝路徑的發炎反應

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Background: Reactive oxygen species produced by neutrophils contribute to signal the inflammatory response and a variety of arachidonic acid (AA) metabolites also have similar effect. We have previously shown that CC10, the main secretory product of bronchiolar Clara cells, plays an important protective role in the respiratory tract against inflammatory processes. To this end, the potential involvement in mediating CC10's anti-inflammatory effects was evaluated in human neutrophils.
Methods: The functional effects of CC10 on fMLP+TNF-α-induced superoxide generation in human neutrophils were determined. In addition, the inhibitory activity of CC10 on the AA/COX-2 or 5-LO pathway and release of inflammatory lipid mediators in fMLP -induced neutrophils was determined by Western blotting and ELISA.
Results: In human neutrophils, it was shown that CC10 significantly suppressed the superoxide production induced by fMLP+TNF-α. Moreover, functional studies revealed that fMLP-induced expression of COX-2 synthase, but no 5-LO synthase was significantly inhibited by CC10. Furthermore, CC10 was shown to be able to significantly inhibit the fMLP-induced generation of AA metabolites, PGE2, (but not the AA metabolite LTB4), in neutrophils. A composite of serum CC10, PGE2 and 11β-PGF2α levels was significantly distinguishable between asthmatic and healthy subjects; also, a negative correlation was noted between the levels of CC10 and PGE2 ($r=0.78$; $p<0.01$).
Conclusions: These data suggested that modulation of the superoxide generation and AA/COX-2 pathway could be a novel mechanism for the anti-inflammatory effects of CC10.

58 Effect of Long-acting Beta-2 Receptor Agonist on IL-25 Expression in Human Bronchial Epithelium

長效乙二型受體刺激劑對於人類呼吸道上皮細胞分泌之IL-25之影響

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Background: Asthma is a chronic inflammatory airway disease and could be induced exacerbation by many environmental factors. interleukin-25 (IL-25) are important initiators of asthma-associated mucosal inflammation. The predominantly epithelial cell–derived cytokine—IL-25 has emerged as important initiators of type 2 cytokine production. Long-acting β2-agonists (LABAs) are useful for prolonged bronchodilation in asthma, usually in combination with inhaled corticosteroids (ICSs). Bronchial epithelial cells are first-line barrier against invasive pathogen and also have immunomodulatory effect. However, little is known of the effects of salmeterol and formoterol and a new extra-LABA (indacaterol) on IL-25 expression and potential mechanisms of cytokine production in bronchial epithelial cells.
Methods: The human bronchial epithelium cell line (A549) was pre-treated with different concentrations of salmeterol, formoterol (two LABAs) or indacaterol (a new extra-LABA) without other stimulation. A549 were pre-treated with ICI-118551, a selective beta2-adrenoreceptor antagonist, 30 min before salmeterol, formoterol or indacaterol treatment. The level of IL-25 was measured by RT-PCR.
Results: Salmeterol, formoterol and indacaterol could induce IL-25 expression in A549. ICI-118551 could reverse the effects of formoterol on IL-25 expression in A549. Fluticasone and budesonide could also suppress LABA-induced IL-25 expression in A549.
Conclusions: LABAs and extra-LABA could induce IL-25 expression in human bronchial epithelial cells via, at least, partly the beta2-adrenoreceptor pathway, implicating that LABAs alone may enhance inflammatory effect and exacerbate asthmatic patients by induction of IL-25 expression. ICSs could suppress LABA-induced IL-25 expression in bronchial epithelium.

59 Effect of Leukotriene Receptor Antagonist on IL-25 Expression in Human Bronchial Epithelium

白三烯素受體刺激劑對於人類呼吸道上皮細胞分泌之IL-25之影響

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Background: Asthma and allergic diseases are Th2-related inflammatory diseases. The group 2 innate lymphoid cells (ILC2s) and Th2 cells were largely thought to be the primary source of type 2 cytokines. Epithelial derived cytokines IL-25, IL-33, and TSLP as activators of ILC2s, and recent studies have identified these cytokines are involved in ILC2-mediated Th2-related cytokine production. The leukotriene receptor antagonist (LTRA), e.g. montelukast is recommended for the treatment of asthma, exercise -induced bronchospasm and allergic rhinitis. In the present study, we investigated the effect of LTRAs on the production of IL-25 in bronchial epithelial cells.
Methods: The human bronchial epithelial cell line (A549 l cells) was pre-treated with different concentrations of montelukast at the different time points with or without DEHP stimulation or budesonide treatment for 30 minutes. The production of IL-25 was measured by RT-PCR.
Results: Montelukast and zafirlukast could induce IL-25 mRNA expression in A549 cells. Fluticasone (ICS) could suppress montelukast-induce IL-25 mRNA expression in A549 cells. Another ICS, budesonide also reduced montelukast-induced IL-25 expression in A549 cells. DEHP, a plasticizer, could also induced IL-25 expression in A549 cells. Montelukast has suppressive effect on DEHP-induced IL-25 expression in A549 cells.
Conclusions: LTRAs alone had a potent effect to induce epithelium-induced ILC2-related cytokine IL-25. However, LTRAs suppressed plasticizer-induced IL-25 expression in bronchial epithelial cells.

60 Time Trend Prevalence of Asthma among Elementary School Students in Southern Taiwan from 2004 to 2018

西元2004年至2018年南台灣小學學童氣喘盛行率之趨勢

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Background: The prevalence of asthma in children is increasing in developed countries as well as in Taiwan.

However, several studies showed the possibility that increase trend has slowed or ceased. Therefore, we would like to know whether the same trend of increasing childhood asthma also occurred in Tainan and to verify the relationship between potential risk factors and the prevalence of childhood asthma and current respiratory symptoms.
Methods: From 2004 to 2018, we use ISAAC-Chinese version questionnaire to conduct a survey for allergic diseases and current symptoms in the elementary school student grouped from grade 1 to grade 6 in Tainan city. A total of 20,193 school children were enrolled. We analyzed annual asthma prevalence of 19,572 cases who completed 4 core questions about asthma. Multivariable logistic regression analysis was used to examine whether the prevalence of asthma and current respiratory symptoms over time could be explained by any selected determinants, such as age, gender, breast feeding, family history and environmental factors.
Results: The prevalence of physician-diagnosed asthma remained constant from year 2004 to 2012, and deceased in years 2017 and 2018 (10.72% in 2004, 10.88% in 2008, 10.99% in 2009, 10.73% in 2010, 10.64% in 2011, 11.18% in 2012, 8.35% in 2017, 9.56% in 2018). In contrast, the prevalence of reported paternal asthma increased significantly. Environmental factors remained virtually unchanged. The prevalence of breastfeeding were significantly increased in year 2017 and 2018 as compared to previous years (35.68% in 2004, 42.21%% in 2008, 42.87% in 2009, 49.53% in 2010, 47.89% in 2011, 51.90% in 2012, 79.15% in 2017, 71.13% in 2018). Multivariable logistic regression results shows that children who had ever been breast fed had a reduced risk of having asthma and current respiratory symptoms compared with children who had never been breast fed.
Conclusions: This survey shows the prevalence of physician- diagnosed asthma and current respiratory symptoms ceased to increase from 2004 to 2018. Increased prevalence of breast milk feeding seems to be the possible protective factor responsible for the decreases trend of childhood asthma in Tainan area.

61 The Perinatal Risk Factors of Acute Bronchiolitis before One Years Old

一歲前急性細支氣管炎的周產期危險因素

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Background: Bronchiolitis is one of the leading causes for infant hospitalization and is associated with lower respiratory tract infections, which caused by virus. We evaluated effectiveness of breastfeeding and other perinatal factors affecting occurrence of hospitalization for bronchiolitis.
Methods: In a prospective case-control cohort study, 150 infants with age no elder than 1 year old were enrolled in 2 medical centers from southern Taiwan. Questionnaires were distributed and by medical professionals. Children were grouped as “exclusive breastfeeding” and “mixed and exclusive formula milk feeding”. The risk of hospitalization for bronchiolitis was evaluated by using univariate analysis. Logistic regression was applied to evaluate risks of hospitalization for bronchiolitis. Odds ratios (OR) with 95% confidence interval (95% CI) were calculated.
Results: Among enrolled infants 36.7% were diagnosed with acute bronchiolitis, and 15.3% were “exclusive breastfed”. The risk of hospitalization for bronchiolitis was significantly lower in the “exclusive breastfeeding” group (OR: 0.222, 95% CI: 0.058-0.847). Also, history of respiratory viral infection during pregnancy was associated with significant increased risk of children’s hospitalization for bronchiolitis (OR: 2.758, 95% CI: 1.095-6.948).
Conclusions: Exclusive breastfeeding reduced the risk of hospitalization for bronchiolitis in children within first year of life. Also, maternal respiratory infection during pregnancy increased risks of acute bronchiolitis for children. Exclusive breastfeeding might be effective measure of prevention of lower respiratory tract infection in infant younger than 1 year old.

62 Clinical Features of Gingivostomatitis due to Primary Infection of Herpes Simplex virus in Children in Northern Taiwan: An Experience in Tertiary Medical Center

北台灣兒童皰疹性齒齦炎的臨床表徵

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Background: To define clinical features of primary herpetic gingivostomatitis (PHGS) in children, we studied pediatric patients with culture-confirmed herpes simplex virus (HSV) infection during 2012 to 2016.
Methods: Between January 2012 to December 2016, 284 patients aged less than 19 years had culture-proved HSV infection in Chang Gung Memorial Hospital. Clinical data were retrospectively collected.
Results: Among 284 isolates, 187 cases were considered as PHGS and were enrolled for analysis. All of them were infected by serotype 1 (HSV-1). Of 185 inpatients, 99.5% had fever, which could be as long as 17 days (5.11±2.24). Oral manifestations were the most common clinical symptoms including oral ulcers (84.3%), which equally resided in the anterior and posterior part of the oral cavity (65.4% vs. 63.2%), gum swelling or bleeding (67.6%), sore throat (49.2%) and exudate coated tonsils (16.8%).

Laboratory findings included leukocytosis (28.1% ＞ 15,000/mm3) and elevated C-reactive protein (29% ＞40 mg/L). Meanwhile, only 35% cases could be diagnosed as PHGS in the very beginning. Compared to others, these patients were more likely had ulcers over the anterior oral cavity (76.1% vs. 26.7%) and gum swelling/bleeding (76.2% vs. 7.5%, p all ＜0.001) and were less likely to receive antibiotics treatment (16.9 vs. 36.7%, p=0.009). Altogether, only 4 cases had complications including 3 central nervous system involvements and 1 disseminated infection. None of them died.

Conclusions: Though PHGS in children was usually self-limited, it might mimic bacterial infection clinically. Early diagnosis by identified specific oral manifestation could reduce unnecessary prescription of antibiotics and hospitalization.

63 Antiviral Activity and Mechanism of Pharmaceutical Combination of Echinacea Purpurea and Fresh Salvia Miltiorrhiza

紫錐花及丹蔘萃取物抗病毒組合物之抗病毒作用及機轉

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Background: EV71 causes many fatal cases worldwide and adenoviruses are highly transmissible with great disease burden in children, but there is no available commercial antiviral medication against adenoviruses or enterovirus 71.

Methods: we screened antiviral activities of plants and herbs with different methods of extraction and different combinations. We measured the IC50 (50% inhibitory concentration) against adenovirus type 3 and enterovirus 71 (EV71) by plaque assay, CC50 (50% cytotoxicity concentration) by XTT cytotoxicity assay and calculated the selective index (SI: CC50/IC50).

Results: According to IC50 and SI, 2 best candidates (the water extract of Echinacea purpurea aerial component, EPA-W, for adenovirus serotype 3 with IC50 of 4.6 ug/ml; the ethanol extract of fresh Salvia miltiorrhiza, SMf-2-E, for EV71 with IC50 8.3 ug/ml) were chosen to make this antiviral pharmaceutical combination. The optimal combination ratio of EPA-W: SMf-2-E was 3:7 to have the best antiviral activity. We further investigated their antiviral mechanism and found that the antiviral mechanism of EPA-W was mainly through inhibiting attachment and that of SMf-2-E was mainly through inhibiting penetration.

Conclusions: This antiviral pharmaceutical combination of EPA-W and SMf-2-E, safe and effective with different antiviral mechanism, can be applied to make antiviral therapeutic or preventive products in the future.

64 Highly Antimicrobial-resistant Nontyphoid Salmonella Infection in Children in Northern Taiwan

北台灣兒童的高度抗藥性非傷寒沙門氏菌感染分析

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Background: Nontyphoidal Salmonella (NTS) is a major food-borne pathogen for enteric infection worldwide. The epidemiology of NTS resistant to ciprofloxacin or ceftriaxone and its impact on patients' outcome are rarely reported.

Methods: Children with culture-proven salmonellosis treated in a medical center in northern Taiwan in 2017 were enrolled. Antimicrobial susceptibility was performed by disc diffusion test, and susceptibility to ciprofloxacin or ceftriaxone was further measured by E-test. The serotypes of highly resistant Salmonella were determined. Food samples from markets at hot zones, mapped by residences of the patients, were examined for NTS.

Results: Among the 453 isolates, 122 (26.9%) were highly resistant strains, as defined by resistance to ciprofloxacin or ceftriaxone or both. The most prevalent highly resistant serotypes was S.Anatum (54.1%, 66), followed by S. Typhimurium (15.5%, 19), and S. Enteritidis (9.8% , 12). S. Anatum often showed multidrug resistance (resistance to 3 or ＞3 drug classes) (98.5 %). Salmonella was detected in 94.1%, 66.7%, and 8.6% of pork, chicken, and vegetables examined, respectively. S. Anatum (23.0%), S. Derby (19.2%), and S. Albany (15.3%) were the top three serotypes isolated from food samples. Of the S. Anatum from food, 83.3% was highly resistant. Patients with ceftriaxone-resistant NTS infections had prolonged hospital stay than those with ciprofloxacin- resistant only NTS and those with non-highly resistant infections (9.0±8.6 vs 4.9±2.3 and 5.8±3.7 days, both P＜0.001). Totally 33 (7.2%) presented with invasive disease, including 31 (6.8%) bacteremia, 1 intestinal perforation (0.2%), and 1 septic arthritis (0.2%). Risk factors for invasive disease included prolonged fever for more than 5 days (OR =4.7, 95 % CI: 2.2-11.2, P＜0.001), and infection during warmer seasons from May to October (monthly average temperate, ＞ 25 o C) (OR= 3.6, 95 % CI: 1.0-12.9, P＜0.044).

Conclusions: The incidence of highly antimicrobial-resistant NTS infection in children was high in northern Taiwan. Retail meat was the major source of these NTS. Highly antimicrobial resistance significantly impacted the clinical course and treatment of the patients.

65 Emergence of Multidrug-Resistant Salmonella Enterica Serovar Anatum Infection in a Medical Center in Central Taiwan, 2015-2018

台灣中部一家醫學中心多重抗藥性沙門氏菌感染的出現，2015-2018

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Background: Nontyphoidal Salmonella causes bacterial gastroenteritis, bacteremia and other invasive diseases in humans. Salmonella antimicrobial resistance is increasing and can cause treatment failure. Since 2015, multidrug-resistant Salmonella strains have emerged, complicating antibiotic use in patients with invasive diseases in Taiwan. In this study, we report the epidemiology of Salmonella enterica Serovar Anatum infection.
Methods: From 2015 to 2018, 1,200 nontyphoidal Salmonella strains obtained from patients in China Medical University Hospital were sent to the Taiwan Centers for Disease Control for serotyping by using PFGE pattern comparison and conventional methods. The clinical features and antimicrobial drug sensitivity were retrospectively reviewed.
Results: A total of 68 patients were included [33 (49%) male; 50 (73.5%) < 18 years of age]. Seventy one Salmonella enterica Serovar Anatum strains were obtained from stool (n=59), blood (n=5), pus (n=5) and urine (n=2). The number of Salmonella Anatum infection increased between 2015 and 2018, and accounted for 0.17%, 4.58%, 8.61% and 10.23%, respectively. Fever (73.5%), diarrhea (69%) and vomiting (25%) were the most common symptoms. The diagnoses were as follows: gastroenteritis (n=59), bacteremia (n=5), cellulitis (n=4), osteomyelitis (n=1) and urinary tract infection (n=1). There was no resistance to levofloxacin. The highest resistance was observed in response to ampicillin (100%), trimethoprim/ sulfamethoxazole (100%) and nalidixic acid (100%), followed by ceftriaxone (24.3%) and ciprofloxacin (18.3%). Multidrug resistance was detected in 22.5% of Salmonella Anatum isolates.
Conclusions: Multidrug-resistant Salmonella enterica Serovar Anatum strains have emerged. Our study will provide useful information for treating invasive Salmonella infections. Urgent control measures are needed to prevent spreading of these multidrug-resistant strains.

66 The Epidemiology and Antimicrobial Susceptibility of Nontyphoid Salmonella Bacteremia in Children in Southern Taiwan during 2008~2016

2008至2016年南台灣兒童非傷寒性沙門氏菌血症之回溯性分析

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Background: Despite the significant improvement in public health in Taiwan, non-typhoidal salmonella (NTS) bacteremia remains a common cause of bacteremia in children. This study aims to investigate the epidemiological, clinical and microbiologic characteristics of patients with NTS bacteremia in a tertiary center in Southern Taiwan.
Methods: We retrospectively reviewed children with blood culture positive for NTS bacteremia treated at Kaohsiung Chang Gung Memorial Hospital from May 2008 to November 2016. Clinical data from the initial visits and any follow-up visits or hospitalizations were recorded.
Results: We studied 114 patients. 63 (55.2%) were male children and 102 (89.4%) were below 36 months of age. The majority of cases (94%) had no documented underlying immunodeficiency, malignancies or conditions requiring immunomodulatory agents. Fever (100.0%) and diarrhea (83.3%) were the most common initial presentations. Salmonella serogroup B(35.1%, 40/114) was the most common serotype isolated from blood culture, followed by serogroup D(30.7%), and C2(21.9%). Focal suppurative infections were found in 4 previously healthy children (3.5%), with 2 meningitis and 2 osteomyelitis. Recurrent disease was found in 1 children. Extra-intestinal complication is not associated with underlying immunocompromised condition, persistent bacteremia or in-appropriate antibiotic use. No fatalities occurred in this study. Antimicrobial resistance was found among ampicillin (23.5%), trimethoprim-sulfamethoxazole (19.1%), and ciprofloxacin (11.3%). All of the isolates were found susceptible to ceftriaxone.
Conclusions: In healthy children, NTS bacteremia was relatively benign and extraintestinal focal suppurative infections were not commonly seen. In this study, Salmonella remained susceptible to empirical use of ceftriaxone or ampicillin in children.

67 Minocycline in Enterovirus 71 Infections

Minocycline在腸病毒71型感染的作用

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Background: Enterovirus 71 (EV71) brain stem encephalitis (BE) was stratified into uncomplicated BE, autonomic nervous system (ANS) dysregulation, and pulmonary edema (PE) based on cytokine-mediated systemic and central nervous system inflammatory responses. Minocycline has been found to have anti-apoptotic, anti-inflammatory and immunomodulatory properties in infectious and inflammatory disease models.
Methods: The effects of minocycline on cytokine expressions and viral replications were investigated in rhabdomyosarcoma (RD), U-87MG, and THP-1 cells. The mouse-adapted-EV71 strain (MP4)-infected 7-day-old ICR model was used to explore the anti-inflammatory and antiviral effects of minocycline for the treatment of EV71 infection.
Results: The levels of interleukin (IL)-6 and IL-8 and relative mRNA expressions of IL-12p40, IL-1β, and tumor necrosis factor (TNF) decreased in U-87MG cells after minocycline treatment. The levels of TNF, IL-1β, IL-6, and IL-8 decreased with a single dose of minocycline in EV71-infected THP-1 cells. Double-dose minocycline treatment demonstrated more effective cytokines reduction. In the MP4-infected animal model, clinical scores and mortality rates were decreased evidently after double-dose minocycline treatment. Minocycline treatment markedly reduced viral titers in various brain tissues. Minocycline inhibited IL-6 and granulocyte colony-stimulating factor (G-CSF) in plasma and TNF in the cerebellum.
Conclusions: Minocycline has properties that enable it to function both as an anti-inflammatory and antiviral agent in EV71 infection. These results evidence its potential usefulness in clinical treatment.

68 Divergent Serotypes in Pneumococcal Carriage between Children with Otitis Media, Sinusitis, and Middle Ear Effusion and Matched Healthy Children in the PCV13 Era

PCV13世代中耳炎、鼻竇炎、中耳積液與健康兒童肺炎鏈球菌鼻咽部帶菌血清型差異

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Background: Pneumococcal conjugate vaccines have significantly decreased the incidence of pneumococcal disease and carriage in children. However, little is known about the serotype distribution of pneumococcal carriage in children with acute otitis media, acute sinusitis, and middle ear effusion and healthy children.
Methods: Nasopharyngeal swabs for S. pneumoniae were performed in children with acute otitis media, acute sinusitis, middle ear effusion (disease group) and healthy children (control group) by culture and PCR from Aug. 31, 2016 to Apr. 30, 2018. Antibiotic susceptibility testing and serotyping were examined.
Results: Totally 397 children were enrolled, including 200 children in the disease group and 197 healthy children in the control group. Pneumococcal carriage was identified by culture in 72 children (18.1%, 38 in the disease group and 34 in the control group). By PCR, pneumococcal carriage was identified in 74 children (18.6%, 42 in the disease group and in 32 in the control group). Among 72 pneumococcal isolates, 90.3% and 87.5% isolates were susceptible to penicillin and cefotaxime, respectively. Among 74 isolates identified by PCR, non-vaccine serotypes accounted for 59 (79.7%) isolates and vaccine serotypes accounted for 15 (20.3%) isolates. The first three common serotypes were 23A, 19A, and 15B/C. Among colonized children, vaccine serotypes were more common in the disease group (28.6%) than in the control group (9.4%) ($p = 0.0475$).
Conclusions: In the PCV13 era, nearly 20% of children had pneumococcal carriage. Among colonized children, vaccine serotypes were more common in children with acute otitis media, acute sinusitis, and middle ear effusion than in healthy children.

