

臺灣兒科醫學會第二四四屆學術演講會時間表

民國109年11月14日(星期六)			民國109年11月15日(星期日)		
第一會場	第二會場	第三會場	第一會場	第二會場	第三會場
<p>08:30 第一單元： 腸胃學、營養學 (1~7題)</p> <p>09:40 休息</p> <p>09:50 第一單元： 腸胃學、營養學 (8~15題)</p> <p>11:10 休息</p> <p>11:20 第二單元： 腎臟學 (16~18題)</p> <p>12:00 附加研討會 主持人：李宏昌理事長、 劉明發醫師 主 題：配方奶與過敏相關 研究 演講者：劉明發醫師、 王志堯教授</p> <p>13:30</p>	<p>08:30 第四單元： 感染學 (38~44題)</p> <p>09:40 休息</p> <p>09:50 第五單元： 小兒預防醫學及 流行病學 (45~48題)</p> <p>10:30 休息</p> <p>10:40 第六單元： 肺臟學 (49~55題)</p> <p>11:50 附加研討會 主持人：鐘育志教授 主 題：探討脊髓性肌肉萎 縮症之呼吸照護新 知 演講者：Prof. Dong In Suh</p> <p>13:20</p>	<p>08:30 第九單元： 神經精神醫學 (77~85題)</p> <p>10:00 休息</p> <p>10:10 第十單元： 急診學 (86~91題)</p> <p>11:10 休息</p> <p>11:20 第十一單元： 重症學 (92~97題)</p> <p>12:20</p>	<p>09:00 教育演講 主 題：一般兒科門診實務經驗 分享 主持人：陳武元教授、 王玲醫師 演講者：曾崇芳醫師、 林應然醫師、 林鈞尚醫師、 林黑潮醫師</p> <p>12:00 附加研討會 主持人：陳志榮教授、 黃高彬副院長 主 題：母嬰免疫：疫苗新知 研討 演講者：陳伯彥主任、 林曉娟主任</p> <p>13:30</p>	<p>09:00 特別演講 主 題：建立以婦幼醫學為 主軸的精準醫療專 案計畫 主持人：李宏昌理事長、 鄭敬楓教授 演講者：胡務亮教授、 陳燕彰教授、 王淑麗教授、 張鑾英教授、 牛道明教授</p> <p>11:40 附加研討會 主持人：黃立民教授 主 題：流感抗病毒藥物治療 之新里程碑 演講者：紀 鑫醫師、 鄭名芳醫師</p> <p>13:30</p>	<p>09:00 第十五單元： 血液、腫瘤學 (120~130題)</p> <p>10:50 休息</p> <p>11:00 第十六單元： 醫學人文與教育 (131~134題)</p> <p>11:40</p>
第一會場	第二會場	第三會場	第一會場	/	
<p>13:30 第三單元： 新生兒學 (19~28題)</p> <p>15:10 休息</p> <p>15:20 第三單元： 新生兒學 (29~37題)</p> <p>16:50</p>	<p>13:30 第七單元： 過敏免疫風濕病學 (56~62題)</p> <p>14:40 休息</p> <p>14:50 第七單元： 過敏免疫風濕病學 (63~69題)</p> <p>16:00 休息</p> <p>16:10 第八單元： 心臟血管學 (70~76題)</p> <p>17:20</p>	<p>13:30 第十二單元： 醫學遺傳學、 新陳代謝學 (98~105題)</p> <p>14:50 休息</p> <p>15:00 第十三單元： 內分泌學 (106~116題)</p> <p>16:50 休息</p> <p>17:00 第十四單元： 青少年醫學 (117~119題)</p> <p>17:30</p>	<p>13:30 頒獎</p> <p>14:00 休息</p> <p>14:10 醫學的科學、倫理與 法律講座 主持人：李宏昌理事長 主 題：醫師如何面對媒體暨 兩性議題 演講者：蔣志偉主播、 林靜儀醫師</p> <p>16:10</p>		

地址：台中榮民總醫院研究大樓(台中市西屯區臺灣大道四段1650號)

一般演講：口頭報告

第一單元：腸胃學、營養學

日期：民國109年11月14日(星期六)

時間：08:30~11:10

地點：第一會場

主持人：吳孟哲、陳偉燾

- 08:30~08:37
1. YqiC蛋白寡聚體態對鼠傷寒沙門氏菌定植和入侵人類腸道上皮細胞有決定性影響
林盈秀^{1,2}、陳玓蓁³、陳威廷³、張珮茹^{1,2}、黃姿雯⁴、張語曲³、方旭彬^{1,2,5}
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；臺北醫學大學醫學院醫學系生化學暨細胞分子生物學科³；臺北醫學大學醫學院醫學系微生物及免疫學科⁴；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⁵
- 08:37~08:44
2. 幽門桿菌感染者發生系統性紅斑狼瘡的風險增加
吳孟哲¹、黃彥筑¹、廖子涵¹、曾瑞如¹、王建得¹、魏正宗²
臺中榮民總醫院兒童醫學中心兒童肝膽胃腸科¹；中山醫學大學附設醫院過敏免疫風濕科²
- 08:44~08:51
3. 早期根除療法對幽門桿菌感染患者系統性紅斑狼瘡風險的影響
吳孟哲¹、黃彥筑¹、廖子涵¹、曾瑞如¹、王建得¹、魏正宗²
臺中榮民總醫院兒童醫學中心兒童肝膽胃腸科¹；中山醫學大學附設醫院過敏免疫風濕科²
- 08:51~08:58
4. 新興、變異型諾羅病毒株造成的兒童腸胃炎之病毒排出研究
鄭弘彥¹、李忠城²、張猷忠³、蔡七女⁴、趙舜卿⁵、陳世彥¹
部立雙和醫院兒科部胃腸肝膽科¹；長庚醫院分子感染症醫學研究中心²；銘傳大學生科系³；長庚醫大學臨床醫學研究所⁴；林口長庚醫院兒童胃腸肝膽科⁵
- 08:58~09:05
5. 便秘對於氣喘的影響：臺灣的全國性世代追蹤研究
黃彥筑¹、吳孟哲¹、廖子涵¹、曾瑞如¹、王建得¹、魏正宗²
臺中榮民總醫院兒童醫學中心兒童肝膽胃腸科¹；中山醫學大學附設醫院過敏免疫風濕科²

第二四四屆學術演講會

- 09:05~09:12 6. 微糖體核酸29a的外源性療法通過調節磷酸肌醇3激酶p85 α 減輕膽汁淤積動物模型中肝纖維化的發展
黃瀛賢、楊雅玲¹、林宏昱²
高雄長庚醫院兒童內科部；高雄長庚醫院麻醉科¹；高雄長庚醫院粒線體中心²
- 09:12~09:19 7. 使用全外顯子定序診斷罕見肝臟疾病之經驗
陳其柏¹、陳慧玲¹、簡穎秀²、吳恩婷¹、周弘傑¹、劉明發³、陳善銘⁴、周言穎⁵、胡務亮²、李妮鍾²
國立台灣大學醫學院附設醫院小兒部¹；國立台灣大學醫學院附設醫院基因醫學部²；新光吳火獅紀念醫院小兒部³；中山醫學大學醫學院附設醫院小兒部⁴；國立成功大學醫學院附設醫院小兒部⁵
- 09:19~09:40 討論
- 09:40~09:50 休息

主持人：黃一菲、陳安琪

- 09:50~09:57 8. 丁酸重編程產婦高脂飲食誘導的胎兒肝損傷
黃仔均、刁茂盟、廖祐玄、盧怡庭
高雄長庚紀念醫院兒童內科
- 09:57~10:04 9. 二甲雙胍重編程母體高脂飲食引起的母體菌叢不良驅動的胎兒肝變異
廖祐玄、刁茂盟、盧怡庭、黃立同
高雄長庚醫院小兒科
- 10:04~10:11 10. 兒童急性闌尾炎臨床表徵相似於感染性腸炎的預測因子探討：病例對照研究
盧怡庭¹、黃福辰¹、陳柏成²
高雄長庚醫院兒童內科部¹；高雄長庚醫院復健科²
- 10:11~10:18 11. 兒童腸套疊合併腺病毒感染的臨床表徵與腸套疊的復發率探究
曾文禹、趙舜卿、陳建彰、賴明璋
長庚醫療財團法人林口長庚紀念醫院小兒腸胃科
- 10:18~10:25 12. 利用口水血球凝集抑制試驗來分析北部健康台灣人的分泌型狀態
周昱吟^{1,2}、劉明發¹、陳瓊汝³、郭恬伶¹、林姪慧¹
新光吳火獅紀念醫院小兒科¹；基督復臨安息日會醫療財團法人臺安醫院小兒科部²；新光吳火獅紀念醫院病理檢驗科³

- 10:25~10:32 13. 兒童(4~7歲)血中微量元素濃度與偏挑食、營養狀態與體智能的相關性研究
趙舜卿¹、朱世明²、盧章智³
林口長庚紀念醫院兒童胃腸科¹、新生兒科²、兒童內科部、兒童醫學中心、
檢驗醫學部³
- 10:32~10:39 14. 肥胖兒童和青少年非酒精性脂肪肝疾病發病和緩解的預測因子
林裕誠¹、張碧峰¹、倪衍玄²
亞東紀念醫院小兒部¹；國立台灣大學醫學院附設醫院小兒部²
- 10:39~10:46 15. 南臺灣青少年之肥胖盛行率調查
楊喬喻、羅筱涓、楊耀榮
國立成功大學醫學院附設醫院小兒部
- 10:46~11:10 討論
- 11:10~11:20 休息

第二單元：腎臟學

日期：民國109年11月14日(星期六)

時間：11:20~11:50

地點：第一會場

主持人：田祐霖、**邱益煊**

- 11:20~11:27 16. 大腸桿菌所致泌尿道感的抗生素感受性發生率及趨勢，2004-2018台灣兒童的世代研究
陳宏恩¹、田祐霖¹、郭曉菁²、許茜甯^{2,3}
高雄長庚醫院兒科部兒童腎臟科¹；高雄長庚醫院藥劑部²；高雄醫學大學藥學系³
- 11:27~11:34 17. 利用紅外顯微光譜和光譜診斷技術擷取腎臟組織影像及偵測血液變化並以電腦自動分析成為診斷兒童紅斑性狼瘡腎炎和追蹤治療效果的創新健康照護方法
余美靜^{1,2}、黃香娣^{1,2}、林盈儀¹、黃珮瑜³、李耀昌³
林口長庚紀念醫院兒童腎臟科¹；長庚大學醫學系²；國家同步輻射研究中心生命科學小組³

- 11:34~11:41 18. 血管收縮素原基因突變導致腎小管發育不全之致病機轉研究
曾敏華¹、黃世明²、蔡政道³、丁肇壯⁴、林石化⁵
林口長庚紀念醫院兒童內科部腎臟科¹；國防醫學院生化所²；馬偕兒童醫院
腎臟科³；三軍總醫院兒科部⁴；三軍總醫院內科部腎臟科⁵
- 11:41~11:50 討論

附加研討會
配方奶與過敏相關研究

日期：民國109年11月14日(星期六)
時間：12:00~13:30
地點：第一會場

主持人：李宏昌理事長、劉明發醫師

- 12:00~12:10 1. 開幕致詞
李宏昌理事長
臺灣兒科醫學會
- 12:10~12:25 2. 羊奶粉的迷思
劉明發醫師
新光醫院小兒科
- 12:25~13:10 3. 預防過敏氣喘要從懷孕開始
王志堯教授
國立成功大學醫學院附設醫院
- 13:10~13:30 4. 問題討論與結語
劉明發醫師
新光醫院小兒科

第三單元：新生兒學

日期：民國109年11月14日(星期六)

時間：13:30~16:50

地點：第一會場

主持人：曹珮真、林湘瑜

- 13:30~13:37 19. Roxadustat藉由提升血管內皮生長因子以降低高氧下新生小鼠肺臟傷害
黃亮迪、周琇珠¹、陳中明
台北市立萬芳醫院兒科部；台北醫學大學醫學系小兒學科、解剖學科¹
- 13:37~13:44 20. 基於關聯的腸道和肺臟菌叢失衡預測新生仔鼠高氧誘導的肺損傷
陳中明^{1,2}、周琇珠³、楊宇辰⁴、蘇家玉⁵
台北醫學大學附設醫院小兒部¹；台北醫學大學小兒學科²、解剖暨細胞生理學科³、聯合人體生物資料庫⁴、醫學資訊研究所⁵
- 13:44~13:51 21. 非常早產新生兒歷經長時間早產早期破水之短期及長期預後
吳佳玲、張瑞幸、許瓊心、張弘洋、彭純芝、詹偉添、林佳瑩、陳佳慧、曾愷悌
馬偕兒童醫院小兒部新生兒科
- 13:51~13:58 22. 於早產兒使用高流量氧氣鼻導管來脫離經鼻式連續性正壓呼吸器之適用性及安全性：初步報告
楊書婷¹、鐘浩瑋¹、何鳳青¹、杜文綾¹、陳秀玲^{1,2}
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
- 13:58~14:05 23. 以非侵襲性方式給予一氧化氮來治療新生兒低氧血症合併肺高壓
陳俐如¹、王杏安²、蕭建洲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新生兒科²
- 14:05~14:12 24. 早產雙胞胎發生開放性動脈導管或腦室內出血併發症的研究
賴筱晴¹、李忠興²、詹耀龍³、朱世明²、林瑞瑩²
長庚大學醫學系，林口長庚醫學中心¹；兒童內科部新生兒科²、婦產部³
- 14:12~14:19 25. 極低體重早產兒開放性動脈導管之血液動力學研究
黃萬恆、徐仲庭、李德敏、林怡瑄、林明志、許雅淇、王德明
臺中榮民總醫院兒童醫學部新生兒科

- 14:19~14:26 26. 經皮中央靜脈導管的消毒頻率影響新生兒加護病房中導管引起的血流感染率：單一中心，隨機對照試驗
劉又禎¹、陳宜綸、黃新純、蘇立婷、張心瑜、陳志誠、歐陽美珍、鍾美勇、陳豐順、陳淑華¹
高雄長庚紀念醫院兒童內科部、護理部¹
- 14:26~14:33 27. 周產期HIV預防處置措施對減少HIV垂直感染的效益：8年的經驗分析
陳俐如¹、王杏安²、蕭建洲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新生兒科²
- 14:33~14:40 28. 生理性脫水之最低點對於非常低體重早產兒發展的影響
許雅淇、林怡瑄、林明志、董舒婷
台中榮民總醫院兒童醫學中心新生兒科
- 14:40~15:10 討論
- 15:10~15:20 休息

主持人：蕭建洲、江明洲

- 15:20~15:27 29. 早產兒早發性低血磷與早期積極營養的關聯性：初步報告
林湘瑜、陳映廷、蔡明倫、邱曉郁、林鴻志、蘇百弘
中國醫藥大學兒童醫院
- 15:27~15:34 30. 早產兒接受眼內注射抗血管內皮生長因子治療視網膜病變後呼吸狀態預後：匹配病例對照研究
黃盈甄¹、許凱翔^{2,3}、吳為吉¹、朱世明²、林瑞瑩²、徐任甫²、傅仁輝²、江明洲^{2,3}、楊長祐²、李建忠^{2,3}
林口長庚紀念醫院眼科¹、兒童內科部新生兒科²；長庚大學臨床醫學研究所³
- 15:34~15:41 31. 產婦飲食對母乳成分與嬰幼兒成長之影響
吳雅慧¹、許雅淇²、黃延君³、林明志²
臺中榮民總醫院護理部¹、兒童醫學中心²；靜宜大學食品營養學系³
- 15:41~15:48 32. 代謝物圖譜分析發現母乳哺餵方式的不同與牛奶致敏化間的關係
唐青敏¹、葉國偉²、黃璟隆³、蘇冠文⁴、蔡明翰⁴、花曼津⁴、廖穗綾⁴、賴申豪⁵、邱志勇⁵
長庚醫療財團法人林口長庚紀念醫院兒童內科部¹；長庚醫療財團法人林口長庚紀念醫院兒童過敏免疫風濕科²；長庚醫療財團法人新北市立土城醫院兒科³；長庚醫療財團法人基隆長庚紀念醫院兒科⁴；長庚醫療財團法人林口長庚紀念醫院兒童胸腔科⁵

- 15:48~15:55 33. 嚴重黃疸新生兒經加強照光成功治療後仍具有黃疸腦病變風險
陳元昕¹、許凱翔^{1,3}、林芝¹、吳怡萱¹、賴美吟^{1,3}、莫澤儀²、許時耘²、江明洲^{1,3}、朱世明¹、林瑞瑩¹
林口長庚紀念醫院兒童內科部新生兒科¹；新北市立土城醫院²；長庚大學臨床醫學研究所³
- 15:55~16:02 34. 出生後發生早期急性腎損傷為罹患雙胞胎輸血症候群早產兒之死亡危險因子
李忠興¹、陳又寧¹、詹耀龍²、林瑞瑩¹
林口長庚紀念醫院兒童內科部新生兒科¹、婦產部²
- 16:02~16:09 35. 新生兒致命性遺傳疾病（腎小管發育不全）之盛行率，臨床表現及預後研究
曾敏華¹、林瑞瑩²、朱世明²、江明州²、徐壬甫²、林石化³
林口長庚紀念醫院兒童內科部腎臟科¹；林口長庚紀念醫院兒童內科部新生兒科²；三軍總醫院內科部腎臟內科³
- 16:09~16:16 36. 一個月大嬰兒之延遲性黃疸的風險因子：前瞻性研究
葉育欣、翁逸豪、程劭文
台北長庚紀念醫院兒童內科
- 16:16~16:23 37. 早產兒急性腎臟損傷的誘發因子——一個台灣三級醫院六年期研究
王崧驊、洪依利、謝武勳¹、沈仲敏
國泰綜合醫院小兒科；國立臺灣大學醫學院附設醫院兒童醫院¹
- 16:23~16:50 討論

第四單元：感染學

日期：民國109年11月14日(星期六)

時間：08:30~09:40

地點：第二會場

主持人：邱南昌、謝育嘉

- 08:30~08:37 38. 台灣序列分型3與分型17之抗巨環黴素肺炎黴漿菌所致肺炎的共同傳播與相關臨床表徵
洪慧敏¹、謝育嘉¹、莊智賢²、陳志和³、陳志榮¹、邱政洵¹、黃玉成¹、郭貞嫻¹、黃冠穎¹、林奏延¹
林口長庚紀念醫院¹；桃園聖保祿醫院²；高雄長庚紀念醫院³

第二四四屆學術演講會

- 08:37~08:44 39. 2019-2020年南臺灣兒童黴漿菌性肺炎的流行病學,臨床特徵及對巨環類抗生素(Macrolides)的敏感性研究
郭正彥、蔡瑋峻、沈靜芬、李慧鳳、何宗憲、劉清泉
國立成功大學醫學院附設醫院小兒部
- 08:44~08:51 40. 抗藥性金黃色葡萄球菌USA300菌株是否已成為北台灣主要菌株之一?
賴琬淳、陳志榮、黃玉成
林口長庚紀念醫院兒童感染科
- 08:51~08:58 41. 小兒骨髓炎的治療:在社區型抗藥性金黃色葡萄球菌盛行之世代
陳俊安¹、林曉娟^{1,2}、衛琇玫¹、許玉龍¹、賴奐丞¹、劉衍怡¹、邱玉婷¹、黃高彬^{1,2}
中國醫藥大學兒童醫院兒童感染科¹;中國醫藥大學醫學院²
- 08:58~09:05 42. 以冠狀動脈血管大小基礎最大值預測川崎症病童發生冠狀動脈瘤
黃競瑩、紀鑫、邱南昌、黃富源、黃璫寧、張龍、龔妍心
馬偕兒童醫院小兒部
- 09:05~09:12 43. 人類白血球抗原與川崎氏病
邱南昌、張子揚、陳銘仁、紀鑫、楊崑德、黃璫寧、張龍、黃富源、洪偉力、李燕晉
馬偕兒童醫院
- 09:12~09:19 44. 台灣兒童諾羅病毒腸胃炎的臨床表現及危險因子
吳佳頤¹、紀鑫¹、劉清泉²、黃玉成³、黃懿娟⁴、林曉娟⁵、何愉懷⁶、黃立民⁷、熊昭⁸、吳芳姿⁹
馬偕兒童醫院兒科部¹;國立成功大學醫學院附設醫院兒科部²;長庚兒童醫院兒科部³;高雄長庚紀念醫院兒科部⁴;中國醫藥大學附設醫院兒科部⁵;花蓮慈濟醫院感染科⁶;國立台灣大學醫學院附設醫院兒科部⁷;國家衛生研究院群體健康科學研究所⁸;衛生福利部疾病管制署⁹
- 09:19~09:40 討論
- 09:40~09:50 休息

第五單元：小兒預防醫學及流行病學

日期：民國109年11月14日(星期六)

時間：09:50~10:30

地點：第二會場

主持人：張鑾英、徐任甫

- 09:50~09:57 45. 研究使用醫病共享決策在兒童輪狀病毒疫苗接種率的影響
林聖傑^{1,2}、譚家偉^{3,4}、顏玉春⁵、呂孟哲¹、陳瑛芳¹、郭雲鼎¹、林文川¹、陳淑惠¹、羅爾維⁶、陳世彥¹
臺北醫學大學部立雙和醫院小兒部¹；臺北醫學大學醫學院小兒學科²；臺北醫學大學部立雙和醫院外科部³；臺北醫學大學台灣考科藍⁴；臺北醫學大學管理學院生物統計學研究中心⁵；臺北醫學大學雙和醫院醫學研究部實證中心⁶
- 09:57~10:04 46. 腸病毒預後之流行病學研究—世代追蹤研究
曾瑞如^{1,2}、林敬恒³、林明志^{1,4,5}
台中榮民總醫院兒童醫學部¹；國立陽明大學臨床醫學研究所²；台中榮民總醫院醫學研究部³；國立陽明大學醫學系⁴；靜宜大學食品營養學系⁵
- 10:04~10:11 47. 臺灣孩童2002-2012年共用中藥與西藥處方的趨勢
杜小昕¹、黃家榆²、黃元韻¹、顏宏融^{3,4,5,6}
澄清綜合醫院中港分院兒科部¹；佛教慈濟醫療財團法人台中慈濟醫院家庭醫學科²；中國醫藥大學中醫學院中醫研究所³；中國醫藥大學附設醫院中醫部⁴；中國醫藥大學中草藥研究中心⁵；中國醫藥大學中醫藥研究中心⁶
- 10:11~10:18 48. 父母對兒童健康預期指引之認知程度與多媒體學習成效之評估
趙香皓^{1,2}、蘇有村¹、黃意雯³、林其和^{1,4}
財團法人義大醫療義大醫院兒童醫學部¹；衛生福利部旗山醫院小兒科²；國立台南大學數位學習科技學系³；國立成功大學醫學院附設醫院小兒部⁴
- 10:18~10:30 討論
- 10:30~10:40 休息

第六單元：肺臟學

日期：民國109年11月14日(星期六)

時間：10:40~11:50

地點：第二會場

主持人：宋文舉、陳中明

- 10:40~10:47 49. 透明質酸介導的運動因子受體藉調節NLRP3發炎體在新生高氧肺損傷中扮演一重要角色
陳怡真^{1,2}、Jie Liao³、Naeun Cheong³、Christopher Longoria³、Rashmin C. Savani³
高雄醫學大學附設醫院小兒部¹；高雄醫學大學醫學研究所²；美國德州大學西南醫學中心兒科部³
- 10:47~10:54 50. 早產兒氣道軟化症之危險因子探討
邱俊哲¹、李恩沛²、賴申豪³、林建志²、夏紹軒²、陳愛華²、邱志勇³
新北市立土城醫院，長庚紀念醫院及長庚大學¹；林口長庚紀念醫院兒童重症加護科²、兒童胸腔科³
- 10:54~11:01 51. 幼兒施予持續咽腔充氣法時：上氣道腔壓力與管腔變化—以軟式內視鏡監測
宋文舉、陳傑賀、林建亨
中國醫藥大學兒童醫院胸腔暨重症科
- 11:01~11:08 52. 結合代謝質體學和微生物菌叢分析探討兒童氣喘
邱志勇¹、鄭美玲²、江孟翰³、蔡明翰⁴、邱俊哲¹、林吉晉³
長庚醫療財團法人林口長庚紀念醫院兒童內科部胸腔科¹；長庚大學生物醫學系健康老化研究中心²；長庚醫療財團法人林口長庚紀念醫院臨床代謝質體學中心³；長庚醫療財團法人基隆長庚紀念醫院兒科⁴
- 11:08~11:15 53. 脈衝振盪肺功能合併支氣管擴張試驗於兒童氣喘診斷之應用
陳傑賀¹、魏長菁²、林清淵³、廖相如²、林鴻志⁴、林建亨¹
中國醫藥大學兒童醫院胸腔暨重症科¹、風濕免疫科²、腎臟科³、新生兒科⁴
- 11:15~11:22 54. 應用脈衝震盪肺功能測定合併氣管擴張試驗於氣喘治療：一兒童醫院之經驗
彭慧倫¹、陳傑賀²、林建亨²、宋文舉²
中國醫藥大學兒童醫院¹；中國醫藥大學兒童醫院胸腔科²
- 11:22~11:29 55. 檢測兒童肺炎病人唾液中C反應蛋白
蔡智閔、唐國書、鄭明洲、劉大猷、李易臻、蔡長谷、蔡迪安、于鴻仁
高雄長庚紀念醫院兒童內科部
- 11:29~11:50 討論

附加研討會
探討脊髓性肌肉萎縮症之呼吸照護新知

日期：民國109年11月14日(星期六)

時間：12:10~13:20

地點：第二會場

主持人：鐘育志教授

- | | |
|-------------|---|
| 12:10~12:20 | 1. 開幕致詞
鐘育志教授
高雄醫學大學附設中和紀念醫院 |
| 12:20~13:10 | 2. 探討脊髓性肌肉萎縮症之呼吸照護新知
Prof. Dong In Suh
首爾大學兒童醫院 |
| 13:10~13:20 | 3. 問題討論與結語
鐘育志教授
高雄醫學大學附設中和紀念醫院 |

第七單元：過敏免疫風濕病學

日期：民國109年11月14日(星期六)

時間：13:30~16:00

地點：第二會場

主持人：陳力振、歐良修

- 13:30~13:37 56. 在哮喘小鼠模型中，免疫調節蛋白FIP-fve可以改善微角塵蟎所誘導氣道炎症反應
陳大揚¹、呂克桓¹、孫海倫¹、潘蕙嫻¹、顧明修¹、廖培汾¹、郭業文¹、劉玉凡、柯俊良、李育慈
中山醫學大學附設醫院¹
- 13:37~13:44 57. 鄰苯二甲酸酯增加人類呼吸道上皮細胞分泌之IL-28 A and IL-29之表達可由類黃酮反轉
李仲翔^{1,2}、洪志興^{1,2,3}、林宜靜^{1,2,4}、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
- 13:44~13:51 58. 類黃酮Narirutin可經由調節基因轉錄的機轉來抑制TH1細胞激素IP-10
李仲翔¹、洪志興¹、郭昶宏¹、林宜靜¹
高雄醫學大學附設中和紀念醫院小兒部、過敏免疫科¹
- 13:51~13:58 59. 氣喘病童呼吸道敏感反應的程度與血清中鞘氨醇-1-磷酸鹽濃度的相關性
陳力振、王雪君¹、葉國偉²、李文益²、郭敏玲³、吳艾瑄、游琇玥、黃嘯谷⁴、黃璟隆
新北市立土城醫院兒童內科部；中國醫藥大學生物醫學研究所¹；長庚醫院兒童過敏氣喘風濕科²；長庚大學微生物免疫研究所³；國家衛生研究院環境衛生暨職業醫學組⁴
- 13:58~14:05 60. montelukast在氣喘病童的使用不會增加過動症的風險：一健保資料庫研究
張鈴偲¹、郭和昌¹、郭明慧¹、楊曜旭²、王亮人¹、于鴻仁¹
高雄長庚醫院¹；嘉義長庚醫院²
- 14:05~14:12 61. 探討微角塵蟎在台灣中部地區過敏氣喘兒童扮演的角色
徐淑華¹、呂克桓^{1,2}、孫海倫¹、劉玉凡³、柯俊良²、李育慈³、廖培汾¹、顧明修¹、潘蕙嫻¹、郭業文¹
中山醫學大學附設醫院兒童部¹；中山醫學大學醫學研究所²；中山醫學大學生物醫學系³

14:12~14:19 62. 開業兒科醫師利用BMI指數對氣喘控制評估的結果
溫港生^{1,2}、黃哲聖²、林博通³、蘇聿懋⁴、葉介彬⁵、洪志平⁶、李鴻科⁷
台北市宏恩醫院小兒科¹；台北市聯合醫院仁愛院區小兒科²；台北市林阿諾診所³；新北市過敏診所⁴；新北市葉洪兒科診所⁵；台北市洪兒科診所⁶；新北市洋基診所⁷

14:19~14:40 討論

14:40~14:50 休息

主持人：孫海倫、高峻凱

14:50~14:57 63. 不同培養條件影響臍帶間質幹細胞生長與其胞外囊泡的內容差異研究
楊蕙榕^{1,2}、林佳學¹、沈婕如¹、簡銘輝¹、陳治平³、楊崑德^{1,2,4}
馬偕兒童醫院¹；陽明大學臨醫所²；馬偕紀念醫院婦產科、醫研部³；國防醫學院微免所⁴

14:57~15:04 64. 比較骨髓與臍帶間質幹細胞來源的胞外囊泡內容與作用差別
林佳學¹、王韻茹²、廖恩慈²、王恩婕^{1,2}、林葳妮^{1,2}、葉庭吉¹、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、醫研部³；國防醫學院微免所⁴

15:04~15:11 65. 冠狀動脈病變的川崎症病人六個月後的免疫球蛋白M濃度較沒有冠狀動脈病變的川崎病人下降
張鈴偲、黃瀛賢、郭明慧、郭和昌
高雄長庚醫院兒童內科部川崎中心

15:11~15:18 66. 介白質15對紅斑性狼瘡病患周邊血液NK細胞凋亡的調控與影響
徐千雅¹、林思偕¹、黃璟隆¹、李文益¹、葉國偉¹、陳力振¹、歐良修¹、姚宗杰、吳昭儀¹、陳基益³、郭敏玲^{1,2}
長庚紀念醫院小兒科¹；長庚大學醫學系微生物及免疫學科²；長庚紀念醫院風濕免疫科³

15:18~15:25 67. 早發性兒童紅斑性狼瘡臨床特徵和基因分析
李宛芳¹、吳昭儀¹、楊皇煜²、曾敏華³、黃璟隆¹、李文益¹、陳力振¹、葉國偉¹、歐良修¹、姚宗杰¹
林口長庚紀念醫院兒童過敏氣喘風濕科¹、腎臟科²、兒童腎臟科³

15:25~15:32 68. 以人工智慧大數據預測兒童紅斑性狼瘡之全身性類固醇使用
傅令嫻^{1,2}、蔡智鈞³
臺中榮民總醫院兒童醫學中心¹；陽明大學兒科系²；暨南大學資訊工程所³

- 15:32~15:39 69. 台灣性聯遺傳免疫球蛋白低下病患之特殊臨床表徵及基因突變
葉育欣¹、謝孟穎^{2,5}、李文益^{1,3}、黃璟隆⁴、陳力振⁴、葉國偉¹、歐良修¹、
姚宗杰¹、吳昭儀¹、林思偕¹
林口長庚醫院兒童過敏氣喘風濕科¹；台北長庚醫院兒童內科²；長庚大學先天
免疫缺損照護暨研究中心³；新北市立土城醫院兒科⁴；林口長庚醫院兒童
神經內科⁵
- 15:39~16:00 討論
- 16:00~16:10 休息

第八單元：心臟血管學

日期：民國109年11月14日(星期六)

時間：16:10~17:20

地點：第二會場

主持人：葉樹人、林明志

- 16:10~16:17 70. 單一心室術後病人心肌和心室內動能變化
翁根本、簡光仁、林竹川、陳昱潔、吳銘庭¹、謝凱生²、彭旭霞³
高雄榮民總醫院先天性結構性心臟病醫學中心放射線部¹；台北醫學大學兒
科學系²；清華大學生醫工程與環境科學系³
- 16:17~16:24 71. 主動脈逆流為馬凡氏症患者一重要之手術風險因子
范文博^{1,2}、李星原¹、曾思穎¹、阮建彰²、黃碧桃¹、牛道明¹、李必昌¹
台北榮民總醫院兒童醫學部¹；國立陽明大學附設醫院小兒科²
- 16:24~16:31 72. 研究深度學習框架與擴增數據自動判讀心室中隔缺損之超音波影像
戴以信¹、陳世興²、林竹川³、黃大誠³、盧文獻³、簡光仁³、傅雲慶¹、郭和昌⁴、
翁根本³、謝凱生⁵
中國醫藥大學兒童醫院¹；正修科技大學資訊管理學系²；高雄榮民總醫院兒
童醫學部³；高雄長庚川崎病中心⁴；台北醫學大學雙和醫院⁵
- 16:31~16:38 73. 探討川崎病在疑似心肌梗塞年輕病患之盛行率
戴以信¹、吳炯仁²、傅雲慶¹、徐宗正¹、謝凱生³
中國醫藥大學兒童醫院¹；高雄長庚紀念醫院²；衛生福利部雙和醫院³

- 16:38~16:45 74. 隱源性腦中風後經心導管關閉開放性卵圓孔－台灣單一醫學中心經驗
林廷育、林明志、詹聖霖、陳書農、劉瑋莉
臺中榮民總醫院兒童醫學中心兒童心臟科
- 16:45~16:52 75. 以超音波測量小於2.5公斤新生兒的股血管內徑大小研究
劉瑋莉¹、林廷育²、陳書農²、林明志²、詹聖霖²
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
- 16:52~16:59 76. 兒童昏厥病患之傾斜床測試結果分析：單一醫院之經驗
葉樹人、洪偉力、林珊妙、陳銘仁
馬偕兒童醫院兒童心臟科
- 16:59~17:20 討論

第九單元：神經精神醫學

日期：民國109年11月14日(星期六)

時間：08:30~10:00

地點：第三會場

主持人：李秀芬、張通銘

- 08:30~08:37 77. KCNQ2 loss-of-function突變導致兒童長期神經發展預後與異質的Kv7.2鉀離子通道電流改變有關
林純至^{1,2}、楊建洲³、劉英明³、黃瑞喜³、李宣佑⁴、李英齊^{1,2}
中山醫學大學附設醫院兒童學科兒童神經科¹；中山醫學大學醫學院醫學系²；
分子與基因醫學研究室中山醫學大學生物醫學科學系³；國立中興大學生命科學系⁴
- 08:37~08:44 78. 自嗜作用與泛素-蛋白酶體系統失調與NRF2訊息異常是造成GLD白質退化症的病理機轉
林達雄^{1,2}、何啓生³、黃玉文⁴、吳竺燕⁴、李宗翰⁴、黃榮達⁴
馬偕紀念醫院兒科¹；馬偕紀念醫學院醫學系²；馬偕兒童醫院神經科³；馬偕紀念醫院醫學研究部⁴

第二四四屆學術演講會

- 08:44~08:51 79. 212個與癲癇相關基因之變異與孩童失神性癲癇的關聯研究
林瑋德^{1,5}、王仲興³、洪宜羽⁴、蔡輔仁^{1,2,3,6}、周宜卿^{4,7}
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、小兒神經科⁴；中國醫藥大學學士後中醫學系⁵、中醫學系⁶、中西醫結合研究所⁷
- 08:51~08:58 80. 心因性癲癇之臨床表現
王家義^{1,2}、許庭榕^{2,3}、張開屏^{2,4}
新北市立聯合醫院兒科¹；台北榮民總醫院兒童神經科²；國立陽明大學臨床醫學研究所醫學院³；苗栗為恭紀念醫院⁴
- 08:58~09:05 81. Dravet症候群及熱感性癲癇分析—單一醫學中心經驗
劉懿萱¹、蔡孟翰^{2,3}、周怡君^{1,2}、洪伯誠^{1,2}、謝孟穎^{1,2}、王蕙珊¹、陳韻茹¹、郭政諺¹、王輝雄^{1,2}、林光麟^{1,2*}
林口長庚醫院兒童醫院兒童神經科¹；長庚大學醫學院²；高雄長庚醫院神經內科³
- 09:05~09:12 82. 經顱光生物調節療法減緩青春期大鼠之Pentylentetrazole所誘發的癲癇重積狀態
蔡崇敏、張淑芬、張璽¹
臺北醫學大學附設醫院小兒科¹
- 09:12~09:19 83. 次世代全外顯子定序對早期癲癇性腦病變之基因診斷
洪焜隆¹、許書菁¹、王麗君¹、盧志峰²
輔仁大學附設醫院兒童醫學部；國泰綜合醫院小兒科¹；輔仁大學醫學系²
- 09:19~09:26 84. 以智慧型手錶評估注意力不集中及過動症之藥物治療療效
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；義守大學資工系¹、電機系²；屏東大學電通系³
- 09:26~09:33 85. 早期語言環境對嬰兒理解性語言發展之影響
吳淑娟、王馨敏¹、李如蕙²、李俊仁³、曾志朗²
羅東博愛醫院小兒科；國立師範大學人類發展與家庭學系¹；中央研究院²；國立師範大學教育心理與輔導學系³
- 09:33~10:00 討論
- 10:00~10:10 休息

第十單元：急診學

日期：民國109年11月14日(星期六)

時間：10:10~11:10

地點：第三會場

主持人：李 嶸、詹聖霖

- 10:10~10:17 86. 單一兒童急診中心學齡前兒童就診的特徵和結果分析
林亭安¹、陸振芳¹、劉英妹¹、林鈺芳¹、邱若仔¹、李嶸²
長庚科技大學護理學院¹；長庚大學長庚醫院兒童內科部一般兒科²
- 10:17~10:24 87. 自兒童門診區轉診至兒童急診室之病童臨床分析
陳澄如¹、陳俊佑^{1,2}、楊文傑^{1,2}、黃文彥^{1,2}、戴以信^{1,2}、彭義欽^{1,2}、許玉龍^{1,2}、陳浚穠^{1,2}、傅雲慶^{2,3}、吳漢屏^{1,2,4}
中國醫藥大學兒童醫院兒童急診醫學部¹；中國醫藥大學醫學系²；中國醫藥大學兒童心臟科³；中國醫藥大學兒童醫院醫學研究部⁴
- 10:24~10:31 88. 兒童急診返診趨勢
黃一安¹、黃心苑²、吳昌騰³、李嶸³、江東和³
基隆長庚醫院小兒科¹；陽明大學醫管所²；林口長庚醫院一般兒科³
- 10:31~10:38 89. 兒童急性感染性腦炎在兒童急診部的臨床分析
陳浚穠、吳漢屏
中國醫藥大學兒童醫院兒童急診部
- 10:38~10:45 90. sCD40L預測兒童闌尾炎
黃文彥¹、吳漢屏^{1,2}
中國醫藥大學兒童醫院兒童急診部¹、醫學研究部²
- 10:45~10:52 91. 兒少虐待及疏忽門診成效—單一中心二年之經驗
夏紹軒、林建志、陳愛華、林蔚均、許喬婷、王心寧、蔡宜津、葉國偉、邱政洵、黃璟隆
林口長庚紀念醫院兒少保護中心
- 10:52~11:10 討論
- 11:10~11:20 休息

第十一單元：重症學

日期：民國109年11月14日(星期六)

