ASPR 2017

The 13th Congress of Asian Society for Pediatric Research

Hosted by
Hong Kong College of Paediatricians
Hong Kong Academy of Medicine
Jockey Club Building

Excellence in Child Health
From Genes to Communities
Contents

General information

Greetings from the President of ASPR Council 2
Greetings from the Chairman of Organizing Committee ASPR 2017 3
Organizing Committee Members 4
Award Winners 5
Floor Plan 6
Programme at a Glance 8
General information 10
Full Programme of ASPR 2017 13

Congress Lectures

Presidential Lecture 30
Plenary Lectures 31
Lunch Symposia Lectures 37
Symposia Lectures 41
Oral Presentations 97
E-posters 121
All Submitted Abstracts with QR codes 189
Index 209
Sponsors 211
Acknowledgement 224
Welcome to the 13th Congress of Asian Society for Pediatric Research

Dear Friends,

We are immensely grateful to so many distinguished individuals as well as multiple professional and academic societies in helping us and collaborating with our Hong Kong College of Paediatricians to put together such an amazingly rich and diverse scientific programme for the 13th Congress of the Asian Society for Pediatric Research.

The scientific programme comprises more than 120 invited lectures delivered by over 100 speakers, which cover “From Genes to Communities”, connecting basic, clinical and community-based research, in order to ensure “Excellence in Child Health” is firmly at the centre stage. This is only feasible with the contribution of the distinguished invited speakers as well as many local and non-local sponsoring societies. The non-local societies include Asia Pacific Society for Immunodeficiencies (APSID), Chinese Pediatric Society (CPS), Japan Pediatric Society (JPS), ROTA Council and Viva-Asia Blood and Marrow Transplant (VABMT) Consortium. Nearly all the local societies engaged in paediatrics and paediatric nursing are either sponsors or supporting organisations of the Congress. We are truly grateful for their staunch support.

Over 1,600 abstracts were submitted to the Congress and each of these abstracts was scored by multiple reviewers independently. More than 500 were selected for either oral presentation, poster walk or poster presentation based on their aggregate score. Many of these submissions are of very high quality and a number of these will be awarded the Young Investigator Awards and/or Travel Awards. Best oral abstracts and poster walk will also be selected during the Congress. We sincerely wish exciting discussion could accompany these presentations as progress depends on exchange of ideas. We thank all the researchers and paediatricians in submitting these abstracts to our Congress.

Last but not least, I would wish to thank all the members of our Organizing Committee and various committees for their hard work in ensuring the success of the 13th Congress of the Asian Society for Pediatric Research. Without their dedication and contribution, we will not have this Congress. Of course, our secretaries in the College have worked tirelessly and selflessly for many months, to them I am forever grateful.

Finally, on behalf of both the Hong Kong College of Paediatricians and the Asian Society for Pediatric Research, I thank you, the 900 delegates who have registered and are here today in Hong Kong with us to make the 13th Congress of ASPR an exciting, educational and memorable experience.

Yu Lung LAU

President
Asian Society for Pediatric Research
Hong Kong College of Paediatricians
Welcome to Hong Kong to attend the ASPR 2017 Meeting

ASPR is an Asian-based professional society and she embraces medical doctors and allied health professionals caring for children as her members. The Society is oriented towards scientific research works that can improve child health and ASPR encourages collaboration between the various specialized fields of pediatrics. We are very delighted that there are more than 900 registered participants to our meeting this year. That includes many internationally renowned pediatricians and scientists as our speakers. The abstracts received were close to 1600 and it is phenomenal. I have to say that the scientific contents of many of the abstracts are excellent and we have a difficult time to select those for presentations. The programs are packed with high caliber speakers and interesting topics. The most important things are that we have pediatricians and pediatric health care workers from a wide spectrum of Asian countries to attend. This really enriches our academic and scientific exchange atmosphere, which is our utmost objective.

I would like to thank many regional and local pediatric learning societies for their support of making this meeting successful. I also would like to thank our commercial partners and HK Tourism Board for their generous sponsorship.

Wishing all of you to have a wonderful experience in Hong Kong!

Prof. Godfrey Chi-Fung Chan
Chairman of Organizing Committee
ASPR 2017
Organisation for ASPR2017

ASPR2017 Council Members

Prof. Yu-lung LAU (President)  
Prof. Tahmeed AHMED  
Prof. Suwat BENJAPONPITAK  
Prof. Godfrey Chi-fung CHAN  
Prof. (Dr.) Rajeshwar DAYAL  
Prof. Mulyadi M. DJER  
Dr. Anne Eng-neo GOH  
Dr. Assad HAFEEZ  
Prof. (Dr.) Mahbubul HOQUE  
Prof. Takashi IGARASHI, MD, PhD  
Prof. Way-seah LEE  
Prof. Ting-fan LEUNG  
Dr. Woei-kang LIEW  
Prof. Tzou-yien LIN  
Dr. Kyaw LINNN  
Prof. Genesis RIVERA  
Prof. Kun-ling SHEN  
Prof. Takao TAKAHASHI  
Prof. Sei-won YANG

ASPR2017 Organizing Committee

Prof. Godfrey Chi-fung CHAN (Chairperson)  
Dr. Sik-nin WONG (Vice-Chairperson)  
Dr. Winnie Wing-ye TSE (Secretary General)  
Prof. Yu-lung LAU (Ex-officio)  
Dr. Kate Ching-ching CHAN (Member)  
Dr. Gilbert CHUA (Member)  
Dr. Brian Hon-yin CHUNG (Member)  
Dr. Nai-chung FONG (Member)  
Dr. Patrick IP (Member)  
Dr. Gareth Po-wan KO (Member)  
Dr. Yat-wah KWAN (Member)  
Dr. Catherine Chi-chin LAM (Member)  
Dr. Wai-hung LAU (Member)  
Dr. Pamela Pui-wah LEE (Member)  
Prof. Ting-fan LEUNG (Member)  
Dr. Robert Po-yee LOUNG (Member)  
Dr. Euan Tsung-liang SOO (Member)

ASPR2017 Scientific Programme Committee

Prof. Ting-fan LEUNG (Chairperson)  
Dr. Patrick IP (Chairperson)  
Prof. Yu-lung LAU (Ex-officio)  
Prof. Godfrey Chi-fung CHAN (Member)  
Dr. Kate Ching-ching CHAN (Member)  
Dr. Renee Wan-yi CHAN (Member)  
Dr. Frankie Wai-tsoi CHENG (Member)  
Dr. Brian Hon-yin CHUNG (Member)  
Dr. Cheuk-wing FUNG (Member)  
Prof. Ellis Kam-lun HON (Member)  
Dr. Yat-wah KWAN (Member)  
Dr. Pamela Pui-wah LEE (Member)  
Ms. Susanna Wai-yee LEE (Member)  
Dr. Ivan Fai-man LO (Member)  
Dr. David Chi-kong LUK (Member)  
Dr. Grace Wing-kit POON (Member)  
Dr. Kwing-wan TSUI (Member)  
Dr. Eric Kin-cheong YAU (Member)

Editorial Board of the Program Book

Editor: Dr. Wai-hung LAU  
Cover design: Dr. Robert Po-yee LOUNG  
Sub-editors:  
• Dr. Lawrence CHAN  
• Dr. Nai-chung FONG  
• Dr. Sou-chi SIT

Designers:  
• Dr. Gilbert CHUA  
• Dr. Wing-keung NG  
• Miss Natasha TENG
Winners of Awards and Grants

Young Investigator Awards

Chunxue LIU (China): Article #N0795
SHANK3 deletion and related phenotypes in Chinese children with autism and shank3-KO zebrafish display autistic-like behaviours

Mingsheng MA (China): Article #N0399
Molecular diagnosis of hepatic glycogen storage disease by gene panel-based next-generation sequencing: Results in 108 cases

Ishita MOSTAFA (Bangladesh): Article #N0110
Unsafe environment puts slum children in Peril: A cross-sectional study on microbial contamination of complementary food and water in Dhaka, Bangladesh

Steven Lim-cho PEI (Hong Kong): Article #N0173
Using paired-end whole genome sequencing (WGS) to investigate complex chromosome rearrangements (CCRs) associated with congenital anomalies and neurodevelopmental disorders

Le Duc Huy TA (Singapore): Article #N0210
Establishment of the nasal microbiota in the first 18 months of life: Correlation with early onset rhinitis and wheezing

Winnie Wan-yee TSO (Hong Kong): Article #N0292
Mutations in PI3K-AKT-mTOR signaling pathway are the major cause of macrocephaly with developmental delay/autism

Ramya UPPULURI (India): Article #N0273
Haploidentical stem cell transplantation for primary immunodeficiency disorders in children: Challenges and outcome from a tertiary care centre in India

Ce WANG (China): Article #N0740
Long-term prognosis and genotype-phenotype correlations of patients with left ventricular non-compaction

Feng WANG (China): Article #N1068
A TBX5 3’UTR variant increases the risk of congenital heart disease in the Han Chinese population

Qian YANG (China): Article #N1241
MiR-29b regulates cardiomyocytes proliferation via targeting NOTCH2

Travel Grants

Natt ARAYAPONG: Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand

Mindy GUO: Kawasaki Disease Center and Kaohsiung Chang Gung Memorial Hospital, Taiwan

Yasuo KUBOYA: The University of Tokyo, Tokyo, Japan

Chunxue LIU: Children’s Hospital of Fudan University, Shanghai, China

Mingsheng MA: Peking Union Medical College Hospital, Beijing, China

Ishita MOSTAFA: International Centre for Diarrhoeal Disease Research, Bangladesh

Kenji MURATA: Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Le Duc Huy TA: Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Supavich TANNUMSAENG: Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Ramya UPPULURI: Apollo Cancer Institutes, Chennai, India

Ce WANG: Shengjing Hospital of China Medical University, Shenyang, China

Feng WANG: Children’s Hospital of Fudan University, Shanghai, China

Qian YANG: Children’s Hospital of Fudan University, Shanghai, China

Su Boon YONG: Show Chwan Memorial Hospital, Changhua, Taiwan

Xu ZHAO: The Affiliated Hospital of Southwest Medical University, Luzhou, China
Floor Map ASPR2017

Hong Kong Academy of Medicine
Jockey Club Building

Ground Floor
## DAY 1 (6 Oct)

<table>
<thead>
<tr>
<th>Time</th>
<th>Run Run Shaw Hall</th>
<th>Function Room 1</th>
<th>Pao Yue Kong Auditorium</th>
<th>Lim Por Yen Lecture Theatre</th>
<th>Function Room 2</th>
<th>James Kung Meeting Room</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:30-09:00</td>
<td>OPENING CEREMONY (Run Run Shaw Hall)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>09:00-10:20</td>
<td>Plenary Lectures I &amp; II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10:20-10:45</td>
<td>TEA BREAK (with poster viewing)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10:45-12:15</td>
<td>Symposium A1</td>
<td>Symposium A2</td>
<td>Symposium A3</td>
<td>Symposium A4</td>
<td>Best Abstracts Session 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neurology 1</td>
<td>Infectious Diseases 1</td>
<td>General Paediatrics 1</td>
<td>Cellular &amp; Gene Therapy</td>
<td>Medical Genetics</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(10:35-12:15)</td>
<td></td>
<td>(10:35-12:15)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10:45-12:15</td>
<td>e-Poster Sessions 1 &amp; 2 (Foyer)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12:20-13:10</td>
<td>LUNCH SYMPOSIUM 1 (Humanities and Paediatric Education)</td>
<td>Location: Run Run Shaw Hall</td>
<td>p.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13:15-13:55</td>
<td>Presidential Lecture</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14:00-14:35</td>
<td>Symposium B1</td>
<td>Symposium B2</td>
<td>Symposium APSID 2</td>
<td>Symposium B3</td>
<td>Symposium B4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infectious Diseases 2</td>
<td>Infectious Diseases 3</td>
<td>Mechanism of Diseases</td>
<td>Respiratory + Oral Present 1 &amp; 2</td>
<td>General Paediatrics 2 + Oral Present 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p.16</td>
<td>p.16</td>
<td>p.17</td>
<td>p.17</td>
<td>p.17</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(14:00-16:10)</td>
<td></td>
<td>(14:00-16:10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:05-16:30</td>
<td>TEA BREAK (with poster viewing)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:30-18:00</td>
<td>Symposium C1</td>
<td>Symposium C2</td>
<td>Symposium APSID 3</td>
<td>Symposium C3</td>
<td>Best Abstracts Session 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neonatology &amp; Oral Present 4</td>
<td>Neurology 2</td>
<td>Inborn &amp; Acquired Susceptibility to Infections</td>
<td>Gastroenterology &amp; Hepatology 1</td>
<td>p.19</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p.18</td>
<td>p.18</td>
<td>p.18</td>
<td>p.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(16:30-18:10)</td>
<td></td>
<td>(16:30-18:10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16:30-18:00</td>
<td>e-Poster Sessions 3 &amp; 4 (Foyer)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18:00-20:00</td>
<td>GALA DINNER (19:00-21:30)</td>
<td>Location: Run Run Shaw Hall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20:00-21:30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Programme subject to changes; please refer to the website for the most updated programme.
Congress Information
6 October (Friday) – 8 October (Sunday), 2017

Hong Kong Academy of Medicine Jockey Club Building (HKAM Building)
香港醫學專科學院

Address: 99 Wong Chuk Hang Road, Aberdeen, Hong Kong
香港黃竹坑道99號

• Tel: (852) 2871 8888  Website: www.hkam.org.hk/HKAMWEB/pages_6_49.html
• Location: www.hkam.org.hk/images/premises/traffic.jpg

Please refer to the enclosed floor plans (pages 6-7) for the location of Venue Facilities and Meeting Rooms:

<table>
<thead>
<tr>
<th>Ground Floor</th>
<th>1st Floor</th>
<th>2nd Floor</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Exhibition Hall</td>
<td>• Foyer</td>
<td>• Function Room 1</td>
</tr>
<tr>
<td>• Lim Por Yen Lecture Theatre</td>
<td>• Run Run Shaw Hall</td>
<td>• Function Room 2</td>
</tr>
<tr>
<td>• Pao Yue Kong Auditorium</td>
<td></td>
<td>• James Kung Meeting Room;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fung Ying Seen Koon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meeting Room 1 (FYSK1)</td>
</tr>
</tbody>
</table>

Registration & Information

Upon arrival, please approach the Registration Desk (on the Ground Floor) to collect your Name Badge and Congress Bag and Materials. The Registration and Information Desks will be opened during the following hours:

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 October 2017 (Thursday)</td>
<td>16:00 – 18:00</td>
</tr>
<tr>
<td>6 October 2017 (Friday)</td>
<td>07:30 – 18:00</td>
</tr>
<tr>
<td>7 October 2017 (Saturday)</td>
<td>08:00 – 18:00</td>
</tr>
<tr>
<td>8 October 2017 (Sunday)</td>
<td>08:00 – 13:00</td>
</tr>
</tbody>
</table>

Please bring along your Registration Confirmation Letter (or show the eCopy with Registration No. with your Full Name) to check in at the Registration Desk. If you have NOT received the Confirmation Letter, please contact the Conference Secretariat immediately and we will send a copy to you again.

Programme

Please find the Programme of the Conference from pages 13-28  Please visit our Congress website at: www.aspr2017.com for the latest updates of Programme as well as for the information of all pre- and post- Congress workshops. (*Please note you may need to refresh the webpage to view the latest updates.)

Exhibition

The Exhibition Counters are located on the Ground Floor.

e-Poster Presentation

You can view the e-poster presentation from the e-poster screens at the Foyer on the 1st Floor at any time during the Congress on 6-8 October. Active Poster Presentations are located at the Foyer (on the 1st Floor).

Certificate of Attendance

A Certificate of Attendance will be available to all registered Congress participants which will be included in the Congress Bag.

Live-Broadcast when Overflow

Due to the overwhelming response of Congress registration which has exceeded the seating capacity of the Plenary Hall, attendance of Presidential Lecture, Plenary Lectures and Lunch Symposia which will be held in the Run Run Shaw Hall (on the 1st Floor) may need to overflow to 2 lecture theatres (on the Ground Floor) to view the Live-Broadcast if the Hall is full. Please take your seat early for these lectures, and for those who arrive after the Hall is full, please follow the direction of staff to the lecture theatres (on the Ground Floor) to view the Live-Broadcast.
Chairpersons

Chairpersons are requested to be in the session room at least 15 minutes in advance of the scheduled starting time.

Speakers and Best Oral Presenters

Speakers/ Presenters for oral sessions are requested to visit the PowerPoint Uploading Centre (Fung Ying Seen Koon Meeting Room 1) located on the 2nd Floor to submit and check your presentation data at the first thing upon arrival. Please arrive at the session room at least 20 minutes prior to your scheduled session to check your presentation file and meet with the session chairs/other speakers of the session.

ASPR Council Member Business Meeting and Dinner (for ASPR Council)

The ASPR Council Member Business Meeting will be held from 15:00-17:00 on Thursday, 5 October in Function Room 2 (on the 2nd Floor) of HKAM Building and Dinner for ASPR Council Members will be at the Jumbo Kingdom from 18:00-20:00 on Thursday, 5 October. All ASPR Council Members are invited to the event.

*If you bring your own Mac/iPad for your presentation, please be reminded to bring a suitable VGA/HDMI Adaptor and save a Backup PowerPoint file in PC format.

Coffee/Tea and Lunch

- Coffee/tea will be served at designated time on 6-8 October on the Ground Floor and the 1st Floor. Please refer to the serving time of Tea Break and Lunch from the Programme details.
- Light Lunch (both vegetarian and non-vegetarian options are available) will be provided for Lunch Symposia on 6 & 7 October which will be held in the Run Run Shaw Hall (on the 1st floor) of HKAM Building. (Attendees may need to overflow to 2 lecture theatres on the Ground Floor to view the Live-Broadcast if the Hall is full.)
- Another dining option inside the venue at your own cost is available. You may visit the Dining Room (on the 2nd Floor) which is opened during the following hours:
  - Monday to Friday: 12:00 - 20:00
  - Saturday: 12:00 -15:00      Sunday and Public Holiday: closed

Accreditation (For Local Delegates Only)

CME/CNE accreditation, please approach the CME Service Desk on the Ground Floor to sign your attendance.

Internet Access

Complimentary WIFI access is available in the Congress Venue.

Language

The Official language of the Congress is English. Sessions and posters will be presented in English. Simultaneous interpretation will not be provided.

Identification Badges

All participants will receive an Identification Badge upon registration. All Congress participants are kindly reminded to wear their Badges at all times for identification purposes and admission to the various Scientific Sessions and Exhibitions. Please note that accompanying persons and exhibitors will not be admitted to the Scientific Sessions. Should you lose your Name Badge, please proceed to the Registration and Information Desks for a Replacement Name Badge. Each Replacement Name Badge will cost HK$300.

Registration Inclusion

- Admission to all of the Conference Scientific Sessions, Lunch Symposia and Exhibition Hall on 6-8 October
- One set of Conference Materials and the ASPR2017 Programme and Abstract Book
- Entry to Opening Ceremony on Friday, Oct 6 2017 at 08:30am
- Congress Bag and Name Badge
- Lunch on 6-7 October 2017 and the Tea Breaks of the Congress
- Certificate of Attendance

PowerPoint Uploading Centre (for Speakers and Best Oral Presenters only)

Fung Ying Seen Koon Meeting Room 1 (FYSK1) on the 2nd Floor is designated as the Uploading Centre. Computers will be available for speakers to preview and upload their presentations. Speakers are encouraged to bring their presentation files to the Uploading Centre as early as possible and AT LEAST ONE HOUR BEFORE THE START OF your scheduled presentation session. This Centre of slide preview room will be opened during the following hours:

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 October 2017 (Friday)</td>
<td>07:30 – 18:00</td>
</tr>
<tr>
<td>7 October 2017 (Saturday)</td>
<td>08:00 – 18:00</td>
</tr>
<tr>
<td>8 October 2017 (Sunday)</td>
<td>08:00 – 13:00</td>
</tr>
</tbody>
</table>
Smoking Policy
HKAM Building is a smoke-free facility. No internal smoking areas will be provided.

Conference Regulations
- Smoking is prohibited in the Congress Venue.
- Mobile phones must be turned off during oral sessions.
- No recording is allowed in any sessions, including posters.

Adverse Weather Arrangements
1. If Typhoon Signal Number 8 or above, or Black Rainstorm Warning Signal is hoisted or in force at 6:30 a.m. on that day, the morning session of the event will be cancelled.
2. If Typhoon Signal Number 8 or above, or Black Rainstorm Warning Signal is lowered or cancelled after 6:30am and before 12:00 noon, the afternoon session will continue.
3. If Typhoon Signal Number 8 or above, or Black Rainstorm Warning Signal is lowered or cancelled after 12:00 noon, the afternoon session will be cancelled.
Please watch for announcement posted on the Message Boards / Congress Website or contact the Secretariat at (+852 28522333).

Information of Lost and Found
Information of Lost and Found items would be located in the Registration & Information Desk area.

Insurance and Liability
Participants are advised to secure their own insurance to cover any losses incurred in case of cancellation, medical expenses or damage/loss of personal properties.

About Hong Kong

Discover Hong Kong
For the most up-to-date tourist information, please visit the website of the Hong Kong Tourism Board at www.discoverhongkong.com.

Useful Telephone Numbers
L’hotel Island South (Conference Hotel)  
Address: 55 Wong Chuk Hang Road, Aberdeen, Hong Kong  
(852) 3968 8888

Hong Kong Airport Hotline  
(852) 2181 0000

Emergency Number (Ambulance / Fire / Police)  
999

Conference Hotline (5-9 October)  
(852) 2852 2333

Should you have any questions, please do not hesitate to contact the Conference Secretariat via email to enquiry@aspr2017.com.

We look forward to seeing you at ASPR 2017 soon!

Best Regards,

ASPR 2017 Organizing Committee
(c/o Congress Secretariat:  
International Conference Consultants Ltd.  
Tel: (852) 2559 9973  
Fax: (852) 2547 9528  
Email: enquiry@aspr2017.com  
Website: www.aspr2017.com)
### Opening Ceremony

### Plenary Lecture 1

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:00 - 09:40</td>
<td>Role of Pediatric and Child Health Research in Achieving SDGs (40 min)</td>
</tr>
<tr>
<td>Speaker</td>
<td>Samira ABOUBAKER (WHO)</td>
</tr>
</tbody>
</table>

### Plenary Lecture 2

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>09:40 - 10:20</td>
<td>Use of Gene Editing to Treat Inherited Diseases (40 min)</td>
</tr>
<tr>
<td>Speaker</td>
<td>Donald B KOHN (USA)</td>
</tr>
</tbody>
</table>

### Tea Break (with poster viewing)

### Symposium A1

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:35 - 12:15</td>
<td>Theme: Neurology 1 - Gene, Cell and Neurological Diseases</td>
</tr>
<tr>
<td>Co-organizers:</td>
<td>HKCNDP, HKSMG and PNAHK</td>
</tr>
<tr>
<td>Chairpersons:</td>
<td>Catherine LAM (HK) and Wai Hung LAU (HK)</td>
</tr>
<tr>
<td>Speaker</td>
<td>Takao TAKAHASHI (Japan)</td>
</tr>
<tr>
<td>Speaker</td>
<td>Yuh Jyh JONG (Taiwan)</td>
</tr>
<tr>
<td>Speaker</td>
<td>Cheuk Wing FUNG (HK)</td>
</tr>
<tr>
<td>Speaker</td>
<td>Ho Ming LUK (HK)</td>
</tr>
</tbody>
</table>

### Symposium A2

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:45 - 12:15</td>
<td>Theme: Infectious Diseases 1 - Infectious Diseases in Asia</td>
</tr>
<tr>
<td>Co-organizer:</td>
<td>HKSPIAID</td>
</tr>
<tr>
<td>Chairpersons:</td>
<td>Mike KWAN (HK) and Tzou-Yien LIN (Taiwan)</td>
</tr>
<tr>
<td>Speaker</td>
<td>Rajeshwar DAYAL (India)</td>
</tr>
<tr>
<td>Speaker</td>
<td>Kyaw LINN (Myanmar)</td>
</tr>
<tr>
<td>Speaker</td>
<td>Tammy MEYERS (HK)</td>
</tr>
</tbody>
</table>
### Symposium A3

**Theme: General Paediatrics 1 - Policy, Public Health and Development**

Chairpersons: Albert Li (HK) and Thomas CHUNG (HK)

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:35-12:15</td>
<td>Impact of Environment on Child Health (20+3 min)</td>
<td>Patrick IP (HK)</td>
<td>Page 60</td>
</tr>
<tr>
<td></td>
<td>Child and Family Polyvictimization in China - Asian Perspective in Violence Prevention (20+3 min)</td>
<td>Edward CHAN (HK)</td>
<td>Page 61</td>
</tr>
<tr>
<td></td>
<td>Internet Addiction and Digital Device Use (20+3 min)</td>
<td>Thomas CHUNG (HK)</td>
<td>Page 61</td>
</tr>
<tr>
<td></td>
<td>Childhood Obesity, School Environment, and Socioeconomic Status (20+3min)</td>
<td>Frederick HO (HK)</td>
<td>Page 62</td>
</tr>
</tbody>
</table>

### Symposium A4

**Theme: Medical Genetics - Pathway Disorders**

Co-organizer: HKSMG

Chairpersons: Ivan LO (HK) and Stephen LAM (HK)

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:45-12:15</td>
<td>Rasopathies - Noonan Syndrome and Related Disorders (25+5 min)</td>
<td>Yoichi MATSUBARA (Japan)</td>
<td>Page 67</td>
</tr>
<tr>
<td></td>
<td>Mutations in PI3K-AKT-mTOR Signaling Pathway Result in Developmental Mosaic Disorders (25+5 min)</td>
<td>Brian CHUNG (HK)</td>
<td>Page 67</td>
</tr>
<tr>
<td></td>
<td>The Genetic Landscape of Rasopathies in Hong Kong (25+5 min)</td>
<td>Ivan LO (HK)</td>
<td>Page 67</td>
</tr>
</tbody>
</table>

### APSID Symposium 1

**Theme: Cellular and Gene Therapy**

Co-organizer: APSID

Chairperson: Godfrey CHAN (HK) and Woei Kang LIEW (Singapore)

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:45-12:15</td>
<td>Gene Therapy for Adenosine Deaminase (ADA) Deficient Severe Combined Immunodeficiency (SCID)</td>
<td>Donald Kohn (USA)</td>
<td>Page 42</td>
</tr>
<tr>
<td></td>
<td>European Lentiviral Gene Therapy Protocol for Chronic Granulomatous Disease</td>
<td>Reinhard SEGER (Switzerland)</td>
<td>Page 42</td>
</tr>
<tr>
<td></td>
<td>Mesenchymal Stem Cell Therapy</td>
<td>Godfrey CHAN (HK)</td>
<td>Page 43</td>
</tr>
<tr>
<td>Session</td>
<td>Topic</td>
<td>Abstract Title</td>
<td>Abstract #</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
<td>----------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Nutrition</td>
<td></td>
<td>Unsafe Environment Puts Slum Children in Peril: A Cross-sectional Study on Microbial Contamination of Complementary Food and Water in Dhaka, Bangladesh</td>
<td>#110</td>
</tr>
<tr>
<td>Allergy and Immunology</td>
<td></td>
<td>Identification of Potential Transcriptomic Markers in Developing Asthma: An Integrative Analysis of Gene Expression Profiles</td>
<td>#1341</td>
</tr>
<tr>
<td>Allergy and Immunology</td>
<td></td>
<td>Calcineurin Inhibitors Exacerbate Nod1-mediated Coronary Arteritis Via the MyD88 Signaling Pathway</td>
<td>#111</td>
</tr>
<tr>
<td>Genetics &amp; Genomics</td>
<td></td>
<td>Diet Glycemic Index Change During Pregnancy is Associated with Placenta Insulin Related Gene DNA Methylation Variation</td>
<td>#1038</td>
</tr>
<tr>
<td>Developmental Paediatrics</td>
<td></td>
<td>Early Food Allergy and Symptoms of Airway Allergy March on the Risk of Attention Deficit Hyperactivity Disorder In Chinese Children: A Cross-Sectional Study</td>
<td>#721</td>
</tr>
<tr>
<td>Genetics &amp; Genomics</td>
<td></td>
<td>Genome-wide DNA Methylation Analysis Identifies the Crucial Role of β-catenin (CTNNB1) in the Pathogenesis of Kawasaki Disease</td>
<td>#6</td>
</tr>
<tr>
<td>Genetics &amp; Genomics</td>
<td></td>
<td>Molecular Diagnosis of Hepatic Glycogen Storage Disease by Gene Panel-Based Next-generation Sequencing: Results in 108 Cases</td>
<td>#399</td>
</tr>
<tr>
<td>Genetics &amp; Genomics</td>
<td></td>
<td>Using Paired-end Whole Genome Sequencing (WGS) to Investigate Complex Chromosome Rearrangements (CCRs) Associated with Congenital Anomalies and Neurodevelopmental Disorders</td>
<td>#173</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>e-Poster Sessions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Lunch Symposium 1

**Theme: Humanities and Paediatric Education**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:20-13:10</td>
<td>Educating the Humane Physician: The Role of Medical Humanities (20+5 min)</td>
<td>Genesis RIVERA (Philippines)</td>
<td>37</td>
</tr>
<tr>
<td>12:45-13:10</td>
<td>A Humanitarian Mission with MSF in South Sudan - Challenges of Delivering Paediatric Care During a Civil War (20+5 min)</td>
<td>Kai Ning CHEONG (HK)</td>
<td>38</td>
</tr>
</tbody>
</table>

### Presidential Lecture

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>13:15-13:55</td>
<td>From Genes to Communities - Improving Child Health through Education and Research (40 min)</td>
<td>Yu Lung LAU (HK)</td>
<td>30</td>
</tr>
</tbody>
</table>

### Symposium B1

**Theme: Infectious Diseases 2 - Rotavirus: Asia Leads in New Vaccine Development**

Co-organizer: ROTA Council

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:00-16:05</td>
<td>Impact of Rotavirus Vaccines: Better than Anticipated (20+5 min)</td>
<td>Jackie TATE (USA)</td>
<td>72</td>
</tr>
<tr>
<td>14:00-16:05</td>
<td>New Rotavirus Vaccines from Asia: Rotavac, Rotasil, Rotavin, RV3BB (20+5 min)</td>
<td>Carl KIRKWOOD (USA)</td>
<td>72</td>
</tr>
<tr>
<td>14:00-16:05</td>
<td>Chinese Rotavirus Vaccines: What’s Around the Corner (20+5 min)</td>
<td>Xuan-Yi WANG (China)</td>
<td>72</td>
</tr>
<tr>
<td>14:00-16:05</td>
<td>Rotavirus Vaccines Save Money: Herd Effects and Less Convulsions (20+5 min)</td>
<td>Tony NELSON (HK)</td>
<td>73</td>
</tr>
<tr>
<td>14:00-16:05</td>
<td>Opportunities for Asian Rotavirus Vaccine Introductions in Asia (20+5 min)</td>
<td>aveen THACKER (India)</td>
<td>73</td>
</tr>
</tbody>
</table>

### Symposium B2

**Theme: Infectious Diseases 3 - Fight Against Pneumonia in Asian Children**

Co-organizer: Japan Pediatric Society

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:00-16:05</td>
<td>The Factors Influencing Infectious Disease Guidelines - EBM or the Other Factors (30 min)</td>
<td>Kazunobu OUCHI (Japan)</td>
<td>74</td>
</tr>
<tr>
<td>14:00-16:05</td>
<td>Epidemiological Change of Pediatric Community-acquired Pneumonia Before and After Introduction of Pneumococcal Conjugate Vaccine Era in Japan (25+5 min)</td>
<td>Naruhioko ISHIWADA (Japan)</td>
<td>74</td>
</tr>
<tr>
<td>14:00-16:05</td>
<td>Pneumonia Etiological Agents in Vietnamese Children (25+5 min)</td>
<td>Lay Myint YOSHIDA (Japan)</td>
<td>75</td>
</tr>
<tr>
<td>14:00-16:05</td>
<td>Risk Factors for Pneumonia and Pneumococcal Vaccine Serotypes Among Children in Afghanistan (25+5 min)</td>
<td>Bhim Gopal DHOUBHADEL (Japan)</td>
<td>76</td>
</tr>
<tr>
<td>Symposium B3</td>
<td>Theme: Respirology - Common Respiratory Diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------</td>
<td>--------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chairpersons: Alfred TAM (HK) and Ting Yat MIU (HK)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse Consequences of Sleep Deprivation in Hong Kong Adolescents - Cardiovascular Perspective (25+5 min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speaker: Albert Li (HK) Page 88</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood Obstructive Sleep Apnoea Syndrome - What’s New? (25+5 min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speaker: Kate CHAN (HK) Page 89</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air Pollution and Allergy (25+5 min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speaker: So Lun LEE (HK) Page 89</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral Presentations 1 &amp; 2 - Thalassaemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chairperson: Frankie CHENG (HK)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost-Benefit Analysis of Thalassemia Screening in Thai Adolescence (Abstract #112; 8+2 min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speaker: Duantida SONGDEJ (Thailand) Page 113</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unmanipulated Haploidentical Stem Cell Transplantation with Post-transplant Cyclophosphamide in Children with Severe Thalassemia with Good Outcome and Rapid Immune Reconstitution (Abstract #154; 8+2 min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speaker: Kittituch AMORNPRASITPOL (Thailand) Page 114</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symposium B4</th>
<th>Theme: General Paediatrics 2 - Community Paediatrics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chairpersons: Ellis HON (HK) and Genesis RIVERA (Philippines)</td>
<td></td>
</tr>
<tr>
<td>Children’s Right and Child Health Policy (25+5 min)</td>
<td></td>
</tr>
<tr>
<td>Speaker: Chun Bong CHOW (HK) Page 62</td>
<td></td>
</tr>
<tr>
<td>Preventing Student Suicides: A Hong Kong experience (25+5 min)</td>
<td></td>
</tr>
<tr>
<td>Speaker: Paul YIP (HK) Page 64</td>
<td></td>
</tr>
<tr>
<td>Global Status of Child Health and Opportunities (25+5 min)</td>
<td></td>
</tr>
<tr>
<td>Speaker: Samira ABOUBAKER (WHO) Page 64</td>
<td></td>
</tr>
<tr>
<td>Stunting, Socioeconomic Status and Early Child Development in the East Asia Pacific (25+5 min)</td>
<td></td>
</tr>
<tr>
<td>Speaker: Nirmala RAO (HK) Page 64</td>
<td></td>
</tr>
<tr>
<td>Oral Presentation 3 - Developmental Paediatrics</td>
<td></td>
</tr>
<tr>
<td>Prediction of Attention Deficit Hyperactivity Disorder (ADHD) Risk Using an Infant Measure: Externalizing Symptoms at 12 Months and Risk of ADHD at 54 Months (Abstract #48; 8+2 min)</td>
<td></td>
</tr>
<tr>
<td>Speaker: Muhammad Taufeeq WAHAB (Singapore) Page 105</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>APSID Symposium 2</th>
<th>Theme: Mechanism of Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-organizer: APSID</td>
<td></td>
</tr>
<tr>
<td>Chairperson: Alan Kwok-shing CHIANG (HK) and Xiqiang YANG (China)</td>
<td></td>
</tr>
<tr>
<td>The Role of Toll-like Receptor 3 in Viral Encephalitis</td>
<td></td>
</tr>
<tr>
<td>Speaker: Cheng-lung KU (Taiwan) Page 43</td>
<td></td>
</tr>
<tr>
<td>Immunotherapy for EBV-associated Disorders</td>
<td></td>
</tr>
<tr>
<td>Speaker: Wen-wei TU (HK) Page 43</td>
<td></td>
</tr>
<tr>
<td>Wiskott-Aldrich Syndrome Protein Regulates Autophagy and Inflammasome Activity in Innate Immune Cells</td>
<td></td>
</tr>
<tr>
<td>Speaker: Pamela LEE (HK) Page 44</td>
<td></td>
</tr>
</tbody>
</table>

16:05-16:30 Tea Break (with poster viewing)
### Symposium C1

**Theme: Neonatology - Improving Neonatal Care**

**Chairpersons:** William WONG (HK) and King Woon SO (HK)

<table>
<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker(s)</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:30-18:10</td>
<td>Improving Outcome or Premature and Low Birth Weight Babies Through KMC - Experience from Bangladesh (25+5 min)</td>
<td>Mahbubul HOQUE (Bangladesh)</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>The Application of Molecular Assays in Neonatal Infection (25+5 min)</td>
<td>Simon LAM (HK)</td>
<td>79</td>
</tr>
</tbody>
</table>

**Oral Presentation 4 - Neonatology**

**Title:** Prognostic Accuracy of Parent-Reported Ages and Stages Questionnaire in Assessing the Developmental Outcome of Preterm Infants (Abstract #54; 8+2 min)

**Speaker:** Gwen HWARNG (Singapore)

**Antibiotic Use in Neonatal Intensive Care Units (25+5 min)**

**Speaker:** Joseph TING (Canada)

### Symposium C2

**Theme: Neurology 2 - Neuromuscular Disorder, the Treatment, the Multidisciplinary Care, and Quality of Life Issues**

**Chairperson:** Kwing Wan TSUI (HK)

<table>
<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker(s)</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:30-18:00</td>
<td>Diagnosis and Treatment of Neuromuscular Diseases - Local Advancement and Challenges (25+5 min)</td>
<td>Sophelia CHAN (HK)</td>
<td>81</td>
</tr>
<tr>
<td></td>
<td>Developmental, Behavioral and Cognitive Profile of Neuromuscular Diseases in Child Assessment Service and Case Illustration (25+5 min)</td>
<td>Chin Pang CHOW (HK)</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>Spinal Muscular Atrophy: Diagnosis and Management in the New Therapeutic Era (25+5 min)</td>
<td>Yuh-Jyh JONG (Taiwan)</td>
<td>82</td>
</tr>
</tbody>
</table>

### Symposium C3

**Theme: Gastroenterology and Hepatology 1**

**Chairperson:** Chung Mo CHOW (HK)

<table>
<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker(s)</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:30-18:00</td>
<td>Screening of Biliary Atresia for Early Management (30+5 min)</td>
<td>Mei-Hwei CHANG (Taiwan)</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>Towards Eradication of Hepatitis B Infection: What More Can We Do? (30+5 min)</td>
<td>Rosanna WONG (HK)</td>
<td>59</td>
</tr>
</tbody>
</table>

**Oral Presentation 5 - Gastroenterology & Hepatology**

**Title:** Upregulated Genes of Intracellular Salmonella Typhimurium after Invasion into Human Intestinal Epithelial Cells (Abstract #189; 8+2 min)

**Speaker:** Shiuh-Bin FANG (Taiwan)

### APSID Symposium 3

**Theme: Inborn and Acquired Susceptibility to Mycobacterial and Fungal Infections**

**Chairperson:** Cheng-Lung KU (Taiwan)

<table>
<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker(s)</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:30-18:00</td>
<td>Anti-interferon-g Autoantibody: A New Form of Adult Onset Immunodeficiency to Mycobacterial Infection in Southeast Asia</td>
<td>Cheng-Lung KU (Taiwan)</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>Cryptococcal Infections in Children can be Associated with a Myriad of Primary Immunodeficiency Diseases - Our Experience at Chandigarh</td>
<td>Surjit SINGH (India)</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Endemic Mycoses: When to Suspect Primary Immunodeficiency?</td>
<td>Pamela LEE (HK)</td>
<td>45</td>
</tr>
</tbody>
</table>
### Best Abstracts Session 2

<table>
<thead>
<tr>
<th>Time</th>
<th>Foyer</th>
<th>RRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:30-18:00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergy &amp; Immunology</td>
<td>Reference Values for Peripheral Blood Lymphocyte Subsets of Healthy Children in China: A Multi-Centered Study (Abstract #304; 8+2 min)</td>
<td>Speaker: Yuan DING (China)</td>
</tr>
<tr>
<td>Cardiology</td>
<td>A TBX5 3'UTR Variant Increases the Risk of Congenital Heart Disease in the Han Chinese Population (Abstract #1068; 8+2 min)</td>
<td>Speaker: Feng WANG (China)</td>
</tr>
<tr>
<td>Haematology and Oncology</td>
<td>The Tetraspanin CD9 is an Adverse Prognostic Factor in Pediatric B-precursor Acute Lymphoblastic Leukemia and Can Be Effectively Targeted by Neutralizing Antibody in Preclinical Animal Models (Abstract #211; 8+2 min)</td>
<td>Speaker: Chi ZHANG (HK)</td>
</tr>
<tr>
<td>Nephrology</td>
<td>Distinctive Cytokine Profile Between Acute Focal Bacterial Nephritis and Acute Pyelonephritis in Children (Abstract #182; 8+2 min)</td>
<td>Speaker: Makoto MIZUTANI (Japan)</td>
</tr>
<tr>
<td>Developmental Paediatrics</td>
<td>Effects of Parent-implemented Early Start Denver Model on Chinese Toddlers with Autism Spectrum Disorder: A Non-Randomized Controlled Trial (Abstract #787; 8+2 min)</td>
<td>Speaker: Bingrui ZHOU (China)</td>
</tr>
<tr>
<td>Respirology</td>
<td>Prospective Study of Risk Factors for Wheezing Phenotypes in Hong Kong Children (Abstract #237; 8+2 min)</td>
<td>Speaker: Agnes LEUNG (HK)</td>
</tr>
<tr>
<td>Allergy &amp; Immunology</td>
<td>Haploidentical Stem Cell Transplantation for Primary Immune Deficiency Disorders in Children: Challenges and Outcome from a Tertiary Care Centre in India (Abstract #273; 8+2 min)</td>
<td>Speaker: Ramya UPPULURI (India)</td>
</tr>
<tr>
<td>19:00-21:30</td>
<td></td>
<td>Gala Dinner</td>
</tr>
</tbody>
</table>

**e-Poster Sessions**
- 3 (Kiosk A: 16:30-18:00) / 4-1 (Kiosk B: 16:30-17:20) / 4-2 (Kiosk B: 17:20-18:00)
### Plenary Lecture 3

**Chairpersons:** Chok Wan CHAN (HK) and Genesis RIVERA (Philippines)

**Constructing a National Research Network for Pediatrics and Child Health in China (40 min)**

**Speaker:** Kun-Ling SHEN (China)  
Page 33

### Plenary Lecture 4

**Chairpersons:** Yen Chow TSAO (HK) and Kyaw LINN (Myanmar)

**Injury Prevention - Research to Effective Intervention (40 min)**

**Speaker:** Chun Bong CHOW (HK)  
Page 34

### 10:20-10:45  
**Tea Break (with poster viewing)**

### Symposium D1

**Theme:** Inborn Errors of Metabolism - Paediatric Neurotransmitter Diseases  
Co-organizers: Joshua Hellmann Foundation / HKSIEEM

**Chairpersons:** Joannie HUI (HK) and Sophelia CHAN (HK)

- **Synaptic Metabolism: A new Approach to Neurotransmitter Disorders (25+5 min)**
  **Speaker:** Angela GARCIA-CAZORLA (Spain)  
  Page 77
- **6- Pyruvoyl-tetrahydropterin Synthase (PTPS) Deficiency: Hong Kong Experience (25+5 min)**
  **Speaker:** Grace POON (HK)  
  Page 78
- **Tyrosine Hydroxylase (TH) Deficiency: Hong Kong Experience (25+5 min)**
  **Speaker:** Wai Lan YEUNG (HK)  
  Page 78

### Symposium D2

**Theme:** Advances in Pediatric Haematology and Oncology 1  
Co-organizer: HKPHOSG

**Chairpersons:** Chi Kong LI (HK) and Daniel CHEUK (HK)

- **Cellular Therapy for Pediatric Cancer (25+5 min)**
  **Speaker:** Dario CAMPANA (Singapore)  
  Page 68
- **Advances in Stem Cell Transplant for Pediatric Cancer (25+5 min)**
  **Speaker:** Wing LEUNG (USA)  
  Page 68
- **Advance in Childhood Leukaemia Research in Chinese Population (25+5 min)**
  **Speaker:** Chi Kong LI (HK)  
  Page 68

### Symposium D3

**Theme:** Paediatric Dermatology Practice Update - Dermoscopy and Atopic Dermatitis  
Co-organizer: HKPADS

**Chairpersons:** David LUK (HK) and Ellis HON (HK)

- **Assessing Naevi in Children Using a Useful Dermoscopic Classification (25+5 min)**
  **Speaker:** Maria GONZALEZ (UK)  
  Page 56
- **Complementary and Alternative Medicine for Childhood Eczema and Atopic Diseases: Friend or Foe? (25+5 min)**
  **Speaker:** Ellis HON (HK)  
  Page 56
- **The Use of Dermoscopy in Daily Paediatric Practice (25+5 min)**
  **Speaker:** David LUK (HK)  
  Page 56
### APSID Symposium 4

10.45-12.15

**Theme: Inflammatory Manifestations in Primary Immunodeficiencies**
Co-organizer: APSID

**Chairpersons:** Bee Wah LEE (Singapore) and Surjit SINGH (India)

**Understanding Mechanisms Underlying Monogenic Autoinflammatory Disease**
Speaker: Yu Lung LAU (HK)  Page 46

**Identifying Primary Immunodeficiency Diseases in Children Suffering from Refractory Diarrhea**
Speaker: Wen-I LEE (Taiwan)  Page 46

**Primary Immunodeficiencies Presenting with Inflammatory Bowel Disease**
Speaker: Melanie WONG (Australia)  Page 47

### Best Abstracts Session 3

10.45-12.15

**Chairperson:** Nai Chung FONG (HK):
**Adjudicators:** Alan KS CHIANG (HK)

#### Haematology and Oncology

**Integrated Genomic Analysis of Pediatric Germ Cell Tumors** (Abstract #56; 8+2 min)
Speaker: Yasuo KUBOTA (Japan)  Page 112

**Haploidentical Stem Cell Transplantation with Post-Transplant Cyclophosphamide in Pediatric High-Risk Acute Leukemia with Good Disease Controls and Immune Reconstitution** (Abstract #151; 8+2 min)
Speaker: Supavich TANNUMSAENG (Thailand)  Page 113

#### Allergy & Immunology

**IVIG Replacement is Essential for DOCK8 Deficiency Patients** (Abstract #291; 8+2 min)
Speaker: Yunfei AN (China)  Page 100

#### Gastroenterology & Hepatology

**A Gain-of-function SYK Mutation in a Very Early Onset Inflammatory Bowel Disease Patient** (Abstract #944; 8+2 min)
Speaker: Lin WANG (China)  Page 109

#### Allergy & Immunology

**Turning Weakness to Strength - Lessons Learnt in Delivering Cure for Primary Immune Deficiency Disorders in India** (Abstract #274; 8+2 min)
Speaker: Ramya UPPULURI (India)  Page 100

#### Respiratory

**Effects of a Group-based Acceptance and Commitment Therapy Versus Asthma Education for Training Parents to Manage Their Children with Asthma: A Randomized Controlled Trial** (Abstract #22; 8+2 min)
Speaker: Yuen Yu CHONG (HK)  Page 118

#### Respiratory

**ORMDL3 May Participate in the Pathogenesis of Bronchial Epithelial-mesenchymal Transition in Asthmatic Mice with Airway Remodeling** (Abstract #618; 8+2 min)
Speaker: Qi CHENG (China)  Page 119

#### Cardiology

**Long-term Prognosis and Genotype-Phenotype Correlations of Patients with Left Ventricular Noncompaction** (Abstract #740; 8+2 min)
Speaker: Ce WANG (China)  Page 103

#### e-Poster Sessions

**e-poster sessions 5-1 (Kiosk A: 10:45-11:10) / 5-2 (Kiosk A: 11:10-12:15) / 6 (Kiosk B: 10:45-12:15)**
### Lunch Symposium 2

**Theme:** Vaccine-preventable Diseases  
**Chairpersons:** Yuichiro YAMASHIRO and Rajeshwar DAYAL (India)

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:20-12:45</td>
<td>Having a Population based Surveillance of Invasive Pneumococcal Disease to understand Vaccine Pressure and Failure (20+5 min)</td>
<td>Yu Lung LAU (HK)</td>
<td>39</td>
</tr>
<tr>
<td>12:45-13:10</td>
<td>Cervical Cancer Prevention: Past, Present and Future (20+5 min)</td>
<td>Ting Fan LEUNG (HK)</td>
<td>40</td>
</tr>
</tbody>
</table>

### Plenary Lecture 5

**Chairpersons:** Chap Yung YEUNG (HK) and Kun-ling SHEN (China)

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>13:15-13:55</td>
<td>Liver Cancer Prevention - From Fetus to Adults (40 min)</td>
<td>Mei-Hwei CHANG (Taiwan)</td>
<td>35</td>
</tr>
</tbody>
</table>

### Plenary Lecture 6

**Chairpersons:** Louis LOW (HK) and Tzou-Yien LIN (Taiwan)

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>13:55-14:35</td>
<td>Rare Disease - Challenges in Diagnosis and Management (40 min)</td>
<td>Yoichi MATSUBARA (Japan)</td>
<td>36</td>
</tr>
</tbody>
</table>

### Symposium E1

**Theme:** Infectious Diseases 4 - Update on Infectious Diseases  
**Co-organizer:** HKSPIAID

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:45-15:10</td>
<td>Enterovirus 71 Infections in Children: Current Update (25+5 min)</td>
<td>Tzou-Yien LIN (Taiwan)</td>
<td>76</td>
</tr>
<tr>
<td>14:45-15:10</td>
<td>Rhinovirus Infections and Their Receptors in the Human Respiratory Tract (20+5 min)</td>
<td>Renee CHAN (HK)</td>
<td>77</td>
</tr>
<tr>
<td>14:45-15:10</td>
<td>What You May or May Not Know About Influenza (20+5 min)</td>
<td>Susan CHIU (HK)</td>
<td></td>
</tr>
</tbody>
</table>

### Symposium E2

**Theme:** Advances in Pediatric Haematology and Oncology 2  
**Co-organizer:** HKPHOSG

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>14:45-15:10</td>
<td>How to Target the Ultra-high-risk Neuroblastoma (25+5 min)</td>
<td>Akira NAKAGAWARA (Japan)</td>
<td>69</td>
</tr>
<tr>
<td>14:45-15:10</td>
<td>Targeting Epstein-Barr Virus in EBV-associated Malignancies (20+5 min)</td>
<td>Alan CHIANG (HK)</td>
<td>69</td>
</tr>
<tr>
<td>14:45-15:10</td>
<td>New Era in the Management of Childhood Cancers (20+5 min)</td>
<td>Godfrey CHAN (HK)</td>
<td>70</td>
</tr>
</tbody>
</table>
### Symposium E3

**Theme:** Allergy 1 - Emerging Concepts about Food Allergies  
**Co-organizer:** HKSPIAID

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
</table>
| 14:45-16:05 | Carbohydrate Allergens - How Clinically Relevant? (20+5 min)  
Speaker: Bee Wah LEE (Singapore)  
Page 52 |
|         | ChildhooCow's Milk Allergy (20+5 min)  
Speaker: Suwat BENJAPONPITAK (Thailand)  
Page 52 |
|         | Fish and Shellfish Allergies (20+5 min)  
Speaker: Agnes LEUNG (HK)  
Page 53 |

### Symposium E4

**Theme:** General Paediatrics 2 - Child Health  
**Co-organizer:** HKPS

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
</table>
| 14:45-16:05 | Child Health Priorities in Asia Pacific Region - Developing a Network for Collaborative Research (25+5 min)  
Speaker: Naveen THACKER (India)  
Page 65 |
|         | Adolescent Health - A Neglected Domain in Global Child Health (20+5 min)  
Speaker: Chok Wan CHAN (HK)  
Page 65 |
|         | Epidemiology of Paediatric Trauma in Hong Kong: a Multicentre Cohort Study (20+5 min)  
Speaker: Ming LEUNG (HK)  
Page 66 |

### APSID Symposium 5

**Theme:** Therapy  
**Co-organizer:** APSID

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
</table>
| 14:45-16:05 | Ig Replacement Therapy in Primary Immunodeficiency  
Speaker: Hua-wei MAO (China)  
Page 47 |
|         | Subcutaneous Immunoglobulin  
Speaker: Theresa COLE (Australia)  
Page 48 |
|         | Management of Invasive Fungal Infection in PID Patients  
Speaker: David Christopher LUNG (HK)  
Page 48 |

#### 16:05-16:30
**Tea Break (with poster viewing)**
<table>
<thead>
<tr>
<th><strong>Symposium F1</strong></th>
</tr>
</thead>
</table>
| **Theme:** Nursing - Towards Better Nursing Practice and Training  
Co-organizer: HKCPN  
Chairpersons: Susanna LEE (HK), Rebecca HUI (HK) and Maria CHAN (HK)  
Music as a Mnemonic Aid in Basic Life Support (BLS) Training on Improving the Skill Mastery of Trainee: A Pilot Study (15+5 min)  
Speaker: Tomcy LEUNG (HK) | Page 91  
Research in Paediatric Simulation Education - Education Model, Clinical Practice and the Big Data (15+5 min)  
Speaker: Jacky CHAN (HK) | Page 92  
Development and implementation of the Victorian Children’s Tool for Observation and Response (VICTOR) (25+5 min)  
Speaker: Sharon Bridget KINNEY (Australia) | Page 92  
Professional Standards for the Advanced Nurse Practitioner (25+5 min)  
Speaker: Gill COVERDALE (UK) | Page 93  
The Effectiveness of a Guided Participation Discharge Programme on improving Parental Outcomes for Very Premature Infants: A Pilot Randomised Controlled Trial (15+5 min)  
Speaker: Billie LEE (HK) | Page 93 |

<table>
<thead>
<tr>
<th><strong>Symposium F2</strong></th>
</tr>
</thead>
</table>
| **CPS**  
Co-organizer: Chinese Pediatric Society  
Chairperson: Kun-Ling SHEN (China)  
Asthma Action Plan (25+5 min)  
Speaker: Kun-Ling SHEN (China) | Page 94  
Disease Severity and Genetic Variation of Glycoproteins in the Respiratory Syncytial Virus-A ON1 Genotype in Chongqing of China, From 2009 to 2016 (25+5 min)  
Speaker: Enmei LIU (China) | Page 95  
Pediatric Sleep Disordered Breathing (25+5 min)  
Speaker: Zhifei XU (China) | Page 95  
Growth and Metabolic Abnormalities in Children Born Small for Gestational Age (25+5 min)  
Speaker: Xiaoping LUO (China) | Page 96 |

<table>
<thead>
<tr>
<th><strong>Symposium F3</strong></th>
</tr>
</thead>
</table>
| **Theme:** Allergy 2 - Management and Prevention of Allergic Diseases  
Co-organizer: HKSPIAID  
Chairpersons: Ting Fan LEUNG (HK) and Jaime S ROSA DUQUE (HK)  
Do Asian Children Have Less Peanut Allergy? (25+5 min)  
Speaker: Marco HO (HK) | Page 53  
Early Introduction of Allergenic Foods for the Prevention of Food Allergy - The Asian Perspective (25+5 min)  
Speaker: Bee Wah LEE (Singapore) | Page 54  
Improved Allergy Diagnosis and Treatment using Novel Technological Platforms (25+5 min)  
Speaker: Ting Fan LEUNG (HK) | Page 54 |
### Symposium F4

**Theme: Nutrition - Common Nutritional Disorders**

**Chairpersons:** Chun Fai CHENG (HK) and Takashi IGARASHI (Japan)

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:30-18:00</td>
<td>In Search for a Solution for Stunting - The Most Common Childhood Nutritional Disorder (25+5 min)</td>
<td>Tahmeed AHMED (Bangladesh)</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>Malnutrition and Chronic Illnesses in Early Life and Long Term Health Outcome (25+5 min)</td>
<td>Way-Seah LEE (Malaysia)</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>The Obesity and Growth in Korean Children and Adolescents (25+5 min)</td>
<td>Sei-Won YANG (Korea)</td>
<td>86</td>
</tr>
</tbody>
</table>

### APSID Symposium 6

**Theme: Haematopoietic Stem Cell Transplantation (HSCT) for Primary Immunodeficiencies**

**Co-organizer:** APSID

**Chairpersons:** Tomohiro MORIO (Japan) and Alka KHADWAL (India)

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>16:30-18:00</td>
<td>Hematopoietic Cell Transplantation for Primary Immunodeficiency Diseases: Current Situation and Future Direction</td>
<td>Tomohiro MORIO (Japan)</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>Reduced Intensity HSCT for Chronic Granulomatous Disease</td>
<td>Reinhard SEGER (Switzerland)</td>
<td>49</td>
</tr>
<tr>
<td></td>
<td>HSCT for Haemophagocytic Lymphohistiocytosis</td>
<td>Theresa COLE (Australia)</td>
<td>49</td>
</tr>
</tbody>
</table>

### Foyer

**e-Poster Sessions**

7 (Kiosk A: 16:30-18:00) / 8 (Kiosk B: 16:30-18:00) / 9 (Kiosk C: 16:30-18:00)
### Symposium G1
**Theme: Gastroenterology and Hepatology 2 - Diarrhoeal Diseases**

**Chairpersons:** Po Wan KO (HK) and Rosanna WONG (HK)

#### Burden and Management of Persistent Diarrhea in Low and Middle Income Countries (20+5 min)
- **Speaker:** Tahmeed AHMED (Bangladesh) Page 59

#### Paediatric Inflammatory Bowel Disease: An Asian Perspective (20+5 min)
- **Speaker:** Way-Seah LEE (Malaysia) Page 60

#### Paediatric Inflammatory Bowel Disease: Hong Kong Experience (20+5 min)
- **Speaker:** Chung Mo CHOW (HK) Page 60

#### Oral Presentation 6 - Gastroenterology & Hepatology
- **Title:** Dynamics of the Gut Bifidobacterium Microbiota During the First Three Years of Life: A Quantitative Bird’s-eye View (Abstract #136; 8+2 min)
- **Speaker:** Yuichiro YAMASHIRO (Japan) Page 107

### Symposium G2
**Theme: Neurology 3 - Neuro-modulation for Epilepsy**

**Chairperson:** Sam YEUNG (HK) and Eva FUNG (HK)

#### Prospects for Non-invasive Brain Stimulation in Epilepsy (25+5 min)
- **Speaker:** Alexander ROTENBERG (USA) Page 83

#### Invasive Brain Stimulation for Epilepsy (20+5 min)
- **Speaker:** Xian-lun ZHU (HK) Page 83

#### Vagal Nerve Stimulation for Epilepsy (20+5 min)
- **Speaker:** Eva FUNG (HK) Page 83

### Symposium G3
**Theme: Endocrinology - Bone Health**

**Chairpersons:** Betty BUT (HK) and Wilson YEUNG (HK)

#### The Prevalence of Vitamin D Deficiency and its Relationship of Bone Health and Glucose Metabolism in Korean Children and Adolescents (25+5 min)
- **Speaker:** Sei-Won YANG (Korea) Page 57

#### Bone Health Assessment in Children (25+5 min)
- **Speaker:** Yuet-Ling TUNG (HK) Page 58

#### Oral Presentation 7 - Rheumatology
- **Title:** Efficacy and Safety of Infliximab in Juvenile Idiopathic Arthritis and Juvenile Ankylosing Spondylitis: A Randomized, Double-blind, Controlled Study (Abstract #767; 8+2 min)
- **Speaker:** Ying XIE (China) Page 120

### APSID Symposium 7
**Theme: Genetics**

**Chairpersons:** Yoichi MATSUBARA (Japan) and Brian CHUNG (HK)

#### Investigational Gene Analysis for Primary Immunodeficiency Diseases
- **Speaker:** Tomohiro MORIO (Japan) Page 49

#### Molecular Characterization of Severe Combined Immunodeficiency in North India
- **Speaker:** Surjit SINGH (India) Page 50

#### The Challenges in Analyzing Next Generation Sequencing (NGS) Data for Molecular Diagnosis of Primary Immunodeficiency Diseases
- **Speaker:** Wanling YANG (HK) Page 50
### Best Abstracts Session 4

**Chairperson:** David LUK (HK)  
**Adjudicators:** Ting Fan LEUNG (HK)

#### Respirology

**Sleep Duration is Negatively Associated with Carotid Intima-media Thickness in Adolescents (Abstract #62; 8+2 min)**  
**Speaker:** Jade Li (HK)  
*Page 118*

#### Cardiology

**Myocardium Specific Gene Therapy Can Partly Rescue Cardiac Troponin T Deficiency Related Cardiomyopathy (Abstract #1059; 8+2 min)**  
**Speaker:** Lian LIU (China)  
*Page 103*

**The Construction of SENP1 Specific Lentiviral Vector and its Effects on Apoptosis of Alveolar Epithelial Cells Induced by Hyperoxia (Abstract #1143; 8+2 min)**  
**Speaker:** Xu ZHAO (China)  
*Page 120*

#### Allergy & Immunology

**Establishment of the Nasal Microbiota in the First 18 Months of Life - Correlation with Early Onset Rhinitis and Wheezing (Abstract #210; 8+2 min)**  
**Speaker:** Le Duc Huy TA (Singapore)  
*Page 98*

#### Cardiology

**MiR-29b Regulates Cardiomyocytes Proliferation via Targeting NOTCH2 (Abstract #1241; 8+2 min)**  
**Speaker:** Qian YANG (China)  
*Page 104*

#### Gastroenterology & Hepatology

**Liver and Spleen Stiffness for Predicting the Presence and Severity of Esophageal Varices in Children with Chronic Liver Diseases (Abstract #225; 8+2 min)**  
**Speaker:** Pornthep TANPOWPONG (Thailand)  
*Page 108*

#### Genetics & Genomics

**Asthma Diagnosis was Associated with Single-nucleotide Polymorphisms of the Gene Encoding Human Rhino-virus-C Receptor in Children (Abstract #1771; 8+2 min)**  
**Speaker:** Yu Ping SONG (HK)  
*Page 112*

#### Developmental Paediatrics

**SHANK3 Deletion and Related Phenotypes in Chinese Children with Autism and Shank3-KO Zebrafish Display Autistic-like Behaviours (Abstract #795; 8+2 min)**  
**Speaker:** Chunxue LIU (China)  
*Page 106*

### Day 3 (8 Oct)

#### 10:20-10:45  
**Tea Break (with poster viewing)**

#### Symposium H1

**Theme: Rheumatology - From Genetics to Clinical Practice**

**Chairpersons:** Kwok Piu LEE (HK) and Godfrey CHAN (HK)

**Autoinflammatory Disease and Genetic Tests - Friends not Turning to Foes (25+5 min)**  
**Speaker:** Grace CHIANG (HK)  
*Page 90*

**Defining Complex and Monogenic SLE with GWAS and Exome Sequencing (25+5 min)**  
**Speaker:** Yu Lung LAU (HK)  
*Page 90*

**Pediatric Antiphospholipid Syndrome (25+5 min)**  
**Speaker:** Surjit SINGH (India)  
*Page 90*
### Symposium H2

**Theme:** Neurology 4 - Epilepsy: From Cellular Biology to a New International Classification  
**Co-organizers:** HKSIEM / PNAHK  
**Chairpersons:** Kam Tim LIU (HK) and Grace POON (HK)

<table>
<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:45-12:15</td>
<td>Astrocyte Biology in Epilepsy (25+5 min)</td>
<td>Alexander ROTENBERG (USA)</td>
<td>Page 84</td>
</tr>
<tr>
<td>10:45-12:15</td>
<td>Epilepsy in Inborn Errors of Metabolism (25+5 min)</td>
<td>Angels GARCIA-CAZORLA (Spain)</td>
<td>Page 84</td>
</tr>
<tr>
<td>10:45-12:15</td>
<td>ILAE Seizure and Epilepsy Classification (25+5 min)</td>
<td>Ada YUNG (HK)</td>
<td>Page 84</td>
</tr>
</tbody>
</table>

### Symposium H3

**Theme:** Common Orthopaedic Problems in Adolescents  
**Chairpersons:** Wai Hong LEE (HK) and Winnie TSE (HK)

<table>
<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:45-12:15</td>
<td>Application of Scolioscan for Child Spine Health (25+5 min)</td>
<td>Yong Ping ZHENG (HK)</td>
<td>Page 86</td>
</tr>
<tr>
<td>10:45-12:15</td>
<td>Adolescent Idiopathic Scoliosis (25+5 min)</td>
<td>Jack CHENG (HK)</td>
<td>Page 87</td>
</tr>
<tr>
<td>10:45-12:15</td>
<td>Adolescent Sports Injuries of the Knee: From Prevention to Treatment (25+5 min)</td>
<td>Patrick YUNG (HK)</td>
<td>Page 88</td>
</tr>
</tbody>
</table>

### Symposium H4

**Theme:** Cardiology - Update on Cardiovascular Diseases  
**Chairpersons:** Lok Yee SO (HK) and Kai Tung CHAU (HK)

<table>
<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:35-12:25</td>
<td>State of the Art in the Management of Congenital Heart Disease (25+5 min)</td>
<td>Mulyadi DJER (Indonesia)</td>
<td>Page 54</td>
</tr>
<tr>
<td>10:35-12:25</td>
<td>Long-term Arterial Sequelae of Kawasaki Disease (25+5 min)</td>
<td>Yiu Fai CHEUNG (HK)</td>
<td>Page 54</td>
</tr>
<tr>
<td>10:35-12:25</td>
<td>Cardiovascular Sequelae of Kawasaki Disease at a Single Hospital Between 1982 and 2016 (Abstract #192; 8+2 min)</td>
<td>Yumi MIZUNO (Japan)</td>
<td>Page 102</td>
</tr>
<tr>
<td>10:35-12:25</td>
<td>Genetic Profile of Inherited Arrhythmias in Hong Kong Children (25+5 min)</td>
<td>Tak Cheung YUNG (HK)</td>
<td>Page 54</td>
</tr>
</tbody>
</table>

### APSID Symposium 8

**Theme:** Immune Dysregulation  
**Co-organizer:** APSID  
**Chairpersons:** Wen I LEE (Taiwan) and Huawei MAO (China)

<table>
<thead>
<tr>
<th>Session</th>
<th>Title</th>
<th>Speaker</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:45-12:15</td>
<td>Hyper-IgE Syndrome (HIES), Clinical Phenotypes, Molecular Characteristics and Therapeutic Options</td>
<td>Hans OCHS (USA)</td>
<td>Page 51</td>
</tr>
<tr>
<td>10:45-12:15</td>
<td>Complement Deficiency and Susceptibility to Autoimmune Disease</td>
<td>Melanie WONG (Australia)</td>
<td>Page 51</td>
</tr>
<tr>
<td>10:45-12:15</td>
<td>Conventional Treatment of Infection/Inflammation in Chronic Granulomatous Disease</td>
<td>Reinhard SEGER (Switzerland)</td>
<td>Page 52</td>
</tr>
</tbody>
</table>

### Closing Ceremony

Day 3 (8 Oct)

---

Closing Ceremony
From Genes to Communities

–Improving Child Health through Research & Education

Prof. Lau Yu-Lung

Department of Paediatrics and Adolescent Medicine
The University of Hong Kong, China

Health has been defined by the World Health Organisation as “a state of complete physical, mental and social well-being and not merely the absence of disease.” Hence child health is more than survival, absence of diseases, but also about achieving the full developmental potential of each child. Therefore, curing and preventing diseases is but one of many tasks for improving child health, nevertheless an important task at individual level. At societal level, policy support and universal implementation of evidence-based cost-effective interventions to improve child health is the key to success.