69 Relationship between Childhood Otitis Media and Mental Stress

兒童中耳炎與心理壓力之關係

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Background: Stressful life are linked to poor developmental and health outcomes in children, but it is not clear whether children's mental stress is related to otitis media as well. As part of a long-term study surveying characteristics of child care and development of children, we tested the relationship between otitis media and sources of mental stress in children including daycare attendance, maternal depression and parental harsh discipline.
Methods: We analyzed data on 1998 children at 3-year-old. In bivariate and multivariate logistic regression models, several risk factors were tested as independent predictors of two outcomes: parent-reported child health and rate of otitis media.
Results: Daycare attendance, maternal depression, and parental harsh discipline were related to parent-report rate of otitis media.
Conclusions: The rate of otitis media was associated with sources of child mental stress. This finding suggests providing psychosocial support to both parents and children may be a new strategy in prevention of otitis media.

70 Antibacterial Activity of Silver Nanoparticles (AgNP) Confined to Mesostructured Silica sgainst Methicillin-Resistant Staphylococcus Aureus (MRSA)

二氧化矽孔洞結構上的奈米銀粒子（AgNP）對抗藥性金黃色葡萄球菌（MRSA）的殺菌能力

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Background: Staphylococcus aureus infections accounts for more than 50% of the joint replacement surgery failure, methicillin-resistant Staphylococcus aureus (MRSA), have appeared and are causing a significant reduction in the efficacy of traditional antibiotics. In this study, silver nanoparticles (AgNP) confined to mesostructured silica (MSAg) powders were prepared to evaluate their antibacterial activity against MRSA.
Methods: 1. Prepared AgNP confined to mesostructured silica (MS-Ag) powders with composition ratios of Si to Ag of 100 to x, where x= 0, 1, 5, or 10. 2. Use Fourier transform infrared spectroscopy (FTIR) and X-ray diffraction (XRD) analyzed the structure of MS-Ag. 3. Disk diffusion method analysis for antibacterial efficacy and Time-killing curve analysis for different concentration of MS-Ag1, MS-Ag5 and MS-Ag10 powders to investigate the growth of methicillin-resistant Staphylococcus aureus (MRSA) during the time.
Results: 1. The results of the disk diffusion method showed that MS-Ag5 had the best antibacterial efficacy due to having the largest inhibition zone. 2. The results of Time-killing curve analysis revealed MS-Ag5 extract concentration was in the range of 5-20 mg/mL, the OD600 showed a flat trend during the 24 h test interval, which indicated that they could effectively inhibit the growth of MRSA.
Conclusions: 1. According to the results of the TGA, there was no weight loss when the temperature was greater than 600C. This result showed that the water, alcohol, non-ionic surfactant F127 and PUF in the silicone-containing colloid were completely removed. These results indicated that the calcination temperature for total dehydration was at least 600C. 2. The MS-Ag5 powders had the lowest MIC against MRSA in the range of 2.5-5 mg/mL according to the time-killing curve analysis. This result was supported by the disk diffusion method as the MS-Ag5 powders had greater antibacterial efficiency against MRSA than the MS-Ag1 or MS-Ag10 powders.

71 Is Urine pH Value one of the Clinical Characteristics of Common Uropathogens in Children

兒童泌尿道感染致病菌與尿液ph值之關聯性研究

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Background: Urinary tract infections (UTIs) are one of the most common pediatric infections worldwide. This study aimed to systematically describe the distribution of urine pH across age, sex, and common uropathogens among urine specimens. We also provide, for the first time, epidemiologic evidence based on a large sample size, to shed insight into the role of urine pH in predicting uropathogen and risk management in pediatric UTI.
Methods: The source population was 26,066 paired urinalysis (UA) and urine culture (UC) obtained from the pediatric patients during 2003 and 2016 at China Medical

University Hospital (CMUH). We further classified paired UA-UC into having UTI (N = 6,348) and not having UTI (N = 19,718) based on the colony forming unit (CFU) and the sampling source. We restricted our study population to pediatric UTIs that were caused by single species of pathogen (N = 5,201). We compared the characteristics between controls and study population to study the association between urine pH and pathogens causing UTI.

Results: Of 5,201 pediatric UTIs included in the current study, the mean pH of urine samples from patients with UTI was 6.27 and that from matched patients without UTI was 6.24. We broke down the UTI samples by the 10 most common uropathogens. Urine that grew P. mirabilis or P. aeruginosa demonstrated the most alkaline pH (mean pH = 6.72 and 6.62, respectively) and were significantly more alkaline than the urine without UTI. Urine with K. pneumonia and E. coli showed the most acidic pH (mean pH = 6.18 and 6.21, respectively). After stratifying UTI samples by their pH range (＜6, 6 – 6.9, 7 – 7.9, ＞=8), we observed that the distribution of the proportion of uropathogens shifted across different pH range, especially the distribution of E. coli and P. mirabilis. P. mirabilis showed an increasing trend in prevalence across incraeasing pH categories.

Conclusions: This is a population-based cohort study described the distribution of urine pH of different uropathogens. Alkaline urine is particularly associated with the P.mirabilis or P. aeruginosa infections that help early guide empirical therapy in pediatric UTI.

72 Clinical Characteristics of Echovirus 11 and Coxackievirus B5 Infections in Taiwanese Children Requiring Hospitalization

伊科病毒第十一型與克沙奇病毒第五型在台灣兒童所造成之疾病特色與表現

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Background: Seasonal outbreak with different types of enterovirus infection had been reported frequently in Taiwan. Severe illness can occur in young children infected with certain types of enteroviruses including echovirus 11 (Echo11) and coxsackievirus B5 (CoxB5). The manifestations and outcomes of Echo11 and CoxB5 diseases across all ages of children remained not comprehensively characterized in Taiwan.

Methods: A total of 80 children with culture-confirmed Echo11 (52 patients) or CoxB5 (28 patients) infections were identified during 2016 and 2018 in a teaching hospital. Information including demographics, clinical presentations, laboratory data and outcomes were abstracted from medical records. Aseptic meningitis was defined as positive viral yield from CSF, and acute liver failure was defined as ＞ 3-fold increase of normal liver enzymes.

Results: Of all patients, male accounted for 50 (62.5%) patients and the median age was 11.5 months [range 1 day – 14.5 years]. For infants ＜ 3 months old, Echo11 (19 cases) was associated with greater incidences of aseptic meningitis (42% vs. 20%, P = 0.23) and sepsis-like syndrome (37% vs. 10%, P = 0.12), though of marginal significance, but a significantly lower rate of upper respiratory tract infection (URI) (21% vs. 70%, P = 0.01) compared to CoxB5 (10 cases) infections. For patients ＞= 3 months old, URI was the cardinal clinical presentations for both viruses and accounted for 63% and 72% of Echo11 and CoxB5 infections, respectively (P = 0.48). The other manifestations for Echo11 and CoxB5 infections included aseptic meningitis (22% vs. 11%, p = 0.34), sepsis-like syndrome (3% vs. 0%, P = 0.45), herpangina (6% vs. 13%, P = 0.23) and hand-foot-and-mouth diseases (6% vs. 0%, P = 0.28). Acute liver failure was identified in four patients with Echo11 infections and all of them were younger than 3 months of age.

Conclusions: Echo11 and CoxB5 were associated with similar disease spectrum in children. However, Echo11 tended to cause more severe diseases including aseptic meningitis, sepsis-like illness and acute liver failure in young children.

73 Echovirus Type 11 Infections in Children at a Medical Center in Southern Taiwan, 2017-2018

伊科病毒11型感染於南台灣一醫學中心

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Background: An increase in reports related to severe echovirus 11 (Echo 11) infections was noted since May 2018. There were seven fatal Echo 11 infections in neonates and young infants in 2018, according to Taiwan Centers for Disease Control. This report describes the epidemiological, clinical and laboratory characteristics of Echo 11 infection cases at one medical center during 2017-2018.

Methods: A retrospective, hospital-based, cross-sectional study was performed at National Cheng Kung University Hospital (NCKUH) between 2017 and 2018. All virological confirmed patients were enrolled. Echo 11 was isolated from sterile (cerebrospinal fluid) or non-sterile sites (throat, and anal). Demographic characteristics, clinical, laboratory and virological findings were reviewed.

Results: Thirty-five Echo 11 isolates were obtained (2 from cerebrospinal fluid, 27 from throat swab, and 6 from rectum swab) from 30 patients (16 male and 14 female). Echo 11 infections are most likely to circulate in the community during June to August (57%, 17/30) in 2018. Thirty percent (9/30) patients were ＜ 1 year of age (3 aseptic meningitis, 2 acute tonsillitis, and 2 viral exanthem, 1 sepsis syndrome, and 1 enterocolitis). In patients ≧ 1 year of age (70%, 21/30), 9.5% (2/21) complicated with aseptic meningitis.

Other Echo 11 associated clinical diagnosis included acute pharyngitis (43%, 9/21), acute tonsillitis (19%, 4/21), herpangina (14%, 3/21) and others (14%, 3/21). All patients recovered uneventfully without complication. Echo 11 was more common to isolate from throat swab (77%, 27/35).
Conclusions: Echovirus 11 infections in 2018 demonstrated the potential of enteroviruses to circulate widely and unpredictably and cause various clinical diseases. It underscores the continued need for enterovirus surveillance.

74 Group B Streptococcal Infections in Children in Southern Taiwan: from Neonates to Adolescents

南臺灣兒童乙型鏈球菌感染：自新生兒到青少年

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Background: Streptococcus agalactiae (Group B Streptococcus, GBS) is a beta-hemolytic gram-positive cocci, which may cause life-threatening infections in susceptible hosts, especially newborn and elderly. The purpose of this study was to determine the prevalence of GBS infections in children during a period of 13 years.
Methods: This retrospective study was designed to explore the clinical, laboratory and microbiological characteristics of GBS infections in children from Jan. 2006 to Dec. 2018 at National Cheng Kung University Hospital. Seasonality, clinical presentations, laboratory data, and antimicrobial susceptibility were reviewed and analyzed.
Results: Overall, 85 patients were identified and enrolled. Patients were divided into early-onset disease (EOD) (n=14, 17%) and late-onset disease (LOD) (n=16, 19%), or invasive group (n=29, 34.1%) and noninvasive group (n=56, 65.9%). There was no difference in seasonal distribution among study groups during the study period. Sepsis (n=8) in the EOD group, bacteremia without focus (n=9) in the LOD group, and soft tissue infections (n=16) in older children were the most common clinical diagnosis. In invasive group, CNS infection (n=8) was associated with worse long term neurologic sequelae (P=0.004). The mortality rate of the group was 10.3%. There was no difference of white blood cell (WBC) counts between invasive (13351± 9119/mm3) and non-invasive (15523± 5244 /mm3) group, but invasive group had high hospitalization rate (P=0.000) and ICU admission rate (P=0.000). As to antimicrobial susceptibility, these GBP were 100% susceptible to penicillin, vancomycin, ampicillin, ceftriaxone, and cefepime, but only 40% susceptible to clindamycin and erythromycin. From our minimum inhibitory concentration (MIC) data, the empirical drug of choice for invasive disease is aqueous penicillin.
Conclusions: Our study shed a new light on the epidemiologic, clinical, laboratory, and antibiotic susceptibility of GBS infections, and will pave a new way for the prevention of invasive infections.

75 Echocardiographic Screening of Kiribati Teenager School Students, a Midterm Result

吉里巴斯學童風濕性心臟病篩檢：期中結果

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Background: Kiribati, a country in Pacific island countries with diplomatic tie with Taiwan, suffered from endemic acute rheumatic fever, yet the prevalence of rheumatic heart disease (RHD) remained uninvestigated.
Methods: Mackay Memorial Children Hospital activated echocardiographic screening for teenager students of Kiribati with hand-on echocardiographic machine since 2016 to estimate the prevalence of RHD. School-based echocardiographic screening was performed in Tarawa island, Kiribati, since 2016. The criteria for diagnosis of RHD screening proposed by world heart federation 2012 was adopted. Those screened positive students were assigned to “borderline” and “definite” groups and received subsequent regular penicillin prophylaxis according to the suggestion of guideline published by American heart association.
Results: We reported the preliminary result of our first screening in 2016 (RHD prevalence: 2.11% of 947 students screened). Among 1579 succeeding screened students, 31 students were diagnosed to have RHD. 19 case of borderline RHD and 12 definite RHD students were detected. The prevalence rate of RHD was estimated of 1.96%. Among those students detected, 58% (7/12) and 21% (4/19) were diagnosed already before our screening for definite and borderline RHD group, respectively. in the meantime, 5 cases of congenital heart disease were diagnosed with the prevalent rate of 0.38%.
Conclusions: Instead of congenital heart disease, RHD is the major cardiac problem in Kiribati students due to tremendous disease burden of RHD in this pacific island country. School based echocardiographic screening of RHD is mandatory since nearly two thirds of RHD cases were not detected yet before this survey.

76 Reference Ranges and Z-scores for Fetal Cardiac Measurements from Two-dimensional Echocardiography in Taiwanese Population

以二維心臟超音波定義正常胎兒心臟結構之參考值

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Background: Currently available fetal echocardiographic reference values are derived mainly from North American and European population studies, and there is a lack of reference values for fetal echocardiographic measurement in Taiwanese population. The aim of this study was to establish normal ranges of echocardiographic measurements in healthy Taiwanese fetuses.
Methods: From September 2016 till December 2017, a total of 600 healthy pregnant Taiwanese with the gestational age (GA) from 14 to 40 weeks were enrolled voluntarily for this observational study. They were divided into 14 groups according to the gestational age at two weeks' interval. Standard two-dimensional echocardiography was performed to obtain measurements of the cardiac chambers and great arteries of the developing fetuses.
Results: After excluding missing data (24) and abnormal fetuses (4), a total of 575 qualified healthy fetuses were ultimately enrolled. In contrast to other studies, our sample was more evenly distributed between GA ($p < 0.001$). All cardiac measurements and developmental markers are normally distributed. We present percentile graph, regression equations for 13 fetal echocardiographic measurements from the knowledge of GA, BPD, HC, AC, FL. All structures and developmental markers had linear models as the best-fitting. Our findings indicate that gestational age was generally the best model for heart growth. But for transverse diameter of aortic isthmus and ductus arteriosus, femur length has a better correlation. Lastly, we developed nomograms for the 13 fetal heart structures, along with on-line z-score calculator to bypass manual check-up in clinical setting.
Conclusions: In Taiwanese fetuses, LV seemed smaller in the third trimester, greater variation of AO/PA ratio. It may be related to: body weight of the pregnant women, birth weight of the neonates, racial differences, and sample number distribution in groups. In conclusion, this is the first study providing echocardiographic reference values for Taiwanese fetuses.

77 Impacts of Right Ventricular Outflow Tract Geometry, Pulmonary Valve Annulus Diameter, and Discrepancy in Branch Pulmonary Arteries on Adverse Outcome Indicators in Patients with Repaired Tetralogy of Fallot

法洛氏四重症術後病患之右心室出口型態、肺動脈瓣環直徑、與雙側肺動脈不均等對患者之不良預後指標的影響

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Background: Right ventricular outflow tract (RVOT) dysfunction is common in patients with repaired tetralogy of Fallot (rTOF). The geometry of RVOT also has great impact on decision-making of pulmonary valve replacement (PVR). However, large-scale detailed quantification of RVOT geometry and its associations with right ventricular (RV) size, function and clinical outcome have yet been investigated. Our objectives were to explore RVOT geometry and its clinical relevance using cardiac magnetic resonance (CMR) and 3-dimensional magnetic resonance angiography (3D-MRA).
Methods: In our CMR database of rTOF, 420 patients were identified between 2007 and 2018. A total of 206 patients (25±11 years of age) met the inclusion criteria were enrolled. Images of 44 patients who had both cardiac catheterization angiography (CCA) and 3D-MRA within one year were compared to validate the reliability of 3D-MRA. Main pulmonary artery and branch pulmonary arteries (BPA) diameters were measured in detail on 3D-MRA. Discrepancy in bilateral BPA was defined as the diameter of the smaller one is less than half of the larger one.
Results: Measurements of 3D-MRA showed good correlation with CCA (mean difference: -0.79±1.21 mm). Larger PVA diameter z-score was associated with larger RV end diastolic/systolic volume index ($p < 0.001$), and higher PR fraction ($p < 0.001$). Of the 4 shapes of RVOT geometry we defined: tubular (n=85), pyramid (n=39), inverted trapezoid (n=11), and hourglass shape (n=71), pyramid shape had largest RV size while inverted trapezoid shape was more resistant to ventricular remodeling. Discrepancy in bilateral BPA (8%) was independently associated with poorer peak oxygen consumption (57.75% vs 48.43% of predicted, p=0.023) and was also significantly associated with higher probability of PVR at follow-up (p=0.006) in Kaplan-Meier analysis.
Conclusions: Using 3D-MRA, we demonstrated the impact of RVOT geometry, PVA diameter, and discrepancy in BPA

on RV size, exercise capacity, and risk of subsequent PVR in rTOF patients. The relationships between morphological characteristics and adverse outcome indicators may have important implications for interventions of RVOT, BPA or future PVR.

78 Pulmonary Arterial Pressure as the Key to Predict Perioperative Outcomes of Patients after Fontan Operation: A Singe-Center Experience

肺動脈壓是預測Fontan手術預後最重要的因子：單一醫學中心之經驗

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Background: Fontan operation is the standard operation to achieve long-term survival in single-ventricular complex congenital heart diseases. There are limited studies about perioperative outcomes after Fontan operation. Objectives: To identify the perioperative outcomes of all patients who had a Fontan operation at the National Taiwan University Children's Hospital.
Methods: Medical records of all patients who received a Fontan operation and born between 1997 and 2017 were reviewed. Pre-operative, operative, and post-operative risk factors for perioperative mortality and morbidity were analyzed. Totally 154 patients were enrolled and M/F was 92/62.
Results: Overall perioperative event-free survival to discharge was 91.6%. Risk factors associated with death or Fontan take down (primary endpoint) included operation prior to 2010, heterotaxy syndrome, elevated pre-operative pulmonary arterial pressure (PAP), elevated preoperative N-terminal pro-brain natriuretic peptide (NT-proBNP), non-extracardiac conduit Fontan type, and elevated post-operative central venous pressure (CVP) in univariate analysis; non-extracardiac conduit Fontan type, and elevated post-operative CVP (odds ratio 43.478 and 1.579, p = 0.023 and <0.001) in multivariate analysis. A cut point of pre-operative PAP ≥14 mmHg and post-operative CVP ≥16 mmHg to predict primary endpoint had a sensitivity of 0.600 and 0.800, and a specificity of 0.687 and 0.769 respectively. A scoring system including heterotaxy syndrome, pre-operative PAP, and non-extracardiac conduit Fontan operation type could predict primary endpoint. For secondary outcomes, pre-operative PAP, McGoon index, and post-operative CVP were associated with prolonged intensive care unit (ICU) stay and prolonged chest tube drainage in multivariate analysis.
Conclusions: Pre-operative PAP and post-operative CVP are the most important factors predicting perioperative death or Fontan take down, prolonged ICU stay, and prolonged chest tube drainage after Fontan operation.

79 Genetic Test in the Survivors of Sudden Cardiac Arrest in Pediatric Population

兒童心因性心跳停止生存者的基因檢測

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Background: Sudden cardiac death (SCD) in pediatric population is a rare but important disease, and causes great loss of social productivity. The clinical characteristics and genetics of pediatric SCD patients have been reported. However, the survivor of sudden cardiac arrest (SCA) in pediatric population, which may be of great clinical interest, has been rarely studied.
Methods: From Jan 1995 to Jun 2018, all patients of SCA aged 1 to 18 years, who survived to discharge from hospital in a tertiary pediatric cardiology center were enrolled. Patients of syncope with ventricular arrhythmia during the events were also included in our study population. Patients with underlying congenital heart disease related arrhythmia, myocarditis related events, and with cause of arrest other than heart origin were excluded. The charts were reviewed and genetic test with gene panel of 103 channelopathy genes and 363 cardiomyopathy genes were analyzed.
Results: Totally 37 patients were included in our study. Male/Female was 25/12, and mean onset age was 13.0±4.5 years. Prior events, including syncope or dyspnea, were found in 15 (40.5%) of the patients. The attack situation was during exercise in 13 (35.1%), and daily activity in 7 (18.9%). The attack symptom was sudden cardiac arrest in 29(78.4%) and syncope in 7 (21.6%). After meticulous evaluation, including supplement by genetic test, the diagnosis was idiopathic ventricular fibrillation in 10 (27%), long QT in 9 (24.3%), and catecholaminergic polymorphic ventricular tachycardia in 5 (13.5). The genetic test was performed in 73% of the patients, and yield rate increase from 44% to 74% using new genetic panel. After 5.8±5.5 years follow-up, the 10 years transplantation free survival rate was 90%, but 7 of the patients has early loss of follow-up. Implantable cardioverter defibrillator is necessary in 77.8% of the patients, and appropriate shock is common in these patients despite adequate medical control.
Conclusions: The survivors of SCA in pediatric population carries a relative good long term survival with aggressive intervention. The yield rate of genetic test using modern gene panel is good.