時間：11:20~12:20

地點：第三會場

主持人：王玠能、夏紹軒

- 11:20~11:27 92. 葉克膜於新生兒呼吸衰竭的應用：台灣一家醫學中心的經驗
王怡方、吳恩婷、王景甲、陳倩儀、周弘傑、曹伯年、顏玳安、呂立
國立台灣大學醫學院附設醫院小兒部
- 11:27~11:34 93. 及時視診超音波在兒科急性照顧之前期經驗
周正哲¹、江舒欣²、陳瑛芳³、郭雲鼎¹、王傳育¹、謝凱生⁴、呂孟哲⁵、林聖傑⁵
臺北醫學大學部立雙和醫院小兒部小兒神經科¹、小兒急診科²、新生兒科³、
小兒心臟科⁴、風濕過敏科⁵
- 11:34~11:41 94. 兒童壞死性腦炎臨床表現，南部一家醫學中心經驗
蘇亭毓、徐美欣、林盈瑞、郭玄章、洪碧蓮
高雄長庚醫院兒童內科部
- 11:41~11:48 95. 免疫調節治療方法(免疫球蛋白或高劑量類固醇治療)對於急性壞死性腦病
變的預後改善
張涵碧、李恩沛、夏紹軒、林建志、陳愛華
長庚醫療財團法人林口長庚紀念醫院兒童重症加護科
- 11:48~11:55 96. 受虐型腦傷—兒科加護病房內嚴重創傷型腦傷主要原因及死因
劉怡慶、吳彥賢、陳怡真、戴任恭、徐仲豪*
高雄醫學大學附設中和紀念醫院兒科部
- 11:55~12:02 97. 使用一個新穎研發的穿戴裝置測量體溫的先導性研究
謝凱生¹、張榮森²、張焜傑²、周正哲¹、陳世彥¹、林奏延³
雙和醫院兒科--台北醫學大學¹；國立中央大學光電科學研究所²；長庚大學
醫學院³
- 12:02~12:20 討論

第十二單元：醫學遺傳學、新陳代謝學

日期：民國109年11月14日(星期六)

時間：13:30~14:50

地點：第三會場

主持人：侯家瑋、蘇本華

- 13:30~13:37 98. 自嗜作用與泛素-蛋白酶體系統失調導致泛素與p62堆積及NRF2訊息異常造成GLD髓鞘細胞死亡
林達雄^{1,2}、何啓生³、黃玉文⁴、吳竺燕⁴、李宗翰⁴、黃榮達⁴
馬偕紀念醫院兒科¹；馬偕紀念醫學院醫學系²；馬偕兒童醫院神經科³；馬偕紀念醫院醫學研究部⁴
- 13:37~13:44 99. 台灣黑尿症患者之HGD基因分析
賴建亦¹、李妮鍾¹、蔡宜蓉²、邱寶琴³、簡穎秀¹、胡務亮¹
國立臺灣大學醫學院附設醫院基因醫學部、小兒部¹；國立臺灣大學醫學院附設醫院兒童醫院兒童腎臟科²；高雄榮民總醫院兒童醫學部³
- 13:44~13:51 100. 台灣纖毛病變症候群病人的基因調查：全外顯子定序的運用
歐宗穎¹、蔡孟哲^{1,2}、周言穎¹、潘好玟¹、陳芃潔²、邱寶琴³、林如立⁴
國立成功大學醫學院附設醫院小兒部¹；國立成功大學臨床醫學研究所²；高雄榮民總醫院兒童醫學部³；林口長庚紀念醫院兒童內分泌暨遺傳科⁴
- 13:51~13:58 101. 自1985至2019年的35年間，175位台灣黏多醣症病患的生存與確診年齡
林翔宇^{1,2,3,4}、林炫沛^{1,2,3,5}、莊志光²、邱寶琴⁶、簡穎秀⁷、牛道明⁸、蔡輔仁⁹、胡務亮⁷、林秀娟¹⁰、林如立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；高雄榮民總醫院兒童醫學部⁶；國立台灣大學醫學院附設醫院小兒科部⁷；台北榮民總醫院兒童醫學部⁸；中國醫藥大學附設醫院小兒科部⁹；台南奇美醫學中心小兒科部¹⁰；林口長庚醫院兒童遺傳科與長庚大學醫學系¹¹
- 13:58~14:05 102. 台灣黏多醣症患者其耳鼻喉症狀的治療經驗
李忠霖^{1,2}、李國森^{3,5}、莊志光^{4,9}、蘇晉輝^{3,5}、邱慧菁⁴、塗如意⁴、林翔宇^{4,5,6,7,8}、林炫沛^{4,5,6,10}
新竹馬偕醫院兒科部¹；陽明大學臨床醫學研究所²；台北馬偕醫院耳鼻喉科³；台北馬偕醫院兒科部與罕見疾病中心⁴；馬偕醫學院⁵；馬偕醫院醫學研究部生化遺傳研究組⁶；馬偕醫護管理專科學校⁷；中國醫藥大學附設醫院醫學研究部⁸；輔仁大學醫學院⁹；臺北護理健康大學嬰幼兒保育系所¹⁰

- 14:05~14:12 103. 台灣黏多醣症第二型的確診患者與無症狀嬰兒的基因型、表現型與生物標記之分析
林翔宇^{1,2,3,4}、林炫沛^{1,2,3,5}、莊志光²、塗如意²、陳樹人²、羅允廷⁶、張雅惠¹、曾紫蕾²、李忠霖⁷、牛道明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；馬偕紀念醫院檢驗醫學部⁶；新竹馬偕紀念醫院小兒科⁷；台北榮民總醫院兒童醫學部⁸
- 14:12~14:19 104. 台灣黏多醣症第二型患者的心臟特徵自然進程與酵素替補治療的長期效果
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^{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
- 14:19~14:26 105. FN1引起的角落骨折：從骨髓炎到兒虐
蔡俊慧^{1,2}、游佳瑜^{1,3}、John-Paul¹
科羅拉多大學小兒科科¹；奧克拉何馬大學小兒科²；和信治癌中心醫院³
- 14:26~14:50 討論
- 14:50~15:00 休息

第十三單元：內分泌學

日期：民國109年11月14日(星期六)

時間：15:00~16:50

地點：第三會場

主持人：朱德明、黃秀莉

- 15:00~15:07 106. 血清嗜中性白血球明膠酶相關脂質運載蛋白作為兒童第一型糖尿病腎病變的生物標記
李如浩^{1,3}、楊豐榮^{2,3}、蔡文友¹、李正婷¹、劉士嶢^{1,3}、楊偉勛^{3,4}、童怡靖¹
國立台灣大學醫學院附設醫院小兒部¹；國立台灣大學醫學院附設醫院雲林分院內科部²；國立台灣大學醫學院臨床醫學研究所³；國立台灣大學醫學院附設醫院內科部⁴

- 15:07~15:14 107. 益生菌對於第一型糖尿病病人的臨床成效
黃彥宇¹、林鴻志¹、呂文莉¹、林瑋德²、蔡輔仁^{1,2,3}、王仲興¹
中國醫藥大學兒童醫院¹；中國醫藥大學附設醫院醫學研究部²；中國醫藥大學中醫學院中醫學系³
- 15:14~15:21 108. 在糖尿病診斷當下的非刺激的C肽數值，是否可作為診斷後兩年的胰島素使用狀況的良好預測因子？
周威志、蔡孟哲、潘妤玟、周言穎
國立成功大學醫學院附設醫院小兒部
- 15:21~15:28 109. 女性荷爾蒙療法在透納氏症兒童之臨床效益
李翊誠^{1,5}、丁瑋信^{1,2}、黃琪鈺^{1,2}、黃世綱^{1,3}、葉淑寧¹、林昭旭⁴、鄭弼文⁴、李燕晉^{1,6,7,8}
馬偕兒童醫院兒童內分泌科¹；馬偕醫護管理專科學校護理學科²；馬偕紀念醫院淡水院區小兒科部³；馬偕紀念醫院新竹院區小兒科部⁴；國泰醫院小兒科部⁵；馬偕紀念醫院淡水院區醫學研究部⁶；台北醫學大學醫學院醫學系小兒科⁷；馬偕醫學院醫學系⁸
- 15:28~15:35 110. 108名台灣透納氏症候群患者的心臟代謝危險因素分析：來自一個醫療中心的經驗
陳冠銘、羅福松、許薰惠、邱巧凡、林如立
林口長庚醫院兒童內分泌暨遺傳科、長庚大學醫學系
- 15:35~15:42 111. 女童中樞性早熟之診斷
葉淑寧^{1,2}、丁瑋信^{1,3,4}、黃琪鈺^{1,3}、李燕晉^{1,3,5,6,7}、黃世綱¹、李翊誠¹、蔡維鍵¹、林昭旭^{8,9}、鄭弼文^{8,9}
馬偕兒童醫院兒童內分泌科¹；沙爾德聖保祿修女會醫療財團法人聖保祿醫院兒科部²；馬偕醫學院³；馬偕醫護管理專科學校⁴；淡水馬偕醫學院醫學研究部⁵；馬偕醫學院生物醫學研究所⁶；臺北醫學大學醫學系兒科部⁷；新竹馬偕醫院兒童內分泌科⁸；國立交通大學生物科學技術學院⁹
- 15:42~15:49 112. 以單一醫學中心為經驗：台灣病人的特發性低性腺促素低性腺功能症的臨床及基因特徵
卓芷伊^{1,2}、蔡文友¹、李正婷¹、劉士嶢¹、黃淑媛³、簡穎秀^{1,3}、胡務亮^{1,3}、李妮鍾^{1,3}、童怡靖¹
國立台灣大學醫學院附設醫院小兒部¹；國立台灣大學醫學院臨床醫學研究所²；國立台灣大學醫學院附設醫院基因部³
- 15:49~15:56 113. 評估以Greulich and Pyle圖譜判讀骨齡之適用性及與生理年齡間之差異性
喻永生^{1,2}、周定遠^{3,4}、董道興⁵
振興醫院兒童醫學部¹；國防醫學院小兒學系²；耕莘醫院放射診斷部³；輔仁大學醫學系⁴；振興醫院教學研究部⁵

- 15:56~16:03 114. 鈣敏感受體基因(CASR)新變異所致低血鈣：家族個案報告
黃羽薇、王禎鞠¹、郭珮雯¹、王碩郁、陳百薰、黃道揚²、蕭惠彬
小兒遺傳及內分泌新陳代謝科，兒科部，遺傳諮詢中心¹，高醫大附設醫院
癌症研究所²/國衛院
- 16:03~16:10 115. 孕婦和哺乳期攝入白藜蘆醇可通過脂肪代謝調節雄性後代的肥胖，並改善
其後代對瘦素的抗性
劉大猷、于鴻仁、黃立同、刁茂盟、田祐霖、沈俊明、陳志誠
高雄長庚紀念醫院兒科
- 16:10~16:17 116. 隨機對照評估沒下降睪丸兒童在台北市、基隆市及新北市的分佈情形
溫港生^{1,3}、李鴻科²、朱紀洪⁴
台北市宏恩醫院小兒科¹；新北市三重區洋基診所²；台北市聯合醫院仁愛院
區小兒科³；台北市宏恩醫院一般外科⁴
- 16:17~16:50 討論
- 16:50~17:00 休息

第十四單元：青少年醫學

日期：民國109年11月14日(星期六)

時間：17:00~17:30

地點：第三會場

主持人：陳武元、林昭旭

- 17:00~17:07 117. 青少年時期之社會生態因子在預測青壯年期的糖尿病發生率分析
黃瑞妍¹、李笙平、王碩郁²
高雄醫學大學附設醫院小兒部、青少年醫學科¹、小兒遺傳內分泌暨新陳代
謝科²
- 17:07~17:14 118. 台灣兒童及青少年高血壓盛行率之研究
徐萬夫¹、高翊璋^{2,3}、陳世彥⁴、謝邦昌^{3,5}、謝凱生⁴
國防醫學院三軍總醫院小兒科部¹；輔仁大學管理學院企業管理研究所²；臺
北醫學大學管理學院大數據研究中心³；衛生福利部雙和醫院兒科部(臺北醫
學大學)⁴；臺北醫學大學管理學院⁵；臺北醫學大學管理學院生物科技高階
管理碩士在職專班⁶

第二四四屆學術演講會

- 17:14~17:21 119. 經濟弱勢青少年的糧食匱虞與物質使用之間的相關性：全國世代研究的長期分析
蔡孟哲¹、陳立成^{2,3}、李芷婷⁴
國立成功大學醫學院暨附設醫院小兒科¹；國立成功大學醫學院護理學系²；
印尼西爪哇巴查查蘭大學護理系³；國立成功大學醫學院暨附設醫院家庭醫學科⁴
- 17:21~17:30 討論

教育演講：
一般兒科門診實務經驗分享

日期：民國109年11月15日(星期日)

時間：09:00~12:00

地點：第一會場

主持人：陳武元教授、王玲醫師

- | | |
|-------------|---|
| 09:00~09:25 | 1. 基層兒科門診常見的治療處置、檢查及健保給付相關規定
曾崇芳醫師
崇芳小兒科家庭醫學科聯合診所 |
| 09:25~09:45 | 2. 會員面對健保兒科醫療政策應有的態度及努力
林應然醫師
林應然小兒科診所 |
| 09:45~10:30 | 3. 基層兒科門診如何做呼吸道及耳鼻喉局部處置
林釗尙醫師
林釗尙小兒科診所 |
| 10:30~10:45 | 4. 討論 |
| 10:45~11:45 | 5. 健康享瘦，享受健康——體重管理的觀念與實務
林黑潮醫師
林黑潮診所 |
| 11:45~12:00 | 6. 討論 |

頒 獎

日期：民國109年11月15日(星期日)

時間：13:30~14:00

地點：第一會場

14:00~14:10 休息

醫學的科學、倫理與法律講座： 醫師如何面對媒體暨兩性議題

日期：民國109年11月15日(星期日)

時間：14:10~16:10

地點：第一會場

主持人：李宏昌理事長

- 14:10~15:00 1. 醫療新聞曝光效應暨媒體溝通
 蔣志偉主播/資深醫藥記者
 TVBS新聞部主播/資深醫藥記者
- 15:00~15:10 討論
- 15:10~16:00 2. 提升醫療中的性別敏感度
 林靜儀醫師
 中山醫學大學附設醫院婦產部
- 16:00~16:10 討論

附加研討會
流感抗病毒藥物治療之新里程碑

日期：民國109年11月15日(星期日)

時間：12:00~13:30

地點：第二會場

主持人：黃立民教授

- | | |
|-------------|---|
| 12:00~12:05 | 1. 開幕致詞
黃立民教授
臺大醫院兒童醫院 |
| 12:05~12:40 | 2. Baloxavir Marboxil最新臨床證據
紀鑫醫師
馬偕兒童醫院 |
| 12:40~13:10 | 3. Peramivir於小兒流感患者之臨床經驗
鄭名芳醫師
高雄榮民總醫院 |
| 13:10~13:30 | 4. 問題討論與結語
黃立民教授
臺大醫院兒童醫院 |

第十五單元：血液、腫瘤學

日期：民國109年11月15日(星期日)

時間：09:00~10:50

地點：第三會場

主持人：巫康熙、王士忠

- 09:00~09:07 120. 甲氨蝶呤藥物治療後空間記憶功能表現及腸道菌叢生態改變：一個小鼠研究模式
謝馨儀¹、黃立同^{2,3}、蕭志誠^{1,3}、沈俊明^{1,3}、王素貞¹、陳昱潔^{1,3}
高雄長庚醫院兒童血液腫瘤科¹；高雄長庚醫院兒童神經內科²；長庚大學³
- 09:07~09:14 121. 薑黃素透過抑制阿糖胞苷耐藥之髓樣白血病細胞的BCAT1表達和mTOR信號而誘導細胞凋亡
林佩瑾^{1,2,3}、楊瑞成^{1,4}、邱世欣^{1,2,3}、曾羽辛¹
台灣高雄醫學大學附設中和紀念醫院小兒部¹；台灣高雄醫學大學附設中和紀念醫院小兒部血液腫瘤科²；台灣高雄醫學大學醫學院醫學系小兒學科³；台灣高雄醫學大學醫學院醫學研究所⁴
- 09:14~09:21 122. 有骨頭肌肉關節症狀的兒童急性淋巴性白血病病人之臨床表現及預後分析
林彥臻¹、葉庭吉¹、侯人尹¹、黃鼎煥¹、蔡佩珊²、汪靖哲²、宋家瑜³、劉希哲¹
馬偕兒童醫院血液腫瘤科¹；馬偕紀念醫院放射科²；彰化基督教兒童醫院³
- 09:21~09:28 123. 比較青少年/年輕人和兒童之間急性骨髓性白血病於異體造血細胞移植的類似結果
張從彥¹、江東和¹、陳世翔¹、溫玉娟²、楊兆平¹、洪悠紀¹
林口長庚紀念醫院兒童醫學中心兒童血液腫瘤科¹、護理部²
- 09:28~09:35 124. 急性淋巴性白血病病童結束化療後「鐵調素-運鐵素機制」失調的探討
劉希哲¹、葉庭吉¹、侯人尹¹、黃鼎煥¹、宋家瑜²、林純卉¹、葉宣佑³、陳采瑩³
馬偕兒童醫院血液腫瘤科¹；彰化基督教兒童醫院²；馬偕醫院醫學研究部³

- 09:35~09:42 125. 碘-131-間碘苜蓿(¹³¹I)MIBG)標靶放射治療應用於復發性/頑固性神經母細胞瘤的初期臺灣經驗
王士忠¹、王連嚴²、盧孟佑³、許文明⁴、顏秀如⁵、葉庭吉⁶、劉希哲⁶、侯人尹⁶、J.S. Miser^{7,8}、劉彥麟^{3,7,9,10,*}
彰化基督教兒童醫院兒童血液腫瘤科¹；彰化基督教醫院核子醫學科²；國立臺灣大學醫學院附設醫院兒童醫院小兒血液腫瘤科³、小兒外科⁴；臺北榮民總醫院兒童血液腫瘤科⁵；馬偕兒童醫院兒童血液腫瘤科⁶；臺北醫學大學臺北癌症中心⁷、醫學科技學院⁸、醫學院醫學系小兒學科⁹；臺北醫學大學附設醫院小兒血液腫瘤科¹⁰
- 09:42~09:49 126. 尤文氏肉瘤及其他小圓細胞肉瘤病患接受療程壓縮之化學治療的反應與毒性觀察
黃嘉蕙¹、陳淑惠^{4,7,8,11}、高郁茜^{5,9,11}、黃棣棟^{2,7}、張璽^{1,8}、蔡明蘭^{1,8}、李欣倫^{3,6,11}、張家堯^{1,8}、王錦莉^{6,8}、劉彥麟^{1,7,8,11,*}、J.S. Miser^{7,10,11}
臺北醫學大學附設醫院小兒部¹、兒童神經外科²、放射腫瘤科³；衛生福利部雙和醫院(委託臺北醫學大學興建經營)兒科部⁴、病理科⁵；臺北市立萬芳醫院-委託財團法人臺北醫學大學辦理兒科部⁶；臺北醫學大學臺北癌症中心⁷、醫學院醫學系小兒學科⁸、醫學院醫學系病理學科⁹、醫學科技學院¹⁰；臺北醫學大學肉瘤及肌肉骨骼腫瘤團隊¹¹
- 09:49~09:56 127. 繼發於惡性生殖細胞瘤的畸胎瘤增長症候群之探討
謝明芸¹、洪君儀²、李致穎²、陳世翔³、江東和³、張從彥³、賴勁堯³、鄭兆能⁴、陳建旭⁴、顏秀如²
高雄榮民總醫院兒童醫學部¹；台北榮民總醫院兒童血液腫瘤科²；林口長庚紀念醫院兒童內科部血液腫瘤科³；國立成功大學醫學院附設醫院小兒部⁴
- 09:56~10:03 128. 兒童視網膜母細胞瘤的RB1基因突變分析：單一醫學中心之經驗
陳世翔¹、高玲玉²、江東和¹、蔡悅如²、劉峻秀²、張從彥¹、楊兆平¹、洪悠紀¹
林口長庚紀念醫院兒童血液腫瘤科¹、林口長庚紀念醫院眼科²
- 10:03~10:10 129. 嚴重A型血友病患者依藥物動力學工具來進行個人化治療
侯人尹、劉希哲、葉庭吉、黃鼎煥
馬偕兒童醫院
- 10:10~10:17 130. 以口服mTOR治療TSC之臉部纖維瘤之成效
吳孟軒¹、吳季棠¹、吳岳庭¹、高碩彥¹、蔡政道^{1,2}
中山醫學大學醫學系¹；中山醫學大學附設醫院兒童部²
- 10:17~10:50 討論
- 10:50~11:00 休息

第十六單元：醫學人文與教育

日期：民國109年11月15日(星期日)

時間：11:00~11:40

地點：第三會場

主持人：陳昭惠、朱紹盈

- 11:00~11:07 131. 兒科臨床醫療場域的敘事醫學課程
朱紹盈
花蓮慈濟醫院兒科部教學部
- 11:07~11:14 132. 導入「論壇劇場」於跨領域醫學人文的創新教學*
黃奕傑、郭慈安¹、顏文娟¹、蔡明哲¹、呂克桓、孫海倫
中山醫學大學附設醫院附設兒科部；中山醫學大學醫學院¹
- 11:14~11:21 133. 運用遊戲學習平台及手機應用程式增進醫學教育成效
田智瑋、彭純芝、葉樹人
馬偕兒童醫院
- 11:21~11:28 134. 兒童罕見疾病全人醫療教學對PGY醫師學員之影響探討
楊峻育¹、江珈瑋²、王俐婷³、葉玟伶⁴、葉怡嘉⁵、陳淑儀⁶、陳淑芬⁷、
張雅琪⁸、錢新南¹、遲景上¹
童綜合醫院兒童醫學部¹、癌症中心²、護理部³、營養部⁴、復健部⁵、神經科⁶、
呼吸治療科⁷、社工部⁸
- 11:28~11:40 討論

一般演講：口頭報告

1 The Oligomeric State of YqiC is Critical for Colonization and Invasion of Salmonella Typhimurium in Human Intestinal Epithelial Cells

YqiC蛋白寡聚體態對鼠傷寒沙門氏菌定植和入侵人類腸道上皮細胞有決定性影響

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Background: Gene yqiC of Salmonella Typhimurium is required for colonization/invasion and innate immunity in human cells. Several conserved Arg and Leu residues in the C-terminal half of YqiC are important for coiled-coil trimer formation. However, whether oligomerization of its encoding protein YqiC related to bacterial colonization/ invasion and which YqiC oligomers affect trimer formation are unknown.

Methods: For crosslinking study, we used BS3 as the crosslinker on SDS-PAGE to see trimer formation of the mutant YqiCs. SEC-MALS was for evaluating trimer forms of the mutant YqiCs. For bacterial phenotyping of YqiC oligomerization mutants, we purified three point mutations of YqiC and complemented two double mutation YqiC (R50L/L60E, L60E/L70E) and one triple mutation YqiC (R50L/L60E/L70E) into the yqiC-deleted S. Typhimurium (Δ yqiC). In colonization/invasion assays, 4-5d Caco-2 cells were infected with S. Typhimurium wild-type SL1344, Δ yqiC, pACYC184 yqiC-complemented strain, Δ yqiC R50L/L60E, Δ yqiC L60E/L70E, Δ yqiC R50L/L60E/L70E, and pACYC184 vector-complemented strain for 2h. After washed with PBS, the infected cells were incubated in the media without (colonization) or with (invasion) gentamicin for 1h. At 3h, the infected cells were lysed and the lysates were diluted, plated out on LB agar, incubated overnight, and colonies counted for calculating colonization/invasion

rates.

Results: In crosslinking study, R50L/L60E weakly diminished the trimer formation while L60E/L70R and R50L/L60E/L70R strongly interfered with the trimer formation of YqiC. SEC-MALS results confirmed wild-type YqiC is mainly in a trimer form with a M.W. ~39 kDa and YqiC with mutations at L60E/L70R is predominantly in the monomer form with the M.W. ~14 kDa. In the colonization and invasion assay, the colonization and invasion rates of Δ yqiC, Δ yqiC R50L/L60E, Δ yqiC L60E/L70E, Δ yqiC R50L/L60E/L70E were all significantly attenuated compared with SL1344 (all $p < 0.05$).

Conclusions: The oligomeric state of YqiC at the location of key residues 50-70 in the C-terminal region is critical for YqiC trimer formation and its bacterial phenotype of colonization and invasion of S. Typhimurium, which might contribute for developing novel antibiotics.

2 Increased Risk of Systemic Lupus Erythematosus in Patients with Helicobacter Pylori Infection

幽門桿菌感染者發生系統性紅斑狼瘡的風險增加

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Background: Helicobacter pylori (HP) infection is associated with systemic lupus erythematosus (SLE), but the related results have been controversial. Therefore, this study investigated the association between HP infection and SLE by using a nationwide longitudinal population-based cohort study.

Methods: We identified 41,651 patients with HP infection and 83,302 matched controls between 2000 and 2013 from the Longitudinal Health Insurance Database of the NHIRD. Age, sex, comorbidities, and medical visits were matched at a 1:2 ratio by using propensity score analysis. The adjusted hazard ratio (aHR) of SLE was calculated by multiple Cox regression. Furthermore, sensitivity and stratified analyses were performed.

Results: The SLE incidence rate was 1.17 (95% confidence interval [CI]: 0.89–1.54) per 100,000 person months in the HP cohort, and the hazard ratio was 1.63 (95% CI: 1.12–2.37) in comparison with the propensity score-matched control cohort. After multivariate adjustment, patients with HP infection had a significantly high overall aHR (1.58; 95% CI: 1.08–2.30) of SLE. Stratified analysis revealed that

the aHR of 8.23 (95% CI: 1.77–38.32) in patients <30 years old, and the p for interaction between age and HP infection was 0.039. For age–sex subgroup analysis, the highest aHR of 12.74 (95% CI: 1.55–104.59) in young (aged <30 years) female patients with HP infection.

Conclusions: The 13-year population-based cohort proved a high SLE risk in patients having HP infection, particularly among female patients aged <30 years. Clinicians should provide appropriate monitoring of SLE in patients with HP infection. Future research may elucidate the possible mechanisms for these associations.

3 Effect of Early Eradication Treatment on Risk of Systemic Lupus Erythematosus in Patients with Helicobacter Pylori Infection

早期根除療法對幽門桿菌感染患者系統性紅斑狼瘡風險的影響

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Background: To explore whether early eradication treatment would influence the risk of systemic lupus erythematosus (SLE) in patients with Helicobacter pylori (HP) infection.

Methods: 41,653 patients with HP infection in Taiwan from 2000 through 2013 were identified from the Longitudinal Health Insurance Database of the NHIRD. The patient population was divided into early (within 3 months) and late (after 3 months) eradication cohorts; age, gender, comorbidities, and medical visits were matched at a 1:1 ratio. Multiple Cox regression was used to estimate the SLE adjusted hazard ratio (aHR). Furthermore, sensitivity and stratified analyses were performed to determine the time-dependent association between HP eradication and SLE risk.

Results: The SLE incidence rate was 1.28 (95% confidence interval [CI]: 0.84–1.97) per 100,000 person months in the early eradication cohort, and the crude relative risk was 0.75 (95% CI: 0.43–1.31) compared with the late eradication cohort. After multivariate adjustment, the overall SLE risk was non-significantly lower in the early eradication cohort than in the late eradication cohort (aHR: 0.74, 95% CI: 0.42–1.29). Stratified analysis revealed that early eradication could significantly reduce SLE risk during the 3-year follow-up period (aHR: 0.16, 95% CI: 0.05–0.53, p for interaction: 0.0013). Compared with eradication within 3 months of diagnosis, eradication within 3–36 months and >36 months corresponded with SLE aHRs of 4.78 (95% CI: 1.19–19.20) and 7.66 (95% CI: 2.17–27.05), respectively, when follow-up period was less than 3 years.

Conclusions: Early HP eradication could significantly reduce SLE risk, especially in the first 3-year follow-up. We recommend administering HP eradication early and appropriately monitor patients with HP infection for SLE during the follow-up.

4 Viral Shedding in Gastroenteritis in Children Caused by Variants and Novel Recombinant Norovirus Infections

新興、變異型諾羅病毒株造成的兒童腸胃炎之病毒排出研究

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Background: Human norovirus (NoV) is the leading cause of acute gastroenteritis and the rapid transmission of NoV renders infection control problematic. Our study aimed to investigate viral shedding in gastroenteritis in children caused by variants of emerging norovirus strains infections.

Methods: We used RdRp sequencing to measure NoV genome copies in stool to understand the relationship between the clinical manifestations and viral shedding in hospitalized patients. The near full-length NoV genome sequence was amplified via RT-PCR and NoV recombination was analyzed using the RAT analysis tool.

Results: From January 2015 to March 2018, 77 fecal specimens were collected from hospitalized pediatric patients with confirmed NoV gastroenteritis. The NoV genotypes were GII.4 (n=22), non GII.4 (n=14), GII.4 Sydney (n=21), and GII.P16-GII.2 (n=20). Viral load increased from days 2 to 9 from the illness onset, resulting in an irregular plateau without peaks. After day 9, the viral load declined gradually and most viral shedding in feces ceased by day 15. The average viral load was highest in GII.4 Sydney followed by GII.P16-GII.2 infections and lowest in non-GII.4 infections. GII.4 unclassified infections showed the longest viral shedding time, followed by GII.4 Sydney infections, GII.P16-GII.2 recombinant infection resulted in the shortest duration. NoVs evolved to form a group of GII.P16-GII.2 variants during the 2017–2018 period.

Conclusions: The viral load and shedding period and was different in variants of NoV infections in children. High mutation rate of emerging and re-emerging variants was observed which enhanced epidemic risk rendering continuous surveillance.

5 Influence of Constipation on Asthma: A Nationwide Population-Based Cohort Study in Taiwan

便秘對於氣喘的影響：臺灣的全國性世代追蹤研究

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Background: Asthma is the chronic respiratory disease both affects in childhood and adulthood worldwide. Growing evidences disclose gut dysbiosis contributes to asthma via the gut-lung axis. Constipation can result in alteration of the gut microflora. The clinical impact of constipation on asthma has not been researched. Therefore, we aim to assess the risk of asthma in constipated patients by the population-based cohort study.

Methods: We collected 82421 patients with constipation and 82421 patients without constipation between 1999 and 2013 from the LHID, which is a subset of Taiwanese NHIRD. Propensity score analysis was performed to match age, gender, comorbidities, and medications at a ratio of 1:1. Multiple Cox regression analysis was utilized to estimate the adjusted hazard ratio of asthma. Moreover, sensitivity tests and a stratified analysis were conducted.

Results: The incidence of asthma was 10.8 per 1,000 person-years in the constipation group, which was higher than the rate of 5.6 per 1,000 person-years observed in the non-constipation group. After adjustment for age, gender, comorbidities, and medications, patients with constipation had a 1.91-fold greater risk of asthma compared to those without constipation (adjusted hazard ratio [aHR]: 1.91 (95% C.I. 1.98-2.24). In subgroup analyses, patients aged 20-39 years had a 2.04-fold highest risk of asthma in the constipation cohort (aHR:2.04, 95% CI, 1.84-2.26). In addition, the severity of constipation is associated with an increased risk of asthma in the analysis from usage of laxatives; the aHR was 1.76 (1.69-1.85), 2.15 (2.03-2.27), and 2.29 (2.10-2.49) for < 3 times, 3-12 times, and ≥12 times of laxatives within one year, respectively. (p<0.001) Moreover, patients with constipation had a higher likelihood of asthma, regardless of gender, and with or without comorbidities, as well as the usage of corticosteroids, and antihistamines.

Conclusions: Constipation is associated with a significantly increased risk of asthma. Furthermore, the severity of constipation is also associated with asthma. Clinicians should be aware of the possibility of asthma in people with constipation.

6 Exogenous Therapeutics of MicroRNA-29a Attenuates Development of Hepatic Fibrosis in Cholestatic Animal Model through Regulation of Phosphoinositide 3-kinase p85 Alpha

微糖體核酸29a的外源性療法通過調節磷酸肌醇3激酶 p85 α 減輕膽汁淤積動物模型中肝纖維化的發展

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Background: Recent studies have found that microRNA-29a (miR-29a) levels are significantly lower in 20 fibrotic livers as shown with human liver cirrhosis. Such downregulation influences the activation 21 of hepatic stellate cells (HSC). Phosphoinositide 3-kinase p85 alpha (PI3KP85 α) is implicated in the 22 regulation of proteostasis mitochondrial integrity and unfolded protein response (UPR) and 23 apoptosis in hepatocytes.

Methods: This study aimed to investigate the potential therapeutic role of miR-29a 24 in a murine bile duct ligation (BDL) -cholestatic injury and liver fibrosis model. Mice were assigned 25 to 4 groups: sham, BDL, BDL+scramble miRs, and BDL+miR-29a-mimic. Liver fibrosis and 26 inflammation were assessed by histological staining and mRNA/protein expression of 27 representative markers.

Results: Exogenous therapeutics of miR-29a in BDL-stressed mice significantly 28 attenuated GOT/GPT and liver fibrosis, and caused a significant downregulation in markers related 29 to inflammation (IL-1 β), fibrogenesis (TGF- β 1, α -SMA and COL1 α 1), autophagy (p62 and LC3B II), 30 mitochondrial unfolded protein response (UPRmt; C/EBP homologous protein (CHOP), heat shock 31 protein 60 (HSP60) and Lon protease-1 (LONP1, a mitochondrial protease)), and PI3KP85 α within 32 the liver tissue. An in vitro luciferase reporter assay further confirmed that miR-29a mimic directly 33 targets mRNA 3'UTR of PI3KP85 α to suppress its expression in HepG2 cell line.

Conclusions: Our data provide 34 new insights that therapeutic miR-29a improves cholestasis-induced hepatic inflammation and 35 fibrosis and proteostasis via blocking PI3KP85 α , highlighting the potential of miR-29a targeted 36 therapy for liver injury.

7 Using Whole Exome Sequencing in the Diagnosis of Rare Genetic Liver Diseases – Advantages and Challenges

使用全外顯子定序診斷罕見肝臟疾病之經驗

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Background: Genetic liver diseases often presented as common symptoms such as jaundice, hepatosplenomegaly and failure to thrive, and are difficult to diagnose by phenotype. Whole exon sequencing (WES) has provided a new platform in the diagnosis of genetic diseases, especially in difficult cases without typical presentation. This study aimed to clarify the yield of WES in the diagnosis of rare genetic liver diseases.

Methods: During the period from May 2018 to Oct 2019, 13 patients suspected with abnormal liver function suspected to have genetic cause of liver disease but not typical for specific single gene disorder were examined by whole exome sequencing. Clinical presentation, molecular diagnosis, and implication for clinical management of these patients were summarized in this presentation.

Results: The clinical manifestation of liver disease in our cohort including jaundice (6/13), liver cirrhosis (6/13), chronic elevated liver function test (5/13), extra-liver manifestations (8/13) and fulminant hepatitis (1/13). Seven patients (53.8%) achieved genetic diagnosis using WES. The final diagnosis including Sensenbrenner syndrome, citrullinemia, Zellweger syndrome, trichohepatoenteric syndrome, renal-hepatic-pancreatic dysplasia 1, immunodeficiency 47 and transaldolase deficiency. Reviewing the clinical manifestations of patients with genetic diagnosis, only the patient with Zellweger syndrome had clinical and biochemical features sufficient for differential diagnosis.

Conclusions: WES is a powerful tool in the diagnosis of rare genetic liver diseases, especially in the patients with multiple anomalies or without typical manifestations of known liver diseases.

8 Butyrate Reprogramming of Maternal High-fat Diet-Induced Fetus Liver Stress

丁酸重編程產婦高脂飲食誘導的胎兒肝損傷

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Background: The maternal high-fat diet can impact offspring rat liver and development of NAFLD. Our aim is to study the effect of butyrate on fetus liver injury caused by maternal high-fat diet.

Methods: After confirmation of pregnancy on the 14th day after mating, pregnant females Sprague-Dawley rats are randomly divided for the maternal high-fat diet (MH) group exposure paradigm or normal control diet (NC) until delivery. The other maternal high-fat diet rats were fed with sodium butyrate as MHS group. The fetus was sacrificed at gestation 21 days.

Results: Shortened ileum villi in MH group in both pregnant mother and fetus were recovered in MHS group. Maternal liver histology of lipid accumulation with steatosis in MH group was recovered in MHS group. Fetal liver histology of increased IL6 in MH group was decreased in MHS group. The Western blot of caspase 3 (apoptosis), TNF-alpha (inflammation) in fetus liver was decreased in MHS group compared to MH group ($P < 0.05$). Phosphor-AKT (survival), GPX1 (antioxidative stress) was higher in MHS group than MH group ($P < 0.05$).

Conclusions: Oxidative stress with inflammation plays a vital role in the fetus liver after maternal high fat diet, and prenatal butyrate may reprogram this.

9 Metformin Reprogramming of Maternal High-fat Diet-Induced Maternal Dysbiosis-driven Fetus Liver Outcomes

二甲雙胍重編程母體高脂飲食引起的母體菌叢不良驅動的胎兒肝變異

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Background: The deleterious effects of high-fat diet can impact fetal rat liver and this can cause later development of NAFLD. Our aim is to study the fetus liver caused- by maternal high-fat diet-induced maternal dysbiosis and the effect of metformin in this model.

Methods: After confirmation of pregnancy on the 14th day after mating, pregnant females Sprague-Dawley rats are randomly divided for the prenatal high-fat diet exposure paradigm (HFD) or left undisturbed (NC) until delivery. The other HFD was fed with metformin (HMf). The fetus was sacrificed at gestation 21 days.

Results: The Western blot of caspase3 (apoptosis),

TNF-alpha (inflammation) in male fetus liver was significantly decreased ($P < 0.05$) in HMf compared to HFD. Phosphor-AKT (survival), GPX1 (antioxidative stress) was significantly higher ($P < 0.05$) in HMf than HFD group. The relative microbiota abundance was different among the 3 groups. Maternal stool in HFD during pregnancy was demonstrated to increase Verrucomicrobiales in Order (related to fatty liver), and this is decreased after metformin given.

Conclusions: Oxidative stress, inflammation and the regulation of maternal gut microbiota plays a vital role in the fetus liver and may possible programming adult liver steatosis, and prenatal metformin may reprogram this.

10 Clinical Predictors of Acute Appendicitis in Children Mimicking Infectious Enterocolitis: A Case-Control Study

兒童急性闌尾炎臨床表徵相似於感染性腸炎的預測因子探討：病例對照研究

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Background: Acute appendicitis is one of the most common abdominal emergencies in pediatrics. Early diagnosis is vital for the clinical outcomes. However, it may present with diarrhea initially that mimics enterocolitis, causing the delay of prompt surgery. Therefore, it is challenging to differentiate acute appendicitis and infectious enterocolitis in time. The purpose of this study is to investigate the clinical predictors that help to distinguish acute appendicitis from infectious enterocolitis.

Methods: A retrospective case-control study was conducted in a medical center in Taiwan from 2015 to 2020. We reviewed medical records of children who were admitted due to abdominal pain with diarrhea. Subjects were divided into two group according to final diagnosis: acute appendicitis (group 1) and infectious enterocolitis (group 0). Multiple logistic regression analysis was used to identify the independent predictors of acute appendicitis. The area under the receiver operating characteristic curve was used to quantify the overall discriminative power of the significant predictors.

Results: A total of 32 patients diagnosed with appendicitis (group 1) and 82 patients diagnosed with enterocolitis (group 0) were enrolled. Five independent predictors of acute appendicitis, were vomiting (odds ratio[OR], 6.69; 95% confidence interval [CI], 1.37–32.72; $p = 0.019$), right lower quadrant (RLQ) pain (OR, 9.06; 95% [CI], 2.06–39.80; $p = 0.004$), stool occult blood (OB) (OR, 0.05; 95% [CI], 0.00–0.73; $p = 0.028$), white blood cell (WBC) count (OR, 1.2; 95% [CI], 1.07–1.34; $p = 0.002$), and C-reactive protein (CRP) level (OR, 1.19; 95% [CI], 1.19–1.30; $p < 0.001$). The combined model of these five predictors (AUC = 0.93) for prediction of appendicitis was more significant than pediatric appendicitis score (PAS) model (AUC = 0.80); $p = 0.0023$.

Conclusions: A vomiting, RLQ pain, negative of stool OB, higher CRP level and higher WBC level are significant predictors for acute appendicitis. This five-combined model has better diagnostic performances than PAS does. Our study would be helpful for assessing cases with abdominal pain with diarrhea, in order to distinguish appendicitis from infectious enterocolitis more accurately in children.

11 Pediatric Adenovirus Infection Related Intussusception - Clinical Characteristics and Recurrence

兒童腸套疊合併腺病毒感染的臨床表徵與腸套疊的復發率探究

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Background: Non-enteric adenovirus was observed to be associated with pediatric intussusceptions. This study aimed to identify the clinical significance of adenovirus infection in pediatric patients with intussusception.