Therefore we have designed a scientific program for our 2017 ASPR Congress that encompasses the full spectrum of child health, from caring and managing rare genetic diseases (individual level) to advocating and implementing the WHO Sustainable Development Goals (SDG societal level) which are extremely ambitious with 169 targets embedded in 17 goals. One of these 17 SDGs relates to health, SDG3 with 9 targets covering a range of topics such as injuries, mental health, noncommunicable diseases in addition to child survival.

Our 2017 ASPR Congress program has addressed many of the above topics. Notably for rare genetic diseases which collectively are not rare, affecting 6% to 8% of the population and 3% to 4% of births, as estimated by the European Union. Use of next generation sequencing and gene editing has transformed rare diseases diagnosis and will revolutionise treatment. I believe experience in managing rare diseases will have positive impact on how to manage common diseases eventually. Health and diseases do not know man-made boundaries. As for societal and policy issues, many topics including absolute and relative poverty, social inequality, injuries and family violence are also discussed within our Congress. In between the spectrum from genes to communities, different disease categories, vaccinations and nursing topics are also earnestly discussed in our Congress. Above all, humanities are given the due prominence to remind us the trap of “Excellence without a Soul”. Science and humanities should travel side by side. I hope the range of chosen topics has reflected our Congress goal to achieve “From Genes to Communities – Improving Child Health” amply.

Now I shall discuss how a young paediatrician may appreciate and acquire the skills of research and education as a means to improve child health, which is the core value and mission of the Asian Society for Pediatric Research and the Hong Kong College of Paediatricians.

Curiosity and passion for clarity and truth are the fundamental attributes that drive science forward for advancing the practice of medicine. Nurturing these attributes should ideally start at home in the family and during the early school and college years. Students should be judged by their questions and not by their answers just as the Chinese term for “knowledge” which literally means “Learning to ask questions”. Asking a question is akin to constructing a hypothesis, very much like a working diagnosis. The next step is to be able to critically search and review literature. Then, followed by testing the hypothesis with clinical studies or experiments, interpreting the results and drawing conclusion supported by evidence. Even for hypothesis-free research, the subsequent steps still involve asking a question and try to answer with humility, realizing our limitations.

Now come the practical steps. For a young paediatrician, writing up an interesting case report will be a good start, followed by a case series, asking a broader question. Depending on one’s interest, the next step could be a clinical study comparing two groups, an epidemiological study or experimental bench research. The format is always the same with a question asked, followed by searching an answer. Please note not “the” answer, because scientific truth can be elusive and provisional, which may change with time, context, and tools that are used. I shall reflect on my personal journey which started over 30 years ago, writing my first case report. Using case reports, clinical and epidemiological studies as well as basic experimental work that I was involved as examples, I hope to illustrate certain principles, which include local relevancy, opportunities, feasibility, situational issues, collaborative spirit, impact and educational value.
Role of Pediatric and Child Health Research in Achieving SDGs

Dr. Samira ABOUBAKER

Policy, Planning and Programmes  
Maternal, Newborn, Child and Adolescent Health and Development (MCA)  
World Health Organization

With the end of the Millennium Development Goal era on 25 September 2015, the UN General Assembly adopted the new development agenda “Transforming our world: the 2030 agenda for sustainable development”.

The SDGs come with new sets of ambitious goals that go beyond survival to ensure healthy lives and promote well-being for all at all ages. Among the targets set for Goal 3 which address all major health priorities, there is a specific goal for reducing newborn mortality to as low as 12 deaths/1000 live births and under five mortality to as low as 25 deaths/1000 live births. These goals can be achieved if we can translate the existing knowledge that we have into actions and address some knowledge gaps to deliver known interventions at scale through implementation research. Additionally, through research we should improve diagnosis and treatment of high burden common newborn and childhood conditions as well as improve measurements of our progress. The child health and paediatric community is well placed for guiding and leading research that provides the answers and options for achieving the ambitious targets of the SDGs.
Use of Gene Editing to Treat Inherited Diseases

Donald B. Kohn

Departments of Microbiology, Immunology & Molecular Genetics; Pediatrics; and Molecular & Medical Pharmacology, University of California, Los Angeles

Techniques for precise editing of the human genome have emerged in the past decade. Gene editing may be used to correct pathogenic mutations for many diseases. The major technical advance that is enabling effective gene editing is the development of “designer nuclease” that can be directed to introduce a DNA double-stranded break (DSB) (ideally) at a single site in the human genome. Zinc finger nucleases, TALENs and, more recently, CRISPR/Cas9 are exquisitely site-specific endonucleases. They can stimulate gene editing by thousand-folds, by inducing the activity of endogenous DNA DSB repair mechanisms. We focus on gene editing in hematopoietic stem cells (HSC) for genetic blood cell diseases, and examples from that area will be used. Gene editing of autologous HSC and transplantation may provide safe and effective therapies for primary immune deficiencies, hemoglobinopathies, storage and metabolic diseases, as well as defects of HSC per se. Gene editing may be performed in isolated HSC in the lab by introducing the gene editing reagents (plasmids, mRNA, proteins) through electroporation or with transient viral vectors; the gene-edited HSC may then be reinfused for engraftment. Three major types of gene edits can be induced, depending on which DNA repair mechanism is used: gene disruption, gene correction and gene insertion. Gene Disruption can be achieved by introducing the gene editing nuclease into cells to produce a DSB at a target locus. The non-homologous end joining (NHEJ) repair pathway will re-connect the cut ends of the DNA, but will introduce variably-sized insertions and deletions (indels) at the joint; these indels disrupt the gene sequence and “knock-out” the gene. Clinical trials are evaluating the efficacy of disrupting the CCR5 HIV-1 co-receptor to treat HIV-1 infection and the BCL11a transcription factor to induce production of fetal hemoglobin for beta-globinopathies. Gene Correction is performed by introducing both a nuclease to produce a targeted DSB, and also a “homologous donor template”, which is a DNA sequence matching the target sequence but containing the sequence change to be introduced. The homology-directed repair (HDR) pathway can use the homologous donor template to direct the repair of the DSB and the sequence variations it carries will be inserted into the genome, editing-out the mutation. The uniform single base-pair transversion in the beta-globin gene causing sickle cell disease makes it an ideal target for gene correction in HSC. Relatively efficient correction of the sickle cell disease mutation has been achieved by several groups in pre-clinical studies with human HSC and is being advanced to clinical trials. Gene Insertion can be used to introduce entire genes into a specific target site. For example, a normal cDNA version of a gene can be inserted site-specifically into that target gene locus to be expressed from the endogenous control elements, in situ. Gene insertion can be used to over-ride any mutation in the gene and when the relevant gene needs to be expressed under regulated control. Translating these techniques to clinical applications in the setting of autologous hematopoietic stem cell transplantation is underway. Applications of gene editing for genetic diseases affecting other organ systems present the additional major challenge of in vivo delivery; novel nanotechnologies are being developed that may be capable of meeting this challenge. Gene editing provides unprecedented opportunities to truly cure genetic disorders and the applications are expected to expand.
The under-five mortality is one of the most important indexes to evaluate the health level of one country. China is a developing country with high under-five mortality. But the report on Women and Children’s Health Development of China in 2011 showed that mortality of children under five years old in 2010 reduced 58.7% compared with that of 2000 with the development of economy and environment. Constructing a national research network for pediatrics and child health could reduce the mortality of children.

Recent years our society has established several research network aims to protect, prevent and treat pediatric patients in China to further reduce the mortality rate. On the basis of Chinese Society of Pediatrics, Chinese Medical association, we have established the research network for pediatric asthma in China and investigate the prevalence and risk factors throughout 42 research centers, conduct basic research, develop guidelines for diagnosis and treatment of childhood asthma, and establish a Cohort study for child-adult asthma now after developed China National Clinical Research Center for Respiratory Diseases. We have also conducted many other multi-center reaches for pediatrics, including investigate the pathogens of pneumonia in children to understand the characteristics of pathogen distribution in different areas and bacterial resistance, thus to direct the appropriate use of the antibiotics and reduce drug resistance. In 2008, human enterovirus 71 responsible for the outbreak of hand foot and mouth disease in Fuyang city of China was found and approximately 490,000 infections and 126 deaths in infants and young children were reported. Chinese Center for Disease Control and Prevention reported the outbreak timely and disseminating prevention knowledge for the public and conducting basic research for preventing and treating severe cases. In 2015, the EV71 vaccine provided protection against EV71-associated hand, foot, and mouth disease or herpangina in infants and young children successfully. Universal vaccination of EV71 has decreased the mortality of children with severe EV71 infection.

When joined the campaign of WHO to reduce the death of children less than five years of age, our programs of save life of children never give up. In the future, we will continue depending on Chinese Society of Pediatrics, Chinese Medical association, China National Clinical Research Center for Respiratory Diseases and Chinese Center for Disease Control and Prevention to construct a national research network for pediatrics and child health in China. By this, we estimate the mortality of children in China would be further reduced in the future.
Injury prevention – from Research to Effective Intervention

Dr. CB Chow

Globally more than 875,000 children die from preventable injuries annually. However, injury is one of the most underrecognized public health problem in the world. To prevent injuries, CDC and WHO advocate using the step-wise Public Health Model – firstly define the problem, secondly identify causes, thirdly develop and test intervention, finally adoption and widespread use. A recent review on the world literature published in 12 leading public health and health promotion journals have found that 63% of publications were descriptive (ie stage 1 – defining problem), 11% were concerned on method development and 16% were intervention based (stage 3 – develop and test interventions) while only 5% were concerned with institutionalization or policy implementation research and fewer than 1% contained diffusion research (stage 4 – adoption and wide spread use). A recent review has found 12 effective intervention strategies for prevention of childhood injuries and should these be implemented globally we could prevent between 8,000 to 80,000 child deaths for each type of injury. The concluded that while there were urgent need to research and identify new intervention strategies, but if we could enhance coverage of existing interventions tremendous benefits – up to 1,000 child lives a day would be saved.2

In Hong Kong, it is the major cause of mortality and morbidity beyond 1 years of age for the past three decades. While there is a very slow decrease in mortality, morbidity rates are on increase with increasing variations among the 18 districts related to socio-economic factors. Assuming that all districts could achieve the lowest rate in Hong Kong around 30-50% of injuries are potentially preventable resulting in 33 fewer deaths, 1,946 less years of life lost, 3953 less hospitalizations, 19488 less AED attendances and a saving of HK$50 million per year in Hospital Authority. Effective interventions have already been established through international and local studies, including our own, but the major challenge is how to raise awareness and empower communities to implement evidence-based interventions in a systemic and sustainable way. Utilization of new social media or technology will another way forward. However, establishment of a good injury surveillance system that can inform local decision makers in prioritizing resources and empower communities to implement evidence-based intervention programmes are keys to success. However, most injury surveillance systems suffer from a lack of timeliness, relevancy, and sustainability. Hong Kong is fortunate to have an excellent public hospital system that electronically captures patient information. Using new geo-spatial and internet technology, an electronic geo-information injury surveillance system has been developed that satisfies most of the criteria for an injury surveillance system according to the World Health Organization and the Center of Disease Control and Prevention. The information can be translated into useful information for the development of injury intervention programmes through the Safe Community platform. PRECEDE-PROCEED and collaborative multiplier were found to be useful tools for implementing interventions. A three-pronged approach at the policy, district, and local levels is proposed for the coordination and implementation of child safety strategies using information collected from the geo-spatial injury surveillance system with Safe Community as the coordinating platform.

References
3. CB Chow. Childhood Injuries in Hong Kong – from epidemiology to community intervention. MD Thesis 2015
Liver Cancer Prevention – from Fetus to Adults

Mei-Hwei Chang, M.D.

Mei-Hwei Chang, M.D., Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan

Liver Cancer is the 2nd most common cause of cancer death in the world. Chronic hepatitis B virus (HBV) infection is closely related to chronic hepatitis, liver cirrhosis, and liver cancer. Asian people have high rates of HBV infection and liver cancer in both children and adults.

We have provided serial sequential evidences to demonstrate that the HBV immunization program has successful reduced approximately 90% of chronic HBV infection in the vaccinated birth cohorts. We have also provided the first evidence to support HBV vaccine as the first cancer preventive vaccine in human, which reduced approximately 70% of liver cancer in children and adolescents. Successful liver cancer prevention effect was later also reported in other areas in the world, such as Khon Kaen, Thailand and Alaska, U.S.A. More recently we have provided further evidence to demonstrate that the cancer preventive effect of hepatitis B vaccination in infancy has been extended from children and adolescents to young adults.

In spite of the great success, still there are problems to be overcome for the better prevention of hepatitis B and liver cancer. Vaccine failure is the main cause of vaccine failure. Other causes include hepatitis B surface gene mutation, and immune hypo- or non-responsiveness to hepatitis B vaccine. Developing effective strategies to block maternal transmission of HBV is very important to prevent vaccine failure, and to achieve better prevention for hepatitis B and liver cancer. Short term antiviral therapy against HBV for highly B viremic mothers at third trimester of pregnancy is effective in further reducing the HBV vaccine failure rate in their infants.

In conclusion, to prevent liver cancer in children and adults, we should work hard to block mother-to-infant transmission of HBV starting from fetal and neonatal period.
Rare Disease - Challenges in Diagnosis and Management

Yoichi Matsubara

*National Center for Child Health and Development, Japan*

To date molecular bases of 5,000 genetic diseases have been identified, while more than 3,000 genetic conditions still await to be elucidated. Since most of the genetic diseases are rare and present with obscure and/or unfamiliar combination of signs and symptoms, patients and their physicians often struggle to search for correct diagnosis for many years (i.e., a diagnostic odyssey). To this end we have initiated a national consortium, the Initiative on Rare and Undiagnosed Diseases in Pediatrics (IRUD-P) funded by the Japan Agency for Medical Research and Development (AMED). The aims of the project are to make diagnosis on patients with rare and undiagnosed diseases using next-generation sequencing, to construct their genome database with clinical information, to make banking system of precious specimens. The IRUD-P assigned 17 regional core clinical centers across Japan which evaluate clinical symptoms of patients who are referred from local hospitals/clinics and perform first-line laboratory examinations. The obtained data are carefully examined by experts specialized in rare diseases and selected patients are enrolled into IRUD-P. So far we have received DNA specimens from 1,542 patients and their parents. Our overall diagnostic rate was 33%. The diagnostic rate was as high as 45% when trio samples were available.

Once the diagnosis is made, an appropriate treatment and management is provided to the patient. In some cases, molecular targeted therapies remarkably ameliorated patients’ disease conditions. IRUD-P not only benefits patients with rare diseases, but also is expected to facilitate the discovery of important medical findings and the development of novel drugs for common diseases, as evidenced by the examples of PCSK9 inhibitors for hypercholesterolemia and SGLT2 inhibitors for diabetes.
EDUCATING THE HUMANE PHYSICIAN:
THE ROLE OF MEDICAL HUMANITIES

GENESIS C. RIVERA, M.D., M.A., FPPS

Executive Director, Center for Medical and Allied Health Sciences
New Era University, Quezon City, Philippines

The previous and present centuries witnessed the tremendous strides in medicine. Modern diagnostic procedures, advanced therapeutic modalities and modern, novel and safer drugs and surgical procedures benefited greatly the whole of mankind in general. As a result of these benefits from modern medicine, normal life span increased and people were able to enjoy life better and longer. Doctors themselves are now better trained due to the modern discoveries, the modern technology at their disposal and the advanced and novel methods in medical education.

However, together with these progress in the science of medicine, there is now a growing dissatisfaction and mistrust of patients of their physicians. There has been a noticeable detachment of doctors from their patients; the traditional patient–doctor rapport is slowly being eroded. Too much reliance on technology in the absence of sound clinical judgment is partly a reason for this, among many others. What is even more alarming is the noticeable decline in empathy and the increase in cynicism among medical students as they progress through medical school and residency. The lack of observational and communication skills, deficient sensitivity to patients’ emotions all lead to a physician without empathy.

The medical humanities as a discipline in medical education was introduced several decades ago to address this issue. Many medical schools in Europe, United States and Asia had integrated the course in their medical curricula. There are various methods in introducing the discipline to medical students; different approaches are being utilized. Basically, the courses included are literature, poetry, visual arts, music, film, theatre, as well as the social sciences like medical anthropology, sociology as well as philosophy, history and ethics. Through these wide area of non-medical fields of study, the medical student could develop better observational skills, analyze human situations sometimes unfamiliar to them, communicate better in a more humane way to patients and better understand and interpret human emotions. All these qualities point to a more humane physician.
A Humanitarian Mission with MSF in South Sudan – Challenges of Delivering Paediatric Care During a Civil War

Dr. Kai-ning CHEONG

Resident Specialist in Paediatrics, Queen Mary Hospital, University of Hong Kong, Hong Kong
Paediatric Immunology, Allergy and Infectious Diseases subspecialty trainee
Honorary Tutor in Paediatrics and Adolescent Medicine, University of Hong Kong
Honorary Clinical Lecturer in Medical Humanities, University of Hong Kong
Bill Marshall Memorial Fund Fellowship awardee 2017

Dr. Kai N. Cheong had the privilege of being the first paediatric trainee from Hong Kong to successfully interrupt her paediatric training for a humanitarian mission, all done using her own annual leave. She spent five arduous and rewarding months in South Sudan with the NGO Médecins Sans Frontières (MSF), working at Gogrial and Doro Refugee Camp field hospitals as the only paediatric doctor (at times only doctor) for those large-scale projects. MSF was able to provide care for general paediatrics, neonatal and paediatric intensive care, and maternity patients; for populations where sometimes they were the only NGO in the area.

In a country still actively at civil war, the vast and overwhelming geopolitical, economical and social problems hampering access to and provision of healthcare, provided innumerable challenges and training opportunities for a young paediatric trainee. Other than being a full-time frontline doctor, she also had to fulfil leadership roles of hospital administrator, manager and educator - and sometimes even cook!

Despite being faced with infectious disease outbreaks, limited healthcare resources and skills, widespread malnutrition - the MSF team was still able to train the next generation of local nurses and staff, drastically reduce infant and maternal mortality rates, and bring some hope to the local population. When faced with helpless medical and ethical situations due to circumstances out of their control, healthcare professionals can still reaffirm the human dignity of their patients - by being present, by bearing witness, and by speaking out.

This is Kai’s story with MSF in South Sudan - only one of million stories about humanity that happen daily, that should change how we think about healthcare and medical education globally. It is her hope that sharing it, can bring light to a desperate situation in a country with immeasurable needs.

More importantly, she hopes to underscore how having the opportunity to carry out this kind of service and work, trains young doctors in their communication, empathy, creativity, ingenuity and leadership. This can only ultimately make them better doctors and better human beings, by pushing them to explore and experience the complex lessons of the medical humanities - through living through them and sharing that human connection.
Having a Population-based Surveillance of Invasive Pneumococcal Disease to understand Vaccine Pressure and Failure

Prof. Lau Yu-Lung

*Chairman, Working Group on Pneumococcal Vaccination
Centre for Health Protection*

In September 2009, 7-valent pneumococcal conjugate vaccine (PCV7) was included in the Hong Kong Childhood Immunisation Programme (HKCIP). In October 2010, it was replaced by 10-valent pneumococcal conjugate vaccine (PCV10), which was in turn replaced by 13-valent pneumococcal conjugate vaccine (PCV13) in December 2011. Having a population-based surveillance of invasive pneumococcal disease (IPD) is critical to understand serotype replacement due to vaccine pressure, persistence of vaccine serotype due to vaccine failure and unexpected changes of IPD epidemiology after introduction of universal childhood pneumococcal vaccination.

In Hong Kong, The Centre for Health Protection (CHP) conducts surveillance of invasive pneumococcal disease (IPD) at different levels, including (1) a laboratory surveillance system established in 2007 to cover all microbiology laboratories in public and private hospitals in Hong Kong with the Public Health Laboratory Services Branch (PHLSB) of the CHP to process all pneumococcal isolates from sterile sites for serotyping, antimicrobial susceptibility testing and characterization; (2) from 2014, doctors were requested to report IPD cases in children under the age of 18 years old to the CHP, which was extended by including IPD as one of the notifiable infectious diseases from January 2015; (3) clinical data related to hospitalized IPD cases are obtained from the Hospital Authority (HA). The data from the different surveillance systems are analysed to monitor the trend of IPD in Hong Kong, with particular focus on issues of serotype replacement, emergence of serotype 3 as the dominant serotype locally and apparent increase in cases of complicated pneumococcal pneumonia and empyema. The latest epidemiology of IPD from this surveillance will be presented, with implications on vaccine choice and development discussed.
Cervical Cancer Prevention: Past, Present and Future

Ting Fan LEUNG

Department of Paediatrics, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong

Oncogenic human papillomavirus (HPV) infection is the most important cause of cervical cancer. Although close to 20 oncogenic HPV types were found, HPV types 16 and 18 account for about 70% of cases of cervical cancer worldwide. The bivalent (Cervarix™, HPV-16/18 AS04-adjuvanted [2vHPV]; GlaxoSmithKline Biologicals) and quadrivalent (Gardasil®, HPV-6/11/16/18 [4vHPV]; Merck & Co., Inc.) HPV vaccines target these two important HPV types. Licensure studies found both vaccines to have excellent efficacy against precursors of cervical cancer, and post-marketing surveillance also reported substantial fall in cervical cancer incidence in many countries. For practical reasons, there has been limited data on the efficacy of these vaccines in preventing the already rare occurrence of genital warts and cervical cancers in teenagers who would be the ideal population for any universal vaccination programme. Despite this, a number of immunobridging studies showed excellent safety and strong immunogenicity of 2vHPV and 4vHPV in adolescence. Therefore, many countries have approved the 2-dose regime of these vaccines in this age group. A recent multi-national randomised clinical trial found superior immunogenicity against HPV-16 and HPV-18 for up to 36 months among teenage girls who received a 2-dose schedule of 2vHPV when compared to 2-dose and 3-dose schedules of 4vHPV. More recently, the marketing of 9-valent HPV vaccine (Gardasil 9 [9vHPV]; Merck and Co., Inc.) covers five more oncogenic HPV types (31, 33, 45, 52, and 58) that account for about 15% of cervical cancers. Phase III efficacy and immunobridging trials confirmed non-inferiority of efficacy and immunogenicity for 9vHPV compared with 4vHPV. In conclusion, the excellent clinical trial and surveillance results of all currently licensed HPV vaccines strongly support their impact as high value public health intervention to prevent anogenital HPV infections and their associated neoplasia. It is also important to emphasise the need for all female vaccinees to undergo cervical cancer screening when they reach young adulthood.
<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy and Immunology</td>
<td>42</td>
</tr>
<tr>
<td>Cardiology</td>
<td>55</td>
</tr>
<tr>
<td>Dermatology</td>
<td>56</td>
</tr>
<tr>
<td>Endocrinology</td>
<td>57</td>
</tr>
<tr>
<td>Gastroenterology and Hepatology</td>
<td>58</td>
</tr>
<tr>
<td>General and Community Paediatrics</td>
<td>60</td>
</tr>
<tr>
<td>Genetics and Genomics</td>
<td>67</td>
</tr>
<tr>
<td>Haematology and Oncology</td>
<td>68</td>
</tr>
<tr>
<td>Infectious Diseases</td>
<td>70</td>
</tr>
<tr>
<td>Inborn Errors of Metabolism</td>
<td>77</td>
</tr>
<tr>
<td>Neonatology</td>
<td>78</td>
</tr>
<tr>
<td>Neurology</td>
<td>80</td>
</tr>
<tr>
<td>Nutrition</td>
<td>85</td>
</tr>
<tr>
<td>Orthopaedics</td>
<td>86</td>
</tr>
<tr>
<td>Respirology</td>
<td>88</td>
</tr>
<tr>
<td>Rheumatology</td>
<td>90</td>
</tr>
<tr>
<td>Nursing</td>
<td>91</td>
</tr>
<tr>
<td>Chinese Pediatric Society</td>
<td>94</td>
</tr>
</tbody>
</table>
Gene Therapy for Adenosine Deaminase (ADA)-Deficient Severe Combined Immune Deficiency

Donald B. Kohn, Adrian Thrasher, and Bobby Gaspar.

Departments of Microbiology, Immunology & Molecular Genetics; and Pediatrics, University of California, Los Angeles, UCL Great Ormond Street Institute of Child Health

Inherited deficiency of adenosine deaminase (ADA), an enzyme of purine metabolism, is the cause of 10-15% of human Severe Combined Immune Deficiency (SCID). Transplantation of hematopoietic stem cells (HSC) from a healthy donor can be curative of SCID. But, there are risks from graft versus host disease caused by an immune reaction by the donor’s cells against the patient. Transplantation using the patient’s own (autologous) HSC that are treated to add a normal copy of the ADA gene (gene therapy) may have similar benefits as a transplant from a donor, without the immunologic risks. From initial studies to insert a normal ADA gene into T cells that began in the early 1990’s, gene therapy for ADA-SCID has been developed to be a highly effective and safe therapy. Use of reduced intensity conditioning with busulfan to “make space” in the hematopoietic niche is essential to achieve engraftment of sufficient gene-modified HSC. Initial metabolic detoxification using ADA enzyme replacement therapy for several months allows the gene therapy transplant to be done when the patient is clinically well and without infections. Murine retroviral vectors were used for initial studies at several centers and led to consistent immune reconstitution in the majority of patients. The first of these, developed in the TIGET Institute in Milan, has been brought to licensure in the European Union by GSK. Currently, our groups in Los Angeles and London are performing trials of gene therapy for ADA SCID with HSC using a lentiviral vector and reduced intensity conditioning. The lentiviral vector achieved high levels of ADA gene transfer and expression than did a murine retroviral used in our preceding clinical trial, and more consistent and robust immune reconstitution. Efforts are underway to advance this therapeutic to licensure to make it widely available for ADA SCID patients. Over 25 years, gene therapy for ADA SCID has advanced from early investigations to becoming potentially a standard of care.
Mesenchymal Stem Cells Therapy

Prof. Godfrey Chi-fung CHAN
Department of Paediatrics & Adolescent Medicine, Queen Mary Hospital & HKU-Shenzhen Hospital, The University of Hong Kong

Mesenchymal stem cells (MSCs, or known as are mesenchymal stromal cells) are multi-potent adult stem cells that can be extracted from bone marrow, adipose tissue and cord blood. MSCs have the potential to differentiate into a wide spectrum of tissue cells. It was initially proven to improve the clinical phenotype of osteogenesis imperfecta but there is no clinical evidence of long term engraftment. For tissue regeneration, MSCs have been used for bone, cartilage or even skin repair in various degenerative or congenital diseases. The other potential applications of MSCs are immunomodulation for various immune disorders such as GvHD, SLE or multiple sclerosis. It appears that MSCs exert such function by both secreting soluble factors and also via cell-cell interaction in the targeted site. However, the immunosuppressive function is often transient and may not work if the recipients are suffering from aggressive inflammatory condition. It is due to the effects of various cytokines and chemokines may alter the survival and function of the MSCs. In addition, one has to be aware that MSCs can also enhance tumor growth and metastasis so its use in cancer setting has to be carefully looked into. Recently, we have been exploring the use of MSCs as vehicle for gene therapy or source for induced pluripotent stem cells. It appears that they have specific advantages over the conventional methodology.

The Role of Toll-like Receptor 3 in Viral Encephalitis

Dr. Cheng-Lung KU
Associate Professor, Graduate Institute of Clinical Medical Sciences, Chang Gung University, Taiwan

The spectrum of diseases of childhood caused by enterovirus 71 (EV71) is broad, ranging from asymptomatic infection or self-limited hand-foot-and-mouth diseases (HFMD) to life-threatening encephalitis, however, the molecular mechanisms underlying these different clinical presentations remain unknown. We hypothesized that severe EV71 infection in children might reflect an intrinsic host single gene defect of anti-viral immunity. We searched for mutations in Toll-like receptor 3 (TLR3), which have been previously found in children with herpes simplex encephalitis (HSE) in young patients with severe EV71 infection. We sequenced TLR3 and tested the impact of the mutation found. We tested dermal fibroblasts from our patient and other patients with known genetic defect in TLR3 or related genes, for their response to both poly(I:C) stimulation and EV71 infection. We found that three children were heterozygous for the TLR3 mutations, which are shown to have severe impact on the TLR3 function. One patient’s fibroblasts with heterozygous mutation had impaired but not abolished response to TLR3 agonist poly(I:C). We also showed that TLR3 was crucial in cellular defense against EV71 infection, as TLR3-deficient or TLR3 heterozygous mutation fibroblasts were highly vulnerable to EV71 infection. In Summary, our results demonstrated that TLR3 deficiency may underlie severe EV71 infection and TLR3 signaling is crucial in human immunity against EV71. Children with severe EV71 infection should be tested for inborn errors of TLR3 immunity.

Immunotherapy for EBV-associated Disorders

Prof. Wen-wei TU
Department of Paediatrics & Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong. Hong Kong

Immunotherapy is a therapeutic strategy by regulating the patients’ immune function to treat diseases, i.e. enhancing the immune responses to fight cancer; inhibiting the immunity to control autoimmune diseases or induce immune tolerance, etc. Here, we share our own research experience by regulating host Vγ9Vδ2-T cell function to treat EBV-associated disorders using EBV-induced lymphoproliferative disease (EBV- LPD) as a model. We showed
that the aminobisphosphonate pamidronate-expanded human Vy9Vδ2-T cells efficiently killed EBV-transformed autologous lymphoblastoid B cell lines (EBV-LCL) through g/d-TCR and NKG2D receptor triggering, and Fas and TRAIL engagement. By inoculation of EBV-LCL in Rag2−/−gc−/− mice and humanized mice, we established lethal EBV-LPD with characteristics close to the human disease. Adoptive transfer of pamidronate-expanded Vy9Vδ2-T cells alone effectively prevented EBV-LPD in Rag2−/−gc−/− mice and induced EBV-LPD regression in EBV+ tumor-bearing Rag2−/−gc−/− mice. Pamidronate treatment inhibited EBV-LPD development in humanized mice through selective activation and expansion of Vy9Vδ2-T cells. This study provides proof-of-principle for a novel therapeutic approach using pamidronate to control EBV-LPD through Vy9Vδ2-T-cell targeting. As pamidronate has been already used for decades in osteoporosis treatment, this ‘new application of an old drug’ potentially offers a safe and readily available option for the treatment of EBV-LPD.

Wiskott-Aldrich Syndrome Protein Regulates Autophagy and Inflammasome Activity in Innate Immune Cells

Dr Pamela Lee
Clinical Associate Professor
Department of Paediatrics and Adolescent Medicine
Queen Mary Hospital,
LKS Faculty of Medicine, The University of Hong Kong

Dysregulation of autophagy and inflammasome activity contributes to the development of auto-inflammatory diseases. Emerging evidence highlights the importance of actin cytoskeleton in modulating inflammatory responses. Wiskott-Aldrich syndrome (WAS) is an X-linked recessive primary immunodeficiency disorder characterized by microthrombocytopenia, defective immunity and eczema. Autoimmune disorders occur in 20-70% of patients with WAS; common manifestations include autoimmune haemolytic anaemia, neutropenia, vasculitis, arthritis and inflammatory bowel disease. There are some features of WAS that resemble paradigmatic auto-inflammatory syndromes, but this has not been mechanistically explored. We tested the hypothesis that deficiency of the WAS protein (WASp) which signals to the actin cytoskeleton through the actin nucleating complex Arp2/3, modulates autophagy and inflammasome function. In a model of sterile inflammation utilizing Toll-like receptor 4 ligation followed by treatment with ATP or nigericin, we observed enhanced inflammasome activation in monocytes from WAS patients and in WAS knockout murine bone marrow-derived dendritic cells. In ex-vivo models of enteropathogenic Escherichia coli or Shigella flexneri infection, WASp deficiency resulted in defective bacterial clearance, exaggerated inflammasome activation and increased host cell death. These events were associated with dysregulated septin cage-like formation and impaired autphagic p62/LC3 recruitment and defective formation of canonical autophagosomes. Taken together, we propose that dysregulation of the autophagy and inflammasome activities partly contribute to the autoinflammatory manifestations of WAS, thereby offering targets for potential therapeutic intervention.

APSID Symposium 3
Inborn and Acquired Susceptibility to Mycobacterial and Fungal Infections

Anti-interferon-γ Autoantibody: a New Form of Adult Onset Immunodeficiency to Mycobacterial Infection in Southeast Asia

Dr. Cheng-Lung KU
Associate Professor, Graduate Institute of Clinical Medical Sciences, Chang Gung University, Taiwan

Anti-Interferon (IFN-γ) autoantibodies are an emerging etiology to cause the adult-onset immunodeficiency with mycobacterial or other opportunistic infections in patients. IFN-γ has an important role in antmycobacterial immunity and is produced principally by T cells and natural killer cells after stimulation with microbial products and interleukin-12. Genetic defects in IFN-γ-mediated immunity cause Mendelian susceptibility to mycobacterial disease (MSMD) in children and young adults, who contract disseminated mycobacterial infection from weakly virulent mycobacteria, such as bacille Calmette-Guérin (BCG) vaccines and nontuberculous mycobacteria. The striking clinical similarities between such individuals and those with MSMD strongly suggest that autoantibodies against IFN-γ are the cause of mycobacterial infection, rather than a consequence.

Our laboratory had identified a high prevalence of anti-IFN-γ autoantibodies in patients with disseminated mycobacterial infections in Taiwan. We found that this disease is strongly limited to the individuals with HLA-DRB1*15:02/16:02 and –DQB1*05:01/05:02 in South-East Asia, which provides genetic basic to explain the ethnic/region restriction of this disease. Moreover, we found that these anti-IFN-γ autoantibodies recognize a major epitope (P121–131) at the C-terminus of IFN-γ. The amino acid sequence of this epitope is 100% homologous to a stretch of amino acids in the Noc2 protein of Aspergillus terreus, a fungus present in the environment, and autoantibodies from patients bound Noc2. We also generated an epitope-erased IFN-γ (EE-IFN-γ), in which the major neutralizing epitope region was modified. The binding affinity of anti-IFN-γ autoantibodies
for EE-IFN-γ was reduced by about 40% compared with unmodified IFN-γ and activated the IFN-γR downstream signaling pathway ex vivo, in the presence of patients’ plasma. In brief, we identified a common, critical B cell epitope that bound to anti-IFN-γ AutoAbs in patients and propose a molecular mimicry model underlying the production of these antibodies.

In conclusion, our effort shows the under-estimated clinical impact of anti-IFN-γ autoantibody disease in Taiwan and our study reveals the molecular mechanism of this particular disease.

Cryptococcal Infections in Children can be Associated with a Myriad of Primary Immunodeficiency Diseases
– Our Experience at Chandigarh, North India
Prof. Surjit SINGH
Professor of Pediatrics and Incharge Allergy Immunology Unit, Advanced Pediatrics Centre,
Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India
Principal Investigator, ICMR Centre for Advanced Research in Primary Immunodeficiency Diseases

Cryptococcal infections have been described in children with certain immune deficient states like Human Immunodeficiency Virus infection, diabetes mellitus and malignancies. We describe here 4 cases who had cryptococcal infections and search for underlying immune defect led to the finding of a myriad of primary immunodeficiencies in some of them.

**Case 1:** 3 year girl, symptomatic since 6 months of age in form of recurrent pneumonia, otitis media and oral thrush, failure to gain weight and height, now presented with history of cough, fever and respiratory distress. On examination, she was severely malnourished, had tachypnea (RR- 60/min), clubbing, oral thrush and diffuse crepitations on auscultation over chest. Investigations revealed anemia (hemoglobin 76gm/L), CT guided fine needle aspiration cytology (FNAC) from lung showed Cryptococcus sp. Search for immune deficiency was carried out. Immunoglobulin G was elevated (2.2 gm%) with CD3 (57%), CD20 (15.7%) and CD56 (27.3%) being within normal limits. Further evaluation uncovered the presence of CD4 lymphocytopenia (CD4+ T cells: 5.7% as compared to 46.4% in age matched control). Search for causes of CD4 lymphocytopenia was unremarkable and a diagnosis of idiopathic CD4 lymphocytopenia was concluded.

**Case 2:** 3 year boy, presented with fever and pain abdomen for 3 months. Had jaundice 1 month back. Examination revealed generalized lymphadenopathy, jaundice and hepatomegaly. Investigations showed anemia, conjugated hyperbilirubinemia with elevated alkaline phosphatase and gamma glutamyl transferase. Biopsy from axillary lymph node revealed multiple necrotizing granulomas with numerous refractile fungal yeasts in the giant cells, histiocytes and in the necrotic tissue confirming to the morphology of Cryptococcus. A diagnosis of disseminated cryptococcosis was made. Evaluation for underlying immune defect revealed elevated serum immunoglobulin E (>10,000 U/l) with reduced Th17 cells (0.9% as compared to 2.1% in age matched control) and p-STAT3 (10.9% as compared to 30.8% in control).

**Case 3:** 4 year boy, presented with fever, rash and pain abdomen for 6 weeks. Examination showed cervical and axillary lymphadenopathy, hepatosplenomegaly and discrete umbilicated lesions over trunk and limbs. FNAC from cervical lymph node showed granulomatous inflammation and numerous intracellular and extracellular round to oval capsulated organisms consistent with Cryptococcus. Search for immune deficiency was unrewarding. With a diagnosis of disseminated cryptococcosis, Amphotericin B and flu cytosine are initiated. On follow-up, skin lesions were healing and organomegaly disappeared.

**Case 4:** 4 year boy, presented with fever, headache, seizures and altered sensorium for 1 month. Investigations: Ultrasonography of abdomen showed altered echo texture of liver with multiple hypo dense lesions in spleen. Cerebro-spinal fluid (CSF) examination showed Cryptococcus on India-ink staining. CSF as well as blood culture revealed Cryptococcus neoformans. A diagnosis of disseminated cryptococcosis was arrived at. Evaluation for underlying immune defect showed reduced expression of IL12Rβ1 on lymphocytes (10.0% as compared to 46.4% in age matched control). This was one of the uncommon cases of disseminated cryptococcal infection with IL12Rβ1 defect.

Cryptococcal infections including disseminated cryptococcal infections have been reported in immunocompetent children (1,2). However, these children should not be termed as immunocompetent only because no apparent immunodeficiency could be demonstrated in them. At best, these children may be called as “apparently immunocompetent”.


Endemic Mycoses: When to Suspect PID?

Dr. Pamela Pui-wah LEE
Clinical Assistant Professor,
Department of Paediatrics and Adolescent Medicine,
LKS Faculty of Medicine,
The University of Hong Kong
Hong Kong

The global burden of fungal diseases has been increasing, as a result of the expanding number of susceptible individuals including people living with human immunodeficiency virus (HIV), hematopoietic stem cell or organ transplant
recipients, patients with malignancies or immunological conditions receiving immunosuppressive treatment, premature neonates and the elderly. Opportunistic fungal pathogens such as Aspergillus, Candida, Cryptococcus, Histoplasma capsulatum, and Pneumocystis jiroveci are distributed worldwide and constitute the majority of invasive fungal infections (IFI). Dimorphic fungi such as Histoplasma capsulatum, Coccidioides spp., Paracoccidioides bucculanti, Blastomyces dermatitidis, Sporothrix schenckii, Talaromyces (Penicillium marneffei) and Emmonsia spp. are geographically restricted to their respective habitats and cause endemic mycoses. Disseminated histoplasmosis, coccidioidomycosis and T. marneffei infection are recognized as AIDS-defining conditions, while the rest also cause high rate of mortalities and mortalities in patients with HIV infection and other immunocompromised conditions. In the past decade, a growing number of monogenic immunodeficiency disorders causing increased susceptibility to fungal infections have been discovered. In particular, defects of the IL-12/IFN-gamma pathway and T-helper 17-mediated response are associated with increased susceptibility to endemic mycoses. In this talk, I am going to take the audience on a journey around the world to examine how cellular and molecular defects of the immune system predispose to invasive dimorphic fungal infections, including primary immunodeficiencies, individuals with autoantibodies against interferon-gamma, and those receiving biologic response modifiers. Though rare, these conditions provide important insights to host defense mechanisms against endemic fungi, which can only be appreciated in unique climatic and geographical regions.

**APSID Symposium 4**

- **Inflammatory Manifestations in Primary Immunodeficiencies**

Understanding Mechanisms underlyin Monogenic Autoinflammatory Diseases may Lead to Targeted Treatment

**Prof. Yu-lung LAU**

*Doris Zimmern Professor in Community Child Health*

*Chair Professor of Paediatrics*

*Department of Paediatrics & Adolescent Medicine*

*LKS Faculty of Medicine*

*The University of Hong Kong, Hong Kong*

Monogenic autoinflammatory diseases (MAD) are characterized by fever, systemic and/or organ-specific inflammation due to mutations of genes involved in innate immunity. Mechanisms underlying MAD have been clarified over the last 20 years to involve that of inflammasomes with IL-1β activation, NF-kB activation with dysfunctional ubiquitination, interferonopathies, cytokine signaling and protein-folding disorders.

The prototypic MAD due to inflammasomopathies with IL-1β activation includes familial Mediterranean fever (MEFV mutation) and cryopyrin-associated periodic syndromes (NLRC3 mutation). Other IL-1β activation disorders include Majeed syndrome (LPIN2 mutation), NLRC4-MAS (NLRC4 mutation), MKD/HD5 (MVK mutation), PFAPA (PSTPIP1 mutation), FKLC (NLRP1 mutation) & PFT1 (WDR1 mutation). Blockade of IL-1 with anakinra or canakinumab is a treatment of choice, except for FMF for which colchicine is the drug of first choice. For NLRC4-MAS, addition of IL-18 blockade is necessary.

NF-kB activation disorders include Blau syndrome (NOD2 mutation) and ubiquitination disorders, which include HA20 & otulipenia (insufficient debiquitination), HOIL-1 & HOIP deficiency (impaired ubiquitination). These MAD generally respond well to TNF-α blockade probably because of activation of NF-kB pathways by TNF-α receptors.

Interferonopathies include SAVI (GOF mutations in dsDNA sensor STING), AGS (multiple genes/proteins defects in intracellular sensing of nucleic acids) and PRAAS-CANDLE (multiple proteasome genes/proteins defect). Patients with SAVI are being treated with inhibitors of JAK, TBK1 and IKKE which are signaling molecules of type 1 interferon pathway.

Cytokine signaling disorders driving autoinflammation include DIRA (defect in IL-1 receptor antagonist), DITRA (defect in IL-36 receptor antagonist) and IL-10/IL-10R deficiency. These MAD have been treated with both TNF-α and IL-1 blockade with variable responses. IL-17 blockade has been used for DITRA. HSCT has been performed for IL-10R deficiency with successful outcome.

**Identifying Primary Immunodeficiency Diseases in Children Suffering from Refractory Diarrhea**

**Prof. Wen-i LEE**

*Professor of Pediatrics, Chang Gung Memorial Hospital and University*

*Director of the Primary Immunodeficiency Care And Research (PICAR) Institute*

*Taiwan*

Diarrhoea lasting longer than 14 days and failing to respond to conventional management is defined as severe and protracted diarrhoea (SD). In our referral centre, we investigated the prevalence, pathogens and prognosis of SD in primary immunodeficiency diseases (PIDs). Among 246 patients with predominantly paediatric-onset PIDs from 2003-2016, 21 with mutations of the Btk, IL2RG, WASP, CD40L, gp91, gp47, and RAG2 genes and five [CVID and SCID] without identified mutations had SD before prophylactic treatment. Detectable pathogens by rank included pseudomonas, salmonella, E. coli, cytomegalovirus, coxsackie virus and cryptosporidium, all of whom improved
after a mean 17 days of antibiotics and/or IVIG treatment. Seven (7/26; 27.0%) patients died of respiratory failure (four), lymphoma, sepsis and intracranial haemorrhage (one each). The patients with WAS, CGD and CD40L and SD had a higher mortality rate than those without. Another five males with mutant XIAP, STAT1, FOXP3 (one each) and STAT3 (two) had undetectable-pathogenic refractory diarrhoea (RD) that persisted >21 days despite aggressive antibiotic/steroid treatment and directly resulted in mortality. For the patients with RD without anti-inflammatory optimization, those with mutant XIAP and FOXP3 died of Crohn’s-like colitis and electrolyte exhaustion in awaiting transplantation, while transplantation cured the STAT1 patient.

Primary Immunodeficiencies Presenting with Inflammatory Bowel Disease

Dr. Melanie WONG
Consultant
Department of Allergy and Immunology,
The Children’s Hospital at Westmead, Australia

A balance between immune responses to harmful microorganisms and tolerance to nonpathogenic antigens is essential for immune homeostasis in the gastrointestinal tract. This generally favors the development of tolerance. Multiple immune factors including barrier function, neutrophils, cytokines, IgA and regulatory T cells are essential to the process.

Inflammatory conditions affecting the bowel are common complications of primary immunodeficiency, occurring at any age. The onset of inflammatory bowel disease at an early is most commonly the manifestation of a monogenic disorder. Over 50 genes are known to cause early onset IBD but not all appear to primarily affect immune function, although the majority impact in some way. Four genes are listed in the 2015 version of IUIS tables under heading of immune dysregulation with colitis (IL-10 deficiency, IL-10Ra deficiency, IL-10Rb deficiency, NFAT5 haploinsufficiency), but ‘IBD’, ‘diarrhoea’, ‘enteropathy’ and ‘colitis’ appear frequently amongst the typical presenting features of many recognised immunodeficiencies including chronic granulomatous disease, Wiskott Aldrich syndrome, IPEX, XIAP, LRBA, CTLA4 and a range of auto-inflammatory conditions. Differences in the prognosis and management argue that a genetic diagnosis should not be missed. As a group, these diseases are rare but have high morbidity and subgroups have high mortality if untreated. Understanding the pathophysiology of a disorder can identify unconventional biological treatment options that interfere with specific pathogenic pathways. So early diagnosis, preferably genetic, is important.

This talk will highlight some of the pathogenic mechanisms leading to early onset inflammatory bowel disease in the setting of primary immunodeficiency, investigation and implications to management.

Ig Replacement Therapy in Primary Immunodeficiency

Dr. Hua-wei MAO
Associate Consultant, University of Hong Kong-Shenzhen Hospital
Vice Chairman, Youth Committee, Chinese Society of Pediatric Immunology
Deputy Director, Shenzhen Key Laboratory of PID Diagnosis & Therapy

Immunoglobulin (Ig) therapy is indicated as replacement treatment for patients with primary immunodeficiency (PID) characterized by absent or deficient antibody production. In 1946, Cohn developed an ethanol fractionation method to separate plasma proteins into stable fractions. In 1952, Bruton showed the effectiveness and benefit of Cohn fraction II for the treatment of agammabloulumina. This landmark case began the modern era of Ig replacement. Ig therapy has served as lifesaving treatment in PID for over six decades. Approximately 70% of PID patients require Ig replacement to maintain their health during the disease course. Ig therapy reduces significantly the incidence of pneumonia and hospital admission, preserves organ function and improves life quality. Ig therapy should be individualized in terms of preparation, dose and frequency. The decision of Ig preparation, such as form, stabilizer, sodium and osmolarity, must be matched to specific patient needs and situations. The individualization of dosage does relate to the optimization of therapy. The target dose is that protecting the patient from significant infection. Trough level monitoring is helpful but should not be misinterpreted as benchmarks for therapy. Other factors including patient’s condition, clinical course, treatment response and ongoing infection should be taken into consideration. Biologic IgG level represents the minimal serum IgG level that renders a patient as disease free as possible, which could be identified and maintained as the goal of Ig therapy. However, the current concept of Ig therapy is challenged by the findings that even the patient receives seemingly optimal treatment and shows no apparent clinical infections, silent lung airway disease progresses. Adverse reactions to Ig treatment are occasionally encountered, and classified as mild, moderate and severe. Thrombosis, anaphylaxis and hemolysis are very rare but serious complications. Use of SCIG has continued to grow in PID. In comparison to IVIG, it has similar efficacy in preventing infection, but is associated with minor local side effects and fewer systemic effects. In addition, the IgG level remains relatively consistent without the fluctuation characteristic of IVIG. According to the 2015 global network survey by Jeffrey Modell foundation, 42.9% of PID patients with an antibody deficiency received Ig replacement therapy. And the rate was even much less in Asia. Efforts are needed to improve the coverage of Ig replacement therapy in PID for the goodness of patients in Asian areas.
Subcutaneous Immunoglobulin

Dr. Theresa COLE
Paediatric Immunologist Allergist
Department of Allergy & Immunology, Royal Children’s Hospital, Melbourne, Australia
Murdoch Children’s Research Institute, Melbourne, Australia

Immunoglobulin replacement is the mainstay of treatment for primary immunodeficiency resulting in hypogammaglobulinaemia. Immunoglobulin is also used for acquired hypogammaglobulinaemia and for immunomodulation in a range of conditions. Historically, immunoglobulin has been provided via the intravenous route. However, in recent years the provision of immunoglobulin via the subcutaneous route has become more common. Subcutaneous immunoglobulin (SCIg) is safe, effective and has been demonstrated to provide patients with good quality of life. It is easy to administer and patients and their families can be taught a range of different techniques to use at home. Infusions can be provided via a range of mechanical or electronic pumps, or can be administered via a manual push. Dosing can vary from multiple times per week to once every second week (in small infants). Patients report few side effects and often tolerate large volumes of SCIg administered at one site. New developments include the development of SCIg with hyaluronic acid and the increasing use of the subcutaneous route of administration for immunomodulation, not just replacement dosing.

Management of Invasive Fungal infection in PID Patients

Dr. David Christopher LUNG
Associate Consultant,
Department of Clinical Pathology,
Tuen Mun Hospital, Hong Kong

Fungal infection can be classified according to the etiological agents or the severity of the infection. Invasive fungal infection can be caused by yeast, mould and dimorphic fungi, where the fungal agent invading into sterile site. Yeast could be found in the environment and is a normal flora of the human body. Infection usually arises from endogenous flora of the human GI tract, resulting in fungaemia and other metastatic infection, especially during the neutropenic phase with the presence of a portal of entry. However yeast can also result in subacute or chronic infection, especially during the post-neutropenic state, which usually occurs in the form of hepatosplenic infection. Mould infection is characterized by the affinity to invade into blood vessels, hence resulting in infarction and tissue necrosis, common examples include Aspergillosis and Mucormycosis. However it is uncommon to see mould causing blood stream infection, except Fusarium, which is one of the rare examples of mould that can be recovered from blood culture.

Dimorphic fungal infection depends on the geographical location. In South East Asia, the most common dimorphic fungal infection is Penicillium (Talaromyces) marneffei. This fungus is found in bamboo rats in the natural environment in South East Asia and commonly affects AIDS patients. If the infection occurs in non-AIDS patients, further investigation is warranted to look for underlying immunodeficiency state.

Management of invasive fungal infection requires the combined medical and surgical treatment, and more importantly, the reversal of the immunocompromised state.

APSID Symposium 6

- Haematopoietic Stem Cell Transplantation (HSCT) for Primary Immunodeficiencies

Hematopoietic Cell Transplantation for Primary Immunodeficiency Diseases: Current Situation and Future Direction

Prof. Tomohiro MORIO, MD., PhD.
Deputy Executive Director (Research), Tokyo Medical and Dental University, Japan

Special Adviser to the President and Dean of School of Medicine, TMDU

Professor and Chairman, Department of Pediatrics and Developmental Biology (Pediatrics), TMDU Graduate School of Medical and Dental Sciences

Director, Center for Cell Therapy and Perinatal Medicine Center, TMDU Medical Hospital

Hematopoietic cell transplantation (HCT) provides curative therapy for patients with severe form of primary immunodeficiency diseases (PIDs). Recent improvements in HCT have led to better outcome with less transplant related adverse effects. In this session, we show the results of HCT carried out in Japan for PIDs including severe combined immunodeficiency (SCID), Wiskott-Aldrich Syndrome (WAS), CD40L deficiency, Chronic granulomatous disease (CGD), X-linked lymphoproliferative disorder (XLP) type 2, Chronic mucocutaneous candidiasis (CMCD), and Hyper-IgE syndrome (HIE). 5 year overall survival (OS) for most of the disorders receiving HCT was around 70-80%. Similar OS was observed in the patients receiving cord blood transplantation. HCT for some of the PIDs, such as CMCD and activated PI3K delta syndrome was associated with poor engraftment, high rate of rejection, or both. HCT is one of the curative therapeutic measures, but still needs modification and optimization of conditioning regimen, monitoring system, and supportive therapy for the better outcome. Gene therapy is expected to provide safer treatment option with better outcome in some of the disorders.
Reduced Intensity HSCT for Chronic Granulomatous Disease

Reinhard Seger and Tayfun Güngör
Switzerland. Children’s Hospital Zürich, Switzerland

HSCT is now offered early to patients with X-CGD and severe a/r CGD with evidence of absent O2- production or one life-threatening infection/severe inflammatory disease. This lecture compares two reduced toxicity conditioning regimens (full dose treosulfan/fludarabin versus low dose/targeted busulfan/fludarabin) with balanced in vivo T-cell depletion (by serotherapy) and double immunosuppressive therapy for prophylaxis of GVHD and graft rejection/failure.

Both regimens can completely cure CGD patients of their disease, even if suffering from ongoing therapy-refractory infection or steroid-dependent granulomatous disease, provided an HLA-matched donor (sibling/family or unrelated 9-10/10 HLA compatible) can be found. Using the myelo-suppressive low busulfan regimen a 2 year probability of overall survival of 96%, an event-free survival of 90%, equivalent outcomes between matched siblings and unrelated donors and low incidence of acute/chronic GVHD are achieved. To prevent underdosing low busulfan conditioning requires real-time drug monitoring and dose adjustment. If unavailable, a fixed submyeloablative busulfan dose (e.g. 14 mg/kg iv < 10 yrs and 12 mg/kg > 12 years) or the treosulfan regimen (dosed according to age) can be used instead.

Mismatched (haploidentical) donor HSCT is still experimental. A new strategy for patients lacking a conventional donor with first promising results in CGD, the posttransplant cyclophosphamide technique, will be discussed.

Investigational Gene Analysis for Primary Immunodeficiency Diseases

Prof. Tomohiro MORIO, MD., PhD.
Deputy Executive Director (Research), Tokyo Medical and Dental University, Japan
Special Adviser to the President and Dean of School of Medicine, TMDU
Professor and Chairman, Department of Pediatrics and Developmental Biology (Pediatrics), TMDU
Graduate School of Medical and Dental Sciences
Director, Center for Cell Therapy and Perinatal Medicine Center, TMDU Medical Hospital

Whole exome sequencing (WES) is an effective tool for elucidation of genetic defects in patients with primary immunodeficiency diseases (PIDs). Diagnosis for most of PIDs is made based on typical clinical presentation and laboratory data, followed by protein expression analysis when applicable, and is finally confirmed by gene sequencing. WES has currently been used for dissecting the etiology of undiagnosed cases.

We carried out WES for 79 cases with PIDs from 2012 to 2015, and for 97 cases in 2016 and 2017 with 128 family members as a reference. Identified known genes include TRNT1 in B cell deficiency and periodic fever, TNFAIP2 in SLE, and IKZF1 in B cell deficiency. We present novel responsible genes for PIDs identified in our laboratory in this session. iPS technology and knock-in mice model have been used as an important tool to elucidate molecular pathogenesis of these disorders.