80 Transcatheter Closure of Perimembranous-type Ventricular Septal Defect: a Single Center's Experience

經心導管關閉膜周邊型心室中隔缺損：單一醫學中心的臨床經驗

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Background: Transcatheter occlusion for perimembranous type ventricular septal occlude (pmVSD) is a popular alternative to surgical closure. Various occluders were designed for this propose. Lifetech pmVSD occluder was commonly used in Taiwan due to national health insurance imbursement. However, the reports for its efficacy and safety were lacking. The aim of this study was to provide local experiences in VSD transcatheter occlusion with VSD occluder.
Methods: Patients who received transcatheter occlusion of congenital pmVSD were enrolled retrospectively. Baseline patient characteristics; hemodynamic and angiographic data during catheterization; echocardiography and electrocardiography data before and after the procedure were collected. We followed up the patient at 1, 3, 6, 12 months post-implantation and yearly thereafter. Complications were recorded and analyzed.
Results: From August 2017 to November 2018, 45 patients with 47 attempts of transcatheter closure of VSD were enrolled. The mean age was 15.6 years (3 - 40) and mean body weight was 45 kg (11.6 – 96.4). Acute successful rate was 89 % (42/47), the mean VSD size in ventriculography was 4.4 mm; mean device-defect difference was 2.8 mm. After the procedure, no atrioventricular block occurred, other arrhythmia/conduction disturbances occurred in 7 patients (16.7%), but none of these arrhythmia/conduction disturbances became permanent. Two patients had residual shunt (4.3%) and 1 (2.2) had newly onset valve regurgitation. The mean follow-up time was 6.3 month (0 - 13).
Conclusions: We keep pace with experienced centers for transcatheter pmVSD occlusion. We have similar acute successful rate and complication rate compared to other experienced centers. Longer follow-up duration is warranted to evaluate long-term efficacy and safety.

81 Initial Experience of Transcatheter Closure of Perimembranous VSD with the Amplatzer Vascular Plug II

經心導管利用安普拉茲第二型血管塞治療膜邊型心室中膈缺損的初步經驗

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Background: The traditional treatment of perimembranous ventricular septal defect (pmVSD) was open heart surgery. This study aimed to evaluate the feasibility, safety and outcome of transcatheter closure with the Amplatzer vascular plug II (AVP-II).
Methods: Between August 2017 and October 2018, a total of 15 patients (9 males and 6 females) with perimembranous VSD who underwent transcatheter closure with the AVP-II were enrolled retrospectively. Their age ranged from 2.2 to 74.3 years, with the median of 17.8 years; their body weights ranged from 12.7 to 83 kg with the median of 62.8 kg. Mild aortic regurgitation was noted in 4 (26.6%) patients.
Results: Left ventriculogram showed VSD entry size ranged from 4.0 to 11.5 mm with the median of 7.9 mm. The device was successfully implanted in 100% (15/15) of the patiens without complication noted. Complete closure rate was 80%, 82%, 100% and 100% at 1-day, 1-month, 6-month and 12-month follow-up, respectively. Four patients developed new aortic regurgitation (trivial) during follow-up.
Conclusions: Transcatheter closure of perimembranous VSD with AVP-II is technically feasible and safe. However, development of aortic regurgitation requires long-term follow-up.

82 Clinical Responses of Patients with Kawasaki Disease to Two Different Brands of Intravenous Immunoglobulin

兩種不同品牌靜脈注射免疫球蛋白球對川崎病患者的臨床療效

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Background: The intravenous immunoglobulin (IVIG) in our hospital before August, 2017 was supplied by Taiwan Blood Services Foundation and they was replaced by Privigen[TM/®] Human normal immunoglobulin Solution (10%) (CSL Behring AG, Switzerland). To determine whether two brands of IVIG administered to children with Kawasaki disease (KD) result in different outcomes.
Methods: We retrospectively reviewed the charts of all the children who were diagnosed as having KD and who were

treated with IVIG at Changhua Christen Children's Hospital from January 2015 to December 2018. We analyzed children with KD and divided them into 2 groups according to the brand of IVIG.
Results: A total of 158 cases of KD were collected in this study. No significant differences in demographic data and pretreatment laboratory data were found among the two groups of patients. Eighteen (11.4 %) were nonresponsive, Fourteen (8.7%) had coronary arteries aneurism at convalescence, and one (0.6%) had giant aneurysm. When comparing the patient's response to IVIG therapy and coronary artery evaluation, we found significant differences in the duration of fever after IVIG ($P < 0.001$), the length of hospital days after IVIG treatment and nonresponsiveness IVIG treatment (P=0.016). There were no difference in the length of total hospitalization days, the rate of coronary artery abnormalities at convalescence, and the development of giant aneurysms . The Generalized Linear Model revealed that an initial CRP, conjunctival injection, high risk group (Formosa score) and treatment with Privigen IVIG were significantly associated with nonresponsiveness to IVIG.
Conclusions: Compared with the efficacy of two brands, this study found that Privigen prolonged febrile days, the length of hospital days after IVIG treatment and increased the proportion of nonresponsiveness IVIG treatment, but did not infer the coronary arteries sequelae.

83 Evaluating the Efficacy of Immunoglobulin plus Steroid for Prevention of Coronary Artery Abnormalities in Taiwanese Patients with Refractory Kawasaki Disease (RAST Study): a Randomized Open-label Trial

頑固型川崎病的最適治療—免疫球蛋白併用類固醇與否的前瞻性隨機研究

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Background: To evaluate whether intravenous immunoglobulin (IVIG) administered together with prednisolone is more effective than IVIG monotherapy in achieving defervescence and reducing coronary aneurysms in patients with refractory Kawasaki disease (KD).
Methods: Patients with refractory KD were randomly assigned to 2groups on the basis of rescue therapy, IVIG alone (I group),or IVIG plus prednisolone (S group, prednisolone 2 mg/kg/day for 5 days). When the C-reactive protein concentration normalized (≤ 0.5 mg/dL) in the patients, we tapered the prednisolone dosage (Clinicaltrials.gov: NCT03200561).
Results: Between 2013 and 2018, we enrolled 70 patients with refractory KD (Male: 50). 37 and 33 patients were allocated to I and S groups, respectively. No significant difference existed in age, sex, fever duration before first IVIG treatment, presence of major diagnostic criteria, laboratory data, and initial maximal coronary Z scores between the 2 study groups. Nine patients in the I group and 1 in the S group failed to achieve defervescence (9/37 vs 1/33, P=.015). The median difference inthe maximal coronary Z score between the acute phase and 1 month after disease onset was +0.34 (I group) and −0.40 (S group), respectively (P = .025). Two patients had medium/giant aneurysms (coronary Z score ≥ +5.0), and both are in the I group.
Conclusions: In total, 14.3% of patients with refractory KD failed to become afebrile after rescue therapy. The defervescence rates of the I and S subgroups were significantly different. Additional therapy with prednisolone also significantly reduced the risk of coronary disease progression.

84 Methylprednisolone Pulse Therapy for Kawasaki Disease Patients with Aneurysm Formation

研究脈衝療法對川崎病動脈瘤之成效

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Background: Kawasaki's disease is the most common systemic vasculitis in children. Coronary artery aneurysms may develop in 20-25% of untreated patients. Intravenous immune globulin (IVIG) can reduce coronary-artery aneurysms to 3-5%. Numerous studies and clinical trials had pointed out that corticosteroid treatment (pulse therapy or usual dosage) could lower the incidence of coronary artery abnormality in high-risk KD patient. However, the therapeutic effect of corticosteroid in KD patients with aneurysm formation was never mentioned. There are also no effective treatment for aneurysm formation in KD after acute stage.
Methods: We conducted a retrospective study of methylprednisolone pulse therapy (MP pulse) for coronary aneurysm. We reviewed the medical chart and found KD patients who had persisted medium or large coronary aneurysm($Z > 5$) upon serial echocardiography for 1 month at least and had received MP pulse (30mg/kg, Max:1g) for treatment.
Results: Three patients were enrolled: patient 1 and 2 were 4-year-old boy who were treated with MP pulse in 2.6 months and 2 months after acute KD illness, respectively. Patient 3 was a 6- year-old girl who suffered from recurrent KD (her first KD episode induced KD-shock syndrome). She underwent MP pulse after 1 month of 2nd course KD onset. Of coronary aneurysm dimension, patient 1 had RCA aneurysm with 6.6mm (Z score:12.61) before MP pulse, and it regress to 3.8mm (Z score:5.27) 1-month after MP pulse. Patient 2 had LAD aneurysm with diameter 5.9mm (Z score:12.12) before MP pulse, and it regress to 4.2mm (Z score:7.29) 1.5 month after MP pulse. Patient 3 had change of LMCA aneurysm dimension (diameter 7.2 to 3.1mm, Z score 11.91 to 1.74) in 2.5 months after MP pulse.
Conclusions: This study first demonstrated that, KD

patients with aneurysm showed regression after MP pulse therapy.

85 Decreased DNA Methyltransferases Expression and is Associated with Coronary Artery Lesion Formation in Kawasaki Disease

降低DNA甲基轉移酶的表達並與川崎病中的冠狀動脈病變形成有關

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Background: Kawasaki disease (KD) is the most common acute coronary vasculitis disease to occur in children. Although we have uncovered global DNA hypomethylation in KD, its underlying cause remains uncertain. In this study, we performed a survey of transcript levels of DNA methyltransferases and demethylases in KD patients.
Methods: We recruited 145 participants for this study. The chip studies consisted of 18 KD patients that were analyzed before undergoing intravenous immunoglobulin (IVIG) treatment and at least 3 weeks after IVIG treatment, as well as 36 control subjects, using Affymetrix GeneChip® Human Transcriptome Array 2.0. An additional study of 91 subjects was performed in order to validate real-time quantitative PCR.
Results: In our microarray study, the mRNA levels of DNMT1 and DNMT3A were significantly lower while TET2 was higher in acute-stage KD patients compared to the healthy controls. Through PCR validation, we observed that the expression of DNMT1 and TET2 are consistent with the Transcriptome Array 2.0 results. Furthermore, we observed significantly lower DMNT1 mRNA levels following IVIG treatment between those who developed CAL and those who did not.
Conclusions: Our findings provide an epigenetic study of DNA methyltransferases and demethylases changes and are among the first evidence that transient DNA hypomethylation is induced during KD's acute inflammatory phase.

86 Mir-182-5p Enhances in Vitro Neutrophil Infiltration in Kawasaki Disease Complicated with Coronary Artery Lesions

Mir-182-5p增加川崎症併有冠狀動脈病灶的體外白血球浸潤

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Background: The previous study identified KD related miRNAs which were able to discriminate KD patients from febrile controls. Of the identified KD related miRNAS, miR-182-5p was shown to promote cell invasion and proliferation. In this study, we aimed to test the hypothesis miR-182-5p could promote leukocyte transendothelial migration, triggering coronary artery lesions (CAL) in KD.
Methods: To examine this hypothesis, we enrolled KD patients with CAL complication, followed by qPCR examination on miR-182-5p and miR-183-5p. By meta-analysis, we first confirmed that miR-182-5p and miR-183-5p were differentially expressed between the KD patients without CAL and the KD patients with CAL. Further analysis with machine learning algorithm demonstrated a high performance of predicting CAL formation using the expression data of the two miRNAs. Finally, we used in vitro cell model to demonstrate that miR-182-5p and miR-183-5p enhanced leukocyte infiltration.
Results: miR-182-5p and miR-183-5p kept higher levels in the KD patients with CAL than those without CAL (p-value <0.05 for miR-182-5p). miR-182-5p and miR-183-5p were able to predict CAL formation, with an auROC value of 0.86. miR-182-5p over-expression, compared with scrambled control, significantly ($p < 0.05$) enhanced neutrophil cells to infiltrate the endothelial layer which was composed of human coronary artery endothelium cells. Microarray assay demonstrated the genes altered by miR-182-5p involved in immune-related responses. Over-expression of miR-182-5p activated the leukocyte trasendothelial migration pathway.
Conclusions: Our result showed the genes activated with miR-182-5p over-expression were significantly enriched in the leukocyte transendothelial migration pathway (kegg_pathway_194, $p < 0.05$). Therefore, our study suggested that miR-182-5p enhanced in vitro leukocyte infiltration through activating the leukocyte transendothelial migration pathway in CAL formation in KD.

87 Dynamic Changes of Eosinophil in Kawasaki Disease and the Association with Coronary Artery Lesions Formation

研究嗜酸性球在川崎病患之動態變化與冠狀動脈病變之關連性

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Background: Kawasaki disease (KD)is a systemic vasculitis which most affect children less than 5 years-old especially in Asia countries. Eosinophilia (peripheral blood eosinophil＞3%) has been reported in a patient with KD and associated with intravenous immunoglobulin (IVIG) treatment response previously. This study further investigates the dynamic change of peripheral blood eosinophilia in different stages of KD till one year after treatment.

Methods: We reviewed medical records of children who were admitted and met the criteria of KD between 2011 and 2015 in the institution retrospectively. A total of 108 KD patients and 108 febrile age-matched controls were enrolled for this study. Patients with any history of allergic diseases were excluded in controls. We collected percentages of peripheral blood eosinophil at 5 different stages including KD1: before IVIG treatment, KD2: 3 days after IVIG treatment, KD3: 3 weeks to 6month after IVIG treatment, KD4: at least 6 months after IVIG treatment, and KD5: 1-2 years after IVIG treatment.
Results: There were 55 boys and 53 girls in KD group. The eosinophils percentage showed significant higher at 5 different stages when compared with controls. The absolute eosinophil counts also showed significantly higher at 5 different stages of KD when compared with controls (all $p < 0.001$). At KD2 stage, patient with eosinophilia had lower rate of coronary artery lesion formation (10/58 vs. 19/50, $p=0.015$). KD patients had higher rate of eosinophilia one year after disease onset (23/84 vs. 5/108, <0.001) than controls.
Conclusions: This is the first study to show dynamic changes of eosinophil in KD over one year, which indicated eosinophil percentages remain higher when compared with controls even after 1 year after IVIG treatment. Eosinophil may play a protective role in coronary artery lesions formation. In addition to the regular scheduled echocardiography, eosinophil-related diseases, especially with the allergic origin, should also be recorded carefully during the follow-up of KD patients.

88 Apoptosis May Play a Major Role in Mediating Diastolic Dysfunction in Adolescent Obesity

細胞凋亡與青少年肥胖引起之心室舒張功能異常相關

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Background: Obesity in adolescence has been shown to be related to cardiac diastolic dysfunction. In adult obesity, the mechanisms responsible for cardiac functional changes were chronic inflammation, insulin resistance, and apoptosis. The mechanisms of diastolic dysfunction in obese adolescents have never been well studied previously. Our aim was to investigate the possible mechanisms of cardiac functional alternations in adolescent obesity.
Methods: Adolescents between 10 and 20 years old were enrolled in this study. Participants were divided into normal-weighted participants and obese participants according to body mass index (BMI) z score. Cardiac function was determined by echocardiography and tissue Doppler images. Glucose metabolism, high sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and apoptosis marker M30 level were measured. The association between serum biomarkers and echocardiographic function parameters was analyzed in obese adolescents.
Results: There were 181 participants, including 104 normal-weight adolescents, and 77 obese adolescents. Diastolic functional alternations were documented in obese adolescents. Main changes in glucose metabolism in obese adolescents were the elevation of C-peptide and insulin resistance. Hs-CRP, IL-6, and M30 level also increased in adolescent obesity. Multivariate regression analysis showed M30 was the major biomarker that highly correlated to diastolic dysfunction in obese adolescents, rather than insulin resistance, hs-CRP, IL-6 or TNF-α.
Conclusions: Diastolic dysfunction was the main change in adolescent obesity. Insulin resistance, apoptosis, elevation of hs-CRP and IL-6 were all related to adolescent obesity. Apoptosis may play a major role in mediating LV diastolic dysfunction among obese adolescents, rather than inflammation or insulin resistance.

89 Adenovirus Infection and Subsequent Risk of Kawasaki Disease and Coronary Artery Lesions: A Population-based Cohort Study

腺病毒感染和後續得川崎症與冠狀動脈併發症風險相關性探討：世代研究

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Background: There is still no clear relationship between adenovirus infection and Kawasaki disease(KD). The aim of this study is to determine the relationship between adenovirus infection and KD, based on a population cohort study in Taiwan.
Methods: We used the Taiwan National Health Insurance program (between 2000 and 2008) to conduct a population-based cohort study, analyzing children that was under 18 years old. In total, 5280 children with adenovirus infection and 5280 children without adenovirus infection were included and followed up. The major outcome event was subsequent KD and coronary artery lesions.
Results: There was significantly higher cumulative incidence of KD in the adenovirus-infected cohort than in the non-adenovirus-infected cohort ($P < 0.001$). The overall incidence of KD was 5.17 times higher in the adenovirus-infected cohort than in the non-adenovirus-infected cohort (adjusted HR 5.29, 95% CI: 2.48-11.3). There was no significant difference of coronary artery complication rate between two cohorts. There was also higher KD risk associated with previous adenovirus infection in children aged 3-5 years, in female gender, in children living in less urbanization levels, and in allergic children.
Conclusions: There is a higher association between previous adenovirus infection and KD in Taiwanese children, particularly in children aged 3-5 years, in female

gender, in children living in less urbanization levels, and in allergic children.

90 Comparison of Hemodynamic Changes of Surgical Ligation versus Transcatheter Closure of Patent Ductus Arteriosus in Preterm Infants Weighing Less Than 1800 Grams: a Case Series of 30 Preterm Infants in Southern Taiwan

體重小於1800克且存有開放性動脈導管之早產兒，接受傳統手術及心導管治療前後之血液動力學的比較：南台灣30例早產兒病例回溯性分析

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Background: Transcatheter closure of patent ductus arteriosus (PDA) occlusion is a safe interventional cardiac procedures in older children and adults, but use among lower weight infants (＜6 kg) has not been characterized adequately. The aim of this study is to compare the hemodynamic and respiratory outcomes of surgical ligation to transcatheter closure of PDA in preterm infants weighing less than 1800gm.
Methods: A total of 30 preterm infants weighing below 1800gm with significant PDA during Jan. 2014 to Dec. 2018 at National Cheng Kung University Hospital were reviewed. Surgical ligation (n = 17; 57%) or transcatheter closure (n = 13; 43%) were performed. Mean blood pressure(MBP), urine output(UO), heart rate(HR), inotropic equivalence(IE), and oxygen demand(FiO2) were sampled before and after ductal closure. We analyzed the results retrospectively.
Results: The mean body weight at the time of the procedure was 855.4 ± 348.5 gm. The gestational age(GA) ranged from 22 to 32 weeks. No significant differences were found in baseline characteristics including gender, age, and birth body weight. The MBP, UO, HR, and IE before and after ductal closure between the groups revealed no significant difference. However, the transcatheter group was associated with less urine output on the first day (p=0.02) and greater decreasing level of FiO2 5 days after the intervention (p=0.043).
Conclusions: Our study clarified the changing of hemodynamic status should not be a major concern of procedure selection for PDA closure. Percutaneous closure of PDA for low weight preterm infants is a safe and reliable alternative to surgical ligation.

91 Application of Umbilical Vein Catheterization for Neonatal Intervention

臍靜脈於新生兒介入性治療之應用

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Background: Percutaneous approach for cardiac catheterization was sometimes difficult in neonate, especially in prematurity. Umbilical catheter was common in NICU care. Umbilical vessel used for cardiac catheterization was rarely mentioned recently. Reported applications for umbilical vein includes cardiac catheterization like angiography, balloon atrial septostomy.
Methods: We retrospective chart review of patient age ＜ 1 months old and admitted to Cheng-Kung University Hospital, Tainan Neonatal Intensive Care Unit (NICU) and used umbilical vein access for cardiac catheterization or double lumen insertion from Mar 2017 to Dec 2018. Patient character including age, gestational age, body weight and indication were reported.
Results: Eleven cases were retrieved, most were preterm infants (n=9) and most were male infant (n=7). Gestational age ranges from 22 to 39 weeks and birth body weight ranges from 462g to 3555g. Patient received intervention 3.64±5.36 days old and mean body weight was 3015g and 45.4% were less than 1 kg (n=5). One case received double lumen insertion (8Fr.) through umbilical vein for continuous venous-venous hemofiltration (CVVH) use. Most patients received cardiac catheterization through umbilical vein (n=10), including patent ductus arteriosus (PDA) occlusion (n=8), balloon atrial septostomy (n=1) and balloon dilation for critical pulmonary valvular stenosis (n=1). The mean procedure time at cath room was 83±35 minutes. The sheath size was 4Fr or 5Fr and one case changed to 11Fr double lumen catheter for CVVH use after PDA closure. In PDA cases, 6 were closed with Amplatzer ADOII-AS (n=5) and Amplatzer VPII (n=1) device successfully. One case was failed for ductus venosus was already closed. Other success cases age ranged from 2 to 14 days old. One case had hemorrhagic ascites and vital sign was stable after intensive blood transfusion.
Conclusions: Umbilical vein may be a useful alternate route for CVVH or cardiac catheterization in neonate age less than 14 days old. The 8Fr. or even 11Fr catheter may be used in infant umbilical vein catheterization carefully. More cases may be needed for further evaluation of application and complication.