Methods: In a 5-year period (2015–2020), medical records of pediatric patients diagnosed with intussusceptions associated with adenovirus infection in a single tertiary center were retrospectively reviewed. Adenovirus antigen test or viral culture of throat swab or rectal swab/feces were used to detect adenovirus infection in those intussusception patients with evidence of fever or upper respiratory tract symptoms. Clinical characteristics evaluated included gender, age, onset and duration of fever, sonographic features of intussusception and enlarged mesenteric lymph nodes, therapeutic efficacy, rate of surgical intervention, and recurrence rate of intussusception. Clinical outcome was measured by the therapeutic efficacy of pneumatic reduction and recurrence rate of intussusception.

Results: A total of 16 patients were included in this study. The mean age of the patients was 2.2 years. Fourteen patients were ileocolic intussusception. 62.5% of the patients had recurrence and 56.3% had enlarged mesenteric lymph nodes. Only half of the patients had fever at diagnosis. Intermittent abdominal pain or irritable crying (75%) was the major clinical presentation, 43.8% had vomiting and 37.5% had upper respiratory tract symptoms. Pneumatic reduction were performed in 15 patients with successful rate of 95.7% (22/23). One patient required surgical intervention, the operative findings revealed ileo-ileo-colic intussusception without pathological lead point. Onset age of intussusception was positively correlated with intussusception recurrence, a higher rate of recurrence was observed in those aged > 2 years ($p = 0.042$). Otherwise, enlargement of mesenteric lymph nodes showed positive correlation with intussusception recurrence of ($p = 0.024$).

Conclusions: This study indicates that pneumatic reduction is very effective to treat pediatric adenovirus infection related intussusception, we observe that non-enteric adenovirus infection is a risk factor for the recurrence of intussusception.

12 Determination the Secretor Status on Human Milk Oligosaccharides Profile by Using Hemagglutination Inhibition Method of Saliva in Healthy Northern Taiwanese

利用口水血球凝集抑制試驗來分析北部健康台灣人的分泌型狀態

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Background: Breast milk contains abundant and different profile of human milk oligosaccharides (HMOs), which is determined by Lewis blood type and secretor (Se gene) status in different population. All data suggest that infants of secretor mothers have a better health outcome than those there of non-secretors. Currently the secretor status of Taiwanese is still unclear. The aim of this study is to determine the secretor status on human oligosaccharide profile through saliva blood group determination among northern Taiwanese population

Methods: From July to December 2019, 65 healthy individuals with known blood type from different sites of Taipei city were enrolled and 5 to 10ml of saliva samples were collected in test tube. The samples were heated in 100 ° Celsius water bath for 10 minutes and centrifuge with 3000 revolutions per minute for 10 minutes. The supernatants were analyzed by using hemagglutination inhibition method to determine the saliva blood group within 24 hours.

Results: Among 65 healthy Taiwanese with different blood groups, age 20 to 65 years old. 14 (21%) were male and 51 (79%) were female. The proportion of blood groups A, B, O and AB were 26%, 38%, 31% and 4%, respectively. All 65 (100%) of the saliva samples tested were compatible to known individual's blood group, the result showed that all of Northern Taiwanese population were secretors in this study.

Conclusions: All of the healthy Taiwanese of Northern Taiwan in our study were secretor. Further genetic studies were needed to confirm secretor status in this population.

13 Correlation of Serum Trace Element (Iron, Zinc, Copper) Levels with Picky Eating Behavior, Nutritional Status, Development, and Physical Activity in Young Children (4-7 Years)

兒童 (4~7歲) 血中微量元素濃度與偏挑食、營養狀態與體智能的相關性研究

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Background: This study aims to assess the prevalence of micronutrient deficiency and its association with nutritional status, picky eating behavior, and physical activity in young children

Methods: A cross-sectional descriptive study with structured questionnaires to assess picky eating behavior, development, and physical activity, and blood examinations of serum trace element (iron, zinc, copper) were conducted in children aged 4-7 years. The correlations among nutritional status, picky eating behavior, development, and physical activity and serum levels of trace elements were compared statistically.

Results: The mean age, height, weight, and BMI were 5.21 ± 0.87 years, 107.83 ± 7.59 cm, and 18.18 ± 3.90 kg, and 15.47 ± 2.12, respectively. Fifty-six (29.4%) were underweight and 30 (15.8%) were overweight. The mean levels of iron, zinc, and copper were 83.41 ± 32.46, 74.57 ± 10.97, and 115.28 ± 23.52 ug/dl, respectively. Results revealed deficiencies of iron (< 50 ug/dl) in 31 cases (16.3%), zinc (< 70 ug/dl) in 71 cases (37.4%), and copper (< 90 ug/dl) in 20 cases (10.5%). Sixty-eight (45.7%) experienced at least one deficiency, and 24 (12.6%) experienced multiple deficiencies. A total of 126 children (66.3%) were found to have picky-eating behavior. Picky eaters had higher prevalence of single or multiple deficiencies than the non-picky eaters (single: 45.2% v.s. 21.8%; multiple deficiencies: 15.9% v.s. 6.3%). Compared to non-picky eaters, picky eaters had significantly lower zinc levels [73.22 ± 10.53 v.s. 77.23 ± 10.79 (ug/dl), p < 0.001]. Those children with better state of development, and physical activities had higher serum levels of iron, zinc and copper levels. Serum zinc levels were significantly higher in those children with better state of development status and physical activities (p = 0.002, and < 0.001, respectively).

Conclusions: The prevalence of trace element deficiency is high among Taiwanese children aged 4-7 years particularly in picky eaters. Zinc deficiency is common and serum zinc level show significantly positive correlation with development status and physically activity levels.

14 Predictors for Incidence and Remission of Nonalcoholic Fatty Liver Disease in Obese Children and Adolescents

肥胖兒童和青少年非酒精性脂肪肝疾病發病和緩解的預測因子

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Background: The status of non-alcoholic fatty liver disease (NAFLD) can wax and wane over time in children. However, the factors affecting its incidence and remission remain elusive. We aimed to investigate NAFLD incidence, remission and predicting factors in obese children.

Methods: Obese children aged 9-10 and 12-13 years were recruited from schools and followed up for 2 years. Liver ultrasonography was performed at baseline and Year 1. Alanine aminotransferase (ALT) concentrations were measured at baseline, Year 1 and Year 2. Elevated ALT was defined as above 26 U/L for boys and 22 U/L for girls. The genes responsible for NAFLD susceptibility, including PNPLA3, GCKR, TM6SF2 and MBOAT7, were genotyped. We analyzed the effects of these risk factors on the incidence and remission of NAFLD and elevated ALT.

Results: At baseline, 86 of 440 (19.5%) subjects had ultrasonography-diagnosed NAFLD. At Year 1, of 264 subjects without NAFLD at baseline, 20 (7.6%) developed NAFLD. The baseline BMI z-score and increment in BMI z-score independently predicted incident NAFLD. Of the 68 subjects with NAFLD at baseline, 36 (52.9%) had NAFLD remission. Decrement in BMI z-score independently predicted NAFLD remission. The four studied NAFLD susceptible genes were not significantly associated either the incidence or remission of NAFLD. In addition, changes in BMI z-score predicted the incidence and remission of elevated ALT from Year 1 to Year 2.

Conclusions: Obese children with increasing BMI are more likely to develop NAFLD and those with decreasing BMI are more likely to have NAFLD remission.

15 The Prevalence of Obesity in Adolescents in Southern Taiwan

南臺灣青少年之肥胖盛行率調查

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Background: Obesity is a global public health disease and leads to comorbidities, such as insulin resistance, dyslipidemia, nonalcoholic fatty liver disease, hypertension, and cardiovascular diseases. The prevalence of adolescent obesity has increased worldwide in the past two decades. Previous studies have reported that most obese adolescents

remain obese in their adulthood. Therefore, monitoring the prevalence of obesity is important for public health programs focusing on reducing or preventing obesity. This study aimed to investigate the prevalence of obesity in adolescents in southern Taiwan.

Methods: This study analyzed the disconnected data, including the age, gender, body weight and height, from junior and senior high schools by random sampling in Tainan City in 2020. Obesity was defined according to the table of childhood and adolescent body mass index published in 2013 by Health Promotion Administration, Ministry of Health and Welfare, Taiwan. The categorical data were analyzed using the chi-square test by SPSS version 26. P values of < 0.05 were considered as statistically significant.

Results: A total of 6075 adolescents (2971 boys and 3104 girls) aged 12 to 18 years were enrolled from three junior high schools and two senior high schools in Tainan City. The overall prevalence of obesity was 17.5% among enrolled adolescents. The boys had significantly higher prevalence of obesity than girls (21.4% vs 13.7%, $p < 0.001$). The significant gender difference in the prevalence of obesity occurred in both junior and senior high schools. The prevalence of obesity in adolescents of senior high school did not higher than those of junior high school (16.7% vs 18.1%, $p = 0.18$).

Conclusions: The overall prevalence of obesity was 17.5% among adolescents in Tainan City in 2020. Moreover, the prevalence of obesity was significantly higher among boys than girls in both junior and senior high schools.

16 Incidence and Trends in Antibiotic Susceptibility of Urinary Tract Infections Caused by Escherichia Coli in a Taiwanese Child Cohort from 2004 to 2018

大腸桿菌所致泌尿道感染的抗生素感受性發生率及趨勢，2004-2018台灣兒童的世代研究

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Background: Escherichia coli (E. coli) -caused urinary tract infections (UTIs) occur commonly in communities worldwide, but data evaluating the incidence of E. coli-caused UTIs in a pediatric cohort are scarce. It is unclear how the incidence of E. coli-caused UTIs and antibiotic susceptibilities changed in pediatric population over time.

Methods: A cross-sectional study was conducted using a large electronic database of medical records combining hospital admission and microbiological data between 2004 and 2018. The multicenter study used data from the Chang Gung Memorial Hospitals in Taiwan for children under 18 years of age with E. coli-caused UTIs.

Results: E. coli-caused UTIs occurred in 10756 unique individuals among 41,8799 hospitalized children, with 92.58% being community associated. The overall IRR for community acquired E. coli-caused UTIs was 1.01 (95% confidence interval [CI] 0.99-1.02). The trend in 3GCs resistance increased (IRR 1.18, 95% CI 1.13-1.24) in community acquired E. coli-caused UTIs. Complex chronic disease (adjusted odds ratio [aOR], 2.04; 95% CI, 1.47-2.83) and antibiotics therapy less than 3 months prior (aOR, 1.49; 95% CI, 1.15-1.94) were associated with increased risk of 3GCs-resistant E. coli-caused UTIs. Mortality was 0.36%, and length of stay was higher in the 3GCs-resistant group than susceptible group (8.09 ± 4.59 days vs 6.78 ± 3.53 days, P < .0001).

Conclusions: The study results suggested little or no change in the trend of community acquired E. coli-caused UTIs in Taiwanese youths over the 15-year study period. Nevertheless, the increase in 3GCs-resistant E. coli-caused UTIs was substantial. Interventions for children with complex chronic comorbidities and prior antibiotic treatment could be effective in reducing the incidence of 3GCs-resistant E. coli-caused UTIs in this region and more generally.

17 Diagnosis and Therapeutic Surveillance of Pediatric Lupus Nephritis Using Innovative Integrated IR-based and Computer Aided Health Care Technology: Wax-Physioption-Kinetics-based FTIR Imaging on Biopsied Kidneys and ATR-FTIR Kinetic Change in Blood

利用紅外顯微光譜和光譜診斷技術擷取腎臟組織影像及偵測血液變化並以電腦自動分析成為診斷兒童紅斑性狼瘡腎炎和追蹤治療效果的創新健康照護方法

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Background: SLE is a complex autoimmune disease characterised by the production of autoantibodies and deposition of Ag-Ab complexes in multiple organs. Lupus nephritis (LN) is one of the most severe manifestations in SLE patients. Numerous studies have shown that renal survivals are much poorer in childhood-onset LN than adult-onset LN. In our previous experiment, with WPK-FTIR imaging on biopsied kidneys, higher population of aberrant glycan structure of glycoprotein induced by acute immune reaction was observed in childhood-onset LN, showing a more amount of n-octacosane residue (AC28) on inflammatory glomeruli than n-docosane residue (AC22). Taken it further, in the present study, we analysed spectroscopic profiling of serum from the paediatric LN patients using ATR-FTIR with the aim of develop sensitive and innovative diagnostics of real-time monitoring of disease status and progression, and therapeutic responses.

Methods: A series of serum were collected from LN

patients in outpatient clinics inpatient care at CGMH. Serum was centrifuged at 2500 rpm for 10 minutes and then stored at -80 °C. After thawing at room temperature, serum was kept in ice-water bath at ~3 °C and ready for ATR-FTIR measurements. Subsequently, the IR data analysis was conducted by home-designs software, 'iPathologist'.

Results: Hydrophobic index (HPI), the peak height ratio of the absorption band of vas (CH2) at 2929 cm⁻¹ to vas (CH3) at 2960 cm⁻¹, and the ratio of δ (CH2) at 1457 cm⁻¹ to δ (CH3) at 1400 cm⁻¹ were markedly elevated in dried serum of paediatric LN patients compared with the healthy volunteers. The δ (CH3) band is known attributed mainly from serum albumin, which implies its important role in the pathogenesis of renal inflammation. Furthermore, the HPI value was higher (> 1) in the beginning of immunosuppressive treatment for paediatric LN, whereas this value was gradually reduced while the remission of LN was achieved.

Conclusions: The spectral marker package including kidney AC28/AC22 ratio, serum HPI index and δ (CH2) / δ (CH3) ratio is of great potential to become an emerging automated diagnostic platform of autoimmune GN such as LN in clinical settings.

18 Pathogenesis of Renal Tubular Dysgenesis Caused by Large Deletion of AGT

血管收縮素原基因突變導致腎小管發育不全之致病機轉研究

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Background: Autosomal recessive renal tubular dysgenesis (ARRTD) caused by inactivation mutations in AGT is an extraordinarily rare but highly fatal disorder with poor prognosis, and incomplete knowledge about pathogenesis.

Methods: Six Taiwanese with ARRTD caused by large deletion of AGT were diagnosed by molecular analysis. In vitro functional studies were conducted.

Results: All patients carried the same homozygous E3_E4 del:2870bp deletion+9bp insertion in AGT. The expressions of wild-type AGT and this truncated AGT protein was in a dose-dependent manner with a relatively low expression of truncated AGT, but the truncated AGT protein was more

stable at the longer CHX treatment time. This mutation results in skipping of exons encoding the serpin domain of AGT important for renin interaction and the generation of truncated protein. In silico modeling revealed a diminished interaction between mutant AGT and renin, and proximity ligation assay demonstrated a significant decrease in the amount of this truncated protein indicative of diminishment of Renin-AGT interaction.

Conclusions: This AGT mutation leads to the diminished interaction with renin and decreased Ang I and II generation.

19 Roxadustat Attenuates Hyperoxia-induced Lung Injury by Upregulating Vascular Endothelial Growth Factor in Newborn Mice

Roxadustat藉由提升血管內皮生長因子以降低高氧下新生小鼠肺臟傷害

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Background: Premature infants who require oxygen (O₂) therapy for respiratory distress syndrome often develop bronchopulmonary dysplasia (BPD), a chronic lung disease characterized by interrupted alveologenesis. Disrupted angiogenesis inhibits alveologenesis, but the mechanisms of disrupted angiogenesis in the developing lungs are poorly understood. Hypoxia-inducible factors (HIFs) are transcription factors that activate multiple oxygen-sensitive genes, including those encoding for vascular endothelial growth factor (VEGF), but angiogenesis in O₂-induced lung injury modulated by HIFs is incompletely understood. Herein, we explored the effects of roxadustat, a HIF stabilizer that had been proven to promote angiogenesis, in regulating pulmonary angiogenesis upon hyperoxia exposure.

Methods: C57BL/6 mice pups were reared in room air or 85% O₂ from postnatal days 1 to 7 and received PBS, 5mg/kg or 10 mg/kg roxadustat intraperitoneal injection Q.O.D respectively. The daily body weight and survival rate were recorded. The lungs were excised for histology and angiogenic factors expression analyses on postnatal day 7.

Results: Exposure to neonatal hyperoxia was observed to reduce body weight and survival rate and von Willebrand factor (vWF) and HIF-1 α and phosphor mammalian target of rapamycin (mTOR) and VEGF and endothelial nitric oxide synthase (eNOs) expression respectively, and increase mean linear intercept (MLI) values. Roxadustat administration reversed the hyperoxia-induced vWF and HIF-1 α and phosphor mTOR and VEGF and eNOs reduction, and reduced MLI.

Conclusions: Hyperoxia suppressed pulmonary vascular development and proangiogenic factors in newborn mice. Roxadustat promoted pulmonary angiogenesis upon hyperoxia exposure by stabilizing HIF-1 α and upregulating

proangiogenic factors expressions, indicating potential clinical and therapeutic applications.

20 Predicting Hyperoxia-Induced Lung Injury Based on Associated Intestinal and Lung Dysbiosis in Neonatal Mice

基於關聯的腸道和肺臟菌叢失衡預測新生仔鼠高氧誘導的肺損傷

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Background: Preclinical studies have demonstrated that hyperoxia disrupts the intestinal barrier, impairs intestinal function, and injures lung in newborn animals. The effects of neonatal hyperoxia on intestinal and lung microbiota and the role of the intestinal microbiota in the pathogenesis of hyperoxia-induced lung injury have not been investigated.

Methods: We evaluated the effect of neonatal hyperoxia on intestine and lung microbiota alterations in neonatal C57BL/6N mice reared in either room air (RA) or hyperoxia (85% O₂) from postnatal days 1 to 7. On postnatal day 7, lung and intestinal microbiota were sampled from the left lung and lower gastrointestinal tract for 16S ribosomal RNA gene sequencing. Right lung and terminal ileum were harvested for Western blot and histology analysis.

Results: Neonatal hyperoxia exposure during the first week of life induced intestinal and lung dysbiosis and promoted bacterial translocation from the intestine to the lung. These findings suggest that changes in the intestinal microbiota composition contribute to hyperoxia-induced lung injury and demonstrates that the combination of intestinal and lung microbiota may identify hyperoxia-induced lung injury in neonatal mice.

Conclusions: Neonatal hyperoxia exposure during the first week of life induced intestinal and lung dysbiosis and promoted bacterial translocation from the intestine to the lung. These findings suggest that changes in the intestinal microbiota composition contribute to hyperoxia-induced lung injury and demonstrates that the combination of intestinal and lung microbiota may identify hyperoxia-induced lung injury in neonatal mice.

21 Short-Term and Long-Term Outcomes of Very Preterm Infants with Prolonged Preterm Premature Rupture of Membranes

非常早產新生兒歷經長時間早產早期破水之短期及長期預後

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Background: Preterm premature rupture of membranes (PPROM) in very preterm period may be associated with high perinatal mortality and morbidity. Prolonging gestation may allow gains in fetal maturity to reduce mortality and morbidities. However, it may also prolong fetal exposure to deleterious inflammation and/or infection. The purpose of this study was to explore the clinical characteristics and outcomes and to assess the effect of prolonged PPRM > 7 days on growth and neurodevelopment in very preterm infants.

Methods: A total of 41 neonates born at gestation age (GA) < 31 weeks with PPRM > 7 days from January 2016 to December 2019 were enrolled as study group. 41 preterm infants born at GA < 31 weeks without PPRM were used as matching controls. Our primary outcome measures were neonatal survival rate and neonatal morbidities. The neurodevelopmental outcomes were assessed using the Bayley Scales of Infant Development, 3rd edition (BSID III) at 2 years of age.

Results: There were no significant differences in GA (26.80 ± 1.80 vs 26.80 ± 1.80 weeks), birth weight (979.00 ± 245.80 vs 928.10 ± 243.80 gm), and gender distribution (male 53.7% vs 39.0%) between PPRM group and controls. Mortality in PPRM group (19.5% vs 4.9%) was significantly higher than that in controlled group. There were no differences between groups for respiratory distress syndrome, necrotizing enterocolitis, early/late -onset sepsis, severe retinopathy of prematurity, severe intraventricular hemorrhage, cystic periventricular leukomalacia and bronchopulmonary dysplasia. 31 infants in PPRM and controlled groups (15 in PPRM group, 16 in controls) received 2-year-old follow up. There were no significant differences in BSID III cognitive scores, language scores and motor scores between these 2 groups. The incidence of cerebral palsy and growth parameters were also similar.

Conclusions: In conclusion, prolonged PPRM in very preterm status was associated with increased risk of neonatal mortality. But it may not increase the risk of morbidities during hospitalization and poor 2-year-old growth and development.

22 The Feasibility and Safety of Weaning Protocol for NCPAP by Cyclic Use of HFNC in Premature Infants- preliminary Report

於早產兒使用高流量氧氣鼻導管來脫離經鼻式連續性正壓呼吸器之適用性及安全性：初步報告

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Background: Nasal continuous positive airway pressure (NCPAP) has been widely use for premature infants with respiratory distress syndrome (RDS). High flow nasal cannula (HFNC) is defined as a flow more than 2L/min in neonates to overcome respiratory distress with less risk of injury to nares and increase of patient comfort; however, the variability in distending pressure is the main concern. Hence, HFNC has been thought to be a weaning device from NCPAP in premature infants. We designed a new protocol for weaning NCPAP by using HFNC in premature infants. The aims of this study is to check the feasibility and safety of this new protocol for weaning NCPAP by cyclic use of HFNC in premature infants.

Methods: Preterm infants (gestational age < 37 weeks) with RDS under NCPAP support, who were ready to wean NCPAP, were enrolled. The weaning protocol was to use NCPAP and HFNC cyclically every 3 hours for 3 days after starting weaning for each patient in neonatal intensive care unit at Kaohsiung Medical University Hospital. Heart rate, respiratory rate, pulse oximetry (SpO₂), transcutaneous carbon dioxide (PtcCO₂) and cerebral tissue oxygen saturation (StO₂, measured by near infrared spectroscopy) were measured and recorded during weaning period.

Results: Between June 2019 to May 2020, 27 preterm infants (18 males, 9 females) suffered from RDS were enrolled. Mean gestational age was 28.4 weeks, and mean birth weight was 1120 gram. Mean post-menstrual age to start weaning NCPAP was 35.6 weeks, and mean body weight was 1977 gram. There were no statistical differences on heart rate, respiratory rate, SpO₂ and StO₂ under wearing NCPAP and under using HFNC. However, mean PtcCO₂ (48.5mmHg) under NCPAP was statistically lower than the period of HFNC (50.0 mmHg), with p value 0.0039. Among these 27 preterm infants, four infants suffered from failure to wean at first when they used HFNC at the first day of weaning protocol.

Conclusions: Our results showed the feasibility and safety of weaning protocol for NCPAP by cyclic use of HFNC in premature infants. However, due to limited patient enrolled now, further evaluation is needed later with larger case numbers.

23 Non-invasive Inhaled Nitric Oxide for the Treatment of Hypoxemia and Pulmonary Hypertension in the Newborn Infants

以非侵襲性方式給予一氧化氮來治療新生兒低氧血症合併肺高壓

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Background: Inhaled nitric oxide (iNO) is effective in conjunction with tracheal intubation (TI) and mechanical ventilation (MV) for treating pulmonary hypertension and hypoxemic respiratory failure in near-term and term newborn infants. Non-invasive respiratory support with nasal continuous positive airway pressure (nCPAP) or nasal intermittent positive pressure ventilation (nIPPV) is increasingly used to avoid morbidity with TI and MV.

Methods: Between January 2017 and March 2019, a total of 32 newborn infants with hypoxemia and pulmonary hypertension were included in this study. Group 1 (n=20) received TI and MV combined with iNO therapy. The mean birth weight (BW) was 2667.2 ± 448.1 grams, the mean gestational age (GA) was 35.25 ± 1.92 weeks (ranged from 31+2 to 40+1 weeks) and the age at initiation of iNO therapy was 1.5 ± 0.7 days in group 1. Group 2 (n=12) received nCPAP or nIPPV combined with iNO therapy. The mean BW was 2920.1 ± 601.8 grams, the mean GA was 37.17 ± 2.66 weeks and the age at initiation of iNO therapy was 1.25 ± 0.62 days.

Results: The average duration of O₂ therapy was 17.55 ± 9.56 days, 10.42 ± 4.22 days ; the average duration of MV was 11.65 ± 6.22 days , 0 ; the average duration of NICU stay was 24.80 ± 9.73 days, 17.08 ± 4.74 days ; total duration of admission was 31.5 ± 10.82 days, 20.67 ± 5.25 days in group 1 and group 2, respectively. There was a significant shorter duration of duration of O₂ therapy (p=0.008), duration of MV (p<0.001), duration of NICU stay (p=0.005), duration of total admission (p<0.001) in nCPAP or nIPPV with iNO group (group 2) than TI and MV with iNO group (group 1). None infant died in this study. Analysis of environmental gases during non-invasive iNO therapy revealed all ambient nitrogen dioxide (NO₂) and nitric oxide (NO) were less than 0.30 p.p.m.

Conclusions: Non-invasive nCPAP or nIPPV iNO therapy is associated with improving oxygenation for newborn infants with hypoxemia and pulmonary hypertension. Non-invasive iNO therapy can reduce the duration of O₂ therapy, duration of MV therapy, duration of NICU stay and duration of total admission than TI and MV with iNO therapy.

24 Patent Ductus Arteriosus (PDA) and Intraventricular Hemorrhage (IVH) in Preterm Twins: Comparisons among Mono-/Di-chorionic and Concordant/Discordant Twins

早產雙胞胎發生開放性動脈導管或腦室內出血併發症的研究

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Background: Genetic pre-disposition and in-utero hypoperfusion share a recent highlight of prenatal etiologic factors of PDA. So far neither observational studies nor animal experiments could conclude if fetal hypoperfusion is a risk of hindering postnatal ductal closure, or conversely, is a protective factor of PDA. Both IVH and PDA are short-term postnatal complications that may have common pathophysiological pathways. Our study aims to describe the incidence of PDA and IVH in monozygotic-monochorionic twins (genetically identical) with and without birth weight discordance (in-utero hypoperfusion), in comparison to dizygotic twins (genetically non-identical) twins, so as to define the impacts of genetic and/or hypoperfusion on the development of PDA and IVH.

Methods: Inborn very preterm (≤ 32 weeks) twins with both twins survived the 1st week of life during Jan 2013–Dec 2018 were enrolled. Twin zygosity and mono-/dichorionicity was confirmed by perinatologists. Exclusion criteria were congenital heart defects and chromosomal anomalies. Demographic data, zygosity, chorionicity, and birth weight discordance was recorded and analyzed using Pearson's chi-square Analysis.

Results: 206 pairs of very preterm twins were born during the study period, including 84 pairs of mono- and 122 pairs of dizygotic twins. 25 pairs were excluded. The mean GA was 29.6 ± 2.2 wks. and mean BW was 1340 ± 398 gms. and no difference between mono and dizygotic twins. SGA was noted in 10.5% and 5.9% of the mono- and dizygotic twins, respectively. Total 42 pairs (23.2%) had BW discordance, including 38.7% of the mono- vs. 15.1% of the dizygotic twins. PDA and IVH incidence was 29.6%, 33.9%, and 27.3%; and 5%, 4.8%, and 5.0% as a whole, in mono- and dizygotic twins, respectively. The association between both PDA and IVH occurrence and BW discordance was significant in monozygotic but not in dizygotic twins.

Conclusions: In the susceptible neonates, PDA, and possibly IVH as well, is associated with in-utero hypoperfusion.

25 Evaluation of Stress-velocity Relationship of Patent Ductus Arteriosus in Extremely Low Birth Weight Infants

極低體重早產兒開放性動脈導管之血液動力學研究

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Background: After birth, the left-to-right shunting patent ductus arteriosus (PDA) may cause an increasing preload of left ventricle (LV). The immature myocardium in extremely low birth weight (ELBW) infants has limited ability to respond to the cardiac loads. It results in some of them may experience hemorrhagic complications such as pulmonary hemorrhage or intraventricular hemorrhage (IVH). Therefore, our study aims to detect the hemodynamic change of cardiac performance and intervene adequately to prevent hemorrhagic complications. We also evaluate the effects of administration of inotropic agents which are considered to improve cardiac contractility and reduce LV afterload.

Methods: We enrolled ELBW infants who didn't have complex congenital heart disease nor chromosomal abnormalities. The tailor-made circulatory management strategy was introduced by echocardiography after birth to evaluate a series of hemodynamic parameters, such as LVEF (ejection fraction of LV), RVCO (cardiac output of right ventricle), mVcfc (left ventricular contraction) and ESWS (systemic peripheral vascular resistance). General clinical data were recorded. Inotropic agents were administrated by variation of hemodynamic parameters or downhill clinical conditions. We also followed up PDA associated complications, such as pulmonary hemorrhage, chronic lung disease, IVH, and acute kidney injury.

Results: A total of 18 ELBW infants were studied. The gestational age was 26.8 ± 1.5 (25-30) weeks and the birth weight was 797 ± 128.8 (450-980) grams. Pulmonary hemorrhage only occurred in 2 preterm infants. None had advanced IVH. 12 cases had chronic lung disease. 2 cases had acute kidney injury. Dobutamine was prescribed in 4 cases. The ESWS, before and after Dobutamine administrated, were 45.36 ± 3.97 (40.47-52.17) g/cm² and 35.44 ± 7.85 (27.1-49.14) g/cm². The ESWS significantly decreased after administration of Dobutamine ($P=0.046$).

Conclusions: No advanced hemorrhagic complications were observed in ELBW infants except 2 cases with pulmonary hemorrhage after introduction of the tailor-made circulatory management strategy. A significant reduction of systemic peripheral vascular resistance in ELBW infants was observed after administration of Dobutamine.

26 The Frequency of Dressing Changes for Percutaneous Central Venous Catheters in Catheter-related Blood Stream Infection in NICU – A Single Center, Randomized Controlled Trial

經皮中央靜脈導管的消毒頻率影響新生兒加護病房中導管引起的血流感染率：單一中心，隨機對照試驗

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Background: Complications of percutaneous central venous catheters (PCVCs) include catheter-related blood stream infection (CRBSI), occlusion, leakage, and phlebitis, which may lead to sepsis or prolonged hospitalization. The frequency of dressing changes for PCVCs may affect CRBSI incidence, but information on the best frequency of dressing changes to prevent CRBSI in NICU is lacking. This randomized controlled trial aimed to determine the effects of different frequencies of dressing change, every week regularly vs. non-regularly, in CRBSI for PCVCs in premature neonates in NICU.

Methods: Patients in NICU requiring PCVCs from March 2019-May 2020 were enrolled. The protocol of sterilization before and after indwelling PCVC included cleaning the skin with normal saline, followed by povidone-iodine, using maximum sterile barrier precautions. Enrolled patients were randomly assigned into 2 groups: the regular dressing group (RD), for which dressings were changed every week regularly, or additionally when oozing was noticed; and the non-regular dressing group (ND), for which dressings were changed only when oozing was visible. The incidence of CRBSI, occlusion, leakage, and phlebitis were compared between the two groups using the Chi-squared test. The incidence of catheter-related complications was defined as numbers of episodes per 1,000 catheter-days.

Results: A total of 197 PCVCs were enrolled. The ND and RD groups had 99 and 98 PCVCs, respectively. The average CD interval was 9.3 days in ND group and 5.8 days in RD group. The incidence of CRBSI in the RD group was 0%, which was significantly lower than that of the ND group, 2.0% ($p=0.048$), but no significant differences were found between groups in the incidence of occlusion, leakage, and phlebitis of PCVCs.

Conclusions: Regular dressing changes every week and when oozing occurs while maintaining the protocol of maximum sterile barrier precautions is the best method and frequency of dressings of PCVCs.

27 The Effectiveness of Perinatal Human Immunodeficiency Virus (HIV) Intervention on Reducing Vertical Transmission of HIV: An 8-year Experience

周產期HIV預防處置措施對減少HIV垂直感染的效益：8年的經驗分析

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Background: Mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV) has become an essential global health issue and its elimination is a crucial target. In recent 3 years, maternal screening rate and MTCT rate were 99% and 2.27% in Taiwan. We describe the clinical management of infants born to HIV infected mothers.

Methods: Between January 2012 and December 2019, there were 12 newborn infants born to HIV infected mothers were included in this study. Maternal viral loads and CD4 counts were measured. All the HIV infected mothers had received antiretroviral therapies (ART), and all of them were delivered by elective Cesarean section. The newborn infants were followed up with viral load by ribonucleic acid (RNC) polymerase chain reaction (PCR) or HIV antibody testing. All the infants received formula feeding. The mean birth weight (BW) was 2875.0 ± 254.5 grams (ranged from 2505 to 3290 grams) and the mean gestational age was 37.17 ± 0.72 weeks (ranged from 36+2 to 38+1 weeks). All the infants had received oral zidovudine 4mg/kg BW/dose with 6-12 hours after birth, twice a day, for 6 weeks. Only 1 infants received Nevirapine 12 mg, 3 times within the first week of age and combined with oral zidovudine for 6 weeks.

Results: None of the babies born to HIV infected mother were infected with HIV, MTCT rate was 0%.

Conclusions: None of babies born to HIV infected mothers were infected with HIV in this study. Current policy for preventing mother-to-child transmission of HIV in Taiwan is effective.

28 Effect of the Nadir Point of Postnatal Adaption on the Development Outcome of Very Low Birth Weight Infants

生理性脫水之最低點對於非常低體重早產兒發展的影響

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Background: The prevalence of prematurity is almost

around 10% in the whole world. As the improvement in the survival rates of prematurity, we focus on how to improve the neurological outcomes of prematurity, especially those in very low birth weight infants. There are many known factors affecting the neurodevelopment outcomes. The objective in our study is analysis how the early nutrition status influences the neurodevelopment outcomes using Bayley III at 6, 12 and 24 months corrected age.

Methods: This was a prospective cohort study in the very-low-birth-weight premature infants, cared in Taichung Veterans General Hospital during Oct. 2015 and Jan. 2017. In the study the infants received a standard nutritional strategy during hospitalization. Perinatal-demographic characteristics, medical interventions, and outcome parameters were collected. Licensed child psychiatrists administered the Bayley III tests randomly when the participants were around 6 and 12 months' corrected age and 24 months old.

Results: 52 patients were followed at corrected age 12 months old and 50 patients were till at the time of 24 months old. The mean birth weight of our cohort was 1070.5 gm (± 245.50gm) and the mean gestational age was 29.0 weeks (± 2.41weeks). From the univariate analysis, the nadir point has a significant impact on the neurodevelopment score. Then we used the linear regression model to adjust the confounding factors and found the nadir point was associated with the motor scores, especially the gross motor development at 12 and 24 months. Finally, we utilized the generalized estimating equation (GEE) model to integrate the longitudinal follow up results. Even we took all the known important cofactors, such as the nutrition status during hospitalization, the gestational age, and the growth condition, the nadir point was still achieved statistical significance with the motor scores.

Conclusions: The nadir point during postnatal adaption had a significant influence on the motor development. The mechanisms of the nadir point to impair the neurodevelopment are not completely understood and further studies should be done.

29 Early Hypophosphatemia in Preterm Infants, an Emerging Problem in Ear of Early Aggressive Nutrition: a Preliminary Report

早產兒早發性低血磷與早期積極營養的關聯性：初步報告

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Background: Electrolyte imbalance as hypophosphatemia, hypokalemia and hypomagnesemia, related to higher energy and amino acid supplementation in early preterm life in recent years had been noticed. We would like to survey the prevalence of hypophosphatemia during the first week of life in preterm infants receiving parenteral nutrition and to analyze population variables with severe hypophosphatemia.

Methods: Retrospective review of medical records of extremely low birth weight infants (ELBWIs) admitted to China Medical University Children's Hospital (CMUCH) during 2019 were reviewed. Hypophosphatemia and severe

hypophosphatemia were defined as serum level < 4 mg/dL and < 2.5 mg/dL, respectively. Correlation of maternal characteristics, birth weight, serum level of electrolytes and nutrition intake with hypophosphatemia were analyzed.

Results: Medical records of 41 ELBWIs were reviewed and only 51% (21/41) of patients had serum phosphate levels measured in the first week of life. The prevalence of hypophosphatemia is 52% (11/21), and severe subtype accounts for 54% (6/11). The risk of early hypophosphatemia was higher in newborn with small for gestational age (SGA) ($p=0.013$). The SGA infants also have a higher risk ($p=0.021$) of severe hypophosphatemia compared to the non-SGA infants.

Conclusions: While early aggressive nutrition declines the incidence of extrauterine growth restriction in the modern era, refeeding-like syndrome is an emerging problem that might be ignored by neonatologist. The prevalence of hypophosphatemia in early life is high, especially in SGA infants. Further studies are needed to adjust early nutrition regimen for preterm infants.

30 Respiratory Outcomes of Preterm Infants Following Intravitreal Anti-VEGF Injection for Retinopathy of Prematurity – A Matched Case-Control Study

早產兒接受眼內注射抗血管內皮生長因子治療視網膜病變後呼吸狀態預後：匹配病例對照研究

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Background: Intravitreal injection (IVI) of anti-vascular endothelial growth factor (anti-VEGF) agents has gained preference in treating retinopathy of prematurity (ROP). Since VEGF are crucial to lung maturation and anti-VEGF agent is known to enter the bloodstream after IVI, there is a concern of decreasing maturation and worsening oxygenation in the lung in preterm infants. The aim of our study was to evaluate respiratory outcomes in ROP infants following IVI of anti-VEGF agents.

Methods: We retrospectively screened preterm infants of < 34 weeks' gestation age (GA) and < 1500 g, and included those having bilateral type 1 ROP and receiving only one dose IVI. The anti-VEGF agents were bevacizumab (Avastin), ranibizumab (Lucentis) or aflibercept (Eylea). Infants with a major anomaly, receiving ≥ 2 doses IVI or laser therapy, or no need of additional oxygen at the IVI treatment were excluded. After identifying the IVI group, 1:1 matched controls were recruited based on the criteria: GA ± 1 week, postnatal age ± 7 days, the same ventilatory mode, and respiratory severity score (RSS (mean airway pressure (MAP) X fraction of inspired oxygen (FiO₂)) \pm

10%). Outcomes were serial respiratory changes of MAP, FiO₂ and RSS, and overall respiratory improvement at 28 days after matching. Respiratory improvement was defined as either extubation, downgrading of ventilatory mode, reduction in MAP $> 25\%$, or decrease in FiO₂ $> 25\%$. Time to extubation and duration of O₂ use after matching were compared.

Results: The study enrolled 98 infants (GA 26.0 ± 1.5 weeks, birthweight 822 ± 165 g) in the IVI group and 98 paired controls. No difference was seen in demographics or major clinical events before matching. In general, both groups had downward trends of MAP, FiO₂ or RSS over the study period, but there was no between-group difference. The percentage of overall respiratory improvement was without difference between IVI and control group, as well as time to extubation and O₂ use duration.

Conclusions: This is the first matched case-control study to evaluate the possible negative effects of anti-VEGF agents on lung maturation, and we found IVI of anti-VEGF agents did not worsen respiratory outcomes in preterm infants

31 Influence of Maternal Diet on Breast Milk Composition and Infant Growth

產婦飲食對母乳成分與嬰幼兒成長之影響

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Background: In 2018, the rate of exclusive breastfeeding was 67.2% in the first month after delivery, and 46.2% was still in the sixth month. In the National Nutrition Survey, women aged 19-44 were found not reaching the recommended amount in dairy products, nuts and seeds, vegetables and fruits. We focused on evaluating the mothers diet at postpartum period influencing the breastmilk content and infant growth in Taiwan.

Methods: After delivery, the included mothers filled the dietary frequency questionnaire and measured the body composition at the first, second and fourth postpartum months. Breast milk samples were collected at the same time. Human milk analyzer was used to analyze breast milk macronutrients and atomic absorption spectroscopy was checked for the mineral calcium, magnesium, iron and zinc. Meanwhile, the infants' growth was measured.