About 70% of the samples were left undiagnosed after WES; and detection of large deletion or splice anomaly with the aid of software is sometimes useful to reach a diagnosis. Regional and international collaboration is critically important to obtain complete picture of, and to find suitable treatment for, the patients with a novel gene defect.
Molecular Characterization of Severe Combined Immunodeficiency in North India

Prof. Surjit SINGH
Professor of Pediatrics and Incharge Allergy Immunology Unit, Advanced Pediatrics Centre,
Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India
Principal Investigator, ICMR Centre for Advanced Research in Primary Immunodeficiency Diseases

INTRODUCTION- Severe combined Immunodeficiency (SCID) is one of the most severe forms of primary immunodeficiency and a medical emergency. It manifests clinically in the form of severe, life-threatening infections during early infancy. Mutations in more than 30 different genes have been detected in different forms of SCID. The clinical and immunological phenotypes are quite variable and dependent on the underlying genetic defect. However, environmental factors and gene modifiers have also been implicated because different clinical and immunological phenotypes have been observed in siblings with the same genetic defect. The genetic basis of severe combined immunodeficiency also depends on the geographical location largely due to the affects of consanguinity and endogamy. Data on SCID from India is limited to case reports only. We have diagnosed 52 cases of SCID over the last 2 decades. Molecular defects were characterized in 22/52 cases.

MATERIALS AND METHODS- Mutation analysis was performed at the Department of Pediatrics and Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, Kazusa DNA Research Institute, Kisasaru, Chiba, Japan, National Defense Medical College, Saitama Japan and Duke University Medical Center, Durham, North Carolina, USA.

RESULTS- Mutations in the RAG1 and RAG2 genes were the commonest and detected in 4 patients each. One patient had a mutation in RAG1 gene on one allele and mutation on the RAG2 gene on the other allele. IL2RG mutations were detected in 6 patients. Mutations in IL7RA and ADA gene were detected in 2 patients each. Mutations were also detected in PNP, DCLRE1C and NHEJ1 genes in one patient each.

CONCLUSION: This series of 22 SCID patients with a well characterized underlying genetic defect is the largest from India. Mutations in the recombinase activating genes 1 and 2 were commonest being detected in 9 patients followed by mutation in the IL2RG gene in 6 patients. Two patients from unrelated families had similar mutation in the IL2RG gene indicating a possible founder effect.

The Challenges in Analyzing Next Generation Sequencing (NGS) Data for Molecular Diagnosis of Primary Immunodeficiency Diseases

Prof. Wan-ling YANG
Associate Professor
Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine,
The University of Hong Kong, Hong Kong

Recent advances in next-generation sequencing (NGS) technology provide a cost-effective approach to large-scale resequencing of human genome for medical diagnosis. In recent years, whole exome sequencing (WES), the targeted sequencing of protein-coding regions, has become a powerful and widely-used tool for dissecting the genetic basis of Mendelian diseases. We have performed whole exome sequencing on nearly a hundred patients with primary immunodeficiency disease (PID) and made molecular diagnosis for more than half of these patients. NGS also showed superb power by detecting the causal mutations in cases that were missed by Sanger sequencing technology. In addition, the new sequencing platform allows us to discover novel PID genes and in certain cases, the molecular diagnoses prompted us to revisit the clinical phenotypes. Thus, NGS technology has become an integral part of clinical diagnosis of Mendelian diseases, particularly PID.

However, many challenges remain. Nearly half of the patients cannot reach definitive molecular diagnosis by WES. There are likely a number of different reasons for the failure in finding the causal mutations. Certain regions of the genome are not covered well, especially for the regions with repeats and paralogous sequences. The short reads of NGS platform and the discontinuous nature of coverage of the genome make it difficult to detect structural mutations such as copy number variations, deletions and duplications, balanced translocations and inversions. Many of the causal genes may not be realized even when the mutations are detected and for known causal genes, mutations in non-coding regions, such as in the regulatory regions are poorly characterized and as a result, may not be realized as disease causal. Extreme genetic heterogeneity for PID and many other Mendelian diseases makes it difficult to draw references from different families.

Thus, improving coverage of the genome and improved analysis of NGS data, broader collaboration in studies of rare Mendelian diseases, building up of population genetic databases with population-specific genetic data from large number of samples, and functional characterization of the disease genes and regulatory elements are the needed steps to improve molecular diagnosis rate. In the meantime, targeted approach combining whole exome sequencing and sequencing of targeted whole genes might be a practical way of improving NGS success rate at the time being.
Symposia Lectures

APSID Symposium 8
- Immune Dysregulation

Hyper IgE Syndromes (HIES), Clinical Phenotypes, Molecular Characteristics and Therapeutic Options

Prof. Hans D. OCHS
Professor of Pediatrics,
Jeffrey Modell Chair of Pediatric Immunology Research,
Center for Immunity and Immunotherapies,
Seattle Children's Research Institute,
University of Washington

Several well-defined genetically determined primary immunodeficiency diseases (PID) are associated with elevated serum IgE levels. The “classic” HIES are rare PIDs inherited in autosomal dominant (AD) or autosomal recessive (AR) manner. Patients with AD-HIES often present with Staphylococcus aureus abscesses, recurrent episodes of pneumonia with pneumatocele formation, very high IgE levels, and eczema. The entity was reported in 1966 as Job syndrome, and as Hyper IgE syndrome in 1972 when elevated IgE levels and coarse facial features were noticed. Other findings include hyperextensible joints, delayed shedding of primary teeth, scoliosis and bone fractures with minimal trauma. In 2010, several groups reported that AD-HIES/Job syndrome is caused by heterozygous mutations in STAT3 which belongs to the STAT family of transcriptional regulators. The generation of both mutated nonfunctional and wild type STAT3 alleles results in decreased wild type STAT3 dimers (~25%) which affect the development of IL–17 producing TH17 effector T cells, that play a prominent role in controlling infectious agents commonly observed in HIES. However, the precise mechanisms by which heterozygous STAT3 mutations cause the multitude of pathologies characteristically seen in AD–HIES patients are only partially understood. A second form of HIES (AR-HIES) complicated by recurrent viral infections and involvement of the central nervous system but without connective tissue and bone abnormalities was recently associated with DOCK8 mutations. Other single gene defects resulting in PID with eczema, increased serum IgE, and recurrent infections include Omenn Syndrome (caused by hypomorphic mutations in RAG1/RAG2, ARTEMIS, ADA or RMRP); Wiskott-Aldrich Syndrome caused by mutations in the WAS gene; Immune Dysregulation, Polyendocrinopathy, Enteropathy, X-linked syndrome (IPEX) caused by mutations in the gene FOXP3; and Netherton syndrome caused by mutations in SPINK5. These syndromes, unlike atopic dermatitis, are caused by single gene defects and have in common abnormal cognate and innate immunity, increased susceptibility to infections, elevated IgE and therapy resistant eczema. Treatments include symptomatic measures (antibiotics, antifungals and IVIG for Job Syndrome and Netherton Syndrome; immune suppressive therapy for IPEX) and hematopoietic stem cell transplantation (Omenn Syndrome and DOCK8 deficiency).

Complement Deficiency and Susceptibility to Autoimmune Disease

Dr. Melanie WONG
Consultant
Department of Allergy and Immunology,
The Children’s Hospital at Westmead, Australia

The complement system involves a cascade of proteins that recognise, bind and facilitate the elimination of invading pathogens. Complement is important for the identification, opsonization, and proper disposal of apoptotic cells, cellular debris and immune complexes. Inability to efficiently clear apoptotic cells could result in a source of autoantigens and drive autoantibody production. In addition, delivery of complement opsonised self-antigens to autoreactive B-cells contributes to anergy and diverts them from germinal centre reactions.

Deficiencies of early complement components (C1q, C1r, C1s, C4 and to a lesser extent C2) are strongly associated with increased risk of developing SLE or a lupus-like disease. Affected individuals with autosomal recessive disease tend to present in early childhood and experience severe morbidity with significant mortality.

This talk will concentrate on C1q deficiency, which is associated with high risk of lupus-like disease and infection, disease response to replacement via plasma infusions and the potential role of haematopoietic stem cell transplantation. HSCT is a viable option because unlike most other complement components in blood, the primary site of C1q biosynthesis is not in the liver, but in myeloid cells including macrophages, monocytes, and dendritic cells.
Conventional Treatment of Infection/Inflammation in Chronic Granulomatous Disease (CGD)

Prof. Reinhard SEGER
Div Immunology /HSCT, Univ Childrens Hospital, Zürich, Switzerland

CGD is a complex immune deficiency with both infection susceptibility and dysregulated inflammation pointing to two protective NADPH oxidase functions: Inactivation of pathogens and resolution of inflammation. Balanced pharmacologic targeting of the two pathways is the basis of CGD management and has resulted in new approaches of conventional treatment.

Currently glucocorticoids are used empirically as main anti-inflammatory agents in CGD. Their cautious use is best illustrated in three conditions:

Liver abscesses are mostly due to S. aureus. The septated, pyogranulomatous lesions once required invasive surgical excision. Today surgery is best avoided and replaced by prednisone 1mg/kg/day 2-3 wks (plus antibiotic therapy).

Fulminant mulch pneumonitis by massive inhalation of Aspergillus spores results in miliary inflammatory infiltrates requiring ventilation. An iv combination of antifungals AND steroids is life-saving.

„Sterile“ granulomatous colitis mimicking Crohn’s disease is again responsive to prednisone 1 mg/kg/day 1-2 wks, slow taper.

Immunosuppressed CGD patients must be covered by antimicrobials. Ongoing molecular dissection of anti-inflammatory pathways (e.g. of PPAR gamma activation) will yield novel interventions avoiding many of the steroid side effects in the near future.

Symposium E3
- Emerging Concepts about Food Allergies

Carbohydrate Allergens – How Clinically Relevant?

Prof. Bee-wah LEE
Department of Paediatrics
Yong Loo Lin School of Medicine
National University of Singapore, Singapore.

Clinicians and academics are constantly challenged to discover ‘new’ concepts in our understanding of disease with the ultimate hope to improve diagnostics and management of disease. In the field of allergy, one example is the changing concept of carbohydrates as allergens. Carbohydrates have been considered weak allergens of little clinical significance. These cross-reactive carbohydrate determinants (CCD) result in non-specific cross reactivity between allergens leading to false positive in-vitro IgE testing. This long-accepted dictum has been challenged with more recent reports of carbohydrate allergenic epitopes resulting in anaphylactic allergic food reactions. The carbohydrate galactose-alpha-1,3-galactose (alpha-gal) which is the epitope in red meat allergy and cetuximab anaphylaxis has been well described in populations residing in the United State and Europe. Closer to home, anaphylaxis to the prebiotic, galacto-oligosaccharide, present in infant and maternal milk formula has been described in the South East Asian population and Japan. This latter allergy is peculiar in that the allergen is a pure carbohydrate. The distinct geographical distribution of these allergens points to a primary sensitizer that is unique to the region. These recent observations parallel the rising trend in food allergies. It is possible that the environmental influences that are responsible for our diminishing gut tolerance and increasing prevalence of food allergy, is also responsible for recent recognition of allergic reactions to carbohydrates. If so, this may signal our propensity to develop new environmental allergies.

Cow’s Milk Allergy

Prof. Suwat BENJAPONPITAK, M.D.
Clinical Professor of Pediatrics (Allergy/Immunology)
Vice President for Education, Mahidol University, Thailand
Board of Directors, World Allergy Organization (WAO)

Cow’s milk allergy is increasing to be the leading cause of food allergy in infants and young children. The recent understanding of its pathophysiology and immunological response including both IgE-mediated and T cell-mediated reactions. The clinical spectrums are varies from IgE-mediated hypersensitivity to intermediate and late-onset
reactions, including urticaria, angioedema, atopic dermatitis, gastro-oesophageal reflux, infantile proctocolitis, food-protein induced enterocolitis, and constipation. The diagnostic approach to cow’s milk allergy shows variations among different experts. double-blind, placebo controlled food challenge, the gold standard diagnostic test for cow’s milk allergy, is increasingly being replaced by the measurement of food-specific IgE antibodies, and/or combination with skin-prick testing. The treatment of cow’s milk allergy relies on allergen avoidance and hypoallergenic formulae, or maternal elimination diets in breast-fed infants. The challenges for therapy and prevention of cow’s milk allergy are common interested among scientific communities.

Fish and Shellfish Allergies

Dr. Agnes Sze-yin LEUNG
Clinical Lecturer
Department of Paediatrics, Prince of Wales Hospital The Chinese University of Hong Kong, Hong Kong

Fish and shellfish are considered one of the commonest food allergens, much more so in the past 50 years as the supply of seafood nearly doubled, outpacing population growth. As seafood consumption continues to increase, the adverse allergic reactions to seafood intake have become an eminent global health issue. This specifically concerns Asia, as China accounts for two-thirds of the world aquaculture production of fish, crustaceans and molluscs. In addition, fish is often introduced early as weaning food and that shellfish is easily encountered in this part of the world.

Parvalbumin and tropomyosin have long been identified as the major fish and shellfish allergen respectively, and extensive efforts have been directed to characterize the allergenic properties of these two allergens in different species. A number of novel seafood allergens have also been discovered in recent decade. Here we will discuss the current understanding of the molecular characteristics of seafood allergens, such as the molecular identity, cross-reactivity, and the methods of detection of seafood allergens. It is generally believed that management of seafood allergies relies on strict intake avoidance with no preventive or curative treatment available, but recently allergen-specific immunotherapies are being developed and are potentially disease-modifying.

Symposium F3
- Management and Prevention of Allergic Diseases

Do Asian Children Have Less Peanut Allergy?

Dr. Marco Hok-kung HO
Consultant in Paediatrics, Queen Mary Hospital
Clinical Associate Professor, Department of Paediatrics & Adolescent Medicine, The University of Hong Kong
Service Director (Quality and Safety), HKWC, Hospital Authority
Deputy Hospital Chief Executive (III), Queen Mary Hospital
Vice-President, The Hong Kong Society for Paediatric Immunology Allergy & Infectious Diseases
Founder & Immediate Past Chairman, Allergy Hong Kong
Honorary Advisor, Hong Kong Asthma Society
President-elect, Hong Kong Institute of Allergy

Some of us, allergists in Asian at times aren’t very impressed why peanut allergy draws so much attention and is regarded as the prototype of food allergy in Western countries. Population prevalence studies conducted in highly developed Asian cosmopolitan cities showed the peanut allergy is perhaps ~0.1-0.3% which is almost 10-fold less than many English-speaking nations [1-4]. The mortality due to peanut allergy is almost unheard to me in last 15 years allergy practice in Hong Kong. While the world allergy community is celebrating the breakthrough in high risk infant prevention by the game-changer studies: Learning Early About Peanut Allergy (LEAP) and LEAP-ON [5-7] and shifting the pendulum from delayed to early introduction of allergenic food at 4-11 month of age, as stipulated in international infant feeding guidelines. Amidst all the entusiasms, the latest Growing Up in Singapore Towards Healthy Outcomes (GUSTO) study found all food allergy rates including PA in Singapore are low despite delayed introduction of allergenic foods [4]. That raised a salient counter argument that early introduction of allergenic foods may not be the “gold standard” or even necessary in populations in which overall food allergy prevalence is low. Therefore, infant feeding recommendations should be carefully tailored to Asian populations.

Intriguingly, Asian infants born in Australia are three times more likely to develop nut allergy than non-Asian infants, and rates of challenge-proven food allergy in infants have been found to be unexpectedly high in metropolitan Melbourne. Such high peanut allergy prevalence among infants of Asian-born parents appears to have occurred in a single generation and was not present among infants with parents migrating from other countries, suggesting gene-environment interactions are important [8-9]. What are the protective factors of Asian children? Why migrant children have lost such protection? Would a reverse migration from West to East regain the protection? These are interesting research questions to be elucidated.
If you ask me again, do Asian children have less peanut allergy? My answer is perhaps yes and no. It depends...

References
1. Leung TF et al, PAI 2009
2. Shek LP et al, JACI 2010
3. Ho MH et al, APJACI 2012
4. Tham EH et al, JACI 2017
5. Du Toit G et al, JACI 2013
8. Koplin JJ et al, Allergy 2014

Early Introduction of Allergenic Foods for the Prevention of Food Allergy –The Asian Perspective

Prof. Bee-wah LEE
Department of Paediatrics,
Yong Loo Lin School of Medicine
National University of Singapore, Singapore.

There is now emerging evidence for the early introduction of allergenic foods, such as peanut and egg, in the prevention of food allergies in at risk infants. This has led to recent publication of guidelines in the US and Europe recommending early peanut introduction for high-risk infants with severe eczema or egg allergy. Peanut allergy is, however, much less prevalent in Asia compared to the West. Varying patterns of food allergy are seen even within Asian countries - such as a predominance of wheat allergy in Japan and Thailand and shellfish allergy in Singapore and the Philippines. Whether the same benefit can be derived from early introduction of other allergenic food such as cow’s milk, shellfish and wheat are still uncertain. Customs and traditions, such as diet and infant feeding practices, also differ between adapting guidelines on early allergenic food introduction to the Asian setting. It is therefore debatable whether rationale guidelines can be formulated for the timely introduction of allergenic food in high-risk infants in Asia.

Improved Allergy Diagnosis and Treatment Using Novel Technological Platforms

Prof. Ting-fan LEUNG
Department of Paediatrics, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong

The pathogenesis of allergic diseases involves complex interplay between genetic predisposition and a wide array of environmental factors such as microbial encounter, dietary intakes, tobacco smoke and pollutant exposure and psychosocial factors. Traditional labour-intensive but low throughput methods have limited capacity to generate the vast amount of laboratory data that are required to decipher such gene-environmental interactions. For example, culture-based studies failed to identify up to 80% of bacterial flora when compared with molecular approaches. The advent of powerful next generation sequencing (NGS) greatly facilitates the omics approach by identifying genomic, metagenomic, epigenomic and transcriptomic signatures of various allergic diseases. Our studies reported substantial differences in the epidemiology of asthma genes and loci between Chinese and Caucasians. Microbial characterisation at different body sites also enhanced our understanding of immunomodulatory roles of microbiota. Supported by improvements in sequencing technology and analytical support, recent NGS studies revealed the microbiota at body sites such as skin, airway and gut. The detection of cutaneous microbes in an ongoing birth cohort provided evidence that microbial compositions soon after birth modulated the risk for eczema development. This approach also confirmed the findings between atopic eczema and Staphylococcus aureus colonisation as well as between eczema flare and reduced skin microbiota diversity from cross-sectional studies. For children with asthma or recurrent wheeze, metagenomics analyses of their nasopharyngeal secretions revealed lower microbiota diversity and some suggestive microbial signatures. Very recently, dual RNA sequencing approach yielded exciting data on both transcriptomic (host) and metatranscriptomic (microbiota) sequences from the airway epithelium. Such sequencing data helped to unravel the human genes differentially expressed in asthmatics that regulated immune and inflammatory responses, the spectrum and functions of microbial genes that were related to asthma, and the interactions between microbiome and host upstream regulators that could explain patients’ clinical manifestations. In conclusion, the development of novel technological platforms such as NGS opens a new horizon for deciphering the complex pathogenetic processes of allergic diseases. Such information will ultimately improve the precision of our diagnosis and treatment for these allergy sufferers.
Congenital heart disease (CHD) is the most common congenital abnormality in children. The incidence of CHD is 8-10 every 1000 live birth. With total population of 254.9 million and birth rate of 2.3%, it is estimated 50,000 babies born with CHD in Indonesia. Early detection and education to parents are equally important. Management of CHD consists of medical treatment, interventional cardiology and surgery. Before the development of interventional cardiology, all patient with CHD underwent cardiac surgery. The advantages of interventional cardiology are shorter duration of hospital stay, avoiding the use of cardiopulmonary bypass machine, thoracotomy procedure, long post-operative care on ICU and chest scar. Currently, interventional cardiology is a treatment of choice in management of certain CHD. Procedures that can be delivered by interventional treatment of CHD consists of: 1) defect closure, 2) dilatation of stenotic valve or blood vessel, 3) occlusion of unwanted collateral or fistulae, 4) radiofrequency perforation and dilatation of atretic valve, 5) valve implantation, and 6) and palliative treatment such as balloon atrial septostomy (BAS) and PDA stenting.

**Keywords:** Interventional cardiology, cardiac surgery, congenital heart disease, state of the art.

### Long-term Arterial Sequelae of Kawasaki Disease

Prof. Yiu-fai CHEUNG, MD

**Bryan Lin Professor in Paediatric Cardiology, Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong.**

Kawasaki disease (KD) remains to be the most common acquired paediatric cardiovascular disease in developed countries. It is five decades since its first description and reports of ischaemic heart disease in young adults with a history of KD are accumulating. While the sequelae of arterial inflammation in the acute phase of the illness are well documented, the long-term effects of KD on coronary and systemic arterial function are just emerging. Structural damage during the acute illness with development of persistent giant coronary arterial aneurysms no doubt constitutes the most significant morbidity and mortality after KD. Functional alterations of the coronary and systemic arteries beyond the sites of aneurysmal dilatation as characterized by endothelial dysfunction, arterial stiffening, active arterial remodeling, and persistent low grade inflammation years after the acute illness have been demonstrated. Coupled with the late structural change of thickened arterial intima-media thickness, these findings have generated concerns regarding predisposition to premature atherosclerosis. There is further evidence to suggest genetic influence on the development of long-term arterial sequelae. Detailed assessment of arterial sequelae in the long-term has significant implications on risk stratification, approach to longitudinal monitoring of cardiovascular complications, medical management including transitional care, and patient education and counselling.

### Genetic Profile of Inherited Arrhythmias in Hong Kong Children

Dr. Tak-cheung YUNG

**Consultant Paediatric Cardiologist & Electrophysiologist, Chief of Service, Department of Paediatric Cardiology, Queen Mary Hospital Division of Paediatric Cardiology, Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong**

Long QT syndrome, short QT syndrome, Brugada syndrome, catecholerminergic polymorphic ventricular tachycardia are now increasingly recognized in paediatric age group. They are arrhythmic problems with clear genetic causes due to mutations of a single gene. On the whole, they are uncommon but very important causes of sudden cardiac death. Patients with these clinical diagnoses should have investigation of the genetic profile. The genetic diagnosis can confirm the clinical suspicion. When the index case is confirmed, predictive testing for relatives will be able to identify other mutation carriers within the family. With medical treatment and preventive measures, symptoms and sudden death in the at-risk relatives may be prevented. Within each genetic arrhythmia syndrome there are numerous subtypes according to the genetic mutation. The risk of sudden death of each subtype is related to the specific gene, as well as to the mutation type and location. Genetic diagnosis also facilitates cardiologists to determine the best treatment option for patients with inherited arrhythmias. For example, clinical studies have demonstrated that different beta-blockers have different efficacy in reducing symptoms in each long QT syndrome subtypes.

In this presentation, the development of genetic testing and genetic profile of inherited arrhythmias in Hong Kong children will be discussed.
Assessing Naevi in Children Using a Useful Dermoscopic Classification

Dr. Maria GONZALEZ
Consultant Dermatologist at the Royal Gwent Hospital, Wales
Private Practice, Specialist in Dermatology, United Kingdom

Dermoscopy has clear and unarguable relevance in the diagnosis of malignant melanoma in adult patients. However, in the UK there is increasing anxiety among parents for even young children to be assessed to rule out the possibility of malignant melanoma. In caucasian groups children often present with multiple congenital naevi which can be a cause of significant concern among anxious parents. Dermoscopy offers a unique opportunity to classify these lesions enhancing diagnostic certainty without resorting to excision biopsies. This discussion provides an overview of a useful dermoscopic classification of naevi with an emphasis on those commonly seen in children.

Complementary and Alternative Medicine for Childhood Eczema and Atopic Diseases: Friend or Foe?

Prof. Ellis Kam Lun HON
Professor, Department of Paediatrics
Faculty of Medicine,
The Chinese University of Hong Kong

Atopic eczema (AE) is one of the most common chronic relapsing childhood illnesses. According to the theory of atopic march, young children with atopic eczema may subsequently develop airway allergies such as asthma or allergic rhinitis (AR). AR and asthma are significantly more prevalent in patients with atopic eczema. Physicians, patients and their families often do not appreciate the significance of these comorbid diseases. AE is a distressing disease that is typically associated with pruritus, sleep disturbance and a reduced quality of life. Its clinical course is often complicated and difficult to manage. It is crucial to perform a detailed diagnostic evaluation on important history and physical features, as well as to review trigger factors. Taking into account quality of life outcomes, a patient-centric integrative approach to diagnosis and management should be adopted.

Despite advances in many aspects of the management of atopic eczema, there is as yet no cure for the disease. Emollients and topical corticosteroids remain the mainstay of therapy for maintenance and acute exacerbations, respectively. However, the treatment of AE is suboptimal due to the psychology of parents regarding steroid therapy, as well as skepticism regarding conventional western medicine.

These fears are compounded by the misplaced belief that complementary and alternative medicines (CAM) are not associated with any adverse effects. Of particular concern is the practice of prescribing corticosteroids in the name of CAM. Consequently, many steroid-phobic parents may, in fact, be unknowingly using potent over-the-counter corticosteroids. It is also important to evaluate whether patients are genuinely ‘allergic’ to certain foods. Management of AE is suboptimal if children with food allergy and severe disease continue to consume the culprit food in the name of CAM. Conversely, avoidance of common foods in children without food allergy could result in food faddism or malnutrition.

There is no substitute for a good rapport between physicians and their patients and families to ensure optimal management. The first step in patient care is to accurately assess the patient and his or her family, and to evaluate the possible concerns, anxiety and phobia that could impede therapeutic efficacy.

The Use of Dermoscopy in Daily Paediatric Practice

Dr. David Chi-kong LUK
Specialist in Paediatrics, Associate Consultant
Department of Paediatrics and Adolescent Medicine
United Christian Hospital

Dermoscopy is a simple handheld medical device with an established role in the examination of skin lesions. It is a standard clinical examination technique to differentiate malignant from benign skin lesions. In children, it has been found to be very useful in diagnosing common paediatric skin lesions including various birthmarks, nevus, wart, molluscum contagiosum, alopecia, etc. It has many advantages as a bedside clinical examination tool and the reduction of the need for skin biopsy being particular helpful. Routine use of dermoscopy in managing paediatric skin problems is now recommended.

In this lecture, the current clinical use of dermoscopy in daily paediatric practice will be discussed.
The Prevalence of Vitamin D Deficiency and its Relationship of Bone Health and Glucose Metabolism in Korean Children and Adolescents

Prof. Sei Won YANG, MD, PhD

Professor, Division of Pediatric Endocrinology & Metabolism
Department of Pediatrics, Seoul National University Children’s Hospital (College of Medicine), Korea
President, Korean Pediatric Society

There has been great interest in the role of vitamin D on multiple health outcomes. Vitamin D has been traditionally known as essential for skeletal health, but there has been increasing evidence linking vitamin D deficiency with non-skeletal health outcomes, such as metabolic syndrome and cardiovascular disease.

In 2011, The Endocrine Society published “evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline”. The Society recommended screening for vitamin D deficiency in individuals at risk for deficiency and did not recommend population screening for vitamin D deficiency in individuals who were not at risk. They recommended using the serum circulating 25-hydroxycholecalciferol [25(OH)D] level, measured by a reliable assay, to evaluate vitamin D status in patients who were at risk for vitamin D deficiency. They defined the level of 25(OH)D below 20 ng/ml as vitamin D deficiency and a level of 25(OH)D of 21-29 ng/ml as insufficiency. The Society suggested that daily reference intakes (DRIs) for infants and children aged 0-1 yr were at least 400 IU/d of vitamin D and for children 1 yr and older were at least 600 IU/d to maximize bone healthy. They also suggested that whether 400 and 600 IU/d for children aged 0-1 yr and 1-18 yr, respectively, were enough to provide all the potential nonskeletal health benefits associated with vitamin D to maximize bone health and muscle function was not known. However, they recommended at least 1000 IU/d of vitamin D to raise the blood level of 25(OH)D consistently above 30 ng/ml.

However, the DRI for vitamin D for Korean children was reduced from 400 IU/day in 2005 to 200 IU/day in 2010 by the Korean Nutrition Society, based on little evidence about the role of vitamin D on health outcomes in Korean children and adolescents and the assumption that exposure to sunlight guarantees adequate vitamin D status in childhood and adolescence.

Despite growing evidence that hypovitaminosis D is prevalent among healthy children worldwide, little is known about the prevalence of vitamin D deficiency in Korean children and adolescents. In addition, there has been a paucity of data on the importance of vitamin D status for health outcomes as well as on the predictors for vitamin D deficiency in Korean children and adolescents. Thus, we analyzed the prevalence and predictors of vitamin D deficiency and its relationship with bone and glucose metabolism.

Based on the Korea National Health and Nutrition Examination Survey (KNHNES) 2008–2009, the prevalence of vitamin D deficiency was 89.4% in spring, 57.8% in summer, 64.4% in fall and 92.2% in winter among 1,510 healthy adolescents (mean age 14.7 ± 1.9 years, 806 males). Winter, older age, female, obesity, a lack of vitamin D supplementation and lower milk intake (<200 ml/day) were unadjusted predictors (all P<0.05) for vitamin D deficiency.

We also evaluated the risk factors for low 25(OH)D status and its relationship with bone health in prepubertal and early pubertal nonobese children living in Seoul or Gyeonggi Province. One hundred nonobese children (mean age 9.3 years, 71 prepubertal, 45 boys) participated in the winter (n = 38) and summer. Twenty-nine percent of children (47.4% in winter, 17.7% in summer) were vitamin D deficient [25(OH)D level of <20 ng/mL]. In winter, low vitamin D intake (P = 0.019) and fewer sunlight exposure (P = 0.015) were associated with low 25(OH)D levels. Simultaneously, Body composition and bone mineral density were measured by dual-energy X-ray absorptiometry (DXA). The 25(OH)D levels were positively correlated with bone mineral content (BMC), total body bone mineral density (BMD), and lumbar spine BMD (all p< 0.05), independently of sex, puberty, fat mass, lean mass, physical activity, and calcium intake. Fat mass was independently correlated with BMC, lumbar spine BMD (P < 0.001 for both), and total body BMD (P = 0.037). Adequate vitamin D status and adiposity contributed to good bone health in nonobese children.

We also examined the association between vitamin D status and the markers of insulin resistance (IR) and the prevalence of impaired fasting glucose (IFG) in Korean adolescents aged 10-19 years. Serum 25(OH)D levels were temporarily stratified into the three categories; lowest (<15 ng/mL), 15 to <20, and ≥ 20 ng/mL (highest group). Insulin resistance was estimated by homeostatic model assessment for IR (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI). Z-scores for total body fat (g), % body fat, and body fat mass index measured by DXA were used to adjust adiposity in multivariate analysis. After adjusting the age, sex, physical activity, and adiposity, the risk of IFG and IR indices were inversely related to the levels of 25(OH)D.

These Korean results suggest that vitamin D deficiency was highly prevalent in Korean adolescents. Almost half of prepubertal nonobese children were vitamin D deficient in winter. In winter season, older age, lower milk and vitamin D intake, and fewer sunlight exposure were risk factors for vitamin D deficiency. At the same time, Vitamin D deficiency is associated with low bone density and a disorder of glucose metabolism in Korean children and adolescents,
Gastroenterology and Hepatology

Symposium C3

Screening of Biliary Atresia for Early Management

Prof. Mei-Hwei CHANG, M.D.
Distinguished Chair Professor,
Department of Pediatrics,
College of Medicine,
National Taiwan University, Taipei, Taiwan

Biliary atresia (BA) is a progressive cholangiopathy starting from fetal or neonatal period, which may lead to rapid liver cirrhosis and liver failure. BA is the most common cause of liver related death and transplantation in children.

The incidences of BA in Taiwan (1.5-2.0/10,000 live birth) and French Polynesia (3.2/10,000) were higher than other part of the world, such as Japan, Australia, Europe or U.S.A.

Hepatic porto-enterostomy (Kasai operation) should be conducted as early as possible to improve the long term outcome of infants with BA. Prolonged neonatal jaundice can be caused by BA or non BA causes (such as unconjugated hyperbilirubinemia or intrahepatic cholestasis). Therefore BA neonates are easily overlooked, leading to delayed diagnosis and treatment. This phenomenon occurred often because breast milk jaundice is much more frequently found than BA.

Screening for BA in infants is mandatory to enhance earlier diagnosis and intervention, which could save children’s life.

There are several screening methods for BA, such as blood conjugated bilirubin, bile acids, urine sulfated bile acid, fecal conjugated bile acids, and stool color card.

The concept of screening newborns for BA using a stool color card was initiated in Japan by Professor Akira Matsui in the early 1990s. With high incidence of BA, Taiwan established the world first universal stool color card screening program for BA since 2004. The rate of Kasai operation <60 days of age increased from 47% in the era before stool color card screening program to 60-74% after the program. The 5-year jaundice free native liver survival rate also increased from 27% before the program to 64% after the program. With the improvement of the rate of earlier Kasai operation and survival rate, still there are needs of further efforts to improve the rate of earlier Kasai operation and outcome of biliary atresia. We investigated the causes of delayed Kasai operation and found that continuous education of the caretakers and medical personnel are both very important.
In conclusion, screening to early detect BA is needed for early management and better outcome. Stool color card screening program is a simple, safe, low cost, non-invasive, applicable and effective screening method for BA.

Towards Eradication of Hepatitis B Infection: What More Can We Do?

Dr. Rosanna Ming-sum WONG
Consultant, Department of Paediatrics and Adolescent Medicine, Queen Mary Hospital
Clinical Associate Professor, Department of Paediatrics and Adolescent Medicine, The University of Hong Kong

Following the universal vaccination program to all newborns since 1988, the incidence of hepatitis B infection has fallen drastically in Hong Kong. Nevertheless, there is chance of immunoprophylaxis failure of infants born to hepatitis B carrier mothers and vertical transmission remains the most important mode of transmission to account for new cases. We have found from a recent multi-centre study that the immunoprophylaxis failure occurred in 1.1% of infants born to mothers with positive HBsAg status. Positive HBeAg and HBV DNA > 8log10 copies/ml at 28-30 weeks were found to be significant predictive factors. Thus, in order to further reduce the vertical transmission of Hepatitis B, pregnant women with positive HBeAg and high HBV DNA load should be identified. Treatment of these women with anti-viral drug can potentially eradicate vertical transmission as shown by a randomized controlled trial using tenofovir 300mg daily starting from the third trimester. It is also important that infants born to HBsAg positive mothers should have post-vaccination serologic testing at 9 to 12 months of age or 1 to 2 months after completion of the vaccination. Infants who remain HBsAg negative and anti-HBs negative should receive extra three doses of Hepatitis B vaccine. Those with positive HBsAg due to immunoprophylaxis failure should be evaluated for chronic liver disease and treated according to protocol. Apart from infants born to carrier mothers, there are special consideration and recommendations on vaccination for other high-risk group such as premature infants and immunocompromised children.

Symposium G1
- Diarrhoeal Diseases

Burden and Management of Persistent Diarrhea in Low and Middle Income Countries

Prof. Tahmeed AHMED
Senior Director, Nutrition & Clinical Services
Division, International Centre for Diarrhoeal Disease Research,
Bangladesh (icddr,b)
Professor, Public Health Nutrition, James P. Grant School of Public Health, BRAC University, Dhaka

The scaling up of oral rehydration salt solution has dramatically reduced mortality due to diarrhea. Yet diarrhea is still one of the most common causes of child death. Most of the episodes of diarrhea are acute and last less than 7 days. When the duration of diarrhea extends to 14 days or more, it is termed as persistent diarrhea (PD). PD is responsible for 32-62% diarrhea associated deaths of young children in low and middle-income countries. It is predominantly a disease of infancy, with 90% of affected children being less than 1 year old. Certain factors predispose to PD; these include young age, malnutrition which is characterized by mucosal injury and delayed repair of mucosal damage, lack of breastfeeding, infection, poor immunity, and inappropriate use of antibiotics. The multi-country study, MAL-ED, showed that the incidence of PD is 4.9% in the first year of life and the pathogens associated with the disease include Enterotoxigenic E. coli (both stable and labile toxin producing), Cryptosporidium species, Astrovirus and Shigella species. The incidence is reduced with age and is 1.8% in the second year with Astrovirus and Shigella species being associated with PD.

In 2012-13 at the icddr,b Dhaka Hospital, 551 children were treated for PD among 8,638 admitted children (6.4%). One-third of these children had severe acute malnutrition, 10% were never breastfed, and major stool pathogens were Campylobacter, Salmonella and Shigella species. 50% of patients came with severe PD, characterized by the presence of signs of some (46.5%) or severe (3.5%) dehydration. 23% of children developed PD after admission to the hospital for treatment of acute diarrhea. Case fatality rate was low at 2%.

A child with PD should be treated in a hospital if there is a serious systemic infection, signs of dehydration of the age is less than 4 months. Dietary manipulation usually aiming to reduce the lactose load is the key to successful management in a developing country context. Diets should be given with an energy density of ~1 kcal/g. Energy and protein intakes should be ~100 kcal/kg and 2-3 g/kg per day respectively. Children should be supplemented with zinc, folic acid, magnesium, potassium etc.

Proper diagnosis and treatment is warranted for quick recovery and preventing deaths. Higher cost of treatment and high case fatality rate reiterate PD as an important public health problem.
Inflammatory bowel disease (IBD) is a heterogeneous group of conditions, comprising of Crohn's disease (CD), ulcerative colitis (UC), and indeterminate colitis (IBD-U). The pathogenesis of IBD is multifactorial. IBD develops in genetically susceptible hosts with altered intestinal response to external stimuli as a result of intestinal dysbiosis. There is a worldwide increase in the incidence of IBD. The incidence of IBD in Asian children is increasing as well, although it is still much rarer as compared to the Caucasian population. The prevalence of IBD is not homogeneous in Asia. It is more common in Indian subcontinent and less prevalent in East Asians. Most studies on childhood IBD in Asia focused on clinical features and descriptive epidemiology. There are no population-based studies in Asia outside Japan or Taiwan. In addition, many aspects of children IBD in Asian children, including genetics, natural history, extra-intestinal manifestations, and intestinal dysbiosis are well not well described. Because of its relative rarity in Asia, many paediatricians and gastroenterologists are not familiar with childhood IBD. This often lead to delayed diagnosis and management. Differentiating CD from intestinal tuberculosis may be challenging, particularly in region where tuberculosis is prevalent. Many management algorithm on the management of childhood IBD have been published. Most are from Western Europe and North America where health resources are more abundant. There are urgent needs to have management algorithm from this part of the world where health care resources are more limited.

Paediatric Inflammatory Bowel Disease: Hong Kong Experiences

Dr. Chung-mo CHOW

President, The Hong Kong Society of Paediatric Gastroenterology, Hepatology and Nutrition

Honorary Clinical Associate Professor, Department of Paediatrics, The Chinese University of Hong Kong

The worldwide incidence of inflammatory bowel diseases (IBD) had been rising over the past few decades, as shown by epidemiological studies from Western developed countries and Asia-Pacific region. However, there is lacking paediatric data in Hong Kong. In this presentation, we would review the data of paediatric inflammatory bowel disease of Hong Kong. And some of the local data will be shared.

General and Community Paediatrics

Symposium A3

- Policy, Public Health and Development

Impact of Environment on Child Health

Dr. Patrick IP

Clinical Associate Professor

Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong

Early life experience is built into our body and significant adversities in a child’s growing environment become the roots of impairments in health, learning and behavior. Long term scientific studies showed that the yield of capital investment in human life drops exponentially as age increases while early childhood is the most rewarding period worth investing. Hence it is most logical to invest more resources into early human life to promote child health and development.

In the first ever Child Health Survey conducted in 2006 on more than 7000 children aged less than 14, we found the key role of parenting and family influence on child development. Almost 30% of children living in poverty and suffering from inequality in health, development and early education opportunity. Hong Kong children of low income families are less likely to receive preschool education but more likely to have poor physical and mental health problems, while their parents tend to have fair parenting coping skills. In another population study commissioned by Central Policy Unit, we found alarmingly increase in child maltreatment cases in Hong Kong and seasonal clustering of abuse as a result of parental stress facing school examinations. All these findings suggested the importance of environmental influence including parenting on children’s development and well being.

More recent studies using Chinese Early Development Instrument found significant gradient relationship between school readiness of preschool children and the family socioeconomic backgrounds of Hong Kong children. A significant proportion of the gradients could be accounted by mediators from both family processes involving parenting (e.g. parent-child interactive activities, use of digital devices) and kindergarten resources (e.g. teacher education level, education relevance and working experience). Optimal sleep and proper use of digital devices were also found to be important predictors of children’s development and behavior.

Given the importance of these scientific findings, policy-makers and stakeholders should pay more attention to evidence-based practice in parenting and promoting early childhood development. Key facilitators and barriers need to be identified in order to design effective intervention
programs at both population and individual level. There is an urgent need of integrating the existing education, health and child care services in order to provide an optimal platform and a more stimulating environment for our children to develop. Building a solid foundation for children in the early years provides the best chance for children to have optimal health and educational success, and impacts on children right and development throughout the course of their lives.

**Child and Family Polyvictimization in China - Asian Perspective in Violence Prevention**

**Prof. Edward CHAN, Ph.D.**

Professor

*Department of Applied Social Sciences The Hong Kong Polytechnic University*

Prof. Chan is the first to develop and apply the concept of family polyvictimization in his research studies. When studying the co-occurring victimization within a family, current literature often focuses on individual violence and fails to cover three forms of violence or more in a family. Prof. Chan’s studies fill the research gap by using families, instead of individuals, as units and investigating the prevalence and patterns of family polyvictimization.

Recently in 2015, he, as the sole author, published an article in which this insightful concept first appeared in the field. His development of the concept of family polyvictimization has brought to him integrative perspective of understanding family as a whole, providing irreplaceable implications for future research and practice. In the presentation, he will review the most up-to-date studies on child and family polyvictimization.

While addressing violence in family context and his research on culture-specific interventions, Prof. Chan started exploring the use of informal social control (including bystanders in informal network such as grandparents, relatives and neighbours) for the prevention of family violence. He, together with his research team, has made use of international and local grants to develop intervention programmes using the Asian perspective, and published impactful articles on this theme. The development of the unique perspective of Asian has led to an approach that allows one to see family as a whole, and to utilize the powerful informal social network to help Asian families build safety support nets for the violence victims.

**Internet Addiction and Digital Device Use**

**Dr. Thomas Wai-hung CHUNG**

*Consultant Community Medicine*

*Student Health Service*

*Department of Health Hong Kong*

The rapidly developed Internet and related mobile technology allows us to accomplish different tasks anytime, anywhere. We are spending longer time online and the age of start using Internet is becoming younger. The resulting problems like parenting difficulties, excessive online gaming, lacking of real life communication warrant our concerns. Relevant government departments, non-governmental organisations and other institutions in Hong Kong have made efforts to create a supportive environment for healthy use of Internet and to tackle the health problems relating to its use.

In 2013, the Department of Health convened The Advisory Group on Health Effects of Use of Internet and Electronic Screen Products which issued a report in 2014 providing recommendations on different areas of health impacts and health tips on using Internet and related products. The general principles “SAFE ACTS” to help parents and teachers to guide the kids has been recommended:

1. Show children the right attitude
2. Aware of the benefits and risks
3. Facilitate a balanced life
4. Empower children to face challenges
5. Agree with children on the rules of use
6. Communicate openly
7. Trust and respect children
8. Seek help when needed

The World Health Organization held three meetings from 2014 to 2016 in response to global concerns about the impact of a range of Internet-based activities with focus on public health implications of excessive use of the Internet, smartphones and similar electronic devices; clinical descriptions, diagnostic guidelines and priorities for international research on the related disorders as well as policy and program responses. The main tasks in the coming future will include information sharing and cross-cultural collaboration; clarification of the public health impact of gaming disorder and other disorders associated with excessive use of the Internet and electronic devices; more research, including effectiveness of prevention programs, randomised control trials of treatment interventions and longitudinal studies exploring impact of excessive Internet use on psychosocial development and last but not least, to improve education, training and awareness of issues related to excessive gaming amongst educators, clinicians and general public.

More information is available at the designated website on Healthy Use of Internet & Electronic Screen Products. The relevant link and QR Code access are as follows:

*http://www.studenthealth.gov.hk/english/internet/health_effects.html*
**Childhood Obesity, School Environment, and Socioeconomic Status**

**Mr. Frederick Ka-wing HO**  
*Department of Paediatrics and Adolescent Medicine, The University of Hong Kong*

**Introduction:** Childhood obesity is a global public health threat and behavioural interventions have been relatively ineffective. A socio-ecological model has been proposed to tackle the issue using a holistic multilevel approach. This study aims to investigate the association between childhood obesity, school physical activity environment, and socioeconomic status (SES) in Hong Kong.

**Methods:** Two cross-sectional studies were conducted. The first one was a population-based school survey measuring students’ body height, weight, and blood pressure in schools. Family SES was reported by parents; neighbourhood SES retrieved from census. The second was a multi-level data linkage study. Students’ body height and weight were retrieved from Student Health Service database and school surveys were conducted to assess school physical activity environment.

**Results:** 14842 children (age 6–19 years) included in the first study. Children whose mother only completed secondary school or below had higher risk of childhood obesity (RR 1.41, 95% CI 1.13–1.76, p=0.003) and hypertension (1.18, 1.01–1.36, p=0.03). Meanwhile, children in the lowest neighbourhood SES group had higher risk of childhood underweight (1.61, 1.04–2.49, p=0.03), overweight (1.35, 1.05–1.72, p=0.02), and obesity (2.07, 1.11–3.88, p=0.02). The second study included 208,280 students (6–18 years) from 438 schools (45% of Hong Kong). A reduced obesity risk was associated with higher teachers’ perceived PA benefits (0.96, 0.94–0.99, P=0.02), PA teaching experience (0.93, 0.91–0.96, P=0.001), school campus size (0.93, 0.87–0.99, P=0.02), PA ethos (0.91, 0.88–0.94, P<0.001), number of PA programmes (0.93, 0.90–0.96, P<0.001), and PA facilities (0.87, 0.84–0.90, P<0.001). Students in schools with at least three PA-friendly environmental factors (11.7%) had a much lower risk of obesity (0.68, 0.62–0.75, P<0.001) than those without (23.7%).

**Conclusions:** Childhood obesity was found to be associated with various school, family, and neighbourhood factors. Future intervention studies on obesity should consider a multi-component intervention for optimal effectiveness.

---

**Symposium B4**  
- Community Paediatrics

**Children’s Right and Child Health Policy**

**Dr. Chun-bong CHOW, BBS, JP**  
*Hon. Clinical Professor, Department of Paediatrics and Adolescent Medicine, The University of Hong Kong  
Honorary Consultant, Hospital Authority Infectious Disease Centre and Paediatrics & Adolescent Medicine, Princess Margaret Hospital  
Consultant Paediatrician, University of Hong Kong  
– ShenZhen Hospital*

Why children, Why investing in children – because they are our future and investing in children means investing in society and is most cost-effective

While children constituted around 20% of our population, they are 100% our future. But while our future is our children, our children’s future is the present. Children’s health is mediated by a complex and dynamic social, economic and physical environment that affects every aspect of a child’s wellbeing. Hence children have multidimensional needs across the areas of social protection, health, nutrition, and education. Recent science has clearly demonstrated children are most vulnerable to adverse events and environmental influences which have persistent lifelong impact on their health, and their gaining the full potential. This highlights the importance of investing in children within a developmental ecological framework.

Why right-based approach? – place health and wellbeing of individuals at centre of programme policy design and recognize importance of equality, means no one will be left behind

Children have no choice over their birth nor their parents hence growing up environment. These and other rapidly changing societal transitions demand a new framework for conceptualising children’s health and well-being, and a new set of principles to guide child health practice to ensure its relevance to children. The Convention on the Rights of the Child provides this framework, these principles, and an architecture to support the application of children’s rights to health, safety and security also as an obligation of government to support children.

What is right based approach? – refers to using human rights as framework for health development Traditional approach to fulfil a child’s need is needs bases and often fails to recognize the holistic and integrated needs of children and often provided too late only after permanent damage has occurred.

<table>
<thead>
<tr>
<th>NEEDS-BASED APPROACH</th>
<th>RIGHTS-BASED APPROACH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Works toward outcome goals</td>
<td>Works toward outcome and process goals</td>
</tr>
<tr>
<td>Emphasizes meeting needs</td>
<td>Emphasizes realizing rights</td>
</tr>
<tr>
<td>Recognizes needs as valid claims</td>
<td>Recognizes that rights always imply obligations of the State</td>
</tr>
<tr>
<td>Meets needs without empowerment</td>
<td>Recognizes that rights can only be realized with em-powerment</td>
</tr>
</tbody>
</table>
This international CRC legal framework calls for comprehensive economic, social, cultural and political process with the objective of constant improvement of the health and wellbeing of the entire population and of all individuals, on the basis of their active, free and meaningful participation in development and in the fair distribution of the resulting benefits. It implies the:

1. Right to equality and non-discrimination
2. Best interest of the child
3. Right to highest standards of health, survival and development
4. Right to participation
5. Child right-based budgeting and spending that holds accountability of duty bears and allows monitoring, evaluation and audit on progress made

A cornerstone of human rights law is accountability, or in its simplest terms, the ability to make certain that those charged with protecting and fulfilling the child rights actually do what they are supposed to do, and if they do not or cannot, that children and their representatives have some recourse. (UNICEF Accountability for children’s rights 2015)

How has Hong Kong fared?

While Hong Kong children may be enjoying accessible care by dedicated staff, services in Hong Kong are found to be:

- Services are fragmented and poorly coordinated to meet the changing needs of our children
- Support is poorly targeted – proportionate universalism that most vulnerable will receive more targeted and intensive care rather than just universal access
- Support often not catered for the true needs – needs assessment poorly coordinated
- Failure to share information
- Support often comes too late to make significant improvement and
- Services for most vulnerable children are stigmatized
- Mainly remedial rather than preventive or protective and building on strength of families
- Training to front-line staff not structured and inadequate
- Lack definition of good practice and evaluation
- Lack of accountability, good governance, management and strong leadership
- Lack for vision, foresights and strategic planning on impending needs of children, family and society

Cases reports indicated

- Some children and families are not getting the help they need when they need it especially the hidden most vulnerables – children under care, children of substance abuse parents, children of parents with complex medical needs...
- Some children are not adequately protected
- The needs of children often lose out to the needs of the system or adults
- Piecemeal approach to incorporating the provision of Convention of Right of the Child into law
- Inability to specify what resources are spent on children with what outcome

Service in Hong Kong

- More radical approach rather than incremental process
- We need an overarching aim, which is both visionary and relevant for all agencies and enable each organization an professionals to understand their contribution to achieve the shared vision rather than a separated role and responsibility.
- We need a continuum of responsibilities from all agencies to promote health and prevent diseases and manage disorders. All services have a contribution to make a child and adolescent healthy along this continuum of promotion, prevention and care and no one agency has a monopoly on helping children and youths to achieve good health.
- Need strong leadership to ensure implementation of strategy

In short, right-based approach is never used on policy and service development.

Joint Future

- To develop a whole child approach and children are being seen in the context of their families and wider social cultural and/or spiritual grouping
  - Focus on needs of children and their families - determine what children need rather than reacting to their problems – promote effective parenting within strong and cohesive families, supportive and enabling schools, supportive and inclusive communities
  - Cross-sectoral approach – services integrated across education, social care, health and youth justice
  - Clear accountability at all levels
- Contain a clearer shared vision for integrated working to create a framework of broad support
- Set out core responsibilities of each of the key partners and how they should contribute to the larger shared vision
- Describe models of integrated/joined-up working
- Explicitly set out a framework of activity to support implementation
- Set timescales for agencies to put joint structure in place
- Establish a network of local champions to drive the agenda forward
- Emphasize the contribution of voluntary organizations

The Global Strategy for Women’s, Children’s and Adolescent’s Health (2016-2039) came into effect alongside the Sustainable Development Goals (SDGs) in January 2016. It aims to advance the 2030 Agenda for Sustainable Development by guiding transformative change that enables every woman, child and adolescent – in every setting – to realize their full potential and their human right to the highest
attainable standard of health. It is high time that we should follow this strategy and integrate a right-based approach into clinical care and into the development of health services and policies in Hong Kong.

Preventing Student Suicides: A Hong Kong Experience

Prof. Paul Siu-fai YIP
The Hong Kong Jockey Club Centre for Suicide Research and Prevention
The University of Hong Kong, Hong Kong

Student suicide had a sharper surge in early 2016. Based on the media reports, 36 student suicides occurred in 2016, with 20 of those incidents took place in the first four months of that year. This exceeds the usual number of student suicides in Hong Kong, which was around 20 annually between the years of 2003 and 2015. All these suicides were full-time students, ranging from primary schools to universities.

Based on our investigation, the risk factors are multifactorial and interacting with one another, ranging mental health, academic, family and peer relationship problems. Over 97% of them have two and more of these problems. Single parent household cases were overrepresented. The talk will report some of the preventive measures adopting a public health approach to prevent student suicide in the future. It includes the intervention at three different levels: (i) indicative, (ii) selective and (iii) Universal. Also, the work to interacting with the media professional will also be discussed.

Global Status of Child Health and Opportunities

Dr. Samira ABOUBAKER
Policy, Planning and Programmes
Maternal, Newborn, Child and Adolescent Health and Development (MCA)
World Health Organization

In 2015 the millennium development goals came to an end and the world celebrated the progress made between 1990 and 2015 particularly in reducing maternal and child mortality. Although progress was insufficient to achieve the MDG 4 target of a two thirds reduction by 2015, globally, deaths in children aged under 5 years declined by approximately 53% from 12.7 million in 1990 to 5.9 million in 2015. The two top causes of death in children under five in developing countries are prematurity and pneumonia. Other main causes are diarrhea and malaria associated with malnutrition in 45% of the cases. Among those children who survive an estimated 200 million children are unable to attain their full developmental potential.

Today congenital anomalies, non-communicable diseases, and injuries are becoming increasingly important causes of morbidity and mortality in childhood there by highlighting the dual burden of childhood diseases, affecting most countries in the coming years.

The coming years provide excellent opportunities for accelerating action to ensure that every child receives the services and care it needs and that no child is left behind. Building on the lessons learned from the MDG era, supported by ambitious SDG goals and targets with governments on the driving seat and stakeholders at large united behind the Universal Health Coverage framework, the coming years can be a turning point towards a reinvigorated agenda in which children are enabled not only to survive but also to thrive.

Stunting, Socioeconomic Status and Early Child Development in the East Asia Pacific

Prof. Nirmala RAO
Serena H.C. Yang Professor in Early Childhood Development and Education, Professor, Faculty of Education, The University of Hong Kong, Hong Kong

Stunting (being >2 SDs below the median height-for-age of the reference population) impairs cognitive ability and psychosocial competencies throughout childhood and adolescence, and continues to have long-term detrimental impacts on adult cognitive ability and achievement. This paper examines the relationships among stunting, socioeconomic status (SES) and early child development.

The sample included 6,352 children (3,168 girls) ranging in age from 36 to 71 months from Cambodia (n=1,178), China (n=1,557), Mongolia (n=1,226), Papua New Guinea (PNG) (n=1,697), and Vanuatu (n=674). Children’s height was measured and WHO growth standards were used to determine the presence of stunting. SES was determined based on family wealth. The Cognitive Development, Language & Emergent Literacy and Socio-Emotional Development domain scores of the East Asia-Pacific Early Child Development Scales (EAP-ECDS) (Rao et al., 2014) were used to determine early child development.

Stunting prevalence was highest in PNG (50.3%), followed by Vanuatu (44.4%), Cambodia (29.9%), Mongolia (11.1%), and China (1.1%), respectively. The wealth gap was highest in PNG, Cambodia, Mongolia, Vanuatu, and China, respectively. Stunted children had significantly poorer development relative to non-stunted children in all five countries and the prevalence of stunting was higher for children in the bottom SES quartile compared to children in the top quartile.

In general, the lower the level of economic development in a country, the higher the rates of stunting. Further, smaller wealth gaps and lower stunting prevalence go hand in hand, supporting recent evidence highlighting that the poorest children in the poorest countries have the highest rates of stunting. Results highlight the importance of addressing chronic malnutrition for the poorest children who face the greatest disadvantage.
Child Health Priorities in Asia Pacific Region – Developing a Network for Collaborative Research

Dr. Naveen THACKER, MD FIAP
President - Asia Pacific Pediatric Association
Past President - Indian Academy of Pediatrics
Coordinator of Development- International Pediatric Association
Ex CSO representative- GAVI Alliance Board
Secretary - Child Health Foundation

Asia-Pacific region with over 4.5 billion people in 2016, is home to nearly 60 per cent of the world’s population. It is a diverse region, with seven of the world’s ten most populous countries, and also some of the world’s smallest island nations in the Pacific. In the Asia pacific region except few countries all others struggled to achieve its Millennium Development Goals (1990-2015) despite substantial gains and child health remains to be highly focused and critical area under sustainable development goals with new set of target to “end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live birth” under SDG -3 by 2030.

Asia Pacific Pediatric Association (APPA) represents pediatricians from over 21 countries, enabling them to work together to improve the physical, mental and social health and wellbeing of all children, from birth through adolescence. As per APPA Action Plan 2016-18, various health issues of significance were identified. These were identified after extensive discussions with the experts in APPA. The major child health priorities in the region are: reduction in Newborn mortality, reduction in birth defects, increasing equitable coverage of immunization with both routine and newer vaccines, delivering adolescent health, measures to improve environmental health of children, identifying and mitigating early child developmental problems, dealing with the “double burden” of nutritional problems of malnutrition and obesity and research in child health issues.

The Technical Advisory Groups (TAGs) are expert groups of APPA working on important child health issues. Total 9 TAGs are established to enable leaders of National Pediatric associations in APPA region who are interested in the specific areas of interest to meet for the purpose of discussing and developing ideas, programs and projects which will improve the care of every child.

APPA have shared detailed Questionnaire with all APPA member societies prepared by respective TAG groups, the responses are received from most of the Technical Advisory Group. Based on the survey analysis results were shared with respective TAG for further actions. APPA have formed task forces on Antimicrobial Resistance and Obesity and in process of forming a task force on TB.

The translation of evidence into practice is critical. There is a need to develop a network for collaborative research for APPA member societies. APPA is increasing focussing on ways to encourage knowledge transfer from policy level to ground level. Collaborative research networks have been touted as a solution for enhancing knowledge translation. Many studies recommend that collaborative network act as a catalyst to facilitate more rapid exchange of information and new evidence.

APPA TAGs with the support of collaborative research network have the potential to translate knowledge across the research, policy and practices in APPA member’s countries and will be a crucial step for child health in APPA region.

Adolescent Health – A Neglected Domain in Global Child Health

Dr. Chok-wan CHAN
Past President, International Pediatric Association (IPA) (2007-2010)
Honorary President, the Asia Pacific Pediatric Association (APPA)
Director of Subspecialty Boards, Hong Kong College of Paediatricians
President, the Hong Kong Society of Child Neurology and Developmental Paediatrics
Board Chairman, the Hong Kong Paediatric Foundation

It is estimated that there are around 1.8 billion adolescents worldwide nowadays. This is the largest generation of adolescents and young people in human history. In May 2016, the third report of Lancet Series on Adolescent Health themed “Our Future: A Lancet Commission on Adolescent Health and Wellbeing” published has highlighted the updated health data on adolescents and the appropriate approach in addressing the health challenges faced by this significant group of world population. Adolescence is a life phase in which the opportunities for health are great and future patterns of adult health are established. The changing patterns of adolescents’ health have the potential to undermine future population health as well as global economic development unless timely and effective strategies can be implemented. On the World Population Day in July 2014, UN Secretary-General Ban Ki-moon had made the following statement – “I call on all with influence to prioritize youth in development plans, strengthen partnerships with youth-led organizations, and involve young people in all decisions that affect them. By empowering today’s youth, we will lay the groundwork for a more sustainable future for generations to come.” Investment in children and youth at present stage will bring along more cost-effective returns to the entire population in future. This is why a focus on adolescence is crucial to the success of many public health agendas, including the Millennium Development Goals (MDG) and Sustainable Developmental Goals (SDG). Hong Kong, in 2017, regrettable is still facing the same problems such as youth suicides and other adolescent problems. While the Hong Kong Special
Administrative Region Government, as usual, plays a lot of lip-services on these issues and proposes a long list of completely useless procedures to deal with the conditions which are totally routine, bureaucratic and ineffective. It is high time that all the healthcare professionals should work together to find out root-cause problems and try to eradicate the underlying causes and not just to hide the rubbish underneath the carpet. Problems for all these are mainly due to total failure of our education system (focusing too much on scholastic performance), lack of time to play, lack of moral education, failure of our younger population to grasp the core values for existence (life education), parenting problems, too much materialistic life styles, lack of positive life attitude, poor resilient ability and others. Detrimental results are reflected in the significant number of non-engaged adolescents in the community and the recent upheavals of physical/social violence in Hong Kong including the umbrella revolution (in Central) and the street riot (in Mongkok). It is highly lamentable to witness these behaviours in our masters for tomorrow.

In order to tackle the problem effectively and efficiently, the Hong Kong Paediatric Foundation and the Hong Kong Paediatric Society invited world expert Dr. Charles E. Irwin, Jr. from the United States to host a series of professional activities on the subject in Hong Kong and in Macau featuring “Adolescent Health Update from the Clinical, Research, Training, Policy and Advocacy perspectives” as well as a survey on adolescent health at the secondary schools aiming to advise the Government, the professionals and the public as to plan strategic action plans to solve the problems in Hong Kong.

Epidemiology of Paediatric Trauma in Hong Kong: a Multicentre Cohort Study

Chow C B1, M Leung2, Gilberto K K Leung3,4, W Y Shen5,6, C W Kam7, H M Cheung8, K L Au Yeung5, Patrick Ip1

Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong, Princess Margaret Hospital,
Department of Surgery, The University of Hong Kong, Queen Mary Hospital,
Queen Elizabeth Hospital,
Hospital Authority, HK,
Tuen Mun Hospital,
Department of Paediatrics, Chinese University of Hong Kong

Introduction

Trauma is the commonest cause of death and major morbidities in children and adolescents worldwide (Bhatti et al., 2016; Chichom-Mefire & Fokou, 2013; Kristiansen, Rehn, Gravseth, Lossius, & Kristensen, 2012; Mitchell, Bambach, Foster, & Curtis, 2015; Snyder, Muensterer, Sacco, & Safford, 2014). There has been a lack of data on the epidemiology of trauma among children in Chinese cities include Hong Kong. Therefore, the current study was conducted to examine the spectrum of paediatric trauma in Hong Kong and to address knowledge gaps in its epidemiology and prevention.