92 Maternal H1 Antihistamine in Breast-milk: a Possible Trigger in Prolongation of QTc Intervals and Seizure?

母親服用H1抗組織胺藥可能引發其哺乳嬰兒抽搐及QTc延長

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Background: The human ether-a-go-go related gene (hERG) encodes the pore-forming subunit of the rapid component of the delayed rectifier K+ channel, Kv11.1. It contains three subfamilies: Kv10.x, Kv11.x and Kv12.x. The Kv11.x has three members, including Kv11.1 . Mutation in the Kv11.1 may result in long QT syndrome. Drugs block Kv11.1 causes acquired long QT syndrome. H1 antihistamine is a Kv11.1 blocker, which is breast-milk transferable, might be a trigger to QTc prolongation in breast-milk fed infants, and possibly seizure.
Methods: Here, we report 2 cases of breast-fed infants, who had QTc prolongation and seizure after the mather took antihistamine.
Results: Case1: A six-month-old female infant who was breast-milk fed since her birth. Her breast-fed- mother suffered from acute generalized urticaria, so H1 antihistamines were used. The next day, the infant's parents found the infant had seizure during sleeping. Electrocardiogram showed the QTc reached 462ms and 509ms respectively. Holter ECG showed daily QTc over 500 ms without circadian shift- shortening during sleeping. After discontinuation of maternal H1 antihistamine usage, the infant's QTc gradually returned the normal ranges. Electroencephalogram and brain MRI were abnormal, so anticonvulsants were prescribed, after that, no more seizure recurred. Case 2: A 3-months old baby was breast-fed since birth. However two episodes of focal seizure with impaired awareness noted. EKG showed QTc prolonged over 500ms without circadian shift-shortening during sleeping was noted. Tracing back to maternal history, the mother took antihistamine due to acute pharyngitis for several days before the seizure onset. The Brain MRI and EEG were abrnomal, which showed suspect pachygyria and dysgenesis of corpus callosum, while EEG showed multifocal seizures . After discontinue the breast feeding, the EKG return to normal, and there was no more seizure under anticonvulsants.
Conclusions: H1 antihistamine is a Kv11.1 blocker that may prolong the QT interval, induce torsade de pointes from early after-depolarization and works as an acquired LQTc syndrome. As H1 antihistamine is breast-milk transferable, so it should beuse with cautious during lactating.

93 Autophagic Dysfunction Underlying Pathomechanism of Pluripotent Cell Model of MELAS Syndrome

自噬作用失調是造成MELAS症候群的病理機轉_以iPS細胞模型的研究

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Background: Mitochondrial Encephalopathy, Lactic Acidosis and frequent Strokes syndrome (MELAS) is most commonly caused by the A3243G mutation of mtDNA, which leads to deficiency of respiratory enzyme complex, impairment of oxidative phosphorylation and subsequently energy deficiency. To this date, role of autophagy upon MELAS syndrome was not fully explored and warranted more studies to unveil the mechanism.
Methods: Both isogenic iPS cell lines carried 85% heteroplasmy (MELAS iPS) and undetectable A3243G mutation (control iPS) were culture in the presence or absence of Carbonyl cyanide m-chlorophenylhydrazone (CCCP). Autophagy markers, mitochondrial membrane potential, oxidative stress, ATP production, bioenergetics and cell viability were determined.
Results: Western blot analysis revealed a significant increase of LC3II/LC3I ratio in MELAS iPS cells at basal level (2.65 v.s. 1.0), treatment with either CCCP (15.90 v.s. 8.33) or bafilomycin (11.32 v.s. 4.90) alone, and combination with CCCP and bafilomycin (17.10 v.s. 8.40), respectively. MELAS iPS cells showed more large punctate structures (autophagosomes) in comparison with the control iPS cells upon exposure to CCCP, while quantification analysis revealed a significance elevation (123 % v.s. 151%) of fluorescence in MELAS iPS cell. Furthermore, MELAS iPS cells showed significantly strong intensity of MitoSox fluorescence in the cytoplasm (1.81 v.s. 4.87), increased calcium flux into cytoplasm (1.27 v.s. 2.61), and decreased polarization of mitochondria (0.38 v.s. 0.24) in the presence of CCCP. The OCR % (66.9 v.s. 79.3), ATP production (19.5 v.s. 14.5) and cell viability (57.1 % v.s. 50.4 %) were significantly decreased in MELAS iPS cells under the treatment of CCCP.
Conclusions: Oxidative insults induced bulk macroautophagy with the accumulation of autophagosomes and autolysosomes upon marked elevation of ROS, overload of intracellular calcium, and robust depolarization of mitochondrial membrane potential, while mitochondria respiratory function was impaired and widespread mitophagy compromised cell viability.

94 Clinical Effect and Long-term Sequelae of Radiation Therapy on Pediatric Brain Tumors

放射治療對兒童腦瘤治療效果與長期追蹤

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Background: Pediatric brain tumors are the second most common malignancy in children. The goal of surgical resection of brain tumors or radiotherapy is the maximal resection or shrinkage of tumor tissue to relieve symptoms, increase survival, and provide an accurate histological/molecular diagnosis combined with minimal disruption of the patient's sensorimotor, language, and cognitive abilities. Radiation therapy (RT) is a major treatment for brain tumor after surgery. The debilitating long-term neurocognitive effects of RT have been increasingly apparent with improvements in treatment and survival. In each of these cases changes were observed in the brain magnetic resonance imaging (MRI) of the tumor.
Methods: We compared the effect of neurosurgical excision plus radiotherapy and compared with radiotherapy alone in one hospital center (VGH-TPE) evaluable patients with a radiological diagnosis of single brain tumor. We will analyze the clinical effect and the long-term sequelae for the brain tumor patients who had accepted the treatment of neurosurgical excision plus radiotherapy and compared with radiotherapy alone. And the patients continued for follow-up care more than 3 months in our hospital center.
Results: There are 29 cases of brain tumor under 18 years old. Male : Female was 17:12. Mean diagnosis age was 8.0 years old and mean follow-up time was 11.4 years. This data analysis about the long-term sequelae of radiation therapy, the complication rates about secondary tumor was 3%; vasculopathy was 25% which including stroke ,AVM, and moyamoya disease. The endocrine disorders was 37% which the major complication was hypothyroidism and the Growth hormone deficiency (26%). The combined treatment compared with radiotherapy alone led to a longer survival. Improvement in functional status occurred more rapidly and for longer periods of time after neurosurgical excision and radiotherapy and after radiotherapy alone.
Conclusions: The brain tumor patients follow-up care more than 3 months after treated with surgical excision and radiotherapy. Pediatric brain tumors is also responding well to the treatment of radiotherapy alone and completely remission .

95 Analysis of Sleep Disorders in Children — Two Years' Experience of a Sleep Clinic

兒童睡眠疾病的分析—兒童睡眠特別門診的兩年經驗

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Background: Sleep-related problems are common complaints at pediatric clinics, which could have significant impact on the daily life of patients and their family. A Sleep Clinic was set up, which is responsible for a sleep-specific certificated pediatrician and focus on resolving sleep disorders for pediatric population since January 2017. This clinic has been lasting for two consecutive years and we would like to share the clinic experience about sleep disorders from a pediatric neurologist's perspective
Methods: The consecutive patients from pediatric Sleep Clinic at Chang Gung Children's Hospital between January 2017 and January 2019 with a discharge diagnosis including sleep-related disorders were retrospectively identified. Records of patients who met criteria for sleep-disordered breathing, parasomnia, sleep-related movement disorders, hypersomnia, enuresis, behavioral sleep disorders and other complaints related with sleep were included.
Results: Total 119 patients were enrolled, 91 males and 28 females. The age distribution is between 4 months old and 56 years old. The diagnosis of these patients were sleep-disordered breathing (n=39), behavioral sleep disorders (n=32), sleep movement disorders (n=18), parasomnias (n=17), narcolepsy (n=7), enuresis (n=5), nocturnal epilepsy (n=2) and others sleep disorders (n=2).
Conclusions: The sleep disorders in pediatric patients are common. The different treatments for diversity of diagnosis are important for the comprehensive care of pediatric sleep disorders. Therefore, pediatric neurologists play important roles to provide professional medical service for children with sleep disorders.

96 Multiple Subependymal Pseudocysts in Neonates Play a Role in Later Attention Deficit Hyperactivity and Autistic Spectrum Disorder

新生兒時期發現之Multiple subependymal pseudocysts與後續注意力不足過動症及自閉症譜系發生之關聯性

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Background: To assess the long-term neurodevelopmental outcome of normal-term neonates who were accidentally

found to exhibit subependymal pseudocysts (SEPCs), frontal horn cysts, or choroid plexus cysts through cranial ultrasound (CUS) examination in a neonatal health examination.
Methods: In total, 5569 neonates received CUS examination as an item in a health examination during the first week of birth between 2002 and 2012. Among them, 5147 infants fulfilled the inclusion criteria. The participants were aged between 5 and 15 years at the time when the data were collected. We retrospectively collected these data and interpreted their statistical significance by using one-way analysis of variance, Chi-square test with Yate's correction and odds ratios
Results: The presence of SEPCs was significantly correlated with developmental delay, particularly with attention deficit hyperactivity disorder (ADHD) and autistic spectrum disorder (ASD). The risk of ADHD or ASD was significantly higher in participants with multiple SEPCs, among whom the odds ratios for ADHD and ASD were 6.50 (95% confidence interval [CI] = 2.27–18.64) and 28.54 (95% CI = 5.98–136.36), respectively, higher than those for the total study population.
Conclusions: Our data revealed multiple SEPCs in normal-term neonates as a risk factor for neurobehavioral outcome, particularly in ADHD and ASD. Simultaneously, the utility of CUS examination as a health examination item for neonates was confirmed.

97 Cytomegalovirus Infection in Infancy may Increase the Risk of Subsequent Epilepsy and Autism Spectrum Disorder

嬰幼兒時期巨細胞感染可能增加之後癲癇及自閉症之風險

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Background: Cytomegalovirus (CMV) infection in childhood ranges from asymptomatic or mild disease to severe and life-threatening disease. Children who survived from a CMV infection early in life might have higher risk of developing neurodevelopmental sequelae including intellectual disability, attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD), cerebral palsy, hearing loss and seizures. The aim of this study is to investigate the association of childhood CMV infection and subsequent epilepsy and neurodevelopmental disorders: Attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD).
Methods: We retrospectively analyzed our data of one medical center on children aged ＜18 years, who had definite CMV infections with positive serums findings from January, 1 2005, to December, 31 2017. The patients were followed in order to evaluate the risks of epilepsy and neurodevelopmental disease (ADHD and ASD) after CMV infections (CMV group), compared with those with other infections (control group).
Results: A total of 69 patients were included in CMV group, with average age of 3.78 year. A total of 292 patients with other infections were included in control group, with average age of 3.16 years. The risk of developing epilepsy in group 1 was 16.4 (95% CI=3.32-80, p=0.001) compared to group 2. The risk of developing ASD in the age interval of 0-2 years in CMV group was 17.9 (95% CI=1.96-162.8, p=0.01) compared to control group. However, the incidences of ADHD in CMV group were not significantly higher than those in control group.
Conclusions: CMV infection in infancy is associated with increased risk of subsequent epilepsy and ASD, but is not associated wih ADHD. The mechanism needs further research.

98 Assisting Diagnosis of ADHD by Gyroscope and Accelerometer

以陀螺儀及加速度計輔助注意力不集中併過動症之診斷

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Background: The diagnosis of Attention-deficit/hyperactivity disorder (ADHD) is mostly dependent on criteria and checklists. However, many authors have pointed out that the criteria and checklists used to diagnose ADHD are subjective. In present study, we use gyroscope combined with accelerometer to assist diagnosis of ADHD.
Methods: This study cohort comprised 15 patients with ADHD and 15 age-matched control subjects. The sensor including gyroscope and accelerometer together was put in a wristwatch for recordings. The watches were worn on the patient's and control's non-dominant wrist at the same time in the same class. Each time one ADHD patient and one control received recording for 2 hours per day for 3 consecutive days.
Results: In this study, we compared the measurements, including mean, variance, skewness, kurtosis, and zero crossing rate (ZCR) of gyroscope and accelerometer between patients with ADHD and controls. All average variance values of three axes (x, y, and z) were higher in patients with ADHD than in controls. Significant differences in average variance values of gyroscope and accelerometer were observed across three axes, including x ($p = 0.0268$, $p = 0.0010$), y ($p = 0.0003$, $p = 0.0004$), and z ($p = 0.0071$, $p < 0.0001$).
Conclusions: In present study, we found that average variance values were significantly higher in patients with ADHD than in controls. Our proposed method may be a promising tool for differentiating between children with ADHD and controls.

99 The Characteristics of Perampanel-Effective, and Ineffective Patients with Pharmacoresistant Epilepsy

癲控達有效及無效之頑固性癲癇病人特性分析

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Background: Perampanel (PER), a selective, non-competitive α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor antagonist, had been approved to monotherapy of focal onset seizures, and been proved of the efficacy as add-on therapy in pharmacoresistant epilepsy. According to previous researches, about 30% of seizure reduction of ＞ 50%, and 10% of seizure free rate respectively, after perampanel add-on therapy had been yield. In this study, we aimed to find the different characteristics between PER-effective, and ineffective groups.
Methods: We reviewed the medical records of patients with epilepsy aged ≤18 years who received PER as adjunctive therapy in ChangGungMemorialHospital from 2016 to 2017. The demographics, etiology, seizure types, epilepsy syndrome, brain image, EEG, epilepsy duration before treatment with PER, previous and concomitant antiepileptic drugs, highest dosage of PER, seizure frequency before and after treatment initiation, and reasons for PER discontinuation were documented from the medical records. According to the responses to PER, we had divided patients into three groups as seizure free, lack of efficacy, and worse group respectively. The characteristics of the three groups were analyzed.
Results: Total 75 patients were enrolled (mean age 14.9 ± 2.3 years). There were 16 people in seizure free group, 12 lack of efficacy group, and four worse group. The median disease onset age in the three groups were 6, 5, and 6.5-year-old, and the median used antiepileptic drugs numbers before PER in three groups were 2, 4, and 2.5 respectively. The positive rate of brain MRI were 44%, 58%, and 25%, and the cognitive impairment rate were 31%, 33%, and 75% respectively in the three group.
Conclusions: PER were less effective and even worsen seizure controlled in epilepsy with encephalopathy and cognitive impairment population in this study.

100 Epilepsy and Neurodevelopmental Outcomes in Children with Etiologically Diagnosed Central Nervous System Infections: A 12-Year Observational Study

探討一群患有具病源體診斷的中樞神經系統感染兒童其癲癇和神經發展預後：一項為期12年的觀察性研究

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Background: Central nervous system (CNS) infection in childhood can lead to neurological sequelae, including epilepsy, and neurodevelopmental disorders, such as attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). This study investigated the association of etiologically diagnosed childhood CNS infection with the subsequent risks of epilepsy and neurodevelopmental disorders.
Methods: We retrospectively analyzed the data of children aged ＜18 years who had definite CNS infections with positive cerebrospinal fluid cultures from January 1, 2005, to December 31, 2017. These patients were followed to evaluate the risks of epilepsy and neurodevelopmental disease (ADHD and ASD) after CNS infections (group 1) in comparison with the risks in those without CNS infections (group 2).
Results: Results: A total of 145 patients with an average age of 41.2 months were included in group 1. The most common etiology of infection was Enterovirus, followed by group B Streptococcus. A total of 292 patients with an average age of 44.8 months were included in group 2. Compared with group 2 (reference), the 12-year risk of epilepsy in group 1 was 10.7 (95% confidence interval [CI], 2.30–49; p ＜ 0.01). Compared with group 2 (reference), the risk of ASD in the age interval of 2–5 years in group 1 was 21.3 (95% CI, 1.33–341.4; p = 0.03). The incidence of ADHD in group 1 was not significantly higher than that in group 2.
Conclusions: Conclusions: This study identified the common etiological causes of CNS infections in Taiwanese children. Enterovirus accounted for the majority of infections, followed by group B Streptococcus, S. pneumoniae, and herpes simplex virus. The highest-risk neurodevelopmental sequelae associated with CNS infection was epilepsy. Only children with enteroviral encephalitis during the preschool age interval had a higher risk of ASD.

101 Medical Exome Sequencings Application after Negative Candidate Genes Analysis in Childhood Severe Neurodevelopmental Disorder

醫源性外顯子定序檢查在兒童嚴重癲癇合併神經發展障礙病人的應用

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Background: The genetic cause of childhood neurodevelopmental disorder is complex and challenging to be diagnosed. Although whole-exome sequencing (WES) is the gold standard for the diagnosis of neurodevelopmental disorders (NDDs), it remains an ineffective approach due to its low coverage, not fully validated, and inability to efficiently detect copy number variations. Commercially available, clinically validated medically relevant exome that contains all currently known disease genes, known as MES (medical exome sequencing), with the ability to simultaneously detect single nucleotide variants, copy number variations, chromosomal rearrangements and uniparental disomy, becomes an effective alternative strategy to WES.
Methods: DNA samples from 3 patients tested negative for causative variants in candidate genes were subjected to MES that analyzes 4200 medically relevant genes and sequenced to an average coverage of 200X. Patient 1 was a 5 years old female had clusters of seizures since day 7 and with severe neurodevelopmental disability and ataxia. Initially clinical diagnosis was ion-channel associated with neonatal epilepsy. Patient 2 was a 6 year old boy who had seizures since 1 year old. He developed refractory seizures, prominent myoclonus, ataxia and cognitive regression since 5 years. The first clinical diagnosis is progressive myoclonic epilepsy. Patient 3 was a 6 years old boy, had severe autistic behavior since 3 years. He had a status epilepticus and unfortunately died at age of 6 years. The genetic data analysis is based on ACMG guideline.
Results: Case 1 harbored heterozygous CACNA1C (p.G1994R) and LRRK2 (p.A211V) after KCNQ2, SCN1A and KCNQ3 genes were tested negative. Case 2 showed heterozygous PRNP (p.E196A), SYN2 (p.L82F and p.R74P) and WWOX (p.G372RG) after negative epilepsy panel (203 genes) negative. Case 3 showed BSCL2 (p.I326Hfs12), GCNT2 (p.R385H), and UPF3B (p.D86E and p.T87K) after a negative epilepsy panel.
Conclusions: The medical exome could be an effective alternative method.

102 Developmental Outcomes and Prevalence of SLC2A1 Variants in Febrile Young Infants with Hypoglycorrhachia

嬰兒時期發燒合併低腦脊髓葡萄糖之嬰兒其發展預後及帶有SLC2A1 變異之比率

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Background: Using the data from febrile young infants who were neurologically asymptomatic in CSF analysis, this study examined: (1) the prevalence rate of hypoglycorrhachia, (2) the type of neurodevelopmental disorders at follow-up, and (3) the genetic diagnosis of GLUT1DS in young infants with hypoglycorrhachia.
Methods: 1655 neurologically asymptomatic infants aged ＜ 4 months had cerebrospinal fluid (CSF) examinations for fever workup from 2006 to 2016. Among the infants with normal CSF cell counts and without isolated pathogens, therewere hypoglycorrhachia group who had CSF glucose levels that met the GLUT1DS criteria, and age- and gender-matched non-hypoglycorrhachia group. Both groups underwent a mean duration of 71 months of follow-up. Mutational analysis of solute-carrier-family 2, which facilitated the glucose transporter member 1 (SLC2A1) gene was performed.
Results: 30 (4.2%) met the hypoglycorrhachia criteria of GLUT1DS. In the 25 infants with hypoglycorrhachia available for follow-up, four (16%) had abnormal outcomes, three (12%) showed mixed-type developmental delay and one (4%) had type 1 diabetes mellitus. In 50 non-hypoglycorrhachia infants, two (4%) showed abnormal outcomes, both with pure speech delay. The hypoglycorrhachia group had a higher rate of mixed-type developmental delay than the non-hypoglycorrhachia group (P = .034).
Conclusions: Hypoglycorrhachia may be an early biomarker for neurodevelopmental delay instead of GLUT1DS in neurologically asymptomatic infants.