Results: Sixteen women were recruited into the study, and seven of them completed the postpartum breast milk collection. Among the six major types of food intake, about 40% included women did not reach the recommended amount in the whole grains and legumes, fish, eggs, meat and their products, more than 60% were under the needs in the category of dairy products and more than 80% failed to meet the requirement of fruits and nuts with seeds. The energy and fat in breast milk correlated positively with the intake frequency of beans and their products. Lactose in

breast milk correlated positively with the frequency of aquatic products, and negatively with the frequency of meats. Calcium and magnesium in breast milk correlated positively with the frequency of meats. Magnesium in breast milk correlated negative with the intake frequency of whole grains and vegetables. Protein in breast milk correlated positively with the mothers weight, body fat percentage, BMI, fat weight, total body water, and cortical thickness.

Conclusions: Although there is no strong correlation between the composition of breast milk and infant growth, it is observed that infants who are exclusively breastfed can maintain their original birth percentile growth and development.

32 Metabolomic Profiling Reveals Association between Different Breastfeeding Patterns and Milk Sensitization

代謝物圖譜分析發現母乳哺餵方式的不同與牛奶致敏化間的關係

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Background: The associations between different breastfeeding patterns and sensitization to milk have been studied. However, longitudinal metabolic analysis toward the development of milk sensitization in different breastfeeding patterns has not been investigated.

Methods: Children aged 0 through 4 years from a birth cohort in the Prediction of Allergies in Taiwanese Children (PATCH) study were enrolled. Urinary metabolites were assessed at 6 months, 1, and 2 year of age by using 1H-nuclear magnetic resonance (NMR) spectroscopy coupled with multivariate statistical analysis and partial least-squares discriminant analysis (PLS-DA). Associations between metabolites and total serum and food allergen-specific IgE levels in different breastfeeding patterns and milk sensitization sets were measured sequentially at 6 months as well as at 1, and 2 years of age.

Results: A total of 153 urine samples collected from 33

exclusively breast-fed children and 22 formula-fed children were enrolled and analyzed. Twenty-two metabolites were predominantly obtained at age 0.5 in the set of different breastfeeding pattern, whereas nine metabolites were predominantly obtained at age 1 in the milk sensitization set. Eight metabolites including 3-methyl-2-oxovaleric acid, glutarate, lysine, N-phenylacetyl glycine, N, N-dimethyl glycine, 3-indoxyl sulfate, 2-oxoglutaric acid, and pantothenate were significantly associated with formula feeding and milk sensitization with same trend variation from 6 months to 1 year of age. Among them, 3-methyl-2-oxovaleric acid, lysine, and glutarate were significantly positively associated with total serum IgE ($P < 0.05$). Further metabolic pathway analysis revealed amino acid metabolisms and metabolism of cofactors and vitamins linked to formula feeding related to milk sensitization.

Conclusions: Longitudinal analysis of urinary metabolomics disclosed crucial metabolic changes of formula feeding associated with sensitization to milk from 6 months to 1 year of age. In formula-fed infants, a significant decrease in 3-methyl-2-oxovaleric acid, lysine, and glutarate after age 6 months appeared to be strongly associated with IgE levels contributing to milk sensitization.

33 Severe Jaundice Infants Who Successfully Treated with Intensive Phototherapy Are Still at Risk for Bilirubin Encephalopathy

嚴重黃疸新生兒經加強照光成功治療後仍具有黃疸腦病變風險

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Background: Bilirubin encephalopathy is a severe morbidity for infants with exceedingly high total serum bilirubin (TSB). Blood exchange transfusion (BET) is the rescue therapy but related to several complications. With the advancement of phototherapy, most infants with severe jaundice could be successfully treated. However, the possibility of bilirubin encephalopathy is often overlooked for infants treated with intensive phototherapy (IP). This study aims to compare the neurologic outcomes between infants treated with BET and IP.

Methods: We retrospectively screened infants of ≥ 35 weeks' gestation admitted between 2014–2019 who had TSB above the threshold for BET according to the American Academy of Pediatrics 2004 guideline. Infants with major anomaly, severe perinatal events or nervous system disease were excluded. Serial TSB levels as well as the reduction in TSB (from the highest to the first TSB below phototherapy criteria) were collected. Demographics, etiology of hyperbilirubinemia, intervention and neurologic

outcomes were analyzed.

Results: A total of 55 infants (12 received BET and 43 IP-only) were included. There was no difference between BET and IP groups in gestational age (37.9 ± 1.2 vs. 37.9 ± 1.4 weeks), age of initial TSB above BET level (5.0 ± 3.4 vs. 6.3 ± 5.0 days), highest TSB (25.7 ± 4.6 vs. 24.2 ± 4.9 mg/dL), and underlying etiology. The BET group had faster reduction in TSB (0.7 ± 0.4 vs. 0.4 ± 0.3 mg/dL/hr, $p=0.007$). Five (42%) infants in the BET group had undergone a brain auditory evoked potential (BAEP) test, and 2 of them (40%) had hearing impairment. The risk for abnormal BAEP was not lower in the IP group that 17 (40%) infants had done a BAEP test, and 10 (59%) failed. One infant of the IP group had seizure, 3 continued to visit otolaryngologists for hearing impairment, 4 were followed by neurologists and 1 underwent rehabilitation. None of the BET group had seizure or needed the abovementioned follow-ups.

Conclusions: We demonstrate that the risk for bilirubin encephalopathy in infants successfully treated with IP was no less than those received BET. Physicians should recognize those infants are still exposed to the risk for encephalopathy, and a neurologic screening protocol is warranted.

34 Early Postnatal Acute Kidney Injury as an Indicator for Neonatal Mortality in Preterm Infants with Twin-to-twin Transfusion Syndrome

出生後發生早期急性腎損傷為罹患雙胞胎胎輸血症候群早產兒之死亡危險因子

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Background: Twin-to-twin transfusion syndrome (TTTS) complicates 10-15% of monozygotic monochorionic twin pregnancies and results in an unbalanced shunting of circulation between the fetuses. Acute kidney injury (AKI) is one of the common postnatal complications in neonates with TTTS. Thus, we aim to describe the occurrence of AKI in neonates with TTTS and to establish a correlation between AKI and TTTS neonatal outcome.

Methods: TTTS twins with a gestational age of less than 34 weeks born in our hospital between Jan 2013 and Dec 2019 were enrolled in the study. Diagnosis and treatment of TTTS was based on Quintero et al. The serum creatinine levels within a week and urine output within 3 days of birth were used in establishing early postnatal AKI according to the modified KDIGO definition. Demographic data, prenatal interventions, laboratory results and outcomes were collected and compared between newborns with AKI and those without.

Results: A total of 46 neonates with TTTS were included in our study. The mean gestational age was 30 ± 3 weeks and birth weight was 1237 ± 437 grams. Based on the neonatal

modified KDIGO criteria, nineteen (41%) neonates were found to have AKI and eight neonates were eventually expired with the mortality rate of 17%. The AKI incidence was not significantly different between donor (48%) and recipient (35%) twins ($P=0.38$). In AKI group, gestational age at birth (29 ± 3 weeks vs 31 ± 2 weeks, $p=0.002$), birth body weight (989 ± 332 grams vs 1411 ± 422 grams, $p=0.001$) and Apgar score (1 minute: 5 ± 2 vs 7 ± 1 ($p=0.002$), 5 minutes: 7 ± 2 vs 8 ± 1 ($p=0.012$)) were all lower than non-AKI group. Furthermore, neonates with TTTS complicated with AKI had a higher mortality rate: the in-hospital mortality rate was 32% in the AKI and 7% in the non-AKI neonates ($p=0.034$) with most of the death occurred within the first 10 days of life.

Conclusions: In our study, the AKI incidence among neonates with TTTS is high (41%) and is associated with an increased risk of neonatal mortality. In preterm infants with TTTS, the occurrence of early postnatal AKI may be used to predict the risk of neonatal mortality.

35 Autosomal Recessive Renal Tubular Dysgenesis Caused by a Founder Mutation of AGT (Angiotensinogen)

新生兒致命性遺傳疾病 (腎小管發育不全) 之盛行率、臨床表現及預後研究

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Background: Autosomal recessive renal tubular dysgenesis (ARRTD) caused by inactivation mutations in AGT, REN, ACE, and AGTR is a very rare but fatal disorder with unknown prevalence.

Methods: We report six Taiwanese with ARRTD from six unrelated families diagnosed by renal histology. Clinical features, outcome, and prevalence of carrier heterozygosity were examined.

Results: All patients exhibited antenatal oligohydramnios, postnatal anuria, pulmonary hypoplasia, and profound hypotension refractory to interventions. AGT (Angiotensinogen) protein levels were diminished in the liver along with reduced serum AGT, angiotensin I (Ang I) and II (Ang II) levels. Neonatal demise occurred in all but one. All carried the same homozygous E3_E4 del:2870bp deletion+9bp insertion in AGT, and led to a truncated protein (1-292 amino acid). The analysis of allelic frequency of this heterozygous AGT mutation suggests that ARRTD may not be exceedingly rare in Taiwan. This mutation results in skipping of exons encoding the serpin domain of AGT, which is important for renin interaction and the generation of truncated protein. In silico modeling revealed a diminished interaction between mutant AGT and renin.

Conclusions: The high frequency of AGT heterozygous

mutation suggests that ARRTD is not rare in Taiwan. ARRTD is not rare This AGT mutation may lead to the diminished interaction with renin and decreased Ang I and II generation.

36 Risk Assessment of Prolonged Jaundice in Infants at One Month of Age: A Prospective Study

一個月大嬰兒之延遲性黃疸的風險因子：前瞻性研究

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Background: Prolonged jaundice is a commonly evaluated condition. The aim of this study was to assess the risk factors of jaundice in healthy infants at one month of age.

Methods: This prospective cohort study enrolled 513 healthy infants from 2013 to 2018. Jaundice was defined as a transcutaneous bilirubin value ≥ 5 mg/dL at 25–45 days of age. Umbilical cord blood samples were obtained to examine seven common gene variants.

Results: The incidence of prolonged jaundice was 32.2%. Prolonged jaundice was more common in infants with exclusive breastfeeding ($p < 0.001$), GA 35–37 w ($p = 0.001$), stool passage > 4 times/d ($p < 0.001$), previous phototherapy ($p < 0.001$), and gene variant of G to A at nt 211 of UGT1A1 ($p = 0.004$). A multivariate logistic regression analysis demonstrated the greatest risk for prolonged jaundice was exclusive breastfeeding (OR=2.818, 95% CI=1.851–4.292), followed by previous phototherapy (OR=2.593, 95% CI=1.716–3.919), GA 35–37 w (OR=2.468, 95% CI=1.350–4.512), and G to A at nt 211 of UGT1A1 (OR=1.645, 95% CI=1.070–2.528).

Conclusions: Infants with exclusive breastfeeding, preterm birth, previous phototherapy, or G to A at nt 211 of UGT1A1 are at greater risk of prolonged jaundice. Physicians should consider these risk factors in their assessment of prolonged jaundice.

37 Predisposing Factors of Acute Kidney Injury in Premature Infants—Six Years' Experience of a Tertiary Hospital in Taiwan

早產兒急性腎臟損傷的誘發因子——一個台灣三級醫院六年期研究

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Background: Acute kidney injury (AKI) is an under-recognized morbidity of premature infants; the incidence remains unclear due to the absence of a unified definition of AKI in this population and because previous studies have

varied greatly in screening for AKI with serum creatinine and urine output assessments. AKI in neonates is often multifactorial and may result from prenatal, perinatal, or postnatal insults. In this study, we conducted a case-control study to investigate the incidence of AKI and the predisposing risk factors in premature infants.

Methods: From January 2014 to December 2019, 270 premature infants with gestational age (GA) less than or equal to 33 weeks were admitted to a level III neonatal intensive care unit. Twenty-nine cases had AKI and 58 were controls closely matched for gestational age and birth body weight. The incidence of AKI in premature infant was 10.74%. We retrospectively reviewed demographic characteristics and various perinatal and postnatal variables. Univariate and multivariate analyses were performed to identify risk factors for AKI in premature infants.

Results: Compared to AKI and non-AKI patients, AKI patients had a higher incidence of perinatal distress, hypotension, ibuprofen or indomethacin given and insensible water loss. However, multivariate logistic regression analysis showed that only perinatal distress, hypotension and the use of NSAID were independent risk factors for AKI (adjusted odds ratio, 95% confidence interval=4.752, (1.368-8.225); $p = 0.315$, 1.482, (0.517-4.338); $p = 0.223$, 6.783, (3.465-11.334); $p = 0.023$) after adjusting for confounding factors.

Conclusions: Perinatal distress, hypotension and NSAID given were significant risk factors for the subsequent development of AKI in our study population. We need to pay more attention to this population. It is very important to early detect and manage AKI in premature infants.

38 Clonal Spread of Macrolide-resistant Mycoplasma Pneumoniae Sequence Type-3 and Type-17 with Recombination on Non-P1 Adhesin in Taiwan

台灣序列分型3與分型17之抗巨環黴素肺炎黴漿菌所致肺炎的共同傳播與相關臨床表徵

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Background: Mycoplasma pneumoniae is currently the most commonly detected bacterial cause of childhood community-acquired pneumonia in several countries. Of note, clonal expansion of macrolide-resistant ST3 occurred in Japan and South Korea. An alarming surge in macrolide resistance complicated the treatment of pneumonia.

Methods: We prospectively enrolled 626 children hospitalized with radiologically confirmed pneumonia at two medical

centers and one regional hospital between 2017 and 2019. *M. pneumoniae* infection was suspected on clinical grounds, and tested by real-time polymerase chain reaction and oropharyngeal swab cultures.

Results: A total of 226 children with *M. pneumoniae* pneumonia were enrolled. Macrolide resistance was found in 77% (174/226) patients. Multi-locus sequence typing revealed that ST3 (48.3%) and its single-locus variant ST17 (41.4%) were the predominant clones among macrolide-resistant strains. ST17 presented clinical characteristics comparable to its ancestor ST3. On multivariate analysis, ST3 with its ST17 variant (OR, 3.4; 95%CI, 1.3–9.4; P=0.02), and C-reactive protein (OR, 1.01; 95%CI, 1.00–1.01; P=0.02) were independently associated with persistent fever after one course of macrolide treatment. By whole genome sequencing, prediction analysis of recombination sites revealed one recombination site in ST3 and ST17 compared with M29 (a macrolide-sensitive ST3 strain isolated from China in 2005): cytoadhesin MgpC-like protein, RepMP4, and RepMP5 at position 643073–645690. ST17 had another recombination site: position 648073–648096 containing an adhesin and RepMP2/3.

Conclusions: In addition to macrolide resistance, ST3 and its ST17 variant might evolve through recombination between repetitive sequences and non-P1 cytoadhesins for persistent circulation in Taiwan.

39 The Epidemiology, Clinical Characteristics and Macrolides Susceptibility of *Mycoplasma Pneumoniae* Pneumonia in Children in Southern Taiwan, 2019-2020

2019-2020年南臺灣兒童黴漿菌性肺炎的流行病學、臨床特徵及對巨環類抗生素 (Macrolides) 的敏感性研究

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Background: Community-acquired pneumonia (CAP) is one of the leading causes of hospitalization of children. After the universal vaccination of pneumococcal conjugate vaccine (PCV), *Mycoplasma pneumoniae* (MP) had emerged as the most common etiology of CAP in children. In recent studies, MP has increasing macrolide resistance rate and causes severe disease in younger children. The study aimed to characterize the changing microbiological epidemiology of MP pneumonia in children in southern Taiwan.

Methods: Patients aged less than 18 years old hospitalized at National Cheng Kung University Hospital from May 2019 to March 2020 were prospectively enrolled. The community-acquired Mp (CAMP) was defined by radiology confirmed segmental or lobar pneumonia and MP infection confirmed by positive PCR and elevated serum antibody titer followed up to 6 months. We analyzed the clinical characteristics, laboratory data, treatment outcome, and macrolides susceptibility and compared with previously published study.

Results: A total of 474 CAP cases were enrolled, and 195 (41%) of them were CAMP. Comparing to 2010-2011-year period, symptoms including chest pain, non-post-tussive vomiting, and decreased spirit appeared less frequently. Decreased hospital stay, ICU admission, mean WBC count, oxygen use, pulmonary consolidation, and pleural effusion were also noted. Children under 5 years had lower level of CRP, lower prevalence for pulmonary consolidation, pleural effusion, and usage of doxycycline; higher prevalence for oxygen therapy, dyspnea, and severe disease. The macrolide-resistant rate was 87.7% (136/155), and the macrolide-resistant group was associated with longer febrile duration after admission and higher prevalence of dyspnea (all p value < 0.05).

Conclusions: The prevalence of CAMP increased in the post-PCV vaccine era, while decreasing disease severity with high resistance to macrolides were noted. Younger children continued to be the vulnerable group for severe disease and inappropriate antibiotic. Prompt diagnosis is needed for precise antimicrobial prescription to avoid complications and macrolide resistance.

40 Methicillin-resistant *Staphylococcus Aureus* ST8 (USA300) Became One of the Major Clones in Northern Taiwan?

抗藥性金黃色葡萄球菌 USA300 菌株是否已成為北台灣主要菌株之一?

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Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a common pathogen in the hospital and the community. There are three major clones of MRSA prevailing in Taiwan, namely clonal complex (CC) 239, ST5 and CC59, and are almost resistant to clindamycin (CL). MRSA USA300 (ST8) prevailed in North America and rarely identified in Taiwan till October 2015. Recently in clinical practice, we found the susceptibility rate of clinical MRSA isolates to clindamycin increased, which prompted us to figure out the changing epidemiology of MRSA in Taiwan.

Methods: Reviewing the antibiograms of clinical MRSA isolates in our hospital in the past decade, we found that clindamycin susceptibility rate increased from 4.9% (293/5979) in 2008 to 33.2% (1058/3184) in 2018. We chose MRSA isolates from pediatric patients for further molecular analysis.

Results: Among MRSA isolates from pediatric patients, CL susceptibility rate increased from 10.3% (23/223) in 2008, 16.6% (56/337) in 2013 to 31.4% (89/283) in 2017 and 32.2% (94/292) in 2018. Molecular analysis revealed that of the CL-S MRSA isolates, USA300 characterized as SCCmec type IV/PVL genes-positive/ACME-positive accounted for none in 2008, 6.5% in 2013, to 44.4% in 2017 and 48.8% in 2018. Of the 69 USA300 isolates, 11 subtypes were identified and one major subtypes accounting for 52.2%.

Conclusions: Molecular epidemiology of MRSA in northern Taiwan changed since 2016 and USA300 seemed to be

among the major clones. Clinical significance should be further studied and empiric antibiotic choice should be adjusted.

41 Management of Pediatric Osteomyelitis: In the Era of Community - Associated Methicillin - Resistant Staphylococcus Aureus

小兒骨髓炎的治療：在社區型抗藥性金黃色葡萄球菌盛行之世代

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Background: Pediatric osteomyelitis is a serious disease requiring early diagnosis and adequate treatment. This study evaluated the clinical characteristics, treatment, and outcomes of pediatric patients with the diagnosis of osteomyelitis.

Methods: This 9-year retrospective study was conducted at a tertiary hospital in central Taiwan. Medical records of all children aged less than 18 years with a diagnosis of osteomyelitis were thoroughly reviewed and analyzed.

Results: In total, 35 patients fulfilled the inclusion criteria. Their median age was 6.5 years and 60% were male. Gram-positive bacteria, especially Staphylococcus aureus (57.9% of identified bacteria), were the main pathogens. The prevalence of methicillin-resistant Staphylococcus aureus was 54.5%. Escherichia coli was the most common gram-negative isolate (10.5% of identified bacteria). Previous trauma was reported in 37.1% children. Surgery was performed in 45.7% of cases. The median duration of intravenous and total antibiotic treatment was 24 days and 52 days, respectively. The overall MRSA coverage rate during empirical and further antimicrobial therapy was 40% and 60%, respectively. Complication and recurrence rates were 11.4% and 5.7%, respectively.

Conclusions: It is important to emphasize that appropriate antibiotic selection, along with adequate and timely surgical intervention, is essential for the successful treatment of pediatric osteomyelitis and to minimize late sequelae.

42 Baseline Maximum Dimension of Coronary Arteries as a Predictor of Late Coronary Aneurysms in Children with Kawasaki Disease

以冠狀動脈血管大小基礎最大值預測川崎症病童發生冠狀動脈瘤

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Background: While coronary artery aneurysms (CAAs) has been established as the most serious complication of Kawasaki disease, to precisely predict the development of CAAs remain a clinical challenge. We aimed to investigate whether z scores of coronary arteries on baseline echocardiography was a predictor of the presence of late CAAs in children with Kawasaki disease.

Methods: We performed a retrospective study in patients who were hospitalized for Kawasaki disease at Mackay Children's hospital and received intravenous immunoglobulin within 10 days of illness. We defined late CAA as a maximum z score (Z_{max}) ≥ 2.5 of the left main, right, or left anterior descending coronary artery at 11-60 days of illness.

Results: Among the 314 included children, 31 (9%) had late CAAs. Thirty-nine (12.4%) patients were classified as incomplete KD. The median age at illness onset was 17.2 months (IQR: 9.8-27.7 months) and the median number of days between onset of fever and IVIg administration was 6 days (IQR: 5-7 days). Late CAAs were significantly associated with baseline $Z_{max} \geq 2.0$ vs < 2.0 (25 [32.5%] vs 6 [2.5%], $P < .001$). The sensitivity, specificity, positive predictive value, and negative predictive value of $Z_{max} \geq 2.0$ for the presence of later CAAs were 80.6%, 81.6%, 32.5%, and 97.5%, respectively.

Conclusions: $Z_{max} \geq 2.0$ on baseline echocardiography may be used to predict children at a high-risk of late CAAs and for targeted early intensification therapy.

43 Human Leukocyte Antigens and Kawasaki Disease

人類白血球抗原與川崎氏病

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Background: Kawasaki disease (KD) is an acute febrile illness of children in all populations, with the highest incidence in Asia. KD is accompanied by vasculitis involving the coronary arteries. Coronary artery lesions occur in 20-25% of untreated patients and 3-5% of treated ones. HLA has been found to be associated with KD by candidate gene approaches and genome-wide association studies. In contrary, other studies have detected no

association. Therefore we investigated the association between HLA-B and KD.

Methods: The patients were 554 unrelated children (311 boys, 243 girls) with KD. Their age at diagnosis of KD was 1.95 [standard deviation (SD), 1.62] years. The control subjects were 403 adults (135 men, 268 women). They included hospital personnel and individuals who underwent routine health examinations or minor surgery. None had a history of KD. All patients and controls were Han Chinese in Taiwan. The diagnosis of KD is according to the diagnostic criteria of the American Heart Association. Treatment consisted of aspirin and intravenous gamma globulin as soon as the diagnosis is made. All patients were examined with two-dimensional echocardiography during the febrile stage and again after discharge from the hospital. The diameter of each coronary artery segment was measured from inner border to inner border. A coronary artery lesion was defined as the inner diameter of a coronary artery Z score ≥ 2.5 . The HLA-B gene was typed using the Dynal RELI SSO HLA-B typing kit (DYNAL, Invitrogen, Warral, U.K.).

Results: The 4 most frequent alleles of HLA-B were B*40:01, 46:01, 58:01, and 13:01 with a frequency of 173 (21.5%), 106 (13.1%), 90 (11.2%) and 64 (7.9%) in controls and 287 (18.5%), 207 (13.3%), 156 (10.4%) and 114 (7.3%) in KD patients. There were no significant difference in the frequency of any allele between the two groups. We analyzed the frequency of each allele between KD patients with and without CALs and also found no significant difference.

Conclusions: The study found no significant association between HLA-B and KD or CALs. Other loci in the HLA complex must be investigated and haplotypes must be analyzed.

44 Clinical Characteristics and Risk Factors for Children with Norovirus Gastroenteritis in Taiwan

台灣兒童諾羅病毒腸胃炎的臨床表現及危險因子

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Background: Norovirus is a common acute gastroenteritis (AGE) pathogen across all age groups worldwide, which is difficult to differentiate from other pathogens. This study aimed to understand the clinical characteristics and risk factors of norovirus gastroenteritis among children in Taiwan.

Methods: A prospective AGE surveillance study was conducted in children aged ≤ 5 years who were hospitalized in 10 major hospitals in Taiwan between 2014 and 2017. The non-AGE control group included healthy children who were matched based on age, gender, season, and geographic area.

Results: Overall, 674 norovirus gastroenteritis patients were enrolled. Fever ($p < 0.001$), mucoid stool ($p < 0.001$), and bloody stool ($p < 0.001$) occurred less frequently among norovirus gastroenteritis patients. Norovirus gastroenteritis patients yielded lower CRP values on admission (21.78 ± 36.81 vs. 46.26 ± 58.12 mg/L, $p < 0.001$) than non-norovirus controls. Norovirus gastroenteritis patients were associated with higher direct contact rates with AGE patients within 1 week (30.5% vs. 0.97%, $p < 0.001$), lower hand wash rates before meals (21.6% vs. 15.4%, $p = 0.001$), lower human milk (15.8% vs. 19.8%, $p = 0.045$), guava (17.8% vs. 24.3%, $p = 0.002$) and beverage consumption rates (44.9% vs. 52.1%, $p = 0.005$) than non-AGE participants.

Conclusions: Body temperature, stool characteristics, and CRP value can help distinguish the norovirus from other pathogens. The major risk factor of norovirus AGE is contact with AGE patient. Higher frequency of hand wash, breastfeeding, guava, and beverage intake may be protective against norovirus gastroenteritis.

45 Study the Influence of Using Shared Decision-Making on Rotavirus Vaccination Rate in Children

研究使用醫病共享決策在兒童輪狀病毒疫苗接種率的影響

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Background: Rotavirus vaccination reduces the incidence and severity of acute gastroenteritis due to rotavirus infection. Lack of understanding and the need to pay for the rotavirus vaccine, the rotavirus vaccination rate is still low in some countries. We used shared decision-making (SDM) with the assistance of patient decision aids (PDAs) to assess on the rotavirus vaccination rate, and the knowledge, confidence, and congruence of value among baby's parents when choosing oral rotavirus vaccine.

Methods: The study is randomized controlled trials. Infants' families who came to the hospital for infant's routine vaccination at 1 month old were enrolled; they were randomly divided into non-SDM group and SDM group. At 2 months old baby, the infants' families from non-SDM group and SDM group will bring baby back again and fill the anonymous questionnaire. The questionnaire consisted general demographic questions and clinical variables including 11 items to assess what variables influence infants' family's choice of letting the baby receive the oral rotavirus vaccine. The 5-item SURE scale measured decision conflict 7. The outcomes of the infants' families let baby receiving oral rotavirus vaccine were recorded.

Results: The study enrolled 180 participants. SDM, parents' education level, and rotavirus vaccination of a previous child were variables that influenced acceptance of rotavirus vaccination. The SDM group scored significantly higher for understanding the information on the oral rotavirus vaccine than the non-SDM group, which helped them to decide whether to vaccinate the baby against rotavirus, to ask questions related to the rotavirus vaccine, to have more confidence in deciding whether to vaccinate the baby against rotavirus, and to understand the advantages and disadvantages of the rotavirus vaccine. The rotavirus vaccination rate was higher in the SDM group than the non-SDM group.

Conclusions: SDM assisted with PDAs gives more information and helps infants' families to understand what they need, reduces their decision conflict, and increases the likelihood that their baby will receive rotavirus vaccine, which promotes public health.

46 Long Term Outcome of Enterovirus Infection in Taiwan: A Population-based Cohort Study

腸病毒預後之流行病學研究—世代追蹤研究

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Background: The major burden of diseases in childhood has shifted from infectious diseases to chronic health conditions in recent decades. Although the rates of infectious diseases have decreased, the incidence of chronic diseases stemming from infectious agents continues to grow. Enterovirus is a major infectious disease of childhood and has been linked to numerous chronic diseases. We analyzed population-based data from Taiwan's National Health Insurance Research Database (NHIRD) to investigate the correlations between enterovirus infection and major chronic health conditions in children.

Methods: Children diagnosed with enterovirus (EV) infection during 1999–2003 were identified from the Longitudinal Health Insurance Database 2000 (LHID 2000), a subdata set of Taiwan's National Health Insurance Research Database (NHIRD). A total of 14,168 patients were selected after excluding patients with existing chronic diseases and missing data. Another 14,168 children matched by age and sex were selected as the control group. Five primary outcomes, including attention deficit and hyperactivity disorder (ADHD), epilepsy, asthma, allergic rhinitis, and atopic dermatitis, were recorded.

Results: The risks of ADHD, asthma, allergic rhinitis, and epilepsy were significantly increased in the EV group compared with the control group. The risk of atopic dermatitis was significantly increased in the crude model. However, there were no significant differences in the adjusted model. The risks of ADHD, asthma, allergic rhinitis, and epilepsy were also significantly increased in patients with severe EV infection compared with patients with non-severe EV infection.

Conclusions: Chronic diseases, such as ADHD, epilepsy, asthma, allergic rhinitis, and atopic dermatitis were shown to be associated with enterovirus infection during childhood. EV infection during early childhood might have long-term public health implications and thus prevention strategies should be implemented.

47 Trends of Coprescription Ordered by Western Physician and Traditional Chinese Physician among Taiwanese Children from 2002-2012

臺灣孩童2002-2012年共用中藥與西藥處方的趨勢

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Background: Coprescription is a potential medical problem for children that could induce polypharmacy and following complications. In Taiwan, children could accept perceptions from Western physician, and traditional Chinese physician. Investigating the coprescription trends from the two sources is helpful avoiding unnecessary polypharmacy.

Methods: The Longitudinal Health Insurance Database 2000 (LHID 2000) in our database. Children <18 years old accepted coprescription from Western physician, and traditional Chinese physician from 2002-2012 were included in analysis. The odds ratio (OR) and 95% confidence interval (95% CI) were estimated by a logistic regression model for evaluating the correlation between basic characteristics and coprescription.

Results: A total of 158,313 children were included for the analysis. The trends in the children using prescriptions from Western physician alone decreased over time, but the cohort using prescriptions from traditional Chinese physician maintained stable. Decreased trends in coprescription with age were noted, but teenagers had opposite presentation. The trends in the proportion of coprescription and the number of days of coprescription increased with the calendar year. Increased trend in the proportion of children with coprescription were also found. Children who were female, aged 3-5 years and residents in middle, southern Taiwan prone to receive coprescription.

Conclusions: Coprescription in children is not uncommon in Taiwan. Healthcare providers and policymakers should be aware of the complex coprescription pattern in the children.

48 Evaluation of the Parents' Knowledge of Children's Care Acquired from the Anticipatory Guidance and the Efficacy of Multimedia Assisted Learning

父母對兒童健康預期指引之認知程度與多媒體學習成效之評估

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Background: Children's Health Booklet has been given to new parents by The Health Promotion Administration, Ministry of Health and Welfare. However, it's a challenge for young parents to read the booklets printed with texts while busy nurturing the babies. There is no comprehensive evaluation of parents' knowledge about anticipatory

guidance so far. In addition, we speculate that the younger generation parents may be benefited from the aids of multimedia in learning information about child care. This study was intended to evaluate parents' current knowledge level on children's care guidance and whether it is better with introduction of multimedia learning opportunity.

Methods: We enrolled parents visiting well-baby care clinics in a university hospital. Participants were divided into 2 groups: parents with infants 1-3 months of age and older. A pre-test was given to the participants. Parents of preterm infants, children who'd been admitted to ICU, children with congenital anomalies, refused to take test or incomplete test were excluded. After pre-test, 5 animations designed according to the age of children and content of the booklet were introduced to each group for about 25 minutes, then the parents retook a post-test. Information about the age, gender, parity, occupation and education status of parents and their test scores were collected and analyzed.

Results: We had 214 parents enrolled, 64 of them excluded and finally 150 parents; 75 in the first and rest 75 in the second group were used for analysis. The correct answer rates of the pretest was 69 and 76%, and greatly improved in the post test of both groups (88, 91%, $p < .001$). Female parents, multiple parity and college or higher education levels performed better. Parents with infants of 1-3 months of age had doubts for fever management and the contraindications of vaccination. For parents of children aged >3 months, the timing and what content of giving supplemental food to babies are major issues.

Conclusions: Parents' knowledge about the guidance of Children's Health Booklet varied among parents of different gender, parity, education levels and children age and could be enhanced with the aids of multimedia learning during clinical visit.

49 The Receptor for Hyaluronan-Mediated Motility (CD168) Regulates the NLRP3 Inflammasome in Neonatal Hyperoxic Lung Injury

透明質酸介導的運動因子受體藉調節NLRP3發炎體在新生高氧肺損傷中扮演一重要角色

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Background: Bronchopulmonary dysplasia (BPD), a devastating disorder, is the most common chronic inflammatory lung disease of prematurity. The causes of BPD are often from life-saving settings, such as mechanical ventilation and oxygen supplementation. Currently, the pathogenic pathways driving BPD are not well-delineated and cell interactions with the extracellular matrix (ECM) is one of the proposed reasons. The glycosaminoglycan

hyaluronan (HA), a chief components of the ECM, and one of its receptors for HA-Mediated Motility (RHAMM, CD168) have been implicated in the response to acute lung injury, but not in BPD yet. We hypothesized that, compared to wild type (WT) mice, RHAMM knockout (KO) mice would have protected effect in a rodent BPD model.

Methods: WT and RHAMM-KO mice were exposed to either normoxia (21%) or hyperoxia (95%) during the sacular phase of lung development from postnatal day (PN) 1 to PN5, and then maintained in normoxia until PN14. Bronchoalveolar lavage (BAL), cells from BAL, and lung tissue were obtained on PN7 and PN14. Lung morphometric evaluation included histology and Radial Alveolar Count (RAC) in inflation-fixed lungs. Expression of key molecules such as IL-1 β was analyzed in BAL by ELISA and in lung tissue by qPCR. Neutrophils and macrophages were quantified by Myeloperoxidase (MPO) and N-Acetyl Glucosaminidase (NAG) activities, respectively.

Results: Both hyperoxic WT and RHAMM KO mice had increased IL-1 β (PN7, $P < 0.05$), MPO (PN7, $P < 0.05$) and NAG activities (PN14, $P < 0.05$) when compared to normoxic WT and RHAMM KO mice. There is no significant change in IL-1 β , RAC, MPO and NAG activities (PN7 and PN14) between normoxic WT and RHAMM KO mice. In hyperoxia, compared to WT mice, RHAMM KO mice had increased alveolarization (PN14), decreased MPO (PN7, $P < 0.05$) and NAG activities (PN14, $P < 0.05$), as well as decreased IL-1 β (PN7 and PN14, $P < 0.05$).

Conclusions: RHAMM KO mice have increased alveolarization and decreased inflammatory response in hyperoxia, suggesting RHAMM could be a potential therapeutic target for BPD.

50 Risk Factors Associated with Development of Tracheobronchomalacia in Preterm Infants

早產兒氣道軟化症之危險因子探討

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Background: Tracheobronchomalacia (TBM) is an abnormal collapse of central airway and had long been recognized as an important complication of prolonged positive pressure ventilation in neonates and infants. The major aim of this study is to investigate the risk factors that contribute to the development of TBM in hospitalized preterm infants.

Methods: Infants diagnosed with TBM by flexible fiberoptic bronchoscope in a tertiary pediatric referred center in northern Taiwan were enrolled and retrospectively reviewed. Demographic and clinical data include gestational age, birth

body weight, apgar score, ventilator setting, duration of intubation, and outcomes were collected and analyzed. Student T test was used for comparison between infants with and without TBM.

Results: A total of 80 preterm infants were enrolled. Among them, 35 (43.8%) were diagnosed as having TBM based on flexible fiberoptic bronchoscope examination. Peak inspiratory pressure (19.6 ± 9.9 vs 10.3 ± 10.0 , $P < 0.001$) was significantly higher in the week before bronchoscopy exam among infants with TBM, and intubation days (89.9 ± 53.5 vs 46.2 ± 35.6 , $P < 0.001$) were significantly longer in infants with TBM than those without TBM. Furthermore, preterm infants with TBM require longer hospital stay (187.9 ± 56.3 vs 110.4 ± 56.3 , $P < 0.001$) and had higher in-hospital mortality (20% vs 4.4%, $P = 0.029$) than those without TBM.

Conclusions: Higher peak inspiratory pressure and longer intubation days could contribute to the development of TBM in preterm infants. Therefore, judicious use of ventilatory support and wean the patient from the ventilator as soon as possible are both essential to avoid adverse outcomes related to TBM formation.

51 Sustained Pharyngeal Inflation with Nasopharyngeal Oxygen Effects on Upper Airway Pressure and Lumen Changes in Infants—Flexible Endoscopy Measurement

幼兒給予持續咽腔充氣法時：上氣道腔壓力與管腔變化—以軟式內視鏡監測

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Background: Sustained pharyngeal inflation (SPI) can create peak inspiratory pressure (PIP) with prolonged inspiration time. Traditionally, SPI is executed via facemask. The “nasopharyngeal O₂ with close-nose and abdomen-compression (NPO₂-NC-AC)” is a novel non-invasive ventilation (NIV) which has demonstrated can provides adequate oxygenation/ventilation to assist flexible bronchoscopy (FB) in children. Closely measuring and monitoring these pressures are important for further management. In this study, we try to use this NIV with PhO₂ flow via a catheter, without any artificial device, with controllable nose-close (NC) to create a SPI in the upper airway lumen.

Methods: A total 20 of consequent children: age ≤ 3 year-old, requiring elective FB, with parental consent were enrolled. By using pharyngeal airway method, we gave the patients 1 L/kg of oxygen flow and measured the trans-pharyngeal pressure of 0 secs, 1 secs, 3 secs and 5 secs after mouth closure.

Results: The mean age of study was 6.8 ± 2.4 kg (Mean \pm SD) and age of 11.6 ± 2.4 month-old. The mean pressure was 4.1 ± 3.3 cmH₂O at 0 secs, 21.9 ± 3.3 cmH₂O at at 1 secs, 42.2 ± 12.3 cmH₂O at 3 secs, and 65.5 ± 18.5 cmH₂O at 5 secs. ($P < 0.001$) The transpharygeal pressure strongly correlated with time length of mouth closure.

Conclusions: In these four SPI–NIV supportive modes, a prolong SPI mode is simple and safe skill which could provides controllable & enough PIP (up to 65.5 ± 18.3 cmH₂O in 5 sec.) in the pharynx to expand the upper airway space. Moreover, it may benefit FB performance for comprehensive upper airway check in small children.

52 Integrative Analysis of Metabolomics and Microbiomics for Childhood Asthma

結合代謝質體學和微生物菌叢分析探討兒童氣喘

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Background: A comprehensive metabolomics-based approach to address the impact of specific gut microbiota on allergen sensitization for childhood rhinitis and asthma is still lacking.

Methods: Eighty-five children with rhinitis (n = 27), with asthma (n = 34), and healthy controls (n = 24) were enrolled. Fecal metabolomic analysis with 1H-nuclear magnetic resonance (NMR) spectroscopy and microbiome composition analysis by bacterial 16S rRNA sequencing were performed. An integrative analysis of their associations with allergen-specific IgE levels for allergic rhinitis and asthma were also assessed.

Results: Amino acid, β-alanine, and butanoate were the predominant metabolic pathways in the gut. Among them, amino acid metabolism was negatively correlated with the phylum Firmicutes, which was significantly reduced in children with rhinitis and asthma. Levels of histidine and butyrate metabolites were significantly reduced in children with rhinitis (P=0.029) and asthma (P=0.009), respectively. In children with asthma, a reduction in butyrate-producing bacteria including Faecalibacterium and Roseburia spp., and an increase in Clostridium spp., were negatively correlated with fecal amino acids and butyrate respectively (P<0.01). Increased Escherichia spp. accompanied by increased β-alanine and 4-hydroxybutyrate appeared to reduce butyrate production. Low fecal butyrate was significantly associated with increased total serum and mite allergen-specific IgE levels in children with asthma (P<0.05).

Conclusions: A reduced fecal butyrate is associated with increased mite-specific IgE levels and the risk of asthma in

early childhood. Fecal β-alanine could be a specific biomarker connecting the metabolic dysbiosis of gut microbiota, Clostridium and Escherichia spp., in childhood asthma.