Objective

This study aimed to describe the epidemiological features of paediatric trauma and explore the characteristics in the low-income group which would help to guide the design of effective interventions and future research on prevention of paediatric injuries.

Method

A descriptive study on the epidemiology of trauma in children ≤18-year-old using a standardised injury registry embedded within a population-based hospital database. Information on demographics, injury type, mechanism, injury severity score (ISS) and injury prevention prioritization score (IPPS) were collected to identify the epidemiological features and prevention initiatives.

Result

The overall female to male ratio was 1: 1.97, which increased with age from 1:1.45 (infant; below 2 years old) to 1:2.67 (adolescent; 12-18 years old). The overall mean ISS was 7.98 (SD 9.18), ISS increased with age significantly (rho = 0.143, P<0.001). The most common context of trauma included travelling (IPPS: 59.94, mean ISS 10.2 + 10.23, n=402), leisure activities (IPPS: 52.04, mean ISS 5.6 + 6.77, n=312), street/highway (IPPS: 70.22, mean ISS 10.48 + 10.53, n=475) and home (including garden and out buildings) (IPPS: 69.56, mean ISS 6.64 + 7.94, n=539). Severity of paediatric injuries among low-income group did not differ from the general population.

Conclusion

The study provided updated data on the epidemiological characteristics of paediatric trauma and helped to highlight further study initiatives including injury surveillance, geographical analysis and environment survey. This study model could be replicated to explore the characteristics of trauma among other age groups for enhancing injury prevention at population level.
Genetics and Genomics

Symposium A4 - Pathway Disorders

Rasopathies – Noonan Syndrome and Related Disorders

Prof. Yoichi MATSUBARA
Director of Research Institute, National Center for Child Health and Development (Japan)
Professor Emeritus, Tohoku University, Japan
President, the Japan Society of Human Genetics

Rasopathies or RAS/MAPK syndromes are a group of phenotypically related syndromes caused by germline mutations of genes encoding components of the RAS/MAPK signaling pathway, which controls cell proliferation, differentiation and survival. These disorders include Noonan syndrome, Noonan syndrome with multiple lentigines (formerly called LEOPARD syndrome), Costello syndrome, cardiofaciocutaneous (CFC) syndrome, Noonan-like syndrome, neurofibromatosis type I, Legius syndrome, hereditary gingival fibromatosis and capillary malformation-arteriovenous malformation. Although each Rasopathy has a unique phenotype, these syndromes have many overlapping characteristics, including craniofacial dysmorphology, cardiovascular abnormalities, musculoskeletal abnormalities, cutaneous lesions, neurocognitive impairment and increased risk of tumor. To date various disease-causing genes have been identified, such as PTPN11, SOS1, SOS2, RAF1, NRAS, RIT1, RRAS, RASA2, LZTR1, A2ML1, KRAS, BRAF, HRAS, MAP2K1/2, SHOC2, CBL, NF1, SPRED1, and RASA1. The identification of the causative genes that underlie the Rasopathies has facilitated molecular diagnosis of these disorders, enabled the evaluation of genotype-phenotype relationships and aided in the development of possible therapeutic approaches. Inhibitors of the RAS/MAPK signaling cascade may offer a means of therapeutically treating disorders that involve dysregulation of the RAS/MAPK pathway. Indeed, MEK inhibitors have been shown to ameliorate the phenotype of knock-in mouse models for NS and CFC syndrome, suggesting that the phenotypes that are produced by Rasopathies can be ameliorated by manipulating RAS/MAPK activity.

Mutations in PI3K-AKT-mTOR Signaling Pathway Result in Developmental Mosaic Disorders

Dr. Brian Hon-yin CHUNG
Clinical Associate Professor
Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine,
The University of Hong Kong

Mutation in PIK3CA, one of the genes involved in the PI3K-AKT-mTOR pathway, is associated with developmental mosaic disorders which are now collectively termed as PIK3CA-Related Overgrowth Spectrum (PROS). PROS can be further divided into two subgroups based on the affected body systems, which are body asymmetrical overgrowth and central nervous system (CNS) overgrowth respectively. Body asymmetrical overgrowth includes diseases such as CLOVES Syndrome, Klippel-Trenaunay Syndrome, Cystic Hygroma and Fibrodipose Hyperplasia. More than 90% of these patients have somatic mutations in one of the 4 mutation hotspots in PIK3CA. CNS overgrowth includes diseases such as Megalencephaly-Polymicrogyria-Polydactyly- Hydrocephalus Syndrome (MPPH) and Megalencephaly-Capillary Malformation Syndromes (MCAP). Nowadays, it is known that germline/somatic mutations in other genes in the PI3K-AKT- mTOR signaling pathway can also result in to CNS overgrowth. Patients who have CNS overgrowth have megalencephaly and at the same time developmental delay and/or autistic spectrum disorder. In this lecture, I will present the clinical spectrum of this group of developmental mosaic disorders, and discuss the challenges for genetic diagnosis.

The Genetic Landscape of Rasopathies in Hong Kong

Dr. Ivan Fai-man LO
Consultant Clinical Geneticist
Head of the Clinical Genetic Service of the Department of Health (CGS, DH)
Hong Kong

Rasopathies are a genetically heterogeneous group of genetic diseases characterized by disturbance of the RAS-MAPK signaling pathway. With an incidence of 1/1,000-2,500, the most common condition among the rasopathies is Noonan syndrome, a well-known dysmorphic syndrome and a common reason for referral to the Clinical Genetic Service. Since the identification of the PTPN11 gene in 2001, there are more than 10 genes implicated in Noonan syndrome. Diagnosing Noonan syndrome has moved from a "genetic" approach to a "genomic" one. This presentation summarized the molecular defects found in over 180 local patients with Noonan syndrome and two other phenotypically overlapping disorders known as Cardiofaciocutaneous syndrome and Costello syndrome. The distinguishing molecular and clinical features were highlighted.
The potency and specificity of immune cells suggest the possibility that their infusion in patients with cancer could overcome the resistance of cancer cells to standard treatment modalities while sparing normal tissues. Evidence is mounting indicating that administration of autologous T cells induced to express anti-CD19 chimeric antigen receptors (CARs) ex vivo can exert major anti-leukemic activity in patients with CD19+ B-cell acute lymphoblastic leukemia (ALL). This has resulted in durable remissions for many patients who were refractory to standard therapy. These initial trials have also revealed the potential serious toxicities that CAR-T cell therapies can produce, including cytokine release syndrome and neurotoxicity. Moreover, recurrent leukemic subclones lacking CD19 may escape monotherapy with anti-CD19 CAR-T cells. In these instances, CAR directed against other B-cell antigens, such as CD22, may prove to be useful.

Simplifying ex vivo cell processing, widening the range of targetable antigens and generating safer and more effective cell products are important objectives to move this field forward. Besides CAR-T cells, several other cell therapy approaches are being explored, using different receptor formulations and different cell types with the vision of building an array of immunotherapeutic options that can complement or replace standard therapy of cancer.

Acute lymphoblastic leukaemia (ALL) is the commonest childhood malignancy and the cure rate is now approaching 90%. Over the past few decades, research studies on various aspects of ALL were conducted in Hong Kong (HK). Initially the research studies were on epidemiological studies, including timing of exposure to infection and impact of SARS on ALL. The clinical studies were firstly local multicenter study, the HKALL 1993 which showed suboptimal results. The next local study extended to regional collaboration with Singapore achieved a marked improvement in survival outcome. Due to small sample size in a city, HK then participated in the International-BFM Study Group and formally joined the large international IC-BFM ALL 2002 Study with countries in Europe and S. America, and recruited over 5000 patients. The participation in the I-BFM group facilitated the HK group to join in more international clinical studies, EsPhALL Study and Interfant Studies. Through the international collaborative studies, new advances in laboratory diagnostic and monitoring methods were introduced in HK. Minimal Residual Disease monitoring by Flow Cytometry and PCR methods were developed and validated in HK laboratories. The treatment and research standard could be elevated to international level. HK also takes active participation in the mainland China multicenter clinical studies, and sharing the international experience with the mainland counterparts. The CCLG2008 Study had been completed with more than 2000 patient recruited. The current ongoing CCCG2015 studies is a much larger study with randomization arm for Ph ALL with two different TKI treatment. The study aimed at recruiting 5000 patients in coming 5 years study. With such a large study, the conduct of study is monitored and audit of data is now also incorporated. The research experience gained through international studies actually helped to promote the research standard in the national studies. Other than the multicenter studies, HK is now also starting the pharmacogenetics studies specific for Chinese
children including the NUDT15 genetic polymorphism on thiopurine metabolism. Scientific research on new targets for resistant or refractory leukaemia is also ongoing, new target is tested in xenograft model based on human leukaemia samples. National and international collaborative studies have brought new advances in the treatment, and basic scientific research will look for the new treatment approach.

Symposium E2
- Advances in Paediatric Haematology and Oncology

How to Target the Ultra-High-Risk Neuroblastoma?

Dr. Akira NAKAGAWARA, MD, PhD
CEO, Saga Medical Center Koseikan, Saga, Japan
CEO, Saga HIMAT Foundation, Tosu, Saga, Japan

The prognosis of neuroblastoma (NB) has significantly improved for the last decades according to the development of multidisciplinary therapy. However, the outcome of the patients with high-risk NB is still poor. Based on our data set in Japan, the 10-year overall survival rate of stage 4 NB, which covers about a half of NB, showed 41% (n=282). In addition, it is getting obvious that NB in stage 4 is highly heterogeneous in its biology and genetics and shows variable survival rates. Therefore, we need to identify a specific group of NB possessing ultra-high-risk characteristics to improve the prognosis as well as to achieve the precision medicine of NB.

The International NB Risk Group (INRG) has recently published an improved risk grouping. However, since it does not include ultra-high-risk NB group, we challenged to identify such group of NB.

Our analyses showed that array CGH-based genome subgroup P2a and P2s (both with 1p loss, 11q loss and 17q gain) with and without MYCN amplification showed ultra-high-risk phenotype of NB. The methylene analysis also indicated that Ps tumors can be clearly divided into four clusters, two of which showed high-risk or ultra-high-risk phenotype. Furthermore, our study suggested that genomic landscape, including the three transcription factors-related networks (DNA-damage response, RB and TP53 mutations) and the mutations in chromatin remodeling/ regulating genes, seems to be very helpful to indentify the ultra-high-risk of NB. Thus, the combination of “methylene profile” may be useful for defining the ultra-high-risk group of NB to construct new therapeutic strategies especially in the subsets without MYCN amplification.

As for the therapies against ultra-high-risk NB, new target molecules, novel immunotherapies, new chemotherapeutic reagents, innovative particle beam radiation therapy, etc. will be discussed.

Targeting Epstein-Barr Virus (EBV) in EBV-associated Malignancies

Alan KS CHIANG 1, 2, KF HUI 1, 2
1Department of Paediatrics and Adolescent Medicine;
2Center for Nasopharyngeal Carcinoma Research,
The University of Hong Kong, Hong Kong SAR, China

Epstein-Barr virus (EBV) persists in tightly latent forms in every tumour cell in EBV-associated malignancies. Re-activation of lytic cycle or suppression of anti-apoptotic function of EBV may result in therapeutic effects on these malignancies.

We tested a class of chemical compounds known as histone deacetylase (HDAC) inhibitors in activating the EBV lytic cycle. Two clinically relevant compounds, suberoylanilide hydroxamic acid (SAHA) and romidepsin, strongly induced the lytic cycle in EBV-positive nasopharyngeal and gastric carcinoma cells. Induction of the early phase of lytic cycle without the need for full viral lytic production resulted in apoptosis of the cancer cells. Furthermore, romidepsin, a specific inhibitor of class I HDACs (HDAC1-3), could induce EBV lytic cycle at picomolar to low nanomolar concentrations through activation of protein kinase C-delta pathway.

In contrast, EBV-positive Burkitt lymphoma (BL) and lymphoblastoid cells (LCL) were found to be resistant to induction of EBV lytic cycle by HDAC inhibitors. However, adding a proteasome inhibitor, bortezomib, to either SAHA or romidepsin could overcome the resistance and result in synergistic killing of LCL and a subset of BL which expressed the EBNA3 proteins. By testing BL lines harboring EBNA-3A, 3B or -3C knockout EBV genome and its respective revertant, we found that the drug combination counteracted EBNA-3C’s anti-apoptotic and cell cycle regulatory function to potently induce apoptosis of the lymphoma cells.

In conclusion, we have shown novel therapeutic strategies against EBV-associated epithelial and lymphoid malignancies by activating viral lytic cycle and antagonizing anti-apoptotic function of latent viral protein, respectively.

The work is funded by NPC Area of Excellence (AoE/M 06/08 Center for Nasopharyngeal Carcinoma Research) and EBV research (#200004525) grants of AKSC.
New era in the management of childhood cancer

Prof. Godfrey Chi-fung CHAN

Department of Paediatrics & Adolescent Medicine, Queen Mary Hospital & HKU-Shenzhen Hospital, The University of Hong Kong

Chemotherapy, surgery and radiation therapy are the conventional approaches for cancers. Patients may need either one, two or all 3 forms of therapy for cancer control. But such approaches carry significant acute and long term side effects. Over the past decades, new modalities such as small molecule targeted therapy and immunotherapy started to emerge. For cancer with identifiable genetic target, using small molecules to block the aberrant expression of genes can achieve significant disease control or even cure in a number of relatively rare childhood cancers such as CML, or solid tumors such as subependymal giant cell ependymoma in tuberous sclerosis, gastrointestinal stromal tumor and anaplastic Ki-1 lymphoma. However, children cancers with treatable gene target accounts for a very small patients’ proportion only. On the other hand, immunotherapy includes a spectrum of new strategies and they have different mechanisms. Such approaches include monoclonal antibody targeting at particular tumor specific antigens; immune check-point inhibitor by blocking the immune evasive mechanism of cancers; immune cellular therapy using chimeric antigen receptor T cells (CAR-T) to attack cancers with specific surface antigen; bispecific antibody to guide the T cells against cancers with specific surface antigen; and allogeneic KIR mismatched natural killer cells to eradicate residual cancer cells, etc. All these fascinating advances provide us new hope with lesser therapy related side effect profile. However, they are usually very expensive and require high level of technological support so the chance of benefiting a large population is slim. In addition, one has to understand the basic mechanism of these approaches so rational utilization of these strategies can be adopted.

Infectious Diseases

Symposium A2
- Infectious Diseases in Asia

Early Diagnosis Of Childhood Mycobacterial Infections-Tuberculosis & Leprosy

Prof. (Dr.) Rajeshwar DAYAL

National Vice President, Indian Academy of Pediatrics, 2011

Dr. B.C. Roy National Awardee, 2016

Head, Department of Pediatrics, Medical College, Agra, India

Department of Paediatrics,S.N.Medical College, Agra, India

The genus Mycobacterium includes pathogens known to cause serious diseases, mainly tuberculosis (Mycobacterium tuberculosis), leprosy (Mycobacterium leprae) and Non Tuberculous Mycobacterial infections( M avium, M intracellulare and M fortuitum). Early diagnosis of T.B. in children is often challenging due to vague clinical manifestations and difficulty in isolating M.Tb. Cheap and easy microscopy using Ziehl nelson stain has been employed as the initial diagnostic tool for tuberculosis. Poor sensitivity remains a major drawback of this method. Culture in liquid media has been the gold standard for bacteriological confirmation of TB. Imaging tools aid in the diagnosis especially where bacteriological confirmation maybe difficult. Molecular methods such as polymerase chain reactions (PCRs) allow direct identification of M.Tb in clinical specimens. Molecular LPAs allow rapid detection of resistance to rifampicin (alone or in combination with isoniazid) in AFB smear-positive sputum specimens or on M. tuberculosis isolates grown by conventional culture methods. However, various recent studies including our own have demonstrated the efficacy of CBNAAT-XpertMTB/RIF and it is now recommended as the initial diagnostic test. Early diagnosis of leprosy requires a high index of clinical suspicion. It is based on detection of 2 of the following features, namely, characteristic skin lesions, loss of sensation and thickened peripheral nerves or the detection of AFB in skin or nasal smear. We have conducted a number of studies, evaluating various newer techniques for early detection of the disease. Fluorescent leprosy antibody absorption technique (FLA-ABS) and Lepromin tests are of immense value for identification of “at risk” population and for detecting subclinical infection. Gene probes developed at our institute detected all smear positive and lepromin negative cases and majority of smear negative cases. Evaluation of the In-situ PCR technique revealed that whereas histopathology detected 45% of total cases, In Situ PCR detected as much as 60% of the total cases. In another study, In-situ hybridization technique helped in diagnosing children with negative skin smear and non specific histopathology. RLEP
PCR is a new technique. Our pioneer study has shown its immense potential in early diagnosis of leprosy specially where skin smears are negative and skin biopsy is not feasible. With the great morbidity and mortality associated with mycobacterial infections early diagnosis is the need of the hour.

Central Nervous System Infections: Developing Country Perspective

Prof. Kyaw Linn
Professor (Paediatric Neurology)
FRCPCH Senior Consultant Paediatrician
Yangon children hospital, Yangon, Myanmar
Secretary, Myanmar Pediatric Society

Central nervous system (CNS) infections are the third leading cause of under-five mortality in Myanmar. Both viral and bacterial infections including CNS tuberculosis are common. Out of total admission of 17,000 children in 2016 in Yangon children hospital, there were 191 children with meningitis (13 mortality), including 49 children with tuberculous meningitis and 118 children with encephalitis (11 mortality). In one study on 83 children with acute encephalitis syndrome in Yangon children hospital in 2016, 35 children were positive for Japanese encephalitis virus. Another study on 66 children with viral encephalitis in three university hospitals in 2013 revealed dengue virus, Japanese encephalitis virus and Herpes simplex viruses as common etiologies.

There are significant sequelae in these children. Developmental and behavioral complications, movement disorders like dystonia are common, serious sequelae. Management of dystonia is quite challenging.

There are still many other challenges like lack of local epidemiology and etiology data, lack of easily available diagnostic tests, lack of facilities like intensive care units and neuroimaging, delayed arrival or referral to health centers.

The Framework to Eliminate Mother to Child Transmission of HIV, Syphilis and Hepatitis B in Asia and the Pacific

Dr. Tammy Meyers
Head of International Exchange, Centre for Global Health
Adjunct Assistant Professor, Jockey Club School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong
Honorary Associate Professor, University of the Witwatersrand, South Africa

The sustainable development goal (SDG) agenda, in particular SDG3, targets elimination and/or control of major infectious diseases including HIV, viral hepatitis and sexually transmitted infections for which global health sector strategies have been set. Included in these are plans to eliminate mother to child transmission (eMTCT) of HIV, syphilis and hepatitis B, which are all congenitally acquired from infected pregnant women. The targets set for the elimination these diseases include; zero new HIV infections among infants (≤50 new paediatric infections per 100 000 live births and a transmission rate of either <5% in breastfeeding populations or <2% in non-breastfeeding populations) by 2020, for syphilis: ≤50 cases congenital syphilis per 100,000 live births in 80% of countries by 2030 and for Hepatitis B: 1% HBsAg prevalence among children by 2020 and 0.1% by 2030. Progress in countries and territories in the Asia Pacific Region towards eMTCT of HIV, syphilis and hepatitis B in infants will be discussed and compared with the global situation. The Asia-Pacific region has already witnessed some success in the quest to eliminate mother to child transmission (MTCT) of HIV and syphilis, with Thailand becoming the first country in the region to be validated for eliminating these diseases in 2015. Traditionally, control programmes for these diseases have operated vertically. However, efforts to eliminate mother-to-child transmission of HIV, hepatitis B and syphilis are essential components of quality maternal, newborn and child health care. China has implemented a triple eMTCT programme, which is coordinated through Maternal Child Health, and the talk will cover the processes required and the challenges faced by countries towards implementing an integrated eMTCT programme within the Asia Pacific Region.
Impact of Rotavirus Vaccine: Better than Anticipated

Dr. Jacqueline TATE

Epidemiologist, Viral Gastroenteritis Team,
Division of Viral Diseases
US Centers for Disease Control and Prevention (CDC), USA

Since 2006, two oral live-attenuated rotavirus vaccines, Rotarix (GlaxoSmithKline Biologics) and RotaTeq (Merck Vaccines), have been licensed for use globally to combat the leading cause of severe gastroenteritis for children under-5 years of age. In pre-licensure trials, rotavirus vaccines showed high efficacy (85%-98%) against severe rotavirus disease in high and middle income countries of the Americas and Europe but modest efficacy (50%-64%) in low income countries in Africa and Asia. As of May 2017, 85 countries have introduced rotavirus vaccines into their national immunization programs. Marked reductions in rotavirus hospitalizations and all-cause diarrhea hospitalizations and mortality have been observed in numerous countries that have introduced rotavirus vaccine since the licensure of rotavirus vaccines a decade ago. Among children <5 years of age, all-cause diarrhea hospitalizations have decreased by 41%, 30%, and 46% in low, medium, and high child mortality countries, respectively, that have introduced rotavirus vaccines. Hospitalizations and emergency department visits due to rotavirus have been reduced by 71%, 59%, and 60% in low, medium and high child mortality countries, respectively. In addition to declines in disease burden among children directly protected by rotavirus vaccination, declines in rotavirus vaccine have also been seen in children too old to have received rotavirus vaccine and as well as in adults in some settings. Reductions in seizures have also been observed following rotavirus vaccination in some settings. The impact of rotavirus vaccines should continue to be monitored as they are introduced into new settings and countries that have not yet introduced rotavirus vaccine should consider including them into their national immunization program.

New Rotavirus Vaccines from Asia: Rotavac, Rotasiil, Rotavin, RV3BB

Dr. Carl KIRKWOOD

Senior Program Officer, Enteric and Diarrheal Diseases, Bill and Melinda Gates Foundation, Seattle, USA
Senior Research Fellow, Murdoch Childrens Research Institute, Victoria, Australia
Associate Professor of Virology, Department of Microbiology, La Trobe University, Victoria, Australia
Fellow, Department of Paediatrics, The University of Melbourne, Victoria, Australia

Rotavirus disease remains a major global cause of mortality and morbidity in children under 5 years of age. Rotavirus vaccines, RotaTeq and Rotarix, have been introduced into over 90 countries globally and have demonstrated substantial impact in reducing diarrhea mortality and diarrhea hospitalizations in young children. The vaccines are cost effective interventions for young children, particularly in countries with high diarrhea disease burden.

Significant advances have been made demonstrating the impact of the vaccines in low- and lower-middle income countries, yet, the full potential impact of rotavirus immunization is yet to be realized. Countries with large birth cohorts and where disease burden is high in Africa and Asia have not yet implemented rotavirus vaccines at all or at scale. In addition, despite the enormous strides forward, the effectiveness and impact is reduced in developing country settings, where the burden and mortality is highest.

New rotavirus vaccines, including live oral rotavirus candidates and non-replicating approaches continue to be developed, with the aim to improve the global supply and cost of rotavirus vaccines, and improve vaccine effectiveness in developing settings. This presentation will provide an overview of the new oral rotavirus vaccines from Asia, including Rotavac, RotaSiil, vaccines developed by Indian manufacturers as well as others that are under clinical development.

Chinese Rotavirus Vaccines: What’s Around the Corner

Prof. Xuan-yi WANG

Research Scientist, Institutes of Biomedical Sciences,
Professor, Key Laboratory of Medical Molecular Virology of MoE/MoH,
Fudan University, China
Deputy Director, National Engineering Laboratory for Therapeutic Vaccines

Rotavirus (RV) is the leading cause of severe gastroenteritis in children worldwide both industrialized and developing countries. In China, hospital-based studies indicated that RV-associated hospitalizations accounted for 32%-50% of all hospitalizations, our population-based surveillance measured an occurrence of ~10/100person/year in children less than 5 years of age. Shortly after the licensure of the first rotavirus vaccine – RotaShield in August 1998, the Lanzhou lamb rotavirus vaccine (LLR, is characterized as G10P[12]), originally isolated from a lamb with diarrhea was licensed in China since 2000. As of 2016, a total of >70 million doses of LLR had been distributed to children countrywide. However, the efficacy of LLR has not been recognized internationally as it has not been confirmed by a properly designed pre-licensure clinical trial. Effectiveness identified by the case-control design nested in our popula-
among children suffered moderate/severe severe RV gastroenteritis. Two oral rotavirus vaccines marketed internationally, namely Rotarix® (GlaxoSmithKline Biologicals, the monovalent (RV1)) and RotaTeq® (Merck & Co. Inc., the pentavalent (RV5)) have completed the clinical test in China in 2012 and 2015 respectively, however, due to the concern of porcine circovirus (PCV) contamination with master seed, the licensure of Rotarix® was shelved, while RotaTeq® is most likely approved in the coming months. At the moment, two reassortant candidates were developed by China National Biologicals Group (CNBG). Of these, the hexavalent (bovine and human reassortant) that is composed of G1, G2, G3, G4, G8 and G9 has passed phase I, and the phase II trial is ongoing. The trivalent (lamp and human reassortant) including G2, G3, G4 has completed phase III, and submitted NDA, a protection against severe diarrhea of >75% was demonstrated. With regard to the causality association between replicable vaccines and intussusception, an inactivated vaccine candidate based on a high replicable strain characterized as G1P[8] is being developed by Institute of Medical Biology, Chinese Academy of Medicine Science, and IND application was submitted in 2016. It is foreseeable that in the near future, adequate products can meet the demand of both EPI and catch-up immunization in China. In contrast, a feasible immunization policy as well as a financial mechanism suiting to China’s national conditions is an urgent challenge.

**Rotavirus Vaccines Save Money : Herd Effects & Less Convulsions**

Prof. Tony NELSON

*Department of Paediatrics, The Chinese University of Hong Kong*

The World Health Organization (WHO) recommended in 2009 that rotavirus vaccines should be included in all National Immunisation Programmes (NIP). Despite this recommendation and the availability of two WHO prequalified rotavirus vaccines, only 81 (42%) or the 194 WHO member states had introduced these vaccines by December 2016. A review of 27 rotavirus vaccine introducing countries of all income groups showed an overall median 67% reduction in hospitalizations and emergency department visits due to rotavirus gastroenteritis. A 42% reduction in diarrhoea mortality was witnessed in the low- and middle-income countries. Introduction of rotavirus vaccines in low-income countries have been subsidised by GAVI, the Vaccine Alliance, but vaccine price plays a key role in introduction decisions in middle- and high-income countries.

Economic evaluations of rotavirus vaccine typically include only reduced diarrheal morbidity and mortality (QALYs and DALYs), averted medical costs from diarrhoea, direct non-medical costs and indirect or productivity costs. The vaccine price used in the model will typically be based on the private sector market price which may not reflect the eventual NIP price. Different regions and different countries have different mechanisms to negotiate price with industry. The broader economic benefits of vaccination are increasingly being recognised and many of these have not been included in rotavirus vaccine economic evaluations e.g. herd immunity, non-diarrheal health benefits (prevention of convulsions and other mortality, improved nutrition), demographic adaptive response, macro-economic effects from impoverishment and equity effects. In low-income countries children are 8.5 times more likely to die in the 2 months following a diarrhoea hospital admission and are more likely to have their growth stunted.

Reductions in both febrile and afebrile seizures have been reported in high-income countries following vaccine introduction. Inclusion of these benefits in economic evaluations will further enhance the economic benefit of rotavirus vaccines. However understandably governments wish to pay a fair price for vaccines and lack of price transparency has likely delayed vaccine introduction decisions. Vaccine research and development costs may be overstated and fair prices of vaccines should be established. WHO has launched a platform designed to increase the transparency of vaccine prices, and this information should help countries negotiate cost-effective prices with industry.

**Opportunities for Rotavirus Vaccine Introduction in Asia**

Dr. Naveen THACKER MD FIAP

*President - Asia Pacific Pediatric Association*

*Past President - Indian Academy of Pediatrics*

*Coordinator of Development- International Pediatric Association*

*Ex CSO representative- GAVI Alliance Board*

*Secretary - Child Health Foundation*

*University of Washington*

Rotavirus (RV) is the most common cause of diarrhea and one of the leading causes of under 5 child-mortality. Each day, RV kills more than 260 children under 5 in Africa and more than 170 in Asia. Safe and effective WHO prequalified vaccines exist to protect children against RV which is one of the important interventions to prevent morbidity and mortality due to severe rotavirus gastroenteritis (RVGE).

According to a recent IVAC report 2017, an estimated 62% of the world’s infants (83.8 million) live in countries or subnational regions within countries that have not yet introduced RV vaccine into their National Immunization Program (NIP). Only 92 countries out of total 194 have introduced RV vaccine till March 2017, nearly 25 countries are in planning phase to introduce but a major proportion i.e. 73 countries are still not clear about introduction of RV vaccine.

Asia is home to 1/3 of the world’s RV related mortality and despite this a large number of Asian countries have
not opted for RV vaccine in their NIP. The reasons for delayed vaccine introduction in Asia are many and likely differ by country, with multiple stages along the pathway to implementation posing hurdles, including - evidence gathering, decision-making, planning, and introduction. The drivers for introduction may also differ; for e.g., perceived health benefits may be the primary reason in one area, and economic benefits may be more important in another. Some policy makers from Asian countries have been slow to introduce RV vaccine due to a misconception that the vaccine is not cost-effective. The limited data from low-resource populations across Asia, which are needed to provide evidence of the clinical protection against severe diarrhoea due to RV vaccination, have also likely stalled the uptake.

Remarkable benefits of the RV vaccine introduction are visible in countries like Austria, Belgium, and Finland as they observed decreases of up to 80% in the annual rate of RV hospitalizations following vaccine introduction. Herd Immunity has been well demonstrated in Australia, Austria, Belgium, Brazil, El-Salvador & Finland following RV vaccine introduction in infants, with RVGE hospitalizations decreased by up to 89%.

With the full support of GAVI, Rota Council and development partners, Asian countries have the opportunity to learn from peer countries that have successfully reduced the morbidity and mortality burden related to rotavirus. Vaccine efficacy data from few Asian countries is also an encouraging factor which will help many decision makers to adopt the RV vaccine in their respective NIP. As of March 2017, 43 GAVI supported countries have introduced RV vaccine into their NIP, with India and Pakistan having introduced in a phased manner. GAVI supported countries in Asia thus have an excellent opportunity to accelerate the process of RV vaccine introduction in their respective countries. As per Rota Council recommendations, GAVI technical and co-financing model can support eligible Asian countries to speed up their efforts to introduce RV Vaccine introduction at the earliest and for non-GAVI eligible countries, governments & funding agencies should continue to support research & development of new, low-cost rotavirus vaccines using public, social business, & public-private models for introduction.

Thus, with nearly half of all rotavirus deaths occurring in Asia, there is an urgent need for action in the region.

**Bibliography.**

1. IVAC report March 2017


---

**Symposium B2**

- Japanese Pediatric Society Symposium

**Fight Against Pneumonia in Asian Children**

**The Factors Influencing Infectious Disease Guidelines - EBM or the Other Factors**

Prof. Kazubobu OUCHI

*President, the Japanese Society for Pediatric Infectious Diseases*

*President, the Japanese Society of Travel and Health since 2016*

*Chairman, Department of Pediatrics, Kawasaki Medical School, Japan*

Pneumonia is recognized as the most common cause of death among children less than 5 years of age in the world, especially in underdeveloped countries. It has also many societal burdens in developed countries. Under these situations, several EBM guidelines have been published especially in developed countries. However, these guidelines sometimes gave us the different recommendations, although they use the same evidences. I think there are many factors influencing these guidelines more than our common evidences, such as various causative organisms, various antibiotic resistant situations, general medical situation, available antibiotics, and so on. I think it is better to make our own original guidelines in each country. In this symposium, three speakers talk about the most important factor, that is the latest epidemiology of etiological agents causing community-acquired pneumonia in three different Asian countries.

**Epidemiological Change of Pediatric Community-acquired Pneumonia Before and After Introduction of Pneumococcal Conjugate Vaccine Era in Japan**

Naruhiko Ishiwada, Sachiko Naito, Noriko Takeuchi, Misako Okhusu, Koo Nagasawa, Katsuaki Abe, Yuko Omata, Haruka Hishiki, Tadashi Hoshino

1. Department of Infectious Diseases, Medical Mycology Research Center, Chiba University, Chiba, Japan
2. Department of Pediatrics, Chiba University Hospital, Chiba, Japan
3. Department of Pediatrics, Chiba Kaihin Municipal Hospital, Chiba, Japan
4. Department of Pediatrics, Chiba Medical Center, Chiba, Japan
5. Division of Infectious Diseases, Chiba Children’s Hospital, Chiba, Japan
Background
Community-acquired pneumonia (CAP) is a serious cause of morbidity and one of the leading causes of hospital admission in children. *Streptococcus pneumoniae* is considered to be the most important pathogen identified from children aged <5 years with bacterial pneumonia. Introduction of the pneumococcal conjugate vaccine (PCV) has been shown to provide significant protection against childhood CAP in European and American countries. However, publications detailing the etiology of CAP are scarce in Asian countries. The heptavalent pneumococcal conjugate vaccine (PCV7) was introduced in Japan in February 2010 and switched to the 13-valent vaccine (PCV13) in November 2013.

Methods
To clarify the epidemiologic and microbiologic change of CAP before and after the introduction of PCV in Japan, a population-based surveillance study was conducted to cover CAP cases in children, admitted to hospitals in Chiba city, Japan. Patients with a positive blood culture or cultured sputum dominant for pathogenic bacteria were diagnosed as bacterial pneumonia. Serotype and antibiotic susceptibility testing of isolated pneumococcal strains were examined.

Pneumonia Etiological Agents in Vietnamese Children

Prof. Lay-myint YOSHIDA

Professor

Department of Pediatric Infectious Diseases

Institute of Tropical Medicine

Nagasaki University, Japan

Background: Acute respiratory infections (ARI) remain a main cause of morbidity and mortality in children. The World Health Organization (WHO) estimates about 156 million new pneumonias each year in children aged less than 5 years, of which 151 million episodes occurs in developing countries. Acute respiratory infections are caused by a broad range of viruses and bacterial pathogens. We utilize our ongoing population based pediatric acute respiratory infection surveillance established at Khanh Hoa General Hospital (KHGH) in Nha Trang, Vietnam in 2007 to investigate to role of viruses and bacterial on pediatric pneumonia in Vietnam.

Method: All children from our target population hospitalized at KHGH which is the only hospital in the region were enrolled to the study. Clinical-epidemiological information, nasopharyngeal samples were collected, routine blood testing and chest Xray were taken to all enrolled cases. Multiplex PCR assays were performed to determine the common respiratory viruses and bacteria. Periodical cross section viral and bacterial carriage surveys were perform to the healthy children in the community.

Results: We found that respiratory viruses were associated with 65 to 70% of hospitalized ARI cases, and Rhino, RSV and influenza A viruses were major viral pathogens. Multiple viral infection were detected in 12 to 15% of the cases, and RSV and HMPV infections independently increased the risk of pneumonia.

*Streptococcal pneumoniae* (SP) is the major bacterial pathogen for pneumonia and commonly colonize in the nasopharynx of children. We investigate the association of pneumococcal bacteria load and viruses in healthy, children with radiologically confirmed pneumonia (RCP), lower respiratory tract infection (LRTI) and healthy children. We found that SP load was higher in children with RCP compared with healthy controls or other LRTIs. SP load was 15-fold higher in pneumonia children with viral co-infection compared with those without (1.4x10^7/ml versus 9.1x10^5/ml; P =0.0001). SP load was over 200-fold higher in serotypeable SP compared with non-typeable SP (2.5 x10^6/ml versus 1x10^4/ml; P < .0001).

Vietnam introduced Hib vaccine into the national immunization program in 2010 so we investigated the role of Hib vaccine on hospitalized pneumonia cases on Vietnam. We found a substantial decline (17-29%) of RCP following Hib vaccination by statistical model. Reduction in healthy carriage was also observed. Our ongoing ARI surveillance has allowed us to determine the minimal clinical impact of 2009 pandemic influenza and high impact RSV ON-1 emergence in central Vietnam.

Conclusion: RSV, rhino, and influenza viruses and SP play important role among hospitalized ARI cases in Vietnam. Population based ARI surveillance study plays a crucial role to monitor newly emerging viruses.
Risk Factors for Pneumonia and Pneumococcal Vaccine Serotypes Among Children in Afghanistan

Rahmani Zabihullah a, Bhim Gopal Dhoubadhel b,*, Ferogh Abdul Rauf b, Sahab Ahmad Shafiq b, Motoi Suzuki a, Kiwao Watanabe a, Lay Myint Yoshida a, Michio Yasunami a, Kiwao Watanabe a, Lay Myint Yoshida a, Michio Yasunami a, Salihi Zabihullah c, Christopher M Parry b, Rabi Mirwais d, Koya Ariyoshi a

a Institute of Tropical Medicine, Graduate School of Biomedical Sciences, Nagasaki University, Japan; b School of Tropical Medicine and Global Health, Nagasaki University, Japan; c Abu Ali Sina Balkhi Regional Hospital, Mazar-e-Sharif, Afghanistan; d Public Health Department, Balkh Province, Afghanistan.

Objective: To investigate risk factors for death due to pneumonia at the time of hospitalization, and pneumococcal serotype distribution in children in Afghanistan.

Methods: We enrolled 639 under-5 children who fulfilled the World Health Organization (WHO) criteria for clinical pneumonia in a regional hospital in Afghanistan. Epidemiological, clinical and laboratory data were collected, and nasopharyngeal carriage of pneumococcus and its serotypes were determined. Findings: Malnutrition was detected in 39.9%, anaemia in 46.3%, and maternal illiteracy was reported in 85.9%. The case fatality ratio (CFR) of pneumonia was 12.1% (75/617) (95% CI: 9.6-14.9) with three quarters of the deaths occurring within 2 days of hospitalization. Age less than one month and malnutrition were the major risk factors for death, whereas female sex was also found to be a risk factor among malnourished group of children. BCG vaccination was protective. Pneumococcus was detected in 38.0% (124/326), which was characterized by 22 different serotypes. The thirteen-valent pneumococcal conjugate vaccine (PCV13) covered 41.1% of the circulating serotypes.

Conclusion: Early detection and treatment of serious pneumonia cases, and dietary interventions for malnutrition are urgently needed in Afghanistan. Although pneumococcal conjugate vaccine serotypes cover less than 50% of the circulating serotypes, the vaccination programme still can save many children’s lives.

Symposium E1
- Update on Infectious Diseases

Enterovirus 71 Infections in Children: Current Update

Prof. Tzou-yien LIN
Chair of the Board of Directors, National Health Research Institutes
Distinguished Professor, Chang Gung University, College of Medicine, Taiwan
Emeritus Superintendent, Chang Gung Children’s Medical Center, Taiwan

Enterovirus 71 (EV71) usually causes mild infections in children; however, a few of them can develop encephalomyelitis that resulted in fulminant cardiopulmonary collapse. Outbreaks with high mortality continue to threat health in children in West Pacific and European regions.

Early detection and prompt treatment is the mainstay of management. Currently no antiviral is available and the treatment is mainly supportive. We developed a stage-based management program for frontline pediatricians to provide the best of care and improve the clinical outcome. Meanwhile, neurological and respiratory rehabilitation program remains necessary to ensure the quality of life for some survivors with neurologic & psychiatric sequelae.

Genetic recombination is a well-known phenomenon for enteroviruses. Phylogenetic analysis indicated the intratypic recombination between C and B genotypes of EV71. Comprehensive recombination analysis showed the evidence of genome recombination of subgenotype C4 sequences between structural genes from genotype C EV71 and non-structural genes from the prototype strains of CAV16. This intertypic recombination C4 viruses were first seen in 1998 and became the predominant endemic viruses circulating for at least 18 years.

There has been rapid progress in the development of EV71 vaccine. Three inactivated, adjuvanted subgenotype C4 vaccines show efficacy in the phase III clinical trial and have been approved by China FDA. In Taiwan, we have completed phase II clinical trials for two inactivated subgenotype B4 vaccines and the results showed promising safety and immunogenicity.

The recent advances in our understanding of regulation of viral translation (FBP2 protein and vsRNA), EV71 3D polymerase, and human EV71-neutralizing antibody repertoire, provide new insight into the design of antiviral agents and an attenuated live vaccine.

Importantly we believe the enhancement of international collaboration & information sharing would be an important step toward a world free of EV71 in the near feature.
Rhinovirus Infections And Their Receptors In The Human Respiratory Tract

Dr. Renee Wan-yi CHAN
Assistant Professor, Department of Paediatrics, The Chinese University of Hong Kong
Co-Director, “The Chinese University of Hong Kong–University Medical Center Utrecht Joint Research Laboratory of Respiratory Virus and Immunobiology”

“It’s just a cold!” is the most common comment when people look at the rhinovirus (RV) infection. However, RVs are the dominant infectious causes of hospitalization in the paediatric population. It is not only an acute respiratory infection causing virus, it also contributes to the exacerbations of underlying respiratory diseases, such as asthma and chronic obstructive pulmonary disease. In addition, it is also the most frequently detected pathogen for the community acquired pneumonia in the adult.

With the tremendous number of RV infection, which is comparable to (or even exceeding) the number of influenza virus or the pneumococcal infections, there is yet an effective antiviral nor a vaccine against the human rhinovirus.

There are more that 100 serotypes of RV grouped into RV species A and B and vigorous research using standard cell line, primary human cells, animal models or even inoculation of human volunteers were performed. In contrast, due to the lack of susceptible cell lines in previous years, RV-C is understudied, though it is the species causing more viremia cases than the other two species while in epidemiology studies, RV-C has a similar prevalence to RV-A.

With the identification of cadherin-related family member 3 (CDHR3) as the cell-entry factor in 2015, on one hand, we got the tool to study RV-C and, on the other hand, we started to examine the distribution of this receptor, together with the two receptors ICAM-1 and LDLR utilized by the major and minor groups of the RV, respectively in human respiratory tract.

Our laboratory is currently working on the surveillance of human RVs of different genotypes and their functional grouping in association with clinical presentations.

Acknowledgements

RV efforts in my group are supported by CUHK Direct Grants 2015.1.055 and 2016.077. I thank Prof John Nicholls and Mr. Kevin Fung in the Department of Pathology, HKU for the immunohistochemical staining work and Dr Mars KP Tao, Dr Joseph GS Tsun, Mr Marvel HC Wang, Ms Waii WY Yu and Miss Tiffany TJ Li for their dedications to the laboratory works. I would like to express my special thanks to the patients who donate their biological samples to make our study possible. Special gratitude to Prof TF Leung and Prof Paul KS Chan of CUHK for their support in this research.

Inborn Errors of Metabolism

Symposium D1
- Paediatric Neurotransmitter Diseases

Synaptic Metabolism: a New Approach to Neurotransmitter Disorders

Dr. Angela GARCIA-CAZORLA
Department of Neurology
Neurometabolic Unit and Synaptic Metabolism Laboratory
Institut Pediatric de Recerca
Hospital Sant Joan de Deu, Barcelona, Spain

The synapse is a highly specialized structure with specific chemical composition devoted to neuronal communication. The concept of synaptic metabolism deals with the connection between metabolic pathways and functions that have been described by classical cell neurobiology. In other words, it tries to describe how metabolites and biochemistry regulate the function of key synaptic structures such as the vesicle cycle, ion channels and neurotransmitter receptors. From a practical point of view, it aims to gain knowledge in our approach to the pathophysiology and treatment of neurologic disorders in which neuronal communication is predominantly involved.

In summary, the learning objectives of this talk are:

- To update the classical concept of “inborn errors of neurotransmitters” which is now restricted to the synthesis, catabolism and transport of these molecules.
- To introduce new categories of neurometabolic diseases based on the description of biochemical pathways, trafficking and signaling functions at the synapse, and to recognize the main clinical manifestations.
- To introduce new therapeutic options based on this approach.
**Neonatology**

**Symposium C1 - The Improving Neonatal Care**

**Improving Outcome of Premature and Low Birth Weight Babies through Kangaroo-Mother Care (KMC) - Experience from Bangladesh**

Prof. (Dr.) Mahbubul HOQUE

Department of Neonatology

Dhaka Shishu (Children) Hospital & Bangladesh Institute of Child Health, Dhaka, Bangladesh

Immediate Past Secretary General, Bangladesh Neonatal Forum

Vice President, Bangladesh Paediatric Association

Member, Asia Pacific Society for Immunodeficiencies (APSID)

In Bangladesh about 77000 newborns die each year and almost 9 babies die every hour largely due to preventable causes. Major killers are Prematurity and its complications, Perinatal asphyxia and Sepsis. According to World Bank data, NMR in Bangladesh was 23.3/1000 live births in 2015. Our target is to reduce this NMR to 12 by 2030 to fulfill the SDG goal. To meet this huge challenge Bangladesh Government has prioritized KMC intervention to reduce death from prematurity. It is evidenced that it reduces nosocomial infection, hypothermia by 50-60% and improves rate of exclusive breastfeeding and thereby reduces neonatal mortality. In Bangladesh, a missionary hospital in the northern district has been practicing KMC since 1990. In 2013 Government of Bangladesh took steps to introduce KMC at the facility level.

Development partners like WHO, UNICEF, Save the Children came forward to help Bangladesh Government in scaling up KMC. Dhaka Shishu Hospital (DSH), the largest Pediatric hospital in the country launched KMC in Aug 2013. Following that some other tertiary and secondary level facilities also started KMC. In a district at Northern part of Bangladesh KMC started in 6 hospitals and till this April 262 babies received KMC and showed incredible success. Upto Dec 2016 total 1704 preterm babies were admitted in neonatal ward of DSH and out of these 522 babies were managed by KMC. Average weight of KMC babies was 1340gm. We have observed that rate of exclusive breastfeeding increased upto 90% which is 60% in non KMC babies. Rate of wt gain was found better in KMC babies than non-KMC babies (18±6g/day vs 13±5g/day).

---

**6-Pyruvoyl-tetrahydropterin Synthase (PTPS) Deficiency: Hong Kong Experience**

Dr. Grace Wing-kit POON

President of Hong Kong Society of Inborn Errors of Metabolism Associate Consultant in Paediatrics, Queen Mary Hospital

Honorary Clinical Assistant Professor, Department of Paediatrics & Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong

Council Member of The Education University of Hong Kong

Tetrahydrobiopterin is an essential cofactor of three important aromatic amino acid hydroxylase enzymes which are crucial in neurotransmitter metabolism and 6-Pyruvoyl-tetrahydropterin synthase (PTPS) is one of the enzymes involved in the biosynthesis of tetrahydrobiopterin. PTPS deficiency is a rare but important cause of severe metabolic encephalopathy in our locality and we would like to report our experience in managing this rare disorder and the long-term outcome of our patients.

---

**Tyrosine Hydroxylase (TH) Deficiency: Hong Kong Experience**

Dr. Dr. Wai-lan YEUNG

Associate Consultant, Department of Paediatrics and Adolescent Medicine,

Alice Ho Miu Ling Nethersole Hospital, Hong Kong

Honorary Clinical Assistant Professor, the Chinese University of Hong Kong and the University of Hong Kong

Vice President, Paediatric Neurology Association of Hong Kong

Tyrosine hydroxylase (TH) deficiency is a rare autosomal recessive monoamine neurotransmitter disorder. Tyrosine hydroxylase converts L-tyrosine to L-dihydroxyphenylalanine (L-dopa), which is essential for biosynthesis of catecholamines - dopamine, norepinephrine and epinephrine. The phenotype of TH deficiency ranges from 1) mild form with dopa-responsive dystonia, 2) moderate to severe form presenting as infantile parkinsonism with motor delay to 3) very severe form of progressive infantile encephalopathy. Only a few dozen cases have been reported in medical literature by 2003. Since our first case of TH deficiency in a Chinese family was diagnosed genetically in 2004, we have had more than 16 cases in Hong Kong over the past 13 years. Their clinical manifestations, biochemical findings, genetic mutations and treatment.
KMC babies suffered less from hypothermia (3% vs 30%). Apnoea episodes was less in KMC babies (8% vs 15%). KMC is KMC is an effective intervention, especially for developing countries to reduce neonatal mortality and morbidity from prematurity.

**The Application of Molecular Assays in Neonatal Infection**

Dr. Hugh Simon Hung-san LAM

*Associate Professor*

*Department of Paediatrics Faculty of Medicine*

*The Chinese University of Hong Kong*

Bacterial infection remains a major cause of morbidity and mortality amongst neonates. Delayed and/or inappropriate antibiotic treatment could have fatal consequences. The search for biomarkers to accurately diagnose bacterial infection early has therefore been an important area of research. Conventional biomarkers such as C-reactive protein, although widely used, have several limitations, e.g., upregulation several hours after clinical presentation, inability to distinguish between non-infective inflammatory conditions and genuine systemic bacterial infections and inability to derive information that could help rationalise therapy. Newer biomarkers based on inflammatory mediators involved earlier in the inflammatory cascade can achieve earlier detection of bacterial infections. However, despite the possibility of earlier detection of systemic inflammatory conditions which include bacterial infection, it is still challenging to determine specific information regarding the pathogen, e.g., bacterial identity and antibiotic resistance patterns. With molecular assays, e.g., polymerase chain reaction-based tests, it has become possible to detect Gram-negative bacteria and their antibiotic resistance patterns within hours of clinical presentation. These novel biomarkers and molecular assays can potentially improve outcomes of these infected neonates.

**Antibiotic Use in Neonatal Intensive Care Units**

Dr. Joseph Yuk TING

*Staff Neonatologist, British Columbia Women’s Hospital; Clinical Investigator, British Columbia Children’s Hospital Research Institute; Clinical Assistant Professor, Division of Neonatology,*

*Department of Pediatrics, University of British Columbia, Vancouver BC, Canada.*

Antimicrobial agents are the most commonly prescribed class of medications in neonatal intensive care units (NICUs). Suspicion of infection is often difficult to differentiate from other evolving pathologic processes in neonates, yet it can progress rapidly, with potentially disastrous consequences. This often leads to challenges in the initiation, selection, and duration of antimicrobial therapy. Early and decisive treatment with powerful antimicrobials tends to be the preferred clinical mantra. Broad-spectrum antibiotic exposure has been associated with altered bacterial colonization, resulting in the emergence of resistant organisms and increased rates of fungemia, necrotizing enterocolitis (NEC), and mortality. Our group recently demonstrated that among infants without culture-confirmed sepsis or NEC, the highest antibiotic utilization rate (AUR) quartile had significantly greater morbidity and mortality than the other three AUR quartiles. We also identified an association between high AUR and a composite outcome of death or adverse neurodevelopmental outcomes at 18-21 months’ corrected age. These findings highlight the importance of using antibiotics judiciously in NICU settings, which may minimize the collateral damage associated with antibiotic therapy and benefit neonatal outcomes. Therefore, NICU is a key location in which to deploy and perfect Antimicrobial Stewardship principles.
Early Events of Neocortical Histogenesis: Proliferation and Differentiation of Neural Progenitor Cells

Prof. Takao TAKAHASHI
Professor and Chair, Department of Pediatrics
Chief, Pediatric Neurology Service
Vice-Dean, Keio University School of Medicine
Keio University School of Medicine
President, Japanese Pediatric Society
President, Japanese Society of Child Neurology
Executive Board Member, International Child Neurology Society

The process of neuron production through proliferation/differentiation of neural stem/progenitor cells (NSPCs) and its contribution to the laminar formation of the neocortex will be reviewed.

Main topic of this lecture is “the decision-making characteristics of NSPCs”, that is, either to remain in the proliferative population or to exit the cell cycle and regulatory mechanisms that govern those behaviors.

Neocortical neuron number is precisely controlled by cell cycle exit probability (Q) of NSPCs.

A subtle change in Q leads to a significant modulation in the neuron number and the brain size.

The total number of neurons to be produced during neocortical neuronogenesis will ultimately determine the size of the brain and layer architecture of the neocortex, and hence define the higher cortical function of human being. In such a context, as an example of application of stem cell biology to child neurology, a mouse model of “in utero exposure to valproic acid” will be presented. The model shows that the antiepileptic drug valproic acid, also known as a histone deacetylase inhibitor, induces neocortical dysgenesis by Q alteration due to a nonspecific increase of G1-phase regulatory proteins; this illustrates the mechanisms of higher cortical function deficits reported in children prenatally exposed to this drug.

Inherited neuromuscular diseases (INMDs) are genetically and clinically heterogeneous diseases, mainly involving spinal motor neurons, neuromuscular junctions, nerves, and muscles. The majority of INMDs are hereditary, degenerative, rare, and delayed diagnosis. A timely molecular diagnosis of INMDs is crucial for providing precise drug treatment, genetic counseling including prenatal diagnosis, therapeutic strategies including standard of care, the available clinical trials, long-term care plans, and to avoid preventable complication such as malignant hyperthermia, to expand phenotype-genotype correlations, and to predict long-term prognosis.

With the ever-increasing numbers of causative genes, and phenotypic and genetic heterogeneity, a comprehensive molecular approach with the feasibility to add newly discovered genes for analysis in a cost- and time-effective manner is needed. The recent development of next-generation sequencing (NGS) including customized target capture panels, whole exome sequencing, and whole genome sequencing has accelerated the discovery of novel INMD phenotypes and genotypes. Compared with the traditional one gene at-a-time Sanger sequencing, NGS is a radically different approach to genetic sequencing. NGS allows for a large number of genes to be captured and sequenced in parallel, making a huge amount of data in a relatively short period of time at much lower cost “per gene.”

In this presentation, we will share our experiences of using target capture/deep sequencing approach to improve the molecular diagnosis of INMDs, and demonstrate the power of NGS in confirming and expanding phenotypes/genotypes of the extremely heterogeneous INMDs. We would stress the importance of deep phenotyping including physical and neurological examinations, electrophysiological, muscle radiological and histopathological findings, ancillary investigations of multiple systems, and familial aggregation will aid in interpreting NGS data.
Mitochondrial Diagnostics: Challenges in the Genomic Era

Dr. Cheuk-wing FUNG
Honorary Clinical Assistant Professor / Associate Consultant
Division of Paediatric Neurology, Developmental Behavioural Paediatrics, NeuroHabilitation, Department of Paediatrics and Adolescent Medicine,
The University of Hong Kong
Queen Mary Hospital / Duchess of Kent Children’s Hospital, Hong Kong

Next generation sequencing (NGS) has been a very promising technology for medical diagnoses. Use of NGS in diagnosing mitochondrial disorders (MD) has a positive yield of up to 60%. Duchess of Kent Children’s Hospital is a tertiary / quaternary referral centre for the diagnosis and management of MD in this locality. In collaboration with the Radboud Centre for Mitochondrial Medicine (Nijmegen), a total of 46 patients, recruited from 2009 to 2017, with the clinical suspicion of MD underwent NGS from a gene panel analysis to the opening of the whole exome if the former was negative. There was a positive diagnostic yield of 26% including 5 and 7 patients confirmed to have MD and non-mitochondrial neurogenetic disorders respectively. Significant clinical phenotypic overlap occurred in patients with MD and non-MD, necessitating the inclusion of a group of MD mimickers in the gene panel analysis. The phenotypic spectrum of our patients with a confirmed diagnosis will be illustrated including a non-specific cerebral palsy-like clinical picture. 6 patients had variants of uncertain clinical significance and further functional studies are ongoing. The power of NGS may have an impact on the use of conventional tissue biopsies for respiratory chain enzymologies as a first-line mitochondrial diagnostic test. On the other hand, functional analyses including respiratory chain enzymologies are still essential to validate some variants found by NGS. Recently, several biomarkers were found to be both sensitive and specific for MD including fibroblast growth factor 21 (FGF21) and growth and differentiation factor 15 (GDF15). However, our data suggested that these markers were not as specific as previously thought. They could be raised in other non-MD including channelopathies. A proposed diagnostic algorithm for MD would be discussed.

CNVs Discovered in Local Patients with Intellectual Disability and Autism

Dr. Ho-ming LUK
Senior Medical and Health Officer Clinical Genetic Service Department of Health, Hong Kong

Copy number variation (CNV) is the major cause of intellectual disability, dysmorphisms, multiple congenital anomalies and autism spectrum disorders in paediatric population. Currently, array comparative genomic hybridization is the first line investigation for the above condition. In this talk, a review of CNV in a cohort of 1,100 local patients with Intellectual Disability and Autism has been performed. The diagnostic yield and some interesting cases would be shared.

Symposium C2 - Neuromuscular Disorder, the Treatment, the Multidisciplinary Care and Quality of Life Issues

Diagnosis and Treatment of Neuromuscular Diseases – Local Advancement and Challenges

Dr. Sophelia Hoi-shan CHAN
Clinical Assistant Professor
Honorary Associate Consultant
Division of Neurology, Developmental Paediatrics & Neurohabilitation
Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine,
The University of Hong Kong, Hong Kong

Paediatric neuromuscular diseases (NMDs) describes a group of hereditary condition associated with disorders in the spinal motor neurons, peripheral nerves, neuromuscular junction and muscles, that often lead to muscle weakness, motor difficulties and sometimes other systems are also involved. Some of these conditions could have a progressive deteriorating course. In this review, an update regarding the most common neuromuscular diseases like spinal muscular atrophy and Duchenne muscular dystrophy, as well as the rare hereditary NMDs including non- 5q SMA, congenital muscular dystrophy, congenital myopathy and congenital myasthenic syndrome will be discussed focusing on the contemporary approach to diagnosis and treatment in our locality.

Several promising therapeutics are now being actively tested in clinical trials for some common neuromuscular diseases with the current better understanding of the underlying genetic pathogenic mechanism causing the important protein loss or dysfunction. While we are actively
participating in some of these internationally collaborated trials, the local patient registry, the standardization of care and the closely collaborated teamwork allows the early identification and recruitment of the suitable patients. With the recent overseas approval of some of the expensive treatment, we will also face a new era of management for our patients and families, with new challenges too very soon.

Developmental, Behavioral and Cognitive Profile of Neuromuscular Diseases in Child Assessment Service and Case Illustration

Dr. Chin-pang CHOW  
Senior Medical and Health Officer  
Tuen Mun Child Assessment Centre  
Child Assessment Service  
Department of Health, Hong Kong

The Developmental, Behavioral and Cognitive Profile of Neuromuscular Diseases (NMD) in Child Assessment Service and the quality of life of their caretakers will be presented.

An adolescent with a deteriorating course in an NMD will be presented as a case illustration. Issues in transition to tertiary education will be discussed including the liaison and conferences with the education institute regarding the special furniture, handwriting allowance and examination allowance, peer support.

Spinal Muscular Atrophy: Diagnosis and Management in the New Therapeutic Era

Prof. Yuh-Jyh JONG, M.D., D.M.Sc.

Department of Biological Science and Technology,  
College of Biological Science and Technology,  
National Chiao Tung University, Hsinchu, Taiwan

Graduate Institute of Clinical Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Departments of Pediatrics and Laboratory Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

Spinal muscular atrophy (SMA) is an autosomal recessive, progressive motor neuron disease mainly manifested with muscle atrophy and limb weakness in childhood, which caused by deletions or mutations in the survival motor neuron 1 (SMN1) gene with retained at least 1 SMN2 gene, and lead to deficiency of full-length SMN protein. To date, SMA is the leading genetic cause of infant mortality in the world.

There is no current active therapy other than supportive standard of care (SOC) for SMA until 2007. Even so the clinical care of infants and children with SMA has advanced significantly over the past two decades. Newer technologies, such as cough assist machines, non-invasive positive pressure ventilation, and gastrostomy tube feeding now offer home-based pulmonary and nutritional management, and have prolonged the survival of severe SMA infants. In 2016, there is a revisiting the consensus statement for SOC in SMA in 8 care areas: diagnostic and genetic counseling, pulmonary, acute care management in the hospital setting, orthopaedics (spinal curvature, joint contractures, fractures), physical therapy and rehabilitation, gastrointestinal and nutrition, other organ systems involved in SMA, ethical considerations and palliative care.

In the past decade, there has made a significant progress in understanding of both SMA molecular genetics and pathomechanisms. Multidisciplinary investigators have identified different SMN-dependent therapeutic approaches including SMN2 ISS-N1 targeting antisense oligonucleotides, SMN2 targeting small molecules, and SMN1 gene therapy that show promise in treating SMA. Until recently FDA has approved nusinersen, the first treatment drug for children and adults with SMA in US (December, 2016) and marketing authorization in Europe (June, 2017). Numbers of disease modifying interventions are rapidly bridging the translational gap from the bench to clinical trials. In this presentation, we will outline the most interesting therapeutic strategies that are currently developing, which are represented by multidisciplinary ways for the treatment and a changing landscape in this new therapeutic era of SMA.
Symposium G2

- Neuro-modulation for Epilepsy

Prospects for Non-Invasive Brain Stimulation in Epilepsy

Dr. Alexander ROTENBERG
Associate Professor of Neurology, Boston Children’s Hospital,
Harvard Medical School, the United States of America
Director, Boston Children’s Hospital Neuromodulation Program

Noninvasive brain stimulation methods are emerging as diagnostic and therapeutic tools in epilepsy. Two among these, transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) already have appreciable preclinical and clinical data to support their deployment either in large trials, or in day-to-day patient management. This lecture will focus on summarizing the basic neurobiology of TMS and tDCS, and will review their application in clinical and experimental epilepsy. Specific topics will include measures of cortical function and cortical excitability by TMS, seizure suppression by TMS and tDCS, and logical drug-device coupling.