103 English Title: Limb-girdle Muscular Dystrophy in Taiwan
肢帶型肌失養症在台灣

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Background: Limb-girdle muscular dystrophy (LGMD) is a hereditary disease entity characterized by limb-girdle weakness and histologically dystrophic change although genetically heterogeneous. The prevalence of each subtype of LGMD varies among different ethnic populations. This study aims to analyze the phenotypes and genotypes of Taiwanese patients with LGMD in a referral center for neuromuscular diseases.
Methods: We enrolled 110 patients clinically suspected to have LGMD who had received muscle biopsy and/or mutation analysis from 2007 to 2018 in Kaohsiung Medical University Hospital. Detailed information in medical records of these patients including disease history, physical/neurological examinations, muscle computed tomography, muscle pathology and molecular test were carefully reviewed and analyzed.
Results: In this cohort, one patient with type 1B, 6 with 1E, 5 with 2A, 6 with 2B, 6 with 2D, 8 with 2I, 3 with 2G and one with 2N have been diagnosed. The 1B patient with LMNA mutation presented with mild limb-girdle weakness and elbow joint contracture but no cardiac conduction defect. All 1E patients with DES mutation showed predominantly proximal but also distal weakness. Sudden cardiac death occurred in one patient. Muscle pathology of 3 in 5 LGMD2A patients with CAPN3 mutations showed prominent lobulated fibers. All LGMD2B patients diagnosed by complete dysferlin deficiency showed a bit slower progression, compared with type 2A. Six patients harbored a common homozygous mutation in SGCA, leading to the diagnosis of LGMD2D. All LGMD2I patients with FKRP mutations have developed dilated cardiomyopathy except for the youngest one. Muscle pathology of two in 3 LGMD2G patients with TCAP mutations showed vacuolar change. One LGMD2N patient with POMT2 mutations presented with slowly progressive weakness without significant intelligence impairment.
Conclusions: Our study showed that muscle pathology remains helpful in guiding further molecular analyses and is crucial for establishing the genotype-phenotype correlation. We also determined the frequencies for different types of LGMD in our cohort which is important for developing specific care system for each disease.

104 Pediatric Restless Legs Syndrome-A Case Series Report
兒童不寧腿症候群~病例系列報告

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Background: The prevalence of restless legs syndrome (RLS) in children was about 2%. The diagnoses depend mainly on the discomforts reported by patients. However, this description ability varies in the different age group. The aims to ours study are to know the major complaints and risk factors in these children with RLS.
Methods: We retrospectively collected and reviewed the medical records of children who visited the outpatient clinic and sleep centers because of the sleep problems from Aug 2015 to Nov 2018. The enrolled criteria are as follows: the patient's age is younger than 18 years old; the International Classification of Diseases (ICD-10) diagnosis code includes G25.81 (restless legs syndrome). Demographic data, polysomnographic findings and iron profiles were analyzed.
Results: 11 children (Age (Mean +/- S.D)=8.5 +/- 3.71) were enrolled in this analysis. The first two reasons of OPD visiting were legs jerks in sleep (45.5%) and leg pain (36.4%). 63.6% participants in our cases has elevated periodic limb movements index. As for the PSG findings, prolonged sleep onset latency and decreased sleep efficiency were noted. Besides, serum Ferritin level less than 50ng/ml was noted in 5 children, and transferrin saturation less than 20% was also found in 8 cases. 9 of 11 children received iron therapy, and 8 kids have subjective improving sleep quality.
Conclusions: Restless legs syndrome impaired sleep quality. The caregiver should aware of limb jerks in sleep and leg pain at bedtime. Iron supplement may help these children with RLS.

105 Stormorken Syndrome with STIM1 Mutation: The First Report in Taiwan

STIM1突變之Stormorken症候群：臺灣第一例

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Background: Stormorken syndrome is a rare autosomal dominant disease characterized by thrombocytopenia, muscle weakness, asplenia, miosis, migraine, and ichthyosis. It is caused by heterozygous mutation in the STIM1 gene, which encodes a multidomain protein, essential for calcium homeostasis. When Ca2+ store depletion, STIM1 unfolds and activates the Ca2+ entry channel through store-operated Ca2+ entry (SOCE). The STIM1 mutations in Stormorken syndrome patients cause gain of function leading to excessive Ca2+ entry which results in platelet consumption and defective muscle contraction. So far, only 11 typical patients have been reported globally.
Methods: We reviewed the medical record of a 13 years old boy diagnosed with Stormorken syndrome. Detailed information about history, physical examinations, muscle computed tomography (CT), muscle pathology and genetic test was analyzed and delineated.
Results: We reported a 13-year-old boy who was initially diagnosed as idiopathic thrombocytopenic purpura at age 3. Mild motor development delay was noticed in childhood. He was referred to Neurologist at age 13 due to persistent hyperCKemia. Physical examinations showed short stature, bilateral miosis, and generalized muscle weakness with predominance in proximal lower extremities. Laboratory data demonstrated borderline thrombocytopenia (150000/ul), hypocalcemia (Ca2+: 4.0 mg/dl), and hyperCKemia (3971 IU/L). Muscle CT displayed mild muscular atrophy and fatty degeneration in the supraclavicular, pectoralis, gluteal, and hamstrings regions. Muscle pathology revealed tubular aggregates, highlighted on modified Gomori trichrome and NADH-TR staining. Based on above features, we analyzed the STIM1 gene and identified c.910C＞T(p.ARg304Trp), a common mutation reported in Stormorken syndrome.
Conclusions: This is the first report of Taiwanese patient with typical Stormorken syndrome. Stormorken syndrome should be considered when tubular aggregates myopathy is present with extra-muscular features, such as miosis, thrombocytopenia, and hypocalcemia. Although currently there is no curative therapy, inhibitor of store-operated calcium may become a potential therapeutic agent according to ongoing studies.

106 NUT Midline Carcinoma (NMC): Clinical Features and Molecular Pathology

NUT中線上皮癌（NMC）：臨床表現與分子病理

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Background: NUT midline carcinoma (NMC) is a rare but highly aggressive tumor that mainly occurs in the head and neck or mediastinum of children and young adults, with a median survival of only 6.5 months. NMC is genetically defined by chromosomal rearrangement of the nuclear protein in testis (NUTM1) gene, such as BRD4-NUTM1 (accounting for approximately 80% of the cases) or other variants. Histologically, NMC has been considered as a poorly differentiated squamous cell carcinoma, whereas cases identified from undifferentiated soft tissue sarcomas have also been reported.
Methods: The medical record, imaging, and histopathology of a young child with NMC of the posterior neck were reviewed. Fluorescent in situ hybridization (FISH) and RNA sequencing (Illumina TruSeq) were performed and analyzed to study the molecular characteristics of the tumor.
Results: A 1-year-and-11-month-old Taiwanese girl was taken to the hospital due to progressive neck pain and right-sided weakness for 1 week. Neuroimaging revealed an epidural tumor at the cervical C1-C2 level with spinal cord compression. After C1 laminectomy and partial resection, her symptoms had partially improved. A subsequent gross total resection of the tumor was performed 2 weeks later. Histopathology showed an undifferentiated round cell sarcoma (URCS) with epitheloid and rhabdoid cells showing NUT protein overexpression. FISH studies were negative for EWSR1 or CIC rearrangements. A consultation was made to the NMC Registry (www.nmcregistry.org) and the diagnosis of NMC was confirmed by international review. RNA sequencing revealed a cryptic CIC-NUTM1 rearrangement. A modified Scandinavian Sarcoma Group (SSG) IX protocol using vincristine, doxorubicin, ifosfamide, and cisplatin in alternating cycles was applied

and focal radiotherapy to the primary site was given right after the third chemotherapy cycle. The girl remained in Complete Response at 9 months after initial diagnosis.
Conclusions: NMC is a highly aggressive tumor which may constitute a subset of undifferentiated sarcoma of childhood. Gross total resection and early local control with radiotherapy may be beneficial to survival. The role of systemic chemotherapy with SSG IX or similar protocols remains to be investigated.

107 Prophylactic G-CSF Administration in Children with Acute Lymphoblastic Leukemia Undergoing Induction Chemotherapy

兒童急性淋巴性白血病引導期治療間G-CSF預防使用之經驗

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Background: Life-threatening infections in children with acute lymphoblastic leukemia (ALL) undergoing induction chemotherapy can be prevented successfully by prophylactic antimicrobials. Breakthrough bloodstream and invasive fungal infections are concerning. In this study, we evaluate the administration of granulocyte-colony stimulating factor (G-CSF) prophylaxis to reduce life-threatening infections.
Methods: This study enrolled 152 children aged ≤ 18 years with newly diagnosed ALL received the treatment of Taiwan Pediatric Oncology Group-ALL 2002 and 2013 between January 1, 2010 and December 31, 2018. Prophylactic ciprofloxacin, vancomycin, and micafungin were administered during induction chemotherapy. G-CSF (at a dose of 200ug/m2/day, subcutaneously) was administered when a patient continue profound neutropenia (absolute neutrophil count ＜100/μL) after the second dose of epirubicin chemotherapy since June 1, 2015. G-CSF therapy was discontinued when ANC recovered to ＞ 500/μL. All episodes of life-threatening bloodstream, fungal infection, febrile neutropenia occurring, duration of neutropenia, duration of induction chemotherapy, antibiotics exposure were recorded.
Results: From January 2010 to May 2015, 81 children experienced a total of 11 (13.6%) episodes of bloodstream infection and 2 (2.5%) episodes of invasive fungal infection (IFI). In contrast, 5 (7%) episodes of bloodstream infection occurred and one (1.4%) IFIs were reported to occur in 71 patients received prophylactic G-CSF therapy since June 2015. Reduction of life-threatening infections occurring did not achieve statistically significant during G-CSF prophylaxis. Compared with patients who received no G-CSF prophylaxis, patients who received G-CSF prophylaxis had a significant reduction of empiric antibiotics, cefuroxime or amikacin, exposure ($p < 0.001$), duration of neutropenia ($p=0.010$), and duration of induction chemotherapy ($p=0.037$).
Conclusions: Prophylactic G-CSF administration in children with ALL underwent induction chemotherapy cannot significantly reduce the rates of life-threatening infection. However, the empiric antibiotics exposure, duration of neutropenia and induction chemotherapy were shortening.

108 Malignant Testicular Tumors in Children: A Single Institution's 12-Year Experience

兒童惡性睪丸腫瘤：單一機構的12年經驗

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Background: Testicular neoplasms are not commonly found in children. However, there is no consensus concerning their management. The aim of this study was to present an undated picture of integrated management of pediatric testicular tumors based on our 12 years' experience.
Methods: Records of children who were treated for malignant testicular tumor in our institution from 2006 to 2018 were reviewed retrospectively. Information recorded for each patient included age, clinical characteristics, diagnostic procedures, treatment methods, histopathological findings, and outcome.
Results: Forty-one patients with a median age of 7.7 years were treated for malignant testicular tumors. All patients presented with a testicular mass. Seventeen patients had mixed germ cell tumors, 14 pure yolk sac tumors, 2 immature teratoma, 2 teratocarcinoma, and 1 had sex cord stroma tumor. Five lesions were diagnosed as non-germ cell tumors: 2 embryonal rhabdomyosarcoma, 2 lymphoma, and 1 AML. At initial presentation, retroperitioneal (n = 2), bone marrow (n =1), and mediastinal (n = 1) metastases were recorded in 4 (10%) patients. Initial operative procedures were radical inguinal orchiectomy (RIO; n = 5), scrotal orchiectomy (SO; n = 30), and testicular biopsy or testis-sparing enucleation of the tumor (n = 6). Postoperatively, 18 patients received adjuvant chemotherapy (n = 13) or chemoradiation (n = 5). Five patients with mixed germ cell tumor (n = 2), group IV paratesticular rhabdomyosarcoma (n = 2), and AML with myeloid sarcoma (n =1) died of progression of the disease. One patient with yolk sac tumor who was alive despite progressive disease at 25 months of follow up. One patient was clinically diagnosed with growing teratoma syndrome 10 months after treatment of mixed germ cell tumor. All remaining patients were alive and disease free at their last outpatient appointment.
Conclusions: Childhood testicular tumors deserve special diagnostic attention from the therapeutic point of view. A solid scrotal mass should be considered malignant until proved otherwise. Any suspicion of the testicular tumor warrants an inguinal approach to prevent scrotal violation by the tumor.

109 Clinical Features and Treatment Outcome of Children with Langerhans Cell Histiocytosis: a Single Center Experience

兒童蘭格罕氏組織細胞增生症的臨床特徵與治療成果：單一機構之經驗

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Background: Langerhans cell histiocytosis (LCH) is a rare disorder which most often affects children under 2 years of age. The aim of this report is to describe the clinical features and treatment outcome of analyze children with LCH in a single institution in Taiwan.
Methods: Medical records of children with diagnosis of LCH between 2001 and 2018 and being treated in Linkou Chang Gung Memorial Hospital were retrospectively reviewed. Data on clinical features, laboratory intervention, and treatment outcomes were collected and analyzed.
Results: Forty-nine pediatric patients with LCH were identified. There were 25 boys and 24 girls. The median age at diagnosis was 2.1 years (range, 0.1 to 13.4 years). Bone was the most frequently affected organ (71.4%) followed by skin (26.5%). Thirty-six patients (73.5%) had single system (SS) disease, and 13 patients (26.5%) had multisystem (MS) disease. The median age of patients with MS-LCH was significantly younger than patients with SS-LSH (0.9 vs. 3.8 years, $P < 0.01$). Among 13 patients with MS-LCH, 9 had risk organ involvement. None of patients with SS-LCH had risk organ involvement. Fourteen patients (28.6%) underwent local treatment only, and 35 patients (71.4%) received systemic chemotherapy. Eleven patients (22.4%) had disease progression. Two patients were transferred to other hospitals within one month of disease progression. Both patents were not included in the survival analysis. The 5-year progression-free survival (PFS) rate and overall survival (OS) rate were 75.9% and 97.6%, respectively. The PFS tended to be lower in patients whose age at diagnosis $<$ 2 years compared to those older than 2 years old (70.3% vs. 82.7%, $P = 0.12$). Patients with MS-LCH had significantly lower PFS than those with SS-LCH (43.6% vs. 84.4%, $P < 0.01$). At the last follow-up, six patients had sequelae related to disease or treatment.
Conclusions: In our study cohort, some patients with progressive disease could be successfully managed by salvage therapy. Vigilant long-term follow-up would be essential for detection and management of sequelae related to disease or treatment.

110 High Dose Chemotherapy with Autologous Stem Cell Rescue in Pediatric High Risk Ewing Sarcoma: a Single Institute Experience

高風險伊汶氏肉瘤病患接受高劑量化學藥物治療併自體幹細胞移植：單一機構治療經驗

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Background: The combination treatment of surgery, chemotherapy and radiotherapy were reported to improve the overall survival in pediatric patients with Ewing sarcoma. However, the prognosis remains poor for the patients with metastatic disease at diagnosis or recurrent tumor. Other high risk features include large tumor burden, tumors of the axial skeleton and poor histologic response after initial chemotherapy. Several studies have documented high dose chemotherapy with autologous stem cell rescue (HDC-ASCR) to be effective in such high risk patients. Herein, we present the results of HDC-ASCR for pediatric high risk Ewing sarcoma at our institute.
Methods: From April 2003 to December 2018, pediatric patients with Ewing sarcoma who were younger than 25 years old at transplant and received HDC-ASCR as part of treatment were included. The patients' characteristics, disease status, stem cell dose, engraftment status, post-transplant complications and outcome were analyzed.
Results: There were 12 pediatric patients with Ewing sarcoma, who received HDC and ASCR at complete response (CR, n=6), partial response(PR, n=5), and stable disease (SD, n=1) were enrolled. Ten patients had metastatic disease. The male to female ratio was 5 to 7. Median age at diagnosis and transplant was 15 years old (ranged 3-25) and 16 (ranged 4-27), respectively. The conditioning regimen included TBI/melphalan/etoposide in 4, ifosfamide/ carboplatin/etoposide in 1, melphalan/carboplatin/etoposide in 6, and busulfan/melphalan in 1. The median duration of follow-up is 42 months (ranged 13-113).The median infused nucleated cell dose, and CD34+ cells was 8.31 $x10^8$/kg (ranged 4.50-17.51 $x10^8$/kg), and 7.11 $x10^6$/kg (ranged 0.47-37.32 $x10^6$/kg), respectively. All patients achieved successful engraftment. The median days for absolute neutrophil count>500/mm^3, and platelet>20000/mm^3 were 10days (ranged 8-19), and 16.5 (ranged 12-30). The post-transplant complications included 12 neutropenic fever episodes, 5 mucositis, 5 candidiasis,2 diarrhea, 1 skin rash, 1 gingivostomatitis,1 esophagitis,1 pneumonia,1 cellulitis, 1 hypokalemia and 1 hemorrhagic cystitis. No transplant-related mortality was recorded. The 5-year progression-free and overall survival are 50%, and 63.5%.The causes of death (n=4) are all contributed to disease progression.
Conclusions: With successful engraftment & limited toxicity, the role of in HDC-ASCR pediatric high risk Ewing sarcoma seems encouraging. For small numbers of our patients and limited observation period, the efficacy of

HDC-ASCR in pediatric high risk Ewing sarcoma patients should be explored by well-designed prospective and randomized study.

111 Efficacy and Safety of Denosumab Therapy for Low Bone Mineral Density in Childhood Cancer Survivors: A Report of Preliminary Experience

Denosumab對兒童癌症存活者之骨密度低下治療的效果與安全性：初步經驗報告

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Background: Low bone mineral density (BMD) is one of the bony consequences in childhood cancer survivors. Denosumab is an effective therapy for adult with osteoporosis, while these experiences are limited in children. In this study, we reported our results of denosumab therapy for low BMD in childhood cancer survivors.
Methods: From May 2010 to January 2018, the lumbar BMD of children with cancer were monitored by dual energy x-ray absorbtiometry (DXA) after completion of chemotherapy with a 6-month interval. For those patients with low BMD, Calcium carbonate and vitamin D3 supplements were administered with approximately dose initially. Once low BMD continued at least 6 months, denosumab therapy was introduced. We investigated their BMD change and adverse effects during denosumab therapy.
Results: There were 20 patients received denosumab treatment. The median height adjustment Z-scores of BMD before denosumab treatment was -2.43 (-1.61~-4.17), and increased to -1.86 (0.08~-3.39), -1.56 (-.098~-3.97), -1.28 (-.067~-1.90) at 0.5, 1, 1.5 years after denosumab treatment respectively (P=0.035). Hypocalcemia occurred in 40% (8/20) of the patient. These hypocalcemic patients recovered well after continuous calcium supplement except for one patient who died for relapsed leukemia.
Conclusions: Denosumab is an effective and safe treatment for low BMD in children with cancer.

112 Dose Cisplatin-induced Nephrotoxicity Precede Ototoxicity? A Zebrafish Animal Model

順鉑引起之腎毒性早於耳毒性？一個斑馬魚動物模式

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Background: Zebrafish lateral line hair cells and skin ionocytes are functionally resembling inner ear hair cells and renal tubular cells in humans. This study aimed to demonstrate cisplatin induced toxicities by using zebrafish as a model animal.
Methods: Zebrafish embryos were incubated in different concentrations of cisplatin at 0~96 h post-fertilization. Using a non-invasive, scanning ion-selective electrode technique (SIET), we measured the functions of hair cells (Ca2+ influx) and ionocyte ([H+] gradients). The survival rate, phenotype, body length, whole-body ion (Na+, Cl-, and Ca2+) and Pt contents were also determined.
Results: The effects of cisplatin on zebrafish embryos were demonstrated as first impairing hair cell function (at 1 μM of cisplatin), the hair cell number, and body ion content of Cl- (at 10 μM of cisplatin), then decreasing ionocyte acid secretion and overall body ion contents of Na+ and Ca2+ (at 50 μM of cisplatin). The body length and ionocyte density decreased at 100 μM of cisplatin, and survival decreased at 500 μM of cisplatin. As the cisplatin concentration increased, the accumulation of Pt in fish embryos also increased.
Conclusions: By determining the lowest observed effective concentration of cisplatin that caused in vivo functional alterations of zebrafish hair cells and skin ionocytes, the results revealed that hair cells are significantly more susceptible to cisplatin toxicity than ionocytes. Our results imply that cisplatin-induced ototoxicity could precede nephrotoxicity in humans.

113 Apoptosis of Human Peritoneal Mesothelial Cells in vivo Exposed to Peritoneal Dialysis Solutions and the Associated Mechanism

由腹膜透析引流液分離人類腹膜間皮細胞之細胞凋亡與相關機轉

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Background: Peritoneal dialysis (PD) is an established treatment for end stage renal disease. Human peritoneal mesothelial cells (HPMCs) form a monolayer, lining the

surface of the peritoneal membrane and form the permeability barrier. Approximately 20%-30% of patients treated with PD gradually lose peritoneal membrane function and loss of HPMCs develops in a majority of these patients. Thus, to clarify the possible mechanism of cell death in HPMCs during PD therapy is critical in long-term preservation of the peritoneum as a dialyzing organ.

Methods: To examine the cell death pattern in HPMCs during PD therapy, we investigated the expression of apoptosis associated molecules in HPMCs separated from peritoneal dialysis effluents. Peritoneal dialysis effluents with different dextrose concentration were analysis. The possible apoptosis related molecule was evaluated in vivo by immunofluorescence staining to determine the possible molecular mechanisms.

Results: We determined annexin V expression by immunofluorescence staining in HPMCs separated from peritoneal dialysis effluents. We found that the HPMCs separated from peritoneal dialysis effluents undergoing apoptosis and presented with annexin V expression. The peritoneal dialysis effluents of different dextrose concentration were analysis also. The apoptotic rate is 31.6 ± 7.0%、37.6 ± 8.3 and 40.1 ± 7.3 (%, Mean ± SD) respect to separate from 2.5% dextrose, 4.25% dextrose and 7.5% icodextrin PD solutions. We further exam the possible role of microtubules in apoptosis of HPMCs separated from peritoneal dialysis effluents. We found different stages of microtubules involvement in apoptotic HPMCs by immunofluorescence staining. This suggests microtubules may involve in the process of apoptosis in HPMCs separated from peritoneal dialysis effluents.