53 The Application of Impulse Oscillometry in Combination with Bronchodilator Test for Diagnosis with Childhood Asthma

脈衝振盪肺功能合併支氣管擴張試驗於兒童氣喘診斷之應用

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Background: Impulse oscillometry (IOS) is simple and sensitive in diagnosis of small airway diseases especially for elderly or children with decreased pulmonary function and unable to perform spirometry properly. IOS measures static airway resistance of airway rather than dynamic forced airflow velocity in spirometry. Increase in peripheral airway resistance is suggestive of obstructive lung diseases. Bronchodilator test is one of the standard tools for measuring reversibility of airflow obstruction. Reduction of airflow resistance by more than 30% in children or 40% in adults after bronchodilator use is suggestive asthma in IOS. Here, we analyze the results of IOS-based bronchodilator test in children with clinician diagnosed asthma.

Methods: Patients aged less than 20 year-old with clinical diagnosis of asthma at China Medical University Children's Hospital were recruited in this study. We measured the airway resistance at 5 Hz and 20 Hz, reactance and resonance frequency before and 10 minutes after 2 puffs of 100mcg albuterol MDI inhalation. Patient's basic information, including age, sex, body weight and height were included for evaluation as well.

Results: A total of 213 patients were included in this study. The median age was 5 year-old (2-19 year-old); 54.9% patients were male (N=117). The median airway resistance at 5 Hz (R5) was 174.68% (95% CI=163.66–196.54) of the reference in baseline, and 119.88% (95% CI=117.67 - 124.14) at 20Hz (R20). The median resonance frequency was 5.09 Hz (95% CI=4.5143 - 5.3001). After standard bronchodilator test, the The median airway resistance at 5 Hz (R5) was 123.1% (95% CI=163.66-196.54). There was a significant reduction of airway resistance with median reduction of 52.8% (95% CI= 49.6311 - 56.3651, P < 0.0001)

Conclusions: In patient unable to perform spirometry properly, impulse oscillometry in combination with bronchodilator test provide a convenient and feasible method for diagnosis and monitoring the severity of asthma.

54 The Application of Impulse Oscillometry Combined with Bronchodilator Test for Asthma Management: A Children's Hospital Experience

應用脈衝震盪肺功能測定合併氣管擴張試驗於氣喘治療：一兒童醫院之經驗

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Background: Impulse oscillometry (IOS), a kind of noninvasive PFT, could easily performed during tidal breathing and requires only minimal patient cooperation. It can provide early detection of small airway disease and more sensitivity of diagnosing asthma. Bronchodilator test (BDT), one of the standard tools for measuring reversibility of airflow obstruction, should be done when patients with suspicion of asthma presented obstructive airflow pattern. The aim of this study is to analyze the results of IOS-based bronchodilator test in children with clinician diagnosed asthma.

Methods: Patients with suspicion of asthma received IOS from August 1, 2019 to May 31, 2020, presented obstructive airflow obstruction, and revealed positive BDT findings were retrospectively enrolled into this study.

Results: A total of 225 patients with median age of 5 year (male to female 123:102) were included. The median airway resistance at 5 Hz (R5) was 175.34% (95% CI=17.166—178.62) of the reference in baseline, and 121.68% (95% CI=118.73 - 127.12) at 20Hz (R20). The median small airway resistance (R5-R20) was 52.32% (95% CI=49.89 - 57.14). The median resonance frequency was 5.11 Hz (95% CI=4.62 - 5.35). After BDT, the median airway resistance at 5 Hz (R5) was 123.56% (95% CI=119.07-126.77). There was a significant reduction of airway resistance with median reduction of 52.8% (95% CI= 49.48 - 56.08, P<0.0001). There is moderate correlation between age and R20 values (r=0.51, P < 0.001) but weak correlation in pre-BD R5 (r=0.16, P=0.014), post-BD R5 (r=0.24, P<0.001), R5-R20 (r=0.28, P< 0.001), Resonance frequency (r=0.30, P< 0.001) but no correlation in X5 (r=0.09, P=0.319) and AX5 (r=0.05, P=0.423).

Conclusions: Our study show that the static proximal airway resistance of asthmatic patients increases with age, inferring different airway inflammation mechanism between pediatric and adult group. IOS combined with BDT provides a convenient and feasible method to evaluate the reversibility of airflow obstruction. Patients with suspicion of asthma should receive IOS, which can optimize management and improve outcomes.

55 Detecting Salivary C-reactive Protein in Children with Pneumonia

檢測兒童肺炎病人唾液C反應蛋白

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Background: Serum C-reactive protein (CRP) is a sensitive biomarker for inflammation and thereby broadly used to clinically diagnose infectious disease, including pneumonia, because of its high correlation with etiology and severity. However, blood test is fraught with technical difficulties in children. Salivary analysis may be considered as a new diagnostic tool, as it is noninvasive, patient-friendly, and easy to perform in children. This study aimed to evaluate the use of salivary CRP as a biomarker for children with pneumonia.

Methods: A prospective study was conducted for children aged 2–17 years admitted for pneumonia. Salivary and serum samples were collected at the initial admission and during follow-up as indicated for CRP and chemokine determination. Salivary samples were also collected from healthy children as control.

Results: A total of 60 healthy children (control group) and 106 children with pneumonia were enrolled in this study. The salivary CRP level was much higher in children with pneumonia than those in the control group (48.77 ± 5.52 ng/ml vs. 14.78 ± 3.92 ng/ml, $p < 0.001$). Salivary CRP level was highly correlated with serum CRP level in children with pneumonia ($r=0.679$, $p < 0.001$). Therefore, salivary CRP level (≥ 40.307 ng/ml) can be used to predict high serum CRP level (≥ 80 mg/L) with area under curve of 0.810 (95% confidence interval, 0.740–0.881). As the pneumonia improved, both salivary and serum CRP levels decreased during follow-up.

Conclusions: Salivary analysis can be an alternative biomarker for serum CRP in children with pneumonia. This is especially beneficial for pediatric patients, as salivary collection is simple, noninvasive, and patient friendly.

56 Dermatophagoides Microceras could Induce Airway Inflammation and Alleviated by Immune Modulation Protein FIP-fve in Asthma Mouse Model

在哮喘小鼠模型中，免疫調節蛋白FIP-fve可以改善微角塵蟎所誘導氣道炎症反應

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Background: Asthma is one of the most common chronic

inflammatory diseases. People with asthma have sensitive airways which react to triggers causing the mucosa swelling and airways narrowing. The incidence of asthma is increasing every year. Recently, several findings demonstrated that asthma/allergy may be caused by living environment, including food, dust mites, climate and air pollutants, etc. 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. In this study, we used *Dermatophagoides microceras* (Der m) which might be one of the most important allergens in Taiwan, especially in central area.

Methods: We used Der m to induce female BALB/c mice allergic reaction. The mice received intraperitoneal Der m sensitization on day 1 to day 3 and intranasal Der m sensitization on day 14, 17, 21, 24, and 27. This animal asthma model had been established. Besides, the Der m-sensitized mice were randomly assigned to two groups. One was fed FIP-fve on day 1 to 14; the other was fed on day 14 to 27. The normal control group was the non-sensitized mice who received normal saline.

Results: According to the results, FIP-fve treatment groups, no matter before or after Der m sensitizing, can suppress the airway inflammatory reaction, reduce IgE and Th2 cytokines and raise the IFN- γ and TGF- β . Moreover, FIP-fve also decreased IL-6 and IL-8 in Der m sensitization groups.

Conclusions: In conclusion, oral FIP-fve can prevent and treat Der m-sensitization airway inflammatory reaction. Therefore, oral FIP-fve may have a role in allergic airway disease prevention and treatment.

57 DEHP Induced-IL-28A and IL-29 Expression Reversed by Flavonoids in Human Bronchial Epithelium

鄰苯二甲酸酯增加人類呼吸道上皮細胞分泌之IL-28 A and IL-29之表達可由類黃酮反轉

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Background: The exposure to phthalates remains a significant risk factor for both the development of asthma and the triggering of asthma symptoms. Type III interferons (IFN λ s), or IL-28 and IL-29 mRNA levels have been reported to be higher in asthmatic children. Phthalates have been explored for their toxic potentials through estrogen receptor (ER), aryl hydrocarbon receptor (AhR) or peroxisome proliferator-activated receptors (PPARs). Some flavonoids are potent AhR or other nuclear receptor agonists

inducing cell cycle arrest and modulate xenobiotic metabolisms. We investigated whether phthalates could induce IL-28A and IL-29 expression in human bronchial epithelium. We hypothesized flavonoids may reverse the effect of phthalate-induced IL-28A and IL-29 expression in human bronchial epithelium.

Methods: The human bronchial epithelium (HBE) and A549 cells were pre-treated with DEHP or MEHP at different concentrations for 3 hours and isolated RNA for RT-PCR measurement. To identify the involved receptors or signaling pathways, cells were pre-treated with ICI 182780 (ER antagonist,) and CH-223191 (AhR), PPAR- α inhibitor (GW6741, Sigma-Aldrich, St. Louis, MO), PPAR- γ inhibitor (GW9662) or several flavonoids (apigenin, fustin, and narirutin) 1 hour before DEHP or MEHP treatment; 3 hours after DEHP or MEHP treatment, the cells were harvested for RT-PCR measurement. RT-PCR and ELISA were used to evaluate the effect of phthalates on IL-28A and IL-29 levels in human bronchial epithelium cells.

Results: DEHP and MEHP could induce IL-28A and IL-29 expression in human bronchial epithelial cells, HBE and A549 cells. Nuclear receptors, including ER and AhR, PPAR- α and PPAR- γ receptor antagonists could reverse DEHP or MEHP induced-IL-28A and IL-29 expression in A549 cells. Flavonoids including apigenin, kaempferol, fustin, and narirutin could also reverse DEHP or MEHP induced-IL-28A and IL-29 expression in A549 cells. These results implied that the reversing effect flavonoids on phthalate-induced IL-28A and IL-29 could be mediated through AhR, PPAR- α or PPAR- γ receptors.

Conclusions: Flavonoids may be the natural antidotes for DEHP through nuclear receptors, such as ER, AhR, PPAR- α or PPAR- γ .

58 Narirutin Suppress M1-related Chemokine IP-10 Production in Monocyte-derived M1 Cells via Epigenetic Regulation

類黃酮Narirutin可經由調節基因轉錄的機轉來抑制TH1細胞激素IP-10

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Background: Flavonoids are groups of natural phytonutrients found in fruits and vegetables that have recently become popular because of their anti-oxidation and anti-inflammatory ability. Narirutin is a flavanone which has been proven to have anti-inflammation effects, although its fundamental mechanisms are not understood.

Methods: To confirm our hypothesis, human THP-1 cells (1×10^6 cells/mL) were initially treated with 20 ng/mL phorbol 12-myristate 13-acetate (PMA) for 24 h. The PMA-differentiated THP-1 cells were treated with various levels of narirutin 2 h before lipopolysaccharide (LPS) stimulation, after that the cells were cultured for 24–48 h

and then examined. The concentration of interferon-gamma-inducible protein-10 (IP-10) was measured using enzyme-linked immunosorbent assay (ELISA). Epigenetic regulation mechanisms were explored by chromatin immunoprecipitation assay (ChIP).

Results: Narirutin significantly suppressed IP-10 production in M1 macrophage cells, and the suppressing effect was partly reversed by the estrogen receptor (ER) antagonist, the aryl-hydrocarbon receptor (AhR) antagonist, the peroxisome proliferator-activated receptor (PPAR)- α antagonist, and the PPAR- γ antagonist. We also found that narirutin-induced IP-10 suppression can be modulated by both histone H3 with H4 acetylation.

Conclusions: Our study suggests the potential of narirutin for the treatment of inflammatory disease by suppressing IP-10.

59 Level of Circulating Sphingosine-1-phosphate is Associated with Bronchial Hyper-responsiveness in Asthmatic Children

氣喘病童呼吸道敏感反應的程度與血清中鞘氨醇-1-磷酸鹽濃度的相關性

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Background: Sphingosine-1-phosphate (S1P) is involved in inflammatory cell influx into the airways and has been reported to exert potent effects on airway smooth muscle cells. ORM DL3, an asthma candidate gene, is known to regulate sphingolipid metabolism, but their relationship with the bronchial hyper-responsiveness in asthmatic children is currently unknown.

Methods: Using human plasma samples, mast cells, epithelial cells, and a mouse model, aryl hydrocarbon receptor (AhR) -mediated, ORM DL3-dependent S1P generation was examined using various molecular, cellular methods, the level of which was evaluated for its relationship with exercise pulmonary function test.

Results: In a case-control design, the levels of plasma S1P were significantly higher in subjects with asthma as compared to those in normal control subjects. A significant positive correlation was noted also between the levels of S1P and those of BMI, ECP, and eosinophils in asthmatic subjects, but not with those of IgE, FEV1, FeNO, PC20, and histamine. Significantly, analysis of S1P levels and the time spent during the exercise pulmonary function test showed

that higher S1P levels clearly led to positive results more swiftly. Subjects with lower S1P levels needed to exercise longer before receiving positive results. AhR ligands, including environmental PAHs, were shown to induce S1P generation in antigen/IgE-activated mast cells and mouse lungs exposed to AhR ligand alone or in combination with antigen challenge. Also, a significant reduction in the level of S1P was found in HMC and A549 cells with ORM DL3 knockdown, as compared to those seen in cells transduced with control sh-RNAs (sh-NC).

Conclusions: In this study, we discovered that increased levels of plasma S1P was associated with the bronchial hyper-responsiveness in children with asthma, and that AhR ligands induced S1P generation, which was ameliorated when the cells had ORM DL3 knocked down.

60 Montelukast does not Increase the Risk of Attention-deficit/hyperactivity Disorder in Pediatric Asthma Patients: a Nationwide Population-based Matched Cohort Study

montelukast在氣喘病童的使用不會增加過動症的風險：一健保資料庫研究

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Background: Attention-deficit/hyperactivity disorder (ADHD) has been linked to pediatric asthma patients treated with montelukast. This study is the first to use a nationwide health insurance research database (NHIRD) to study whether asthmatic children using montelukast are at an increased risk of ADHD.

Methods: We used data from the Taiwan NHIRD, which is a longitudinal database of one million randomly selected subjects. The enrolled patients were followed up until 2013. Patients with new-onset asthma (ICD-9 CM code 493.X) diagnosed between 1997 and 2013 under the age of 18 years old were enrolled. A competing risk-adjusted Cox regression analysis was conducted to evaluate the association between montelukast treatment and risk of ADHD. The incidence of ADHD (ICD-9-CM code 314.X) was determined.

Results: A total of 58,830 asthmatic children who had at least one claim of inpatient admission or at least two claims of an ambulatory visit were enrolled. Montelukast users and match controls were identified using propensity score matching in a 1:1 ratio. The matched cohort (n=16,378 in the montelukast and 16,378 in the non-montelukast group) created. The montelukast group had a similar risk of ADHD (n=712, 4.35%) as the non-montelukast group (n=655, 4%) [adjusted hazard ratio 1.06; 95% confidence interval, 0.96 to 1.18]. In children treated with montelukast, high cumulative days of montelukast use did not increase the risk of ADHD.

Conclusions: This nationwide population-based cohort study reveals that asthma children taking montelukast were not at an increased risk of developing ADHD. Validation of our retrospective survey requires further prospective study.

61 To Explore the Role of Dermatophagoides Microceras in Allergic Childhood Asthma in Central Taiwan

探討微角塵蟎在台灣中部地區過敏氣喘兒童扮演的角色

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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, including food, dust mites, climate and air pollutants, etc. The house dust mites (HDMs) are one of the most important allergens that have been identified in the household environment.

Methods: Der m main allergen breeding and use of E. Coli system to produce recombinant protein and used NGS technology to complete the dust mite gene analysis. Der p, Der f sequence data was used as a template to predict up to 31 different allergens, of which Der m1, Der m2 are the two main allergens. The laboratory used recombinant protein and sensitized mouse technology to generate specific Der m 1, Der m antibodies. Serum, nasal brush and HDMs environment samples from about 22 children with allergic asthma and sensitized with single and multiple house dust mites were collected and used chemiluminescent reaction to detect Der m, Der p, Der f, Der m2 specific IgE antibodies and ciELISA method to detect Der m allergen in nasal mucosa and environment dust for further general statistical analysis.

Results: We were the first to expose the presence of Der m in allergic patients in central Taiwan, and there were 68.2% (Der m), 77.3% (Der p), 72.7% (Der f) and 59.2% (Der m2), respectively. Moreover, we further analyzed house dust mite environmental sample, the dust mite distribution in central Taiwan is quite diverse.

Conclusions: HDMs, including Der p, Der f and Blomia tropicalis (Blo t) were important allergens in the Taiwan's asthma research field. Moreover, according to our results, Der m was an important allergen too. There are important to complete analysis of Der m distribution and pathogenesis.

62 The Effectiveness of Body Mass Index for Evaluating Bronchial Asthma Control Outcomes in Private Clinic Physician's

開業兒科醫師利用BMI指數對氣喘控制評估的結果

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Background: A persistently high body mass index during childhood increased the risk of doctor-diagnosed asthma at school age. Also, high body mass index was associated with asthma in females was proposed.

Methods: A retrospective cohort study was performed and chart review to evaluate urban asthmatic children from nine private pediatric clinics locate at difference communities in Taipei city, new Taipei city and Shen Zhen district. Overweight and obesity of children was defined by the BMI percentile according to the NIH guideline from Taiwan Health association (lean < 85%, normal weight=85%, overweight 85%-95%, obese >=95%).

Results: A total 100subjects aged 3 to 18 years were recruited in this studied. Body mass index percentile was recorded, which showed underweight 21%, normal weight 50%, overweight 17% and obesity 12% respectively. The percentile in male children results in 10%, 30% 10% and 8% respectively. In females asthmatic they showed 11%, underweight, 20% normal weight, 7% overweight, and 4% obesity.

Conclusions: In our current study, asthmatic children is predominant in the normal weight group and there's no sex differentiation. Also, not like the literature reports, overweight and obesity were not favored for asthma development in Taiwan.

63 Influences of Different Culture Conditions on Umbilical Cord Mesenchymal Stem Cell (ucMSC) Growth and the Contents of ucMSC Exosomes

不同培養條件影響臍帶間質幹細胞生長與其胞外囊泡的內容差異研究

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Background: Different culture conditions may affect the growth of mesenchymal stem cells (MSCs) and the contents of its secretary exosomes. Exosomes derived from MSCs may present MSCs to function as a cell-free transplant therapy. To find a higher growth capability and better bio-contents in exosomes may provide a useful immunoregulatory therapy of MSCs and MSC-derived exosomes. This study investigated effects of different culture conditions on cell growth of umbilical cord MSCs (ucMSCs) and the contents of exosomes derived from ucMSCs.

Methods: ucMSC harvested from umbilical cord Wharton jelly were cultured in normoxia or hypoxia conditions for measurement of cell growth. Sizes and particles of exosomes were analyzed by NanoSight nanoparticle tracking analyzer, the contents of exosomes were measured by millipore multiplex arrays, and the immune functions were analyzed by de novo expression of T cell transcription factors by RT-PCR analysis.

Results: ucMSCs cultured in hypoxia condition grew much better ($p < 0.01$) than those in normoxia condition. We then used hypoxia condition to harvest exosomes in naïve, preconditional and post-incorporated situations. The number of naïve ucMSC exosomes (ucMSC-EVs) was 4.4×10^{11} (vesicles/ml). EVs harvested from MSCs with preconditional treatment of bryostatin (Bryo-EV) and aspirin Asp-EV were respectively 2.3×10^{11} and 6.9×10^{11} (vesicles/ml). The mean size was larger in aspirin-primed EVs (Asp-EVs) and smaller in EVs with curcumin incorporation (EV-Cur). The miRNA profiles of ucMSC-EVs and EV-Cur were different, and the incorporation of curcumin increased the expression of 5 miRNAs and decreased the expression of 2 miRNAs. EV-Cur appeared to influence some of the cytokine contents, and aspirin tended to modulate T cell differentiation of Th17 as reflected on lower ROR γ T expression.

Conclusions: ucMSC appeared to grow better in hypoxia condition. The EVs derived from ucMSCs with and without precondition or incorporation of small molecule have different contents for immunoregulation, by which different immunologic disorders may be targeted for a better immunotherapy.

64 Different Contents and Functions between Exosomes Derived from Umbilical Cord Mesenchymal Stem Cell (ucMSC) and Bone Marrow (bmMSC)

比較骨髓與臍帶間質幹細胞來源的胞外囊泡內容與作用差別

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Background: Exosomes derived from mesenchymal stem cells (MSCs) of different tissues may have different contents and functions. To compare the difference between exosomes derived from bone marrow MSCs (bmMSCs) and umbilical cord MSCs (ucMSCs), we prepared different MSCs in accordance with our previous publication (Kuo, Yang, et al. J Proteome Res. 2011;10 (3) :1305-15; Shiue, Yang, et al. Pain. 2019; 160 (1) :210-23.) made from decoded samples.

Methods: The cell markers of bmMSC and ucMSC were analyzed by flow cytometry. Exosome biomarkers were studied by Western blot. Size and number of exosomes were measured by nanoparticle tracking analyzer (NTA). Contents of exosomes were measured by multiplex beads immunoassay. Cell growth was assessed in a human cortical neuron 2 (HCN-2) line with and without rotenone (0.25 μ M) treatment using CCK-8 cell counting kit.

Results: Compared to ucMSC, bmMSC had a higher expression level of CD105, but lower expression of CD44. Both ucMSC and bmMSC did not express hematopoietic cell markers of CD45, CD34 or CD11b. The bmMSC-exosomes expressed a higher CD63 expression but lower CD81 expression in Western blots (a representative set of 3 reproducible experiments). The contents of growth factors were also significantly different between bmMSC- and ucMSC-exosomes, in which ucMSC-exosomes contained significantly higher levels of FGF2 and HGF, while bmMSC-exosomes contained significantly higher levels of endoglin and VEGF-A. ucMSC-exosomes, but not bmMSC-exosomes, significantly ($p < 0.01$) protected the HCN-2 cells from the treatment of neurotoxin (0.25 μ M Rotenone). In an 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) -induced Parkinson disease (PD) mice, we traced the animal mobility and found that ucMSC-exosomes, but not bmMSC-exosomes, significantly ($p < 0.01$) improved the mobility of the MPTP-treated PD mice.

Conclusions: Results from these in vitro and in vivo studies indicated that ucMSC-exosomes prepared from Wharton jelly had significant effects on in vitro neuron cell protection and in vivo rescue of mice with PD induction better than bmMSC-exosomes. This study model may provide a useful immunoregulatory therapy of MSC-derived exosomes.

65 Patients with Coronary Artery Lesions Had Significantly Lower Immunoglobulin M on Six-Month Follow-up Data in Kawasaki Disease

冠狀動脈病變的川崎症病人六個月後的免疫球蛋白M濃度較沒有冠狀動脈病變的川崎病人下降

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Background: Intravenous immunoglobulin (IVIG) administration can up-regulate immunoglobulin (Ig) M in Kawasaki disease (KD). IVIG preparation contains very little amounts of IgM. The long-term expressions of IgM on KD remain unknown. FCMR-encoded Fc μ R is a receptor of IgM. The relationship between IgM and the IgM receptor is uncovered. We aimed to explore the role of immunoglobulin M in the prognosis of Kawasaki disease and correlate the IgM level with transcriptional expression of the IgM receptor.

Methods: We enrolled 40 pre-IVIG KD, 40 post-IVIG patients and 23 non-KD controls. We unfreeze plasma stored in -80 ° Crefrigerator. We used rate nephelometry to quantify the value of IgM in plasma. Each plasma consisted of a sample taken before IVIG was administered in acute stage and those taken at six months later. Whole blood leukocytes in the same subjects with IgM data were isolated and the mRNA expression for FCMR was determined.

Results: Of the 40 KD patients six months after KD, 20 had coronary artery lesions (CAL), while 20 did not. After six months of treatment, patients with CAL apparently have lower IgM compared patients without CAL (89.01 ± 5.41 vs. 122.4 ± 10.50 mg/dL, $p=0.012$). Gender and age distributions were similar between the two groups. We found no significant difference in IgM levels between pre-IVIG KD patients and controls. We observed no remarkable difference in the IgM levels between pre-IVIG patients with and without CAL (84.19 ± 7.99 vs. 111.4 ± 10.98 mg/dL, $p=0.068$). Before and after six months of IVIG treatment, IgM levels revealed no significant difference. Plasma IgM levels do not correlate to mRNA of FCMR in KD patients.

Conclusions: The current study is the first to long-term follow IgM in patients with KD. Interestingly, lower IgM levels in patient with CAL after six months of KD reflect their compromised immunity.

66 Apoptosis of Natural Killer Cells in Patients with Systemic Lupus Erythematosus -Regulation with IL-15

介白質15對紅斑性狼瘡病患周邊血液NK細胞凋亡的調控與影響

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Background: The accumulation of apoptotic cells may play an important role in the pathogenesis of systemic lupus erythematosus (SLE). Interleukin (IL) -15, a essential cytokine for natural killer (NK) and CD8+ T cell survival , is a potent inhibitor of apoptosis.

Methods: To examine the degree of NK cell apoptosis, marker of apoptosis, and apoptosis-related cytokines in SLE patients, and to determine the effect of IL-15 on these parameters compared to controls. Peripheral blood mononuclear cells obtained from SLE patients and healthy controls (HC) were stimulated with or without IL-15 (10 ng/ml) for 18 hours. We then assessed the expression of Annexin V/PI, caspase 3, caspase 8, Bcl-2, Bcl-xL, and STAT-5 gated on CD3-CD56+ NK cells by flow cytometry. Serum cytokines including IL-12p70, TNF- α , IL-10, IL-6, IL-1 β , IL-8, sFAS, FasL, TRAIL were determined by ELISA. Cytoplasmic and nuclear proteins were extracted from control and IL-15-treated purified NK cells and analyzed by proteome profiler assay.

Results: We observed 1. Low level of early apoptosis (Annexin V+/PI -) was observed in both SLE and HC NK cells; 2. SLENK cells showed decreased caspase 8 expression compared to HC; 3. The anti-apoptotic protein Bcl-2, Bcl-xL expression were decreased in SLE NK cells compared to HC;4. IL-15 inhibited the early apoptosis of HC, but not SLE NK cells, and enhanced Bcl-2, Bcl-xL expression of both SLE and HC NK cells 5. Increased serum sFas ,but decreased FasL, and TRAIL was found in SLE patients with active disease ; 6. Pro-apoptotic p27/kip1 and anti-apoptotic catalase, HMOX1, and HMOX2 may be involved in IL-15 mediated NK anti-apoptotic response.

Conclusions: Our study demonstrated the differential NK apoptosis related molecule expression and their response to IL-15 in SLE patients. Aberrant circulating death-related signaling cytokines production in SLE patients may serve as a disease marker. Possible IL-15 related NK apoptosis pathway will be highlighted.

67 Characteristics and Genetic Analysis of Cases with Early-onset Systemic Lupus Erythematosus

早發性兒童紅斑性狼瘡臨床特徵和基因分析

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Background: Systemic lupus erythematosus (SLE) is a complex, multisystem autoimmune rheumatic disease that can be rather severe, especially among the pediatric population especially before the age of 5. The aim of this study was to examine genetic associations and clinical phenotype in patients with early-onset SLE.

Methods: It is a cross-sectional study. Clinical and laboratory data from the 140 pediatric-onset SLE (pSLE) patients were included. The clinical and laboratory characteristics of pSLE patients followed at the Department of Pediatrics of Chang Gung Memorial Hospital (CGMH) were analyzed. They were combined with those collected from the literature by performing a systematic literature search on PubMed using the following keywords: SLE, early-onset, monogenic lupus.

Results: A total of 7 patients with early-onset SLE in our institution. 4 of 7 (57.1%) were females and 3 were males (42.9%). The age at disease onset ranged from 24 to 60 months. We demonstrated 2 previously reported variants in genes associated with SLE: Shared splicing variant c.625+1 G>A, were found in the SLC7A7 gene in 2 brothers; and a homozygous TREX1 c.292-293 ins A, p.Cys99Met frame shift mutation were discovered. In comparison with other pSLE, early-onset SLE had less female predominance (f:m=1.3:1), more central nervous system (57.1% v.s.17.2%) and renal involvement. (71.4-94.1% v.s. 61.7%)

Conclusions: This report demonstrates the clinical importance of identifying monogenic causes of rare disease to provide a definitive diagnosis, help rationalize treatment, and facilitate genetic counseling.

68 Predicting Systemic Corticosteroid Use in Childhood-onset Systemic Lupus Erythematosus by Artificial Intelligence

以人工智慧大數據預測兒童紅斑性狼瘡之全身性類固醇使用

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Background: Systemic lupus erythematosus (SLE) is a multi-system involved, chronic autoimmune disease, characterized by an unpredictable and fluctuating course with relapses and remissions over many years. Experience from our hospital revealed up to 34.1% of childhood-onset SLE (cSLE) patients can discontinue systemic corticosteroid (SCS) for a period of time. However, it is difficult to predict. This study is to use big data deep learning for predicting SCS use in cSLE.

Methods: We recruited 376 cSLE patients from 2006 to 2016 in Clinical information database in our hospital. The laboratory and drug for cSLE data were retrospectively recorded and analyzed. We classified cSLE patients by daily dosage of SCS (prednisolone or its equivalence). There were 4 groups as follows: Group A,B,C,D : no SCS use, < 10mg/day,10-20mg/day,and > 20mg/day. We use Pandas for classification filtering and excluding incomplete data, and Scikit learn for random sampling and split data to training set and test set. There were three training models in this study. They include Random Forest, Gradient Boosting and XGBoost. We used 80% data for training and 20% data for test. Result analyses were carried by XGBoost. To evaluate the performance of model, we adopted measures for classification model.

Results: The 1,2,3-month accurate prediction rate for training and test groups were 86.3%/ 85.1% , 85.8%/ 78.4% and 89.2%/ 75.3% respectively. Most patients in all subgroups stayed in the same subgroups in the next 1,2,3 months (79.9% ,74% and 68.5% respectively). If we take original group as the control, there was significant improve in accurate prediction in training group in the next 1,2,3 months (p=0.038, <0.00001,<0.00001, respectively). The test groups also achieved better accuracy in the next 1,2,3 months (p=0.02,0.029, 0.008 respectively).

Conclusions: Deep learning from laboratory and drug data cSLE can predict their future systemic corticosteroid use with fair accuracy. It can provide more data for physicians and cSLE patients/family during the short to middle-term care. The prediction may also helpful in selecting cases for cSLE studies.

69 Distinct Clinical Features and Novel Mutations in Taiwanese Patients with X-linked Agammaglobulinemia

台灣性聯遺傳免疫球蛋白低下病患之特殊臨床表徵及基因突變

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Background: X-linked agammaglobulinemia (XLA) is caused by a mutation of the Bruton's tyrosine kinase (BTK) gene and is the most common genetic mutation in patients with congenital agammaglobulinemia. The aim of this study was to analyze the clinical features, genetic defects and/or BTK expression in patients suspected of having XLA who were referred from the Taiwan Foundation of Rare Disorders

Methods: Patients with recurrent bacterial infections in the first 2 years of life, serum IgG/A/M below 2 standard deviations of the normal range, and $\leq 2\%$ CD19+B cells were enrolled during the period of 2004-2019. The frequency of infections, pathogens, B-lymphocyte subsets and family pedigree were recorded. Peripheral blood samples were sent to our institute for BTK expression and genetic analysis

Results: Nineteen (from 16 families) out of 29 patients had BTK mutations, including 7 missense mutations, 7 splicing mutations, 1 nonsense mutation, 2 huge deletions and 2 nucleotide deletions. Six novel mutations were detected: c.504G>T [p.K168N], c.895-2A>G [p.Del K290 fs 23*], c.910T>G [p.F304V], c.1132T>C [p.T334H], c.1562A>T [p.D521V], and.1957delG [Del p.D653 fs plus 45 a.a.]. All patients with BTK mutations had obviously decreased BTK expressions. Pseudomonas sepsis developed in 14 patients, and led to both Shanghai fever and recurrent hemophagocytic lymphohistiocytosis (HLH). Recurrent sinopulmonary infections and bronchiectasis occurred in 11 patients. One patient died of pseudomonas sepsis and another died of hepatocellular carcinoma before receiving optimal treatment. Two patients with contiguous gene deletion syndrome (CGS)

Conclusions: Pseudomonas sepsis was more common (74%) than recurrent sinopulmonary infections in Taiwanese XLA patients, and related to Shanghai fever and recurrent HLH, both of which were prevented by regular immunoglobulin infusions. A 10% of patients belonged to CGS involving the TIMM8A/DDP1 gene and presented with the DDON/MTS phenotype in need of aggressive psychomotor therapy.

70 Myocardial and Intraventricular Kinetic Energy in Patients with Fontan Circulation

單一心室術後病人心肌和心室內動能變化

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Background: Fontan patients may have the problem of progressive ventricular dysfunction and heart failure. The measurement of kinetic energy (KE) using magnetic resonance imaging (MRI) is a new method in evaluating cardiac function. The purpose of this study was to investigate the interaction between systolic myocardial and intraventricular KE in Fontan patients.

Methods: The subjects recruited 16 Fontan patients (17.8 ± 4.1 y/o, M/F 10/6) and 16 sex-matched normal controls (22.0 ± 1.2 y/o, M/F 9/7). The TPM and 4D flow data were acquired in a 3 Tesla MR scanner. The voxel-wise KE in both intraventricular blood flow and myocardium was calculated. The KE delay was calculated by the subtraction of time to peak (TTP) from TTP. The difference of KE and KE delay between two groups was compared.

Results: Compared to normal group, Fontan group showed decreased peak and mean systolic KE (2.29 ± 0.84 mJ vs. 1.45 ± 0.85 mJ, 1.37 ± 0.44 mJ vs. 0.88 ± 0.36 mJ, p<0.01), and decreased peak and mean systolic KE (0.10 ± 0.06 mJ vs 0.02 ± 0.02 mJ, 0.05 ± 0.02 mJ vs 0.02 ± 0.01 mJ, both p <0.001). Fontan group presented more diverse KE delay distribution in comparison with normal group. Longer TTP (59.3 ± 9.1%ES vs 47.4 ± 7.5 mJ, p<0.001) and TTP (39.4 ± 12.1%ES vs 22.1 ± 4.2%ES, p<0.001) was shown in Fontan group. No significant difference of KE delay was shown between two groups, while the Fontan group presented larger coefficient of variation of intragroup KE delay (79.7% vs 29.6%). The KE delay in Fontan group significantly correlated with peak systolic KE (r=0.546, p=0.029) and with mean systolic KE (r=0.584, p=0.018), while no significant correlation was found in normal group.

Conclusions: Our results demonstrated Fontan patients exhibited decreased myocardial and intraventricular KE and prolonged TTP during systole. The correlation between KE delay and KE in Fontan patients was observed and illustrated the adverse impact of abnormal energy transferring mechanism on Fontan circulation.

71 Aortic Regurgitation Stands as a Risk Factor for Surgical Intervention in Marfan Syndrome: A Single-Center Experience

主動脈逆流為馬凡氏症患者一重要之手術風險因子

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Background: Marfan syndrome is an inherited connective tissue disease, which often causes aortic root dilatation and dissection, and eventually requires surgical intervention. The timing for surgical intervention depends on the severity of aortic root dilatation, left ventricular dysfunction, and occurrence of aortic dissection (in current clinical practice). The direct relationship between surgical intervention and aortic regurgitation was seldom mentioned in previous studies.

Methods: A retrospective cohort study was conducted, comparing risk factors for surgery in patients with Marfan syndrome. From January 2009 through May 2019, we enrolled 112 patients, adolescents and young adults, who were treated in the department of pediatric cardiology of Taipei Veterans General Hospital.

Results: Among the participants, nine patients received the Bentall procedure, and the other 103 did not receive surgical intervention. The operation group had larger aortic root size, larger left ventricular inter-diameter, and higher prevalence of moderate and severe aortic regurgitation than the non-operation group.

Conclusions: Among adolescents and young adults with Marfan syndrome, aortic root dilatation, left ventricular dilatation, and significant aortic regurgitation are all significant risk factors for early surgical intervention.

72 Deep Learning Framework and Data Augmentation for Ultrasound Images of Ventricular Septal Defect

研究深度學習框架與擴增數據自動判讀心室中隔缺損之超音波影像

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Background: Congenital heart diseases (CHD) could be detected by ultrasound images that are useful in practice. Although ultrasound can be used for immediate diagnosis, doctors still need much time to read the heart image. Most important of all, this diagnosis is highly relied on doctors' experiences.

Methods: This paper established an ultrasound image classification on deep learning algorithms to solve the challenges. We detect the most common CHD, the first, second, and 4th type of Ventricular septal defect (VSD). We improved the performance of the well-known deep learning algorithms, including InceptionV3, ResNet, and DenseNet. In addition, due to the optimizer algorithm and overfitting problem influences the performance of the deep learning algorithm, we study some optimizer algorithms and early-stopping strategy. To enhance the solution quality, we utilize the data augmentation methods for solving this classification problem.

Results: The selected approach is further compared with Google AutoML which applied the structure search to get a better prediction quality. Our results show most VSD types could be recognized by the deep learning algorithm. However, there is still one type that needs more advanced techniques to be conquered.

Conclusions: Most VSD types could be recognized by the deep learning algorithm. However, there is still one type that needs more advanced techniques to be conquered.

73 Prevalence of Kawasaki Disease in Young Adults with Suspected Myocardial Ischemia

探討川崎病在疑似心肌梗塞年輕病患之盛行率

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Background: Up to 25% of patients with untreated Kawasaki disease (KD) and 5% of those treated with intravenous immunoglobulin will develop coronary artery aneurysms. Persistent aneurysms may remain silent until later in life when myocardial ischemia can occur. We sought to determine the prevalence of coronary artery aneurysms suggesting a history of KD among young adults undergoing coronary angiography for evaluation of possible myocardial ischemia.

Methods: We reviewed the medical histories and coronary angiograms of all adults < 40 years of age who underwent coronary angiography for evaluation of suspected myocardial ischemia at 2 hospital from 2015 to 2019 (n =208). History of KD-compatible illness and cardiac risk factors were obtained by medical record review. Angiograms were independently reviewed for the presence, size, and location of aneurysms and coronary artery disease by 3 cardiologists blinded to the history. Patients were evaluated for number of risk factors, angiographic appearance of their coronary arteries, and known history of KD.

Results: Of the 208 young adults who underwent angiography, 48 had coronary aneurysms. After all clinical criteria were assessed, 20% had aneurysms secondary to KD as the cause of their coronary disease.

Conclusions: Coronary sequelae of KD are present in 20% of young adults evaluated by angiography for myocardial ischemia. Cardiologists should be aware of this special subset of patients who may benefit from medical and invasive management strategies that differ from the strategies used to treat atherosclerotic coronary artery disease. The result may have connection to the fact that Taiwan's higher incidence rate of KD compare with North America.

74 Transcatheter Closure of Patent Foramen Ovale after Cryptogenic Stroke - A Single Center Experience in Taiwan

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Background: Previous studies revealed an increased risk of cryptogenic stroke (CS) associated to patent foramen ovale (PFO). Recent reports also yielded that cardiac or pulmonary shunts were related to agitated saline intravenous injection. We aimed to investigate the association between the grade of transcranial Doppler (TCD) study and the presence of PFO, which needed transcatheter closure, in the patients with CS.

Methods: 62 patients, younger than 60 years of age, with CS who underwent transcatheter PFO closure between September 2013 and January 2020 in Taichung Veterans General Hospital were enrolled in this retrospective study. TCD study was performed in 50 patients. We calculated the grade of TCD study, the risk of paradoxical embolism (RoPE) score, the successful closure rate, complications such as atrioventricular block or new onset of atrial fibrillation (Af), and the efficacy of PFO closure for preventing recurrent cryptogenic strokes.

Results: In all the patients undertook TCD study, 50% were grade I (n=25), 20% were grade II (n=10), 10% were grade III (n=5), 2% was grade IV (n=1), and 18% were grade V (n=9). In these 11 patients without PFO, 36.4% patients did not undergo TCD study (n=4). 63.6% were grade I in TCD study (n=7). In the intention-to-treat population (n=51), successful PFO closures were performed with Amplatzer septal occluders (84.3%, n=43), Amplatzer cribriform multifenestrated septal occluders (11.8%, n=6), or Occlutech Figulla Flex II PFO occluders (3.9%, n=2). In the PFO closure group, only 2 patients developed Af after the procedure. No recurrent ischemic stroke occurred in the PFO closure group.