Invasive Brain Stimulation for Epilepsy

Dr. Xian-lun ZHU
Consultant Neurosurgeon
Division of Neurosurgery
Department of Surgery
Prince of Wales Hospital
The Chinese University of Hong Kong

Invasive brain stimulation for epilepsy refers to a surgical option through electrical stimulation of the brain.

Various structures of the brain have been investigated as the target for stimulation, such as the thalamus, subthalamic nucleus, cerebellum, hippocampus and epileptic focus of cerebral cortex. Brain stimulation can be classified according to the targets and the stimulation modality:

1. To stop seizure onset by direct stimulation of epileptogenic zone, e.g. focus in the eloquent area, mesial temporal. The stimulation modality can be open loop (continuous stimulation), or close loop (responsive stimulation).
2. To stop seizure propagation by stimulation of certain key structure along the pathway to alter the epileptic network, such as deep brain stimulation (DBS) of the anterior nucleus of the thalamus (ANT).

DBS of the Anterior Thalamic Nucleus (ANT) and Responsive neurostimulation have been studied in large randomized trials in adult population.

In the responsive neurostimulation study with long term follow up (2011, 2015), the 50% seizure reduction responder rate was 44%, 53% and 58% at one, two and 3-6 years respectively.

In the ANT DBS study with long term follow up, (SANTE study, 2010, 2015), the 50% seizure reduction responder rate was 43%, 54% and 68 at one, two and five years respectively.

For ANT DBS, recent studies showed improved result by direct visualization of the target and stimulating the site where the mammillo-thalamic tract (MTT) joins the ANT.

Brain stimulation for epilepsy in paediatric population has been reported effective in small series.

In Hong Kong, three cases of ANT DBS have been done for refractory epilepsy since 2015 with encouraging results. Details will be presented.

Vagal Nerve Stimulation for Epilepsy

Dr. Eva Lai-wa FUNG
Honorary Clinical Assistant Professor
Department of Paediatrics
The Chinese University of Hong Kong

Epilepsy is one of the most common chronic neurological conditions in paediatrics. More than 30% of epilepsy patients still have ongoing seizures despite medical treatment, i.e., refractory epilepsy. Among them, only a small proportion of them are suitable candidates for respective surgery. Vagal nerve stimulation (VNS) has been approved for palliative treatment in refractory epilepsy since 1997. More than 85,000 devices have been implanted worldwide and its short-term and long-term efficacy have been documented in many studies. There is also new generation VNS therapy with additional feature of seizure detection algorithm based on ictal tachycardia, followed by automatic stimulation. However, VNS is relatively under-utilized in the territory. We will discuss the local experience of VNS use. We will also review the indications, precautions and side effects of VNS for treatment of epilepsy.
Symposium H2
- Epilepsy: From Cellular Biology to a New International Classification

Astrocyte Biology in Epilepsy

Dr. Alexander ROTENBERG

Associate Professor of Neurology, Boston Children’s Hospital,
Harvard Medical School, the United States of America
Director, Boston Children’s Hospital Neuromodulation Program

Despite introduction of numerous antiepileptic drugs in recent decades, the prevalence of drug-resistant epilepsy remains unchanged. In part, this may be due to persistent targeting of neuronal seizure mechanisms. As the field of astrocyte neurobiology expands, novel therapeutic targets are emerging. This lecture will focus on astrocyte basics, and the contribution of reactive astrocytosis to epileptogenesis. Specific topics will include astrocyte roles in synaptic potassium buffering and glutamate homeostasis, with a focus on novel therapeutic targets that can be engaged by available medications.

Epilepsy in Inborn Errors of Metabolism

Dr. Angela GARCIA-CAZORLA

Department of Neurology
Neurometabolic Unit and Synaptic Metabolism Laboratory
Institut Pediàtric de Recerca
Hospital Sant Joan de Deu, Barcelona, Spain

Seizures and epilepsy are frequent symptoms in inborn errors of metabolism (IEM). Many IEM interfere with important functions of brain metabolism such as the utilization of energy substrates, the metabolic coupling between neurons and astrocytes, the neurotransmitter turnover and signaling pathways, and the transport of substrates across the blood/brain barrier. These functions are involved in the regulation of excitatory/inhibitory balance and the way that brain circuits interact leading to epilepsy. However, although seizures are a very common sign of the “hyperexcitable” brain, only some IEM can cause epilepsy and epileptic syndromes as the predominant (leading) sign in the clinical manifestations.

These epilepsies can present across the life span, in most cases are refractory to anti-epileptic drugs, and very often do not present as an isolated symptom but associated with developmental delay, intellectual disability, behavioral abnormalities and neurological regression. Some of these disorders are treatable and they have to be considered in first place in the differential diagnosis of epileptic syndromes of unknown origin.

In this talk, we will focus on those IEM that present with epilepsy as a major clinical sign, how the onset-age determines what kind of disease and associated symptoms are present, what are the main biological mechanisms that cause epilepsy in IEM, and practical algorithms in the diagnosis and treatment.

ILAE Seizure and Epilepsy Classification

Dr. Ada Wing-yan YUNG

Associate Consultant, Duchess of Kent Children’s hospital, Hong Kong
President, Hong Kong Epilepsy Society
Council Member, the Hong Kong Society of Child Neurology and Developmental Paediatrics
Subcommittee, Epilepsy Surgery Working Group
Associate Member, American Epilepsy Society

The ILAE classification for seizures and epilepsies evolved from the popular versions in 1981 and 1989 to recent 2016 classification scheme. Different versions were compared and new changes were highlighted.
Nutrition
Symposium F4
- Common Nutritional Disorders

In Search for a Solution for Stunting - the Most Common Childhood Nutritional Disorder

Prof. Tahmeed AHMED
Senior Director, Nutrition & Clinical Services
Division, International Centre for Diarrhoeal Disease Research, Bangladesh (iccdr,b)
Professor, Public Health Nutrition, James P. Grant School of Public Health, BRAC University, Bangladesh

Stunting or linear growth retardation is the most common manifestation of childhood malnutrition. Defined as length for age less than 2 standard deviations from the WHO growth standard, stunting is due to chronic malnutrition. Asia has seen a reduction in stunting rates but still accounts for more than 60% of the global burden of stunting, while in Africa the prevalence is in fact increasing. Stunting not only blunts cognitive potentials of children, 14.5% of all under-five deaths in developing countries can be attributed to this condition. The World Health Assembly has declared a target to reduce stunting globally by 40% by 2025. Given the pace at which reduction is taking place, it is unlikely that the target will be met. The causes of stunting are multi-factorial. These include prenatal causes (maternal malnutrition, anemia, hypertensive disease of pregnancy), low birth weight, postnatal causes (inappropriate feeding, repeated infections, zinc deficiency, environmental enteric dysfunction (EED) or enteropathy etc), and environmental toxins such as aflatoxin. The importance of each factor is context-specific. Although food insecurity is a major underlying factor, lack of awareness regarding infant feeding is important. These determinants of stunting should therefore be the focus of programs for preventing stunting. Given the huge burden of stunting, it is imperative also to implement programs that reverse stunting in young children.

EED, caused by repeated exposure to bacterial pathogens which colonize the small gut and disrupt its mucosal architecture, is believed to be the cause of stunting in almost 40% of stunted children. The discovery of a simple, robust test for EED will greatly improve our understanding of the condition and the development of an intervention(s) that prevents/treats it.

Scaling up both nutrition-specific (for example, infant and young child feeding) and nutrition-sensitive interventions (food security, water, sanitation and hygiene etc) appear to be effective in reducing stunting in developing countries. Strong political commitment, budgetary allocation to support implementation of the above mentioned interven-

tions, multi sectoral collaboration and community-based service delivery platforms are essential.


Malnutrition and Chronic Illnesses in Early Life and Long Term Health Outcome

Prof. Way-seah LEE
Professor, Department of Paediatrics, Faculty of Medicine, University of Malaya Medical Centre
Immediate-past President, College of Paediatrics, Academy of Medicine, Malaysia
Head of Department of Paediatrics (2011-2016)
Fellow, Academy of Sciences, Malaysia

Both physical growth and development are highly influenced by genetic, nutritional and environmental factors. Malnutrition in infancy and early childhood is an important factor leading to stunted growth in adulthood. It is estimated that 925 million people are malnourished the world over and 165 million children < 5 years are stunted. Most of these are related to malnutrition during infancy or early childhood. In the period when nutritional intake are compromised, hormones which stimulate growth (such as insulin, IGF-1, growth hormone) are suppressed while hormones suppressing growth (such as corticosteroids) are stimulated. On the other hand, chronic illnesses, especially in diseases characterized by chronic inflammation, cause stunted growth via increased circulating level of various cytokines acting upon the physiological growth plate. For example, TNF-α and IL-6 which suppress levels of IGF-1, an important mediator of growth, are increased in chronic inflammation. Stunted growth in early childhood have been associated with various adverse outcome in adulthood. These include increased risk of metabolic syndrome, development, final adult height, schooling, academic achievement, as well as income. Thus, it is important to identify children at risk of nutritional compromised and treat the cause vigorously.
Obesity is one of the most important health problems in children worldwide. WHO defines obesity as a part of ‘the double burden of malnutrition’ along with nutritional deprivation. It is usually related to metabolic syndrome even in young age groups and the prevalence of obesity is rapidly increasing, especially in developing countries. In Korea, the prevalence of obesity increased from 5.8% in 1997 to 9.7% in 2005 according to the National Growth Survey. For the school age groups, this trend was still prominent. According to the National School Health Examination, the prevalence of obesity increased from 11.7% in 2010 to 13.4% in 2015. Including overweight, which is defined as BMI between 85 percentiles and 95 percentile of standard BMI, the prevalence could rise up to 21.8% in school age groups (7-18 year).

Secular trends of height increment in children has been a striking phenomenon during the last decades. According to the 2005 survey report performed by the Korean Pediatric Society, in association with the government, the mean height of boys was 50.4 cm at birth, 77.3 cm at 12 month of age, and 174.3 cm at 20 year of age. The mean height of girls was 49.9 cm at birth, 76.4 cm at 12 month of age, and 161.2 cm at 20 year of age. For the comparison, the mean heights of boy at 12 months of age were 74.8 cm in 1965, and 77.3 cm in 2005, respectively (2.5 cm of height gain), respectively. The mean heights of girl at 12 month of age were 72.8 cm in 1965, and 76.4 cm in 2005 (3.6 cm of height gain), respectively. The mean heights of boy at 7 year of age were 112.5 cm in 1965, and 124.9 cm in 2005 (12.4 cm of height gain), respectively. The mean heights of girl at 7 year of age were 112.0 cm in 1965 and 123.7 cm in 2005 (11.7 cm of height gain), respectively. The mean heights of boy at 20 year of age were 168.9 cm in 1965, 173.4 cm in 1997 and 174.3 cm in 2005 (4.5 cm and 0.9 cm of height gain, respectively), respectively. The mean heights of girl at 20 year of age were 155.9 cm in 1965, 160.4 cm in 1997 and 161.2 cm in 2005 (4.5 cm and 0.8 cm of height gain, respectively), respectively. Compared to 2015 school health examination data, there was little change in final height of late adolescents since 1997.

In summary, obesity epidemic has been still a big health problem in Korean children. There were great secular changes in final adult height from 1965 to 1997; nevertheless, there were little change in final adult height since 1997. There seems to be a relationship between growth acceleration during puberty and degree of obesity, but which should remained to be clarified for further study.

Orthopaedics

Symposium H3 - Common Orthopaedic Problems in Adolescents

Application of Scolioscan for Child Spine Health

Prof. Yong-Ping ZHENG

Henry G. Leong Professor in Biomedical Engineering

Interdisciplinary Division of Biomedical Engineering, The Hong Kong Polytechnic University

Background and Aims

Scoliosis is a medical condition defined as a 3D spine deformity with curvature of more than 10 degrees in the coronal plane. Scoliosis is usually seen in teenagers and known as adolescent idiopathic scoliosis (AIS). The prevalence of AIS is 2-4% of the general population, and it is regarded as the most common spinal diseases among kids. Scoliosis does not only affect the appearance in adolescents but also the imbalance of muscle tension, which may cause back pain. Severe scoliosis may also affect lung and heart function, even leading to death. Therefore, when the deformity is larger than 45 degrees, complicated surgical procedure is normally required to correct the deformed spine. Recently, a number of organizations, including American Academy of Pediatrics (AAP), have endorsed a position statement on “Screening for the Early Detection for Idiopathic Scoliosis in Adolescents”, indicating the importance of earlier detection and non- surgical management of AIS. (http://pediatrics.aappublications.org/)

The traditional scoliosis examination is X-ray radiography. However, there are some health risks posed by the radiation exposure – including an increased incidence of lung and breast cancers.

Although there are a number of screening approaches, but none of them are accurate enough, thus using X-ray is inevitable for AIS during diagnosis, curve progression monitoring, and treatment outcome evaluation, as well as during brace treatment. Thus, we developed a novel technology that enables safer and more frequent monitoring for scoliosis.
Methods

Scolioscan takes the advantage of 3D ultrasound imaging techniques and can provide 3D view of spine without any radiation (Fig. 1). Ultrasound probe is scanned over the spine to collect a series of image together with spatial information, and advanced imaging processing methods are used to form images in coronal views as well as in 3D [1-6]. Scolioscan has been used for scanning over 3000 scoliosis patients in Hong Kong, China, Macau, and The Netherlands.

Results

As shown in Figure 1, 3D US imaging of the spine is achieved. Excellent intra- and inter-rater repeatability of spinal process angle (ICC>0.8) and good correlation with X-ray Cobb’s angle (R>0.85) were obtained respectively in human trials [5]. In addition, semi-automatic and automatic results obtained using different algorithms showed good agreement with manual and X-ray Cobb’s angle [6].

Conclusions

Scolioscan can provide radiation-free while accurate assessment of scoliosis, and has the ability for evaluating spine deformity in 3D, thus is a unique tool for scoliosis screening and monitoring. Effects on spinal curvature under different postures and properties of spinal muscles can also be investigated in patients with scoliosis or other musculoskeletal diseases in children using Scolioscan.

References


Adolescent Idiopathic Scoliosis

Prof Jack CHENG

Department of Orthopaedics and Traumatology
Choh-Ming Li Professor of Orthopaedics & Traumatology
Faculty of Medicine
The Chinese University of Hong Kong

The term scoliosis was first used by Galen (A.D. 131-201). The most common form is Adolescent Idiopathic Scoliosis (AIS) which typically affects an otherwise healthy girl in the early stage of pubertal growth. The incidence of AIS worldwide is 1-4% and the prevalence in Hong Kong is 3.6% in girls and 1.3% in boys. Scoliosis deformity when not treated or improperly treated may progress and deteriorate leading to significant cosmetic problems and functional disabilities and cardiopulmonary compromises in the severe cases. Considerable advances have been made in the treatment of scoliosis in the past few decades as a result of improved knowledge of the 3D deformity of scoliosis, the availability of new non-operative and surgical treatments and the parallel advances in related supportive techniques. Despite all these advances, the etiology and etiopathogenetic mechanisms of AIS are still unclear. Without being able to prevent and treat the primary cause yet, the current treatments are primarily targeting at controlling further progression of the deformity.

This lecture will present a general overview of the clinical presentation and treatment and briefly touch on some of the latest advances in AIS epidemiology, key concepts and hypotheses arising from some of the current multidisciplinary research related to the etiopathogenesis of AIS.
Adolescence Sports Injuries of the Knee: From Prevention to Treatment

Prof. Patrick Shu-hang YUNG
Professor & Chief, Sports Medicine Team, Department of Orthopaedics & Traumatology, Faculty of Medicine, The Chinese University of Hong Kong
President, Hong Kong College of Orthopaedic Surgeons
President Elect, Asian Federation of Sports Medicine

Because of increasing participation in contact or pivoting sports, such as soccer, Rugby, basketball..., there has been an increasing incidence of sports injuries among the adolescence group, particularly among the girls, with knee injuries high on the list. Apart from acute injuries such as ACL, meniscus & cartilage injuries, which can lead to serious long-term disability, there is also more and more overuse injuries of the knee being seen among this group of young patients. This is probably because of early participation and sub specialization in sports participation among adolescence nowadays, particularly among the elite/competitive group of athletes. Over the past years, advancements in different rehabilitation & surgical techniques have significantly improved the outcome of management of such kind of injuries. Nevertheless, because of the increasing incidence of injuries, more demand and resources have been allocated into the work on sports injuries prevention. This lecture will cover the recent developments in the treatment & prevention of sports injuries, among the adolescence group.

Respirology

Symposium B3 - Common Respiratory Disease

Adverse Consequences of Sleep Deprivation in Hong Kong Adolescents – Cardiovascular Perspective

Prof. Albert Martin LI
Assistant Dean (Development) Professor, Department of Paediatrics
Faculty of Medicine
The Chinese University of Hong Kong

Sleep deprivation is a world-wide phenomenon and the issue is even more concerning for adolescents. Biological changes during adolescence lead to a shift in circadian phase preference from “morning” to “evening” type. The accumulation of sleep drive during daytime is slower relative to younger children, thus adolescents can easily cope with late bedtime. In addition, environmental and lifestyle/social demands such as extracurricular activities and home-work are other important culprits in pushing back sleep time. However, the sleep needs of adolescents do not reduce significantly and therefore a great proportion of them are chronically sleep deprived. In Hong Kong, a significant number of adolescents report to be sleeping for <6.5 hours during school term time, where the recommended sleep duration is 9 hours. Adolescents are well known to sleep compensate during school holidays. A difference of up to 2-3 hours in sleep duration between school term and holiday is often reported.

Chronic sleep deprivation is associated with a number of significant short and long term consequences. Adverse health outcomes that include sleepy driving-related crashes, obesity and metabolic dysfunction have been demonstrated in sleep-deprived adolescents. Impaired mood and behavioural control, neurocognitive deficits, suboptimal academic performance, increased tardiness and absenteeism have also been documented. Sleep duration impacts on blood pressure (BP) and acts as a risk factor for hypertension. Results from cross-sectional studies on adolescents have shown negative relationships between sleep duration and BP. Short sleep duration in adolescents can lead to prehypertension, increased systolic and 24-hr BP.

Maintaining healthy cardiac status in childhood and adolescence is vitally important. Childhood BP tracks into adulthood and the tracking coefficient is greater for adolescents. Forty percent of adolescents with hypertension have already developed left ventricular hypertrophy at the time of diagnosis. One of the risk factors to account for early deaths and coronary heart disease amongst young adults is elevated BP and hypertension in childhood and adolescence. Thus it is essential to tackle any BP abnormality in childhood and adolescence promptly in order to
minimize future adverse cardiovascular events.

In children and adolescents, delaying school start time is a mean to increase sleep duration. Significant improvements are seen in markers of health and academic success in association with later school start times. However, delaying school start time in our locality has met with strong resistance from teachers who have to re-schedule the “lost time” into an already packed timetable, parents as any alteration to the school schedule may jeopardise their children’s after school extra-curricular activities and private academic tuition, and school bus companies as any delay implies a change to their busy schedules and that may affect their overall revenue.

In this talk, the presenter will review the latest literature linking sleep deprivation and cardiovascular adverse outcomes in the paediatric population and will share with the audience his on-going study that takes advantage of changes in sleep duration that occur during school holidays in adolescents to assess whether prolonging adolescents’ sleep would lead to a reduction in their BP.

Childhood Obstructive Sleep Apnoea Syndrome – What’s New?

Dr. Kate Ching-ching CHAN
Assistant Professor
Department of Paediatrics
The Chinese University of Hong Kong

Obstructive sleep apnoea (OSA) is one of the most common forms of sleep disordered breathing in children. The diagnostic gold standard is nocturnal polysomnography (PSG). However this diagnostic service has limited availability particularly in resource scarce settings because it is expensive and labour intensive. Recently developed neural network-based automated analysis of nocturnal oximetry recordings provides reliable identification of OSA severity among children with habitual snoring and high pre-test probability of OSA, and thus may allow a diagnostic alternative for more timely diagnosis and intervention of the disease condition. Childhood OSA is known to be associated with various morbidities, namely cardiovascular, metabolic and neurobehavioural complications. However, it is increasingly recognised that phenotypic variation in terms of end organ complications exists even for the same degree of severity of OSA. Recent research has tried to address the mechanistic pathways in the pathogenesis of paediatric OSA, and to identify biomarkers and factors to predict phenotypic variability of OSA related consequences and treatment response. An overview of recent studies exploring morbidity-related biomarkers in children with OSA will be given through this presentation.


Air Pollution and Allergy

Dr. So-lun LEE
Honorary Clinical Associate Professor
Department of Paediatrics and Adolescent Medicine
LKS Faculty of Medicine
The University of Hong Kong

There is substantial evidence to support the adverse health effect of air pollution. In this presentation, the focus will be on the effect of air pollution and allergic diseases in children, who are most vulnerable to the effect of air pollution. Local studies, for example, effect of smoke-free legislation on childhood asthma, and the effect of indoor and outdoor pollution on childhood allergic diseases will be used as reference to illustrate the relationship.
Autoinflammatory diseases are a group of genetically heterogeneous diseases. In the past, many of these diseases have been misdiagnosed therefore causing delay in starting effective treatment which can result in permanent organ damage e.g. intellectual disability, deafness and blindness or early onset renal failure secondary to amyloidosis. This not only affects the quality of life of the patients but also burdens the families heavily. With the advancement of new technologies in genetic tests, next generation sequencing (NGS) methods (targeted sequencing of a gene panel or whole exome sequencing) has allowed timely genetic characterization of many of the diseases at an affordable cost. However, this is not the ultimate solution and answer for autoinflammatory or any other inheritable diseases. There are on-going and heated discussions on genotype/phenotype correlations, role of environmental triggers of gene expression, the sequencing of non-exomic DNA consisting of introns and regulatory regions of a gene (whole genome sequencing), the dilemma of detecting a carrier state or sequences/variants with unknown clinical significance. Nonetheless, it is undeniable that genetic technologies are a powerful tool. In order to make the best use of this tool and benefit our patients and their families to the best extent, we have to apply the tests wisely and strategically. We can make the headway by promoting three things in our daily clinical practice: acquiring a good knowledge of this ever-expanding group of diseases through easily accessible learning platforms, arranging genetic counselling services to patients and families both before and after genetic tests and contributing to the established genetic database of autoinflammatory diseases.

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by presence of auto-antibodies to nuclear antigens and augmented interferon type 1 production, leading to inflammation that results in multiple organ damage, notably kidneys. There is an ethnic and gender bias in SLE incidence and severity which may be contributed by genetic, hormonal and environmental factors. SLE can be inherited as complex or monogenic disease, which have been investigated by genome-wide association studies and exome sequencing respectively. Twin studies and sibling risk ratio suggesting a high heritability of SLE of 60%.

Genome wide association studies (GWAS) of SLE have identified over 50 potential candidate genes which explain less than 30% of the heritability of SLE. These 50 genes are involved in apoptosis and clearance of apoptotic debris; lymphocyte and innate immunity signaling as well as intra-renal signaling. The limitations of GWAS include not being optimal to identify rare genetic variants and structural variants, requiring large number of subjects and controls for sub-phenotyping. The future genomic studies include investigating role of HLA, micro RNAs, epigenetics and copy number variations.

Exome and genome sequencing (EGS) has identified many types of monogenic SLE. Monogenic SLE include complement deficiencies of C1q, C1r/s, C2 and C4, as well as type 1 interferonopathies with defects in cytosolic DNA and RNA sensing and clearance, which can be due to mutations in DNASE1, DNASE1L3, TREX1, TMEM173, SAMHD1, RNASH2, ADAR1 and IFIH1.
Antiphospholipid syndrome (APS) is an uncommon entity in childhood. The entity was described for the first time in early 1980s and the antibodies implicated were anti-cardiolipin antibodies. About half of children with APS have primary APS. In children, APS is more commonly associated with SLE than in adults. Association of various manifestations of systemic lupus erythematosus (SLE) were found to be associated with the presence of anti-phospholipid antibodies. The common ones being portal and pulmonary hypertension (1), cerebral infarction (2), thrombocytopenia (3), pulmonary hypertension (4) and chorea (5). Diagnosis of APS including paediatric APS is based upon clinical features of either vascular thrombosis or pregnancy morbidity in the presence of antiphospholipid antibodies. It is obvious that pregnancy morbidity is not of relevance in paediatric age group and there are other clinical features like lived reticularis, chorea that suggest the presence of APS in children. These cutaneous, neurological and haematological manifestations are not taken into account while defining APS in children. Evidence- based recommendations for diagnosis and treatment of paediatric APS have been recently published by The Single Hub and Access point for paediatric Rheumatology in Europe (SHARE) (6).

73 children with SLE were tested for anti-phospholipid antibodies. 56 (76.7%) were girls. 7 had LAC (DRVV) positivity, only one had LAC (SCT) positivity. Only 2 had LAC (DRVV) positivity on repeat testing. The one who had LAC (SCT) positivity turned negative on repeat testing, but a new patient tested positive at repeat testing for LAC (SCT). 20 had ACA IgM positivity, 3 had ACA IgG positivity at the time of initial testing. ACA IgG was not detected in any of the patients while ACA IgM was detected in 7 on repeat testing. Anti-β2GP1 was not detected in any of the patients while Anti-β2GP1 IgG was found in one on repeat testing. One patient had triple positivity (on repeat testing). Six patients had thrombotic complications with SLE. Two had pulmonary thromboembolism (PTE), 1 had deep vein thrombosis (DVT) of lower limbs, 2 patients had old CNS infarcts and 1 had acute infarct in CNS. One patient with LA hypoprothrombinemia syndrome presented with refractory coagulopathy and bleeding.


Hong Kong College of Paediatric Nursing (HKCPN) Symposium

Symposium F1 -Towards Better Nursing Practice and Training

Music as a Mnemonic Aid in Basic Life Support (BLS) Training on Improving the Skill Mastery of Trainee: A Pilot Study

Tomcy SF LEUNG¹, Prof Doris SF YU², Prof KC CHOI²

Queen Mary Hospital¹; The Chinese University of Hong Kong²

Background:
Quality of chest compression in resuscitation such as compression rate and depth is associated with the return of spontaneous circulation (ROSC) in victims with cardiac arrest. However, the skills of the providers are often suboptimal even after training. Thus, there is an emerging need in the development of an evidence-based and high quality CPR training programme to enhance the skill mastery of the learners. Nevertheless, prompt devices are incorporated into training to improve the mastery of resuscitation skills in the last decade.

Aim of the Study:
It was aimed to estimate the effects of compression quality by using song as the prompt device in BLS training among paediatric nurses.

Methodology:
This was a prospective randomized study. Paediatric nurses from a local hospital were recruited and allocated randomly into control and song groups. The BLS training consisted of lecture and practice on an infant manikin (Resusci baby QCPR, Laerdal). The song “Stayin’ Alive” by Bee Gees was played during training and practice in the song group. The compression skills from 2-person infant CPR were assessed at three time points: before (T0) and after training (T1), and one week after (T2). Data of the compression quality were collected and analyzed using IBM SPSS 23 (IBM, NY). The generalized estimating equation (GEE) model was used to compare the repeated measures outcomes between two groups.

Results:
Forty paediatric nurses were recruited and three nurses did not turn up (control n=20; song n= 17). The two groups were equivalent in gender, time since previous BLS training, and CPR experience. However, the nurses in the control group were older in age (p=0.025) and had longer work experience (p=0.03). Both groups were able to perform chest compressions with mean rate according to 2010 AHA guidelines, 94% of nurses in the song group performed compressions at correct rate (100-120cpm) at one week after as compared to 75% of nurses in the control group. Yet, this study failed to identify any significant difference in the compression qualities between the two groups.
Conclusion:
Using song as a prompt device in BLS training was feasible. It could serve as a mnemonic aid to guide the nurses for chest compressions.

Research in Paediatric Simulation Education – Education Model, Clinical Practice and the Big Data

Mr. Jacky Chun-kit CHAN
Registered Nurse
Accident & Emergency Training Centre
Runtonjee and Tang Shiu Kin Hospital
Hospital Authority, Hong Kong

Simulation education is popular in recent years. Other than learning outcomes, the clinical impact and related research are also very important. This sharing will show how the research integrate with the Brinkerhoff 6 level of learning evaluation model, with the example from research publications and paediatrics simulation education in Hong Kong:

- NRP (Neonatal Resuscitation Program): usability and efficiency of the NRP Cart
- STABLE program: Using scenario checklist with statistic analysis to determine the number of the scenario
- NETS (Neonatal Emergency Transportation Simulation): Big data research: how to extract data from simulation scenario video recording
- Education 4.0 model - group based learning with virtual patient simulation

Development and implementation of the Victorian Children’s Tool for Observation and Response (ViCTOR)

Dr. Sharon Bridget KINNEY
Senior Lecturer, Department of Nursing, The University of Melbourne
Research Fellow, Department of Paediatrics, The University of Melbourne
Nurse Consultant Research, The Royal Children’s Hospital Melbourne
Australia

Best practice stipulates that patient observation charts should identify thresholds for vital signs (such as respiratory rate) and incorporate a ‘track and trigger’ system to escalate care when deterioration occurs (Australian Commission for Safety and Quality in Health Care, 2011). The Australian Commission for Safety and Quality in Health Care (ACSQHC) developed a suite of standardised observation and response charts for adult patients; however, there were no plans to develop national charts for paediatric or newborn patients.

In Victoria, lack of consistency in the parameters for identifying deterioration, and lack of consistency in design and format of paediatric observation charts, highlighted the need for a standardised statewide approach.

Since 2013, the Victorian government has funded the Victorian Children’s Tool for Observation and Response (ViCTOR) projects. Following sector-wide engagement and drawing on the most recent evidence of respiratory rate and heart rate percentiles for hospitalised children, a set of standardised charts was developed, incorporating age-related vital signs and other clinical observations for children across five age groups. Initially piloted in 12 hospitals and following a multi method evaluation including chart audits, user surveys and focus groups the charts were released for statewide use late 2014.

A subsequent project evaluating the ViCTOR charts suitability for smaller rural health services resulted in the release of a set of ‘ViCTOR Urgent Care’ charts in late 2015. A series of Back to Basics (B2B) videos were also developed demonstrating how to conduct vital signs in children aged 0 – 18 years. To date, more than 70 Victorian health services, both public and private, are using the ViCTOR suite of charts.

On the back of ViCTOR’s success the maternity and newborn sector recognised the need for a similar standardised approach to recognition and response to deteriorating newborns. Two newborn charts were developed and piloted to meet the needs of two main groups of patients: ‘ViCTOR Birth Suite/Postnatal’ for use in all newly delivered babies and ‘ViCTOR Special Care Nursery’ for use in the special care nursery environment. These charts have recently been released for statewide use.

The ultimate goal of the ViCTOR charts and associated escalation of care processes is to provide timely medical care to any deteriorating patient and so eliminate unexpected but preventable mortality, cardiac arrest and other life-threatening events. We are now about to commence an evaluation of the clinical impact that ViCTOR has on quality and safety outcomes.

Further details about the ViCTOR work and resources can be found: https://www.victor.org.au/
Advanced practice is a level of practice, rather than a type or specialty of practice. Advanced practitioners are educated at master’s level in advanced practice and are assessed as competent in practice using their expert knowledge and skills. They have the freedom and authority to act, making autonomous decisions in the assessment, diagnosis and treatment of patients” (Royal College of Nursing, 2016)

With an ever increasing demand for healthcare it has never been more important to have the right staff, educated and competent, able to deliver the best care possible at the right time for patients. Leadership and innovation are the key to developing and delivering the right services and care and improving health and wellbeing outcomes for people. Registered Nurses are increasingly extending and expanding their scope of practice beyond initial registration in all healthcare settings developing their skills, competence and confidence.

Registered nurses working at an advanced level of practice work in various health care settings, in hospital and in the community and within specialities such as paediatrics and neonatal care; in any setting where patients would benefit from nurses with advanced level skills and knowledge.

This presentation will define advanced level nursing practice and signpost listeners to relevant domains and competences for advanced level nursing practice in the UK and internationally. The presentation will also explore the standards for the accreditation of advanced nursing practice educational programmes and outline the new RCN Credentialing framework, which may be of interest to delegates.

Background
Prematurely born infants have immature body organs and body function and thus there are anticipated health problems. The more premature the infants, the more health problems they could have. Despite an increased risk of behavioural and/or developmental deficits, with the advancement of neonatal intensive interventions, more premature infants can survive. Nevertheless, their survivors are not absolutely free from complications, long term impacts on parenting, family and health services could result. Parents of very premature infants are stressful in seeing their fragile infants. This could be related to the alternation in parenting and confronting to the technical environment of neonatal intensive care unit. Evidence suggests that effective discharge interventions enhance parenting competency and mitigate the high level of stress in taking care of the infants after discharge.

A pilot randomised controlled trial was conducted to evaluate whether implementing a guided participation discharge programme in a neonatal intensive care unit can improve parenting sense of competence and parental stress. The population includes very premature (gestational age ≤32 weeks) infants with no congenital abnormalities and required no major surgery right after the infants was born. The sample included 30 very premature infant-parent pairs divided into the intervention and control group. The participants in the intervention group received three bedside guided participation discharge intervention training sessions and one follow-up telephone call after discharge. The control group participants received usual care including three condition updates and a follow-up telephone call after discharge.

Two self-reported questionnaires, the Chinese version of the Parenting Sense of Competence Scale (PSOC) and the Chinese version of the Perceived Stress Scale-10 (PSS-10) were delivered to parents soon after admission when the consent for the trial were obtained at T₀, at the time of discharge T₁, at the time after telephone follow up T₂, and at one month after discharge T₃ to evaluate for the parental outcomes.
Key findings
With adjustment on the confounding factors, the estimated change of parenting sense of competence score in the intervention group was significant ($p=0.01$) at the time when the infant was discharged from hospital ($T_1$). On the other hand, the estimated change of perceived stress score was not significant throughout all the time points except at one month after hospital discharge ($T_3$), the estimated change of perceived stress score in the intervention group was significant ($p=0.03$).

Significance of the study
The study can arouse the awareness of neonatal nurses for the need of further studies on this scope. Despite there were limitations of the study, the guided participation discharge intervention demonstrated significant effect at certain time points to enhance the parenting sense of competency and to mitigate perceived stress of the parents. In the future, further studies with adjustment on the implementation time point, adjustment on the dose of interventions, addition of measurement in parental knowledge, measurement of parental satisfaction, and involvement of different neonatal units are recommended.

Chinese Pediatric Society (CPS) Symposium

Symposium F2

China Children Asthma Action Plan

Kunling SHEN<sup>1</sup>, Jing ZHAO<sup>2</sup>, Ju YIN<sup>1</sup>, Li XIANG<sup>1</sup>, Chuanhe LIU<sup>2</sup>, Yixiao BAO<sup>3</sup>

<sup>1</sup>National Clinical Research Center for Respiratory Diseases, Department of Respiratory Medicine, Beijing Children’s Hospital, Capital Medical University, National Center for Children’s Health, China, Beijing 100045, China

<sup>2</sup>Center for Asthma Prevention and Education, Capital Institute of Pediatrics, Beijing 100020, China

<sup>3</sup>Department of Pediatric Pulmonology, Xinhua Hospital affiliated with Shanghai Jiao Tong University, School of Medicine, Shanghai, China

Childhood asthma is the most common chronic disease to children. Asthma action plan has been advocated by the Global Initiative for Asthma and international asthma guidelines to achieve self-management for more than 20 years and has been proven to be effective to improve asthma-related outcomes. In accordance to National Guideline for Diagnosis and Prevention of Childhood Asthma, the first China’s children asthma action plan, China Children Asthma Action Plan (CCAAP), as well as a mobile phone-based asthma self-management application (APP), have been developed. The principles of CCAAP include tracking changes in child patients’ symptoms and/or peak expiratory flow, using a “traffic light” model with green (well), yellow (caution), and red (danger) zones, to identify patients’ current asthmatic conditions. Each zone consists of both instructions which are intended for parents or caregivers to recognize loss of asthma control, and intervention strategies with various extents that patient could take when loss of asthma control occurs in settings outside of medical care facilities. The mobile phone-based asthma self-management APP (Youran Respiratory) includes an electronic version of CCAAP, peak expiratory flow monitor system, educational resources for asthma, and an interactive function between patients and doctors. The action plan should be provided to asthmatic children when diagnosis is confirmed; update each time when child patient discharged from hospital or emergency; and for patient’s pediatric practitioner to continue to monitor patient’s conditions. CCAAP will help asthmatic children and their caregivers to attain a batter and a more convenient way to achieve asthma control.

CCAAP is a milestone of asthma self-management for children in China, it will be an effective tool for health care providers, children, parents/caregivers to understand the
key points of asthma management and to achieve well control and eventually to improve quality of life.

**Keywords**—Asthma Action Plan, Mobile-Phone, asthma management application (APP), children, China

---

**Symposia Lectures**

---

**Disease Severity and Genetic Variation of Glycoproteins in the Respiratory Syncytial Virus-A ON1 Genotype in Chongqing of China from 2009 to 2016**

Lili WANG¹, Xiaohong XIE², Yu DENG², Na ZANG², Zhengxiu LUO², Zhou FU², Luo REN¹, Enmei LIU²

¹Department of Respiratory Medicine, Children’s Hospital, Chongqing Medical University. Paediatric Research Institute of Children’s Hospital of Chongqing Medical University, Chongqing Key Laboratory of Child Infection and Immunity, Ministry of Education Key Laboratory of Child Development and Disorders, China International Science and Technology Cooperation Base of Child Development and Critical Disorders, Chongqing 400014, China

²Department of Respiratory Medicine, Children’s Hospital, Chongqing Medical University, No. 136, Zhongshan 2nd Road, Yuzhong District, Chongqing, 400014, People’s Republic of China.

Respiratory syncytial virus (RSV) is a leading cause of acute respiratory tract diseases in younger children. ON1 is a new genotype of RSV-A found in 2010, which is characterised by a 72-nucleotide duplication in the G protein gene. To comprehensively understand the prevalence of the ON1 genotype in Chongqing, we monitored the circulation pattern of RSV-A over seven consecutive years (June 2009 to June 2016). We found that ON1 has become the predominant genotype in Chongqing. Compared with the NA1 genotype, children infected with ON1 genotype RSV-A tended to develop a more severe form of the disease. We searched for the reasons for this at the amino acid level and found that the ON1 genotype was subject to insertion of duplicate sequences, positive selection in G proteins, amino acid mutations in neutralising antigenic site Ø and HLA-restricted epitope HLA*B57 in F proteins. The evolutionary rate was $4.2 \times 10^{-3}$ nucleotide substitutions/site/year for G proteins of the ON1 genotype and $8.6 \times 10^{-4}$ nucleotide substitutions/site/year for F proteins. Surveillance of genotype ON1 and analysis of the molecular epidemiology of the G and F proteins may be helpful for the development of vaccines against RSV infection.

**Key words**: human respiratory syncytial virus, ON1 genotype, G protein, F protein, severe lower respiratory tract infections, child

---

**Pediatric Sleep Disordered Breathing in Mainland China**

Prof. Zhifei XU, MD

Associate professor of Pediatrics
Respiratory Department, Beijing Children’s Hospital, Capital Medical University, National Center for Children’s Health, China

Beijing Children’s Hospital (BCH) first established a one-bed sleep lab in 2002 and a new sleep center with 12 beds was opened in 2013. There are several pediatric sleep labs in mainland China now. Besides, sleep services are offered in various departments of children’s hospital and pediatric department in general hospitals. Night time snorers are the major population coming for sleep study. Current data showed that sleep disordered breathing (SDB) are common in Chinese pediatric population and sleep disorders can lead to serious morbidity if left untreated. A questionnaire survey performed in children in eight major Chinese cities showed that 27.1% of 28424 children them had sleep disorders. Another questionnaire survey in Shanghai showed a prevalence of snoring of 16% in 1812 children. A positive relationship between the degree of obesity and the severity of OSAHS was reported as well. Furthermore, a recent study showed a positive relationship between OSAHS and metabolic syndrome. Interestingly, recent studies have demonstrated that an active leukotrienes (LTs) mediated inflammatory response is involved in pathophysiology of SDB, which might provide a theoretical evidence for LTs modify therapy in treating pediatric OSAHS. Besides, the efficacy of various treatments such as surgery, and non-invasive ventilation were also investigated in numerous studies in Chinese pediatric population.

**Key words**: child, sleep disordered breathing, epidemiology, complication, treatment
Growth and Metabolic Abnormalities in Children Born Small for Gestational Age

Prof. Xiaoping LUO

Professor and Chairman, Department of Pediatrics,
Tongji Hospital
Director, Center for the Diagnosis of Genetic Metabolic Diseases, Tongji Medical College, Huazhong University of Science and Technology
President, Chinese Society of Pediatric Endocrinology and Metabolism (CSPEM), CMA
Vice President, Chinese Pediatric Society (CPS)
Past President, Asia Pacific Paediatric Endocrine Society (APPES)
Board of Director, Asia Society of Inherited Metabolic Diseases (ASIMD)
Executive Committee, Global Pediatric Endocrinology and Diabetes (GPED)
Council, Growth Hormone Research Society (GRS)

Small for gestational age (SGA) refers to a group of infants with birth weight and/or length is less than the 10th percentile of the population and the reported incidence was around 6.61% in China, with a multi-factorial etiology. A number of genomic imprinted disorders were associated with SGA, including Prader Willi syndrome, Angelman syndrome and Silver Russell syndrome with characteristic clinical and molecular features. Most SGA infants will develop catch-up in growth, normalizing their height by the age of 2 and achieving a final height within normal range. About 10% of SGA failed to achieve catch-up growth, resulting in childhood and adult height -2SD below the mean. Aside from acute perinatal adverse events, the children born SGA often manifest with long-term metabolic and endocrine consequences including insulin resistance, metabolic syndrome and social neuro-developmental problems. Recombinant human growth hormone (rhGH) was approved as an indication for short SGA by the FDA, EMEM and other authorities at 2 to 4 years of age, and was recommended by consensus guidelines from pediatric endocrine societies. Current data suggest that rhGH treatment can safely improve height and HRQoL in children born SGA. Whether the rhGH treatment should be started at or before the first year of age is under debate.
Allergy and Immunology

Calcineurin inhibitors exacerbate Nod1-mediated coronary arteritis via the MyD88 signaling pathway

Kenji Murata1, Yoshitomo Motomura1,2, Shunsuke Kanno1, Hisanori Nishio1, Yasunari Saka1, Hidetoshi Takada1, Shoichi Ohga1, Sho Yamasaki2, Toshiro Hara2,3

1Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, 2Division of Molecular Immunology, Research Center for Infectious Diseases, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan, 3Fukuoka Children’s Hospital, Fukuoka, Japan

Background and Aims: Calcineurin inhibitors (CNIs) have been used off-label for the treatment of refractory Kawasaki disease (KD). However, it remains unknown whether CNIs show protective effects against the development of coronary artery lesions in KD patients. The aim of this study is to investigate the effects of CNIs on coronary arteries and the mechanisms of their actions on coronary arteritis in a mouse model of KD.

Methods: We performed experiments with FK565, a ligand of nucleotide-binding oligomerization domain-containing protein 1 (Nod1) in wild-type, SCID, CARD9−/−, and MyD88−/− mice. We also performed in vitro studies by using vascular and monocytic cells, and vascular tissues.

Results: Histopathological analyses showed that both cyclosporin A and tacrolimus exacerbated the Nod1-mediated coronary arteritis in a dose-dependent manner. Cyclosporin A induced the exacerbation of coronary arteritis in mice only in high doses, while tacrolimus exacerbated it within the therapeutics range in humans. Similar effects were obtained in SCID and CARD9−/− mice but not in MyD88−/− mice. CNIs enhanced the expression of adhesion molecules by endothelial cells and the cytokine secretion by monocytic cells in our KD model. These data indicated that both vascular and monocytic cells were involved in the exacerbation of coronary arteritis.

Conclusions: The present study revealed the exacerbation of coronary arteritis by CNIs in a Nod1-mediated KD murine model. Activation of MyD88-dependent inflammatory signals in both vascular cells and macrophages appears to contribute to their adverse effects. Particular attention should be paid to the development of coronary artery lesions when using CNIs to treat refractory KD.

Establishment of the nasal microbiota in the first 18 months of life: Correlation with early onset rhinitis and wheezing

Le Duc Huy Ta1, Gaik Chin Yap1, Carina Jing Xuan Tay1, Alicia Shi-Min Lim1, Ching-Hui Huang1, Collins Wenhan Chu2, Paola Florez De Sessions2, Lynette Pei-Chi Shek1, Anne Goh9, Hugo PS Van Bever3, Oon Hoe Teoh9, Jian Yi Soh1, Biju Thomas9, Mahesh Babu Ramamurthy1, Daniel Yam Thiam Goh1, Christophe Lay4, Shu-E Soh1,5, Yiong Huak Chan4, Seang-Mei Saw5, Kenneth Kwek7, Yap-Seng Chong5,9, Keith M Godfrey10, Peter David Gluckman10, Martin Lloyd Hibberd11, Bee Wah Lee1

1Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, 2Genome Institute of Singapore, Agency for Science, Technology and Research, Singapore, 3Department of Paediatrics Allergy and Respiratory, KK Children’s and Women’s Hospital, Singapore, 4Danone Research Centre for Specialised Nutrition, Singapore, 5Saw Swee Hock School of Public Health, National University of Singapore, Singapore, 6Biostatistics Unit, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, 7Department of Maternal and Fetal Medicine, KK Children’s and Women’s Hospital, Singapore, 8Department of Obstetrics & Gynaecology, National University of Singapore, Singapore, 9Singapore Institute for Clinical Sciences, Agency for Science, Technology and Research Singapore, Singapore, 10MRC Lifecourse Epidemiology Unit and NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom

Background and Aims: We hypothesize that the dynamic establishment of the nasal microbiota in early life influences local mucosal immune responses and the susceptibility to develop respiratory disorders in childhood. The aim of this study was to monitor, evaluate and compare the development of the nasal microbiota in early life: (1) children who developed rhinitis in the first 18 months into (1) rhinitis alone (symptoms of sneezing, runny and/or blocked nose lasting for at least four weeks in the first 18 months) (n=28), (2) rhinitis with concomitant wheeze (n=34) and (3) controls (n=60). Controls were selected with similar characteristics (mode of delivery, age,
Oral Presentations

Haploidentical stem cell transplantation for primary immunodeficiency disorders in children: Challenges and outcome from a tertiary care centre in India

Ramya Uppuluri, Dhaarani Jayaraman, Meena Sivasankaran, Venkateswaran Swaminathan, Shivani Patel, Revathi Raj
Apollo Cancer Institutes, Chennai, India

Background: We describe our experience in the use of haploidentical stem cell transplantation (haploSCT) in children with PID.

Patients and Methods: We performed a retrospective study at the blood and marrow transplant unit at Apollo Cancer Institutes, Chennai including children up to 18 years diagnosed to have PID who underwent haploSCT from 2008 to 2016.

Results: Of the total 17 pediatric haploSCTs for PID, 7 were for severe combined immunodeficiency, 2 - Wiskott Aldrich syndrome, 2 - primary HLH,1 each with Chediak Higashi syndrome and Griscelli’s syndrome with accelerated HLH, 2 - MSMD, 1 - Hyper IgM syndrome. Haplograft was from a sibling donor in 5, parent donor in 12 children. PBSC was used in 13, bone marrow in 4. Techniques of T depletion used were 1 each with CD 34 selection and Campath in the bag, TCR alpha/beta depletion 3, CD3/19 selection 1 and post transplant cyclophosphamide (PTCy) in 10 children. 14/17 (82.3%) transplants resulted in engraftment by Day 16-21 post HSCT with sustained complete chimerism in 11 children (64%). Hyper IgM syndrome and MSMD were 2 conditions where primary rejection resulted in autologous reconstitution. One child with WAS dropped his chimerism to 77% around D+90 post HSCT and was salvaged with a donor lymphocyte infusion. One child with ADA deficient SCID has mixed chimerism 5 months post HSCT and remains infection free. Acute skin and gut GVHD responsive to steroids of grade 2-3 was noted in 3/15 (20%), CMV reactivation in 6/15 (40%) children. Overall mortality was found to be 5/17 (29%). Two deaths among infants receiving PTCy were due to sepsis and severe ARDS. Campath use resulted in refractory CMV disease and death. Two children where TCR α/β depletion and CD3/19 selection was used died of progressive leukoencephalopathy probably of viral etiology.

Conclusions: HaploSCT is a feasible option for cure in children with PID where no compatible family or matched unrelated donor has been found with engraftment rates of 82%, durable graft in 64% and overall survival of 70%. In our series, we have had superior outcome with the use of PTCy compared to ex vivo T depletion with survival rates of 80% in this group. The cost of the monoclonal antibodies alone is about 1200,000 Indian rupees making this procedure manifold expensive compared to PTCy. Careful patient selection will improve outcomes using this simple but cost effective method of treating children with PID in the future.
Turning weakness to strength: Lessons learnt in delivering cure for primary immune deficiency disorders in India

Ramya Uppuluri, Dhaarani Jayaraman, Meena Sivasankaran, Venkateswaran Swaminathan, Shivani Patel, Revathi Raj
Apollo Cancer Institutes, Chennai, India

Aim: Haematopoietic stem cell transplantation (HSCT) is the only form of cure in children with primary immune deficiency (PID). We present our experience in cure for PID and lessons learnt.

Patients: All children less than 18 years of age with PIDs who were transplanted at Apollo Cancer Institutes, Chennai from 2008 to 2016 were included in the study where factors affecting morbidity and mortality were analysed.

Results: A total of 62 PID transplants have been performed at our centre till December 2016 - 37 T cell defects, 3 B cell defects, 11 Phagocytic defects, 10 primary HLH, 2 MSDK. The conditioning regimen was myeloablative in children with Wiskott Aldrich Syndrome, Hyper IgM, and Chronic Granulomatous Disease with fludarabine/busulphan. All children with SCID, HLH, CVID, Leucocyte Adhesion Defect Syndrome had non-healing ulcers. Among children with SCID, HLH, CVID, Leucocyte Adhesion Defect Syndrome had dysphagia, dysphonia, and decreased antibody avidity in patients with DIDS. The antibody avidity of haemophilus influenza B antibody in one patient with DIDS was reduced compared to healthy controls (2.871 mol/L VS 5.871 mol/L). The antibody avidity of human tetanus and haemophilus influenza B antibodies was decreased by ELISA using thiocyanate elution. IVIG replacement therapy and infection condition were retrospectively investigated.

Conclusion: This is the first series in India with survival rates of 62% in children with PID. Conditioning regimens need to be chosen based on the genotype of an individual child. The pre-engraftment phase is critical in babies with SCID due to maximum mortality risk due to bacterial sepsis during this phase. Wiskott-Aldrich syndrome poses unique challenges due to immune dysregulation and these children need to be monitored for late immune cytopenias affecting mortality in over 50%. GVHD is a predominant problem in children with CGD with a risk of 80%. In children with primary HLH and less than 6 months of age, acute pulmonary haemorrhage is a risk factor affecting mortality. In all these children, CMV viral load needs to be monitored and treated early. Haploidentical HSCT is a feasible option in children with no matched family donors with success rates on par with unrelated donor HSCT.

IVIG replacement is essential for DOCK8 deficiency patients

Wenjing Tang, Ying Dou, Tao Qin, Xiaodong Zhao, Yunfei An
Chongqing Key Laboratory of Child Infection and Immunity, Children’s Hospital of Chongqing Medical University, Chongqing, China

Background and Aims: DOCK8 immunodeficiency syndrome (DIDS) is a combined immunodeficiency characterized by recurrent viral infections, severe atopy, and early onset malignancy. Immunological abnormalities include lymphopenia, defective antibody function, and variable serum immunoglobulin levels. Here, we analyze the B cell receptor repertoire (BCR) characteristics and antibody avidity of DOCK8 patients, and attempt to understand the possible mechanisms of humoral immunity dysregulation, and to provide the scientific basis for intravenous immunoglobulin (IVIG) replacement therapy of these patients.

Methods: Three patients with DIDS were enrolled in the study. Analysis of BCR characteristics including somatic hypermutation (SHM) frequency was performed by using deep sequencing on multiplex PCR products of BCR heavy chain CDR3s. The antibody avidity of human tetanus and haemophilus influenza B antibodies was determined by ELISA using thiocyanate elution. IVIG replacement treatment and infection condition were retrospectively investigated.

Results: For individual samples, means of 63.635 to 72.384, and 50.048 to 106.868 unique CDR3 sequences were generated in DOCK8 deficiency patients, and healthy controls. Regarding the gene usage frequencies, the usage of IGHV1-2, IGHV3-11, IGHV1-69, IGHV7-4-1 decreased in patients with DIDS compared to healthy controls. While the usage of IGHV1-58, IGHV1-59, IGHV3-53, IGHV4-39, IGHV4, IGHV4-61 increased. Negatively charged amino acids in patients with DIDS compared to healthy controls. The SHM frequency of IGHV3 gene and IGHV4-55 gene were decreased in patients with DIDS. The antibody avidity of human tetanus antibody in one patient with DIDS was reduced compared to healthy control (2.871 mol/L VS 5.871 mol/L). The antibody avidity of haemophilus influenza B antibody in two patients with DIDS was reduced compared to healthy controls (0.302 mol/L VS 2.027 mol/L, 0.369 mol/L VS 2.326 mol/L). Patients received regular IVIG therapy with reduced frequency of infections and improved severity of infections.

Conclusions: Our results reveal skewing of BCR repertoire and decreased antibody avidity in patients with DIDS. Although IgG level is normal in DOCK8 patients, the IVIG replacement therapy is still necessary.
Reference values for peripheral blood lymphocyte subsets of healthy children in China: A multi-centered study

Yuan Ding¹, Lina Zhou¹, Yu Xia², Wei Wang³, Ying Wang⁴, Li Li⁵, Xiaochuan Wang⁶, Hongmei Song⁷, Jun Yang⁸, Xiaodong Zhao¹

¹Chongqing Key Laboratory of Child Infection and Immunity, Children’s Hospital of Chongqing Medical University, Chongqing, China, ²Department of Immunology, Shenzhen Children’s Hospital, Shenzhen, China, ³Department of Pediatrics, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, ⁴Department of Clinical Immunology, Children’s Hospital of Fudan University, Shanghai, China

Background and Aims: Defining abnormality of peripheral blood lymphocyte distribution is the key to suspect primary immunodeficiency and numerous other immune disorders in childhood. Use of domestic reference values is known to improve the accuracy of flow cytometric analysis by integrating local variation due to race, gender, and age. As there were no published estimates, we now report establishment of reference values for peripheral blood lymphocyte phenotypes applicable to the healthy childhood population in China.

Methods: Blood samples were taken from 1075 children aged 0-18 years, and 20 peripheral blood lymphocyte subsets were determined by means of seven-color-flow cytometry. Relative and absolute sizes of each subset were calculated. When absolute numbers were concerned, a dual platform approach was used.

Results: Reference values for age-related lymphocyte subsets in seven age groups of T-, B-, NK-cell subsets were estimated, including naive, central memory, effector memory, terminally differentiated of helper T cell (TH) and cytotoxic T cell, TCRαβ double negative T cell, γδT cell and naive, memory, transitional, plasmablasts of B cell. The distributions of lymphocyte subsets changed by age. Naive CD4 T-cells showed a gradually decrease relative size while the percentage of memory CD4 T-cells increased. As for the CD8 T-cells, similar pattern of changes was observed. Both CD4 and CD8 TEMRA cells showed a low frequency in newborns and a dramatic increase during the first year of life. The absolute numbers of CD4 and CD8 T-cell subsets had parallel changes to the relative numbers. The frequency of TCRαβ-DNT cells showed a gradually increase while the absolute number range changed a little. γδT cells percentage gradually increased and the absolute number of γδT cells had a wide range related to ages. Naive B-cells (CD19+CD27-IgD+) composed the greatest B cell subsets in all age groups, while memory B-cells gradually increased. Transitional B-cells showed obvious age-related variations while plasmablasts did not in both relative and absolute sizes.

Conclusions: This study provides a largest scale research project on peripheral blood lymphocyte subsets analysis of healthy children, which is multicentered and multiparametered. Based on the statistical methods, the reference values reflect the continuous maturation of lymphocyte subsets during childhood. And localized reference values of peripheral blood lymphocytes subsets may be more suitable for clinical evaluation of immune abnormalities for Chinese children.

Identification of potential transcriptomic markers in developing asthma: An integrative analysis of gene expression profiles

Fang Fang, Jian Pan, Yanhong Li, Yiping Li, Xing Feng, Jian Wang

Children’s Hospital of Soochow University, Suzhou, China

Background and Aims: Asthma represents a chronic respiratory disorder characterized by airway inflammation, airflow obstruction, and bronchial hyperresponsiveness to stimuli. Airway epithelial cell (AEC) dysfunction plays an important role in asthma, hence systematic screening is required to identify AEC abnormalities and improve the diagnosis and treatment of asthma. Rapid growth of high-throughput transcriptomic data largely enables gene expression profiling and diagnostic targets identification in disease nowadays. In the past decade, several studies have focused on the transcriptional profiling of asthma using microarrays to identify candidate genes involved in asthma. Analysis of multiple transcriptomic datasets has the likelihood of discovering robust candidates for diagnosis and treatment. Therefore, to identify potential transcriptomic markers in developing asthma, we investigated gene expression patterns in AEC between asthma patients and healthy controls by an integrative analysis of multiple public microarray datasets in this study.

Methods: R software and bioconductor packages were used for data pre-procession, differentially expressed (DE) genes identification, and support vector machine (SVM) model training. Enrichment analysis and co-expression network construction were also performed using DAVID and Cytoscape software, respectively.

Results: 3 microarray datasets (192 cases and 91 controls in total) were collected for this analysis. 62 DE genes were identified in asthma, among which 43 genes were up-regulated, 19 genes were down-regulated, and a set of them were not studied in asthma previously. Enrichment analysis revealed that those DE genes strongly associated with proteolysis, retina homeostasis, humoral immune response, and salivary secretion. A co-expression network of DE genes was also constructed using highly correlated DE genes identification, and support vector machine (SVM) classifier (asthma versus healthy control) was trained. The performance of the SVM classifier was evaluated using 10-fold cross-validation and the cross-validation error was 0.079.

Conclusions: In conclusion, we identified consistently DE genes in asthma that could potentially serve as transcriptomic markers. GO and pathway analyses revealed that those candidates strongly associated with proteolysis, retina homeostasis, humoral immune response, and salivary secretion. A SVM classifier (asthma versus healthy control) was also trained based on candidate transcriptomic markers in this study. These results provide novel insights into the pathogenesis of asthma, and promote the generation of diagnostic gene sets.
Characteristics of patent ductus arteriosus in congenital rubella syndrome

Michiko Toizumi, Giang Do, Hideki Motomura, Tin Do, Hiroyuki Moruchi, LayMyint Yoshida

1Institute of Tropical Medicine, Nagasaki University, Nagasaki, Japan, 2Children's hospital 1, Ho Chi Minh, Vietnam, 3National Hospital Organization Nagasaki Medical Center, Omura, Japan, 4Nagasaki University Hospital, Nagasaki, Japan

Background and Aims: A large-scale rubella outbreak occurred throughout Vietnam between January and July 2011 and many congenital rubella syndrome (CRS) cases emerged. This study aimed to determine characteristics of CRS-associated cardiac complications, particularly morphology and hemodynamics of patent ductus arteriosus (PDA) as compared to those in non-CRS patients.

Methods: (1) Retrospective descriptive study: we reviewed medical records of [1] Laboratory/clinically confirmed CRS cases admitted to Children's Hospital 1 (CH1) between December 2010 and December 2012, identified by the previous published study and [2] Clinically diagnosed CRS cases who had PDA transcatheter occlusion therapy in the Department of Pediatric Cardiology at CH1. (2) Comparative study of PDA: We compared characteristics of PDA between children in (1) with PDA treated by transcatheter closure (CRS-PDA) and those with PDA treated by transcatheter closure at CH1, between July 2014 and Dec 2015, after rubella outbreak was over (non CRS-PDA).

Results: (1) A total of 109 children with CRS were enrolled. Among them, 48% were boys, 67% had laboratory confirmed CRS, and the mean birthweight was 2129g. Cardiac defects (99%), cataract(s) (70%), and hearing impairment (4%) were detected and 17% died at discharge. (2) Fifty-one CRS-PDA and 248 non CRS-PDA cases were analyzed. Compared with non CRS-PDA, those with CRS-PDA had lower median age at closure (p=0.0081), less mean birthweight (p<0.001), more pulmonary stenosis (p<0.001), more aortic stenosis (p<0.001), more pulmonary hypertension measured by catheter (mean main pulmonary artery pressure ≥25 mmHg, p=0.006), more main pulmonary artery pressure and more aortic pressure both in systole and diastole (mean systolic pressure of main pulmonary artery; 48.8 vs 36.3 mmHg, p<0.001, mean systolic pressure of aorta; 93.1 vs 73.6 mmHg, p<0.001). Also, mean aorta side diameter of PDA was larger (p=0.0115) and proportion of tubular type of PDA was more in CRS-PDA (27.5% vs 10.2%, p=0.014).

Conclusion: Tubular type, which is difficult-to-treat by transcatheter closure, and pulmonary hypertension are commoner in PDA in CRS and it needs intervention earlier compared with PDA in non-CRS.