Conclusions: This study in vivo explores apoptosis of HPMCs during PD therapy. The apoptotic rate is different in various dextrose concentration of PD solution. We also found the possible role of microtubules in the process of apoptosis in HPMCs separated from peritoneal dialysis effluents. Therapeutic regimens that modulate HPMCs apoptosis may have important clinical implications during PD.

114 Urine Metabolomic Profiling of Childhood Nocturnal Enuresis

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Background: The pathophysiology underlying childhood nocturnal enuresis is complex and not fully understood. In this study, we analyzed metabolites in urine collected from children diagnosed of monosymptomatic nocturnal enuresis (MNE) with the aim of gaining metabolomics insights into its pathogenesis.

Methods: A total of 70 urine samples were collected from the children with primary MNE (n=43, age: 8.8±2.4 years, male/female: 24/19) and healthy children (n=27, age:7.4±0.5 years, male/female:17/10). In all subjects, their renal functions and urinalysis were normal (i.e. no proteinuria, no hematuria, no proteinuria and no glycosuria). Besides, there were no structural abnormalities of kidneys and urinary tract in ultrasound scans. Analysis of urinary metabolites were conducted using 1 H-nuclear magnetic resonance (NMR) spectroscopy and subsequently, the data was analyzed by multivariate statistics such partial least-squares discriminant analysis and cluster analysis.

Results: Urinary metabolomics identified several metabolites (e.g. 3-hydroxylisovalerate, alanine, creatinine phosphate, glycine, hypoxanthine, isoleucine, lysine, N, N-dimethylglycine, N-isovaleroylglycine and tyrosine, $P < 0.01$ of all) significantly associated with childhood MNE.

Conclusions: This is the first NMR-based metabolomic study of investigating nocturnal enuresis in children. The characteristic urinary metabolites are recognized in children with primary MNE, but the further study is required to elucidate the biochemical pathways, and to explore potential metabonomic marker of refractory NE.

115 Outcome of Low Dose Afinitor for Tuberous Sclerosis Complex Associated Angiomyolipoma-The Result of 48 Months Follow-up

以低劑量Afinitor治療結節性硬化症血管平滑肌脂肪瘤的成效─48個月追蹤結果

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Background: Tuberous sclerosis complex (TSC) presents with multisystem benign neoplasm induced by dysregulation of the mammalian target of the rapamycin pathway. This study aimed to examine the effects of low-dose everolimus on the treatment of TSC-associated angiomyolipoma (AML).

Methods: Between July 2013 and August 2017, patients with TSC-AML were selected for an everolimus therapy protocol. An oral everolimus dose starting at 2.5 mg daily, was gradually increased to 5.0 mg daily. All patients were evaluated using magnetic resonance imaging or computed tomography scanning at baseline, 12, 24, 36 and 48 months after the start of treatment for measuring changes of renal AML mass volume.

Results: Eleven patients were enrolled for investigation in this study. Everolimus therapy resulted in significant shrinkage of TSC-AML volume after 48 months follow-up. Serum levels of everolimus were subdivided into group I

(＜8 ng/ ml, n=6), and group II (＞8 ng/ ml, n=5). The volume reduction rates were 10.6% to 65.2 % in group I and 42.5% to 70.6% in group II. To evaluate the response to treatment, 3 of six (50%) were responders in group I, and all the patients in group II (5/5, 100%) were responders. The differences in AML volume reduction between the groups were statistically significant at 12 months (p=0.011), 24 months (p=0,006), 36 months (p=0.014) and 48 months (p=0.05).

Conclusions: These results suggest that low-dose everolimus therapy is effective in shrinking TSC-AML volume and minimizes adverse effects, subsequently reducing medical costs.

116 Risk Factors of Vesicoureteral Reflux in Children with Imperforate Anus

無肛症病童合併膀胱輸尿管迴流的危險因子分析

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Background: Imperforate anus (IA) is a congenital disease which occurs in approximately 1 newborn per 4000-5000 live births in Taiwan. Urinary tract anomalies are more often seen in children with IA and might increase risk of recurrent urinary tract infection (UTI) and renal damage.

Methods: In this case control study, we used National health insurance research database (NHIRD), aiming to survey the frequency of congenital anomalies of the kidney and urinary tract (CAKUT) in children with IA and to investigate the risk factors of vesicoureteral reflux (VUR).

Results: We collected 613 children during 2000-2008 (367 boys and 246 girls; 489 low position IA and 124 high position IA). The high position IA had significantly increased risk of VUR, compare with those with low position IA (OR 2.68, 95% CI 1.61, 4.45). In addition, IA children with CAKUT, hydronephrosis, or ever UTI had greater risk of VUR (OR 8.57, 95% CI 3.75, 19.6; OR 7.65, 95% CI 4.48, 13.1; OR 31.8, 95% CI 11.5, 88.3, respectively). However, there was no statistical difference of VUR risk stratified by gender and chromosome anomaly.

Conclusions: In conclusion, our study found high position IA had greater risk of VUR, particularly those with CAKUT, hydronephrosis, or UTI. Such high-risk patients should need periodical urinalysis to screen UTI and early VCUG study to survey UVR in order to prevent consequent renal damage.

117 Urinary Microalbumin as a Minor Diagnostic Criterion of Kawasaki Disease

尿中微蛋白量做為診斷川崎氏症的次要標準

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Background: The diagnosis of KD depends on the clinical features. Nonspecific laboratory tests provide support for a diagnosis of atypical KD and are used as minor diagnostic criteria. Urinalysis may show pyuria in up to 80% of KD patients. Correlation of increased microalbuminuria with cardiovascular disease has been reported. There is no previous study about the relationship between KD and urinary microalbumin. The purpose of this study is to examine whether urinary microalbumin could be used as a minor diagnostic criteria of KD.

Methods: This study consisted of 101 KD patients (age: 23.2±24.6 months; male/female: 61/40) who fulfilled the diagnostic criteria at the Department of Pediatrics, Kaohsiung Veterans General Hospital. Medical records were reviewed for age, sex, presenting symptoms, complications, and laboratory data within 7 days of illness. The definition of albuminuria (urine-albumin/creatinine) degree is as follows: normal ＜0.03 mg/mg, microalbuminuria 0.03-0.3 mg/mg, macroalbuminuria ＞ 0.3 mg/mg. The relationship of urine-albumin/creatinine and other laboratory data was analyzed.

Results: The percentages of macroalbuminuria, microalbuminuria, and normal urinary microalbumin are 4%, 36%, and 60% respectively. The percentage of positive urinary protein is 15%. The percentage of pyuria (＞10 WBC/HPF) is 18%. The percentage of low serum albumin (＜ 3 g/dl) is 16%. The percentage of high GPT 46.5%. The percentage of leukocytosis (＞15000/mm3) is 24%. The percentage of high CRP (＞3.0 mg/dL) is 51.5%. There is a significant correlation of albuminuria with CRP level ($p < 0.05$).

Conclusions: Our results suggest urinary microalbumin might be used as a minor diagnostic criterion of KD.

118 Establish a Highly Sensitive and Highly Specific Nephrotoxicity Detection Platform in a Transgenic Mice Model (Shen-Nong Mice)

以基因改造小鼠(神農鼠)模式建立高靈敏且高專一性的腎毒性檢測平台

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Background: With the rapid development of science and technology, many new chemical substances have been developed and applied to food additives, pesticides, environmental drugs, and clinical drugs, which will enter the human body directly or indirectly. In many ways, mice are used as animal survey models. After administration, they were evaluated for toxicity and characteristics by clinical chemistry and histopathology. The nephrotoxicity analysis is the concentration of blood urea nitrogen and creatinine, but there is a lack of specificity and sensitivity. This may result in serious and difficult recovery of human health; in addition, the prevalence of chronic kidney disease in Taiwan is highest in the world and how to improve is a problem that we urgently need to overcome.
Methods: We used the biological luciferase assay technology developed in recent to increase the specificity of detecting kidney damage with its high sensitivity and combined with the genetic modification technology. The key technology is the production of transgenic mice. In this study, we use Bacterial Artificial Chromosome as a gene carrier and the target protein gene X specifically expressed in the renal tubule is artificially implanted into the embryo with luminescent enzyme gene, and the activity of the luciferase enzyme in the blood and urine was quantified to represent the kidney damage condition.
Results: This model has been verified by in vivo imaging system and luciferase assay system to confirm tissue specificity with sensitivity. This core technology develops a highly sensitive and highly specific chemical nephrotoxicity test platform (Shen-Nong mice) to meet the needs of future health care and the biotechnology industry. And build a domestically needed nephrotoxicity analysis and testing platform.
Conclusions: Subsequent validation and evaluation of clinically common nephrotoxic drugs will establish a prototype, promote its application, and be further revised in the future. We hope that it will be approved and incorporated into the health food safety assessment. And the non-clinical safety standard of drugs, to protect the people from kidney toxicity, can gradually reduce the incidence of renal injury in Taiwan.

119 Resveratrol Prevents Combined Prenatal NG-Nitro-L-arginine-methyl ester (L-NAME) Treatment Plus Postnatal High-fat Diet Induced Programmed Hypertension in Adult Rat Offspring through Modulation of Gut Microbiota and Oxidative Stress

白藜蘆醇藉由調控腸道菌群和氧化壓力，避免產前L-NAME治療加上產後高脂肪飲食所造成的計畫性高血壓

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Background: Nitric oxide (NO) deficiency, high-fat (HF) intake, and dysbiosis of gut microbiota are involved in the development of hypertension, a disorder that can originate in early life. Our previous report showed that maternal NO deficiency induced by NG-nitro-L-arginine-methyl ester (L-NAME, an inhibitor of NO synthase) resulted in hypertension in adult offspring. We examined whether postnatal HF diet can aggravate maternal L-NAME treatment-induced programmed hypertension and whether resveratrol therapy can prevent it.
Methods: Pregnant Sprague-Dawley rats received L-NAME administration at 60 mg/kg/day subcutaneously during pregnancy alone, or with additional resveratrol (R) 50 mg/L in drinking water during the entire pregnancy and lactation. The offspring were onto either the regular chow or high-fat diet (D12331) from weaning to 16 weeks of age. Male offspring rats were assigned to five groups (N=8/group): control, L-NAME, HF, L-NAME+HF, and L-NAME+HF+R. Rats were sacrificed at 16 weeks of age. We observed that postnatal HF diet exacerbates maternal L-NAME treatment-induced programmed hypertension in male adult offspring, which resveratrol attenuated.
Results: Combined L-LAME and HF diet-induced hypertension is related to increased asymmetric dimethylarginine (ADMA, an endogenous inhibitor of NO synthase), decreased L-Arginine-to-ADMA ratio, increased oxidative stress, mediating nutrient-sensing signals, and alterations of gut microbiota compositions. L-NAME+HF caused an increase of the Firmicutes to Bacteroidetes ratio, which was prevented by resveratrol therapy. Additionally, the abundances of phylum Verrucomicrobia and genus Akkermansia were increased increases by L-NAME+HF exposures, which were further amplified by resveratrol therapy.
Conclusions: In conclusion, our data highlighted the interactions between maternal NO deficiency, HF diet, and gut microbiota in which the blood pressure of adult offspring can be modified by resveratrol. Targeting gut microbiota and oxidative stress by resveratrol might be a

useful reprogramming strategy to prevent hypertension of developmental origin.

120 Targeting on Gut Microbial Metabolite Trimethylamine-N-Oxide (TMAO) and Short Chain Fatty Acid to Prevent Maternal High-Fructose Diet-Induced Developmental Programming of Hypertension in Adult Male Offspring

針對腸道微生物代謝產物三甲胺-N-氧化物和短鏈脂肪酸預防母親高果糖飲食誘導的程序化高血壓產生

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Background: Consuming a high-fructose diet (HFD) during pregnancy and lactation causes hypertension in adult offspring. Alterations of gut metabolites, like short-chain fatty acids (SCFAs) and trimethylamine (TMA), and microbial composition are associated with the development of hypertension. We examined whether maternal 3,3-dimethyl-1-butanol (DMB, an inhibitor for TMA formation) treatment or the predominant SCFA acetate supplementation can prevent pmaternal HFD-induced hypertension in adult male offspring.
Methods: Male offspring born to Pregnant Sprague-Dawley dams were divided into 4 groups and fed as follows during pregnancy and lactation period: ND: normal diet; HFD: 60% HF diet; ACE: 60% HF diet plus 200 mmol/L magnesium acetate in drinking water; and DMB: 60% HF diet plus 1% DMB in drinking water. Male offspring were sacrificed at 12 weeks of age.
Results: HFD exposure during pregnancy and lactation induced programmed hypertension in adult male offspring, which was prevented by maternal acetate supplementation or DMB treatment. HFD-induced hypertension is relevant to increased plasma levels of TMA (614 ± 199 vs 443 ± 57 ng/mL, $P < 0.05$) and acetate (546 ± 69 vs 477 ± 24 μM, $P < 0.05$), and alterations of gut microbial composition. Dams exposed to HFD, ACE, and DMB results in long-lasting effects on their offspring's gut microbiota at 3 and 12 weeks of age. Despite ACE and DMB treatments show comparable protective effects against HFD-induced programmed hypertension, they produce distinct alterations on gut microbial compositions. The protective effects of acetate supplementation are associated with decreased plasma TMA level and TMA-to-trimethylamine-N-oxide (TMAO) ratio, and increased renal mRNA expression of SCFA receptors. While maternal DMB treatment protects offspring against hypertension is related to reduction of plasma TMA, TMAO, acetate, and propionate levels.
Conclusions: Our results indicated that maternal ACE or DMB treatment prevented HFD-induced hypertension in adult offspring via remodeling gut microbiota, regulating TMA-TMAO metabolic pathway, and mediating SCFAs and their receptors.

121 Factors Associated with the Need for Pediatric Critical Care in Community Acquired Pneumonia versus Hospital Acquired Pneumonia

社區型肺炎和院內感染肺炎可能導致需要兒童加護病房照顧的危險因子

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Background: To compare the need for pediatric critical care in a tertiary children's hospital with a diagnosis of community-acquired pneumonia (CAP) or hospital-acquired pneumonia (HAP). Furtherly, we conduct a pilot study to evaluate the possible medical biomarkers which are associated with longer pediatric intensive care unit stay.
Methods: An observational, retrospective cohort analysis was conducted of children who were admitted to our tertiary children's hospital with a diagnosis of CAP or HAP. The following prospective pilot study was conducted of children who were admitted to our pediatric intensive care unit (PICU).
Results: A total of 548 patients with 598 episodes of pneumonia requiring admission to our children's hospital. 530 episodes were identified as CAP and the other 68 episodes were HAP. CAP had significantly shorter lengths of hospital stay and duration of ICU stay than that with HAP (8.2±10.5 v.s. 36.5±31.5 days, $p < 0.001$; 2±6.9 v.s. 10±18 days, $p < 0.001$). The most common co-morbidities in CAP were neurological diseases, and atopy history. Among them, 90 episodes (17%) experienced ICU admission during the treatment course with most common co-morbidities, neurological diseases. However, in HAP patients, cardiovascular diseases were most common co-morbidities as well as those (38.2 %) who need PICU care. The pilot study included 8 children with the diagnosis of pneumonia in PICU. We divided two groups as PICU stay more than 7 days and less than 7days. The values of pro-BNP, AaDO2, Platelet, CRP, CI in PICU had significant difference in the two groups($p < 0.05$). The levels of sputum 8-isoprostane and urinary 8OHdG revealed the trend of decreasing level after disease relief.
Conclusions: In this study, we found that (1)The possible risk factors for the need of critical care are associated-neurologic disease in CAP and heart disease in HAP; (2) the possible biomarkers of pro-BNP, Platelet, CRP, CI, 8-isoprostane and 8OHdG may predict the duration of PICU stay. These results can not only help further understand the risk of pneumonia in children who requiring critical care but also provide chances for better intensive respiratory care.

122 The Clinical Significant of Filmarray Respiratory Panel in Children with Acute Febrile Respiratory Distress in Pediatric Intensive Care Unit

在兒科加護病房急性呼吸窘迫病童Filmarray呼吸道檢驗的臨床意義

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Background: Acute febrile respiratory distress is the most common cause leading to pediatric intensive care unit admission and viral infection is an important cause. FilmArray Respiratory Panel is a commercial multiplex PCR fast assay that is capable of detecting 17 respiratory viruses and 3 bacteria within 2 hours. The aims of this study were to investigate the capability of FilmArray Respiratory Panel for identification of pathogens and compare the detection rate to the current methods in children with acute febrile respiratory distress.
Methods: We conducted this retrospective cohort study in a tertiary paediatric intensive care unit between January 2018 and December 2018. All children from 1 month to 18 years of age were eligible. Nasopharyngeal aspirates were obtained and sent for viral cultures, multiplex polymerase chain reaction (PCR), and traditional quick tests as well as Filmarray Respiratory Panel. Demographic, clinical, and laboratory data were analyzed.
Results: Among the 27 patients, 21 (77.7%) had detectable pathogens. The quick antigen tests (Influenza A+B test and respiratory syncytial virus), PCR (influenza A+B and mycoplasma pneumonia) and urine pneumococcal antigen test had 29.6% positive rate, which increased to 40.7% when conventional viral cultures were combined. The positive rate further increased to 77.7% when the Filmarray respiratory panel was combined. The etiological pathogens identified were most common in rhinovirus/enterovirus (30.8%), respiratory syncytial virus (23.1%) and adenovirus (23.1%). Three patients had co-infection, and all detected by the Filmarray respiratory panel. The co-infection rate was 11.1% (3/27). The report time of Filmarray respiratory panel are 26.83+/-20.82 hours, that is shorter than PCR (65.58+/-29.51 hours) and viral culture (22.6+/-9.89 days) (both $P < 0.001$).
Conclusions: Viral infections were the main etiologies of acute febrile respiratory distress in children admitted to pediatric intensive care unit. Filmarray respiratory panel is a rapid assay that can shorten the waiting time of result and increase the diagnostic yield rate.

123 High-Flow Nasal Cannula in Children with Acute Respiratory Failure in Pediatric Intensive Care Unit

兒科加護病房在急性呼吸衰竭使用高流量鼻導管的經驗

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Background: High-flow nasal cannula showed potential to improve gas exchange, apply positive pressure, and decrease work of breathing for acute respiratory failure. The aims of this study were to descriptive demographic data and evaluate clinical characteristics of pediatric patients who had high-flow nasal cannula respiratory support.
Methods: We conducted this retrospective cohort study in a tertiary paediatric intensive care unit between January 1, 2018 and December 31, 2018. We developed a protocol of high-flow nasal cannula and it was initiated as the first line therapy for various acute respiratory failure since January 1, 2018. All children from 1 month to 18 years of age with high-flow nasal cannula respiratory support were eligible. The clinical data were reviewed.
Results: Thirty-five patients met the eligibility criteria for the study. Seventeen (48.6%) of the 35 children were male, and the mean age was 5.82+/-5.27 years. 27 (77.1%) of the children had underlying disorders. The primary indications for the utilization of high-flow nasal cannula were pneumonia (14, 40%), bronchiolitis (4, 11.4%), status asthmaticus (3, 8.5%) and status asthmaticus with bronchiolitis/pneumonia (3, 8.5%), and congenital cardiac disease with respiratory distress (3, 8.5%). The failure rate was 11.4% (4 of 35 children), including 3 (8.5%) children required intubation and 1 child (2.8%) required discontinuation due to discomfort.
Conclusions: In our small population, we found high-flow nasal cannula could be initiated as the first line therapy for various acute respiratory failure in pediatric intensive care unit and for all age groups.

124 Urine Catecholamines Study in Children with Severe Enterovirus A71 Infection: Comparison with Pediatric Septic Shock

兒童腸病毒A71型重症感染之尿液兒茶酚胺研究：與兒童敗血性休克比較

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Background: Severe enterovirus A71 (EV-A71) infections in children can result in high morbidity and mortality. Hypercatecholaminemia-related heart failure has been proposed as the main cause of rapid deterioration leading to EV-A71-related early mortality; however, few systemic studies have been conducted. The purpose of this study was to measure urine catecholamine concentrations in children with severe EV-A71 infection.
Methods: A total of 35 children, aged 2.5 ± 2.1 years, were studied. They were divided into three groups. Group I included 15 septic shock patients, group II included 17 EV-A71-stage 2 patients, and group III included 3 EV-A71-stage 4 patients. The demographic data, laboratory results, cardiac biomarkers and urine catecholamine concentrations were statistically analyzed.
Results: There were no statistically significant differences in creatine kinase and MB fraction among the groups. Group III patients had significantly higher urine catecholamine and troponin-I values among the groups. Group I had the highest C-reactive protein (CRP) levels and group II had the lowest B-type natriuretic peptide (BNP) and its N-terminal prohormone (NT-pro-BNP) values among the groups ($p = 0.039$, < 0.01 and < 0.001, respectively). If urine epinephrine $>$ 134 ug/gCr, norepinephrine $>$ 176 ug/gCr, dopamine $>$ 766 ug/gCr and vanillylmandelic acid (VMA) $>$ 11.7 mg/gCr were used as the cut-off points to differentiate group II and III, the sensitivities were all 100%, and the specificity was 100% for epinephrine, 100% for norepinephrine, 41.2% for dopamine and 100% for VMA.
Conclusions: The significantly elevated urine catecholamine concentrations in EV-A71-stage 4 patients found in this study support the hypothesis that hypercatecholaminemia-related heart failure is involved in severe EV-A71 infection. Urine catecholamines could be used as sensitive and reliable biomarkers for differentiation of severe EV-A71 infection with or without heart failure and septic shock. Further investigations and large multi-institutional studies are necessary to definitively establish the role of hypercatecholaminemia in children with severe EV-A71 infection.