Conclusions: TCD study is a good tool for detecting PFO among CS. Closing PFO might be a good strategy for preventing recurrent stroke among those patients.

75 Ultrasonographic Measurements of the Internal Diameters of Femoral Vessels in Neonates Less Than 2.5 kg

以超音波測量小於2.5公斤新生兒的股血管內徑大小研究

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Background: The femoral vein (FV) and femoral artery (FA) are important vessels for access in the pediatric cardiac catheterization. Vascular injury after catheterization occurred more frequently in neonates, especially prematurity and low birth body weight (LBW) infants. The primary aim of this study is to determine the correlation of body weight (BW) to the size of the femoral vessels in LBW and premature infants. The secondary aim is to determine whether weight can be used clinically to predict the size of femoral vessels in these infants.

Methods: A total of 76 premature or LBW neonates less than 2.5kg (0.57-2.4kg) and gestational age of 24 to 38 weeks were enrolled into this study. Echocardiography was performed to measure the size of central blood vessels, including both sides of FA and FV, superior vena cava (SVC), inferior vena cava (IVC), and descending aorta (DAO) by two experienced pediatric cardiologists between January and November, 2019. They were divided in four groups: group A (2-2.49kg, n=20), group B (1.5-1.99kg, n=26), group C (1-1.49kg, n=18), and group D (<1kg, n=12). Simple linear regression analysis was used to estimate the strength of the relationship between variables.

Results: The male to female ratio was 1.38, and forty (52.6%) neonates had patent ductus arteriosus during study. The mean diameters of RFA were 1.97, 1.87, 1.75, and 1.56 mm in group A, B, C, and D, respectively. The mean diameters of RFV were 2.31, 2.25, 2.07, and 1.82 mm, LFA of 1.93, 1.87, 1.78, and 1.59 mm, and LFV of 2.33, 2.22, 2.18, and 1.86 mm in each group, respectively. There was a positive correlation between BW to the size of the femoral vessels (correlation coefficient of 0.61, 0.61, 0.51, and 0.44 between weight and RFA, RFV, LFA, and LFV, respectively). The equations of regression line were RFA=1.36+0.29xBW, RFV=1.62+0.34xBW, LFA=1.46+0.22xBW, and LFV=1.75+0.27xBW.

Conclusions: BW can be a predictor of diameters of femoral vessels in premature or LBW newborns. It can help us choose the vessels and the size of sheath before femoral catheterization to decrease vascular injury. The correlation coefficients showed moderate positive relationships, and a further study is required to validate these findings.

76 Result of Head-up Tilt Table Tests of Pediatrics, a Single Hospital's Experience

兒童昏厥病患之傾斜床測試結果分析：單一醫院之經驗

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Background: Orthostatic related problems were common complaints in pediatric clinics. Most of the pediatric patients experienced orthostatic symptoms were transient and benign clinically. Rarely, significant problems might be encountered. We analyzed our results of head-up tilt table tests (HUT) in recent years in our children's hospital.

Methods: We analyzed our data set of 96 pediatric patient with HUT test with complete study and the results was assigned into: negative, inconclusive, vasovagal syncope (VVS), and postural orthostatic tachycardia syndrome (POTS) respectively.

Results: Our analysis showed 35 cases of confirmed VVS, and 5 cases of POTS was diagnosed according to the criteria proposed of HUT tests. 54 cases were negative and 2 cases remained inconclusive after HUT test.

Conclusions: In our experience, 36% (35/96) of patients referred for HUT test with the impression of syncope or near syncope were vasovagal syncope and 5% (5/96) of referral patients were postural orthostatic tachycardia syndrome.

77 KCNQ2 Loss-of-Function Mutations with Heteromeric Kv7.2 Current Changes are Correlated with Long-Term Neurodevelopmental Outcomes

KCNQ2 loss-of-function突變導致兒童長期神經發展預後與異質的Kv7.2鉀離子通道電流改變有關

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Background: Background: Pediatric epilepsy caused by a KCNQ2 gene mutation can manifest benign familial neonatal convulsions to neonatal-onset epileptic encephalopathy. Patients might manifest mild to profound neurodevelopmental disabilities.

Methods: Methods: Two patients with the KCNQ2 c.740C > T (S247L) and c.853 C > A (P285T) mutations presented with neonatal-onset epileptic encephalopathies and autisms. We analyzed P285T and three mutations that cause KCNQ2

protein change in the 247 position: S247L, S247X, and S247W. S247L and S247W cause neonatal-onset epileptic encephalopathy and poor neurodevelopmental outcomes; S247X cause benign familial neonatal convulsions and normal neurodevelopmental outcome. We investigated the phenotypes correlated with HEK293 cell functional current change and KCNQ2 protein expression.

Results: Results: In S247L, S247W, and S247X, there were more cell current changes in the homomeric-transfected S247X than in the S247L and S247W ($p < 0.05$). But in the heteromeric channel, S247L and S247W had more current impairments than did S247X. The protein expressions of S247X were significantly ($p < 0.05$) lower than in the wild-type, S247L, and S247W. The neurodevelopmental outcomes were most severe in S247L and in S247W, but not correlated with the amount of protein expression. P285T cells expressed significantly ($p < 0.05$) lower current densities than did the wild-type.

Conclusions: Conclusions: Current changes were significant in cells with homomeric transfection of S247X, but currents improved in cells with S247X after heteromeric transfection of wild-type KCNQ2 and KCNQ3. This was not the case in cells with S247L and S247W. Our findings support the notion that heteromeric functional current change is correlated with long-term neurodevelopmental outcomes. P285T mutation can cause reduction in Kv7.2 currents and neonatal epileptic encephalopathy.

78 Impairment of Proteasome and Autophagy with Dysregulation of NRF2 Signaling Pathway Underlying the Pathogenesis of Globoid Cell Leukodystrophy

自嗜作用與泛素-蛋白酶體系統失調與NRF2訊息異常是造成GLD白質退化症的病理機轉

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Background: Impairment of ubiquitin-proteasome system (UPS) and autophagy causing cytoplasmic aggregation of ubiquitin and p62 has been implicated in the pathogenesis of most neurodegenerative disorders, yet, it has not been fully elucidated in Leukodystrophies. The relationship among impairment of UPS, autophagy, and globoid cell leukodystrophy (GLD), one of the most common demyelinating leukodystrophy, is clarified in this study.

Methods: Brain tissues from wild type and twitcher mice were processed for IHC and western blotting. MO3.13 oligodendrocytes were incubated with psychosine concomitant with chloroquine and MG132. Autophagy markers, oxidative stress, cell viability, and bioenergetics were determined.

Results: Spatiotemporal accumulation of ubiquitin- and p62-aggregates located mainly in the white matter of brain and spinal cord at disease progression. Levels of insoluble

LC3-II, p62 and ubiquitin in twitcher brain were elevated to 2.2-, 4-, and 3.2-fold of WT mice. In vivo, levels of insoluble LC3-II, p62 and ubiquitin were exacerbated by Chloroquine and MG132 to 3-/1.8-, 3-/1.5-, and 2.8-/1.8-fold of psychosine-treated cells, while the cell viability, ROS and respiration were 25% of norm, 4-fold increase, and 50% reduction in psychosine treated MO3.13 cells with inhibition of both UPS and autophagy. Of note, levels of NRF2 and insoluble KEAP1 were 25% and 1.8-fold of norm in twitcher brain

Conclusions: For the first time, our studies unveils the impairment of autophagy and UPS leading to accumulation of ubiquitin and p62 in the white matter of CNS in murine model of GLD. Furthermore, in vitro studies validates the dysfunction of autophagy and UPS exacerbating the cytoplasmic aggregation of insoluble ubiquitin and p62, and the dysfunction of NRF2 signaling resulting in reduction of mitochondrial respiration, elevation of ROS and subsequent cell death of oligodendrocytes. These findings open new insights in understanding the molecular mechanism for the pathogenesis of GLD, and a possible therapeutic avenues via targeting specific pathomechanism and modulation of proteostasis as well as providing a sufficient antioxidant system.

79 Association Study of 212 Epileptic-related Genes Variation with Childhood Absence Epilepsy

212個與癲癇相關基因之變異與孩童失神性癲癇的關聯研究

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Background: Epilepsies are a diverse collection of neurologic disorders involving recurrent and unprovoked seizures that are the manifestation of abnormal electrical activity in the central nervous system. Childhood absence epilepsy (CAE) is characterized by a brief loss and return of consciousness, abrupt and sudden-onset impairment of consciousness, interruption of ongoing activities, a blank stare, possibly a brief upward rotation of the eyes, generally not followed by a period of lethargy. CAE occurred commonly in children aging 4 to 14 year. Previous studies have uncovered a growing number of single gene mutations that cause epilepsy. Here, we selected 212 epileptic-related genes which the variants of their locus regions being correlated with neurodevelopmental disorders to elucidate the associated possibility with CAE.

Methods: Eighteen patients diagnosed with CAE according to ILAE and DSM-IV guideline were enrolled. Whole exome sequencing (WES) was performed and 212 epileptic-related genes panel was applied to analyze the participants' sequence data. The variants observed from participants compared with database and only their minor allele frequency (MAF) smaller than 0.001 was conducted to predict the effects of amino acid substitution using: SIFT, PolyPhen-2 and Combined Annotation Dependent Depletion (CADD) and the variants annotation in ClinVar.

Results: After sequencing analysis and MAF filtered (< 0.001), 85 variants in 61 genes were observed in these patients. According to the include criteria based on bioinformatics prediction (SIFT: deleterious; PolyPhen-2: damaging; CADD score >20), 13 variants from 12 genes were isolated. Excluded those site noted benign in ClinVar, only 6 variants in 6 genes [KCNJ10: c.1042C > T (p.Arg348Cys); KCNQ4: c.316T > G (p.Phe106Val); CLCN1: c.1205C > T (p.Ala402Val); CACNA1H: c.2368G > A (p.Val790Met); SCN4A: c.2297T > C (p.Met766Thr); DIAPH1: c.256T > C (p.Met256Thr)] were found in 6 patients.

Conclusions: Our results demonstrated that the variants of epileptic-related genes could be associated with CAE, but no single gene variation was dominated in this disease. Database update and WES data reanalyzed could get some new genetic information, thus we can extend our view for study.

80 Clinical Manifestations of Psychogenic Non-Epileptic Seizures

心因性癲癇之臨床表現

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Background: Psychogenic non-epileptic seizures (PNES) is one of the conversion disorder with paroxysmal attacks mimicking epileptic seizures but no abnormal neuronal discharges can be recognized on electroencephalography (EEG) during the attacks and is considered to be triggered by psychological stressors. Prompt and accurate diagnosis might be a major challenge. This study tries to find out the clinical features of PNES for further accurate differential diagnosis from epilepsy.

Methods: This case series enrolled patients with the diagnosis of PNES between December 2003 and February 2019 retrospectively in Division of Pediatric Neurology, Department of Pediatrics, Taipei Veterans General Hospital. ICD codes were used for screening and the relevant medical records were carefully reviewed. Experienced pediatric neurologists made the PNES diagnosis, mostly from clinical manifestations, and

sometimes with confirmatory video-electroencephalography or simultaneous electroencephalography during the attack. The general information, clinical manifestation, psychological condition and relevant laboratory or imaging test results were collected and analyzed.

Results: Of the 26 patients, PNES occurred in male (34.6%) and female (65.4%) patients with the mean age being 13.6 years old. Ten patients (38.5%) with PNES had established diagnosis of epilepsy before. The duration between the onset of symptoms and diagnosis range from 1 to 120 days (Mean 20.81 days, median: 12 days). Sixteen patients (61.54%) showed the possible causative psychosocial stressors. Multiple subtle features or specific clinical manifestations of PNES that usually differ from epileptic seizures were observed on all patients with PNES.

Conclusions: Detailed information of clinical manifestations and skillful observation are important for the challenging diagnosis of PNES.

81 Analysis of Dravet Syndrome and Fever-sensitive Epilepsy - an Experience of a Single Medical Center

Dravet症候群及熱感性癲癇分析—單一醫學中心經驗

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Background: Dravet syndrome (DS) is a severe developmental and epileptic encephalopathy characterized by the onset of prolonged febrile and afebrile seizures in infancy. In 2001, de novo variants of the SCN1A gene were discovered to cause most cases of DS. In some cases, non-SCN1A genes mutation can present with a phenotype so similar to that of DS. The aim of this study was to compare the phenotype of SCN1A gene with non-SCN1A gene mutation related DS.

Methods: Thirty-six patients with DS-like phenotypes were followed at Chang Gung Memorial Hospital from July 2017 to December 2019. We retrospectively analyzed the variables of clinical profile and genetic survey.

Results: There were 36 patients with DS-like phenotype enrolled in this study. 12 patients (33.3%) with SCN1A mutation, 1 (2.8%) with SCN8A mutation and 5 females (13.9%) with PCDH 19 mutation. The median age of first seizure onset was 7 m/o in SCN1A mutation patients, 1.3 y/o in PCDH19 and 10 m/o for remaining patients. The majority of SCN1A mutation patients had status epilepticus (75% vs 40%) and fever-sensitive seizures (77% vs 31%) compared with patients of PCDH19 mutation. Initially, 8 of 12 SCN1A mutation patients showed a normal interictal EEG, and remained normal during the follow-up in 2 patients. 46.9% were normal in patients (n = 32) underwent

brain MRI. 3 of 5 (60%) patients with PCDH19 mutation showed brain MRI abnormalities. The 3 most commonly used antiepileptic drugs were levetiracetam (69.4% of all patients and 75% in SCN1A cases), sodium valproate, clobazam. 3 of 12 patients with SCN1A mutation used stiripentol. 27.2% genetic mutation identified patient became seizure free and the 76% seizure free in remaining patients at least 6 months.

Conclusions: Patients with SCN1A mutation had high rate of fever-sensitive seizures, status epilepticus, and relatively small seizure onset age. PCDH19 mutation had a relatively high proportion of abnormal brain MRI findings. There was no significant difference of antiepileptic drugs used in the patients of our study. Compared with genetic mutation identified patients, the remaining patients had better seizure outcome.

82 Transcranial Photobiomodulation Attenuates Pentylentetrazole-Induced Status Epilepticus in Periparturient Rats

經顱光生物調節療法減緩青春期大鼠之Pentylentetrazole所誘發的癲癇重積狀態

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Background: Convulsive status epilepticus is the most common neurological emergency in children and adolescents. Although clinically established nonpharmacological treatments such as deep brain and vagus nerve stimulation showed effectiveness, they are invasive. Noninvasive treatments including repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) also showed effectiveness to epilepsy, however, adverse event of rTMS and poor evidence of effectiveness of tDCS were noted. Therefore, new effective, noninvasive and safe treatment for pediatric CSE is needed. Transcranial photobiomodulation (tPBM) reversed elevated rodent neurotransmitters after status epilepticus (SE). However, whether tPBM can attenuate seizure behaviors or even SE remains unknown.

Methods: Near-infrared laser at wavelength 808 nm was applied transcranially to postnatal day 30-36 Sprague-Dawley rats prior to subcutaneous pentylentetrazole (PTZ) injection. Hematoxylin-eosin (H&E), immunofluorescence (IF) staining with anti-parvalbumin (PV) and terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL) assay after IF staining was performed.

Results: Behaviorally, tPBM attenuated the mean seizure score (the slope of curve at tPBM group was 0.01148 ± 0.007081, which was significantly lower than the slope 0.04713 ± 0.009825 at sham group, p < 0.005) and reduced the incidence of SE (70% at sham group vs 60% at tPBM group, severe SE: 85.7% at sham group to 50% at tPBM group) and mortality (42.9% at sham group vs 16.7% at tPBM group). Histochemically, tPBM reduced dark neurons in the cortex, hippocampus, thalamus and hypothalamus according to H&E staining, lessened the apoptotic ratio of

parvalbumin-positive interneurons (PV-INs), and alleviated the aberrant extent of PV-positive unstained somata of principles in the hippocampus.

Conclusions: tPBM with wavelength at 808 nm attenuated PTZ-induced seizures, SE and mortality in peripubertal rats and reduced PTZ-induced neuronal injury, apoptosis of PV-INs and preserved PV-positive perisomatic inhibitory network in the hippocampus.

83 Next-Generation Whole Exon Sequencing in the Genetic Diagnosis of Early-Onset Epileptic Encephalopathy

次世代全外顯子定序對早期癲癇性腦病變之基因診斷

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Background: Early-onset epileptic encephalopathy (EOEE) comprises a group of heterogeneous disorders in which development is impaired by recurrent clinical seizures during the early childhood period. The identification of causative mutations associated with EOEEs is useful for genetic counseling, and possibly for clinical management. The application of next-generation sequencing (NGS) technology highlights the striking impact of its role on genetics and medicine.

Methods: During the recent 2 years, we try to find the pathogenetic causes among cryptogenic epileptic encephalopathy patients through whole-exome sequencing (WES). Hereby we report the primary result data.

Results: A series of 14 (7 males and 7 females) patients exhibiting EOEE with seizure onset within the first 2 years of life were collected and analyzed using WES. They aged 2 months to 23 years (average 5 years 11 months). Mutations were found in 8 (4 boys and 4 girls) probands; the overall mutation identification rate via WES was 57.1%. Two (25%) mutations involve ion channels, including each in GABRG2 and SCN2A. The other 6 (75%) mutations include each in CDKL5, KIDINS220, QARS1, SYNE2, TUBB2B, and IQSEC2. Seven (87.5%) of the identified mutations were confirmed to be de novo and one (12.5%) was parentally transmitted autosomal recessive inheritance. The majority (62.5%) of identified mutations were missense except for two nonsense mutations in CDKL5 and IQSEC2, as well as a frameshift mutation in KIDINS220.

Conclusions: Our data showed the genetic heterogeneity of EOEE. This study demonstrates a detection rate of 57.1% compared to the previous target gene panel analysis (29.5%). The role of WES in the genetic diagnosis of EOEE is hereby emphasized.

84 Objective Evaluation of Therapeutic Effects of ADHD Medication Using a Smart Watch

以智慧型手錶評估注意力不集中及過動症之藥物治療療效

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Background: Attention-deficit hyperactivity disorder (ADHD) is the most common neurobehavioral disorder in schoolchildren. Several methods are used to evaluate ADHD therapeutic effects, including the Swanson, Nolan, and Pelham (SNAP) questionnaire, the Vanderbilt ADHD Diagnostic Rating Scale, and the visual analog scale. However, these scales are subjective. In this study, we employed an objective method to evaluate the aforementioned therapeutic effects.

Methods: Ten patients (9 boys and 1 girl) with ADHD were enrolled. An accelerometer was embedded in a smart watch to record the movements of patients with ADHD. The variance values of the accelerometer before and after 1 month of medication (methylphenidate) use were compared.

Results: The results demonstrated that the variance values along the y- and z-axes of the accelerometers significantly decreased after 1 month of methylphenidate use. Before and after 1 month of methylphenidate use, the variance values were 4.4227 ± 2.1723 and 2.3214 ± 0.6475 ($p = .0119$) on the y-axis, and 4.0933 ± 1.5720 and 2.4091 ± 0.8141 ($p = .0140$) on the z-axis, respectively. In addition, the correlation was moderate-to-strong between SNAP hyperactivity subscale and variance along the y-axis.

Conclusions: Thus, a smart watch with an accelerometer inside is potentially an objective and useful method for evaluating the therapeutic effects of ADHD medications.

85 Language Input from the Beginning: the Nutrition of Infant's Receptive Vocabulary

早期語言環境對嬰兒理解性語言發展之影響

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Background: Early language development in childhood is recognized as central to child's development of learning skills and socialization. Literature has suggested that language ability is strongly influenced by environmental factors, such as the quantity and linguistic diversity that the

caregivers provide in the early years. The American Academy of Pediatrics has recommended that it is a responsibility of pediatricians to encourage reading aloud beginning as soon as possible after birth. Our study conducted two parent-infant interaction settings to observe the quantity and linguistic diversity that the 6-month-old infants received from their mothers and their early language skill was also evaluated.

Methods: A total of 21 mother and 6-month-old healthy infant dyads were included in this study. All infants were born full-term and under Mandarin-acquiring monolinguals. All mothers were native Mandarin-Chinese speakers. Language data of mother-child interactions in the home environment were collected in two 5-minutes settings (book-reading versus toy-playing). The videotaped interactions were transcribed following the CHAT transcription conventions of the CHILd system and the analyses were conducted using the CLAN software. Children's language ability was estimated using the MCDI-T.

Results: The results indicate that mothers tended to speak longer mean length of utterances (MLU, $p < .001$) and higher lexical diversity ($p < .05$) in the setting of book-reading than toy-playing. In addition, mothers' lexical diversity in general was significantly related to the receptive vocabulary of 6-month-old infants ($r = .461$, $p < .05$).

Conclusions: 1. Maternal lexical richness was higher in the book-reading setting, which related to the receptive vocabulary of 6-month-old infants. 2. Quality of the maternal language input (diversity) turned out to be more related to a child's receptive vocabulary than quantity (MLU). 3. The anticipatory guidance of early book reading from pediatricians is important for parents of infants.

86 Characteristics and Outcomes of Preschool Children Presenting to a Pediatric Emergency Center

單一兒童急診中心學齡前兒童就診的特徵和結果分析

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Background: Pediatric emergency medicine is a young subspecialty. Many preschool patients seek emergency care, but little information is available about the needs and current treatment of them. In this observational study, we like to describe the characteristics, chief complaints, diagnosis, and outcomes of preschool patients presenting at a pediatric emergency center.

Methods: This was a retrospective descriptive study. Data were collected from preschool patients under 7 years old (y/o) presenting at the largest pediatric emergency department (PED) in North Taiwan in year 2018.

Results: Clinical records of 34,588 pediatric patients who visited our PED were analyzed. Among them, 77%

($n=26444$) were preschool children younger than 7y/o including 14737 (55.7%) boys and 11705 (44.3%) girls. Their mean age was 2.65 y/o (Standard Deviation [SD] = 1.76 years). Incidence for their PED visit was highest from 6 p.m. to 12 a.m. (45.8%, $n = 12,121$). Of the 136 different presenting complaints, fever (47.2%, $n=12,486$), nausea/vomiting (10.6%, $n=2799$), and cough (8%, $n=2115$) were common complaints for their PED visit. The majority of patients were discharged 19,501 (73.8%). There were 6943 (26.2%) cases, including 303 (1.1%) cases requiring intensive care, need hospital admission and 4 patients died. The mean duration of the ED stay was 3.4 hrs (SD = 4.1 hrs).

Conclusions: Most preschool patients presenting at a pediatric emergency center were young children from 6 p.m. to 12 a.m. . Fever was the leading cause for their PED visit.

87 Clinical Analysis of Children Admitted to the Pediatric Emergency Department Transferred from the Pediatric Outpatient Department

自兒童門診區轉診至兒童急診室之病童臨床分析

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Background: Sick children may visit pediatric outpatient department (OPD), but they may be transferred to the pediatric emergency department (PED) for further managements. We aim to survey children admitted to the PED transferred from the OPD

Methods: From 2018 to 2019, we prospectively conducted children admitted to the PED transferred from OPD. The following clinical information was studied: demographics, (age, gender, distribution of patients by month) diagnosis, and disposition (admission, discharge). We compared the clinical data between the referred patients discharged home from the PED and those admitted to the wards.

Results: During the 16-month study period, 867 patients were enrolled, 468 (54%) were discharged from PED, and 399 (46%) were admitted. In this study, 654 (75.4%) of the 867 children were aged < 6 years. The mean age was 4 ± 0.8 , and mean degrees of triage was 3 ± 0.26 in the transferred children. Among them, 359 children (46.0%) were admitted to the wards, and 422 (54.0%) were discharged home from the PED. The first 3 common transferred subspecialty clinic units were gastroenterology (29.1%), infection (9.0%), and neurology (7.7%). In patients admitted to the wards, the mean length of hospital stay was 7.9 ± 0.5 days, and first 3 common diagnosis included pneumonia (33.7%), acute

gastroenteritis (12.5%), and urinary tract infections (8.3%).

Conclusions: More than half of children transferred to the PED may not require admission, and more than one third of them could not require special tests, interventions, and further consults. In the PED, the most common diagnosis requiring admission to the wards was pneumonia, and the highest length of hospital stay was the diseases of neurology requiring neurosurgery.

88 Return Visit Presentations in Pediatric Emergency Visits, 2000-2015

兒童急診返診趨勢

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Background: Return visit rate was one of most useful quality indicators in pediatric emergency department (PED). Evidence relating to quality of care with available outpatient services and PED was limited and mixed. This study aimed to investigate the trend of PED utilization and quality of care following their outpatient visits from 2000 to 2015.

Methods: A repeated cross-sectional population-based design was adopted and the main data source was the National Health Insurance Database. All PED visits made by children below 18 years old on 2000, 2005, 2010, and 2015 following their outpatient visits were included. Quality indicators of return visit to PED or outpatient and return visit for acute abdomen were analyzed. Descriptive statistics and trend analysis were computed using the statistical software SAS v9.4.

Results: Return visit to PED or outpatient visits following their outpatient visits decreased from 17% on 2000 to 14% on 2015; both return visit to PED and outpatient visits decreased in trends. Return visits for acute abdomen also decreased in acute appendicitis (0.11% on 2000 and 0.07% on 2015) and intussusception (0.06% on 2000 and 0.04% on 2015).

Conclusions: Pending results showed quality of care at PED seems improved in return visits and return visits for acute abdomen following their outpatient visits overtime.

89 Clinical Analysis of Acute Encephalitis in Pediatric Emergency Department

兒童急性感染性腦炎在兒童急診部的臨床分析

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Background: Acute viral encephalitis is a rare but severe infectious disease in the pediatric population, resulting in

serious neurologic dysfunction. A large variety of viruses are associated with encephalitis, but there were only a few studies discussing the initial presentation in the Emergency Department. Our study aims to analyze different symptoms and laboratory data of different pathogens.

Methods: We reviewed the patient who admitted via the Pediatric Emergency Department under the diagnosis of encephalitis, from 2015 to 2019. We analyzed different symptoms and laboratory data. We used Chi-Square Test and T-Test as statistic methods.

Results: We included 31 patients admitted via our Pediatric Emergency Department; 11 patients were boys and 20 patients were girls. Age was 5 ± 4.3 years old; admission length was 13 ± 20.5 days. The seizure is the most often neurologic symptoms at initial presentation (15 patients, 48.3%) Enterovirus accounts for the most common pathogen in our patient group (10 patients, 32.2%); the second common is influenza (8 patients, 25.8%). Comparing with influenza-related encephalitis, the patients whose encephalitis caused by enterovirus had younger age (3.1 ± 3.1 v.s 9.7 ± 3.9), higher white blood cell counts (11640 ± 3140 v.s 6562 ± 3553), higher platelet count (321500 ± 71809 v.s 217520 ± 65497) and lower Hb (11.6 ± 1.1 v.s 13.0 ± 0.7)

Conclusions: This study helps clinical Pediatric Emergency doctors to differentiate the possible pathogen of encephalitis when presenting to the Emergency Department. However, more data should be acquired.

90 sCD40L in Prediction of Pediatric Appendicitis

sCD40L預測兒童闌尾炎

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Background: Appendicitis is one of the most common abdominal emergency in children. Clinicians cannot easily distinguish between non-perforated appendicitis and perforated appendicitis in children on physical examinations and laboratory tests. Abdominal computed tomography is a common tool used in emergency rooms for the diagnosis of appendicitis. However, excess radiation exposure is not suitable for children. Serum soluble CD40 ligand (sCD40L) is an inflammatory biomarker associated with atherosclerosis and sepsis in adults. The purpose of our study was to predict appendicitis and perforated appendicitis in children using sCD40L.

Methods: All patients under the age of 18 suspected of having appendicitis tested once for serum sCD40L within 72 hours of the symptoms of appendicitis. We compared the sCD40L level among patients with normal appendices, appendicitis, and perforated appendicitis. Then, we calculated the diagnostic performance of sCD40L and performed receiver operating characteristic curves in the prediction of appendicitis and perforated appendicitis.

Results: Of a total of 116 patients, 62 had non-perforated

appendicitis, 44 had perforated appendicitis, and 10 had normal appendices. The sensitivity at 90 pg/ml and the specificity at 301 pg/ml of sCD40L in total first 3 days after onset of symptoms are 0.99 and 1.00, respectively. The sensitivity and specificity at the best cutoff point with 178 pg/ml of sCD40L predicting appendicitis and perforated appendicitis are 0.73, 0.90 and 1.00, 0.90, respectively.

Conclusions: SCD40L is a good predictor of pediatric appendicitis. SCD40L below 90 pg/ml can exclude appendicitis, and above 301 pg/ml can confirm perforated appendicitis in children.

91 The Suspected Child Abuse and Neglect Clinic and the Network of Child Protection: A Two-Year Experience of a Single Center

兒少虐待及疏忽門診成效—單一中心二年之經驗

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Background: Child maltreatment is one of the most concerning issues in the World. The case numbers of child maltreatment in Taiwan has been persistently high (> 50,000/year) recently. A multidisciplinary child protection network is in need and a Suspected Child Abuse and Neglect Clinic launched in our hospital. This clinic has been lasting for two consecutive years and we would like to share the experience.

Methods: We reviewed the medical records and database of Children Protection Center of a tertiary medical center in north Taiwan from May 2018 to June 2020. Patients who met certain criteria were arranged to visit the “Children Friendly Clinics” by appointment.

Results: Totally 101 patients are enrolled, 56 male and 45 female. They have 558 visits (from 1 to 38) and 716 doctors consultations (1-4/visit). The mean age on the first visit was 3.4 years old (10 days old -17.7 years old). 58 of them (57.4%) are still in need of follow-up, 22 cases (21.8%) had no need of follow-up and 21 (20.8%) been referred to other hospitals. The reasons for appointment are: 1. Requested for evaluation by Center of Domestic Violence and Sexual Assault Prevention, 11.2%; 2. Reported as suspected child abuse and was severely injured, 38.3%; 3. Requested by physicians to identify child abuse, 5%; 4. children entering foster care with medical needs, 42.4%; 5. Suspected child abuse and neglect patients who needed psychological consultation, 3%. Among the 56 cases for evaluation, 47 of them (83.9%) were positive with evidence of maltreatment. The consulted medical specialties are Pediatric subspecialties other than neurology 30.1%, pediatric neurology 24.5%, orthopedics 9.4%, ophthalmology 8.8%, rehabilitation 7.7% and psychiatry 5.3%.

Conclusions: Child maltreatment often associates with complicated clinical presentations. A multidisciplinary clinic is necessary to provide evaluation and health care for these children.

92 Extracorporeal Membrane Oxygenation Support in Neonatal Respiratory Failure: A Single Medical Center Experience

葉克膜於新生兒呼吸衰竭的應用：台灣一家醫學中心的經驗

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Background: Extracorporeal membrane oxygenation (ECMO) is a life-saving method supplying both cardiac and respiratory support to critical patients with severe cardiopulmonary failure. According to the latest ECLS registry report, pulmonary disease of neonate has the most cases amount and highest survival. We started to apply neck ECMO in neonatal patients from 2000. In the study in 2017, we achieved an overall survival rate of 59.2% with good neurological outcomes for ECMO in neonatal disease from the experience during January 2005 to June 2015. In this study, we summarized the recent result of ECMO of pulmonary support for neonatal respiratory failure and described the long term outcome.

Methods: Data were retrieved from our ECMO database for the neonates (age < 28 days) with respiratory failure who received ECMO support from January 2005 to June 2019.

Results: In summary, 46 neonates who were respiratory failure and unresponsive to conventional therapy received venoarterial ECMO support. The overall decannulation rate was 71% (33/46), and 13 patients (28%) were died on ECMO. 23 (50%) patients survived to hospital discharge, and only 3 patients had a poor neurological outcome (PCPC scale 4-5). About the disease resulted in respiratory failure, persistent pulmonary hypertension of the newborn, including meconium aspiration syndrome related, had a superior outcome (17/24, 70%), and 70% of these patients received PDA ligation through thoracotomy to improve lung recovery. Congenital diaphragmatic hernia had the worst outcome (6/15, 40%). In addition, 80% of neonates (37/46) were born at other hospital and transferred to our hospital for ECMO support; however, the transferral rate decreased (64%) in recent 5 years. It also indicated better neonatal critical care and widely used of ECMO in medical centers.

Conclusions: We focused on ECMO use in neonates with respiratory failure and unresponsive to conventional therapy. We offered fair decannulation rate, acceptable survival rate and good neurological outcomes in neonatal ECMO for respiratory support. Disease associated with persistent pulmonary hypertension of the newborn has the superior survival under ECMO use, and PDA ligation demonstrated a significant role.

93 Feasibility of Point of Care Ultrasound in Acute Pediatric Care Setting, a Prospective Study

及時視診超音波在兒科急性照顧之前期經驗

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Background: Point of care ultrasound (POCUS) is a diagnostic or procedural guidance ultrasound that is performed by a clinician to help guide the evaluation and management of the patient. POCUS was frequently used in the adult emergency room but rarely reported in an acute pediatric care setting. We reported our prospective experience of POCUS practiced at a tertiary referred center of the acute pediatric patients.

Methods: We retrospectively evaluated hospitalized or emergency room pediatric patients who were aged younger than 18 years old, present with acute clinical symptoms in a local hospital from September 2019 to July 2020. We analyzed the patient's symptoms, POCUS technique, POCUS duration, and intervention after POCUS.

Results: A total of 13 patients were completed POCUS during acute symptom illness. Three patients perform POCUS more than once. A total of 33 individual ultrasounds were performed. Common indications of POCUS were hip pain (3/16, 18%), conscious change (3/16, 18%), and respiratory distress (2/16, 12.5%). The most common ultrasound techniques used during POCUS were cardiac echography (7/33, 21%), followed by hip echography (5/33, 15%) and lung echography (4/33, 12%). Intervention after ultrasound included close observation (5/16, 31%), further laboratory diagnosis (4/16, 25%), and further image study (3/16, 18%). The average duration of POCUS was 16 minutes (min: one minute, max: 1 hour and 10 minutes). One case was done over one hour because we used ultrasound to guide the aspiration of joint fluid.

Conclusions: POCUS is a feasible method for pediatric clinicians to perform immediate ultrasound diagnosis to help children with acute illness in time. Pediatricians should be encouraged to increase their readily-accessible ultrasound assessment capability to further strengthen their acute care competency.

94 Acute Necrotizing Encephalopathy of Childhood – A Single-Center Experience in Southern Taiwan

兒童壞死性腦炎臨床表現，南部一家醫學中心經驗

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Background: First described in 1995, acute necrotizing encephalopathy of childhood (ANEC) is a novel form of acute encephalopathy. It causes rapid deterioration of consciousness within 24 hours. Nevertheless, most treatment for this critical disorder seems invalid and its mortality rate maintains high. To get a more precise detail about ANEC, we collected the cases in our medical center and made a summary of their clinical, laboratory, imaging data and the prognosis.

Methods: Retrospectively, we made chart review from patients in the PICU in Kaohsiung Chang-Gung Memorial Hospital for children with the diagnosis of ANEC. The clinical presentations, medical intervention, and laboratory data were collected from the medical record. The brain MRI were collected. Fisher's exact test and binary logistic regression were used to analyze the association between all the data and the mortality outcome.

Results: From 2012 to 2020, 10 children were included, including 8 boys and 2 girls. In the accessible records, 6 presented initially with seizure and 3 of them with confusion. Influenza A/B were the dominant pathogen (5/9). The mean length of prodromal fever was 1.62 (1-3 days) days. Most children had leukocytopenia, thrombocytopenia, elevated serum AST and ALT, and elevated protein levels in CSF. In their cerebral CT/MRI, four illustrated brain stem insult and most of them had bilateral thalamus lesions. 2 children received steroid pulse therapy, 3 received IVIG, and 3 received both. Despite the intensive management, the prognosis was poor. 6 patients died, 3 became comatose, and 2 ended up with confusion. The mean duration of admission to death was 22.17 days; in those who survived, the mean length of PICU stay was 41.67 (3-61) days. Analytically, the above factors had no significant association with the mortality outcome.

Conclusions: According to our experience, our case series of this fulminant ANEC showed the mortality rate was over 50%. Poor prognosis and prolong neurologic sequelae were observed. Neither did the clinical, laboratory, or imaging findings predict its prognosis. Influenza A/B was the major pathogen. Aggressive neurocritical supportive care with prompt immunotherapy may lessen the long term deficit.

95 Outcome of Acute Necrotizing Encephalopathy in Relation to Treatment with Immune-modulator Therapy (IVIG or Steroid Pulse Therapy)

免疫調節治療方法 (免疫球蛋白或高劑量類固醇治療) 對於急性壞死性腦病變的預後改善

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Background: Acute Necrotizing Encephalopathy (ANE) is a rare disorder characterized by fever, seizures and rapid progression to coma after the onset of a viral infection. The most prominent feature of ANE is the presence of multiple, symmetric brain lesions in the bilateral thalami and other specific brain regions including periventricular white matter, internal capsule, putamen, upper brain stem tegmentum, and cerebellar medulla, demonstrated by CT or MRI. Neurological outcome of ANE is very poor and the mortality and morbidity rates are high. The poor prognosis of ANE makes randomization of patients difficult because of ethical problems, and the treatment for ANE is different among hospitals because there is no standard regimen. Several studies have suggested that hypercytokinemia is closely related to the development of ANE. These facts indicate that macrophage activation and hypercytokinemia will be participated in the pathogenesis of ANE. We postulated that anti-inflammatory treatment can be effective for ANE, if the development of ANE is attributable to systemic inflammatory response. We conducted a retrospective study in order to examine the efficacy of anti-inflammatory treatment with steroids.

Methods: From 2001 January to 2020 January we retrospectively collected children with diagnosis of Acute Necrotizing Encephalopathy and admission to PICU in a tertiary center.

Results: Twenty-nine patients were identified. The mortality rate was 41.6%, and 40% of patients survived without or less neurological sequelae. The outcome is better in early steroid pulse therapy group.

Conclusions: The outcome of patients treated with early steroid pulse therapy was better than those without early steroid, if the patients without brainstem lesions.

96 Abusive Head Trauma - A More Severe Etiology and Major Cause of Mortality of Traumatic Brain Injury in Pediatric Intensive Care Unit

受虐型腦傷—兒科加護病房內嚴重創傷型腦傷主要原因及死因

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Background: Traumatic brain injury (TBI) occurs commonly in childhood. Most children with TBI are mild and have no any sequelae. However, some children with severe traumatic TBI may expire or have neurological sequelae. In fact, some episodes of TBI can be prevented. This study was to review the etiology, severity, and prognosis of the TBI in a pediatric intensive care unit (PICU) in order to provide some information for the prevention of TBI.

Methods: We retrospectively analyzed patients with diagnosis of TBI from January 2016 to December 2018 in a PICU of a medical center. The severity of traumatic brain injury severity was divided into mild, moderate, and severe according to initial Glasgow Coma Scale (GCS) or Pediatric GCS score. We collected demographics, pre-hospital events, and outcomes of these patients.

Results: There were 111 patients enrolled in this study. The most common etiology was traffic accident (n=47, 42.3%). Among these patients, there were 28 patients (59.6%) caused by motorcycle. The second most etiology of pediatric TBI was child abuse or neglect (n=41, 36.9%). The age of children with abusive head trauma (AHT) is younger than patients with non-AHT TBI (median age: 0.44 y/o versus 4.48 y/o, p<0.001). 85% (n=12) of children with AHT were less than 1 year old. Besides, the incidence of severe TBI was higher in patient with AHT than patients with non-AHT TBI (42.9% versus 15.5%, p=0.014). The overall mortality rate of pediatric TBI was 2.7% (n=3). However, the mortality rate in patients with AHT is much higher than patient with non-AHT TBI (14.3% versus 1%, p=0.004).

Conclusions: TBI in children usually cause by traffic accident, child abuse, or child neglect. Most of them can be prevented. AHT usually occurs in patient less than one year old and has higher mortality. Early recognition of child abuse is warranted and is the best strategy to improve outcome of TBI in PICU.