Cardiovascular sequelae of Kawasaki disease at a single hospital between 1982 and 2016

Yumi Mizuno, Kohichi Sagawa, Kenji Furuno, Sooyoung Lee, Ayako Kuraoka, Sagano Onoyama, Hiroshi Matsuzaki, Tosiro Hara

Fukuoka Children's Hospital, Fukuoka, Japan

Background and Aim: To evaluate the relation of cardiovascular sequelae of Kawasaki disease and clinical feature or treatment of the patients during acute phase of illness.

Methods: 2908 patients with Kawasaki disease during acute phase were treated at Fukuoka Children's Hospital from July,1982 to December, 2016, 97 patients of them had coronary artery lesions (CALS) beyond 3 months after onset ; 55 male, 42 female, the median age on admission was 1 year 9 months. The relation of cardiovascular sequelae of Kawasaki disease and clinical feature or treatment during their acute phase of illness was analyzed retrospectively. CAL was defined according to the criteria of Japanese Ministry of Health, Labor and Welfare.Main treatments of Kawasaki disease at our hospital were intravenous immunoglobulin (IVIG) from low dose to high dose, aspirin and additional use of steroids until 2010. Infliximab and plasma exchange have been included as additional treatments for the IVIG resistant Kawasaki disease since 2011.

Results: The rates of CAL of 1982-1990, 1991-2000, 2001-2010 and 2011-2016 were 9.5%, 3.4%, 2.1% and 1.0% respectively. The initial treatments of the patients were as follow; 24 with only aspirin, 39 with divided low dose IVIG and 34 with 1~2g/kg of single high dose IVIG (HDIG). CALs of 74 of 97 patients were regressed from 4 months to 7 years. Ten of 23 patients whose CAL was not regressed had giant aneurysm, Seven of 23 patients had stenosis or obstruction of coronary artery and three of them needed surgical treatment. 19 patients of 34 patients who were treated with HDIG were resistant to HDIG (2g/kg), 7 of 34 patients were diagnosed after 8 days of illness.

Conclusion: The rate of cardiac sequelae has decreased due to HDIG and other additional treatments including infliximab, steroids and plasma exchange. Delay of diagnosis and resistance to HDIG may be involved in cardiac sequelae.
Long-term prognosis and genotype-phenotype correlations of patients with left ventricular noncompaction

Ce Wang¹², Yukiko Hata³, Keiichi Hirono², Asami Takasaki¹, Sayaka Watanabe Ozawa², Xianyi Yu¹, Fukiko Ichida²
¹Department of Pediatrics, Shengjing Hospital of China Medical University, Shenyang, China; ²Department of Pediatrics, Faculty of Medicine, Toyama University, Toyama, Japan; ³Legal Medicine, Faculty of Medicine, Toyama University, Toyama, Japan

Background and Aims: Left ventricular noncompaction (LVNC) has since been classified as a primary genetic cardiomyopathy, but the genetic basis is not fully evaluated. The aim of the present study was to identify the genetic spectrum using next-generation sequencing (NGS) and to evaluate genotype-phenotype correlations in LVNC patients.

Methods: We targeted and sequenced 73 genes related to cardiomyopathy in 102 LVNC patients using NGS. Clinical evaluation consisted of clinical presentation and symptoms; a personal and family history; arrhythmia; thromboembolism; electrocardiogram (ECG); two-dimensional Doppler, and color Doppler echocardiography.

Results: A total of 102 patients enrolled in this study; 54 male and 48 female, aged from fetus to 12 years old. We identified 43 pathogenic variants (39 were missense, 1 deletion, 1 nonsense, and 2 splice site variants) in 16 genes in 39 patients (38%), 28 were novel variants. Sarcomere gene variants accounted for 63%, variants in genes associated with channelopathies accounted for 12%. Overall, MYH7 was most commonly mutated (n=19, 44%), followed by TAZ, and rare variant collapsing analysis showed variants in these two genes contributed to the risk for LVNC. Patients carrying MYH7 and TAZ pathogenic variants displayed different phenotypes. Adverse events were noted in 17 patients, including 13 deaths, 3 heart transplants, and one implantable cardioverter-defibrillator insertion. Congestive heart failure at diagnosis and pathogenic variants were independent risk factors for these adverse events.

Conclusions: NGS revealed a wide spectrum of genetic variations and a high incidence of pathogenic variants in LVNC patients. These pathogenic variants were independent risk factor for adverse events. Patients harboring pathogenic variants showed poor prognosis and should be closely followed.

Myocardium specific gene therapy can partly rescue cardiac troponin T deficiency related cardiomyopathy

Lian Liu¹, Yonghao Gui¹, Xu Wang²
¹Children’s Hospital of Fudan University, Shanghai, China; ²Fudan University, Shanghai, China

Background and Aims: Cardiac troponin T (cTnT) gene mutations can lead to cardiomyopathy. Gene supplement therapy is the most direct and viable option for diseases caused by a single structural protein deficiency. We plan to generate a transgenic zebrafish line to study the feasibility of myocardium specific gene therapy on cTnT gene mutated-related cardiomyopathy.

Methods: Firstly, we generated a transgenic zebrafish line of temporal and spatial specific cTnT gene expression by injecting a Tol2-based knock-in vector carrying the cardiac specific promoter, cmlc2, the Tet-on system, and red fluorescence fusion labeled tnt2a cDNA sequence. Then, we screened F1 and crossed it with tnt2a mutant zebrafish (obtained from our lab), the in situ dosage-induced expression transgenic therapy zebrafish tnt2a mutated model was obtained. Lastly, Dox induction rescue test and RNA-seq analysis were performed to observe whether myocardium specific gene therapy can be feasible and find underlying causes.

Results: The Tg (cmlc2-tetone-tnnt2a-p2A-mKate2;cmlc2;EGFP;tnnt2a-/-) was eventually obtained, which was proved by fluorescence reaction and genome sequencing. The phenotype of the Tg zebrafish assembles dilated cardiomyopathy without supplement therapy. Moreover, DOX induction test showed that the partial cardiac abnormal phenotypes of tnt2a mutant could be rescued, such as atrium and ventricle enlargement, no heart beats. However, the optimization of multiple doses and induction time did not completely restore the heart shape. What’s more. That the dysregulation expressions of the valve and outflow tract associated genes had not been rescued efficiently through transcriptomics analysis would be the underlying cause of partial rescue.

Conclusions: Gene supplement therapy was feasible for cardiomyopathy caused by cTnT gene mutant. However, for the treatment of TNNT2-relevant cardiomyopathy, it was necessary to take into account the gene supplementation of myocyte, valve and outflow tract cell.
A TBX5 3'UTR variant increases the risk of congenital heart disease in the Han Chinese population

Feng Wang¹, Dong Liu², Jian-Yuan Zhao³, Ran-Ran Zhang¹, Xue-Yan Yang³, Hong-Yan Wang³, Yong-Hao Gui¹

¹Children’s Hospital of Fudan University, Shanghai, China, ²Co-innovation Center of Neuroregeneration, Key Laboratory of Neuroregeneration of Jiangsu and Ministry of Education, Nantong University, Nantong, China, ³The State Key Laboratory of Genetic Engineering & MOE Key Laboratory of Contemporary Anthropology, Collaborative Innovation Center of Genetics and Development, School of Life Sciences, Fudan University, Shanghai, China

Background and Aims: TBX5 is a vital transcription factor and it contributes to cardiac development in a dosage-dependent manner. But little is known about the potential association of TBX5 regulatory variations with congenital cardiac malformations. This study aimed to investigate the relationship between TBX5 3’ untranscribed region (UTR) variants and risk for congenital heart disease (CHD) susceptibility in two Han Chinese populations, and to reveal its molecular mechanism.

Methods: The relationship between TBX5 3’UTR variants and CHD susceptibility was examined in 1,177 CHD patients and 990 healthy controls in two independent case-control studies. Following the association study, Quantitative real-time PCR and Western blot analysis were performed to confirm TBX5 expression in CHD heat tissues of different genotypes. In addition, luciferase reporter assays, surface plasmon resonance analysis and zebrafish experiments were applied to reveal the function of TBX5 3’UTR variants.

Results: Variant rs6489956 C>T was found to be associated with increased CHD susceptibility in both cohorts. The combined CHD risk for the CT and TT genotype carriers was 1.83 times higher than that of CC genotype, while the risk for CT or TT genotype was 1.94 times and 2.31 times higher than that of CC carriers, respectively. Quantitative real-time PCR and Western blot analysis were performed to confirm TBX5 expression in CHD heat tissues of different genotypes. In comparison, luciferase reporter assays, surface plasmon resonance analysis and zebrafish experiments were applied to reveal the function of TBX5 3’UTR variants.

Conclusions: We concluded that TBX5 3’UTR variant rs6489956 increased susceptibility of CHD in the Han Chinese population because it changes the binding affinity of two target miRNAs that specifically mediate TBX5 expression.

MiR-29b regulates cardiomyocytes proliferation via targeting NOTCH2

Qian Yang, Yong-hao Gui, Qiang Li

Children’s Hospital of Fudan University, Shanghai, China

Background and Aims: Tetralogy of Fallot (TOF) is a developmental cardiac manifestation with an incidence of 3 per 10,000 live births. Recent study have showed that TOF is relevant to altered proliferation, migration, or differentiation of the precardiac cells of the secondary heart field. Researches have addressed the role of microRNA (miRNAs) in cardiac development. The role of miR-29b in adult cardiovascular diseases including cardiac fibrosis, dilated cardiomyopathy and myocardial ischaemia-reperfusion injury has been studied widely, yet the involvement of miRNA-29b in TOF remains unclear. Our aim is to explore the effect and mechanisms of miR-29b on contributing to TOF pathogenesis.

Methods: A total of 13 TOF patients and 7 normal controls were included in our study. All tissue samples were obtained from the right ventricular outflow tract (RVOT) immediately after surgical resection or autopsy. Real-time RT-PCR and Western Blot were used to quantify genes expression. Tg Cmlc2: GFP reporter zebrafish embryo were microinjected with miR-29b to explore its role in cardiac development in vivo. Dual-luciferase reporter assay was designed to validate the target gene. CCK-8, EdU incorporation assay and flow cytometry were performed to evaluate cardiomyocyte proliferation.

Results: (1) We observed that miR-29b-3p was up-regulated in the RVOT of TOF patients when compared with normal controls. (2) Zebrafish injected with miR-29b-3p mimics exhibited abnormal heart morphology and function. The proliferation rate of zebrafish cardiomyocytes was also reduced in vivo. (3) CCK-8 and EdU incorporation assay showed that miR29b-3p mimics potently inhibited cardiomyocytes proliferation in vitro. Conversely, inhibition of miR29b-3p substantially induced cardiomyocytes proliferation. (4) A higher proportion of cells in G2/M stage in miR29b-3p mimics group was observed, which suggest that miR29b-3p could arrest cardiomyocytes in G2/M stage. Positive cell cycle regulators, such as cyclins, catenin beta 1 and PCNA, were down-regulated in miR29b-3p mimics group. (5) We observed that NOTCH2 were significantly decreased RVOT of TOF patients. DLR assay identified NOTCH2 was a direct target of miR-29b-3p. (6) Transfection of NOTCH2 siRNA significantly decreased cardiomyocytes proliferation. Moreover, the promoting effect of miR-29b-3p inhibitor on proliferation were partly abrogated by Notch2 siRNA in cardiomyocytes.

Conclusions: miR-29b-3p functions as a novel regulator of cardiac development and inhibits cardiomyocytes proliferation via direct targeting of the NOTCH2, which provides groundwork for a new therapy approach to TOF.
Prediction of Attention Deficit Hyperactivity Disorder (ADHD) risk using an infant measure:

Externalizing symptoms at 12 months and risk of ADHD at 54 months

Muhammad Taufeeq Wahab1, Daryl Yeo Yuan Chong1, Sherilyn Chan Jin Wen2, Evelyn Chung Ning Law2

1National University of Singapore, Singapore, 2National University Health System, Singapore,

**Background and Aims:** Attention Deficit Hyperactivity Disorder (ADHD) is generally diagnosed at the start of school age. By finding a reliable measure of externalizing symptoms during infancy to predict risk of ADHD, early intervention may be started before school age.

**Methods:** Using the Growing Up in Singapore Towards Healthy Outcomes (GUSTO) cohort, we obtained externalizing symptoms using the Infant Toddler Social Emotional Assessment (ITSEA) tool at 12 months and ascertained risk for ADHD using the Computerized Diagnostic Interview Schedule for Children (C-DISC) at 54 months (N=163). Nonparametric descriptive statistics compared low and intermediate risk of ADHD based on early ITSEA externalizing scores. Binary logistic regression models examined the relationships between the ITSEA externalizing score and risk of ADHD, after controlling for child and family factors.

**Results:** At 12 months, the mean externalizing score was 0.580 ± 0.278. At 54 months, 41.2% were intermediate risk and 58.8% were low risk. Mann-Whitney U test showed that the mean externalizing score of children with intermediate risk of ADHD was higher than those with low risk of ADHD (Ustandardized 3.984, p<0.001). After controlling for gender, birth weight, 3-month postnatal State-Trait Anxiety Inventory (STAI) score, 12-month child media use, and ITSEA 12-month internalizing raw score, the model showed that high externalizing scores at 12 months increased the prediction of ADHD risk at 54 months by the odds of 13.70 times (OR 13.70, 95%CI 2.62-71.50, p=0.002). for final model and included covariates.

**Conclusions:** An infant measure at 12 months has predictive validity of risk of ADHD in preschool years. Thus, clinicians should consider administering this infant measure when concerns are raised about externalizing symptoms and high risk infants should be followed up regularly for behavioral assessments. Future studies should look at how this infant measure correlates with actual ADHD diagnosis in later childhood.

---

Early food allergy and symptoms of airway allergy March on the risk of attention deficit hyperactivity disorder in Chinese children: A cross-sectional study

Chun Shen, Xiaodong Jiang, Fei Li
Xinhua Hospital, Shanghai, China

**Background and Aims:** Few studies investigated the effects of food allergy and the symptoms of allergy march on ADHD in children. We aim to investigate the effects of early food allergy and symptoms of allergy march on the prevalence of attention-deficit/hyperactivity disorder (ADHD) in school-age children.

**Methods:** This cross-sectional study was conducted in school-age children in grade 1-6 in elementary schools in China using cluster-stratified methods from nine cities across China between November and December 2005. A family and social environmental questionnaire including the diagnosis history of ADHD and allergic diseases (food allergy, allergic rhinitis and bronchial asthma), as well as general information of the children were completed by the parents of school-age children. The children were grouped as: no food allergy group, single food allergy group (FA group), food allergy complicated with one airway allergy march symptom group (FA+AR/BA group), and food allergy complicated with two airway allergy march symptoms group (FA+AR+BA group) according to the diagnosis history of airway allergic diseases.

**Results:** The prevalence of allergic rhinitis (20.4%) and asthma (11.6%) in the food allergy group were both significantly higher than in the non-food allergy group (9.0% and 2.8%, respectively) (both p<0.001). The multivariable analysis showed that single food allergy (OR=1.53, 95%CI: 1.13-2.05, p=0.005), food allergy complicated with allergic rhinitis or asthma (OR=3.36, 95%CI: 2.19-5.14, p<0.001), and food allergy complicated with allergic rhinitis and asthma simultaneously (OR=4.08, 95%CI: 2.05-8.11, p<0.001) were independently associated with the increased risk of ADHD.

**Conclusions:** Early exposure to food allergen is a risk factor of ADHD in school-age children. The symptoms of airway allergy march resulted in a synergism with a higher risk of ADHD in children with food allergy. Monitoring food allergy in early life could provide information for the early prediction and intervention for the consequent allergy march and ADHD in children.
Effects of parent-implemented Early Start Denver Model on Chinese toddlers with autism spectrum disorder: A non-randomized controlled trial

Bingrui Zhou¹, Qiong Xu¹, Huiping Li¹, Ying Zhang¹, Yi Wang¹, Sally Rogers², Xiu Xu¹

¹Children's Hospital of Fudan University, Shanghai, China, ²University of California Davis, Sacramento, USA

Background and Aims: It has been a consensus that early screening, diagnosis and intervention can effectively improve the prognosis of autism spectrum disorder (ASD). The trinary screening network and 2-tiered referral system have been primarily established in Shanghai and several other cities. As a result, the disparity between the staggering increase in the prevalence of ASD toddlers and the lack of a systematic intervention approach for them has become increasingly obvious in China.

Objectives: To evaluate the effects of a 26-week, low-intensity, parent-implemented Early Start Denver Model (P-ESDM) intervention on developmental outcomes, ASD severity of ASD toddlers, and on parental stress of their parents.

Methods: The present study is a non-randomized controlled trial. Subjects in P-ESDM group (n=23) were recruited from 1.5~2.5-year toddlers who were screened positive on Checklist for Autism in Toddlers (CHAT-23) in Xuhui and Minhang District and diagnosed with ASD by DSM-V in developmental and behavioral clinic of Children's Hospital of Fudan University. ASD toddlers in the community group (n=20) were recruited from age-matched ASD toddlers coming from other districts or provinces with the same diagnosing procedure as P-ESDM group. Parents and children of P-ESDM group attend 1.5-hour therapy per week for 26 weeks. Children of community group received any interventions available from communities or private services. Assessments were completed at baseline (T1) and 26 weeks later (T2).

Results: After adjusting for baseline differences between the two groups, compared with community group, P-ESDM group demonstrated improvement that was more significant in general development, especially in Personal-Social, Language and Eye-Hand Coordination domains. The both groups did not have much improvement in ASD severity using standardized Autism Diagnostic Observation Schedule (ADOS), but P-ESDM group showed greater improvement in parent-reported social communication and symbolic play than community group did. Although parents in P-ESDM group experienced decreased parenting stress while those in community group showed an opposite trend, the difference was not significantly related to the group assignment.

Conclusions: Parent-implemented Early Start Denver Model on Chinese toddlers with ASD for longer duration have shown some potentials in improving their developmental outcomes as well as social communicational skills reported by parents. Our results also supported the importance of early detection and intervention for ASD.

SHANK3 deletion and related phenotypes in Chinese children with autism and shank3-KO zebrafish display autistic-like behaviours

Chunxue Liu, Chunyang Li, Chunchun Hu, Jia Lin, Bingrui Zhou, Huiping Li, Qiong Xu, Qiang Li, Xiu Xu

Children's Hospital of Fudan University, Shanghai, China

Background and Aims: Autism spectrum disorder (ASD) is well known as a heritable, debilitating neurodevelopmental disorder manifesting in early development. A mount of studies showed that SHANK3 gene had a strong causal relationship with ASD and/or 22q13.3 deletion syndrome. However, the data of Chinese ASD patients with SHANK3 deletion is insufficient and the mechanism is not clear.

Methods: MLPA and Sanger sequencing were carried out to confirm the SHANK3 deficiency of Chinese children. Moreover, systematic and comprehensive evaluations were performed to Chinese-specific features. In addition, shank3 was knock-out (KO) using a CRISPR/Cas9 system in zebrafish to build a transgenic zebrafish model.

Results: As to the patients, six participants lacked the whole gene of SHANK3 with 22q13.3 deletions ranging in size from 55 kb to 4.8 Mb and three participants with de novo SHANK3 mutation were included. They were characterized by high rates (100%) of ASD, developmental delay, hypotonia, several dysmorphologies and perception abreaction. New and rare features were also viewed in this study: ectropion of nostril sparse hair, ankle deformity, whole-body hairy, hanked-3-lap arms, snagletoothed or extra teeth and unusual-dehydrated skin, and extreme hyperactivity/self-stimulation. As to the zebrafish model, the shank3-KO zebrafish displayed varying degrees of developmental retardation compared with the wild-type zebrafish, such as ventral curled body, less melanin, less somites and so on. Moreover, the homozygous zebrafish were more significant than the heterozygotes. What’s more, in zebrafish social interaction test, shank3-KO zebrafish showed less interest exploring conspecific zebrafish both in swimming distance ratio and swimming time ratio. Furthermore, in zebrafish social preference test, shank3-KO zebrafish displayed reduced polarization of fish shoals, looser and larger schools, and higher percentage of fish leaving the group and spending time outside the shoal which implied a disorganized social structure. In addition to social deficits, the trace pattern analysis of zebrafish found several obvious behavioral stereotypies, such as repetitive, stereotypic “repeated self-rotation” swimming behavior.

Conclusions: In our study, the severity of intellectual, hypotonia, and speech impairments were seen in SHANK3 deficiency which highlighted the prominence of SHANK3 in ASD. Zebrafish, a typical animal model, will play a critical role in further studying the relationship between phenotype and genotype of ASD and insighting into the molecular mechanisms underlying the clinical heterogeneity of ASD.
Gastroenterology and Hepatology

Dynamics of the gut Bifidobacterium microbiota during the first three years of life: A quantitative bird's-eye view

Yuichiro Yamashiro1, Ravinder Nagpal1, Hirokazu Tsuji1,2, Takuya Takahashi1,2, Kazunari Kawashima3, Satoru Nagata1,4, Koji Nomoto5,2
1Probiotics Research Laboratory, Juntendo University Graduate School of Medicine, Tokyo, Japan; 2Yakult Central Institute, Tokyo, Japan; 3Yakult Central Institute, Tokyo, Japan; 4Department of Pediatrics, Tokyo Women’s Medical University, Tokyo, Japan; 5Laboratory of Animal Symbiotic Microorganisms, Department of Molecular Microbiology, Faculty of Lice Science, Tokyo University of Agriculture, Tokyo, Japan

Background and Aims: Bifidobacteria represent a major element of infant gut microbiota and impart significant beneficial effects on infant’s gut, immune and metabolic health. We investigated the fecal carriage of eight signature Bifidobacterium species in healthy infants prospectively from first day to 3 years of life, and examined the effect of factors.

Methods: The study included healthy term Japanese infants (n 89; M 49; F 40). Fecal samples (≈1 g) at age 1 day, 7 days, 1, 3 and 6 months, and 3 years were collected. Bifidobacterial groups and species viz. were enumerated by using sensitive reverse-transcription-quantitative PCR assays targeting bacterial 16S rRNA molecules. The study was approved by the Institutional ethical committee, and prior written informed consent was obtained from the parents.

Results: About 21% of babies carried bifidobacteria at first day of life (mean bacterial count: 6.1±1.8 log10 cells/g feces); but this count (and prevalence) gradually increased to 7.7±2.3 (62%), 8.3±2.1 (76%), 9.2±1.9 (97%), and 9.6±1.7 cells/g (99%) at age 7 days, 1, 3, and 6 months, respectively. At 3 years, all babies carried bifidobacteria (mean count: 9.7±1.0 cells/g). B. longum, B. breve, B. catenulatum and B. bifidum were the first colonizers (detected at day 1). B. infantis, B. dentium and B. adolescentis appeared at day 7 whereas B. angulatum was detected only at 3 years. In terms of count as well as prevalence, B. longum, B. breve, and B. catenulatum remained most dominant bifidobacterial clades throughout the study period. Compared to vaginally-born babies, cesarean-born babies had significantly or insignificantly lower carriage of bifidobacteria from age 7 days to 3 months, with difference being most prominent for B. catenulatum. Interestingly, within vaginally-born babies, those who started formula-feed as early as first week of life had higher carriage of bifidobacteria during first 6 months as compared to those who were exclusively breast-fed during first 3 months.

Conclusions: Our study presents a quantitative bird's-eye view of the age-related dynamics of typical infant-associated Bifidobacterium species in infant gut during the critical developmental window of life. The data further demonstrate the effect of various factors such as birth mode, feeding type, gender etc. on bifidobacterial colonization during infancy and early childhood, besides displaying the correlation pattern of bifidobacteria with other gut microbes. Given the fundamental role of gut microbiota in numerous aspects of infant’s long-term health, these data should prove to be informative and important for prospective studies on paediatric microbiota and gastroenterology.

Oral Presentations

Upregulated genes of intracellular Salmonella Typhimurium after invasion into human intestinal epithelial cells

Shih-Bin Fang1,2,3, Ke-Chuan Wang1,2, Ching-Jou Huang1,2, Pei-Ju Chang1,2
1Division of Pediatric Gastroenterology and Hepatology, Department of Pediatrics, Shuang Ho Hospital, Taipei Medical University, Taipei, Taiwan; 2Department of Pediatrics, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan; 3Master Program for Clinical Pharmacogenomics and Pharmacoproteomics, College of Pharmacy, Taipei Medical University, Taipei, Taiwan

Background and Aims: Salmonella pathogenicity island-1 (SPI-1) and SPI-2 genes account for bacterial invasion into host cells and survival of intracellular Salmonella, respectively. Whether additional Salmonella genes after internalization into human intestinal epithelium contribute to bacterial intracellular survival remains unknown. Therefore, we aimed to investigate which genes of Salmonella Typhimurium were significantly regulated after Salmonella invades human intestinal epithelium.

Methods: Caco-2 cells were infected with S. Typhimurium SL1344 (MOI=5) for 2 hours. Then, the cells were treated with gentamicin for 1 hour and remained incubated for an additional 15 hours. After 18-hour incubation, the infected cells were lyzed to obtain intracellular bacteria. Total RNAs of extracellular and intracellular S. Typhimurium SL1344 were isolated from two independent infections, reverse-transcribed to cDNAs, and subsequent cRNAs were processed for RNA microarrays (Agilent Custom Salmonella GE 8 x 15K Microarray), which were scanned, quantified, and analyzed. Transcriptomes of extracellular and intracellular S. Typhimurium SL1344 were compared using the Student’s t test to determine the p values. A p value < 0.05 with > 1 log2 or < −1 log2 fold change was considered
Results: Compared to extracellular *S. Typhimurium*, a total of 1249 genes of intracellular *S. Typhimurium* within Caco-2 cells were significantly regulated, including 831 genes upregulated and 418 genes downregulated. Most of the plasmid genes were significantly upregulated (54 P1 genes and 23 P2 genes; e.g. 3.707 log2 fold-change in SL1344_P1_0060) except for 4 significantly downregulated P1 genes and 23 P2 genes; e.g. 3.707 log2 fold-change in SL1344_P1_0060. The majority of plasmid genes and the genes associated with synthesis of biotin (*bioC, bioA, bioB, bioF, and bioD*), enterobactin (*entD, entE, entA, entB, entC, entF*), ferric bacter (*fepA, fepG, fepC, fepB, fepD, fepE*), colicin (*cirA and imm*), and bacteriophage shock protein (*pspC, pspA, pspD, pspB, and pspE*) were significantly upregulated in intracellular *S. Typhimurium* SL1344. Most of the significantly downregulated genes include those encoding invasion-associated secreted proteins (e.g. *sopE, hilA, OrgA, figE, flc, and flgB*) and SPI-1 genes (e.g. *inv, sip, spa, and prg* genes). The RT-PCR analysis validated mRNA expression of the selected significantly upregulated genes from microarrays, including P2_0016, *bioC, entD, fepA, cirA*, and *pspC*, in intracellular *S. Typhimurium* relative to extracellular *S. Typhimurium* (all p<0.05).

Conclusions: The majority of plasmid genes and the genes associated with synthesis of biotin, enterobactin, ferric bacterin, colicin, and bacteriophage shock protein are important for host-induced bacterial virulence and survival after invasion of *S. Typhimurium* into human intestinal epithelial cells.

Liver and spleen stiffness for predicting the presence and severity of Esophageal varices in Children with chronic liver diseases

Suporn Treepongkaruna, Teera Kijmassuwan, Wasuntara Prabpram, Pornthep Tanpowpong
Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background and Aims: Esophageal varices (EV) caused by portal hypertension among children with chronic liver diseases can lead to significant morbidity and mortality from variceal bleeding. Esophagogastroduodenoscopy (EGD) is currently the most accepted tool to diagnose EV but it is considered invasive. Recent studies have shown that spleen stiffness by using transient elastography (TE) can predict EV in adults. However, studies of spleen stiffness in children are limited and its cutoff for the presence of EV has not been reported. We aimed to determine the correlation of liver and spleen stiffness by TE for the presence and grading of EV and identify the cutoffs of stiffness data for predicting presence of EV.

Methods: Children aged <15 years with chronic liver disease and portal hypertension were invited to enroll for EGD (to evaluate EV) and TE (FibroScan®). Data on liver stiffness measurement (LSM) and spleen stiffness measurement (SSM) were collected. Information on the LSM and SSM was blinded to the endoscopists, and vice versa. LSM and SSM were then analyzed for the potential cutoff values, sensitivity and specificity of the presence and grading of EV.

Results: We studied 40 patients (65% female, 70% with biliary atresia, median age of 20.5 months). Median (interquartile range) of LSM and SSM were 69 (19-75) and 37 (14-75) kilopascal (kPa), respectively. EV grade I, II and III were noted in 10, 9, and 10 patients, respectively. Both LSM and SSM had significant correlations with the presence of EV (r = 0.53, p=0.001 and r = 0.43, p=0.007). Furthermore, significant correlation was noted between SSM and EV grade II-III vs. grade 0-I (r = 0.43, p=0.008) but not for LSM (r = 0.26, p=0.12). Area under the ROC for LSM and SSM with the presence of EV was 0.83 (95%CI 0.66-0.99) and 0.77 (95%CI 0.61-0.93). The combination of LSM and SSM by applying the cutoff of 18.8 kPa for LSM and 16.9 kPa for SSM provided 83% sensitivity and 82% specificity for the presence of EV. SSM <9.6 kPa would predict an absence of large EV (grade II-III) on endoscopy with a negative predictive value of 100%.

Conclusion: Transient elastography defining LSM and SSM can be considered to use as a non-invasive screening method for the presence of EV and of large EV.
Genetics and Genomics

A gain-of-function SYK mutation in a very early onset inflammatory bowel disease patient

Lin Wang¹, Qi Li², Kaiyue Peng¹, Ying Huang¹, Aleixo Muise²

¹Children’s Hospital of Fudan University, Shanghai, China, ²The Hospital for Sick Children, Toronto, Canada

Background and Aims: Severe forms of inflammatory bowel disease that develop in very young children are often caused by single gene defects. This study is aimed to determine the causative mutation in novel gene and pathways by whole exome sequencing (WES) and define precision medicine approaches based on the underlying genetic defect.

Methods: We performed whole-exome sequence (WES) analysis in the parent-child trio samples and confirmed by Sanger sequence. We used luciferase assay, western blot and immunoprecipitation to determine the different effects on NF-kB and MAPK signaling pathway between wild type and mutant group. We also used the inhibitor R406 to investigate its role on the activation of NF-kB and MAPK signaling pathways.

Results: We identified an infantile IBD case who presented in the first two weeks of life with severe colitis and fistulizing disease with a novel de novo autosomal dominant S550Y mutation in the Spleen Tyrosine Kinase (SYK). Functional studies demonstrated that the mutation resulted in hyper-tyrosine phosphorylation of SYK both in vitro and in PBMCs isolated from the patient. The S550Y SYK mutation resulted in enhanced auto-phosphorylation of Y525/526 and subsequent activation of both NF-kB and MAPK signaling through stabilizing the binding of SYK to TAB2 and TRAF3/6. These effects could be partially reversed using the SYK inhibitor R406.

Conclusions: The novel de novo SYK mutation is the first SYK mutation identified to cause human disease and functional studies suggest targeting SYK may be beneficial for treating patients with arthritis and colitis.

A genome-wide DNA methylation analysis identifies the crucial role of β-catenin (CTNNB1) in the pathogenesis of Kawasaki disease

Mao-Hung Lo¹, Kuang-Den Chen², Ho-Chang Kuo¹, Mindy Guo¹

¹Kawasaki Disease Center and Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, ²Institute for Translational Research in Biomedicine, Liver Transplantation Center and Department of Surgery, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

Background: Kawasaki disease (KD), a form of acute febrile vasculitis syndrome, is the most frequent cause of cardiac illness in children under five years old. While KD’s etiology is largely unknown, genome-wide studies in recent years have indicated that epigenetic factors may play a vital role in its pathogenesis.

Methods: We enrolled 24 KD patients and 24 non-KD controls to access their DNA methylation status using HumanMethylation450 BeadChips. Results were confirmed using pyrosequencing at CpG methylation sites according to the array data. Furthermore, another 34 KD patients and 62 control subjects were enrolled for expression validation. Functional study was performed using knockdown target gene expression in endothelial cells.

Results: Of the 3193 CpG methylation regions with a methylation difference ≥ 20% between KD and controls, 3096 CpG loci revealed hypomethylation, with only 3% (97 CpG loci) being hypermethylated. Pathway buildup by subnetwork analysis identified 11 networked genes among hypermethylated regions, including four transcription factors nuclear factor of activated T-cells 1 (NFATC1), v-ets avian erythroblastosis virus E26 oncogene homolog 1 (ETS1), runt related transcription factor 3 (RUNX3), retinoic acid receptor gamma (RARG), and the activator β-catenin (CTNNB1). Ten of these network-selected genes demonstrated a considerable mRNA decrease in KD patients. Furthermore, β-catenin knockdown in endothelial cells with venous (HUVEC) or arterial (HCAEC) origins drastically increased expression of CD40 and CD40L.

Conclusions: This study is the first to identify network-based susceptible genes of hypermethylated CpG loci, their expression levels, and the functional impact of β-catenin which could be involved in both the cause and development of KD.

Significance Statement: This is the first study to identify network-based susceptible genes of hypermethylated CpG loci through HumanMethylation450 BeadChips, their expression levels, and the functional impact of β-catenin which could be involved in both the cause and development of KD. β-catenin also provide future treatment potential for Kawasaki disease.
Using paired-end whole genome sequencing (WGS) to investigate complex chromosome rearrangements (CCRs) associated with congenital anomalies and neurodevelopmental disorders

Gordon KC Leung, Steven LC Pei, Christopher CY Mak, KS Yeung, Mullin HC Yu, Mandy HY Tsang, Gary TK Mok, Brian HY Chung
Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong

Objective: Our aim is to apply paired-end whole genome sequencing (WGS) to study a patient with congenital anomalies and developmental delay and complex chromosomal rearrangements (CCRs). Specifically we would like to improve the resolution of breakpoint analysis and to identify the underlying causes of the clinical manifestations.

Case report: A 10-month-old girl was referred for trigonocephaly and metopic synostosis. She was also found to have global developmental delay. Karyotyping showed a de novo type IV complex chromosomal rearrangement, 46,XX,(t;5;12),t(8,10,18)dn, and chromosomal microarray revealed a 8q23.3 deletion. However, these cytogenetic results can only explain part of her clinical features.

Method: We hypothesized that the unexplained clinical features are related to the CCRs. We aim to map the exact breakpoints using WGS. We performed a high-depth (i.e. 60X coverage) pair-ended WGS followed by bioinformatics analysis. Breakpoints for the CCRs were investigated using MANTA as the structural variant caller, followed by manual visualization of the raw data, with reference to the cytogenetic findings. The results were confirmed by Sanger sequencing with custom designed primers. The breakpoints were further analysed with clinical correlations to see if they can explain the clinical features via a) direct gene disruption; b) cryptic genomic imbalance and/or c) disruption of topologically associated domains (TADs).

Results: WGS confirmed all the known cytogenetic findings and provided a single nucleotide resolution for the CCR breakpoint. It confirms that the 8q23.3 deletion results in haplo-insufficiency of TRPS1 which is known to cause Tricho-Rhino-Phalangeal syndrome. In addition, the CCR breakpoint at chromosome 5 has directly disrupted CTND2 at intron 2, a gene known to be critical in causing intellectual disability in patients with Cri-du-chat syndrome. No additional cryptic genomic changes or TAD alternation involving other known disease-causing genes was identified. Micro-homology signatures were identified at the CCR breakpoints, providing insights into the mechanism underlying these complex rearrangements.

Discussion: Using WGS, we are able to identify the breakpoints of CCRs at single nucleotide level in this patient. The findings revealed that she actually has at least the dual diagnoses of trichorhinophalangeal syndrome and CTN-ND2-related intellectual disability. Compared to conventional methods, WGS has improved the diagnostic precision for CCRs, empowering a more individualized approach for both genetic counselling and management of this child and the family.

Acknowledgement: The study is supported by (i) Seed Fund for Basic Research (HKU201611159197) and (ii) the Society for the Relief of Disabled Children.

Molecular diagnosis of hepatic glycogen storage disease by gene panel-based next-generation sequencing: Results in 108 cases

Mingsheng Ma, Zhengqing Qiu, Zhixing Sun, Mengqi Zhang
Department of pediatrics, Peking Union Medical College Hospital, Beijing, China

Background and Aims: To evaluate the utility of molecular diagnosis for liver-affecting GSD of large sample volume by targeted gene panel-based NGS assay.

Methods: This work reports the use of gene panel-based next-generation sequencing to diagnose patients with hepatic glycogen storage disease. Sequence variants were matched against biochemical and clinical hallmarks.

Results: Altogether 108 Chinese pediatric patients clinically diagnosed with liver-affecting GSD were enrolled in the study. The most common related genes were AGL (GSD type III), PHKA2 (GSD type IXa), G6PC (GSD type Ia), and PYGL (GSD type VI). The molecular diagnosis rate for NGS was 88.0% (95/108) in total. In our study, 168 variations were detected, the majority of which had previously been associated with the phenotype of the disease. Prevalent examples include: a missense mutation (c.648G>T, p.L216L) in G6PC, occurred in 61.5% (16/26) of GSD type Ia alleles; a splicing-site mutation (c.1735+1G>T) in AGL, accounted for 6.9% (4/58) of GSD type III alleles; and a missense mutation (c.884G>A, p.R295H) in PHKA2, made up nearly 12.5% (3/24) of GSD type IXa alleles. Furthermore, we detected 69 variations that have never been reported before; most were either frame-shift or nonsense mutations (31 frame-shift mutations, 25 splicing-site mutations, 22 nonsense mutations, and 3 non-frame-shift deletions), and thus lead to a complete loss of gene function.

Conclusions: Our results clearly indicate that this method is an accurate, prompt, and cost-effective tool for clinical diagnosis of complex diseases with genetic heterogeneity such as GSD, providing a mutation search from large CNVs to SNVs and small indels in a single platform, thus facilitating diagnosis confirmation, appropriate medical care, and genetic counseling.
Oral Presentations

1038

Diet glycemic index change during pregnancy is associated with placenta insulin related gene DNA methylation variation

Wei-Li Yan, Da-Yan Niu, Yi Zhang, Yuan Jiang, Ya-Lan Dou, Ying Ye, Mi Ji
Department of Clinical Epidemiology, Children’s Hospital of Fudan University, Shanghai, China

Background and Aims: Low glycemic index (GI) diet is proved to be a new effective approach to help pregnant women manage body weight and improve the health of offsprings however the mechanism remains unclear. Our study analyzed the association between the change of diet GI during gestation and newborns’ DNA methylation.

Methods: The study sample was from a randomized controlled trial. Two different education programs were provided to overweight pregnant women to achieve glycemic index reduction of their diet. The information of their diets in 3 trimesters was collected by 24 hour diet records and the corresponding GIs were calculated. Placentas tissue were collected to extract DNA. 12 subjects whose diet GI from 1st trimester to the last trimester decreased most remarkably were chose as the case group; 12 subjects whose diet GI increased most were chose as the control group. The genome wide methylation level of two groups was examined by Illumina Human Methylation 450K Bead Chip. Genome-wide differential methylation analyses were performed and followed by various bioinformatics analysis such as Gene Ontology, KEGG Pathways. The probes discovered by significant differential methylation region (DMR) were verified by pyro sequencing.

Results: The diet GI decreased 24.3 (20.1-26.2) averagely in the case group and increased 19.6 (15.2-29.1) averagely in the control group. According to the genome wide methylation analysis, 2259 MVPs were found. Among all the MVPs, the methylation level of 1499 (66.4%) positions increased and 760 (33.6%) positions decreased when the case group was compared with the control group. The genome wide methylation level of two groups was examined by Illumina Human Methylation 450K Bead Chip. Genome-wide differential methylation analyses were performed and followed by various bioinformatics analysis such as Gene Ontology, KEGG Pathways. The probes discovered by significant differential methylation region (DMR) were verified by pyro sequencing.

Conclusions: The change of diet glycemic index change during gestation may have impact on offspring’ insulin resistance level through varying placenta tissue insulin resistance related gene methylation. The findings needs further study to validate.

1338

Association of single nucleotide polymorphisms of IL23R and IL17 with necrotizing enterocolitis in premature infants

Jiayi Tian, Chaoying Yan
The First Hospital of Jilin University, Changchun, China

Background: Necrotizing enterocolitis (NEC) is a severe gastrointestinal inflammatory disease in neonates, particularly in preterm infants. The interleukin (IL) 23/IL17 axis has been shown to play an important role in the gastrointestinal inflammation. However, the association of gene polymorphisms in the IL23/IL17 axis and the development of NEC remains unknown. In this study, we aimed to explore a possible genetic role of IL23R and IL17 in the development of NEC.

Methods: We identified single nucleotide polymorphisms (SNPs) in IL23R (rs10889677), IL17A (rs2275913), and IL17F (rs763780) by polymerase chain reaction and Sanger sequencing. A total of 102 NEC patients (stage II, n=75; and stage III, n=27) and 120 control subjects were recruited for the study. All of the participants were premature (gestational age <37 weeks).

Results: Our results revealed that the combination of the IL17F rs763780 (TC+CC) genotype and the C allele both significantly increased the risk of NEC [odds ratio (OR)=1.89, 95% confidence interval (CI) =1.04–3.43, p=0.035; OR=1.82, 95% CI=1.06–3.13, p=0.028, respectively]. Furthermore, the rs763780 (TC+CC) genotype was associated with increased severity of NEC and the incidence of NEC-related perforation [OR=2.80, 95%CI=1.10-7.12, p=0.031; OR=3.86, 95%CI =1.10-13.53, p=0.035, respectively]. However, IL23R rs10889677 and IL17A rs2275913 were not associated with the susceptibility to NEC.

Conclusion: Our data suggest that a variant of IL17F (rs763780) may contribute to the development of NEC.
Asthma diagnosis was associated with single-nucleotide polymorphisms of the gene encoding human rhinovirus-C receptor in children

YuPing Song, Man-Fung Tang, Agnes Sze-Yin Leung, Renee Wan-Yi Chan, Gary Wing-kin Wong, Ting-Fan Leung

Chinese University of Hong Kong, Hong Kong

Background and Aims: Asthma is a common obstructive lung disease in children. Rs6967330 of CDHR3, being the gene encoding human rhinovirus-C (HRV-C) receptor, was reported to be a risk factor for severe asthma exacerbations in Danish preschoolers. Recent data suggested that the mutant of this single-nucleotide polymorphism (SNP) increased bronchial epithelial susceptibility to HRV-C infection, but the relevance of CDHR3 for asthma diagnosis remains unclear. This study investigated the association between CDHR3 and childhood asthma diagnosis and subphenotypes.

Methods: Ten tagging SNPs located within 5-kb both upstream and downstream from rs6967330 were selected by HaploView 5.0 based on 1000 Genomes database searched at pairwise r² ≥ 0.8 for linkage disequilibrium (LD) for all SNPs with minor allele frequencies (MAFs) ≥ 0.01 in Southern Han Chinese (CHS). These tagging SNPs were genotyped by TaqMan assays on QuantStudio 12K Flex real-time PCR system. Genetic associations between these SNPs and categorical and quantitative variables were analysed by logistic and linear regression, respectively, fitted for recessive and co-dominant models.

Results: 903 Chinese children with asthma and 1205 non-allergic controls were recruited, with their mean (SD) age in years being 11.0 (4.1) and 13.6 (4.5). Atopy, defined as having at least one positive skin prick test or aeroallergen-specific immunoglobulin E, occurred in 75.3% of patients and 37.9% of controls (p<0.0001). The overall genotyping efficiency was ≥ 95%. MAFs of tested SNPs were comparable to those published for CHS, except rs448025 and rs543085868 which were monomorphic. Asthma diagnosis was significantly associated with rs6967330 under additive model (odds ratio [OR] 1.34 and 95% confidence interval [CI] 1.00-1.80; p=0.049) and dominant model (OR 1.40 and 95% CI 1.03-1.90; p=0.032). This SNP, however, was not associated with atopy or spirometric indices. None of the other SNPs was associated with asthma diagnosis or subphenotypes.

Conclusions: Rs6967330 of CDHR3 is associated with asthma susceptibility in Hong Kong Chinese children, but none of the SNPs is associated with patients’ lung function. Whereas these results may reflect the importance of HRV-C infection in modulating asthma susceptibility, prospective studies with larger sample size are needed to confirm this genetic association.

Funding: Direct Grant for Research (4054292) of CUHK

Haematology and Oncology

Integrated genomic analysis of pediatric germ cell tumors

YasuKubota1, Masafumi Seki1, Tomoya Isobe1, Ryosuke Shiozawa1, Kenichi Yoshida1, Keisuke Kataoka2, Yuichi Shiraishi2, Kenichi Chiba2, Hiroko Tanaka4, Yukichi Tanaka4, Satoru Miyano3, Akira Oka3, Yasuhide Hayashi4, Seichi Ogawa2, Junko Takita1

1Department of Pediatrics, The University of Tokyo, Tokyo, Japan, 2Department of Pathology and Tumor Biology, Kyoto University, Kyoto, Japan, 3Human Genome Center, The Institution of Medical Science, The University of Tokyo, Tokyo, Japan, 4Division of Pathology, Kanagawa Children’s Medical Center, Kanagawa, Japan, 5Gumma Children’s Medical Center, Gunma, Japan

Background and Aims: Germ cell tumors (GCTs) arise from primordial germ cells, which migrate during embryogenesis from the yolk sac through the mesentery to the gonads. GCTs include several histological subgroups, such as yolk sac tumor and teratoma. Since they derive from the same cell origin, primordial germ cells, GCTs may have common genetic alterations. The isochromosome of 12p is a common genomic alteration in adult testicular GCTs, and TP53 or KIT mutation has been frequently found in adult testicular GCTs. However, genetic basis of pediatric GCTs is still to be elucidated due to its rarity.

Methods: Forty-six pediatric GCT samples, which included 9 teratomas, 6 dysgerminomas, 2 embryonal carcinomas, 6 mixed germ cell tumors (MGCT), and 23 yolk sac tumors (YST) were used in this study. We applied genome-wide analysis for genetic abnormalities using SNP array analysis to 46 cases, whole-transcriptome sequencing (WTS) to 39 cases, and methylation array analysis to 26 cases. To validate gene mutations detected by WTS, targeted deep sequencing was also conducted.

Results: SNP array analysis revealed that chromosomal gains were predominantly detected rather than chromosomal losses in pediatric GCTs. Among the recurrent gains, 12p gain was the most frequent genetic alteration in this study. Nine samples with 12p gain have been supeculated to have the isochromosome of 12p. Based on the consensus clustering of expression data, GCTs were divided into 3 clusters. Each cluster showed a distinct pattern of gene expression and characterized by histological subgroups. Cluster 1 includes all teratomas. Cluster 2 includes all ECs and most of DGs. Cluster 3 includes most of YSTs. This result enlightened each histological subtypes of GCTs have clearly characteristic gene profiles. Intriguingly, high expression of KIT or CXCR4 pathway genes were commonly detected in all clusters. Activating mutations of KIT (n=2) and NRAS (n=1) were detected in group 2 and group 3, respectively. Consensus clustering of methylation array analysis divided GCTs into two clusters, which were consistent of histological subtypes, teratomas and yolk sac tumors (YSTs), respectively. We also detected several DMRs between two clusters. Cluster of YSTs had hypermethylation of RASSF1, which is known as a tumor suppressor gene.

Conclusions: We identified specific gene expression profiling of pediatric GCTs and upregulation of KIT or CXCR4 signaling in GCTs. Since KIT and CXCR4 signaling is essential for migration and proliferation of primordial germ cells, these findings suggest that KIT or CXCR4 signaling have a potential role in the pathogenesis of GCTs, and might be novel therapeutic targets for GCTs.
Cost-benefit analysis of thalassemia screening in Thai adolescence

Duantida Songdej1, Ampaiwan Chuansumrit1, Nongnuch Sirachainan1, Oraluck Pattanaprateep2, Praguwyn Kadegasem3, Pakawan Wongwerawat-tanakoon1, Werasak Sasanakul1

1Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand 2Sector for Epidemiology and Medical Statistics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Backgrounds: Although a Thai national policy to antenatally screen couples at risk of having affected babies with severe thalassemia has been implemented for decades, at least 12,000 patients were born each year. An important reason for these preventable events is late first antenatal clinic visit. Therefore, thalassemia screening starting from early child-bearing age is required.

Objectives: To identify the most cost-benefit thalassemia screening package for Thai adolescence.

Methods: A total of 97 secondary school students in Ayutthaya province were explored for thalassemia using Mean Corpuscular Volume (MCV), 2,6-Dichlorophenol-Indophenol Precipitation (DCIP), Hemoglobin (Hb) electrophoresis and DNA analysis for 7 common deletional and 2 non-deletional α-thalassemia. Combination of all test results were used as a gold standard for diagnosis of thalassemia. Three potential packages for thalassemia screening were proposed: 1) MCV and DCIP, 2) MCV and Hb electrophoresis, 3) MCV, Hb electrophoresis and DNA analysis for the South East Asian (SEA) deletion. Data from the study group were used as a base to compare relevant costs for each thalassemia screening package and no screening strategy. Cost-benefit analysis was performed using decision tree model, calculated according to health burdens over the patients’ lifetime. Tornado sensitivity analysis was conducted to investigate the effect of parameter uncertainty.

Results: Mean (SD) age of enrolled students were 13 (±0.6) years and 51.5% of the students were female. Twenty-two students (23%) are carriers at risk of having a child with severe thalassemia, including Hb Bart’s hydrops fetalis, β-thalassemia major and β-thalassemia/HbE. The screening using MCV and DCIP showed sensitivity and specificity to detect carriers at risk of 95% and 83% respectively, whereas the screening using MCV and Hb electrophoresis provided a higher sensitivity of 100% and similar specificity of 85%. Surprisingly, detection of the SEA deletion did not show additional benefits. MCV and Hb electrophoresis were also shown to be the most cost-benefit among the three potential screening packages. These two tests cost 360 Baht (US $11) per subject, whereas the cost for taking care of one severe thalassemia patient comprises 2.3 million Baht (US $67,647). Based on this study model, a difference of incremental benefit to incremental cost of thalassemia screening using MCV and Hb electrophoresis, as compared to no screening strategy, is 22,153 Baht (US $652) per capita of general Thai adolescence.

Conclusion: Mean corpuscular volume and hemoglobin electrophoresis are the most cost-benefit thalassemia screening in Thai adolescence.

Haploidentical stem cell transplantation with post-transplant cyclophosphamide in pediatric high-risk acute leukemia with good disease controls and immune reconstitution.

Supavich Tannumsaeng, Kittituch Amornprasitpol, Usanarat Anurathapan, Samart Pakakasama, Surapong Lerthammakiat, Suradej Hongh

Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background and Aims: Acute leukemia is the most common childhood cancer worldwide. Most of the patients, suffering from relapsed or refractory disease, need allogeneic stem cell transplantation; however donor availability is the main obstacle. To solve this dilemma, haploidentical stem cell transplantation has been recently introduced. In this study, we would like to analyze the results and the immune reconstitution of this novel approach at Ramathibodi Hospital.

Methods: We retrospectively reviewed medical record of 23 pediatric patients with high-risk or relapsed ALL and AML, whose age less than18 years old, between August 2012 and February 2017. All patients were in the remission state of disease at the time of the study. HLA studying of the patients and their parents were done by high-resolution technique searching for HLA subunit A, B, C, DR and DQ. Parents with greater HLA matching were selected as a haploidentical donor for their sibling. Before receiving conditioning regimen, patient’s blood was obtained to measure serum IgG and WBC level and then continuously evaluate at 1, 3, 6, 12, 24 month post-transplantation for immune reconstitution analysis. All patients received conditioning regimen, thiotepea based or TBI based, prior to transplantation. Then patients received unmanipulated haploidentical stem cell products at the day 0, then received post-transplantation cyclophosphamide, cyclosporin or tacrolimus, and mycophenolate mofetil as the graft-versus-host-disease prophylaxis. The median follow-up time of this study is 17.1(0.6-51.3) months.

Results: Twenty-two patients had engraftment. One patient, who was not engrafted, deceased due to severe infection. One patient was suffered from grade III-IV acute GVHD; three patients developed moderate-to-severe chronic GVHD. Thirteen patients encountered viral infections especially cytomegalovirus (8 cases), BK virus (6 cases) and adenovirus (4 cases). No patient had primary graft failure. Two patients died of relapsed disease while three patients died of severe infection. The one-year event-free survival and the one-year overall survival were 75.3 and 79.3%, respectively. The relapse rate was 19.1 (0.5-59.4) % meanwhile the transplant-related mortality was 15.0 (0.2-54.9) %. T, B and NK cell numbers were at the lowest values at one month after transplantation. Interestingly, CD4+ T cell was reduced but not to the critical point while memory helper T-cell received little effect.

Conclusions: Our haploidentical transplantation with Post-transplant cyclophosphamide gives a satisfied outcome. But viral reactivation is the major morbidity in our study. This conditioning regimen would not reduce CD4+ T cell to the critical point and be safe for memory helper T-cell.
Unmanipulated haploidentical stem cell transplantation with post-transplant cyclophosphamide in children with severe thalassemia with good outcome and rapid immune reconstitution

Kittituch Amornprasitpol, Usanarat Anurathapan, Samart Pakakasama, Duantida Songdej, Surapong Lertthammakiet, Nongnuch Sirachainan, Ampaiwan Chuansamrit, Suradej Hongeng

Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background and Aims: Thalassemia disease can be treatable by allogeneic marrow transplantation. However, HLA-matched donors are difficult to find. HLA-haploidentical hematopoietic cell transplantation (Haplo-HCT) is an alternative transplant strategy for patients without an HLA-matched donor. Recently, expanding the number of patients treatable by haplo-HCT especially in Thailand. Conversely, lack of the study supported the immune reconstitution outcome. The aim of this study was to evaluate the haplo-HCT in Thai children with thalassemia.

Methods: This retrospective study was conducted at Ramathibodi Hospital, including patients with severe thalassemia who received haplo-HCT in which collected from their parents. Fludarabine, busulfan and anti-thymocyte globulin were used as a conditioning regimen. In addition, all patients were received fludarabine plus dexamethasone at 3 and 6 weeks prior to conditioning regimen. All patients received unmanipulated hematopoietic cell products. Graft-versus-host disease (GvHD) prophylaxis regimen consisted of cyclophosphamide, mycophenolate mofetil, and calcineurin inhibitor. Moreover, patients with positive donor specific HLA were received rituximab additionally.

Results: Fourteen patients, at the median age of 11.8 (3.7-18.8) years, enrolled in the study. Thirteen patients were diagnosed as beta-thalassemia/hemoglobin E disease and 1 patient had beta-thalassemia major disease. Eleven patients received stem cells from their mothers. The average stem cells dose was 10.1 × 10^6 cells/kg of recipient body weight. The median time of neutrophil and platelet engraftment were 14 and 26.5 days after transplantation, respectively. Eight patients developed mucositis; 3 patients had engraftment syndrome. Three patients developed hepatic veno-occlusive disease. In our study, 10 patients developed grade I-II acute GvHD. Mild chronic GvHD was found in 7 patients. Ten patients encountered viral infections especially BK virus(n=8), adenovirus(n=2), and cytomegalovirus(n=3). Secondary graft failure was found in 1 patient. At the median follow-up time of 15.5 (3.3-36.0) months, the one-year event free survival and the one-year overall survival rates were 92.86% and 100%, respectively. Moreover, the number of NK cell, B cell, and T cell decreased to the lowest point (111.5, 5.083 and 442.0 cells, respectively) at one month then the number of B cell and T cell gradually increased to the peak at 1 year after transplantation. Interestingly, the serum immunoglobulin G level decreased gradually to the lowest point (6.358 mg/ml) at three month after transplantation whereas the number of immunity cells were lowest at the first month.

Conclusion: Our haplo-HCT with post-transplant cyclophosphamide gives a good outcome with high rate of viral infection. Immune reconstitution study showed rapidly increase of number of immune cells and immunoglobulin levels.
remained as an independent prognostic factor for adverse survival outcomes. Administration of CD9 antibody substantially reduced leukemic burden and prolonged survival of animals xenografted with the intermediate-risk 697 (TCF3-PBX1+) and high-risk RS4;11 (MLL-AF4+), but not the standard-risk Reh (ETV6-RUNX1+) cell lines. Similarly, CD9 antibody treatment significantly decreased B-ALL progression in patient-derived xenografts with a wide spectrum of genetic and disease features, including TCF3-PBX1+ and MLL-AF4+cases and those with relapsed/refractory diseases. Importantly, CD9 antibody in combination with conventional chemotherapy consisting of vincristine, dexamethasone and L-asparaginase further prolonged animal survival, when compared to animals treated with CD9 antibody or chemotherapy alone.

Conclusions: Expression of CD9 in pediatric B-ALL patients was associated with adverse survival outcomes and could be used for refinement of clinical risk group stratification. CD9 blockade, in adjunct to chemotherapy, was highly effective for suppressing B-ALL progression in preclinical animal models and could be developed as a novel and promising strategy for treatment of high-risk pediatric B-ALL.

Acknowledgements: Supported by the RGC/GRF (14108615), CCF (7104593) and CUHK Direct Grant (4054291).

Neonatology

54

Prognostic accuracy of parent-reported ages and stages questionnaire in assessing the developmental outcome of preterm infants

Gwen Hwarng1, Imelda Ereno2, Selina Ho2, John Allen1, Cheo Lian Yeo2

1Duke-NUS Medical School, Singapore, 2Singapore General Hospital, Singapore

Background and Aims: Preterm birth and low birth weight are associated with developmental delay. Given these risks, early identification and intervention are imperative. However, standardized tests to assess development are often time-consuming and require trained personnel. In contrast, the Ages and Stages Questionnaire (ASQ) is a parent-completed questionnaire which can be used for developmental screening in children up to 5 years of age. Thus, an assessment of the prognostic accuracy of the ASQ compared to standardized assessment tools is essential. The aim of the study is to compare the prognostic agreement between the ASQ (3rd Edition) and standardized assessment tools.

Methods: This was an observational study of preterm infants presenting to the Neonatal Neurodevelopmental Clinic at Singapore General Hospital from January 2014-June 2017. At follow-ups, the ASQ was completed by parents, and standardized assessment tools were administered: Peabody Developmental Motor Scales 2nd Ed (PDM) by the physiotherapist (6, 12 months), Bayley-III Screening test (Bayley) by the neonatologist (12 months), and Preschool Language Scale 4th Ed (PLS) by the speech therapist (18 months), all at corrected ages. ASQ Gross and Fine Motor scores were compared to PDMS at 6 months (n=113) and 12 months (n=106), ASQ Problem Solving score to Bayley Cognitive score at 12 months (n=106), and ASQ Communication score to PLS at 18 months (n=91). Statistical analysis included Spearman and Pearson correlation, McNemar’s test for correlated binary outcomes, logistic regression, and ROC analysis.

Results: At 6 months, ASQ-predicted accuracy of Gross Motor outcome was 81.4% (p≤0.0002) (sensitivity 69.2%, specificity 83.0%, PPV 34.6%, NPV 95.4%); and ASQ-predicted accuracy of Fine Motor outcome was 81.4% (p≤0.0025) (sensitivity 58.3%, specificity 84.2%, PPV 30.4%, NPV 94.4%). At 12 months, ASQ-predicted accuracy of Gross Motor outcome was 79.0% (p≤0.0001)
(sensitivity 65.5%, specificity 84.2%, PPV 61.2%, NPV 86.5%); ASQ-predicted accuracy of Fine Motor outcome was 71.0% (p ≤ 0.0354) (sensitivity 39.3%, specificity 82.3%, PPV 44.0%, NPV 79.3%); and ASQ-predicted accuracy of Cognitive outcome was 50.9% (p ≤ 0.54) (sensitivity 39.7%, specificity 67.4%, PPV 64.1%, NPV 43.3%). At 18 months, ASQ-predicted accuracy of Language outcome was 64.8% (p ≤ 0.0021) (sensitivity 51.0%, specificity 81.0%, PPV 75.8%, NPV 58.6%).

Conclusions: At 6 and 12 months, the Motor domains of the ASQ showed high accuracy in screening both gross and fine motor skills. At 18 months, the Language domain of the ASQ also met acceptable diagnostic accuracy. However, the Cognitive domain of the ASQ at 12 months was not sensitive enough to accurately identify an infant’s cognitive abilities, hence standardized tests are still recommended to screen the cognitive abilities of infants at 12 months of age. In conclusion, the ASQ may be used to screen the motor skills of preterm infants at 6 and 12 months, and language abilities at 18 months.

Nephrology

182

Distinctive cytokine profile between acute focal bacterial nephritis and acute pyelonephritis in children

Makoto Mizutani1, Shunji Hasegawa1, Takeshi Matsushige1, Naoki Ohta1, Setsuaki Kittaka1, Madoka Hoshide1, Takeshi Kusuda1, Kazumasa Takahashi1, Kiyoshi Ichihara2, Shouichi Ohga1,3

1Department of Pediatrics, Yamaguchi University Graduate School of Medicine, Ube, Japan, 2Department of Clinical Laboratory Sciences, Faculty of Health Sciences, Yamaguchi University Graduate School of Medicine, Ube, Japan, 3Department of Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Background and Aims: Acute focal bacterial nephritis (AFBN) is a severe form of upper urinary tract infection (UTI) with neurological manifestations and focal renal mass lesions on computed tomography (CT). Prolonged antibiotic therapy may improve the renal outcome, but the early differential diagnosis of AFBN from acute pyelonephritis (APN) is challenging. We searched for effective biomarkers of AFBN based on the pathophysiology of upper UTIs.

Methods: Of 52 upper UTI cases treated at Yamaguchi University between 2009 and 2016, 38 pediatric patients with AFBN (n=17) or APN (n=21) who underwent ultrasonography and/or CT were enrolled. The clinical data and serum cytokine concentrations were analyzed to differentiate AFBN from APN.