125 Outcomes Analysis of Children Diagnosed with Hemophagocytic Syndrome in Pediatric Intensive Care Unit－An 15-years' Experience in a Medical Center

兒童嗜血症候群死亡預後因子探討

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Background: Hemophagocytic syndrome is a life-threatening disease which can cause rapid clinical deterioration even under intensive care setting. It is essential to identify clinical parameters which related to early mortality and establish prognostic factors correlated with unfavorable outcome for high risk patients who may fail on treatment.
Methods: Patients under 18-year-old who underwent bone marrow exam and fulfilled the diagnostic criteria of HLH-2004 from Jan. 2004 to Dec.2018 in Kaohsiung Chang Gung Memorial Hospital were enrolled. Prognostic factors including serological tests, microscopic reports of bone marrow, which correlated with mortality, length of ICU stay and treatment response, were reviewed retrospectively from medical records. Patients were divided into 4 groups based on etiology including infection associated hemophagocytic syndrome(IAHS), macrophage activation syndrome(MAS), malignancy associated hemophagocytic lymphohistiocytosis(MA-HLH) and idiopathic hemophagocytic lymphohistiocytosis(HLH). Early mortality was defined as death within 30 days. The results were acquired by using statistical analysis of Pearson chi-squared test and Multivariate analysis.
Results: Total 57 patients were enrolled with median age 9 years old, and the overall mortality was 29%. The median length of ICU stay was 11 days. 29 patients (51%) are cases of IAHS, in which 25 patients are case of virus-associated hemophagocytic syndrome(VAHS) with identifiable trigger pathogens. 15 patients (26%) are cases of MAS. 6 patients (7%) were assumed as idiopathic HLH. 9 patients (16%) are cases of MA-HLH, who has underlying hematologic disorders. The mortality rate is 28% in IAHS group, 27% in MAS group, 56% in MA-HLH group and 25% in idiopathic HLH group respectively. In each death group, early morality accounts for 50% in IAHS, and 75% in MAS group, 0% in MA-HLH and 100% in idiopathic HLH group in this review.
Conclusions: There is no significant difference in mortality rate of IAHS, MAS and idiopathic HLH, but higher in MA-HLH. The cause of death in MA-HLH is underlying disease, which is not related to hemophagocytic syndrome. Early mortality accounts for about half of death in IAHS and MAS.

126 Extracorporeal Membrane Oxygenation Support in Neonates: Analysis of Experience in a Medical Center
在新生兒使用葉克膜：一個醫學中心的經驗分析

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Background: Extracorporeal membrane oxygenation (ECMO) is the last management for infants with severe cardiopulmonary failure who have failed to respond to conventional therapy. In this study, we have focused on the influence of ECMO to pulmonary condition in chest radiography in presence of patent ductus arteriosus (PDA) and PDA condition after ECMO support.
Methods: The medical charts of all neonate who required ECMO support were reviewed during the period from June 2009 to June 2017. The patient with congenital heart disease (CHD) was excluded. Chest radiography was evaluated for ventilation condition, pulmonary opacification, presence of air bronchograms and silhouette sign between heart and lung.
Results: A total of 12 neonates received ECMO support during this period. Congenital diaphragmatic hernia (CHD) (50%) was the most common diagnosis in those neonates, followed by meconium aspiration syndrome (MAS) (25%). No significant change was noted in chest radiography between chest X-ray before ECMO support and that after ECMO support for 24 hours. Eleven neonates (91.7%) received echocardiography before ECMO support. All patients had documented pulmonary hypertension, and ten cases had PDA. No patient received PDA ligation under ECMO support. The total survival rate was 58.3% (7/12). All survival patients revealed spontaneous closure of PDA in following echocardiography after removing ECMO support.
Conclusions: In this study, we noted that no significant change in chest radiography in presence of PDA when compared chest X-ray before and after ECMO support. Following echocardiography showed spontaneous closure of PDA in the survival patient. Therefore, PDA ligation may not need in neonate under ECMO support.

127 Role of Initial Radiographic Tracheal Ratio in Predicting the Outcome of Croup in a Pediatric Emergency Department
X光片氣管比值在預測兒童急診哮吼病童結果之角色

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Background: Croup is the major cause of upper airway obstruction in children. We aimed to determine whether various features of neck radiographs can be used to objectively predict outcomes in patients with croup treated in a pediatric emergency department (PED).
Methods: We prospectively recruited 192 patients with croup admitted to the PED between 2012 and 2014. Data regarding clinical factors, fever, age, radiographic findings, and the length of hospital stay were gathered. The initial Westley score (WS), presence of steeple sign, extent of narrowing, and narrowing ratio on soft tissue neck radiographs were determined before and after treatment. The extent of frontal narrowing, extent of lateral narrowing, frontal ratio (FR), and lateral ratio (LR) were analyzed to predict clinical outcomes in patients with croup.
Results: The extent of frontal/lateral narrowing and LR were significantly correlated with outpatient status. Approximately 71% of patients with FR values below 0.23 remained in the hospital for further care, while approximately 98% of patients with FR vales ＞0.65 were discharged to outpatient treatment. Approximately 85% of patients with LR＜0.45 remained in the hospital for further care. Almost all patients with LR values above 0.6 were discharged to outpatient treatment.
Conclusions: Radiographic factors can be used to objectively assess the severity of croup and aid in clinical decision-making. LR and FR are significantly correlated with croup severity and admission rate, and that LR＞ 0.6 and FR ＞0.65 indicate low risk in patients with croup. In contrast, the patients with FR ＜ 0.23 or LR ＜ 0.45, shloud stay in hospital for further treatment and monitor.

128 Risk of Infection and Prognostic Outcomes in Neonates Born from Precipitate Labor with Out-of-Hospital Delivery
院外急產感染風險及預後研究

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Background: Precipitate labor (PL) is defined as expulsion of the fetus within less than three hours of commencement of uterine contractions. PL usually took place outside the delivery units due to unexpected timing of labor. PL is known to associate with higher rates of maternal complications and common problems of neonates. The aim of this study was to investigate the risk of infection and prognosis of neonates born with out-of-hospital delivery (OHD).
Methods: We enrolled neonates with precipitate labor at the Department of Pediatrics, MacKay Children's Hospital, from January 2004 to December 2017. Neonates born in the hospital or delivery units were excluded to meet the criteria of "out-of-hospital" birth. We retrospectively reviewed maternal history, birth records, clinical courses and laboratory data.
Results: A total of 158 newborns were enrolled. The overall

rate of OHD was 0.22%. Twenty-nine neonates (18.4%) were prematurity. Nine patients (5.7%) had positive cultures within seven days old, and two of them (1.3%) had bacteremia. Twenty-nine patients (18.4%) underwent non-sterile umbilical cord care. Six patients (3.8%) had developmental delay, and five of them (3.2%) had seizure disorder. Nine patients had infection while 149 patients had negative cultures. In the multivariate analysis, gestational age (OR, 0.75; 95% CI, 0.56–0.99; p = 0.047) was the factor associated with increased risk of infection. Eleven women (7.0%) were teenagers. Forty-nine women (31%) did not receive any prenatal examinations, and 10 women (6.3%) were even unaware of pregnancy. The newborns with OHD had younger maternal age with relative majority of teenage mothers, higher rates of prematurity, and higher rates of early-onset infection (OR, 5.12; 95% CI, 1.26–20.83; p = 0.011) than those born in hospital.
Conclusions: Poor prenatal care and social issues as teenage mothers were not uncommon in PL. Social support resources should be provided to the vulnerable populations. Preterm delivery is related to PL, and gestational age is the factor associated with infection. Early-onset infection rate of neonates with OHD is higher than general population, so those who born out-of-hospital should be hospitalized for observation.

129 Retrospective Study of Encephalitis in a Pediatric Emergency Department
兒童急診病童腦炎之回顧性研究

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Background: Encephalitis in children are medical emergency and are associated with significant mortality and neurological morbidity throughout the world. The aim of this study was to review and analyze clinical data on the characteristic of encephalitis admitted to our pediatric emergency department.
Methods: From January 2010 to September 2015, a total of 58 children were admitted to our pediatric emergency department with acute encephalitis. Electronic medical records and laboratory test data were initially reviewed to extract demographic characteristics, clinical symptoms, triad level at the time of pediatric emergency department.
Results: The series comprised 29 (50.0%) males. The mean patient age was 8.09 ± 5.069 years; 17 (29.3%) cases were ＞ 12 years of age. Patients with encephalitis were most common in winter (31.0%). Of the 58 included children, 9 (15.5%) were admitted to the pediatric intensive care unit, 10 (17.2%) were prolonged hospital stays (＞14 days). Lower motor responses in the emergency department were the significant higher rate of pediatric intensive care and prolonged hospital stays (p＜0.05).
Conclusions: Early recognition and closely monitor the vital sign is important. Future studies might explore the long-term prognoses of these patients.

130 Adolescent Developmental Assets and Longitudinal Physical and Psychosocial Health Outcomes: Analysis from a Taiwanese Cohort Study
青少年發展資產與長期生理與心理社會健康影響：台灣世代研究分析

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Background: Developmental asset-based youth development has been proposed to be associated with health behaviors and psychological well-being in adolescents. This study aims to extend the current knowledge regarding the effects of positive youth development on physical and psychosocial health outcomes in young adulthood using a large representative longitudinal sample.
Methods: Four waves of data were retrieved from the Taiwan Youth Project that comprised a longitudinal cohort of adolescents (N = 2688) surveyed at grades 7, 8, 9, and 12, and at age 22. We used principal component analysis to validate a set of adolescent developmental assets that was constructed using 35 items selected from the relevant questions in the wave 1. Outcomes included standardized scores of body mass index, self-rated health and happiness, depressive symptomology and deviant behaviors in the subsequent waves. Generalized estimating equation analysis was applied to assess the impact of developmental assets on these repeatedly measured outcome variables.
Results: The factor analysis extracted eight factors of the constructed scale, of which 4 were related to external and the other 4 related to internal assets. As compared to those with the highest quintile level of developmental assets, individual with the lowest quintile level were likely to rate themselves unhealthy (ß=0.33 [0.26, 0.40]) and unhappy

(ß=0.47 [0.41, 0.54]) and report more depressive symptomatology (ß=4.18 [3.35, 5.01]) and deviant behaviors (ß=0.63 [0.44, 0.81]). No association was found between and body mass index and developmental asset scores.

Conclusions: The results conclude a longitudinal association between adolescent developmental assets and psychosocial health outcomes in Taiwanese youth. Further research may be required to investigate whether positive youth development could be translated into long-term benefits in adult physical conditions, such as obesity.

131 Understanding Lived Experiences of At-Risk Teenage Boys in Taiwan through Photovoice

透過Photovoice了解男性高風險青少年的生活經歷

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Background: At-risk adolescents often have a range of unmet physical, developmental, and mental health needs and may suffer from negative outcomes, including substance use, economic instability, and increased likelihood of becoming adult offenders. This study aims to address the lack of research regarding at-risk boys in Taiwan by: 1) identifying common themes about the lived experiences and health needs of at-risk boys in Taiwan, 2) generating compelling evidence to better advocate for these youth, and 3) empowering participants by helping them share their needs and experiences with stakeholders.

Methods: Photovoice is a qualitative research method in which participants use photography and narratives to communicate their perspectives. Thirteen boys from a Taiwan out-of-home placement facility for adolescent boys with backgrounds in foster care or the juvenile court system participated in this study, which was facilitated by a US medical student of Taiwanese heritage. After receiving in-depth training, participants spent three months taking photos relating to their perceived health needs and sources of resiliency and support. Then, in a series of facilitated individual and group meetings, the most powerful photos were chosen, and narratives were added. Key themes were identified. The photos best reflecting the group's experiences and messages will be compiled into an exhibit targeting local community members and stakeholders. Ethics approval was granted by National Taiwan University and the University of Southern California.

Results: Common themes identified by the participants included the lack of and need for companionship, complex relationships with family, the fear of but also benefit of the law, the desire to belong in and be accepted by society, and the impact of activities as a means of encouragement and character development. Post-study reflections are also expected to show that the study led to participant empowerment.

Conclusions: The results shed light on the social determinants of health among at-risk Taiwanese youth and should be used to inform policy recommendations regarding resiliency- and health-promoting services.

132 The Effect of Oral Vitamin D3 Supplementation in Breastfeeding Newborns

口服維生素D補充對於以純母乳哺育新生兒的影響

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Background: Breast fed infants are at high risk of vitamin D deficiency. AAP and Taiwan Pediatrics Association all recommended supplementing exclusively breast-fed infants 400 IU/day of vitamin D during the newborn period. We conducted a clinical trial on vitamin D supplementation for exclusively breast-fed newborns.

Methods: Serum 25(OH)D level were measured in the pregnant women enrolled, and concentration of 25(OH)D, Ca, P, alkaline phosphatase and intact-PTH for newborns. Breastfed newborns were double-blinded, placebo-controlled, and randomized to one of the two regimens at 10 days old. Supplementation continued for 16 weeks. Placebo group was a liquid product with no vitamin D3, and the study group received 400 IU/drop/day vitamin D3. Infants with severe vitamin D deficiency at birth were excluded. We measured serum 25(OH)D, Ca, P, alkaline phosphatase, and bone mineral density of the neonates at 4 months old of age.

Results: A total of 132 pregnant women and infants were analyzed. The mean vitamin D levels were 17.23 ng/mL in pregnant women and 17.52 ng/mL in newborns. Maternal vitamin D level strongly correlated with newborn vitamin D level ($p < .001$). 67 exclusively breastfed newborns fulfilled enrollment criteria and were analyzed. The mean vitamin D levels were 38.92 ng/mL for study group and 14.92ng/ml for placebo group. The serum 25(OH)D, phosphate, intact-PTH level significant differed among the 2 groups ($p < .001$, $p=.019$, $p=.007$). But bone mineral density did not differ between them.

Conclusions: Daily oral vitamin D 400 IU increased vitamin D concentration in exclusively breastfed newborns at 4 months of age but did not affect their bone mineral density.

133 The Clinical and Endocrinological Manifestations in Children with Craniopharyngioma: one Medical Center Report at Taiwan

顱咽管瘤患兒的臨床和內分泌表現：台灣一醫學中心報告

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Background: Craniopharyngioma is a unique tumor of the suprasellar region with an embryologic origin. They may cause headache, visual impairment, increased intracranial pressure, and endocrinologic abnormalities. The endocrine dysfunction includes growth failure, diabetes insipidus, and hypothyroidism. The primary therapy is surgical resection and endocrine dysfunction may happen after the surgery. The aim of the study is to describe the clinical presentation and endocrine dysfunction before and after the major surgical resection of craniopharyngioma.
Methods: We retrospectively reviewed 25 pediatric patients of craniopharyngioma in Linkou Chang Gung Memorial Hospital between 2001 and 2018. We collected and analyzed the data of initial presentation, age at diagnosis, height, weight, initial thyroid function, time to diagnosis, final pathology report, post-operative endocrine dysfunction, and tumor recurrence via electronic medical records (EMRs).
Results: Total 25 patients (12 boys and 13 girls) were included in the study. The mean age at diagnosis was 8.8 years, ranging from 1 to 14-year-old. The initial complaints are headache (n=15, 60%), visual impairment (n=9, 36%), short stature (n= 8, 32%), and fever (n=6, 24%), respectively. After surgery, the prevalence of permanent diabetes insipidus, hypothyroidism, and adrenal insufficiency are 64%(n=16), 80%(n=20), and 80%(n=20). 8 patients (32%) suffered from epilepsy and under oral anti-epileptic drug control. 12 patients (48%) had recurrence tumor subsequently.
Conclusions: The clinical presentation of craniopharyngioma was headache, visual impairment, and short stature. Delay in diagnosis was noted in short patient without any cranial sign. Therefore, craniopharyngioma should be considered in all children with only initial presentation of short stature.

134 Clinical and Endocrine Manifestations of Children with Intracranial Germ Cell Tumors at Diagnosis: one Medical Center Report at Taiwan

顱內生殖細胞腫瘤患兒的臨床和內分泌表現：台灣一家醫學中心報告

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Background: Intracranial germ cell tumors are rare extragonadal neoplasms. The patients with intracranial germ cell tumors may have symptoms and signs such as headache, visual impairment and endocrine disorder, depending on the size and location of the tumor. The aim of this study is to assess the clinical features of patients with intracranial germ cell tumors in one medical center.
Methods: We performed a retrospective chart review of 22 children who were diagnosed with intracranial germ cell tumors from December, 1994 to December, 2018. The initial clinical presentation, tumor markers (hCG and alpha-fetoprotein, etc.), pituitary function, and brain images were reviewed and further analyzed.
Results: Total 22 patients (15 boys and 7 girls) were included in the study. The mean age at diagnosis was 13.67 ± 2.72 years, ranging from 8.43 to 17.92 years. The initial complaints were visual impairment (n=14, 64%), polyuria (n=14, 64%), short stature (n= 9, 41%), headache (n= 7, 32%), and lethargy (n=5, 23%), respectively. Laboratory data showed central hypothyroidism (n = 8, 36%), central diabetes insipidus (n=8, 36%), hypogonadotropic hypogonadism (n= 7, 32%), and growth hormone deficiency (n=5, 13%).
Conclusions: Intracranial germ cell tumors should be considered if patients suffer from visual impairment, polyuria, short stature, headache, and lethargy.

135 Transforming AI into a Medical Assistant in Clinical Hospital: Scalable Bone Age Assessment System

當AI人工智慧成為醫院中的臨床診斷幫手：以AI骨齡評估系統為例

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Background: A deep learning based automatic bone age assessment system (BAAs) demonstrated the application and assessment of a deep learning and artificial intelligence (AI) method in medical imaging and clinical diagnosis for an Asian population in a clinical hospital in Taiwan. This BAAs enhanced accurate, consistent, and timely clinical diagnostics and enlightened research fields of deep learning and AI in medical imaging.
Methods: The goal of this study was to use Deep Neural Networks (DNN) model of machine learning (ML) techniques to establish an algorithm or model for the predicted bone (skeletal) age in months based on a database of pediatric left-hand radiographs. The values of clinical bone age by clinicians were used as references for the trained machine deep learning interpretation and prediction of related symptoms.
Results: A database consisting of 8,061 hand radiographs (7,211 training set and 850 testing set) with their gender and

age (1-18 years) as the reference standard were used. As shown, DNN model for radiographs were assigned age within 0.5, 1 and 2 years of 89.3%, 98.3% and 99.9% ground truth. The Mean absolute error for the study subjects was 0.45 and 0.41 for male and female model, respectively. The efficiency of BAAs only required 4 seconds to complete the whole analysis.

Conclusions: This system was very helpful for clinical teaching and physicians to improve the accuracy and efficiency of bone age assessment, and can greatly reduce the burden on clinical personnel. Further, we look forward to stimulating the development of more AI tools and methods for other medical diagnostics base on this system.

136 Cardiac Features in Taiwanese Patients with Mucopolysaccharidosis III

台灣黏多醣症第三型患者的心臟特徵

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Background: Mucopolysaccharidosis type III (MPS III), or Sanfilippo syndrome, is caused by a deficiency in one of the four enzymes involved in the lysosomal degradation of heparan sulphate. Cardiac abnormalities have been observed in patients with MPS of any types. However, there are only a few studies focusing on cardiac alterations in MPS III.

Methods: We reviewed medical records, echocardiograms, and electrocardiograms of 26 Taiwanese patients with MPS III (5 with IIIA, 20 with IIIB, and 1 with IIIC; 14 males and 12 females; median age, 7.4 years; age range, 1.8-26.5 years). The relationships between age and each echocardiographic parameter were analyzed.

Results: Echocardiographic examinations (n=26) revealed that 16 patients (62%) had valvular heart disease. Four (15%) and fifteen (58%) patients had valvular stenosis or regurgitation, respectively. The most prevalent cardiac valve abnormalities were tricuspid regurgitation (46%), followed by mitral regurgitation (31%) and aortic regurgitation (19%). However, most patients with valvular heart disease had mild cases. Three (12%), five (19%) and none (35%) patients had mitral valve prolapse, a thickened interventricular septum, and asymmetric septal hypertrophy, respectively. The severity of aortic regurgitation, and the existence of the aortic valve abnormality and valvular stenosis were all positively correlated with the increasing age ($p < 0.05$). Z scores $>$ 2 were identified in 0%, 38%, 8%, and 27% for left ventricular mass index, interventricular septum diameter in diastole, left ventricular posterior wall diameter in diastole, and aortic diameter, respectively. Electrocardiograms in 11 patients revealed the presence of sinus arrhythmia (n=3), sinus bradycardia (n=2), and sinus tachycardia (n=1).

Conclusions: Cardiac involvement in MPS III is less common and milder compared with the other MPS types. The existence of the aortic valve abnormality and valvular stenosis of these patients aggravated with the increasing age reinforce the concept of the progressive nature of this disease. These findings and the follow-up data can be used to develop quality of care strategies for them.