97 A Pilot Study on the Temperature Measurement Using a Novel Wearable Device

使用一個新穎研發的穿戴裝置測量體溫的先導性研究

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Background: Since December 1, 2019, our team started to design a novel device capable of multiple physiological parameters including temperature measurement. Coincidentally, Covid-19 pandemic started at Wu-Han, Hu-Bei and then spread to Europe and worldwide, including Taiwan. Our team rapidly responded to this new pandemic disease by designing a wearable device for temperature as well as other physiological parameters. Temperature measurement has been a routine procedure for more than a century. There

have been many changes about temperature measurement since its initial application. However, until now, wearable device is rarely seen. In the Covid-19 pandemic era, we therefore develop a novel wearable device capable of continuous temperature measurement as well as other functions.

Methods: We have made a prototype wearable device which is applicable since February. We also made test measurements. As a preliminary pilot study, we measured temperature measurement at the upper-middle third of people's anterior chest and compared the measurement with right and left ear within 10 seconds using infrared-ear thermometer.

Results: The temperature measurement at the middle anterior upper chest was 36.20± 0.56 Celsius degree. The near simultaneous measurement of right tympanic temperature was 36.18± 0.26 Celsius degree while the left side was 35.99± 0.33 Celsius degree. The p-value for the comparison between chest and right ear temperature was 0.7694 ($p > 0.05$). The p-value for the comparison between chest and left ear temperature was 0.0312 ($p < 0.05$). The p-value for the comparison between right and left ear temperature was 0.0040 ($p < 0.05$). There was no adverse events.

Conclusions: This pilot study showed that our custom-made novel wearable device is capable of measuring skin temperature at the anterior middle chest wall, with its measure values very close to the conventional infrared ear thermometers. This fact is especially important since it provides continuous measurement at non-exposed skin surface. Also, our novel device also can provide additional measurement of other physiological parameters which are now undergoing further validations in the near future.

98 Proteasome and Autophagy Impairment Leads to Progressive Accumulation of Ubiquitin and SQSTM1/p62 Aggregates Underlying the Cell Death of Oligodendrocytes in Globoid Cell Leukodystrophy

自嗜作用與泛素-蛋白酶體系統失調導致泛素與p62堆積及NRF2訊息異常造成GLD髓鞘細胞死亡

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Background: Disturbed autophagy and ubiquitin proteasome system (UPS) on regulation of proteostasis has been implicated in pathogenesis of many neurodegenerative diseases, albeit it has not been fully elucidated in Globoid cell leukodystrophy (GLD).

Methods: Brain tissues from wild type and twitcher mice were processed for IHC and western blotting. MO3.13 oligodendrocytes were incubated with psychosine concomitant with chloroquine and MG132. Autophagy markers,

oxidative stress, cell viability, and bioenergetics were determined.

Results: Twitcher brain presented with profound accumulation of ubiquitin- and p62-aggregates in the brain stem, spinal cord and cerebellar white matter. Levels of insoluble LC3-II, p62 and ubiquitin in twitcher brain at day 35 were elevated to 2-fold of WT mice. In vitro, levels of insoluble LC3-II, p62 and ubiquitin in combination treated cells were 4-, 4-, and 3.5-fold of psychosine-treated cells, while the cell viability were 25% of norm, ROS to 4-fold of norm, and mitochondrial respiration were 50% of norm. Intriguingly, insoluble KEAP1 expression were reduced to 60% of norm after combination treatment.

Conclusions: In this study using both cellular and authentic animal models, for the first time, we report the dysfunction of proteasome and autophagy underscoring the pathogenesis of GLD. We demonstrate a progressive accumulation of cytoplasmic aggregates containing ubiquitin and SQSTM1/p62 in brain and spinal cord of GLD mouse model. Our in vitro study shows a dose- and time-dependent cytotoxicity of psychosine upon autophagy and UPS machinery. Furthermore, inhibition of autophagy and UPS exacerbated accumulation of insoluble p62 and ubiquitinated proteins mediated by psychosine cytotoxicity as well as increased cytoplasmic deposition of p62- and ubiquitin- aggregates. Nonetheless, NRF2-KEAP1 signaling and its downstream antioxidant response elements were not activated, thus, leading to accumulation of reactive oxygen species, and subsequent cell death. Our findings therefore provide an innovative insight into the psychosine cytotoxicity contributing to pathogenesis of GLD.

99 Molecular Analysis of HGD Gene in Taiwanese Patients with Alkaptonuria

台灣黑尿症患者之HGD基因分析

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Background: Alkaptonuria (AKU) is a rare autosomal recessive inherited disease blocking the metabolism of tyrosine, resulting in accumulation of homogentisic acid (HGA). The hallmark of this disease is the large amount of HGA was excreted in the urine with further oxidation into dark color. The prevalence is estimated about 1:250,000 to 1:1,000,000 in most ethnic group. However, the genotype and phenotype information in Taiwanese patients scarce.

Methods: From 2010 Jan to 2020 Jun, patients clinically diagnosed as AKU were enrolled. Clinical information were recorded. Molecular analysis on HGD were arranged with previously not done by targeted panel sequencing using

MiSeq sequencer.

Results: A total 4 patients were enrolled, with 3 male and 1 female. Three patients were noticed in infancy, and 1 patient onseted at 8-year-old. There mean age of diagnosis was 8.62 years old (± 6.54). Current mean age was 19.53 years old (± 10.32). All of the patients have initial presentation of dark color urine. Molecular testing was performed in 4 patients. One reported missense variant c.473C > T (p.P158L) and 6 novel variants on HGD mutation (c.16-2063A > C, T196I, G362R, W97X, G344Dfs*25, L386fs) were identified.

Conclusions: Although AKU is rare but still exists in Taiwanese population. This study provides further information about molecular spectrum of alkaptonuria and expands our knowledge of the molecular basis of this disease.

100 Genetic Investigation in Syndromic Ciliopathies among Taiwanese Patients: Application of Whole-Exome Sequencing

台灣纖毛病變症候群病人的基因調查：全外顯子定序的運用

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Background: Syndromic ciliopathies are a heterogeneous group of congenital disorders with broad and overlapping clinical features and genetic etiologies. The clinical presentations vary considerably, ranging from retinopathy, polydactyly, renal pathology, obesity to mental insufficiency. Several genes involved in ciliary function have been implicated in the pathogenesis, but still in some patients, their genetic causes remained unclear. In order to survey the genetic causes in a timely and economically efficient manner, we apply whole exome sequencing (WES) to extend our knowledge of the specific genotype-phenotype correlation of syndromic ciliopathies among Taiwanese patients.

Methods: During the period from Jan 2015 to Dec 2018, a total of 10 patients with clinically suspected syndromic ciliopathies, including Bardet-Biedle syndrome, Alström syndrome, and Joubert syndrome, were examined using WES. Genetic variants were filtered and manually checked against publicly indexed allele frequencies and bioinformatically predicted protein functions. Sanger sequencing and segregation analysis were finally used to confirm the genetic etiology. Clinical presentations, molecular diagnoses, and managements of these patients were discussed.

Results: Among the recruited 10 patients, we confirmed the genetic diagnosis for 7 patients. In total we found 3 mutations in BBS2 (c.534+1C>A, c.1814G>C, c.563delT), 2 mutations in BBS7 (c.728C > T, c.1688_1689delCT), 4 mutations in ALMS1 (c.6167_6168insAT, c.7970_7976delACTTTAT, c.10290_10291delTA, c.10828_10829delAG), and 2 mutations in C2CD3 (c.2720A>G, c.1730G>A) gene.

Conclusions: Our data demonstrate that WES can help to identify the genetic causes of syndromic ciliopathies and further extend our knowledge of genotype-phenotype information specifically in Taiwanese patients.

101 Survival and Diagnostic Age of 175 Taiwanese Patients with Mucopolysaccharidoses in 35 Years (1985-2019)

自1985至2019年的35年間，175位台灣黏多糖症病患的生存與確診年齡

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Background: Mucopolysaccharidoses (MPSs) are a group of inherited metabolic diseases, which are characterized by the accumulation of glycosaminoglycans, and eventually lead to the progressive damage of various tissues and organs.

Methods: An epidemiological study of MPS in Taiwan was performed using multiple sources. The survival and diagnostic age for different types of MPS between 1985 and 2019 were evaluated.

Results: Between 1985 and 2019, there were 175 patients diagnosed with MPS disorders in the Taiwanese population, with a median diagnostic age of 3.9 years. There were 21 (12%), 78 (45%), 33 (19%), 32 (18%) and 11 (6%) patients

diagnosed with MPS I, II, III, IV and VI, respectively, with median diagnostic ages of 1.5, 3.8, 4.7, 4.5 and 3.7 years, respectively. Diagnosis of MPS patients was significantly earlier in recent decades ($p < 0.01$). Pilot newborn screening programs for MPS I, II, VI, IVA, and IIIB were progressively introduced in Taiwan from 2016, and 48% (16/33) of MPS patients diagnosed between 2016 and 2019 were diagnosed by one of these screening programs, with a median diagnostic age at 0.2 years. For patients born between 2016 and 2019, up to 94% (16/17) were diagnosed with MPS via the newborn screening programs. At the time of this study, 81 patients had passed away with a median age at death of 15.6 years. Age at diagnosis was positively correlated with life expectancy ($p < 0.01$). Life expectancy also significantly increased between 1985 and 2019, however this increase was gradual ($p < 0.01$).

Conclusions: The life expectancy of Taiwanese patients with MPS has improved in recent decades and patients are being diagnosed earlier. Because of the progressive nature of the disease, early diagnosis by newborn screening programs and timely implementation of early therapeutic interventions may lead to better clinical outcomes.

102 Taiwan's Experience of Otorhinolaryngological Management in Patients with Mucopolysaccharidoses

台灣黏多醣症患者其耳鼻咽喉症狀的治療經驗

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Background: Mucopolysaccharidoses (MPSs) are lysosomal storage disorders in which glycosaminoglycans accumulate due to insufficiency of the enzymes to degrade them. Patients have organomegaly, short stature, and/or intellectual disability. The earliest symptoms are otologic and upper

respiratory obstruction and are the main reasons for doctor consultation.

Methods: We reviewed 42 patients (30 male and 12 female), with a median age of 20.5 years, who had MPS (16.7% type I, 35.7% type II, 19.0% type IIIB, 21.4% type IVA, and 7.2% type VI). Otorhinolaryngologic manifestations were collected, and quality of life after surgery was documented.

Results: Ear, nose, and throat (ENT) symptoms occurred in patients with all MPS types. We found recurrent otitis media in 42.9% of cases. We noted hearing loss in 81.0% (mixed in 45.2%, conductive in 19.0%, sensorineural in 16.7%), adenotonsillar hypertrophy in 76.2%, frequent infections of the upper airway in 47.6%, and obstructive sleep apnea syndrome in 26.2%. Seventy-six percent of patients underwent surgery, including adenoidectomy, tonsillectomy, insertion of middle ear ventilation tubes, tracheotomy, and supraglottoplasty.

Conclusions: ENT surgery reduced the severity of hearing loss, and decreased the degree of symptoms related to upper airway obstruction which improved patients' quality of life.

103 Genotype, Phenotype and Biomarker Analysis of Confirmed Mucopolysaccharidosis II Patients and Asymptomatic Infants in Taiwan

台灣黏多醣症第二型的確診患者與無症狀嬰兒的基因型、表現型與生物標記之分析

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Background: Mucopolysaccharidosis II (MPS II) is caused by a defect of the iduronate-2-sulfatase (IDS) gene. Few studies have reported integrated mutation data of Taiwanese MPS II phenotypes. In this study, we summarized genotype, phenotype and biomarker correlations of confirmed MPS II patients and asymptomatic MPS II infants in Taiwan.

Methods: Regular polymerase chain reaction and DNA sequencing were used to identify genetic abnormalities of 191 cases, including 51 unrelated patients with confirmed MPS II and 140 asymptomatic infants referred from the newborn screening program. Urinary glycosaminoglycans

were quantified by mass spectrometry and the IDS enzyme activity was performed using 4-methylumbelliferyl fluorometric assay. IDS activity was analyzed in individual novel IDS variants using in vitro expression studies.

Results: A total of 51 mutations of IDS gene were identified, including 32 missense, three nonsense, two silent, six splicing, four small deletions, three gross deletions, and one complex inversion. In those, 28 variations were reported and verified as being pathogenic to cause MPS II with different severities and the rest 19 were novel mutations. Exogenous-expressing of various mutations in COS-7 cells was applied to understand the affected IDS activity. Among the 19 novel mutations identified, the percentages of IDS activity of the novel missense mutations c.137A>C, c.311A>T, c.454A>C, c.797C>G, c.817C>T, c.998C>T, c.1106C>G, c.1400C>T, c.1402C>T, and c.1403G>A were significantly decreased ($p < 0.001$), c.254C>T and c.1025A>G were moderately decreased ($p < 0.01$), and c.851C>T was slightly decreased ($p < 0.05$) comparing with normal enzyme activity. The activities of the other six missense mutations were reduced but were insignificant. The results of genomic studies and their phenotypes were highly correlated.

Conclusions: A greater understanding of the positive correlations may help to prevent the irreversible manifestations of MPS II, particularly in infants suspected of having asymptomatic MPS II. In addition, urinary glycosaminoglycan assay is important to diagnose MPS II since gene mutations are not definitive (could be non-pathogenic).

104 Natural Progression of Cardiac Features and Long-term Effects of Enzyme Replacement Therapy in Taiwanese Patients with Mucopolysaccharidosis II

台灣黏多糖症第二型患者的心臟特徵自然進程與酵素替補治療的長期效果

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Background: Cardiac abnormalities have been observed in patients with mucopolysaccharidosis type II (MPS II). The

aim of this study was to investigate the cardiac features and natural progression of Taiwanese patients with MPS II, and evaluate the impact of enzyme replacement therapy (ERT) on cardiac structure and function.

Methods: The medical records, echocardiograms, and electrocardiograms of 48 Taiwanese patients with MPS II (median age, 6.9 years; age range, 0.1-27.9 years) were reviewed. The relationships between age and each echocardiographic parameter were analyzed.

Results: The mean z-scores of left ventricular mass index (LVMI), interventricular septum diameter in diastole (IVSd), left ventricular posterior wall diameter in diastole (LVPWd), and aortic diameter were 1.10, 2.70, 0.95 and 1.91, respectively. Z scores >2 were identified in 33%, 54%, 13%, and 46% for LVMI, IVSd, LVPWd, and aortic diameter, respectively. The most prevalent cardiac valve abnormality was mitral regurgitation (MR) (56%), followed by aortic regurgitation (AR) (33%). The severity of mitral stenosis (MS), MR, aortic stenosis (AS), and AR were all positively correlated with increasing age ($p < 0.01$). We also compared the echocardiographic parameters between two groups: (1) 12 patients who had up to 17 years of follow-up echocardiographic data without ERT, and (2) nine patients who had up to 12 years of follow-up data with ERT. The results showed that z-score changes of LVMI significantly improved in the patients who received ERT compared to those who did not receive ERT ($p < 0.05$). However, the severity score changes of MS, MR, AS, and AR all showed gradual progression in both groups ($p > 0.05$).

Conclusions: High prevalence rates of valvular heart disease and cardiac hypertrophy were observed in the MPS II patients in this study. The existence and severity of cardiac hypertrophy and valvular heart disease in these patients worsened with increasing age, reinforcing the concept of the progressive nature of this disease. ERT for MPS II appeared to be effective in stabilizing or reducing the progression of cardiac hypertrophy, but it only had a limited effect on valvulopathy.

105 FN1-Related Spondylometaphyseal Dysplasia (SMD), Corner Fracture Type: From Osteomyelitis to Child Abuse

FN1引起的角落骨折：從骨髓炎到兒虐

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Background: Spondylometaphyseal Dysplasia (SMD) corner fracture type, first reported in 1999, is a rare autosomal dominant skeletal dysplasia consisting of a diagnostic triad of mild vertebral body abnormalities leading to short stature, developmental coxa vara, and metaphyseal irregularities with visible corner fracture-like lesions of the tubular bones on radiography. Recently pathogenic variant in the N-terminal of FN1 (Lee et al. in

2017) and specific variants of the COL2A1 gene has been reported to be causal for this condition.

Methods: The first patient is a 3-y/o girl seen in ED with concerns of osteomyelitis, which presented as wrist edema. ID workup showed mildly elevated CRP (1.6 mg/dL) and low D3. The skeletal survey showed transverse fractures and multifocal erosive patterns on the proximal and distal ulnar, radial, femoral bones. "Corner fractures" were seen on tibial metaphysis. SEM Dysplasia NGS Panel revealed a de novo variant of the FN1 gene: a c.773G>C transversion (p.Cys258Ser) in exon 6. The 2nd patient was a 16-m/o boy with standard height referred to rule out non-accidental trauma (NAT) due to distal metaphyseal fractures. PE show corner fractures without much erosion were seen on long bones and two vertebral bodies. Molecular testing confirmed a de novo known pathogenic variant: p.Cys260Gly.

Results: Fibronectin-1 is a master organizer of extracellular matrices (ECMs) and promotes the assembly of collagens, fibrillin-1, and other proteins as well as controls the cleft formation during the initiation of epithelial branching in the formation of salivary glands. We hypothesize that a gain of function fibronectin increases the cleft formation and branching and results in the corner fracture appearance of the bone. The corner fractures can result from either inappropriate assembling or congenital defective collagens such as COL2A1.

Conclusions: Our patients demonstrated the clinical presentation of FN-1 related SMD corner fracture type in younger patients: less skeletal involvement, features of the triads including bow legs and scoliosis might not have developed, and the metaphyseal erosion is not that extensive. The recognition of this unique type of skeletal dysplasia is an important differential diagnosis to be excluded in the workup of NAT.

106 Serum NGAL as a Potential Biomarker of Diabetic Kidney Disease for Patients with Pediatric-onset Type 1 Diabetes

血清嗜中性白血球明膠酶相關脂質運載蛋白作為兒童第一型糖尿病腎病變的生物標記

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Background: Diabetic kidney disease (DKD) is a major complication in patients with type 1 diabetes (T1D). Microalbuminuria is considered as a marker to predict DKD but with limitations. The aim of this study is to explore the role of serum neutrophil gelatinase-associated lipocalin

(sNGAL) for early detection of DKD in pediatric-onset T1D patients.

Methods: A total 116 patients (mean age 22.3 ± 6.9 years) with diabetes duration over 5 years and eGFR ≥ 60 ml/min/1.73m² were enrolled in this prospective cross-sectional study. Persistent albuminuria (PA) is defined as urine albumin -creatinine ratio > 30 mg/g for consecutive 2 years, and otherwise as non-albuminuria (NA). The patients were divided into adult group (≥ 18y, n=91) and pediatric group (< 18y, n=25), which were further subgrouped as Ad-PA (n=8), Ad-NA (n=83), Ped-PA (n=2) and Ad-NA (n=23). In all groups, sNGAL were determined.

Results: Of total, the mean diabetes duration was 14.2 ± 6.1 years. 8.6% patients had persistent albuminuria and there was no significant difference in sNGAL levels between PA and NA. In adults, notably, sNGAL was significantly higher in Ad-PA than Ad-NA [49.2 (34.5-55.2) ng/mL vs. 36.2 (31.1-40.8) ng/mL, P=0.039]. sNGAL was negatively correlated with eGFR in adults (Rho -0.41, P < 0.001). Multiple linear regression models in adult group showed higher sNGAL levels were independent and significant determinants of lower eGFR (P < 0.001).

Conclusions: Elevated sNGAL significantly correlated with GFR decline even in the range of normal to mildly decreased renal function. It is a potential biomarker for early deterioration of DKD in pediatric-onset T1D.

107 The Beneficial Effects of Probiotics on Type 1 Diabetes Mellitus Patients

益生菌對於第一型糖尿病病人的臨床成效

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Background: Type 1 Diabetes Mellitus (T1DM) is characterized by autoimmune of β-cell destruction, which mainly due to excessive activation of immune cells aroused by antigens from diet and infection. Probiotics residing in gut play essential roles in host immune regulation. In this clinical trial, we evaluated the therapeutic efficacy of probiotic on T1DM patients to suggest a novel and alternative T1DM medical administration.

Methods: A randomized, double-blind, placebo-controlled trial was performed at China Medical University Hospital. 27 patients were daily administered with two capsules containing 5*10⁹ colony-forming units (CFU/capsule, species include Lactobacillus salivarius subsp. salicinius AP-32, Lactobacillus johnsonii MH-68 and Bifidobacterium animalis subsp. lactis CP-9 from glax Biotech Co., Ltd.) for 6 months, while the other 29 patients were treated with placebo. The variations of fasting blood glucose and HbA1c were analyzed at pre-intervention, 3 and 6 months post-intervention. In addition, interleukin-8 (IL-8), IL-17, macrophage inflammatory protein-1β (MIP-1β), regulated

on activation, normal T cell expressed and secreted (RANTES), transforming growth factor-beta 1 (TGF- β 1) and tumor necrosis factor- α (TNF- α) in serum were detected by ELISA to evaluate the immune suppressive effects induced by probiotic treatments.

Results: Fasting blood glucose levels in T1DM probiotics group were significantly reduced to $87.5 \pm 10.3\%$ in reference to the pre-treat level, whereas those in placebo groups showed change of $101.5 \pm 11.7\%$ from baseline to 6 months' supplement ($P < 0.001$). HbA1c levels were also improved by the administration of probiotics, showing the reduction of HbA1c to $91.8 \pm 5.4\%$ and $100.1 \pm 7.8\%$ in probiotic and placebo group respectively after normalized with pre-treat level ($P < 0.001$). The concentrations of IL-8, IL-17, MIP-1 β and TNF- α were significantly decreased and were associated with an increased TGF- β 1 expression after probiotic treatment.

Conclusions: Overall, we found the probiotics attenuate the symptom of T1DM by stabilization of glycemic levels and reduction of HbA1c in T1DM patients through beneficial regulation of immune cytokines.

108 Is Non-stimulated C-peptide at Diagnosis a Good Predictive Value for Insulin Use at Two Years after Diagnosis in Pediatric Diabetic Patients?

在糖尿病診斷當下的非刺激的C肽數值，是否可作為診斷後兩年的胰島素使用狀況的良好預測因子？

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Background: The intervention for type 1 and type 2 diabetes is different due to their underlying biological mechanisms. However, insulin may be initially required to stabilize patients presenting metabolic crisis at the onset of both disease entities. Identifying a convenient and effective predictor for distinguishing them would help to set basis for appropriate treatment and health education provided to these patients.

Methods: We reviewed the medical charts of pediatric patients aged 18 years or younger with diabetes mellitus in a medical center in southern Taiwan from January 2000 to December 2019. In this study, we included a total of 250 patients. The BMI of patients with their age less than 18 years old was quantified to Z score with Taiwan Children and adolescent growth body mass index recommended value in 2010, and with their age more than 18 years old was quantified with the standard of World Health Organization. We will analyze the data of the gender, age of DM onset, BMI of DM onset, insulin, C-peptide, GAD antibody and ketoacidosis to verify whether the above values are effective predicting factors for insulin use.

Results: We calculated the area under the ROC curve between C-peptide and the treatment with the insulin at the time of DM onset, 1 year and 2 years after the DM diagnosed. The best cut off point of C-peptide values were A: 0.955 ng/mL, B: 0.935 ng/mL, and C: 0.955 ng/mL.

Then, after excluding the factors of gender and insulin, we use Backward Elimination (Conditional) binary logistic regression analysis, and classify the age of DM onset (≤ 11 y/o), C-peptide (≤ 0.955 ng/mL), and BMI at the time of DM onset (Z score ≤ 2). To take the most significant impact factors (Entry: 0.05, Removal: 0.1), obtaining the most significant impact factors in three periods. The ages of DM onset, BMI of DM onset, C-peptide, GAD antibody and ketoacidosis, the five above variables corresponding to the three periods after the diagnosis of diabetes, have significant effects. A histogram with 95% CI shows that C-peptide is the most significant predictor among the three factors.

Conclusions: Overall, C-peptides are the most outstanding of all factors for predicting insulin use and are meaningful.

109 The Clinical Effect of Hormone Replacement Therapy on Pediatric Turner Syndrome Patient

女性荷爾蒙療法在透納氏症兒童之臨床效益

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Background: Turner syndrome is a chromosome disorder characterized by short stature, primary ovarian failure, congenital cardiac and renal abnormality. Many experts recommend low dose estrogen supplement at the pubertal stage. In our study, we investigate various pubertal presentations before and after estrogen supplement and the correlations of Turner syndrome karyotype.

Methods: We reviewed the medical records of patients with Turner syndrome age less than 18 years old between January 2000 and December 2019. Eighty-eight patients were enrolled and grouped into 3 categories, including 45,X, X chromosome mosaicisms (without structural abnormalities of the second X) and other karyotype (with structural abnormalities of the second X) for analysis. Sixty-six patients entered puberty and were included for pubertal analysis. Pubertal manifestations were classified as spontaneous puberty, no spontaneous puberty and arrested puberty. All patient's karyotype, phenotype, growth and

pubertal presentations and laboratory data were collected for detail group comparison.

Results: 45,X patients (79.2%) were more likely to receive growth hormone therapy than patients with X chromosome mosaicism (45.5%) and other karyotypes (64.3%), $P=0.004$. However, all patients finally reached similar adult height despite different karyotypes. Regarding pubertal presentations, most 45,X patients (58.3%) had no spontaneous puberty, most patients with X chromosome mosaicism (31.8%) had normal spontaneous puberty while most patients with other karyotypes (38.1%) had arrested puberty. Patients with arrested puberty tended to receive HRT at an older age (15.5 vs 13.6 years, $P=0.01$), but needed shorter interval (1.6 vs 2.7 years, $P=0.01$) to achieve menarche than those without spontaneous puberty. Patients without spontaneous puberty may normalize pubertal tempo after HRT management as compared with spontaneous puberty group (2.3 vs 2.2 years, $P=0.02$).

Conclusions: The necessity of growth hormone therapy and pubertal presentations of Turner syndrome patients were highly correlated to different karyotypes. The thelarche age, menarche age and pubertal tempo could be normalized after HRT management.

110 Analysis of Cardiometabolic Risk Factors in 108 Taiwanese Patients with Turner Syndrome: Experience from one Medical Center

108名台灣透納氏症候群患者的心臟代謝危險因素分析：來自一個醫療中心的經驗

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Background: Turner syndrome (TS) have 2 and 4.5 times increased relative risks of type 2 diabetes mellitus and impaired glucose tolerance, respectively. Increased mortality and morbidity have been reported in TS, possibly relating to an increased frequency of diabetes and cardiovascular diseases. Here we report blood glucose and lipid manifestations of 108 TS patients in a medical center in north Taiwan.

Methods: We conducted a retrospective cohort analysis of 108 local patients with TS between 2000 and 2019 in Chang Gung Memorial Hospital, Linkou. The patients were categorized into 2 groups according to karyotype: X chromosome monosomy (45, X) ($n=48$) and the other X chromosome abnormalities (including mosaicism and structural aberrations) ($n=60$). The profiles of age, family history, blood glucose, HbA1c, total cholesterol (HDL and LDL), triglyceride, and uric acid were reviewed and analyzed. We used independent the Student's t test, chi-square test, Cox proportional-hazards model and log-rank test to compare differences in continuous data, proportions, and Kaplan–Meier survival analysis results between the two TS groups.

Results: The other X abnormalities group had higher mean

fasting plasma glucose (FPG) levels (103.06 vs 86.11 mg/dL) and mean HbA1c levels (5.81 vs 5.28%) at childhood stage. Kaplan–Meier cumulative survival curve analysis showed the other X abnormalities group tended to have higher HbA1c (cut-off point 5.7%) ($p = 0.0004$) and total cholesterol levels (cut-off point 170 mg/dl) ($p = 0.01$), respectively. The hazard ratio of other X abnormalities group was 3.686 in glycohemoglobin A1c higher than 5.7%.

Conclusions: TS girls are at high risk of impaired glucose tolerance, diabetes, hyperlipidemia and hyperuricemia. We recommend annual screening for hemoglobin A1c, fasting plasma glucose, lipid profiles, and uric acid starting at TS adolescents.

111 Diagnostic Evaluation of Central Precocious Puberty in Girls

女童中樞性早熟之診斷

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Background: Gonadotropin-releasing hormone (GnRH) stimulation test is the gold standard for confirming the activation of hypothalamic-pituitary-gonadal axis in central precocious puberty (CPP). However, it is time-consuming and costly. Objective: To search for a simpler diagnostic modality for CPP by 1) evaluate the performance of basal serum luteinizing hormone (LH), 2) construct a practical score system, and 3) determine the optimal single sampling time for serum LH in GnRH stimulation test.

Methods: Retrospective analysis of girls aged between 3 and 9 years at the time of GnRH stimulation test, who attended our endocrine clinic at the MacKay Children's Hospital for signs of puberty between July 2014 and June 2019. We recorded patients' age, height, weight, breast Tanner stage (BS), bone age, serum LH and follicle-stimulating

hormone (FSH). Receiver operating characteristic (ROC) curves and Youden index were used to obtain optimal basal serum LH level. Binary logistic regression was employed to construct a practical score system. Cross-sectional, cumulative frequency, and ROC curves utilized to simplify GnRH stimulation test.

Results: 381 sets of GnRH stimulation test were performed in 313 patients. Basal serum LH ≥ 0.2 IU/L demonstrated 70% sensitivity and 70% specificity for predicting GnRH positive results. Practical score system (3 BS+3 LH+4 FSH) showed 76% sensitivity and 72% specificity. Serum LH value at 30th minute post intravenous gonadorelin showed 99% sensitivity and 100% specificity.

Conclusions: Single sampling of serum LH at 30th minute post-injection demonstrated equivalent diagnostic performance to the traditional GnRH stimulation test in diagnosing CPP. This could become the simplest diagnostic modality.

112 Clinical and Molecular Characteristics in Taiwanese Patients of Idiopathic Hypogonadotropic Hypogonadism: The Experience of a Single Medical Center

以單一醫學中心為經驗：台灣病人的特發性低性腺促素低性腺功能症的臨床及基因特徵

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Background: Idiopathic (isolated) hypogonadotropic hypogonadism (IHH) is a rare disease. It can be classified as Kallmann syndrome (KS) with anosmia and normosmic IHH (nIHH). This study is aimed to investigate the clinical characteristics and molecular diagnosis in Taiwanese patients with IHH.

Methods: Twenty-six unrelated IHH patients were included in this study. Their clinical, hormonal and radiological findings were analyzed retrospectively. Exome sequencing with targeting analysis for 283 IHH-associated genes were performed in these patients to identify the molecular etiology.

Results: These 26 patients (M:F=19:7) were divided to KS group (n=11) and nIHH group (n=15). The suspicious ages were earlier in boys than in girls. Fifteen patients were found to have pathogenic/likely pathogenic variants on IHH-associated genes and the detection rate was 58%. The most common genetic etiologies in this study group are CHD7, FGFR1 and KAL1. Two patients with nIHH were found de novo SOX11 mutations and shared Coffin-Siris syndrome-like features. After treatment, the height outcomes and secondary sexual characteristics were significantly

improved. There were no obvious differences between disease-causing, variants of uncertain significance and idiopathic groups.

Conclusions: Exome sequencing is helpful in patients with IHH and SOX11 gene was first found as a causative gene in this study. We described the clinical, hormonal, molecular characteristics, and treatment outcome in patients with IHH in Taiwan, which is useful in the therapeutic plan and further research.

113 Applicability of the Greulich/Pyle Skeletal Standards for Bone Age Assessment: A Taipei Experience

評估以Greulich and Pyle圖譜判讀骨齡之適用性及與生理年齡間之差異性

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Background: The Greulich-Pyle (GP) atlas of skeletal age determination was based on the data derived from Caucasian children population born between 1917 and 1942. The purpose of this study is to answer the question of whether GP standards currently used are applicable to modern-day Taipei children/adolescents.

Methods: Clinical data from October 1, 2010, till March 31, 2019, were retrospectively collected from a general hospital in Taipei. The data of patients who were diagnosed as endocrine/genetic disorders were excluded. Clinical data included the chronological age (CA) and bone age (BA) X-ray film image. BA was determined by a senior pediatrician and a senior pediatric radiologist using the GP method. The reliability and validity of BA reading were tested. The validity of BA at different CA groups were assessed, and the rates of deformed middle phalanx V and maturation stage were estimated. Relative stages of ulnar and radial bones maturation were evaluated. Data were analyzed statistically.

Results: 969 data of males were collected and 1,189 data of females were collected from 2,185 medical records. After the exclusion of those data with endocrine or genetic diseases and unqualified films, 705 data of males and 836 data of females were analyzed. In boys, mean BA was delayed by 0.7 to 1.5 years compared with CA between 0 to 9 years of age and advanced by 0.8 to 1 years between 15 to 18 years. In girls, mean BA was generally advanced before 2 years old or after 5 years old, especially between age groups of 6 and 15. Ulnar bone maturation tended to be delayed in the early age of males. The rate of deformed middle phalanx V was 8.2%. Middle phalanx V tended to mature earlier than GP standards in males < 15 years old and in females > 7 years old.

Conclusions: There is a discrepancy of deviation pattern between male and female populations. In males, GP

standards tend to underestimate BA at a younger age and overestimate BA beyond age 15. In the female population, GP method tends to overestimate BA beyond age group of 5. The rates of deformed middle phalanx V were high. Ulnar bone maturation tends to delay at the early age of males.

114 A Novel Pathogenic Variant in Calcium-Sensing Receptor (CaSR) Gene Causing Hypocalcemia in a Family

鈣敏感受體基因 (CASR) 新變異所致低血鈣：家族個案報告

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Background: The calcium sensing receptor (CaSR) plays an important role in calcium balance, it expresses in multiple tissue such as parathyroid glands, kidneys, bone marrow, breast, thyroid C-cells, intestine, some areas of the brain, and others. If there has an inactivating (loss-of-function) mutation, the set-point of the CaSR will increase which resulted in hypercalcemia. In contrast, an activating (gain-of-function) mutation of CaSR gene will decrease the set-point of the CaSR, which in turn decreases the secretion of the parathyroid hormone (PTH) at serum calcium concentrations that normally trigger PTH release, thereby causing hypocalcemia. Here, we present a novel pathogenic variant in CASR which causes hypocalcemia in a Taiwanese family.

Methods: A 5-month-old female infant, was brought to our Emergency Department because of generalized tonic-clonic convulsion, upper ward eye gazing and drooling which occurred twice in 2 days. The biochemistry data showed serum ionized calcium of 3.39 mg/dL (4.6-5.32), albumin 4.5 g/dL, phosphate 10.2 mg/dL (2.5-4.6), PTH 15.95 pg/ml (11-62) and Vit D: 22.6 ng/mL (6.6~49.9). Tracing back her birth history, she was an identical twin A with normal prenatal examination and non-eventful perinatal course; her developmental history was as milestone. Her father also had seizure episode with clonic movement and eye deviation to the right while he was 7 days of age which was then diagnosed as hypocalcemia caused by hypoparathyroidism. He was on Calcium Carbonate and Calcitriol supplement since then.

Results: Due to the low level PTH and family history, we performed genetic sequencing in CaSR gene. It revealed a novel variant c.350A>G (p.Gln117Arg) in our patient and her father. We checked this variant in prediction models as below: Polyphen-2 showed damaging and LOVD revealed pathogenic. The ionized calcium and phosphate returned to near normal (4.43 mg/dL, 8.7 mg/dl respectively) under the oral Calcium Carbonate and Calcitriol.

Conclusions: From literature, several mutation of CASR causing hypocalcemia had been reported but there had no

published report in Taiwan yet. Herein, we report a novel pathogenic variant in CASR causing a familial hypocalcemia in Taiwan.

115 Resveratrol Intake during Pregnancy and Lactation De-programs Adiposity and Ameliorates Leptin Resistance in Male Offspring Induced by Maternal High-fat Plus Postnatal High-fat Diets via Fat Metabolism Regulation

孕婦和哺乳期攝入白藜蘆醇可通過脂肪代謝調節雄性後代的肥胖，並改善其後代對瘦素的抗性

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Background: Maternal obesity is an emerging problem in the modern world. Growing evidence suggests that intrauterine high-fat (HF) exposure may predispose progeny to subsequent metabolic challenges. Progeny born to mothers who ate an HF diet also tends to eat an HF diet when growing and aggravate metabolic issues. Thus, the generational transmission of obesity is cyclical. Developing a strategy to prevent the occurrence of metabolic syndrome related to prenatal and/or postnatal HF diet is important. In this study, the reprogramming effects of maternal resveratrol treatment for the progeny with maternal HF/postnatal HF diets were investigated.

Methods: Sprague-Dawley dams were fed either a control or a HF from mating to lactation. After weaning, the offspring were fed chow or an HF diet. Four experimental groups were yielded: CC (maternal/postnatal control diet), HC (maternal HF/postnatal control diet), CH (maternal control/postnatal HF diet), and HH (maternal/postnatal HF diet). A fifth group (HRH) received a maternal HF diet plus maternal resveratrol treatment and a postnatal chow diet to study the effects of maternal resveratrol therapy.

Results: Maternal resveratrol treatment lessened the weight and adiposity of progeny that were programmed by prenatal and postnatal HF diets. Maternal resveratrol therapy ameliorated the decreased abundance of the SIRT1 enzyme in retroperitoneal tissue and the altered leptin/soluble leptin receptor ratio of progeny. Maternal resveratrol therapy also decreased lipogenesis and increased lipolysis for progeny.

Conclusions: Maternal resveratrol intervention can prevent adiposity programmed by maternal and postnatal HF diets by inducing lipid metabolic modulation. This study provides a new reprogramming role for the anti-obesity effect of maternal resveratrol supplements.

116 Randomized Evaluation of Acquired Undescended Testis in School Children in Taipei City, Keelung City and New Taipei City: a Preliminary Study

隨機對照評估沒下降睪丸兒童在台北市、基隆市及新北市的分佈情形

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Background: The physical examination including EENT, heart, lung, abdomen and genital organs especially focusing on acquired undescended testis (AUDT), were performed by the local government

Methods: Groups of doctors were randomized send to the schools of Taipei city, Keelung city and new taipei city to do the students health physical examination, each group is including 4 doctors .

Results: The results are interesting, which showed 5.78% (AUDT=12, R&L=10, R=2, n=207) in grade 1 (6-7yr), 7.97% (AUDT=11, R&L=7, R=4, n=138) in grade 4 (9-10yr), 1.2% (AUDT=5, R&L=4, R=1, n=408) in junior high school (12-13yr), and 0.49% (ADUT=1, n=201) in high school (16yr). No hypospadias was found in the ADUT students. In the meantime, the above student' data was by only one doctor

Conclusions: Although it is proposed that over 50% of boys with AUDT spontaneous descend occurs before puberty but 0.98% (ADUT=6, n=609) still being observed in boys during puberty in our study, which means the risks of testicular cancer, reduced sperm motility, and even infertility could be expected in the future. Therefore, our future planning is to call back the AUTD students for further scrotal ultrasounds examination, and reproductive hormones and semen analysis.

117 Adolescent Social Ecological Factors in Predicting Diabetes Mellitus during Young Adulthood among Different BMI Groups

青少年時期之社會生態因子在預測青壯年期的糖尿病發生率分析

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Background: Diabetes Mellitus is a world pandemic. However, the pathogenesis of diabetes is not fully understood. Scientists proposed that diabetes may arise from a complex interaction among genes and environmental

factors. The impact of potential risk factors during adolescence on the development of diabetes in later life is less studied. The purpose of this research is to examine adolescent social ecological factors in predicting the development of diabetes in young adulthood among different BMI groups.

Methods: Data were derived from the public-use data of National Longitudinal Study of Adolescent Health (Add Health), a nationally representative probability sample of US adolescents. A cohort of 5114 adolescence in grades 7-12 (Wave1, 1994-1995) was followed to their young adulthood (24-32 years, Wave 4, 2008-2009). Social ecological predictors were extracted from the Wave 1 data, while the outcome variable, diabetes, and BMI groups were obtained from Wave 4. Bivariate and multivariable logistic regression was conducted to evaluate the relationship between risk factors and risk of diabetes among different BMI groups.