Results: AFBN patients tended to be older, and have a higher body temperature, longer febrile period, more frequent neurological symptoms, higher immature neutrophil count, lower lymphocyte count, higher procalcitonin and urine β₂-microglobulin levels. AFBN patients showed higher serum levels of IFN-γ, IL-6, IL-10 and soluble TNF-receptor 1 (sTNFR1) (all p<0.05). Although levels of the cytokines were variably correlated among each other, multiple logistic regression analysis revealed that combination of IFN-γ and IL-6 levels were most relevant for distinguishing AFBN from APN. The discriminant power of the logistic equation was 0.86 in terms of the area under the curve by the ROC analysis.

Conclusions: In AFBN, serum levels of 4 out of 7 cytokines examined were higher compared with those in APN. For distinguishing AFBN from APN, IFN-γ and IL-6 were most relevant.
Unsafe environment puts slum children in Peril: A cross-sectional study on microbial contamination of complementary food and water in Dhaka, Bangladesh

Ishita Mostafa1, Nurun Nahar1, Faruque A.S.Golam1, Mustafa Mahfuz1, Manoj Roy2, Tahmeed Ahmed1

1International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh, Environment Centre (LEC), Lancaster University, United Kingdom, Lancaster city, United Kingdom

Background and Aim: Under-nutrition accounts for 3.5 million deaths and 35% of disease burden among children of less than five years of age. In developing countries, inappropriate or inadequate introduction of complementary food causes decline in child’s growth after the age of 6 months resulting in high prevalence of malnutrition. Complementary food prepared without maintaining proper hygienic practices exposes the child to enteropathogens. As a result food and water borne infectious disease like diarrhea has a negative impact on the nutritional status of these children. We conducted a cross-sectional study to examine microbial contamination of complementary food and water, status of household food access, water, sanitation, hygiene practice and nutritional status of children 0-59 months old in four slums of Dhaka, Bangladesh.

Methods: This cross-sectional study took place from December 2015 to May 2016. A total of 360 children aged 0-59 months and their mothers/caregivers participated in the study. Household food security, socio-economic context, nutritional status, hygiene and feeding practices were recorded. Complementary food and water samples were collected from 72 households and tested for microbial contamination. Logistic regression (backward step-wise) model was fit to identify the factors that were significantly associated with malnutrition. Strength of association was determined by calculating adjusted odds ratios (aOR) and their 95% confidence intervals (CI). Probability of < 0.05 was considered statistically significant.

Results: Among the 360 under 5 children, 63.3% (CI 0.58-0.69) were malnourished as evident either by weight-for-height, weight-for-age or by height-for-age Staphylococcus. Yeast and moulds, and coliform were detected in 85.7% (CI 0.74-0.93) and 73.2% (CI 0.59-0.84) of complementary food samples, respectively. About 82.5% of the households had food insecurity. Logistic regression shows that malnutrition was associated with lack of hand washing after cleaning the child’s bottom following defecation (OR 2.04; 95% CI 1.27–3.29), low birth weight as perceived by mothers (OR 1.96; 95% CI 1.11-3.47) and exclusive breast feeding (OR 0.44, 95% CI 0.27-0.70).

Conclusion: children under the age of five were most often stunted. Complementary food and water samples were contaminated which could be attributed to poor quality of water, sanitation and food preparation practices. Integrated efforts may promote healthy complementary feeding practices in the low income settlements.

Acknowledgement: This paper originates from EcoPoor, research programme, which is funded by the UK Government’s ESPA (www.espa.ac.uk) programme (NE-L001616-1)
Respirology

Effects of a group-based acceptance and commitment therapy versus asthma education for training parents to manage their children with asthma: A randomized controlled trial

Yuen-Yu Chong¹, Yim-Wah Mak¹, Alice Yuen Loke¹, Shu-Yan Lam²

¹School of Nursing, The Hong Kong Polytechnic University, Hong Kong, ²of Paediatric and Adolescence Medicine, Tuen Mun Hospital, Hong Kong

Background and Aims: Parents of children with asthma face many psychological difficulties that can adversely affect their asthma care. Acceptance and Commitment Therapy (ACT) is a contextual behavioral therapy to help parents to better accept their psychological difficulties and work towards achieving better health outcomes for their children. This study aimed to examine the efficacy of a parental training program using group-based ACT for childhood asthma management in comparison with an asthma education talk, as measured by the children’s use of healthcare services due to asthma exacerbations at six months after the intervention.

Methods: An assessor-blinded, two-armed randomized control trial was conducted. Parents and their children aged 3-12 years were consecutively recruited in a public hospital in Hong Kong from January to July 2016. The parents were randomly assigned either to four weekly sessions of a group-based ACT intervention (ACT group), or to an asthma education talk as the usual care plus three weekly telephone reminders (Control group). The goal of ACT was to enhance the psychological flexibility of the parents in caring for a child with asthma in the following ways: (i) to be aware of the present moment with thoughts and feelings, (ii) to accept and adapt flexibly to challenging situations, and (iii) to take actions to achieve valued goals in childhood asthma management. The primary outcomes were the number of visits to emergency departments (EDs), outpatient clinics, or hospital admissions due to asthma exacerbations at six months after the intervention. Changes in these outcomes between groups were examined using generalized estimating equations.

Results: 168 parents (age M = 38.4, 88.1% mothers) and their children with asthma (age M = 6.8) participated. 162 (96.4%) parent-child dyads successfully adhered to the follow-up assessments up to six months. When compared to the control group, children whose parents were allocated in the ACT group showed a significant drop compared to the control group, children whose parents were allocated in the ACT group showed a significant drop in ED visits (adjusted [incidence rate ratio] IRR = 0.22, 95% CI [0.08, 0.59], p=0.003), and in outpatient clinic visits (adjusted IRR = 0.27, 95% CI [0.08, 0.84], p=0.024) due to asthma exacerbation. There was no significant effect on the hospital admissions between groups (p=0.455).

Conclusions: The results suggest that parents’ active commitment to engaging in meaningful activities with their children with asthma and accepting the related psychological difficulties might help them to better manage their children’s asthma, thereby producing better health outcomes for their children.

Sleep duration is negatively associated with carotid intima-media thickness in adolescents

Jade Wing-Sum Li, Chun-Ting Au, Ping Chook, Albert Martin Li

The Chinese University of Hong Kong, Hong Kong

Background and Aims: Sleep plays an essential role in maintaining metabolic homeostasis, ensuring memory consolidation and body restoration. However, sleep deprivation is an increasing phenomenon, and in adults, emerging evidence suggests chronic sleep deprivation can lead to adverse cardiovascular events. Sleep pattern tracks from young age and whether sleep deprivation in adolescents is associated with any cardiovascular risks remains unknown. In this study, we aimed to investigate the relationship between sleep duration and carotid intima-media thickness (CIMT) in adolescents. We hypothesised that short sleep duration was associated with increased CIMT in this paediatric population.

Methods: Healthy subjects aged 10-18 years old were recruited from a school-based cohort established to examine the prevalence of obstructive sleep apnoea in Hong Kong. All subjects underwent anthropometric measurements, overnight polysomnography (PSG) and CIMT assessment. Mean sleep duration was obtained from a prospective 7-day sleep diary. Subjects who were overweight or with an obstructive apnoea-hypoapnoea index (OAHI) ≥5 were excluded from the analysis. The subjects were divided into groups according to their mean sleep duration for comparisons, regression analysis was used to assess the association between CIMT and sleep duration and other possible correlates.

Results: One hundred and forty one subjects completed the assessments. Male subjects tended to have shorter sleep duration than females. There were no significant differences in age, BMI, Tanner stage and parental history of hypertension between groups of different sleep durations. Subjects with shorter sleep duration had higher CIMT (r=-0.267, p=0.001). Sleep duration was an independent parameter negatively associated with CIMT.

Conclusions: Sleep duration was found to be negatively associated with CIMT in adolescents. Adult adverse cardiovascular events may take its origin from adolescence as a result of chronic sleep deprivation. Our study endorsed the importance of adequate sleep duration in adolescents, a critical period when various physiological changes are taking place.
Prospective study of risk factors for wheezing phenotypes in Hong Kong children

Agnes Sze-Yin Leung¹, Ting-Fan Leung¹, Man-Fung Tang¹, Wing-Hung Tam², Hing-Yee Sy¹, Gary Wing-Kin Wong²

¹Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong; ²Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, Hong Kong

Background and Aims: Given the importance of early-life wheezing as a strong risk factor for subsequent asthma, the identification of early-life determinants for wheezing phenotypes can improve our prediction for the development of childhood asthma. Ten asthma loci were identified in the genome-wide association study (GWAS) by GABRIEL Consortium. Nonetheless, the relevance of these loci on early-life wheezing remains unclear. This birth cohort study characterized both environmental and genetic determinants for early-life wheezing.

Methods: Early-life factors, environmental factors and occurrence of wheezing phenotypes of 149 healthy Chinese neonates born in September 2012 were prospectively assessed at baseline and 9 and 24 months. Buccal swab samples were genotyped for single-nucleotide polymorphisms (SNPs) reported by GABRIEL using TaqMan genotyping assays. Linear regression and binary logistic regression were used to identify the genetic and environmental risk factors for wheezing.

Results: Adjusted for gender and family history of asthma/eczema as covariates, presence of household smokers (odds ratio [OR] 5.89, 95% confidence interval [CI] 1.02-33.84; p=0.047) and furry pet exposure (OR 6.47, 95% CI 1.21-34.69; p=0.029) at birth were risk factors for current wheeze at 9 months. These exposures were also associated with increased risk for wheeze ever both at 9 months (OR 3.99, 95% CI 1.35-11.84; p=0.012 and OR 3.51, 95% CI 1.06-11.59; p=0.040) and 24 months (OR 2.68, 95% CI 1.03-7.00; p=0.044 and OR 3.81, 95% CI 1.31-11.08; p=0.014). Besides, visible mould or dampness at home increased the risk for current wheeze at 9 months (OR 10.53, 95% CI 1.17-94.47; p=0.035). Concerning the genetic factors, rs2284033 in IL2RB was weakly associated with current wheeze at 9 months (OR 9.32, 95% CI 1.22-71.08; p=0.031), while rs11650680 in TOP2A was associated with wheeze ever at 9 months (OR 0.27, 95% CI 0.08-0.91; p=0.035) and rs1295686 in IL13 with wheeze ever at 24 months (OR 2.51, 95% CI 1.01-6.26; p=0.049). All other SNPs were not associated with any wheezing traits.

Conclusions: This study identifies exposures to passive smoking, pet keeping and domestic visible mould or dampness as risk factors for wheezing phenotypes at 9 and 24 months. IL2RB, TOP2A and IL13 appear to be candidate genes for early-life wheezing, which should be replicated in larger cohorts.

Funding: Research Committee’s One-off Fund for Research (3132910) and Direct Grant for Research (4054292) of CUHK

ORMDL3 may participate in the pathogenesis of bronchial epithelial-mesenchymal transition in asthmatic mice with airway remodeling

Qi Cheng, Yunxiao Shang

Department of Pediatrics, Shengjing Hospital of China Medical University, Shenyang, Liaoning, China

Background and Aims: Asthma is a common chronic respiratory disease in children and is caused by a complex interaction of genetic and environmental factors.Ormocoid-like 3 (ORMDL3) is a candidate gene that has been strongly linked to asthma, but the underlying mechanisms are unknown. ORMDL3 regulates the expression of metalloproteinases and TGF-β, and ORMDL3 transgenic mice exhibit increased airway remodeling. Hence, ORMDL3 may be associated with airway remodeling. We attempted to examine the relationship between ORMDL3 and the severity of airway remodeling in asthmatic mice and to determine whether ORMDL3 induces epithelial-mesenchymal transition (EMT) in the bronchial epithelium.

Methods: BALB/c mice were randomly assigned to control and asthma groups. Lung tissues were collected on days 3, 7, and 14 of ovalbumin (OVA) challenge. We observed airway remodeling in asthmatic mice by hematoxylin and eosin (HE) and Masson staining. Morphological changes in the bronchial epithelium were assessed by transmission electron microscopy. The EMT-related indicators E-cadherin (E-cad), fibroblast-specific protein 1 (FSP1), and Vimentin (VIM) were assessed by western blotting and real-time PCR at different time points of airway remodeling in asthmatic mice to detect the EMT trend. Then, the localization of ORMDL3 was observed by immunohistochemistry, and its protein and mRNA expression was examined by western blotting and real-time PCR, respectively. Furthermore, the bronchial epithelial cell line 16HBE14o- was transfected with an ORMDL3-expressing plasmid, and changes in E-cad, FSP-1, and VIM were detected by immunofluorescence, western blotting and real-time PCR, and cell invasive ability was assessed by microscopy.

Results: ORMDL3 expression in the bronchial epithelium was correlated with airway remodeling and EMT progression in vivo. Transfection of ORMDL3 into 16HBE14o- cells in vitro induced EMT.

Conclusions: ORMDL3 may regulate EMT in the bronchial epithelium, thereby affecting airway remodeling in asthma.
Rheumatology

Efficacy and safety of Infliximab in juvenile idiopathic arthritis and juvenile ankylosing spondylitis: A randomized, double-blind, controlled study

Ying Xie, Huasong Zeng
Guangzhou Women and Children's Medical Center, Guangzhou, China

Objective: The randomized double-blind method was designed to observe the efficacy and safety of infliximab for juvenile idiopathic arthritis (JIA) and juvenile ankylosing spondylitis (JAS).

Methods: The 45 cases of this study were allocated to treatment group and control group using the randomized, double-blind method. The treatment group was divided into JIA subgroups and JAS subgroup. The test group received MTX combined with infliximab intravenous infusion (JIA group: 3 mg.kg\(^{-1}\); JAS group: 5 mg.kg\(^{-1}\)); the control group received MTX combined an equal volume of placebo intravenous infusion.

Results: The treatment groups of this study included 12 JIA cases and 7 JAS cases while the control group included 18 JIA cases and 8 JAS cases. The ASAS 20 response rate of JAS treatment group after two weeks was 85.7%, which was far higher than 25 % , the rate of the control group (p=0.04). The ASAS 20 response rate in the treatment group at the endpoint was 100%, while the rate of control group was 37.5 % (p=0.07) . The total number of infliximab injection was 124, including 24 JIA and JAS cases. One JIA case of penicillin anaphylaxis appeared with systemic wheal -like rash during the 4th injection, and the rash subsided one hour later with the oral phenergan treatment.

Conclusion: This study shows that MTX combined with infliximab can quickly alleviate joint pain and reduce inflammatory markers compared with single MTX in the treatment of juvenile idiopathic arthritis and juvenile ankylosing spondylitis.

The construction of SENP1 specific lentiviral vector and its effects on apoptosis of alveolar epithelial cells induced by hyperoxia

Xu Zhao, Wenbin Dong
Department of Neonatology, the Affiliated Hospital of Southwest Medical University, Luzhou, China

Objective: To construct a SENP1-RNAi lentivirus vector and establish human type II alveolar epithelial cells (HEPApiC) that stably express SUMO specific protease 1 (SENP1). To investigate the relationship between SENP1 and apoptosis induced by oxidative in HEPApiC after exposing to hyperoxia.

Methods: This experiment was divided into two parts. Part one: Preparing for virus particles with constructed plasmid LV3-SENP1-RNAi to infect the HEPApiC cells, and detecting the expression of SENP1 in different groups by qRT-PCR and Western blot. Part two: the experiment was based on SENP1 stably silenced HEPApiC cells and the model of lung injury was induced by mixture gas formed with O2 (900 ml/L) and CO2 (50 ml/L). Cells were randomly divided into 6 groups: control group, empty vector infected group, experimental group, hyperoxia group, hyperoxia and empty vector infected group, hyperoxia and experimental group. After culturing for 12h, 24h and 48h, cells would be collected and the indicators would be detected. Obtaining cells apoptosis situation through flow cytometry instrument after 24h. Then testing the transposition of SIRT1 by immunofluorescence technique after 24h. Measuring the expression of SENP1, SIRT1 separately in cytoplasm and nucleus, P53 and AC-P53 by Western Blot after 24h.

Results: Part one: LV3-SENP1-RNAi was successfully constructed and virus was correctly packaged. Part two: the apoptosis rate increased when cells were dealt with by hyperoxia 24h later according to the results of flow cytometry instrument. Furthermore, the apoptosis rate in hyperoxia and experimental group was lower than another two groups disposed by hyperoxia. Immunofluorescence results showed that SIRT1 protein translocated more in those groups dealt with hyperoxia and the difference between six groups was statistically significant ($\chi^2=99.34$, $p=0.000<0.05$). Finally, compared with control group, at the level of protein, the expression of SENP1, SIRT1 in cytoplasmic, AC-P53 increased, while the expression of SIRT1 came from nucleus and P53 decreased obviously in hyperoxia group. In hyperoxia and experimental group, SENP1, SIRT1 in cytoplasmic, AC-P53 expressed less as SIRT1 in nucleus expressed more than that in hyperoxia group, but both were failed to meet the level of control group ($p<0.05$).

Conclusion: SENP1 and SIRT1 were involved in the oxidative stress induced by hyperoxia in preterm infants. Hyperoxia led to higher expression of SENP1. Then the translocation of SIRT1 increased. SIRT1 decreased in nucleus and increased in cytoplasm, which induced acetylation of P53 and apoptosis.
Adolescent Health.......122  Allergy and Immunology.......123  Cardiology.......129  Developmental Paediatrics.......131  Endocrinology.......136  Gastroenterology and Hepatology.......137  General and Community Paediatrics.......142  Genetics and Genomics.......147  Haematology and Oncology.......154  Inborn Errors of Metabolism.......162  Infectious Diseases.......163  Neonatology.......171  Nephrology.......172  Neurology.......174  Nutrition.......177  Respirology.......179  Rheumatology.......183  Others.......186
**Background and Aims:** A highly conservative nutrition replacement approach has been adopted for adolescents with ED in Hong Kong for many years. This is because of the lack of international consensus on the optimal rate of nutrition replacement for this group of patients and the physicians’ worry about refeeding syndrome, an uncommon complication of nutrition replacement but with high rate of mortality and morbidity.

Increasing evidence in the medical literature has shown that replacing nutrition at a higher rate is both safe and effective and the risk of refeeding syndrome in inpatient NRP is more related to the degree of malnutrition, not the rate of nutrition replacement. Such reports included ED programs in North America and Australia. We performed this case control study to look into the preliminary outcome of our new NRP in local ED adolescents.

**Method:** This is a retrospective case-control study assessing the clinical outcome and safety (weight, electrolyte disturbance or signs of refeeding syndrome) of a new inpatient NRP for adolescents with eating disorder hospitalized in the Department of Paediatrics, Queen Elizabeth Hospital. The standardized inpatient NRP was started in May 2016, aiming at >0.5 kg/week weight gain (measured early morning after voiding according to protocol). Activity Responsibility stages, Nutrition Responsibility stages and house-rules were designed to standardize the treatment with respect to their activities on the ward, homemade food or standard nutrition replacement items if they could not finish the nutrition as prescribed.

**Results:** There was no significant change in the electrolytes level (i.e. serum sodium, potassium or phosphate) between the two groups and there was no sign of refeeding syndrome in any of the included adolescents. All 6 in the intervention group achieved the goal of 0.5kg/week gain in weight on day 14 when compared to 5 of the 12 adolescents in the control group. The difference was statistically significant (Fisher’s exact test; p value 0.038).

**Conclusions:** The case-control study provides preliminary evidence about the safety and improved weight outcome of our new NRP in adolescents with ED. A larger scale study would be able to provide more concrete information on the effectiveness and 1 year outcome of our new NRP.

---

**Assimilation of reality of health index in national health promotion in Japan - as a prospect of flame-work analysis and reaction of external causes**

**Toshiko Sawaguchi**

*NIPH & Showa University School of Medicine, Saitama & Tokyo, Japan*

**Background and Aims:** In Healthy Parent-Child 21 as a Japanese national plan of health promotion, the comprehensive success has been reported and on the other hands, the remarkable contribution with reality could not be impressed. So here we analyzed the Assimilation of reality of health index in Healthy Parent-Child 21 and particularly of the index of child abuse.

**Methods:** (1) The time-dependent process of plural indexes in Healthy Parent-Child 21 in 2000, in 2004, in 2008 and in 2012 as the quantitate variables and three flame works such as the health and medical standards, citizen’s action and some administrative groups and NGO etc’s action and those structured by these plural indexes which could contribute the 5 step appraizal (being bad, not change, not enough improvement, improvement, impossible to be estimated). The logistic regression analysis was carried out as the grouped variables of 4 main topics in Healthy Parent-Child 21 such as adolescence health and education (topic A), safety of pregnancy and child birth and support of infertility (topic B), environmental preparation for child & maternal health and proper development of infant mind and child care support using SAS9.4 (EG7.1). The method of variable selection was the variable increase method and of optimization was the Fishers Scoring method. (2) The health indexes of child abuse in Healthy Parent-Child 21 and other regional health indexes of child abuse were compared.

**Results:** (2) The odds ratio and 95% CI of topic A was 0.041 and 0.002-0.577 and of topic B was 0.193 and 0.032-0.984. (2) The difference and opposite trends between both indexes of child abuses were observed.

**Conclusion:** It was suggested that the contribution of some administrative groups was higher than citizen’s action to the improvement of health indexes. Also in Japan, social capitalized citizen’s action could be recognized most important in national health promotion. The difference and opposite trends between both indexes of child abuses were observed. It seemed that the results of our analysis had shown the in assimilation between national health promotion and reality of health-related matters.
Allergy and Immunology

86

Needle length for epinephrine prefilled syringes in children and adolescents

Wiparat Manuyakorn¹, Buntita Bamrungchaowkasem², Nichanan Ruangwattanapaisarn², Wasu Kamchaisatian³, Suwat Benjaponpitak¹

¹Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, ²Department of Radiology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background: Intramuscular epinephrine is the first line drug in the treatment of anaphylaxis. This study was to identify the appropriateness of 1 inch needle length for epinephrine prefilled syringes in children.

Methods: Children aged 1 month to 18 years were enrolled. Skin to muscle depth (STMD) and skin to bone depth (STBD) were measured using an ultrasonography at the mid-anterolateral thigh. A 1 inch needle was considered as being appropriate if the STBD was more than 1 inch and the STMD was less than 1 inch.

Results: Seventy five infants, 75 pre-school aged children, 75 school aged children and 147 adolescent were enrolled: 196 (52.7%) children were male. A 1 inch needle length was appropriate for 61% of the infants, for 88% of the preschool children, for 99% of the school aged children and for 95% of the adolescents. Thigh circumference ≥23 cm, BW ≥10 kg provided the sensitivity of 98.5-100% in predicting that a 1 inch needle was too short.

Conclusion: One inch needle length may not be appropriate for intramuscular injection at thigh in all children. Thigh circumference, BMI and BW ≥10 kg provided the sensitivity of 95% of the adolescents. Thigh circumference ≥23 cm, BMI ≥13.5 kg/m² and BW ≥6 kg in infants provided the sensitivity of 74%-96% in predicting the appropriateness of 1 inch needle. In preschool group, thigh circumference ≥25 cm, BMI ≥13.5 kg/m² and BW ≥10 kg provided the sensitivity of 98.5-100% in predicting the appropriateness of 1 inch needle.

96

IDO contributes to the pulmonary immunosuppression and the alleviation of pulmonary fibrosis induced by human mesenchymal stem cells in humanized mice

Ke Ni¹, Ming Liu², Jian Zheng¹, Wenwei Tu¹

¹University of Hong Kong, Hong Kong, ²Guangzhou Medical University, Guang Zhou, China

Background and Aims: The contribution of indoleamine-pyrole 2,3-dioxygenase (IDO) is indicated in the human mesenchymal stem cells (MSC)-induced immunosuppression in vitro. However, the involvement of IDO in human MSC-induced immunosuppression and the attenuation of inflammation-related disease in vivo has not been investigated.

Methods: The inflammation is appeared at the early stage of pulmonary fibrosis and related to the pathogenesis of this disease. In this study, pulmonary fibrosis was induced
by bleomycin in the human peripheral blood mononuclear cells (PBMC)-reconstituted humanized mice, which facilitated the direct investigation of human cell interaction in the animal model. The IDO production in human MSC was silenced by shRNA. Then, the IDO-silenced human MSC and control human MSC were injected respectively into humanized mice with bleomycin treatment. The weight loss, the lung function, and the fibrosis in the lung were monitored until day 21 post bleomycin injection. Meanwhile, the activation of human immune cells and the production of human cytokine/chemokine in the lungs of humanized mice were tested.

Results: In humanized mice, the administration of human MSC effectively rescue the weight change, the lung function and the fibrosis in the lung. Compared with the control human MSC, the IDO-silenced human MSC could not significantly induce pulmonary immunosuppression and the attenuation of pulmonary fibrosis.

Conclusions: IDO contributes to the pulmonary immunosuppression and the alleviation of pulmonary fibrosis induced by human MSC in humanized mice.

Development and maturation of polyfunctional Epstein-Barr virus antigen-specific CD4+ and CD8+ T Cell Responses In Children With Infectious Mononucleosis And Primary Asymptomatic Infection

Janice Ki-Pui Lam, Raymond Jia Ning, Xuequn Xu, Kwok-Hung Chan, Kwai-Fung Hui, Alan Kwok-Shing Chiang
The University of Hong Kong, Hong Kong

Background and Aims: Effective control of chronic viral infections was shown to require the generation of polyfunctional T cells (PFCs) which are capable of producing multiple cytokines and possess cytotoxic function. However, the development and maturation of PFC responses in Epstein-Barr virus (EBV) infection are not well understood. We carried out a longitudinal study to assess the development and maturation of T cell responses to EBV from the time of acute infection to recovery in a large cohort of children with infectious mononucleosis (IM) and primary asymptomatic (AS) infection.

Method: Evaluation of IFN-γ secreting CD8+ T cell responses upon stimulation of PBMC by HLA class I-specific peptides of EBV lytic and latent proteins was first performed by ELISPOT assay followed by assessment of CD4+ and CD8+ PFC responses upon stimulation of PBMC by a panel of overlapping peptides of EBV lytic and latent proteins using polychromatic flow cytometric analysis for the co-expression of IFN-γ, TNF-α, IL-2, perforin and CD107a. Cytotoxicity of T cells against autologous lymphoblastoid cell lines (LCLs) as well as viral loads in plasma and PBMC were determined.

Results: A trend of decrease in the magnitude of CD8+ T cell responses towards EBV lytic peptides in contrast to the increase towards latent peptides was demonstrated by the ELISPOT assay. Interestingly, both lytic and latent antigen-specific CD4+ and CD8+ T cells showed increased polyfunctionality (greater or equal to three functions) concurrent with enhanced cytotoxicity and sustained decrease in plasma and PBMC viral loads over time. Immunodominant EBV antigens (EBNA-3A, -3B and -3C) induced higher proportion of CD8+ PFCs than the subdominant ones. No significant difference in the pattern of development of EBV-specific PFC responses was found between the IM and AS patients.

Conclusion: Our data supported that the development and maturation of polyfunctional CD4+ and CD8+ T cell responses to both lytic and latent antigens are important in the long term control of EBV.

The plasticity of innate immune responses to lipopolysaccharide in iron dextran-overloaded mice

Jun-Kai Kao1,2, Shih-Chung Wang3, Cheng-Han Lee4, Tzu-Cheng Su5, Ming-Sheng Lee1, Chien-Sheng Hsu6, Jeng-Jer Shieh, Rei-Cheng Yang1,2
1Frontier Molecular Medical Research Center in Children, Changhua Christian Children Hospital, Changhua, Taiwan, 2Institute of Biomedical Sciences, National Chung Hsing University, Taichung, Taiwan, 3Department of Pathology, Changhua Christian Hospital, Changhua, Taiwan, 4Department of Pediatrics, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

Background and Aims: The disturbance of iron homeostasis is associated with altered immune function. Transfusion-dependent thalassemia patients have more complications in bacterial infections. However, the effect of iron overload on the function of immune system is unclear. In order to identify the differences in the innate immune responses to bacterial infection of iron overload, the present study assessed the subgroups of monocytes and responses of peripheral blood mononuclear cells (PBMCs) to lipopolysaccharide (LPS) in iron dextran-overloaded mice model.

Methods: An experimental model of iron overload was generated by intraperitoneal injections of iron dextran (1 g/kg) administered once a week for 8 weeks in male C57BL/6 mouse strain. The serum levels of ferritin, ferrum, oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT) as well as cytokines including TNF-α, IL-6, IL-10 were measured. Monocytes were identified and gated in a forward-scatter and side-scatter dot plot of PBMCs by flow cytometry. Two main types of monocytes were further defined by classical monocytes (Ly6C<sup>high</sup> CCR2<sup>low</sup>) and non-classical monocytes (Ly6C<sup>low</sup> CCR2<sup>high</sup>). In ex vivo studies, cytokines secreted from PBMCs after LPS stimulation for 12hrs were quantified.

Results: An increase in liver and spleen size with iron deposits was observed in iron overload mice. Compared to controls, the group of iron overload had higher values of serum IL-6 (10.66±3.44 vs 2.52±0.47 pg/ml), ferrum (1096±112.9 vs 201.9±13.29 µg/dl), GOT (260.0±26.56 vs 70.71±12.58 U/l) and GPT (200.5±21.66 vs 30.43±3.37 U/l) but not ferritin level (10.63±0.50 vs 10.73±0.65 ng/dl). Two groups had the same population of inflammatory, classical monocytes (0.53% vs 0.59%) of total monocytes but the group of Iron overload showed a trend of decrease in the proportion of CD8+ PFCs than the subdominant ones. No significant difference in the pattern of development of EBV-specific PFC responses was found between the IM and AS patients.
overload had higher tissue repairing, non-classical mono-
cytes (0.22 % vs 0.08%). At 12 hours after LPS exposure,
the PBMCs of two groups produced the same level of IL-6
(236.3±13.42 vs 227.9±17.62 pg/ml). However, the PBMCs
of monocytes during iron overload, wherein they simul-
taneously had pro-inflammatory and immunosuppressive
phenotypes. These findings may explain the impaired
innate immunity of thalassemic patients with chronic iron
overload.

Conclusions: Our results revealed the functional plasticity
of monocytes during iron overload, wherein they simul-
taneously had pro-inflammatory and immunosuppressive
phenotypes. These findings may explain the impaired
innate immunity of thalassemic patients with chronic iron
overload.

The number of lymphocytes can be a IVIG treatment failure predictor in Kawasaki Disease as well as Neutrophil-lymphocyte ratio, platelet lymphocyte ratio

Masaru Kobayashi, Kenichi Takano, Yoshie Tomita,
Junji Kamizono, Koutaro Ichikawa

Yahata Hospital, Kitakyushu, Japan

Background and Aims: Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are used as systemic inflammatory markers and prognosis of adverse cardio-
vascular events. Recently there have been reports that
NLR and PLR in the acute stage of Kawasaki Disease (KD)
may be a predictor of refractoriness against intravenous
immunoglobulin (IVIG) treatment in Kawasaki disease. To
validate whether NLR and PLR could be predictors of IVIG
treatment in the acute phase of KD.

Methods: A retrospective study was performed with 398
patients with KD that we experienced in our department
between January 2009 and December 2016. And we divid-
ed them into responders and non-responders according to
the initial IVIG responsiveness. NLR, PLR and the absolute
number of differential blood count were calculated. Fur-
thermore, those values were evaluated when they were
used with RAISE (Randomized controlled trial to Assess
Immunoglobulin plus Steroid Efficacy for Kawasaki disease)
treatment in the acute phase of KD.

Results: Both NLR and PLR of non-responders were sig-
ificantly higher than those of responders (P<0.01). The
sensitivity and the specificity were 70.3% and 63.9% re-
spectively by using a cut-off of NLR ≥3.12. The sensitivity
and the specificity were 70.4% and 50.6% respectively by
using a cut-off of PLR ≥100. In addition, IVIG non-respond-
er group showed significantly less number of the absolute
lymphocyte count than responder group (P<0.01). We
determined the cut-off level of absolute lymphocyte count
as 2600 /ml. Then, the sensitivity and the specificity were
61.1% and 68.2% respectively. The positive predictive value
of the refractory prediction combined NLR and RAISE score
≥5 was 33.3% [95% CI 23.9 - 44.4] and the odds ratio was
3.1 [1.1 - 8.0]. The positive predictive value of the refracto-
ry prediction combined PLR and RAISE score ≥5 was 35.1%
[95% CI 25.2-46.5] and the odds ratio was 3.8 [1.3-9.7]. The
negative predictive value of lymphocyte alone was 92.1%
[95% CI 88.1 - 94.8].

Conclusion: We demonstrated that NLR, PLR and the
number of lymphocyte play an important role in predicting
IVIG-resistance in Kawasaki disease. NLR and PLR are val-
ues which can be calculate easily. However, we can see the
number of lymphocytes more quickly. It is crucial to pay at-
tention to lymphocyte count for predicting IVIG-resistance.
Further investigation is necessary to improve the accuracy
of NLR, PLR and the number of lymphocyte.

The relationship of IRF7 and IFN-β in type I IFN pathway in trophoblast

Xiaoyan Dong1, Nanbert Zhong2, Paulomi B Aldo3,
Gil Mor4

1Shanghai Children’s Hospital, Shanghai Jiaotong
University School of Medicine, Shanghai, China, 2New
York State Institute for Basic Research in Developmental
Disabilities, Staten Island, New York, USA, 3Department
of Obstetrics, Gynecology & Reproductive Sciences, Yale
University School of Medicine, New Haven, USA

Background and Aims: Preterm birth effects up to 18% of
births today. Infection have been reported as responsible
for up to 40% of preterm birth cases. Type I IFN pathway
was thought as a mainly inflammation pathway involved
in this process. Furthermore, the expression of IFN-β was
down regulated in this response. However, how does this
process happen was still unknown. The objective of this
study was to reveal the relationship of IRF7 (interferon regu-
laratory factor 7) and IFN in trophoblast in order to un-
derstand further the different expression of gene in type I
IFN pathway in trophoblast when microorganisms affect.

Method of Study: To find a different expression gene (IRF7)
in human’s placenta mRNA array data comparing with the
placenta of mouse with MHV infected by bioinformatics
analysis. Validate this gene’s function in type I IFN pathway
not only in SW71 LPS induced and MHV infected, but also
in cells treated by IFN and poly(I:C) by qPCR and west-
ern-blot.

Results: There was one common gene (IRF7) by bio-
informatics analysis in down regulated genes of human
and mouse placenta. By qPCR, it was showed that the
expression of IRF7 and IFN-β were decreased in mouse
placenta with MHV infected compared to its increasing in
LPS induced cells. Meanwhile, the expression of IRF7 and
IFN-β were elevated in human trophoblast LPS induced as
well. Furthermore, the increased expression of IFN-β was
prior to IRF7. With different expression ORF45 and ORF50
in SW71 infected for 10 days, IRF7 and ISG20 (IRF7’s down-
stream gene) were decreased. On the other hand, in protein
eexpression, total and phosphorylated IRF7expressed later than IRF3 in LPS induced SW71. The
phosphorylated expression of IRF3 was different with IRF7
in poly (I: C) treated and MHV infected trophoblast. IFN-β
could induce total IRF7 expression in trophoblast, but not
IRF3.

Conclusion: It confirmed that the expression of IRF3 was
prior to IRF7 in Type I IFN pathway in trophoblast. We
demonstrate that IFN-β can regulate IRF7 expression in
 trophoblast. From these results, we suggest that there may
be a circle between IFN-β and IRF7 in type I IFN pathway in trophoblast, once virus blocks this circle, then innate immune response will be altered in trophoblast contributing to preterm birth.

Effects of short chain fatty acids and their receptor signaling pathway on intestinal barrier function and regulatory T cells in food allergic mice

Zhenni Zhu, Chijun Hu, Xiaoqin Zhou

Hubei Maternal and Child Health Hospital, Wuhan, China

Objective: Food allergy (FA) has become a worldwide public health problem, in recent years the incidence rate has continued to rise, about 5% of adults and up to 8% of infants and young children for one or more food allergies. Short chain fatty acid (SCFA) is one of the most important markers in intestinal metabolism. It plays an important role in intestinal nutrition, intestinal microflora homeostasis, energy balance maintenance and physiological function regulation. It is generally accepted that SCFAs and its receptors mediate inflammation in the body. In FA, the intestinal tract is a major affected organ, so the intestinal specific microbial community metabolite SCFAs and its receptor may directly or indirectly influence the development of FA through a variety of pathways. At present, the mechanism of short chain fatty acids and their receptor signaling pathways in food allergy has not been reported. This research selects the common food allergens ovalbumin (OVA) of Balb/c mice intestinal sensitization, food allergy research on intestinal barrier function in mice and the effects of regulatory T cells, so as to provide a new target for prevention and treatment of food allergy.

Methods: 30 Balb/c mice fed with no experimental protein, 18-22 g in body weight and half male and female, were randomly divided into two groups: experimental group and control group. The experimental group was given ovalbumin (OVA), the control group was given the same amount of normal saline, the model was made for thirty-first days, the eyeball was taken and the mice were killed. The content of intestinal secretory immunoglobulin A (sIgA) and serum total IgE and DAO were measured by ELISA. Meanwhile, the frequency of CD4+CD25+ regulatory T cells in their splenic cell suspension was analyzed by flow cytometry, using different concentrations of short chain fatty acids and TSA (HDAC inhibitors), CD4+CD25+Foxp3+Treg cells were isolated and stained with intracellular factors, and the expression of IFN-γ, TNF-α and NF-kappa B was detected.

Results: compared with the control group, the serum total IgE and DAO content (A value) of the experimental group increased significantly, and the number of CD4+CD25+ regulatory T cells in the splenic cell suspension decreased significantly. SCFAs may play an anti-inflammatory role in mouse PBMC by inhibiting the activity of NF-kB by inhibiting HDAC.

Conclusion: The food allergen ovalbumin on Balb/c mice intestinal sensitization, food allergy research on intestinal barrier function in mice and the effects of regulatory T cells, to investigate the protective effect of short chain fatty acid and its receptor signal pathway.

Immunosuppressive properties of hTERT mesenchymal stem cell (htMSC)-derived extracellular vesicles on human plasmacytoid dendritic cells (pDCs) and its therapeutic potential in autoimmune diseases

Lin Kui, Godfrey Chi-Fung Chan, Pamela Pui-Wah Lee

Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong

Background: Mesenchymal stem cell (MSC)-based therapy has shown promises in treating inflammatory disorders and tissue damage by means of immunomodulation and promoting tissue regeneration. MSC exert its effect on target cells through cell–cell contact, secretion of soluble molecules and extracellular vesicles (EVs). In systemic lupus erythematosus, TLR7 and TLR9 activation in plasmacytoid dendritic cells (pDC) is recognized as one of the major pathogenetic mechanisms. We previously demonstrated that tumor necrosis factor-inducible gene-6 (TSG-6), a key anti-inflammatory protein secreted by activated MSC, could downregulate TLR-7 and TLR-9 activation in human pDC. Herein, we investigate the effect of MSC and MSC-derived EVs on regulating pro-inflammatory cytokines and interferon production in pDCs, and whether such effect is mediated by TSG-6.

Methods: hTERT-MSC (htMSC) were cultured in serum-deprived CDMF medium for 48 hours. EV were isolated by ultracentrifugation and characterized by transmission electron microscopy, Nanosight, and western-blot. Immunosuppressive effect of EV on TLR9-mediated cytokine production was determined in GEN2.2, a human pDC cell-line, following overnight, 4-hr or 30-min activation by CpG-A, and analysed by qPCR, ELISA and flow-cytometry.

Results: Upon activation of TLR9 signaling by CpG-A, IL-1β, TNF-α and IFN-α transcription was upregulated in GEN2.2. Such response was reduced when CpG-A-primed GEN2.2 were co-cultured with htMSC. Knockdown of TSG-6 in htMSC dampened its capacity to suppress IL-1β, TNF-α, IFN-α and IRF7 transcription in GEN2.2, suggesting the importance of TSG-6 in downregulating TLR9-mediated response. To find out whether MSC exert its immunosuppressive effect by means of EV, we isolated EVs from hTERT MSC. We showed that hMSC-derived EV contained TSG-6 protein by western-blot. Coculture of EV with CpG-A-primed GEN2.2 resulted in downregulation of IFN-α transcription and protein expression, mediated via reduction in total and phospho-IRF7.

Conclusion: For the first time, we showed that MSC could downregulate TLR9 activation in human pDCs, and this was dependent on TSG-6. Furthermore, hMSC-derived EV contain TSG-6 and suppress IFN-α response in CpG-A primed pDCs through reducing total and phospho-IRF7. Our findings revealed mechanistic insights on the immunosuppressive properties of MSC, and their therapeutic potential in autoimmune disorders triggered by TLR9 activation shall be further explored.
Background and Aims: To investigate the effects of adipose-derived stem cells (ADSC) and non-methylated CpG-oligodeoxynucleotides (CpG-ODN) on the expression of peripheral blood CD4+CD25+ regulatory T cell in young mice of food allergy.

Methods: A total of 40 female BALB/c mice were randomly divided into control group, allergic group, ADSC treatment group, and CpG-ODN treatment group. A mouse model of food allergy was established by intraperitoneal injection of ovalbumin (OVA) for sensitization and challenge. The mice in the control group, allergic group, ADSC treatment group, and CpG-ODN treatment group were given intraperitoneal injection of non-methylated CpG-ODN solution (40 ug for each mouse) at 1 hour before OVA challenge, and those in the CpG-ODN treatment group were given intraperitoneal injection of non-methylated CpG-ODN solution (40 ug for each mouse) at 1 hour before OVA challenge. The allergic group had a significantly higher percentage of peripheral blood CD4+CD25+ Treg cells in young mice with food allergy, as well as their immune intervention effects.

Results: The allergic group had significantly higher symptom scores and serum level of OVA-IgE than the control group (p<0.05). There were no significant differences in the allergic symptom score and the serum level of OVA-IgE between the ADSC treatment group and CpG-ODN treatment group (p>0.05), but these two groups had significantly symptom scores and serum level of OVA-IgE than the allergic group and significantly higher allergic symptom scores and serum level of OVA-IgE than the control group (p<0.01). The allergic group had a significantly lower percentage of peripheral blood CD4CD25 Treg cells than the control group (p<0.05). The ADSC treatment group and the CpG-ODN treatment group had a significantly higher percentage of peripheral blood CD4CD25 Treg cells than the allergic group (p<0.05); there were no significant differences between these two groups or between them and the control group (p>0.05). Pathological results showed structural damage and edema in the jejunal villi, a large number of eosinophils, and lymphocyte infiltration in the allergic group, while the ADSC treatment group and the CpG-ODN treatment group had less structural damage and edema in the jejunal villi, a lower number of eosinophils, and less lymphocyte infiltration.

Conclusions: ADSC and non-methylated CpG-ODN have a certain effect in the treatment of food allergy and can increase the percentage of peripheral CD4CD25 Treg cells and reduce the level of OVA-IgE. They may be associated with the induction of immune tolerance.
Comparative analysis of the profiles of short chain fatty acids in stool samples of healthy infants and infants with eczema

James Chun-Yip Chan¹, Chiung-Hui Huang², Dorinda Yan-Qin Kioh³, Eric Chun-Yong Chan⁴, Gaik Chin-Yap⁵, Lynette Pei-Chih Shek⁶, Anne Goh⁷, Hugo PS Van Bever⁸, Oon Hoe Teoh⁹, Jian Yi Soh², Biju Thomas⁵, Mahesh Babu Ramamurthy², Daniel Yam Thiam Goh², Christophe Lay², Shu E Soh²,³, Fabian Yap⁶, Kok-Hian Tan⁶, Yap Seng Chong⁷,⁸, Keith M Godfrey⁹, Peter D Gluckman¹⁰, Bee Wah Lee²

¹Department of Pharmacy, Faculty of Science, National University of Singapore, Singapore, ²Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, ³Department of Paediatrics Allergy and Respiratory, KK Children’s and Women’s Hospital, Singapore, ⁴Department of Paediatrics, KK Children’s and Women’s Hospital, Singapore, ⁵Saw Swee Hock School of Public Health, National University of Singapore, Singapore, ⁶Department of Maternal Fetal Medicine, KK Women’s and Children’s Hospital, Singapore, ⁷Department of Obstetrics & Gynaecology, National University of Singapore, Singapore, ⁸Singapore Institute for Clinical Sciences, Agency for Science, Technology and Research, Singapore, ⁹MRC Lifestage Epidemiology Unit and NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, UK, Southampton, United Kingdom, ¹⁰Singapore Institute for Clinical Sciences, Agency for Science, Technology and Research, Singapore

Backgrounds and Aims: Short chain fatty acids (SCFAs) are metabolites produced by commensal bacteria. These major end products of anaerobic bacteria fermentation in the gut modulate host metabolism and regulate immune function. The aim of this study was to compare the profile of SCFAs in the first year of life between infants with eczema and healthy controls.

Methods: From a larger mother-offspring cohort, Growing Up in Singapore Towards healthy Outcomes (GUSTO), 34 children who developed eczema in the first 18 months of life and 40 non-eczema controls with similar demographic and clinical factors were selected. A total of 160 stool samples obtained over 3 time points (month 3, 6, 12) were analyzed for the amount of short chain fatty acids (acetic-, propionic-, butyric-, isobutyric-, valeric-, isovaleric-, 2-methylbutyric-, caproic- and 4 methyvaleric acids) by liquid chromatography tandem mass spectrometry. Longitudinal multivariate analysis was made and data was adjusted for possible confounders (mode of delivery, feeding pattern, antibiotics at labour and antibiotics in first year of life).

Results: Longitudinal analysis of individual SCFA levels showed higher butyric acid levels (p<0.01) in controls compared to eczema. When the mode of delivery was taken into consideration, vaginally-delivered controls had higher butyric acid (p<0.01) and 4-methyvaleric acid levels (p<0.05) compared to those with eczema. For infants born by caesarean-section, controls had higher concentrations of isobutyric acid (p<0.05) compared to those with eczema.

Conclusions: Specific SCFAs over the first year of life were lower in infants with eczema compared to non-eczema controls, suggesting an influence in eczema development. These differences are likely to result from the perturbation/impairment of the maturation of infant gut microbiome in infants with eczema.

Thrombocytopenia in cytomegalovirus infection can lead to or mislead from the diagnosis of Wiskott-Aldrich syndrome

Deepti Suri¹, Ankur Jindal², Rashmi Rekhi¹, Jitendra Shandilya², Mini Singh², Biman Saikia³, Ranjana Minz³, Anju Gupta¹, Amit Rawat¹, Wing Chan Koon⁴, Yu-Lung Lau⁴, Surjit Singh¹

¹Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India, ²Department of Virology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, ³Department of Immunopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, ⁴Department of Paediatrics & Adolescent Medicine LKS Faculty of Medicine The University of Hong Kong, Hong Kong

Introduction: Cytomegalovirus (CMV) infection is frequently seen in the clinical setting of primary immune deficiency diseases (PIDs). Children with Wiskott-Aldrich syndrome (WAS) are predisposed to CMV infection. Thrombocytopenia is a dominant clinical finding in both congenital and postnatal CMV disease as well as WAS. Thrombocytopenia may sometimes be falsely attributed to the CMV infection alone and thus the diagnosis of WAS can be missed. Here, we describe the case profile of 3 children who had CMV infection and WAS.

Case 1: A 4-month-old boy presented with blood stained loose stools. Family history was noncontributory. On examination, he was pale, had oral ulcers and hepatosplenomegaly. Severe anemia with thrombocytopenia was noted. CMV IgM serology was positive and eye evaluation revealed active CMV retinitis. Colonic biopsy showed colitis with CMV inclusions. Postnatal active disseminated CMV disease was diagnosed and treatment initiated. However, thrombocytopenia persisted. Mean platelet volume was low and WASP protein expression was reduced. Mutation in exon 1 of WAS gene confirmed the diagnosis of WAS.

Case 2*: A 6-year-old boy presented with discharging sinus from right leg and headache. He had been unwell since the first year of life and was diagnosed to have severe atopic dermatitis. He had had blood mixed loose stools, multiple episodes pneumonia, and otitis media in past. He developed Staphylococcus aureus chronic osteomyelitis of right femur. Eye examination revealed elevated intraocular pressure, mild anterior uveitis, and unilateral acute glaucoma. Polymerase chain reaction from the aqueous was positive...
for CMV. CMV serology (IgM) was negative but CMV DNA PCR was positive. Review of old case records showed persistent thrombocytopenia which helped clinch the diagnosis of WAS.

**Case 3:**
A 4-month-old boy presented with recurrent febrile episodes, progressive pallor and skin bleed. On examination, he had eczema, petechiae, and hepatosplenomegaly. He had severe anemia and thrombocytopenia. History of a death of male sibling 2 years back prompted the diagnosis of WAS. However, CMV IgM was found to be positive and CMV viral load was highly elevated. No active eye lesions were found. He received prolonged ganciclovir treatment and prophylaxis is being continued as he awaits transplant.

**Learning Objectives:** Proactively screening of children with CMV infection for WAS as well as children with WAS for CMV disease is necessary. Thrombocytopenia is a masquerader: can lead to or mislead the diagnosis. Eye examination for CMV infection is necessary for children with WAS.

* This case has been published before J AAPOS. 2013 Dec;17(6):646-7. PMID:24210345

---

**Cardiology**

**CYP2E1 gene polymorphisms related to the Formation of Coronary Artery Lesions in Kawasaki Disease**

Ling-Sai Chang¹², Ho-Chang Kuo³⁵⁴

¹Department of Pediatrics and Kawasaki Disease Center, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, ²Institute of Clinical Medical Sciences, College of Medicine, Chang Gung University, Kaohsiung, Taiwan, ³Department of Pediatrics and Kawasaki Disease Center, Kaohsiung Chang Gung Memorial Hospital, Taiwan, Kaohsiung, Taiwan, ⁴Gung University College of Medicine, Kaohsiung, Taiwan

**Background and Aims:** Kawasaki disease (KD) is an acute febrile systemic vasculitis that disturbs coronary arteries. Patients’ risks of adverse cardiovascular events and subclinical atherosclerosis have been found to significantly increase with polymorphisms of the human cytochrome P450. This current study aims to research the possible relationship between Cytochrome P450, Family 2, Subfamily E, and Polypeptide 1 (CYP2E1) polymorphisms with KD.

**Methods:** selected six tag single-nucleotide polymorphisms (tSNPs) of CYP2E1 TaqMan allelic discrimination assay in 340 KD patients and performed analysis on the clinical phenotypes and coronary artery lesions (CAL). CAL associations of tSNPs were adjusted for age and gender in the logistic regression.

**Results:** This study consisted of 340 participants. A total of 35.6% of the KD cases experienced CAL formation. Of these, 12.6% did not respond to the initial intravenous immunoglobulin (IVIG) treatment. Further, 150 patients with acute-phase KD were treated with high-dose acetylsalicylic acid (80 to 100 mg/kg/day). We examined six CYP2E1 gene polymorphisms and their potential association with KD in Taiwanese children. After genotyping six SNPs, we noticed that SNP rs2070676 and rs915906 of the CYP2E1 gene had a strongly association with the risk of CAL in the recessive model. For rs915906, the C/C genotype reflected a higher risk of CAL in KD patients (p=0.009). Regarding rs2070676, the G/G genotype was strongly associated with the risk of CAL formation (p=0.007). However, the of the CYP2E1 gene did not influence CAL formation the participating KD patients either with or without high-dose acid. determine the association between SNPs (rs915906 and rs2070676) of CYP2E1 and gene expression, we retrieved the tissue expression quantitative trait loci (eQTLs) data from the GTEx Portal (http://www.gtexportal.org/home/). The TT genotype of rs915906 had a higher expression of CYP2E1 when compared to the CC genotype in sun-exposed skin tissue (p=3.8e-14). Furthermore, the CC genotype of rs2070676 had a higher expression of CYP2E1 when compared to the GG genotype in esophagus tissue (p=4.9e-15).

**Conclusions:** This study is the first to find that the risk of CAL formation is associated with CYP2E1 polymorphisms in KD patients.
Increased pituitary volumes in Fontan patients: The other portal circulation

Jun Muneuchi, Seigo Okada, Chiaki Iida, Yusaku Nagatomo, Hiromitsu Shirozu, Mamie Watanabe
Japan Community Healthcare Organization Kyushu Hospital, Kitakyushu, Japan

Background and Aims: Current results of Fontan operation are acceptable as the final palliative surgery in patients with single ventricle physiology. There exist two portal systems in human being; the hepatic and pituitary portal systems, and these portal systems become super-portal systems after the completion of Fontan operation. Although the disturbance of the hepatic portal system has been shown to cause Fontan-associated liver disease or protein losing enteropathy, there is little information about the pituitary portal system in Fontan patients. The aim is to investigate pituitary volume measured by brain magnetic resonance imaging (MRI) and to compare pituitary volumes between Fontan patients and control subjects.

Methods: We performed brain MRI in 40 Fontan patients (26 males) and 74 age-matched control subjects (42 males). The median age at Fontan operation was 3.3 (1.6-5.7) years. Brain MRI was performed using a 1.5-T system at 9.3 (7-23) years of age in Fontan patients and at 10.4 (8.8-12.8) years in the control subjects, and T1-weighed images were acquired. The pituitary volume was obtained by multiplying the height by depth by width by 0.52. We also measure the volume of the pons referred to the volume of the pituitary gland.

Results: The median the pituitary volume in Fontan patients was 472 (425-527) mm$^3$, which was significantly larger than that in the control subjects [267 (203-320) mm$^3$, p<0.001]. However, the median pons volume was 7,286 (6,672-8,241) mm$^3$, which was significantly smaller than that in the control subjects [8,331 (7,531-9,148) mm$^3$], p<0.001. In Fontan patients, the larger pituitary volume was significantly related to an increase in central venous pressure, but there was no correlation with age, systemic saturation, cardiac index, and pulmonary arterial resistance.

Conclusions: The present study suggest that not only hepatic portal circulation but also the pituitary portal circulation is impaired in Fontan patients. Increased pituitary volumes in Fontan patients may surrogate congestion of the pituitary portal circulation which becomes super-portal circulation after Fontan operation.

Ventricular mechanics in adolescents and adults late after repair of subarterial and perimembranous ventricular septal defects

Sit-Yee Kwok, Susanna So-Shan Yeung, Wing-Yi Li, Yiu-Fai Cheung
Queen Mary Hospital, Hong Kong

Background and Aims: There have been concerns of ventricular dysfunction late after surgical repair of non-subarterial ventricular septal defects (VSD). We assessed and compared right (RV) and left ventricular (LV) mechanics in adolescents and adults after surgical closure of subarterial and perimembranous defects.

Methods: A total of 75 subjects were studied: 29 patients after subarterial VSD repair (group I), 17 patients after perimembranous VSD repair (group II) and 29 age-matched controls (group III). RV and LV mechanics were assessed using tissue Doppler and speckle tracking echocardiography, while RV outflow systolic function was quantified by systolic excursion and fractional shortening (FS).

Results: Compared with group III, groups I and II had significantly reduced tricuspid annular systolic and diastolic velocities, isovolumic myocardial acceleration, RV global longitudinal systolic and diastolic deformation parameters, and RV outflow systolic excursion (all p<0.05). Group I, but not II, had reduced RV outflow FS (p=0.008) and the lowest global LV longitudinal systolic strain (p=0.008) and systolic strain rate (p=0.014). In group I, postoperative aortic regurgitation was associated with lower LV longitudinal systolic strain (p=0.009) and early diastolic strain rate (p=0.002), while right bundle branch block was associated with lower RV systolic strain rate (p=0.048). As a group, RV outflow excursion (p=0.001) and FS (p=0.001) were correlated with LV global systolic strain.

Conclusion: Adolescents and adults late after repair of subarterial and perimembranous VSDs show impairment of RV systolic and diastolic myocardial deformation. The RV outflow function and LV systolic deformation appear to be worse after repair of subarterial defects.
**Developmental Paediatrics**

**Screen use and its relationship with emotional and behavioural difficulties in pre-school children with neurodevelopmental disorders: Do screen content and context matter?**

Rachel Shi-Hui Chong1,2, Jiayong Lin2, Swati Singhal3, Natasha Riard3, Isabel Ng, Jacqueline Leow4, Sylvia Henn-Tean Choo4,5, Falk Muller-Riemenschneider2,3, Chui-Mae Wong2,5, Iliana Magiati

1Department of Child Development, KK Women’s and Children’s Hospital, Singapore (KKH-DCD), Singapore, 2Department of Psychology, National University of Singapore, Singapore, 3Department of Child Development, KK Women’s and Children’s Hospital, Singapore, 4School of Clinical Medicine, University of Cambridge, Cambridge, United Kingdom, 5NUS Yong Loo Lin School of Medicine, Singapore, 6Yong Loo Lin School of School of Medi, Singapore, 7Saw Swee Hock School of Public Health, National University of Singapore, Singapore

**Introduction:** Use of screen media has been linked to poorer developmental outcomes in typically developing children. Despite increasing use of screen media in children, little is known about screen use in children with neurodevelopmental disorders (NDD), a population already at a higher risk for poorer developmental, emotional and behavioural outcomes. The present study examined the relationship between screen use and emotional and behavioural difficulties (EBD) in Singaporean pre-school children with NDD. Specifically, we explored whether the content (type of programmes) and context (amount of co-viewing with others) of screen use moderates this relationship.

**Methodology:** Parents of 367 children with NDD below the age of six years seeking services at the Department of Child Development, KK Children’s and Women’s Hospital, participated in this cross-sectional study. Children’s screen use patterns and EB difficulties were assessed using parent-report questionnaires.

**Results:** The average daily screen time for children in this study was 3.98 hours. The average age of First Screen Exposure (FSE) was 1.74 years, with 52% exposed to screens at less than 18 months of age. Child video programmes (CVP) was the screen content ranked as being ‘used most often’, followed by interactive educational applications (EA), and mobile games (MG). Use of CVP ‘more often’ was significantly negatively associated with use of EA ‘more often’. Earlier age of FSE was associated with more EBD, with a small effect size. Average daily screen time and screen context (time spent on solitary viewing of screens) was not associated with EB difficulties. Using CVP during screen time was found to be a significant moderator between age of FSE and EBD. Other screen content categories (i.e. screen interactive educational applications, interactive games, and adult programmes) and screen context (i.e. screen interactive educational applications, interactive games, and adult programmes).
context was not found to be significant moderators.

**Discussion/Conclusion:** Screen time of children with NDD in our study exceeded APA recommendations, but was similar to previous Singapore studies in younger children. Children who are introduced to screens at an earlier age had more EBD at recruitment. Mixed results in the moderating effects of screen content and screen context are in line with previous studies, but could also be due to limitations in measurement of screen content and context. For future studies are discussed.

### Rasch Validation of the Chinese Parent-Child Interaction Scale (CPCIS)

Patrick Ip\(^1\), Winnie Tso\(^1\), Nirmala Rao\(^1\), Frederick Ho\(^2\), Ko-Ling Chan\(^3\), King-Wa Fu\(^4\), Sophia Li\(^5\), Winnie Goh\(^6\), Wilfred Wong\(^7\), Chun-Bong Chow\(^8\)

\(^1\)The University of Hong Kong, Hong Kong, \(^2\)The Hong Kong Polytechnic University, Hong Kong, Hong Kong, \(^3\)KK Women’s and Children’s Hospital, Singapore

**Background:** Proper parent-child interaction is crucial for child development, but an assessment tool in Chinese is currently lacking. This study aimed to develop and validate a parent-reported parent-child interaction scale for Chinese preschool children.

**Method:** The Chinese Parent-Child Interaction Scale (CPCIS) was designed by an expert panel based on the literature and clinical observations in the Chinese context. The initial CPCIS had 14 parent-child interactive activity items. Psychometric properties of the CPCIS were examined using the Rasch model and confirmatory factor analysis (CFA). Convergent validity was investigated by the associations between CPCIS and family income, maternal education level, and children's school readiness.

**Results:** The study recruited 567 Chinese parent-child pairs from diverse socioeconomic backgrounds, who completed the CPCIS. Six out of the 14 items in the initial CPCIS were dropped due to suboptimal fit values. The refined 8-item CPCIS was shown to be valid and reliable by Rasch models and CFA. The person separation reliability and Cronbach’s \(\alpha\) of the CPCIS were 0.81 and 0.82, respectively. The CPCIS was shown to be valid and reliable by Rasch models and CFA. The person separation reliability and Cronbach’s \(\alpha\) of the CPCIS were 0.81 and 0.82, respectively. The CPCIS scores were positively associated with family socioeconomic status (\(\eta^2=0.05, p<0.001\)), maternal education level (\(\eta^2=0.08, p<0.001\)), and children’s school readiness (\(\eta^2=0.01, p<0.01\)).

**Conclusions:** CPCIS is an easily administered, valid, and reliable tool for the assessment of parent-child interactions in Chinese families.

### EEG power spectra as early biomarkers of autism spectrum disorder

Bingrui Zhou, Chunyang Li, Yuanfeng Zhou, Qiong Xu, Chunchun Hu, Xiuxu Xu

Children’s Hospital of Fudan University, Shanghai, China

**Objective:** To identify electrophysiological biomarkers of autism spectrum disorders (ASD) and to investigate their diagnostic value of ASD.