137 An At-risk Population Screening Program for Mucopolysaccharidoses by the Measurement of Urinary Glycosaminoglycans

以尿液葡萄胺聚糖的檢測進行黏多醣症高風險族群的篩檢計畫

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Background: The mucopolysaccharidoses (MPSs) are a group of rare lysosomal storage disorders characterized by the accumulation of glycosaminoglycans (GAGs), and eventually causes progressive damage to various tissues and organs. We developed a feasible MPS screening algorithm and established a cross-specialty collaboration platform between pediatricians and medical geneticists based on

at-risk criteria for earlier MPS confirmative diagnosis.
Methods: In pediatric clinics, children (＜19 years of age) with clinical signs and symptoms compatible with MPS were prospectively enrolled between July 2013 and June 2018. The subjects were first collected their urine samples for a non-specific total GAG analysis by the dimethylmethylene blue (DMB) spectrophotometric method and the urine quantitation of three GAGs [dermatan sulfate (DS), heparan sulfate (HS), and keratan sulfate (KS)] by liquid chromatography/tandem mass spectrometry (LC-MS/MS) for the MPS patient screening. For subjects with elevated urinary GAG level, they were recalled for plasma enzymatic activity assay and genetic test for confirmation.
Results: Among 153 subjects enrolled in this study, thirteen patients had confirmative diagnosis with MPS (age range, 0.6 to 10.9 years; three with MPS I, four with MPS II, five with MPS IIIB, and one with MPS IVA). The major signs and symptoms by different systems involvement recorded by pediatricians at the time of decision to test were musculoskeletal system (55%), followed by neurological system (45%) and coarse facial features (39%). For these 13 patients, the median age of MPS diagnosis was 2.9 years. In this cohort, no case had a false positive result or false negative result of urinary DS, HS and KS by the LC-MS/MS method. However, for urinary DMB ratio using the spectrophotometric method, the positive predictive value was only 50%, and negative predictive value was 97%.
Conclusions: We established an at-risk population screening program for MPS by the measurement of urinary GAGs between pediatricians and medical geneticists for increasing awareness and enabling early diagnosis by detection of MPS at initial onset of clinical symptoms.

138 Whole Exome Sequencing as a Diagnostic Platform for Pediatric Rare or Difficult Cases

全外顯子定序作為兒科罕見或困難個案的診斷平台

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Background: Whole Exome Sequencing(WES) represents a significant breakthrough in the field of human genetics. This technology has largely contributed to the identification of new disease-causing genes and is now entering clinical laboratories. Here, we evaluate the usefulness of clinical WES in different clinical indications, such as rare or difficult diseases. In addition to looking for correct diagnosis, we would like to understand the efficacy of WES as a diagnostic tool and the impact on patient management.
Methods: We enrolled 17 pediatric cases of rare or difficult diseases, including 4 cases of neurological disease, 5 cases of hypogonadism, 1 case of recurrent pancreatitis, 2 cases of bone/joint disorders, 2 cases of immune disorder, 1 case of microphthalmia, 1 case of developmental disorder and 1 case of ectodermal disorder. Only the proband was applied for WES analysis. The detected variants were filtered through Human Phenotype Ontology, allele frequency in Human Genome reference, including Taiwan Biobank, ClinVar curation, mode of inheritance and functional prediction. The candidate variants after filtering were confirmed by Sanger sequencing through pedigree segregation analysis.
Results: The WES identified 9 out of 17 test individuals, including 4/4 neurological cases, 2/5 hypogonadism cases, 1 cystic fibrosis case, 1 arthrogryposis/bronchiectasis case and 1 crohn's disease case. In summary, the WES success rate were 9/17 with 100% detection for neurological patients and 40% for hypogonadism patients. Since the emerge of accurate diagnosis, we could adjust our management on patient care. For example, in addition to the hydration and protase therapy for pancreatitis, we extended our care to prevent the lower airway infection after the diagnosis of cystic fibrosis. Another diagnosis of Lowe syndrome alerted us to the presence of renal tubular dysfunction.
Conclusions: With the benefit so intuitive for pediatric rare or difficult cases, and as shown in this survey, WES should be a game changer in clinical and laboratory practice.

139 Mutation Spectrum of Patients Suspected Having Collagenopathies

疑似膠原蛋白病變的基因缺損探究

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Background: Molecular diagnosis of collagenopathies is frequently hampered by the genetic heterogeneity of the diseases and the large size of the genes involved. Next Generation Sequencing (NGS) enables massive parallel sequencing of human genes at a time. We recently developed a NGS-based method for the diagnosis of collagenopathies.
Methods: During the period from Jan 2016 to Dec 2018, 26 patients suspected having collagenopathies were examined by NGS-based targeted gene panel analysis. Clinical presentation, molecular diagnosis, and implication for clinical management of these patients were summarized in this presentation.
Results: Among the 26 patients, 5 patients were clinically diagnosed as Elhers-Dalnos syndrome (EDS) and 21 patients were diagnosed as skeletal dysplasia. Molecular

diagnosis was established in 17 patients with diagnostic yield of 65.4%. For EDS, 3 patients were found to each have PRDM5 (Brittle cornea syndrome 2), COL5A1 (EDS type I), and COL3D1 (EDS type IV) mutations. For patient with skeletal dysplasia, 3 were found to have COL1A1 (Osteogenesis imperfect, OI) mutations, 4 were found to have COL2A1 (COL2A1-related collagenopathy) mutations. Other genes identified in patients included SERPINF1 (OI type VI, n=2), WNT1 (OI type XV, n=1), ITIM5 (OI type V, n=1), TRPV4 (Spondylometaphyseal dysplasia, Kozlowski type, n=1), and B3GALT6 (Spondyloepimetaphyseal dysplasia with joint laxity, n=1). The molecular diagnoses effectively helped the managements and genetic counseling of these patients.

Conclusions: NGS has made possible the molecular diagnosis of collagenopathies. The spectrum of genes involved in these patients is much wider than we previously considered. Therefore, NGS should become a standard diagnostic tool for collagenopathies.

140 Inducible Pluripotent Stem Cell Model Recapitulates Pathogenesis of MELAS Syndrome

以iPS細胞模型重現MELAS症候群的病理機轉

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Background: MELAS syndrome is most commonly caused by the A3243G mutation of mtDNA, which leads to deficiency of respiratory enzyme complex, impairment of oxidative phosphorylation and subsequently energy deficiency. To this date, studies of autophagy upon mitochondrial dysfunction induced by mtDNA A3243G mutation were limited to fibroblasts and cybrids, while these studies showed controversial results.

Methods: Both isogenic iPS cell lines carried 85% heteroplasmy (MELAS iPS) and undetectable A3243G mutation (control iPS) were derived from MELAS fibroblasts. Autophagy markers, mitochondrial membrane potential, oxidative stress, ATP production, bioenergetics and cell viability were determined.

Results: Isogenic iPS cells showed expression of pluripotent markers. MELAS iPS cell demonstrated deficiency of respiratory complexes I (57%) and IV (74%). Under oxidative insults, MELAS iPS cells showed significantly increase of LC3II/LC3I ratio (2.65 to 15.9), autophagic fluorescence levels (110 % to 151%), elevation of ROS fluorescence (1.29 to 2.1), increased calcium flux into cytoplasm (1.27 to 2.61), massive depolarization of mitochondria (0.58 to 0.14), loss of OCR % (100% to 66.9), ATP deficiency (17.7 to 14.5) and compromised cell viability (85.5 % to 50.4 %).

Conclusions: The iPS cellular model recapitulates the pathogenesis of MELAS syndrome and holds promises for the determination of a pathological mechanism. The existence of pathogenic mtDNA alone in mitochondrial disease was not sufficient to elicit the degradation of dysfunctional mitochondria. The combination of the mtDNA mutation and the oxidative insults elicit bulk a macroautophagy with an accumulation of autophagosomes and autolysosomes, and leads to the promotion of cell toxicity, activation of mitophagy and subsequently decrease of cell viability.

141 Airway Anomalies in Infantile-Onset Pompe Disease: A Large-Scale Survey by Flexible Bronchoscopy

新生兒型龐貝氏症呼吸道異常：一大型研究

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Background: Pompe disease is an AR lysosomal storage disorder characterized by the deficiency of acid α-glucosidase. Deficiency of this enzyme leads to the progressive accumulation of glycogen in numerous types of cells and tissues. Early enzyme replacement therapy (ERT) can prolong survival and improve the long-term outcome. Our series jointed nationwide Pompe newborn screening (NBS) from 2008, testing approximately two-thirds of the newborn population in Taiwan. Until 2018, more than one million newborns were included in our series. Now, the average age of our infantile-onset Pompe disease (IOPD) patients started their ERT less than 10 days of age. We compared many prognostic parameters with other study groups and showed that our patients who received very early ERT had better outcomes. However, according to our 10-year follow-up, we found that our patients, even having better outcomes in many aspects, still presented some airway problems.

Methods: The study population included 15 IOPD patients who were referred to the TVGH from Jan. 1, 2008 until now by NBS.They received whole airway survey by flexible bronchoscopy and analyzed the results with respiratory function, speech quality tests and other biomarkers simultaneously.

Results: The results showed that all of them had narrowing oral cavity, compromised oral-pharynx, having difficulty to keep adequate oral cavity and were with dropping uvula. We also found that most of them showing poor vocal cords movement, presenting reduced the movements of vocal cords and silent saliva penetration/aspiration through glottis in respiration. We also did the evaluation of articulation disorders for whom were older than 24-month-old and all the them showed hypernasal resonance, consonant substitution, consonant omission and consonant distortion.

Conclusions: This is the first large-scale study of dynamic whole airway abnormalities of Pompe disease. Even for very early-treated IOPD patients, upper airway abnormalities were still observed. Flexible bronchoscopy is useful tool for airway examination. Early diagnosis for respiratory problems and effective managements were the critical factors for long-term prognosis of IOPD.

142 Newborn Screening for Gaucher Disease
高雪氏症新生兒篩檢之台灣經驗

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Background: GD is an AR lysosomal storage disorder (LSD) characterized by the deficiency of β-glucocerebrosidase. Deficiency of this enzyme results in accumulation of glucosylceramide in macrophages, and transforms them into Gaucher cells. The progressive infiltration of Gaucher cells into organs contributes to the presence of clinical symptoms. Taiwan started the nationwide Gaucher newborn screening (NBS) program from 2015. Our study presented the results from 2015 to 2018 and analysis the current treatment and prognosis of the GD in Taiwan.
Methods: Our series jointed nationwide Gaucher newborn screening (NBS) from 2015, testing approximately two-thirds of the newborn population in Taiwan. Until 2018, more than 500,000 newborns were included in our GD series. Three patients were screened out and confirmed the diagnosis of Gaucher disease.
Results: The 3 patients were all male and were classified as Gaucher type 1, type 3 and type 2 respectively. The genotype of case 1 was c.509G＞A, p. R131H (novel) and c.1448T＞C, p.L483P (L444P). His enzyme activity was 2.6 (＞7.5μmol/hr/L) on dried blood test (DBS) and started the enzyme replacement treatment (ERT) at 2y10m/o. The second patient, which was suspected Gaucher type 3, had homozygous c.1448T＞C, p.L483P (L444P) mutation. His enzyme activity was only 0.01 and started the ERT at 9m/o. The third patient was a Gaucher type 2 and had c.674 A＞G, p.K225R (novel) and c.1448T＞C, p. L483P (L444P) mutation. The enzyme activity was 0.4 (＞7.5μmol/hr/L; DBS) and started the ERT at 8m/o. The neurological symptoms such as stridor, involuntary movement and seizure were deteriorated after 1.5-year-old, so HSCT was done at 2-year-old. Long term prognosis of them will be monitored continuously.
Conclusions: This is the first report of GD NBS applied for Taiwanese population. We collected the results from 2015 January to 2017 December, which included more than 500,000 newborns. We studied on these 3 cases (Gaucher type 1, type 3 and type 2) and found that early diagnosis (through the NBS) can lead to early treatment intervention (ERT). For LSD, early treatment has benefits to slow down the disease progression. This might be thought to have greatly improved the prognosis of the GD.

143 Asian Hotspot Fabry Mutation, IVS4+919G>A, Evidence for Founder Effect and Originated in Asia more than 800 Years Ago
亞洲高好發率的法布瑞氏症IVS4基因突變的遺傳起源研究

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Background: The Fabry hotspot mutation, IVS4+919G＞A, is extremely high in our Taiwan Chinese population. In addition to Taiwan, this IVS4 mutation was also reported to be prevalent in, Kagoshima, Japan and found in the patients with hypertrophic cardiomyopathy in Southeast Asia, such as southeast area of mainland China, Singapore, Malaysia, and Vietnam.
Methods: To investigate the founder effect, estimate the mutation age and the most likely source of this mutation, a total of 33 IVS4 males, including 20 Taiwanese, 6 Japanese, 4 Chinese (3 from northern Fujian & 1 from Guangdong), 1 Singaporean , 1 Malaysian, and 1Vietnamese, as well as 16 male non-carriers as control were enrolled in this study. The llumina Infinium CoreExome-24 microarray was used for the genotyping of 12,975 genomic variants in the human X chromosome.
Results: A common haplotype of the 33 IVS4 males was identified and characterized as founder. The age was estimated with Genetic Mutation Age Estimator to be as far as 887.5 (97.5 ~ 1672.5) years ago.
Conclusions: This result indicates that the IVS4 mutation of GLA gene was originated from a single event on the X chromosome of a Chinese who was traced at least as far as Sung dynasty of the Chinese history.

144 Incidence and Treatment of Femur Fractures in Adults with Osteogenesis Imperfecta: an Analysis of an Expert Clinic of 72 Patients

台灣成人成骨不全症患者股骨骨折的盛行率及治療分析，以一醫學中心72位患者為例

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Background: Purpose Osteogenesis imperfecta (OI) is characterized by increased bone fragility and susceptibility for fractures. A few studies described and compared treatment modalities for femur fractures in children with OI. However, no cohort studies on adults with OI have been published. This study on OI patients aims to give insight into the incidence of femur fractures and non-unions and its best treatment options to avert non-union.
Methods: In this retrospective, descriptive study of the OI expert clinic in The Netherlands, all medical charts of patients16 years or older were analyzed for femur fracture incidence, non-union rate and treatment modality.
Results: Of 72 OI patients, 11 patients suffered a femur fracture with 4 patients having more than 1 femur fracture. For all types of femur fractures, the incidence was 651 fractures per 100,000 person-years annually. In 15 total fractures, 4 fractures resulted in a non-union, mostly shaft fractures of type 4 OI patients. Surgically treated shaft fractures had the best outcomes for non-union.
Conclusions: OI adults were prone to developing femur fractures and non-unions. Especially type 4 OI adults, with conservatively treated shaft fractures, were at high risk for non-unions.

145 To be or not to be Short: Genetic Susceptibility to Familial Short Stature

矮或不矮：家族性矮小症之易感基因研究

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Background: Many genetic variants are associated with human height. Familial short stature (FSS) is the most common short stature with normal or near-normal growth velocity, and bone age similar to chronologic age. It is caused by genetically inherited factors without any identifiable pathogenic causes and represents a suitable model for short stature genetics. To investigate the genetic profile, genetic risk score (GRS), and prediction model for FSS. And to evaluate the relationship between the FSS GRS and human height.
Methods: A follow-up study for FSS initiated in 1999 was introduced in Taiwan. FSS Children and their controls were unrelated Han Chinese with comprehensive clinical and genome-wide association investigations and were randomly assigned into two groups: a training group with 930 FSS cases and 856 controls, and a testing group with 233 FSS cases and 215 controls. A multilocus GRS for FSS, calculated as the weighted sum of alleles of 10 novel genetic variants. The outcome was the odds of FSS.
Results: 10 novel and 9 reported human height-related genetic variants were associated with FSS risk. These 10 novel genetic variants exhibited a continuous increased FSS risk with the cumulative weighted GRS quartile numbers and 90% accurate prediction in the testing group. A regression tendency in the general population showed that each weighted genetic risk score of 10 novel and 9 reported human height-related genetic variants was associated with human height reduction for both male and female participants.
Conclusions: Our results provided a clear FSS genetic profile and FSS GRS exhibits a decreased human height regression tendency. This study is useful for pediatric endocrinologists to distinguish this high-risk FSS population from other kinds of short stature and also

provides a reliable FSS prediction model and possible proper treatment.

146 Association of Menarche-Related Genetic Variants in Taiwanese Girls with Idiopathic Central Precocious Puberty

初經相關基因變異在原發性中樞型性早熟女童的關聯分析

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Background: Precocious puberty, a secular trend seen more frequently in girls, is a mostly normal developmental variant of pubertal ontogenesis caused due to complex genetic and environmental interactions and is characterized by earlier onset of secondary sexual characteristics. Genome-wide association studies (GWAS) have revealed susceptible loci and provided insights into the polygenic nature of age at menarche (AAM) and puberty. Here, we collected girls with idiopathic central precocious puberty (ICPP) and performed replication study with GWAS variants for AAM and puberty to elucidate the relationship between gene variants and phenomenon in the Taiwanese population.
Methods: Girls with ICPP (n=321) and matching controls (n=148) were recruited from a clinic. One hundred thirty SNPs associated with AAM and puberty was selected from previously published papers and subjected to custom-designed chip. Genotyping was attempted to all ICPP and control cases. Data were analyzed according to standard protocols.
Results: After replicated 130 SNPs, 33 SNPs revealed significant association in our ICPP group ($p < 0.05$). Twenty three SNPs located on 6q21, HACE1-LIN28B loci, which is highly associated with menarche and puberty time in several populations studies. Two SNPs observed in FTO locus, which is a nuclear protein and strong association with body mass index, obesity risk, and type 2 diabetes. In addition, two loci in or near DSCAML1 and DLGAP1 exhibited association with ICPP, and they are involved in neuronal differentiation or highly expression in brain. The other 6 SNPs located in far away from gene or gene function unknown regions.
Conclusions: Our findings elucidated that the some genetic variants influencing AAM and puberty in other populations are also important in the Taiwanese ICPP cases.

147 Microarray-based Comparative Genomic Hybridization for Genotype-phenotype Analysis and Clinical Outcomes of Wolf–Hirschhorn Syndrome and Cat Cry Syndrome

比較基因組雜交晶片診斷第四及第五號染色體缺失症候群並探討其臨床症狀及預後分析

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Background: Wolf-Hirschhorn syndrome (chromosome 4p deletion) and Cat cry syndrome (chromosome 5p deletion) are both group B chromosome deletions. They both presented with some phenotypes in common, such as craniofacial anomaly, growth and developmental impairment. However, a wide variety of phenotype has been observed. We aim to analyze the correlation between phenotype and genotype by use of both aCGH and chromosome study.
Methods: From 2016 to 2018, 4 patients and 2 patients were diagnosed with Wolf-Hirschhorn Syndrome and Cat cry syndrome separately in our hospital, either by array comparative genomic hybridization or by cytogenetic study. Clinical manifestations in all aspects, and parameters such as brain magnetic resonance imaging, electroencephalography, and the developmental evaluation were also recorded.
Results: The average age of the diagnosis varies from 1 month-old to 5 year-old. Deletions in chromosome 4p16.3p16.1 and 4p16.3 were found in patients with Wolf-Hirschhorn Syndrome. The sample size of deletion ranged from 1.13 Mb to 10.18 Mb. On the other hand, deletions of chromosome 5p15.33p15.32, 5p15.33p13.3 were found in patients with cat cry syndrome. The sample size of deletion ranged from 5.32 Mb to 28.79 Mb. The deletion amounts correlate with the severity of the phenotype and the prognosis. In one case, the chromosome study was performed first and reported no abnormalities, but further proved deletions by aCGH. All the patients presented with developmental delay, whereas facial dysmorphism varies.
Conclusions: Wolf-Hirschhorn syndrome and Cat cry syndrome are both rare deletion diseases that both presented with facial dysmorphism and developmental delay. Array CGH has its advantage over conventional chromosome study in microdeletion detection and it is more precise for further evaluation. Base on the data we collected so far, we found that the wide variety of phenotype correlates with the amount of deletions. Our experience also show aCGH is a better tool for microdeletion syndrome detection than cytogenetic analysis.

148 Holocarboxylase Synthetase Deficiency: Report of a Novel Mutation and an Unusual Disease Presentation with a Brief Literature Review

羧化全酶合成酶缺乏症：一個新突變和一個非典型臨床表現案例報告，以及文獻回顧

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Background: Holocarboxylase synthetase deficiency (HCSD) is a rare disorder with an estimated annual incidence about 1/200,000. It is also called early-onset form of multiple carboxylase deficiency (MCD) whereas biotinidase deficiency (BTD) is the late-onset form of MCD. Clinical presentation of HCSD includes skin eczema, alopecia, metabolic acidosis and hyperammonemia. Diagnosis is made through enzyme assay or by genetic analysis. To date, only 3 cases were reported in Taiwan before.

Methods: We report two cases of HCSD. One is an early-onset type with a novel mutation and the other is a late-onset type with recurrent hypoglycemia attacks. We searched PubMed by using the MeSH term

Results: Our cases included typical early onset type and an unusual late onset type of HCSD. Three case reports of Taiwan were found after search. We organized their clinical presentations and genotypes. Holocarboxylase synthetase deficiency in Taiwanese population was also reviewed.

Conclusions: Holocarboxylase is a rare disease but it can be fatal if the correct diagnosis is not made. Once the diagnosis is made, the prognosis is good with biotin treatment.