Results: In bivariate analysis, age, race, BMI, family history of diabetes and daily screen time during adolescence were associated with higher risk of diabetes in young adulthood, while the impact of gender, exercise, regular family meal, routine physical checkup, neighborhood fitness center, health education and family income were negligible. However, in multivariable analysis, age, overweight status, and neighborhood fitness center (Odds Ratio [OR]: 1.32; 1.4; 0.2, p < 0.05) are significant adolescent predictors of diabetes for low/normal BMI young adult. As for those with overweight or obesity, race, family history of diabetes and screen time (> 6 hours/day) ([OR]: 2.18; 2.08; 1.82) are the most significant predictors of diabetes in their adolescence.

Conclusions: Demographic features, health behaviors, family history, and community resource during adolescence are related to the risk of diabetes in young adulthood. The impact may vary among different BMI groups. Preventive measures should be tailored according to their potential risk factors.

118 The Prevalence of Hypertension among Children and Adolescents in Taiwan

台灣兒童及青少年高血壓盛行率之研究

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Background: Hypertension is associated with long-term cardiovascular morbidity and mortality. However, the reported prevalence of hypertension during childhood is wide-ranged from different populations. Therefore, in order to promote long-term cardiovascular health, to understand the local prevalence of hypertension among children and adolescents are essential to help establish suitable health-care strategies.

Methods: The study subjects were retrieved from the Taiwan National Insurance Research Database between 2000 and 2015. Children and adolescents younger than 18 years old who were coded with hypertension were identified from each year. The prevalence and trend of hypertension among children and adolescents were calculated.

Results: During the study period, the prevalence of hypertension among children and adolescents in Taiwan were between 0.018% and 0.028%. The overall prevalence of pediatric hypertension was increasing yearly, particularly in the last few years. The prevalence of male patients was higher than that of female patients.

Conclusions: In comparison with other reports, the prevalence of hypertension among children and adolescents in Taiwan was relatively low. The results may reflect the reality of diagnosis and awareness of pediatric hypertension during the study period in Taiwan. To improve the long-term cardiovascular outcome, early diagnosis, and appropriate therapy of hypertension during childhood are important for the health-care providers.

119 Association between Food Insecurity and Substance Use among Economically Disadvantaged Adolescents: Longitudinal Analysis of a Nationwide Cohort Study

經濟弱勢青少年的糧食匱乏與物質使用之間的相關性：全國世代研究的長期分析

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Background: Food insecurity (FI), defined as the limited or uncertain availability of nutritionally adequate and safe foods, remains a major life concern among many poor subpopulations despite national economic growth. Few investigations have been made into its impact on adolescent substance use. Considering this gap in knowledge and less researched Taiwanese social setting, this study aims to examine the relationship between FI and cigarette and alcohol use among economically disadvantaged adolescents.

Methods: Data come from the Taiwan Database of Children and Youth in Poverty, which is a biennial survey on nationally representative cohort of children and youth in

families receiving governmental subsidies or social services. The present study used a subset of data on the 1,243 adolescents (Mage = 13.3 years; 645 males) that completed all the four items relevant to FI (range: 0-4) at wave 3 in 2013. Cigarette smoking and alcohol drinking were self-reported throughout the waves 3 to 5. Covariates included psychological wellbeing and peer substance use. Multiple hierarchical regression analysis based on generalized estimating equation modeling was applied to examine the relationship between food insecurity and substance use in this longitudinal cohort.

Results: Of the sample analyzed, nearly 75% reported having at least one FI item. Regression models adjusted for age and gender found that adolescents with more than one FI item had a 45% increased odds of alcohol drinking (adjusted odds ratio [AOR] = 1.45 [95% confidence interval 1.61–3.21]), compared with food-secure peers. This association was canceled if peer substance use and psychological wellbeing were added as covariates. On the contrary, FI remained significantly associated with cigarette smoking (AOR = 2.16 [1.33–3.51]) in fully adjusted models.

Conclusions: FI appears to be a salient predictor of cigarette smoking in adolescents. There is also some evidence supporting the link between FI and alcohol use, whilst psychological wellbeing and peer substance use may mediate the association. Clinical and public health attention should be given to economically disadvantaged youth who are particularly vulnerable to FI.

120 Changes in Spatial Memory Performance and Gut Microbiota Homeostasis Following Methotrexate Treatment in a Juvenile Murine Model

甲氨蝶呤藥物治療後空間記憶功能表現及腸道菌叢生態改變：一個小鼠研究模式

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Background: Studies on children leukemia survivors revealed impaired intellectual and cognitive functions. Methotrexate (MTX) chemotherapy is responsible for both functional and morphological changes in brain. Our study found MTX treatment caused spatial deficits in developing rats. Gibson et al. had demonstrated that tri-glia dysfunction underlies MTX neurotoxicity was mediated through brain-derived neurotrophic factor (BDNF)-mediated pathways. We focus on the BDNF-mediated regulation of adaptive myelination process following MTX treatment. Increasing studies have highlighted the prominent role of the gut microbiota in gut-brain interactions, with emphasis on gut microbiota change in response to stimuli and the correlation of the neurologic impact. Thus, gut microbiota alteration was examined in the study.

Methods: Male Sprague-Dawley rats (PND 17 ± 1) weighing ~50 g are used. Rats receive intrathecal injection via transcutaneous cisternal magna puncture. The Morris water-maze test was conducted to assess spatial learning and memory change. Brain tissue and plasma were collected for analysis of the brain-derived neurotrophic factor (BDNF) and myelination-related proteins, including myelin basic protein (MBP), Sry-related HMg-box gene 10 (Sox10), gamma-aminobutyric acid receptor subunit alpha-1 (gabaal receptor), and gamma-aminobutyric acid B receptor 1 (GABAB1). Feces collected were used for bacterial 16S rRNA sequencing.

Results: MTX caused spatial memory deficits in developing rats and significant myelin loss. Altered expression of BDNF and myelin-related proteins was noted. MTX group showed a significant decreased relative abundance of Firmicutes while Bacteroidetes were elevated compared to sham groups. The top 10 of order clustering revealed that there were significant increased relative abundance of Bacteroidales in treatment group. Clustering microbiomes based on family indicated significance lower relative abundance of Clostridiaceae and Muribaculaceae. Examination of plasma SCFA concentration found plasma SCFAs were down regulated after MTX treatment.

Conclusions: The study found the association between gut microbiota changes and myelination process after MTX treatment.

121 Curcumin Induces Apoptosis by Inhibiting BCAT1 Expression and mTOR Signaling in Cytarabine-Resistant Myeloid Leukemia Cells

薑黃素透過抑制阿糖胞苷耐藥之髓樣白血病細胞的 BCAT1 表達和 mTOR 信號而誘導細胞凋亡

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Background: Acute leukemia is the most common cancer in children. Cytarabine is one of the key chemotherapy drugs for leukemia treatment, however, chemotherapy-induced multidrug resistance is considered to be an important cause of therapy failure or tumor recurrence. Curcumin is known to fight against tumor development and be used as a chemical sensitizer for cytarabine. Our previous research also showed curcumin induce apoptosis in cytarabine-resistant acute myeloid leukemia cells. Branched-chain amino-acid transaminase1 (BCAT1), an

aminotransferase enzyme, acts upon branched-chain amino acids. BCAT1 is known to play a critical role in the progression of myeloid leukemia and can interfere with the growth of cancer cells by regulating mTOR-mediated mitochondrial biogenesis and function. This study investigated whether curcumin induces apoptosis by interfering the expression of BCAT1 and mTOR signaling in cytarabine-resistant myeloid leukemia cells.

Methods: The cytarabine resistant cell lines and primary cells from bone marrow samples of patients with relapsed cytarabine-resistant myeloid leukemia were cultured and treated with curcumin. Then, real-time PCR or western blot analysis were used to detect whether the expression of BCAT1 and mTOR signaling were regulated by curcumin.

Results: Curcumin induced apoptosis by inhibiting BCAT1 expression and mTOR signaling in Kasumi-1, KG-1, HL60, cytarabine-resistant HL60, and cytarabine-resistant primary myeloid leukemia cells. In addition, the BCAT1 and mTOR signaling may modulate each other. Interesting, tetrahydrocurcumin, a major metabolite of curcumin, and cytarabine have no the effect of BCAT1 inhibition.

Conclusions: The current medical treatment is still unable to solve the problem of multidrug resistance phenotype in chemotherapy treatment of acute myeloid leukemia. The use of phytochemical factors to cancer treatment has received increasing attention. Understanding the mechanism of curcumin-induced apoptosis in cytarabine-resistant cells can help the development of new drugs for leukemia.

122 Clinical Features and Treatment Outcomes of Childhood Acute Lymphoblastic Leukemia with Initial Musculoskeletal Manifestations

有骨頭肌肉關節症狀的兒童急性淋巴性白血病病人之臨床表現及預後分析

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Background: Musculoskeletal manifestations (MSM) can be primary symptoms of childhood acute lymphoblastic leukemia (ALL) with risk of delay diagnosis. In this study, we retrospectively investigated the clinical features and treatment outcomes of patients with MSM at diagnosis (Dx) in children with ALL.

Methods: From April 2007 to April 2020, children (age ≤ 18 years) with ALL diagnosed at out institution were assigned to 2 groups: ALL with MSM (MSM Gr) or without MSM (non-MSM Gr). The symptoms of MSM included bone pain, arthralgia, myalgia or limping gait. The symptom duration, clinical features, and radiological abnormalities at Dx were collected. Differences between categorical variables and continuous data were examined with Fisher exact or χ^2

tests and the Mann-Whitney U test, respectively. The Kaplan-Meier method was used to estimate survival rates with differences compared by the log-rank test.

Results: Totally, 195 newly diagnosed ALL were enrolled in the study. Fifty patients (26%) presented with MSM at Dx. Compared with non-MSM Gr, the patients of MSM Gr statistically significantly had older age (median, 5.2 vs. 4 y, $P = .036$), longer duration of symptoms (14 vs. 7, days $P = .0035$), occurrence of fever (90% vs. 74%, $P = .01$), higher Hb (8.4 vs. 6.8 g/dL, $P = .0008$) and platelet (77 vs. $44 \times 10^3/\mu\text{L}$, $P = .002$), and lower circulating blasts (18% vs. 48%, $P = .002$). Of note, none of the MSM Gr was T-ALL. The median WBC count ($6.8 \times 10^3/\mu\text{L}$) of the MSM Gr was nearly normal, though there was no significant difference with that of the non-MSM Gr. Biochemistry profile (i.e. LDH, ALK-P, Cr and uric acid), CNS status and risk group did not significantly differ between the 2 groups. Further, 20 patients (40%) of the MSM Gr had x-ray of affecting sites. Radiological abnormalities were detected in 14 (70%). There were no significant differences between the MSM and non-MSM in the rates of 5-year event-free survival (85.2% vs. 84.0%; $P = .612$) or overall survival (94.2% vs. 88.8%; $P = .124$).

Conclusions: Musculoskeletal manifestations of childhood ALL may lead to the delay diagnosis, but this delay did not have the impacts on the treatment outcomes.

123 Similar Outcomes between Adolescent/young Adults and Children with AML Following Allogeneic Hematopoietic Cell Transplantation

比較青少年/年輕人和兒童之間急性骨髓性白血病於異體造血細胞移植的類似結果

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Background: Cytogenetics of AML increases exponentially with age. AYA patients have a myriad of specific psychosocial and other challenges which may influence their ability to obtain appropriate treatment. We therefore hypothesized that in the setting of allo-HSCT for AML, inferior outcomes would be observed in AYA patients as compared with children.

Methods: A total of 63 AML patients, ages 1.5-28 years, underwent allo-HSCT at Chang Gung Children's Hospital between 1998 and 2020. In all, 37 (59%) patients were < 15 years at the time of allo-HSCT and 26 (41%) were 15-29 years of age (AYA). The median age at the time of allo-HSCT for those < 15 years of age was 6.3 (range, 1.5-12.8 years) as compared with 15.7 (range, 13.5-28.3 years) for the AYA. The median follow-up was 2.2 (range, 0.2-20.8) years after HCT for patients < 15 years old and 3.8 (range, 0.3-21.6) years for AYA. Overall survival (OS) was defined as the length of time from the HSCT to death from any cause. Disease-free survival (DFS) was defined as

the length of time from the HSCT to the last follow-up or first event (failure to achieve CR, relapse, secondary malignancy, or death from any cause).

Results: Before transplant, 25 (68%) patients < 15 years old were in CR1, 6 (16%) in CR2 and 6 (16%) are transplanted in refractory relapse as compared with 13 (50%) in CR1, 5 (19%) in CR2 and 8 (31%) in refractory/relapsed disease for the AYA group ($P = 0.31$). Eleven patients (30%) < 15 years old had high-risk cytogenetics with FLT3-ITD ($n = 3$), MLL-R ($n = 5$), and monosomy 5 or 7 ($n = 3$) compared with 5 (19%) of the AYA (FLT3-ITD, $n = 3$; MLL-R, $n = 2$; $P = 0.89$). Comparing patients of < 15 years old with AYA using univariate analysis reported no significant difference in the 5-year OS (63.1%, 95% CI 44.9%-80.3% vs 64.1%, 95% CI 44.9%-88.3%; $P = 0.876$) or DFS (44.3%, 95% CI, 27.1%-61.5% vs 49.5%, 95% CI, 29.6%-69.4%; $P = 0.83$).

Conclusions: Our retrospective analysis of children and AYA who received an allo-HSCT for AML identified similar survival regardless of age, but our relatively low numbers may have limited the statistical significance of this finding.

124 The Dysregulation of Hecpudin-Ferroportin Axis in Childhood Acute Lymphoblastic Leukemia Survivors Completing Chemotherapy

急性淋巴性白血病病童結束化療後「鐵調素-運鐵素機制」失調的探討

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Background: The master regulator of systemic iron homeostasis is hepcidin, which controls serum iron through degradation of ferroportin in iron-absorptive enterocytes and iron-recycling macrophages. Here, we aimed to investigate the role of the hepcidin-ferroportin axis in childhood acute lymphoblastic leukemia (ALL) survivors who completed chemotherapy.

Methods: Children with ALL, diagnosed at our hospital and completed TPOG-ALL-2013 protocol before June 30, 2020, were enrolled. Their siblings were selected as the normal controls if the informed consents were obtained. The data of serum iron, total iron-binding capacity (TIBC) and ferritin were collected in ALL patients. Hecpudin and ferroportin (FPN) levels of ALL patients and control groups were performed using peripheral blood (PB) by Enzyme-linked immunosorbent assay (ELISA).

Results: In total, 58 ALL survivors with disease-free were enrolled. Thirteen patients had abnormal ferritin levels (> 300 ng/mL) (range, 387.7-2288.0) in the first 6-month

period after off-therapy and defined as iron overload (IO). Among them, 35 patients (off-therapy group) had PB for ELISA of hepcidin and FPN. Seven (20%) of the 35 patients had IO. And the normal control group (control group) collected 38 siblings after exclusion of acute illness and iron deficiency. There were no significant differences of age or gender in the off-therapy and control groups. The hepcidin and FPN of the off-therapy group were significantly higher than those of the control group ($P = .01$). The difference was particularly significant while comparing the control group with 7 patients with IO in the off-therapy group ($P < .001$). In addition, male and patients after puberty tended to have higher levels. In the off-therapy group, transferrin saturations (iron/TIBC) did not significantly differ between patients with and without IO. Further, the 7 IO patients had significantly higher levels of hepcidin and FPN than those of patients without IO ($P < .0004$).

Conclusions: The dysregulation of hepcidin-ferroportin axis of childhood ALL survivors with iron overload showed high hepcidin and uncontrolled ferroportin hyperactivity, which may point to the impaired down-regulation of ferroportin by hepcidin.

125 Iodine-131-labeled Meta-iodobenzylguanidine (^{131}I)MIBG Targeted Radiotherapy in Relapsed / Refractory Neuroblastoma: Initial Experience in Taiwan

碘-131-間碘苜瓜 (^{131}I)MIBG 標靶放射治療應用於復發性/頑固性神經母細胞瘤的初期臺灣經驗

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Background: Radiolabeled ^{131}I MIBG targets the Norepinephrine Transporter, accumulates in neuroblastoma (NB) cells, and serves as a retrieval therapy in relapsed/refractory NB.

Methods: In 2015, an ^{131}I MIBG Treatment Facility was established at Changhua Christian Hospital with a private

room with lead shields to maintain area dose rates ≤ 0.5 uSv/hr outside the room, independent sanitary pipelines & tank, and patient isolation until dose rate < 50 uSv/hr at 1 meter. Parents were isolated behind lead shields, trained in radiation safety principles and given real-time radiation monitors.

Results: During 2015–19, 4 doses of ^{131}I MIBG were given to 3 patients with MIBG-avid NB aged 13, 24, and 3 years, respectively. All patients tolerated the isolation & infusion without complications. Case #1 was diagnosed with retroperitoneal NB with bony metastases, MYCN non-amplified with segmental chromosomal alterations (SCAs), at 11 years of age (y/o); he was refractory to TPOG-N2002-HR2 and Topo/Cy/Etop. ^{131}I MIBG of 150 mCi (3 mCi/kg) was given 25 months after initial diagnosis. Stable Disease was observed for 1 month. Case #2 was diagnosed with retroperitoneal NB at 12 y/o with marrow & nodal metastases, MYCN low-level gained with SCAs. After CR to TPOG-N2002-HR2, he suffered multiple relapses since 6 years after diagnosis. ^{131}I MIBG of 300 mCi (5 mCi/kg) *2 tandem doses were given at 24 y/o. Stable Disease was observed for 4 months before progression with liver metastases. The patient died of tumor progression 17 months after ^{131}I MIBG. Case #3 was diagnosed with retroperitoneal NB with bone & marrow metastases at 9 m/o. He achieved Complete Response after TPOG-N2002-HR1 induction but relapsed at 10 months after diagnosis. After failing ICE & Irino/Temoz/Dinutuximab beta, he received palliative radiotherapy followed by ^{131}I MIBG of 100 mCi (9.5 mCi/kg) at 3 y/o. Clinical Response was observed for 3 weeks. Further targeted therapy was planned.

Conclusions: Submyeloablative doses of ^{131}I MIBG have been successfully administered to Taiwanese patients with relapsed/refractory NB with clinical benefit. Through interhospital collaborations, ^{131}I MIBG may be further added on to NB therapy in Taiwan.

126 Response and Toxicity of Interval - compressed Chemotherapy for the Treatment of Ewing Sarcoma and Other Small Round Cell Sarcomas

尤文氏肉瘤及其他小圓細胞肉瘤病患接受療程壓縮之化學治療的反應與毒性觀察

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Background: Small Round Cell Sarcomas (SRCS) in children & young adults are highly aggressive tumors that benefit from interval-compressed (ic-) chemotherapy. Data from Asia remain scarce, however.

Methods: Patients < 30 years of age with newly diagnosed SRCS were to begin chemotherapy cycles every 14 days if the neutrophil count $\geq 75 \times 10^6$ /L and the platelet count $\geq 75 \times 10^9$ /L. Patients received Vincristine (2 mg/m²), Doxorubicin (75 mg/m²) & Cyclophosphamide (1,200–2,200 mg/m²) (VDC) alternating with Ifosfamide (9,000 mg/m²) & Etoposide (500 mg/m²) (IE), with Filgrastim (5 mcg/kg/day) between cycles. Carboplatin (800 mg/m²) was added to IE for CIC-rearranged sarcoma. Primary site treatment with surgery, radiation, or both was performed at Week 10–15 for patients with nonmetastatic disease, after maximal systemic control for patients with metastatic disease, or when decompression was needed.

Results: From 2016/12 to 2019/12, nine patients (M:F = 5:4; mean age = 12.9 [range, 3–29] years; stage I/II/III/IV = 0/4/1/4) were treated with 98 cycles of ic-VDC/IE at a median interval of 19 days (interquartile range [IQR], 15–22 days); diagnoses were Ewing Sarcoma (6), MyoEpithelial Carcinoma (1), Rhabdomyosarcoma (1), and CIC-DUX4 Sarcoma (1). The best Overall Response Rate of 6 patients with measurable tumor was 83% (5 Partial Response and 1 Stable Disease [CIC-DUX4 sarcoma]). The other 3 patients whose primary tumor was resected upfront remained in Complete Response during follow-ups. Patients had neutrophil count decreased to a median nadir (IQR) of 134 (35–365) $\times 10^6$ /L at median (IQR) Day 11 (10–12) that recovered by Day 15 (13–17). Patients had their platelet

count decreased to a nadir of 29 (19–54) $\times 10^9$ /L at Day 11 (11–13) that recovered by Day 17 (14–22). 38 episodes of febrile neutropenia (44%), 7 episodes of bacteremia (8%), and 0 episode of septic shock (0%) were observed. At follow-ups, 4 of 4 patients with localized disease were alive with no evidence of disease and 2 of 4 patients with metastatic disease have died of tumor progression.

Conclusions: For Ewing sarcoma and other SRCS in Asian children and young adults, ic-VDC/IE is a very effective regimen with tolerable toxicity.

127 Growing Teratoma Syndrome in Patients of Malignant Germ Cell Tumors: An Unusual Evolution of Clinical Significance

繼發於惡性生殖細胞瘤的畸胎瘤增長症候群之探討

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Background: Malignant germ cell tumor (GCT) may occur intracranially or extracranially. The outcome for patients with malignant germ cell tumor ranges widely, mainly dependent on staging, tumor histology, tumor location and responsiveness to the treatment. The tumor marker, AFP or bHCG, may be a surrogate of disease activity during followup if elevated at initial presentation. We identified a patient of malignant GCT at left testis who developed an abdominal mass after treatment completion, but had normalized tumor markers. Upon histological examination on the excised tumor, absence of any malignant component other than mature tissue was revealed. A diagnosis of growing teratoma (GTS) syndrome was made according to the criteria by Logothetis in 1982.

Methods: Four pediatric patients of GTS are identified in Taipei Veterans General Hospital, Linkou Chang Gung Memorial Hospital and Cheng Kung University Hospital. By medical charts review, clinical characteristics and treatment details are collected.

Results: There are 3 boys and 1 girl. The primary malignant GCT located in pineal region in 1, ovary in 1 and testis in 2. Two have GTS in primary site, and the other two have GTS in abdomen or testis. The interval between diagnosis of primary GTC and GTS is 4, 4, 10, and 48 months respectively. They all received surgery for tumor resection, and three required further treatments upon recurrence. One patient was lost to follow-up. With a median follow-up time

of 83.7 months after diagnosis, three patients were disease free without chemotherapy.

Conclusions: Although GTS is not common, its unique presentation, resistance to chemotherapy or radiotherapy and good outcome if completely resected deserve our attention to avoid unnecessary intensive treatment in such patients. However, its progression may be fast and recurrence is not uncommon. Long term follow-up is required.

128 A Single-center Case Series of Mutational Analysis of RB1 Gene in Children with Retinoblastoma

兒童視網膜母細胞瘤的RB1基因突變分析：單一醫學中心之經驗

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Background: Retinoblastoma (RB) is a rare pediatric cancer caused by the mutation of RB1 gene. Mutational analysis of the RB1 gene is helpful to delineate heritable retinoblastoma for non-hereditary ones for efficient genetic counseling. In this study, we present the mutational analysis of RB1 gene in children with retinoblastoma in a single medical center.

Methods: Tumor and/or blood samples from patients with retinoblastoma were submitted to an outsourced certified laboratory center in Taipei after obtaining the informed consent from the parents. DNA was extracted. Mutational analysis was conducted by a combinatorial approach of Multiple Ligation-dependent Probe Amplification (MLPA) assay, Methylation specific-MLPA assay, and next generation sequencing.

Results: Fifty-seven children were diagnosed with retinoblastoma between 2014 and 2019 in Linkou Chang Gung Memorial Hospital. Mutational analysis of RB1 gene was conducted in 12 (21%) patients (8 bilateral and 4 unilateral retinoblastoma). Six patients (3 bilateral and 3 unilateral retinoblastoma) had genetic tests of both blood and tumor samples. The remaining 6 patients (5 bilateral and 1 unilateral retinoblastoma) who did not undergo enucleation submitted blood samples alone. Overall, 18 mutations were identified. The spectrum of mutation types comprised 27.8% (5/18) splicing site mutations, 27.8% (5/18) promoter hypermethylation, 22.2% (4/18) nonsense mutations, 11.1% (2/18) frameshift mutations, 5.6% (1/18) missense mutations, and 5.6% (1/18) large deletions. Among 8 patients with bilateral retinoblastoma, 6 had germline mutations in RB1 gene. No germline mutations in RB1 gene was detected in 4 patients with unilateral retinoblastoma. Only one mother of the 18 parents tested was positive for a germline mutation which was pathogenic and highly penetrant. She was treated for bilateral

retinoblastoma in her childhood and remained disease-free for more than 20 years.

Conclusions: Mutations in the RB1 gene in this study were heterogeneous. Our study emphasizes that genetic testing should be incorporated into the management plan of all retinoblastoma patients to ensure timely evaluations and appropriate counseling in Taiwan.

129 Individually PK-guided Management in Severe Hemophilia A Patients

嚴重A型血友病患者依藥物動力學工具來進行個人化治療

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Background: Prevention and treatment of bleeding episodes aggressively could improve life quality in severe hemophilic patients. The extended half-life clotting factors provides longer half-life and fewer injection frequency. In view of the diverse pharmacokinetics (PKs) of clotting factor between individuals, it was rational to use PK to personalize hemophilia treatment. Here we report the experience of PK tools in MacKay Children's Hospital.

Methods: The patients with severe hemophilia A were enrolled. We shifted the clotting factor from standard half-life to extended half-life product since November 2019. The PK study was conducted in patients with prophylactic use of extended half-life product. Trough and peak level of factor VIII were examined. The PK tools including WAPPS-Hemo and MyPKFiT were adopted in the study.

Results: There were 20 severe hemophilia A patients treated in MacKay Children's Hospital. Eighteen received prophylactic and two received on-demand treatment, respectively. The PK study was done in 13 severe hemophilia A patients with prophylactic use of Adynovate. The utilization of PK tools included WAPPS-Hemo in 13 patients and MyPKFiT in 10 patients. Then we adjusted the dosage or frequency of clotting factor based on the PK results individually.

Conclusions: According to the application of PK tools, we expect to optimize the management of hemophilia. Patients would have better life quality and minimize the bleeding events.

130 Oral mTOR Inhibitor (Everolimus) for Tuberous Sclerosis Complex–Renal Angiomyolipoma/Subependymal Giant Cell Astrocytoma – The Associated Outcome of Facial Angiofibromas

以口服mTOR治療TSC之臉部纖維瘤之成效

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Background: Facial angiofibromas occur in approximately

75% of individuals with tuberous sclerosis complex (TSC), causing substantial cosmetic and disfigurement. Current therapies are partially effective but uncomfortable, produce scarring, especially expensive. Current study is to evaluate the efficacy of oral everolimus for TSC- angiofibromas.

Methods: This retrospective study reviewed TSC patients being treated of oral everolimus for SEGA /AML, recording the change of facial angiofibromas. Angiofibroma Grading Scale (AGS) changes were recorded according to erythema, average lesion size, lesion density and percent involvement on forehead, nose, cheeks and chin. The sums were recorded before and after administration of oral everolimus.

Results: Twenty- one patients being treated with oral everolimus were enrolled in this study. There were 4 males and 17 females, and the mean age was 20.5 years (5 patients <18 years and 16 patents > 18 years). Clinically meaningful and statistically significant improvement in erythema ($p=0.001$), average lesion size ($p<0.001$), lesion density ($p<0.001$) and percent involvement ($p<0.001$). AGS were all statistically significant in forehead ($p=0.001$), nose ($p<0.001$) cheeks ($p<0.001$) and chin ($p=0.004$).

Conclusions: Everolimus is currently evident and approved for both TSC - SEGA and AML, and limited study proved the treatment of oral everolimus for facial angiofibromas. Meanwhile studies had showed topical rapamycin is evident in reducing facial angiofibromas. Current study showed the efficacy of oral everolimus in reducing facial angiofibromas, demonstrated the parallel benefits of treatment protocol of TSC.

131 Narrative Medicine in Clinical Teaching

兒科臨床醫療場域的敘事醫學課程

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Background: 21世紀初，美國哥倫比亞大學的內科學教授Rita Sharon從文學與歷史、藝術美學等面向開始了敘事醫學的發展，藉由一系列課程讓醫學生練習聆聽、關注與重現病人的故事，期望醫者回歸「人」的價值。敘事醫學期望醫師能將雙眼從檢驗報告與治療準則之外，專注到病人身上。疾病之外，醫師與病人之間將有另一種形式的連結產生，病人豐富的故事將帶來許多值得駐足與凝視的片刻，醫學生的人文素養也將透過敘事醫學的教學而深化。本系列三篇報告，旨在呈現第1篇。兒科臨床醫療場域的敘事醫學課程(花蓮慈濟醫院兒科部 朱紹盈醫師)第2篇。兒童也需要長照資源~從故事的解構與bioecological系統談起(慈大 醫學系五年級 楊芳琦醫學生)第3篇。IDDM病童疾病敘事的面貌(慈大 醫學系六年級 陳文士醫學生)

Methods: Aim: 運用書寫病童與其家庭的psychosocial issues, 提升醫學系五年級醫學生人文素養 Material and Method 兒科臨床學習場域的一箇月中，醫學生在第一週會觀察、接觸、與聆聽病人與家屬的故事，醫學生需辨識除疾病之外的情緒、心理、家庭、經濟，整個系統與社會脈絡下的相關議題，第二週時運用Gibb's 5R反思模式撰寫所發現之psychosocial issues與自己所思，自己的反應與角色，心理社會議題的原因分析與疾病的關係

等，並提出解決的方案。第三週時在小組討論過程中分享與接受老師與同儕的回饋。

Results: 醫學生從被動觀察者變成問題解決者，學習到如何協助病人面對疾病之外的心理社會相關議題，從生理疾病以外熟悉了biopsychosocial (BPS) 的全人觀點，從反思書寫看見病人罹病的歷程，感同身受病人與家人的煎熬與困境。部分醫學生用呈現不同角度分析與解構病人心理社會相關議題，呈現書寫內涵的不同面貌，看見自己與看見病人的關係、位階與狀態。許多醫學生用淺顯易懂的文字書寫或詮釋病人的生病歷程，娓娓道出醫病之間那原本就存在的人性與關懷。

Conclusions: 敘事文本的面貌非常多樣化，醫學生透過書寫觸及生理疾病之外的諸多心理與系統架構下與文化脈絡下的議題。以科學實證為基礎、以醫師角度出發的醫學，強調簡約化主義、實證與成效，不小心就忘記了病人的存在。科學與人文，結構與敘事，醫師與病人，這兩個世界需要更多的連結，需要更多的理解。

132 Introduce "Forum Theater" in Innovative Teaching of Inter-professional Medical Humanities

導入「論壇劇場」於跨領域醫學人文的創新教學 *

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Background: 近幾年來，醫療糾紛或是其他醫療相關議題日漸受到大眾注目，與此同時，醫學人文教育的重要性引起大家重視。傳統的大堂授課方式，例如：講座、會議或公開討論，很難吸引學生，不但引不起學生興趣，也達不到教學的目標。經過這幾年的教學經驗，我們認為透過論壇劇場可以打開一個新的教學思維，可以提升醫學人文教育的教學品質，甚至可以讓學生們對於「同理心」有更深的感受，透過互動方式，讓所有人都參與在討論中為探索困難局面和可能的解決方案提供了多元的思考和想法。

Methods: (一)引進以『論壇劇場』為基礎的互動式教學方式 (二)在課堂上用ZUVIO 雲端即時反饋系統回饋，並用google表單讓學生在每堂課都可以即時匿名回饋。根據國科會統計，只有28%學生勇敢發問，88%擔心自己會說出笨問題。「ZUVIO 雲端即時反饋」系統以及匿名的google表單都可以讓同學隨時發表意見，隱密又快速，透過手機、平板等工具，老師可以及時掌握學習成效，更可進一步利用作答結果的呈現，引導學生進行答案理由之說明與深入討論，藉此促進課堂學生的互動與溝通。(三)使用Jefferson Scale of Physician Empathy Student Version (JSPE)，以半開放式問卷評估醫學生在修習論壇劇場之前和之後的同理心分數。

Results: 此計畫含醫學系、護理系、社工系的參與率為88.37%。共有76名學生 (53名男性，23名女性)，平均年齡為20.47歲。前測平均同理心分數為82.28±6.79，而後測平均同理心分數為84.17±5.55。在一年級學生的部分，前測與後測分數有統計學上明顯的差異(81.94±6.84 vs 84.29±5.36, $p<0.05$)。而進一步分析，我們發現醫學系的學生和20歲以下的學生，後測的分數明顯比前測的分數提高。雖然全體學生前後測的分數沒有明顯的差異，然而一年級全體學生，甚至一年級的醫學生或20歲

以下的學生同理心分數都有明顯的進步。此研究也發現在同理心分數上不同的性別並沒有明顯的差異，與我們去年的研究結果不同，這樣的結果有可能歸因於樣本數少且追蹤的時間不夠¹。因此我們需要更多的研究去找尋是否有其他因素影響同理心分數的表現。

Conclusions: 雖然全體學生前後測的分數沒有明顯的差異，然而一年級全體學生，甚至一年級的醫學生或20歲以下的學生同理心分數都有明顯的進步。此研究也發現在同理心分數上不同的性別並沒有明顯的差異：男性：84.74 ± 5.05，女性：82.87 ± 5.02，P value: 0.18 (> 0.05)。與我們去年的研究結果不同。在去年結果中，女性有較高的分數表現：女性：90.2 ± 17.0，男性：84.7 ± 10.8，P value (< 0.05)。這樣的結果有可能歸因於樣本數少且追蹤的時間不夠¹。因此我們需要更多的研究去找尋是否有其他因素影響同理心分數的表現。在未來應可以更加推廣此一模式於醫學人文的教學中，議題的設定可以更廣，以增加學生的視野。

133 Utilizing Game-based Learning Platform and Mobile Applications to Enhance Learning in Medical Education 運用遊戲學習平台及手機應用程式增進醫學教育成效

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Background: 醫學教育與學習正在快速地演進。教育得融入更多的多媒體、遊戲、手機應用程式和虛擬刺激來增進學習成效。現行學生接觸眾多科技產品和刺激，也同時更加期待課程中有多媒體的呈現。教師也發現運用多媒體教材將提供更豐富的發展方向，但也是一大挑戰。本文目的是展示如何運用遊戲學習平台及手機應用程式進行教程，也評估其對於醫學教育之成效。

Methods: 我們運用了遊戲學習平台及手機應用程式進行多次課程，其中有152位參與者。首先設計案例為導向的思考流程圖，並依此進行問題設計。參與者使用各自手機匿名加入遊戲後，教師介紹課程將將會運用之基本知識並開始遊戲。參與者的回答方式包含選擇題、填充題或是排序答案。每題結束後，他們將知道正確答案、分數並討論。當遊戲結束時，將提供分析（課程時間、答對率、困難問題），結論並頒獎給得分第一的參與者。最後將要求每位參與者填寫問卷。

Results: 本研究以問卷進行。有152位參與者，其中包含五六年級醫學生38名、PGY醫師48名、住院醫師54名及研究醫師12名。問卷中有五項問題，每項問題皆有1至5的分數：授課時間(1=過短，3=適中，5=過長)、增進臨床工作信心、參與感、專心程度及整體滿意度(皆為1=非常低，5=非常高)。在152位參與者中，平均分數為：授課時間2.914、增進臨床工作信心3.941、參與感4.875、專心程度4.914以及滿意度4.941。將五六年級醫學生和其他族群比較，五六年級醫學生以下分數明顯偏低：增進臨床工作信心 (95%信賴區間3.401-3.915, P=0.004)、專心程度 (95%信賴區間4.572-4.902, P=0.003)、整體滿意度 (95%信賴區間4.687-4.945, P=0.007)。

Conclusions: 遊戲學習平台運用容易且有效地增進臨床工作信心、參與感、專心程度及整體滿意度。然而發現五六年級醫學生有顯著較低之臨床工作信心、專心程度及整體滿意度分數。訪談後發現5至10分鐘的課前簡介過短、缺乏基礎知識、答對率較低以及曾經接觸過類似課程而降低新鮮感皆是可能的原因。未來方向上，需要融

入更多元的多媒體運用，以前測、後測及定期測驗的控制組設計來驗證長期學期成效。

134 The Influence and Outcome of Post-Graduate Year Doctors through Pediatric Outpatient Clinic Holistic Health Care Teaching in Rare Diseases

兒童罕見疾病全人醫療教學對PGY醫師學員之影響探討

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Background: 傳統上醫學教育於基礎醫學教育以及臨床技能之培養均有相當不錯地水平，然而於心理及靈性之照顧上卻略顯不足，導致同質性偏高但在領域之連結與同理相對較弱，因此本院在兒科罕見疾病部分採以全人醫療教學之方式，本研究探討提早讓學員接受全人醫療教育，對PGY醫師學員未來執業及醫療人文精神之影響

Methods: 本院於兒科罕見疾病整合門診，採取全人醫療方式照護病患，結合兒童神經科醫師、成人神經科醫師、兒童復健科醫師等以及諮商心理師、營養師、呼吸治療師及社工師等專業人員，提供PGY醫師學員學習。本研究從 107年02月至 108年12月，連續性且前瞻性針對12位PGY醫師學員予以兒科罕見神經學疾病全人醫療教學門診三小時後，接受心理諮商師60分鐘之訪談，採用深度訪談 (In-depth interview) 技巧，透過事先預備之訪談大綱，以導引式訪談，從四個主題切入作分析，包含：1.了解PGY醫師對於人文素養的自我覺察2.了解PGY醫師目前同理心的教育、訓練及應用3.探索PGY醫師對於個人職業認同感、學習動機及生涯4.其他訪談結果觀察發現

Results: 經過完整的訪談後發現PGY醫師學員有幾項特色 1.受訪者對於同理心的學習動機不足，在認知上不認為有必要太多的同理心，其中有3位受訪者因曾經經歷過個人創傷即失去的感受，所以能夠有意願同理個案，有1位受訪者因為對於安寧緩和及照護老人有興趣，本身特質也喜歡與人溝通。 2.受訪者較少思考醫師職業認同議題 成為一個醫師的過程，可能許多 (9位) 受訪者皆表達當初沒有想這樣多，就成為一個醫師，甚至是家庭逼迫選擇的，華人文化給予醫師社會地位高，所以對於醫師角色的認同需要有什麼樣的條件，沒有興趣去做反思。目前只重視生涯選擇選哪一科發展較好、薪資較優、生活品質較佳的生涯決策思考。較少思考職業認同議題。 3.受訪者有能力共感，但對於負向情緒較不熟悉 10位受訪者人格特質是屬於較理智型的，亦即思考與病人的關係，習慣認知先以解決個案問題導向來思維，並且給予處置，雖然在臨床中可能會有一些共感能力，但對於病人及家屬的立場情緒較不熟悉 (痛苦、難過、焦慮、悲傷) 負向情感較難以理解，敏感度明顯較低，故無法提升其同理心層次。 4.受訪者對於重新回憶受挫經驗，能提高受訪者同理心能力 受訪這皆由心理師引導其回憶個人受挫經驗，像是生活經驗的挫折感、失控感以及無奈感受時，受訪者皆願意思考重述其當時罕病門診個案

家屬的心情，而願意學習同理心的動機提高。此部分可以應用在未來人文素養教學。

Conclusions: 研究者觀察受訪者成為醫師後，了解自身社會地位相對較高、也有相對好的收入進而感到有優越感，其中有4位受訪者對於自身聯考當初是考到前1%而感到自信，相當認同自己的智識成分，但對於情緒智識部分沒有覺察到尚有學習空間。有3位受訪者對於自己同理心及情緒智識部分有意願學習，並展現願意關懷他人的精神。有4位受訪者對於醫師的職業並沒有太大的認同，認為相對於其他行業是比較好賺錢的職業。有1位受訪者已經決定不當醫師，沒有任何職業認同。根據本研究發現，台灣醫學教育之下同質性高，專業水平高，但是在多領域交流及醫療人文精神相對欠較少，然而多數PGY醫師學員回饋本身是願意多學習，因此在兒科罕見疾病全人醫療之教育提供了PGY醫師學員一個環境，能更好地思考與成長，進而培養醫療人文精神。