**Methods:** We recruited toddlers aged 18-30 months who diagnosed with ASD and age-matched toddlers with typical development (\(n=20\), respectively) in our study. EEG absolute and relative powers of 17 frequency bands were measured when subjects were awake. Then, we selected the power spectra which were different between toddlers with ASD and typical toddlers, and performed receiver-operator-characteristic (ROC) area-under-the-curve (AUC) analyses using clinical diagnosis as reference to evaluate their application values for early diagnosis of ASD, and to compare the sensitivity and specificity of the EEG power candidates using optimal cutoffs. Finally, we used the EEG power indexes of statistical significance to establish a model for early diagnosis of ASD. Meanwhile, we performed linear regression analysis and correlation analysis to explore the probable relationship between EEG powers and severity of clinical symptoms/developmental outcomes.
Altered functional and structural brain connectivity in ASD individuals with SHANK3 defect

Chunxue Liu, Dongyun Li, Haowei Yang, Bingrui Zhou, Chunchun Hu, Chunyang Li, Huiping Li, Qiong Xu, Zhongwei Qiao, Xiuxu

Children's Hospital of Fudan University, Shanghai, China

Background and Aims: SHANK3 is a postsynaptic scaffolding protein, whose molecular variations is thought to be responsible for 22q13 deletion syndrome (Phelan-McDermid Syndrome) and autism spectrum disorders (ASD). However, it remains unclear how SHANK3 defect are relat-ed to abnormal brain development in ASD. Our study aims to assess the GM and WM development of SHANK3 defect children ascertained for ASD and explore the relationship with clinical phenotypes.

Methods: MLPA and Sanger sequencing were carried out to confirm the SHANK3 deficiency of 8 Chinese children with ASD (SHANK3 group), followed by systematic and compre-hensive evaluations. Then we recruited 24 ASD children without SHANK3 deficiency (ASD group) and 25 typically developing controls (TD group). ADOS scale was applied to examine the severity of autism and Griffith scale was used to assess the development level of SHANK3 group and ASD group. In addition, MRI scans of the three groups were ana-lyzed using voxel-based morphometry (VBM) and Diffusion tensor imaging (DTI). Normalized modulated GM maps were statistically analyzed using the general linear model. The integrity of WM fiber was evaluated using fractional anisotropy (FA).

Results: (1) Compared with those of typical toddlers, the beta relative powers of central (C3, Cz), frontal (F3, Fz, F4), left temporal (T7, T3) and left parietal (P3) areas were signifi-cantly higher in toddlers with ASD.

(2) After performing ROC-AUC analyses, beta relative powers of 3 electrodes (F3, Fz, F4) of frontal area were confirmed with statistical significance. The AUCs were higher than 0.7 (p<0.05). Of these, the AUC of the F4 beta relative power was the best (AUC=0.827, p<0.006). Logistic regression model was established with the 3 beta relative powers, but only the F4 beta relative power entered the equation. The regression equation is logitP=-2.454+0.517*F4 beta RP. (3) The beta relative powers of left frontal (F3) and left anterior temporal (F7) lobe were positively correlated with the developmental quotients (DQs) of hand-eye coordination and performance subscales, and the general quotient (GQ), respectively (r>0.3, p<0.05). No other correlations were founded between EEG relative powers and clinical outcomes.

Conclusions: (1) There are some differences in awake EEG power between toddlers with ASD and typical toddlers, mainly manifesting as higher beta relative powers of some areas in toddlers with ASD, especially in left brain areas. (2) The beta relative powers of frontal areas (F3, Fz, F4) can be the biomarkers for early diagnosis of ASD, and the beta relative power of right fronta l area (F4) might become an independent index for the early diagnosis of ASD. (3) The beta relative powers of left frontal (F3) and left anterior temporal (F7) lobes might be used for predicting cognitive ability of ASD toddlers.

Clinical Practice of CMA in NDD in China

Mingyu Xu, Yiting Ji, Ke Li, Juan Geng, Fei Li

1Xinhua Hospital Affiliated to Shang Jiaotong University School of Medicine, Shanghai, China, 2Hangzhou Joinge-nome Diagnostics, Hangzhou, China

Background and Aims: Neurodevelopmental disorders (NDDs), including intellectual disability, global developmental delay, and autism, affect more than 15% of children. NDDs are a condition of great concern for public health and society which have the complex genetic understanding in its etiology. Chromosomal microarray (CMA) is currently the first-line diagnostic genetic test for patients with idiopathic neuropsychiatric diseases in many countries. Large-scale whole-genome copy number variation (CNV) studies have established the importance of de novo CNV in NDD, CNV study in DD/DD and/or ASD have not been well investigated in non-Caucasian population.

Methods: To evaluate the pathogenic responsibility and clinical impact of chromosomal microarray (CMA) on the paediatic patients in China. We performed CytoScan™ HD system, Affymetrix array on 364 children with intellectual disability (ID)/developmental delay (DD), autism spectrum disorders (ASD) in the department of developmental behavorial pediatrics of Shanghai Children’s Medical Center and Xinhua hospital affiliated to Shanghai Jiaotong University, School of Medicine from July 2014 to August 2016. The medical records of patients were reviewed, focusing on the pathogenic/likely pathogenic CMA findings and their clinical management.

Results: 56 patients were reported to have pathogenic/
likely pathogenic results. This gives a detection rate of 24.4% for DD/ID and 8.33% for ASD with clinically significance. The significant findings have prompted clinical actions in 48 patients (86%). A total of eight recurrent CNVs that spanned in different chromosome were identified. The 22q13.3 deletion is more common in ASD patients of our study cohort. Our study clearly demonstrates a dosage effect of 17q11.1-1q12 copy number on the various clinical findings, and suggests the presence of dosage sensitive genes and level of somatic mosaicism within the rearranged interval.

**Conclusion:** Our effort helped to collect the information of the de novo mutation in Chinese children with DD/ID and/or ASD. Our data shows that CMA provides immediate clinical utility for patients. Our study provided further evidence of an increased diagnostic yield of CMA and supported its use as a first line diagnostic tool for Chinese individuals with DD/ID, ASD. We advocate using diagnostic yield of clinically actionable results to evaluate CMA as it provides information of both clinical validity and clinical utility. The same framework can be applied to other genomic testing strategies enabled by next-generation sequencing.

### 1058

**Collaborative project of medical service and school health system to care for school age children’s mental health in Shanghai**

**Xiaolin Zhang**1,2, **Yiwen Zhang**1,2, **Jun Ma**1,2, **Zengqiang Wu**3, **Zhenzhen Ma**4

1Shanghai Children’s Medical Center Affiliated to Medical School of Shanghai Jiao Tong University, Shanghai, China, 2MOE-Shanghai Key Laboratory of Children’s Environmental Health, Shanghai, China, 3Shanghai Academy of Educational Science, Shanghai, China

**Objective:** The present study aimed to build a mode of collaboration with medical service and school health system to care for school age children’s mental health in Shanghai.

**Methods:** The sample of this study consisted of 4884 children aged 6-9 years (8.10±1.19) from 12 primary schools in four districts in Shanghai. The Strengths and Difficulties Questionnaire (SDQ) was administered to screen. Screening positive children were interviewed with Mini International Neuropsychiatric Interview for Children and Adolescent (MINI-KID) by trained teachers from school health system. Developmental and behavioral pediatricians then further interviewed children with positive results of MINI-KID to made diagnosis. Eight-week individualized intervention for children with mental issues, mainly Attention Deficit Hyperactivity Disorder (ADHD) was done in schools with the monitoring of developmental and behavioral pediatricians and therapists. The intervention includes group play therapy, behavior therapy, language and neuro-motor therapy and medication. The Chinese version of the Swanson Nolan and Pelham, Version IV (SNAP-IV) Scale, Self-esteeem Scale, SDQ and neuro-motor scale were reassessed at the end of the intervention and 3 months later.

**Results:** The positive rate of SDQ screening is 9.38% (468/4884), in which about 80% shows positive in domains of conduct problem, partnership problem and hyperactive and attention problem. MINI-KID positive is 18.85% (69/366, 92 children didn’t attend interview). All 69 children show ADHD pattern and 12 comorbid anxiety, 7 comorbid ODD, 5 comorbid depression, 4 comorbid conduct disorder and 2 comorbid tics. Fifty-eight from 69 MINI-KID positive children accepted interview of developmental and behavioral pediatricians and 46 were diagnosed as ADHD. The detection rate of ADHD by school health system is 79.31%. Eight-week individualized intervention significantly improved ADHD children’s symptoms of inattention and hyperactivity, neuro-motor ability, and self-esteem (p<0.05). The same pattern of improvement showed 3 months later.

**Conclusion:** The mode of collaboration with medical service and school health system to care for school age children’s mental health in Shanghai is feasible and effective. ADHD is the main etiology for primary school children with behavioral and mental health problems.

### 1735

**Efficacy study of family-based early behavioral intervention program BCRI for autism in Chinese population**

**Biyuan Chen, Xiaobing Zou, Yuanyuan Zou**

**Sun Yat-Sen University, Third Affiliated Hospital, Guangzhou, China**

**Background:** Autism Spectrum Disorder (ASD) is considered to be an early-onset neurodevelopmental disorders characterized by qualitative social interaction impairments and repetitive stereotyped behaviors/restricted interests. However, compelling evidence shows that promoting a structural early-intervention model may positively influence outcomes of ASD as well as reduce the burdens of lifetime care demands for society.

**Objective:** BCRI intervention program aims to empower the parents to master appropriated approaches and strategies of BCRI early behavioral intervention, and provide positive effects to the clinical outcome for children with ASD.

**Methods:** 130 children diagnosed with ASD between the ages of 18 and 30 months were randomly assigned to the early BCRI group and CI group (community intervention). Both BCRI group and CI group participate in a two-day ASD seminar to receive basic knowledge about behavioral intervention in Phase-one. In Phase-two, BCRI group participate in a 24-halfday workshop to gain hands-on experience and one-on-one training from master trainers, then these family take another 11 months to implement BCRI intervention to their children in home settings, and CI group receives community service. Psycho-educational Profile-3rd Edition (PEP-3) assessment indexes were collected, and single and multiple Wilcoxon signed rank test were performed for statistical analysis.

**Result:** 85 participants (53 in BCRI group, 32 in CI group) completed primary endpoint at one year after enrollment. Statistically significant post-intervention improvements were found in BCRI group, which included Cognitive Verbal/Proverbial (CVP), Expressive Language (EL), and Receptive Language (RL) subsets in the Communication domain (p<0.05). By Comparison of pre- and post-intervention between BCRI and CI group, significant improvements were...
reported in combined score of Communication domain (CVP, EL, RL) plus Fine motor (FM) subset (p<0.05), and in combined score of Visual Motor Imitation (VMI) subset and FM subset (p<0.05).

**Conclusions:** It’s the initial large sample randomized controlled study for family-based early behavioral intervention for ASD. We suggest that BCRI intervention model have positive effects for children with ASD, to develop early communication skills as well as visual motor imitation and fine motor skills. BCRI model emphasize the initial appliance of behavior management and problem-solving strategies, which following by structural teaching infrastructure with appropriate level of education. BCRI also emphasize to emerge ‘relationship elements’ as part of social interaction intervention throughout every step of BCRI model, to Improve social skills of children with ASD. The study indicated that BCRI model is an effective early behavioral intervention method for child with ASD, and the feasibility to implement in middle-income countries.

**1751**

**Association between maternal gestational diabetes mellitus and offspring’s neurodevelopment delay at one year of age: A prospective cohort study**

Xian Liu¹, Meizhen Tan², Yingyi Lin¹, Jianrong He¹, Fanfan Chan¹, Jinhua Lu¹, Yashu Kuang¹, Fengjuan Zhou¹, Minshan Lu¹, Fang Hu¹, Lisha Zhu¹, Xiu Qiu¹, Huimin Xia¹

¹Division of Birth Cohort Study, Guangzhou Women and Children’s Medical Center, Guangzhou Medical University, Guangzhou, China, ²Department of Child Health Care, Guangzhou Women and Children’s Medical Center, Guangzhou Medical University, Guangzhou, China

**Objective:** The incidence of gestational diabetes mellitus (GDM) is rising rapidly in China. Effects of maternal GDM on offspring’s neurodevelopment remain unclear. We aimed to examine whether children whose mothers were diagnosed with GDM had increased risk of neurodevelopment delay in their first years of life.

**Methods:** We used data from 5107 mother-child pairs recruited from the Born in Guangzhou Cohort Study between February 1, 2012 and April 30, 2015. Maternal GDM status was assessed by 75-g oral glucose-tolerance test (OGTT) at 22 and 28 week’s gestation. Five dimensions of child’s neurodevelopment, including adaptive behavior, gross motor, fine motor, language and social behavior, was evaluated at 12 months of age using the Gesell Development Scale. Neurodevelopment delay for each dimension was defined as a score of <85 respectively. Log-binomial regression models were used to examine the association between maternal GDM status and children’s neurodevelopment outcomes, and risk ratios (RR) and 95% confidence intervals (CI) were calculated after adjustment for child’s sex, birth weight, mothers’ maternal age, pre-pregnancy body mass index (BMI), second-hand smoking status, maternal education, income, parity and feeding practice. Multiple linear regression was applied to explore the relationship between fasting glucose level and neurodevelopment scores.

**Results:** Maternal GDM was statistically associated with lower risk of fine motor development delay (RR=0.59, 95% CI: 0.35-0.97, p=0.04), but not other neurodevelopment dimension (p values >0.05). Fasting glucose levels was positively related to the scores of gross motor (regression coefficient β=0.81, p=0.03), fine motor (β=0.80, p=0.01) and social behavior (β=1.64, p=0.001).

**Conclusions:** We did not observed evident harmful effects of maternal GDM on children’s neurodevelopment at 12 month of age. In contrast, higher fasting glucose level appeared to be associated with improved development of gross motor, fine motor and social behavior. Further research is needed to confirm our findings.

**1890**

**Regional brain chemical alterations between verbal and non-verbal autistic Children: A 1H-MRS study**

Wen-Xiong Chen¹, Hong-Sheng Liu², Zhi-Fang Huang¹, Si-Huiz Zeng², Li Huang², Qian-Qian Wu², Zheng-Qing Liu², Yuan-Yuan Gao³, Ke-Lu Zheng¹

¹Department of Neurology, Guangzhou Women and Children’s Medical Center, Guangzhou, China, ²Department of Radiology, Guangzhou Women and Children’s Medical Center, Guangzhou, China

**Background:** Language deficit is one of most difficult to treat autistic features; around 25% autistic patients remain non-verbal; the pathophysiology of non-verbal is unclear.

**Objectives:** In vivo investigated cellular neurochemicals with proton magnetic resonance spectroscopy imaging (1H-MRS) in the brain regions associated with language in children with autism spectrum disorder (ASD).

**Methods:** The autistic children aged between 2-14 years old were recruited. The concentrations of cerebral N-acetyl-aspartate (NAA), creatine (Cr), choline (Cho), were determined by 3 T 1H-MRS examinations in 91 non-verbal (NV) and 75 verbal (V) autistic children at the inferior frontal cortex (IFC), superior temporal cortex, cerebellum, and hippocampus respectively. The binary multivariate logistic regression analysis was adopted.

**Results:** The higher level of NAA/Cr ratio at the right IFC was associated with increased risk of non-verbal (2.51[1.17-5.38]; p=0.018), whereas the lower levels of Cr (0.60[0.41-0.88]; p=0.01) and Cho (0.73 [0.56-0.97]; p=0.027) at the right IFC, Cho/Cr ratio (0.46 [0.23-0.90]; p=0.023; 70/91 [NV] versus 54/75 [V]) at the left cerebellum, and NAA (0.70 [0.52-0.93]; p=0.015; 53/91 [NV] versus 37/75 [V]) and Cr (0.48 [0.27-0.85]; p=0.011; 53/91 [NV] versus 37/75 [V]) at the right hippocampus were related to decrease risk of non-verbal, after adjusting the confounding factors including age, gender, gestational age, birth weight, developmental quotient /intellectual quotient, severity of autism, maternal education and paternal education.

**Conclusions:** Among autistic children, some regional chemical alterations were associated with the risk of non-verbal feature.
Endocrinology

The interplay of vitamin D levels, vitamin D receptor single nucleotide polymorphism and diets on serum lipid profiles in Chinese Han adolescents

Xiaojuan Liu1,2,3, Siqi Guo1,2, Yongmei Jiang1,3, Dingzhi Fang

1Department of Laboratory Medicine, West China Second University Hospital, Sichuan University, Chengdu, China, 2West China School of Basic Medical Sciences & Forensic Medicine, Sichuan University, Chengdu, China, 3Key Laboratory of Obstetric & Gynecologic and Pediatric Diseases and Birth Defects of Ministry of Education, Chengdu, China

Background and Aims: Abnormal serum lipids and glucose are closely related to the cardiovascular disease leading to high morbidity. Recent studies have shown that vitamin D and vitamin D receptor (VDR) FokI polymorphism as well as dietary patterns are involved in regulating serum lipids and glucose. But the existing conclusions are still controversial and debatable. The aim of this study is to investigate how dietary pattern of Chinese people, vitamin D and VDR polymorphism influence metabolism of serum lipid and glucose.

Methods: 590 volunteers, the eleventh grade students, participated in this study. According to the energy percentage of carbohydrate and fat, they were divided into two groups, high-carbohydrate (high-CHO) diet group and non-high-carbohydrate (non-high-CHO) diet group. Serum lipid, serum glucose and 25-hydroxyvitamin D [25 (OH) D] were measured in laboratory. Based on the VDR FokI polymorphism, the participants were assigned into two groups, TT genotype and CC allele carriers. According to the serum level of 25 (OH) D, the subjects were divided into three groups.

Results: There were quite a few differences in serum lipids and glucose between males and females under different vitamin D levels, dietary patterns and genotypes. To conclude below: (1) Considering dietary pattern, C allele carriers males with medium vitamin D in non-high-CHO diet group had higher HDL-C but lower TC/HDL-C and LDL-C/HDL-C than those in high-CHO diet group. As for females in non-high-CHO diet group, C allele carriers subjects with low vitamin D had lower TG than those in high-CHO diet group. (2) Considering FokI polymorphism, males with medium vitamin D in high-CHO diet group had higher HDL-C but lower TC/HDL-C and LDL-C/HDL-C than those in C allele carriers group. For TT genotype females in high-CHO diet group, subjects with low and medium vitamin D had higher TG than those with high vitamin D. As for C allele carriers females in high-CHO diet group, subjects with low vitamin D had higher TG than those with medium vitamin D.

Conclusion: In the youth China healthy Hans, serum lipid and glucose affected by serum level of vitamin D, VDR FokI polymorphism and dietary pattern, and these influences not only has sex dependent, but also interact with each other. This partly explains why the earlier results were inconsistent.

Waist-to-height ratio remains an optimal and easier index for indicating obesity-related cardiovascular risk in children and adolescents

Yuan Jiang, Ya-Lan Dou, Yi Zhang, Da-Yan Niu, Wei-Li Yan

Department of Clinical Epidemiology, Children’s Hospital of Fudan University, Shanghai, China

Background and Aims: Which obesity measures, including body mass index (BMI), waist circumference (WC) and waist to height ratio (WHtR), better indicate cardiovascular risk remains controversial for pediatric population since cardiovascular disease rarely occur in this population. Recently tri-ponderal mass index (TMI) is reported better correlated with body adiposity than BMI. The current study aims to evaluate the accuracy of body adiposity indexes based on BMI, TMI, WC, WHtR and percentage of body fat (PBF) as indicators for cardiovascular risk in children and adolescents.

Methods: Eligible subjects were recruited from 4 schools in Shanghai and 6 schools in Chongqing by random cluster sampling. Height, weight, WC, blood pressure, fasting blood glucose (FBG) and lipid profiles (elevated triglyceride, total cholesterol, low density lipoprotein cholesterol, decreased high density lipoprotein cholesterol) were examined by standard protocols. PBF were measured by dual energy X-ray absorptiometry and standardized into Z scores using American recommendation. BMI and WHtR were computed. BMI and WC were standardized into Z scores to adjust effect of age by gender. Central obesity was defined by age-specific cutoff recommended by China Children’s Obesity Working Group. Two outcomes were defined. Subjects with any 3 or more the following abnormalities, elevated FBG, lipid profiles, blood pressure, or central obesity, were defined as CVD3 (outcome 1). Subjects with at least 2 above abnormalities were defined as CVD2 (outcome 2). Pearson correlation coefficients were calculated between WHtR, TMI, BMI, WC and PBF. Receiver operation curves (ROC) were performed to assess and compare the performance of WHtR, TMI, BMI, WC and PBF in predicting two CVD outcomes, respectively.

Results: A total of 1863 subjects aged 7 to 18 years with complete data were included in this analysis. WHtR and TMI were very weakly correlated with age (r=0.05 and 0.05, P>0.001). WHtR, TMI, BMI and WC were highly correlated with PBF (r=0.71, 0.67, 0.68 and 0.72, P<0.001). To predict CVD3, AUCs of WHtR, TMI, BMI, WC, PBF were 0.83 (95% CI: 0.79-0.87), 0.82 (95% CI: 0.78-0.86), 0.83 (95% CI: 0.79-0.87), 0.83 (95% CI: 0.79-0.88), 0.81 (95% CI: 0.77-0.85), respectively. In predicting CVD2, AUCs were 0.80 (95%CI: 0.77-0.83), 0.79 (95%CI: 0.77-0.82), 0.82 (95%CI: 0.80-0.84), 0.82 (95% CI 0.80-0.85), 0.78 (95% CI: 0.75-0.81), respectively.

Conclusion: Considering performances in indicating CVD risk and simplicity in application, we believe that WHtR remains an optimal index to evaluate obesity related CVD risk in children and adolescents in public health.
Exclusive enteral nutrition versus infliximab in inducing therapy of pediatric Crohn’s disease
Youyou Luo, Jindan Yu, Jingan Lou, Youhong Fang, Jie Chen
The Children’s Hospital of Zhejiang University School of Medicine, Hangzhou, China

Background and Aims: Infliximab, a monoclonal antibody targeting tumor necrosis factor-alpha (TNF-α), is one of the primary treatment strategies for active Crohn disease (CD), while exclusive enteral nutritional (EEN) therapy have been shown advantages in inducing remission, improving growth and MH in pediatric CD patients. However, adverse reactions (AIR), infections and risk of malignancy are the main concern of patients who are receiving infliximab as induction remission therapy. In the meanwhile, patients’ poor compliance may lead to EEN treatment failure. Thus, the balance between efficacy, risk of side effects and patients’ compliance is an important consideration in choosing therapeutic regimens. Since rare studies showed comparative effectiveness of those approaches, we prospectively compared the efficacies, growth improvements, and adverse effects of the two regimens in children with newly diagnosed CD

Methods: In a prospective study of children initiating EEN or infliximab therapy for CD, we compared clinical outcomes using the pediatric Crohn’s disease activity index (PCDAI), growth improvement as evaluated by height for age (HFA) z score and body mass index for age (BMIFA) z score, endoscopic mucosal healing and adverse effects. Data were measured at baseline and after 8 weeks of therapy.

Results: We enrolled 26 children with CD, of whom 13 were treated with infliximab, 13 with EEN. Clinical response (PCDAI reduction ≥15 or final PCDAI ≤ 10) was achieved by 83.3% in EEN group and 90.9% in IFX group. BMIFA z scores were significantly increased in both 2 groups (p<0.05). No significant differences were observed in PCDAI, HFA or BMI recovery between two groups. Adverse effects were detected in 30.7% on infliximab and 0% on EEN. Mucosal healing was achieved in 71.4% cases in EEN group versus 85.7% in IFX group.

Conclusion: EEN provided similar improvement as IFX in clinical symptoms, mucosal healing and BMI, but not height, in a short term. EEN therapy had less adverse effects when compared with IFX. To our knowledge, this is the first study comparing the efficacy of nutritional status between EEN and IFX.
Background and Aims: It is the key point to choose appropriate antibiotics for the children with congenital biliary atresia Kasai postoperative cholangitis, as the developing of antibiotic resistant and the changing of the bacteria spectrums. To explore the antibiotic selection of cholangitis in children who underwent hepaticoportoenterostomy for congenital biliary atresia.

Methods: The data collected of 300 children with congenital biliary atresia Kasai postoperative cholangitis had been analyzed to analyze pathogenic bacteria and antibiotics sensitivity according to clinical types of the cholangitis in our hospital from 2006 to 2016.

Results: (1) In 300 cases of children with occasional cholangitis accounts for 202 cases, 98 cases of frequent cholangitis; early cholangitis in 166 cases, 134 cases of late cholangitis. (2) The main pathogens of cholangitis followed by Escherichia coli, Pseudomonas aeruginosa, Enterococcus, Acinetobacter baumannii, Enterobacter cloacae and Candida albicans. (3) The sensitivity rates of Escherichia coli and Pseudomonas aeruginosa to cefoperazone sulbactam were 75% and 78%, to piperacillin tazobactam were 82% and 84%, and to meropenem were 93% and 76%. The sensitivity rates of Enterococcus to vancomycin or linezolid were 100%.

Conclusion: Cefoperazone sulbactam and piperacillin tazobactam can be used to the first choice of antibiotics for biliary atresia Kasai postoperative cholangitis. And meropenem should be used to replace them when treatment effect was poor. Late cholangitis and frequent cholangitis should be alert to Enterococcus, Acinetobacter baumannii and other pathogens.

Antibiotics resistance of Helicobacter pylori in children with upper gastrointestinal symptoms in Hangzhou, China

Xiaoli Shu, Mizu Jiang
The Children's Hospital, Zhejiang University School of Medicine, Hangzhou, China

Background and Aims: The decreasing eradication rate of Helicobacter pylori is mainly because of the progressive increase of its resistance to antibiotics. Studies on antimicrobial susceptibility of H. pylori in children is limited. This study aimed to investigate the resistance rates and patterns of H. pylori strains isolated from children.

Methods: Gastric mucosa biopsy samples obtained from children who had undergone upper gastrointestinal endoscopy were cultured for H. pylori and susceptibility to six antibiotics (clarithromycin, amoxicillin, gentamicin, furazolidone, metronidazole and levofloxacin) was tested from 2012 to 2014.

Results: A total of 545 H. pylori strains were isolated from 1390 children recruited. The total resistance rates of H. pylori to clarithromycin, metronidazole and levofloxacin were 20.6%, 68.8%, and 9.0%, respectively. No resistance to amoxicillin, gentamicin and furazolidone was detected. 56.1% strains were single resistance, 19.6% were resistant to more than one antibiotic, 16.7% for double resistance, and 2.9% for triple resistance in 413 strains against any antibiotic. And the H. pylori resistance rate increased significantly from 2012 to 2014. There was no significantly difference in the resistance rates to clarithromycin, met-
ronidazole and levofloxacin between different gender, age groups, and patients with peptic ulcer diseases or non-ulcer diseases.

Conclusions: Antibiotic resistance was observed in H. pylori strains isolated from children in Hangzhou and it increased significantly during the three years. Our data strongly support current guidelines which recommend antibiotic susceptibility tests prior to eradication therapy.

### 1065

**Early nasogastric versus nasojejunal tube feeding in pediatric acute pancreatitis:**

**A randomized controlled trial**

**Jingan Lou, Hong Zhao, Hong Zhao, Jindan Yu, Kerong Peng, Feibo Chen, Jie Chen**

_The Children’s Hospital of Zhejiang University School of Medicine, Hangzhou, China_

**Background and Aims:** Nasojejunal tube feeding is a standard of care in patients with predicted acute pancreatitis (AP) and several recent trials suggested that nasogastric tube feeding (NGT) is as safe and efficient as nasojejunal tube feeding in these patients. However, the efficacy and safety of NGT in pediatric AP has not been investigated yet. The aim of this study was to investigate whether NGT presents any benefit to patients with mild to moderate AP in children.

**Methods:** A total of 49 consecutive pediatric patients with AP were randomized to receive either NG or NJ feeding via a fine bore feeding tube within 72 hours of hospital admission. The primary outcome was tolerance of enteral nutrition support. Complications (tube-associated, infections, feeding-associated) were monitored and comparisons made of both total hospital and intensive-care stays, duration of tube feeding, occurrence of any complications.

**Results:** A total of 49 children with acute pancreatitis were recruited into this study and were randomized to NG group (25) or NJ group (14). There were no significant differences of age, gender, pediatric acute pancreatitis scores, CT Severity Index (CTSI) and gastrointestinal symptoms or abdominal pain between the two groups. Eighty-eight percent (22/25) of NG group and 96% (23/24) of NJ group can tolerate with tube feeding ($p>0.05$). The duration of hospital stay was $14.5 \pm 4.7$ d for NG group and $16 \pm 6.3$ d for NJ group. For duration of tube feeding were $12.5 \pm 7.4$ d and $16 \pm 4.4$ d separately. One children of NJ group has tube-associated complication. 8 patients of NJ group and 9 of NG group have feeding-associated complications such as diarrhea, vomit and abdominal pain. None of all patients has complication of any infection. Clinical differences between the two groups were not significant. Overall mortality was 0.

**Conclusion:** The simpler, cheaper, and more easily used NG feeding is as good as NJ feeding in pediatric patients with AP. This appears to be a useful and practical therapeutic approach to enteral feeding in the early management of patients with AP.

---

**Clinical application of treatment of large colorectal polyps by purse string suture with nylon loop and titanium clips in combination with colonoscopy-assisted high-frequency electrocision**

**Ying Fang, Hong Li, Tian-jiao Gao, Feng Wang, Ku-Ku Ge, Yi Chen**

_Xi’an Children’s Hospital, Xi’an, China_

**Objective and Aims:** Endoscopic high-frequency electrocision has been widely used in the treatment of colorectal polyps in children. But for big polyps with wide base, electrocision is likely to cause complications, such as intestinal perforation and intestinal bleeding. The aim of this study was to assess the effect and safety of high-frequency electric snare used for removal of big polyps with wide base (Diameter $>2.5$ cm) under endoscopy with the assistance of purse string suture with titanium clips and nylon loop.

**Methods:** 27 cases of hospitalized children diagnosed big colorectal polyps with wide base from January 2015 to December 2016 were researched and their clinical data were retrospectively analyzed.

**Results:** 27 cases of big polyps in children include that P-J syndrome was 11 cases, familial polyposis was 9 cases, inflammatory polyps was 6 cases, lymphoma was 1 case. Among the distribution of these 33 polyps, 26 of them were located in colon and 7 in rectum. Fourteen polyps were ligatured by nylon loop firstly and then were cut by high-frequency electric snare, and finnally clipped by titanium folders. Bleeding occurred during operation in 1 case, and delayed hemorrhage after operation had been happened in 3 cases (after intravenous hemostasis treatment, 1 case stopped bleeding; 2 cases used endoscopy again to clip bleeding site with titanium clip, no more bleeding); delayed intestinal perforation after operation had been happened in 1 cases, and the perforation was successfully cured by anti-infection treatment, no diet, and applying titanium folders. Bleeding occurred in 1 case stopped bleeding; 2 cases used endoscopy again to clip bleeding site with titanium clip, no more bleeding; delayed intestinal perforation after operation had been happened in 1 cases, and the perforation was successfully cured by anti-infection treatment, no diet, and applying titanium folders. Bleeding occurred in 1 case stopped bleeding; 2 cases used endoscopy again to clip bleeding site with titanium clip, no more bleeding; delayed intestinal perforation after operation had been happened in 1 cases, and the perforation was successfully cured by anti-infection treatment, no diet, and applying titanium folders.

**Conclusion:** The application of high-frequency electrocision with the assistance of titanium folder and nylon loop can effectively prevent the bleeding and perforation during cutting big colorectal polyps with wide base or after the operation. Compared the two methods, purse string suture is more effective to prevent and cure complications, so it is worth popularizing in clinic.
Disease spectrum in children with inherited intrahepatic cholestasis in China

Neng-Li Wang¹, Jian-She Wang²
¹Jinshan Hospital of Fudan University, Shanghai, China,
²Children Hospital of Fudan University, Shanghai, China

Objective: Genetic causes account for a substantial proportion of pediatric intrahepatic cholestasis. Several genetic defects have been reported in China, but the disease spectrum is still largely unknown. The aims of this study are to explore the disease spectrum of pediatric inherited intrahepatic cholestasis that is still largely unknown in China.

Study Design: Between January 2012 and June 2016, 877 pediatric patients with intrahepatic cholestasis were evaluated by Sanger sequencing, panel sequencing, or whole exome sequencing. Clinical data and sequencing results were retrospectively collected by reviewing the medical records.

Results: A total of 295 (33.6%) received a molecular diagnosis. There were 18 distinct genetic disorders diagnosed. The top 7 resulted from mutations in SLC25A13 (41.4%), JAG1 (25.4%), ABCB11 (9.2%), ATP8B1 (6.1%), ABCB4 (4.1%), ABCC2 (4.1%), and CYP27A1 (2.7%). Patients with disease onset at younger age were more likely to receive a genetic diagnosis. The majority (85.4%) of diagnosed cases developed cholestasis before 4 months of age, and Citrin deficiency was the most common cause. But ABCB4 deficiency became the most common cause of patients with disease onset after one year old. Among the 295 diagnosed patients, 245 distinct mutations were identified in disease genes, including 61 novels. Recurrent mutations were detected in SLC25A13, ATP8B1, CYP27A1, and AKR1D1; and together accounted for 47.0% of the total mutant alleles.

Conclusion: SLC25A13 was the most common disease gene of pediatric inherited intrahepatic cholestasis in China, followed by JAG1, ABCB11, ATP8B1, ABCB4, ABCC2, and CYP27A1.

Activation of the renin-angiotensin system promotes colitis development

Yongyan Shi, Jianhua Fu, Xindong Xue
Department of Pediatrics, Shengjing Hospital of China Medical University, Shenyang, China

Background and Aims: The renin-angiotensin system (RAS) plays pathogenic roles in renal and cardiovascular disorders, but whether it is involved in colitis is unclear. The study was designed to explore the role of the renin-angiotensin system (RAS) in the pathogenesis of colitis.

Methods: RenTgMK transgenic mice that overexpress active renin from the liver, and wild-type mice chronically infused with Ang II or treated with AT1 receptor blocker (ARB), were studied using 2, 4, 6-trinitrobenzenesulfonic acid (TNBS)-induced colitis model. Intestinal mucosal biopsies from IBD patients who were on ARB therapy were also analyzed.

Results: Preterm births with NEC had significantly lower vitamin D levels than those without NEC and healthy subjects. Vitamin D increased the survival rate, lowered the Nadler’s scores in NEC pups. Enterocyte apoptosis and local inflammation, which was very prominent in NEC rats, was...
greatly reduced by vitamin D. Tight junction function was maintained, as demonstrated by normalized expression of tight junction proteins and decreased intestinal permeability. The increase in the expression of TLR4 in NEC models was also suppressed by vitamin D.

**Conclusions:** Vitamin D may increase the survival rate, alleviate structure damage and preserve intestinal barrier function. These were achieved partly through restoration of VDR expression and suppression of TLR4. Therefore, pro-inflammatory cytokines release and enterocyte apoptosis was largely inhibited. Since TLR4 activation is a typical pathological change of NEC, vitamin D therapy may be an effective prevention of NEC.

**1753**

The effect of anti-Gr-1 antibody in rhesus rotavirus induced mouse biliary atresia model

Zefeng Lin¹, Ruizhong Zhang¹, Ming Fu¹, Huiting Lin², Huimin Xia³, Yan Chen¹²
¹Guangzhou Women and Children’s Medical Center, Guangzhou, China, ²The university of Hong Kong, Hong Kong, China

**Background and Aims:** Biliary atresia (BA) is a common obstructive jaundice disease in pediatric patients with poor prognosis and high mortality. The etiology of the BA is not fully understood, but the virus infection, autoimmune dysregulation and genetic background might all get involved. The inflammation was a typical phenomenon in BA, but the immune cells involved and their interaction were not totally clear. The aim the study is to investigate the function of Gr-1+ cells in the mouse BA model.

**Methods:** Rhesus rotavirus inoculated into newborn mice was well established as a mouse BA model. In this study, the virus was injected into the mice at day 5 instead of 24 hours after birth. The anti-Gr-1 antibody was injected 4 hours before virus injection and repeated every 3 days for another 3 times. Isotype control antibody was used in the control group. The morphological changes of the mouse were monitored and the survival curve and body weight were recorded. The liver samples were collected and the Hematoxilin and Eosin and Sirius Red staining were used for histology and fibrosis evaluation.

**Results:** The results showed the similar observation with previous studies that in isotype control groups, no obvious jaundice was observed and the body weight was comparable to that of normal mice. However, in anti-Gr-1 antibody group, the oily hair was developed at day 10-12 and reduced body weight and jaundice were observed, some of them was dying at day 15-17 day after birth. The development of the BA syndrome was similar to that of virus injection at 24 hours after birth others than 5 days time different suggested the similar immune response. Furthermore, the chronic BA was obtained by which, in the liver tissue section the collagen deposition was found indicated the liver fibrosis was in progress.

**Conclusions:** Our data indicated the Gr-1+ cells play an important role in prevention of virus infection induced postnatal biliary atresia in mouse, the detail virus-Gr-1+ cells interaction is still need to further examine for understanding the mechanism in disease process.

1876

Diagnosis and treatment of functional constipation caused by cow milk protein allergy in infants

Hong-Bin Yang, Hong Li, Han-Hua Zhang, Ying Fang
Xi’an Children’s Hospital, Xi’an, China

**Background and Aims:** Functional constipation (FC) account for more than 90% of children with constipation, which often lead to abdominal pain and pain during defecation, and bring children with anxiety and unease. In addition, because of the long period of illness, parents also appear anxious and the quality of family life was affected. Cow Milk protein allergy (CMPA) is an immunological reaction of the body to one or more milk proteins, and its clinical manifestations are diverse, which mainly related to the digestive system, respiratory system, skin and so on. There are few reports about the relationship between CMP and FC at home. The purpose of this study was to analyze the clinical features of infants with functional constipation (FC) associated with CMP and explore its ways of diagnosis and therapy.

**Methods:** The detail clinical information of the infants (<1 year old) diagnosed FC relating to CMPA in our hospital from January 2015 to May 2017 were analyzed retrospectively. All patients completed routine blood test, serum IgE, allergen IgG examination, anal digital examination, thyroid function, barium enema, abdominal B ultrasound, anorectal manometry, and so on.

**Results:** 67 cases of milk protein allergy manifested functional constipation as the main manifestation, accounted for 9.1%(67/736) of all milk protein allergy. Twenty-eight (41.8%) cases were males, and 39 (58.2%) cases were females. The onset age was 17 days to 11 months, and the average age was 4.4 months. The course of disease was 1-8 months, and the average course of disease was 3.5 months. His mother and/or father had an allergic history in 21 cases (31.3%). The proportion of eosinophils increased in 57 cases (85%), and serum IgE elevated in 8 cases (11.9%). Twenty-one cases (31.3%) were positive for allergen IgG test, especially milk, eggs, cod and so on. DRE, thyroid function, abdominal ultrasound, barium enema, anorectal manometry examination showed no abnormality in all cases. Diet therapy: mothers avoid allergic food for breastfeeding children, and free amino acid formula was used for formula fed children. After 2-4 weeks treatment 45 cases (67.1%) of children with constipation has been improved.

**Conclusion:** CMPA may be one of the causes of FC in infants. Avoiding diet in the treatment of some milk protein allergy related functional constipation in infants was effective.
Clinical analysis of gastroscopic results of 525 cases of pediatric abdominal pain

Xiao-Xia Ren, Hongbin Yang, Yi Chen, Ying Fang
Xi’an Children’s Hospital, Xi’an, China

**Background and Aims:** Abdominal pain is one of the main causes of digestive diseases in children, with the characteristics of multiple, and easy recurrence. The invention of gastroscopy provides convenience for people to explore the cause of abdominal pain. The purpose of this study was to observe the microscopic manifestations and analyze the causes of abdominal pain in children, and to provide guidelines for the diagnosis and treatment of abdominal pain in children.

**Methods:** 525 patients with upper abdominal pain who were examined by gastroscopy were collected from Xi’an Children’s Hospital between March 2015 and May 2016. The patients were examined by using electronic gastroscopy OlympusGIF-Q260 and electronic nose gastroscopy GIF-XP290N. Meanwhile, results were recorded in details, including medical history, family history, other signs, biochemical tests results and abdominal imaging results. For children with long history or serious abdominal pain, further endoscopic mucosal biopsy and 13C-UBT test for helicobacter pylori were done to clear etiology of abdominal pain.

**Results:** Gastroscopy results showed 36 cases among 525(6.9%) cases were normal, the other 489 cases (93.1%) were abnormal, and the upper digestive tract diseases were common. Endoscopic biopsy was performed in 122 cases, and the biopsy rate was 23.2%. According endoscopic and biopsy results, Simple chronic superficial gastritis was 284 cases (58.1%), peptic ulcer was 47 cases(9.6%), superficial gastritis complicated with reflux esophagitis, or bile reflux was 61 cases(12.5%), superficial gastritis with duodenitis was 36 cases (7.36%), gastric volvulus was 3 cases (0.6%), erosion gastritis was 18 cases (3.68%), chemical corrosive gastritis (0.6%), eosinophilic gastroenteritis was 3 cases(0.6%), allergic purpura was 34 cases(6.95%). Among them, 385 cases received 13C-UBT test to check Helicobacter pylori, the positive rate was 53%.

**Conclusion:** The causes of abdominal pain in children are complicated and the clinical manifestations are varied. Gastroscopy is an important method for the definite etiology of abdominal pain in children, and the improvement of the rate of biopsy is beneficial to the diagnosis of the disease.

Association between dietary intake, psychosocial status, physical activity and constipation in school children: The results from Toyama Birth Cohort Study

Masaaki Yamada 1,2, Michikazu Sekine 1, Takashi Tatsuse 1
1University of Toyama, Epidemiology and Health Policy, Toyama, Japan, 2University of Toyama, Organization for promotion of Regional Collaboration, Toyama, Japan

**Background and Aims:** Childhood constipation is one of the major causes of clinic visit and affects quality of life of patients. Although psychosocial status (PS) have been thought as a potential risk factor, an epidemiological study in large population have been rarely conducted. Our aim was to clarify the association between PS, lifestyle factors and child constipation.

**Methods:** Children were from Toyama Birth Cohort Study in Japan. A total 7,478 children aged 9-10 years were analyzed by questionnaire. ‘Less frequent than once every two days’ was defined as constipation. We also surveyed children’s lifestyle, food frequency and PS. PS included the frequency of irritation, feeling of school refusal and talk with their parents. Food frequency was divided into three: more than once a day, 3 to 5 days/week, or less frequent. Multivariate logistic regression analyses were performed to explore the association. This research has been approved by an ethical committee.

**Results:** Of all, 276 children (3.7%) had constipation. Girls were more likely to have constipation (2.6% in boy and 4.8% in girl). In multivariate analysis, constipation was significantly associated with girl (Odds Ratio (OR)=1.92), physical inactivity (OR=1.48), obesity (OR=0.52), less frequent intake of milk (OR=1.30), fruits (OR=1.88), and vegetable (OR=1.56). In addition, frequent irritation (OR=1.58), feeling of school refusal (OR=1.81) and insufficient talk with parents (OR=1.42) were associated with constipation. In stratified analysis by sex, OR of physical inactivity became higher (=2.73) in boys, while ORs of psychosocial status became higher in girls (OR of irritation=1.89 and insufficient talk with parents=1.61).

**Conclusions:** Our epidemiological study showed that psychosocial status was as strongly associated with childhood constipation as conventional risk factors, such as fiber intake and physical activity. It is be beneficial for parents and health practitioners to be aware that caring psychosocial status of children can reduce their constipation.
Association between breastfeeding in infancy and cognitive function of adolescents in Santiago, Chile

Adriana Ardy1,2, Sheila Gahagan2, Estela Blanco3, Erin Delker4
1Duke-NUS Medical School, Singapore, 2University of California, San Diego School of Medicine, San Diego, USA, 3UC San Diego, San Diego, USA, 4SDSU/UCSD, San Diego, USA

Background and Aims: The benefits of breastfeeding are well-established in literature, such as immunoprotection for infants, and reduced rates of depression and breast cancer for mothers. However, whether it relates to child intelligence is an ongoing scientific debate. Studies with robust designs have produced mixed results. Few have assessed whether benefits continue into adolescence. The aim of this study was to investigate the association between duration of breastmilk as the sole source of milk in infancy and cognitive function in adolescence.

Methods: Data were from 891 adolescents who completed an infancy iron deficiency anemia preventive trial in Santiago, Chile. Date of the first bottle of formula was collected in infancy, and used to calculate the duration of breastmilk as the sole source of milk. Duration was categorized into 0-3 m, 3.1-6 m and >6 m. Cognitive function was assessed in adolescence using the Wechsler Intelligence Scale for Children-IV: Matrix Reasoning (WISC-MR) and Verbal Similarities (WISC-VS). Generalized linear modeling was used to assess differences in cognitive functioning scores by breastfeeding group. Models were adjusted for sex, birth weight, SES, maternal IQ, HOME score, maternal stress, age of WISC evaluation, randomization group, and infancy iron deficiency anemia.

Results: The sample was 50.2% female, 16.2 +/- 0.2 years of age at follow-up, and low-middle income. The average date of first bottle was 3.6 months (SD= 3.1). 51.6% of participants were breastfed for at least 3 months. The average score for WISC-MR was 7.5 (SD= 2.4), and WISC-VS was 8.4 (SD= 2.1). Longer duration of breastmilk as the sole source of milk was associated with higher scores in WISC-MR (F=4.06, p=0.018). Those who breastfed for 0-3 m scored significantly lower on the WISC-MR at 16 y (M= 7.31, SE=0.12) compared to those who breastfed for 3.1-6 m (M=7.83, SE= 0.15, p=0.004) and >6 m (M=7.72, SE=0.19, p=0.044). There was no difference in scores between the 3.1-6 m and >6 m groups. There were no significant associations between breastfeeding and WISC-VS score.

Conclusion: In a sample of healthy infants, at least 3 months of breastfeeding related to improved WISC-MR score in adolescence. Findings add to existing literature that breastmilk is a superior form of nutrition for infants, and its benefits extend to adolescence. Public policy advocacy campaigns to promote breastfeeding may benefit from this finding.

Association of household tobacco exposure in Hong Kong young children under 2 years of age with lower Family socioeconomic status and medical service utilisation

Siyu Dai, Ching-Ching Chan

The Chinese University of Hong Kong, Hong Kong

Background and Aims: Household tobacco exposure in young children causes great disease and economic burden. Local prevalence of infant household tobacco exposure was previously reported to be 41.2%. Updated prevalence and identification of associated factors of household tobacco exposure in Hong Kong young children are important. This study aimed to examine the updated prevalence of household tobacco exposure in local young children under 2 years of age and to explore the associations between household tobacco exposure and family socioeconomic status, recent respiratory symptoms and medical service utilisation.

Methods: Analysis was performed on data obtained from a community-based cross-sectional pneumococcal carriage surveillance study of healthy children aged under 2 years across 4 main regions of Hong Kong. Information on demographics, household tobacco exposure, family socioeconomic status, children’s recent respiratory symptoms and medical service utilisation was obtained by parent-reported questionnaires.

Results: A total of 1541 subjects (mean age: 11.2 months, male: 50.7%) recruited from June 2013 to June 2014 were included in the final analysis. The overall prevalence of household tobacco exposure was 31.5%, prevalence of prenatal and postnatal maternal smoking was 1.6% and 3.5% respectively. After adjustment for potential confounding factors, low household income (AOR=1.38, 95% CI: 1.08-1.76), overcrowding of household area (AOR=3.13, 95% CI: 2.00-4.89), residing in Kowloon (AOR=1.55, 95% CI: 1.11-2.15) and residing in New Territories West (AOR=1.65, 95% CI: 1.18-2.32) were independently and significantly associated with household tobacco exposure in young children. Practice of breastfeeding was significantly associated with lower odds of having household tobacco exposure (AOR=0.65, 95% CI: 0.50-0.84). For medical service utilisation, household tobacco exposure (AOR=1.33, 95% CI: 1.03-1.70) and postnatal maternal smoking exposure (AOR=2.70, 95% CI: 1.16-6.27) was significantly associated with hospitalisation in recent 3 months. However, household tobacco exposure was not significantly associated with recent respiratory symptoms in our cohort.

Conclusions: The prevalence of household tobacco exposure in young children under 2 years of age in our study was lower than previous local study. Lower family socioeconomic status was significantly associated with household tobacco exposure in young children. Household tobacco exposure in young children was associated with medical service utilisation. As home is the most significant source of environmental tobacco exposure for young children, efforts for reducing such exposure are essential especially in socially deprived population.
Mechanism of hyponatremia in Kawasaki disease: A role of nonosmotic ADH secretion and salt loss

Kenichiro Miura, Yutaka Harita, Naoto Takeda, Haruko Tsurumi, Hiroki Yasudo, Tsuyoshi Isojima, Yoichiro Hirata, Ryo Inuzuka, Keichi Takizawa, Etsushi Toyofuku, Hajime Nishimoto, Masaru Takamizawa, Masahiro Sugawa, Atsuhiko Yanagisawa, Jun Inatomi, Yoshitsugu Nogimori, Akiko Kinumaki, YoshiyukiNamai, Motoshi Hattori, Akira Oka

1 Pediatric Nephrology, Tokyo Women’s Medical University, Tokyo, Japan
2 Pediatrics, the University of Tokyo, Tokyo, Japan
3 Pediatrics, Saitama Citizens Medical Center, Saitama, Japan
4 Pediatrics, Yaizu City Hospital, Yaizu, Japan
5 Pediatrics, Ohta Nishinouchi Hospital, Koriyama, Japan

Background: The mechanisms of hyponatremia in Kawasaki disease (KD) have been reported to be hypotonic dehydration or syndrome of inappropriate secretion of antidiuretic hormone (SIADH). However, the precise mechanism of hyponatremia remains elusive because assessment of volume status based on serial change in body weight is lacking.

Methods: Eighteen patients who were diagnosed with KD and hyponatremia (serum sodium level less than 135 mEq/L) were analyzed. Hyponatremia was diagnosed at febrile state before IVG treatment in all subjects. Plasma arginine vasopressin (ADH), urine electrolytes, and serum cytokine levels were measured at diagnosis of hyponatremia. Increase and decrease in body weight by >3% was defined as hypervolemia and hypovolemia, respectively. A diagnosis of SIADH was based on all the following criteria: (1) absence of hypovolemia, (2) urine sodium level > 20 mEq/L, (3) urine osmolality >300 mOsm/kg, and (4) detectable plasma ADH (> 0.8 pg/mL).

Results: The volume status was hypervolemic in 3 (17%), euvolemic in 14 (78%), and hypovolemic in 1 (6%). The diagnoses were SIADH in 5 (28%) and hypotonic dehydration in 1 (6%). Plasma ADH levels were inappropriately high in 16 (89%). Contribution of decreased total exchangeable cations (salt loss) to occurrence of hyponatremia [5.0 (interquartile range, 2.5-6.5)%] was significantly larger than contribution of increased total body water [1.6 (1.3-3.5)%] (p=0.012). Fractional excretion of uric acid (FEUA) significantly correlated with increased total body water (r=0.57, p=0.01), and serum interleukin-6 levels significantly correlated with salt loss (r=0.66, p=0.04). Twelve patients (67%) other than SIADH or hypotonic dehydration were characterized by euvolemic or hypervolemic hyponatremia, salt loss, inappropriately high ADH levels, and a significant increase in total body water after diagnosis of hyponatremia, which was not significantly different from SIADH patients.

Conclusions: Our study demonstrated that hyponatremia in KD was euvolemic or hypervolemic and might be explained by salt loss and water retention induced by nonosmotic secretion of ADH in the majority of patients. Physicians should avoid infusion of hypotonic solutions with low sodium concentrations. Restriction of infusion rate would also be recommended, especially when FEUA is high.

A sports mentorship program improves adolescent mental health and physical fitness: A randomised controlled trial

Frederick Ho, Lobo Louie, Wilfred Wong, Ko-Ling Chan, Agnes Tiwari, Chun-Bong Chow, Walter Ho, William Wong, Meanne Chan, Eric Chen, Yiu-Fai Cheung, Patrick Ip

1 The University of Hong Kong, Hong Kong
2 Hong Kong Baptist University, Hong Kong
3 The Hong Kong Polytechnic University, Hong Kong
4 Hong Kong Sanatorium & Hospital, Hong Kong
5 University of Macau, Macao
6 University of Toronto, Toronto, Canada

Background and Aims: To assess the effectiveness of a positive youth development (PYD)-based sports mentorship program on physical and mental well-being of adolescents recruited in a community setting.

Methods: This is a randomized controlled trial recruiting students from 12 secondary schools in Hong Kong, China. Participants were randomly assigned in a 1:1 ratio to an intervention or a control arm after stratification for school, from October 2013 to June 2014. Participants were not blinded to allocation due to the nature of intervention. Students in the intervention arm received an after-school PYD-based sports mentorship for 18 weeks. Each weekly session lasted for 90 minutes. Students in the control arm received exclusive access to a health education website.

Results: 664 students (mean age 12.3 [SD 0.76]; 386 females [58.1%]) completed baseline and post-intervention assessments. The intervention improved students’ mental well-being (Cohen’s d 0.25, 95% confidence interval 0.10–0.40, P=0.001), self-efficacy (0.22, 0.07–0.37, P=0.01), resilience (0.19, 0.03–0.34, P=0.02), physical fitness (flexibility [0.28, 0.13–0.43, P=0.02], lower limb muscle strength [0.18, 0.03–0.33, P=0.03], dynamic balance [0.21, 0.06–0.37, P=0.01]), and physical activity level (0.39, 0.24–0.55, P=0.0001). The intervention did not significantly improve physical well-being (-0.01, -0.17–0.14, P=0.86), BMI z-score (-0.03, -0.18–0.12, P=0.69), body fat proportion (-0.15, -0.31–0.00, P=0.051), and social connectedness (-0.03, -0.18–0.12, P=0.72).

Conclusions: A PYD-based sports mentorship intervention improved healthy adolescents’ mental well-being, psychological assets, physical fitness, and PA level.
Accident & emergency department attendances and survival patterns among children with Down syndrome: A population-based cohort study follow-up from birth

Gilbert T Chua, Keith TS Tung, Ian CK Wong, Terry YS Lam, Wilfred HS Wong, Chun-Bong Chow, Patrick Ip

1Department of Paediatrics & Adolescent Medicine, Queen Mary Hospital, Hong Kong, 2Department of Paediatrics & Adolescent Medicine, the University of Hong Kong, Hong Kong, 3UCL School of Pharmacy, London, United Kingdom, 4Department of Social Work & Social Administration, The University of Hong Kong, Hong Kong

Background and Aims: This study aims to, with the use of hospitalisation data, describe the survival patterns and attendance to Accident & Emergency Department (AED) among children with DS in Hong Kong.

Methods: A population-based, retrospective cohort study was conducted on 1010 livebirths with DS delivered from 1995 to 2014, as identified from the territory-wide hospitalisation data. Kaplan-Meier product-limit method was adopted to estimate the survival probabilities of children with DS by selected demographic and clinical characteristics.

Results: Within the study period, the average live birth rate with DS in Hong Kong was 8.0 per 10,000 live births (95% confidence interval (CI): 6.8, 9.3). Throughout the period, a total of 75 of 1010 livebirths with DS died, with the overall half-, 1-, and 5-year survival probabilities 95.8%, 94.4%, and 92.6%. Significant improvement in their survival has been observed, particularly among those born after 2000 compared to those born between 1995 and 1999 (p < 0.05). Moreover, people with DS who were admitted to AED within their first half year of life had poorer survival rate in general.

Conclusions: The early life survival of children born with DS has improved incrementally across the last 2 decades. Further efforts are needed to educate the caregivers and health professionals to prevent the potential early onset of associated complications among children with DS, especially those with early AED visits.

Effect of socioeconomic disparity on childhood injury in Hong Kong

Chun-Bong Chow, Patrick Ip, Sarah Morag McGregor, Matthew Sik-Hon Tsui, Chak-Wah Kam, Paul Hiu-Fai Ho, Esther Wai-Yin Chan, Wilfred Hing-Sang Wong, Ivy Wing-Sze Chiu, Frederick Ka-Wing Ho, Dorothy Sze-Ting Lui

1Department of Paediatrics and Adolescent Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, 2Department of Community Medicine, The University of Hong Kong, Hong Kong, 3Accident & Emergency Department, Queen Mary Hospital, Hong Kong, 4Clinical Skills Training Centre, New Territories (West Cluster), Hong Kong, 5Department of Accident & Emergency, Queen Elizabeth Hospital, Hong Kong, 6Department of Pharmacology and Pharmacy, The University of Hong Kong, Hong Kong

Background: Injury is one of the leading causes of childhood mortality and morbidity globally. In Hong Kong, injury has been consistently the 2nd leading cause of death among children of 0-14 years. Comprehensive injury data is needed in order to design specific intervention strategy and prioritize suitable resources to combat against the public health problem. Hong Kong, although small in size, is one of the most densely populated areas around the world and is divided into 18 districts. Each district has its own characteristics, including demographics, geographical features and housing attributes. The combination creates a unique environment with the district that pose varying injury risks across districts. The study aims to analysis on the difference in injury epidemiology among the 18 districts in Hong Kong and to explore the relationship between childhood injury and socioeconomic indicators.

Methods: A retrospective analysis of Hospital Authority’s Accidents and Emergency Department (AED) visits of 0-19 year-old children due to injury between 2001 and 2012 was conducted through geo-spatial analysis and regression analysis of each injury sub-type. Sub-group analysis of age group and time sub-period were also conducted.

Results: There were a total of 742,552 episodes of AED visits due to injury during 2001-2012. 67% (n=495,207) were male. Rate of attendance of male was 5,839 per 100,000 population, which is 1.9 times more than that of female. Annual injury attendance rate was highest among 0-4 year-old children, at 6,799 per 100,000. There is an overall decreasing trend of children’s AED attendance due to injury. Analysis by residential district revealed that Tai Po (6,500 per 100,000), North (5,290), Sai Kung (5,166) and Kwai Tsing (5,159) have the highest childhood injury risks. Regression analysis also showed that districts of higher socioeconomic indicators have lower risks of injury. Childhood injury’s protective socioeconomic factors include smaller household size, higher household income media and higher employment rate.

Conclusion: Injury pattern varied in the 18 districts in Hong Kong due to the different characteristics in each district. There was also an inequity in injury risks due to socioeconomic disparities in Hong Kong. Further studies should be conducted to look into whether socioeconomic indicators affect the severity and outcome of injury among children, as well as how community level factors affect the risks of injury.
Detection and analysis of fecal intestinal microflora in children with Henoch–Schonlein purpura

Hongwei Hu, Jiang Duan, Jingjing Xiong, Mei Liu, Lizhi Zhang, Yongkun Huang

Department of Pediatrics, The First Affiliated Hospital of Kunming Medical University, Kunming, China

Background and Aims: Henoch–Schonlein purpura (HSP) is the most common systemic vasculitis in children, which mainly involves the skin, joints, and gastrointestinal and renal small blood vessels. More and more studies have found that intestinal microflora play a very important role in autoimmune and allergic diseases. HSP is also an immune-mediated disease, the etiology and pathogenesis of which is not yet fully understood. This study aimed to detect and evaluate the intestinal microflora in children with HSP and to explore the relationship between HSP and intestinal microflora.

Methods: Fecal samples were collected from children without HSP and children with HSP at the active stage and remission period. A 16SrDNA high-throughput sequencing technique was used to detect the intestinal microflora.

Results: The abundance of intestinal microflora (based on OTUs) in children without HSP was significantly higher than that in children with HSP at both the active stage and convalescent phase. The average abundance of the Bacteroidetes phylum in children with HSP at the active stage increased along with Dysgonomonas, Parabacteroides, Prevotella and unclassified Bacteroidetes at the genus level. The average abundance of the Firmicutes phylum decreased significantly, accompanied by a significant decrease in Megamonas, Acetivibrio, Anaerostipes, Butyricicoccus, Clostridium XI, Clostridium sensu stricto, Coprococcus, Dorea, Faecalibacterium, Lachnospira, Lachnospiraceae incertae sedis, Roseburia, and unclassified Lachnospiraceae at the genus level. The average abundance of Proteobacteria phylum significantly increased, accompanied by significant increases in Comamonas, Escherichia/Shigella, Halomonas, Susscinivibrio, and Sutterella at the genus level. In addition, the average abundance of Eggerthella, which belongs to actinomycetes, was significantly higher in patients at the acute phase than that in the children without HSP. The intestinal microflora of children in the convalescent group seemed not to shift back to normal. The abundance of intestinal microflora increased in the children with HSP at the acute phase and was the highest in children at the convalescent phase, while the abundance of intestinal microflora decreased at the acute phase and was the lowest during the remission period.

Conclusion: There is a dysregulation of intestinal microflora in children with HSP at the active stage and recovery stage. The relationship between such disorders and the pathogenesis, clinical and prognosis of HSP is worthy of further study.

NBO intervention improving maternal exclusive breastfeeding with perinatal anxious symptoms

Huiping Zhang¹, Shuya Shao¹, Qian Su¹, Dan Yao¹, Zhongliang Zhu², Hui Li³

¹Department of Neonatology, First Affiliated Hospital of Medical College, Xi’an Jiaotong University, Xi’an, China, ²Shaanxi Province Biomedicine Key Laboratory, College of Life Sciences, Northwest University, Xi’an, China

Background and Aims: The present study aimed to determine whether Neonatal Behavioral Observation (NBO) intervention could ameliorate maternal perinatal anxious symptoms, and further to explore the efficacy of the NBO in improving the rate of exclusive breastfeeding breastfeeding.

Methods: The 14-item Hamilton Anxiety Scale (HAMA) were used to assess the hospitalized pregnant women waiting for delivery within 37-42 weeks of gestation. The number of normal group was 100, 105 subjects were diagnosed with anxious symptoms according to the score of HAMA>14. All of the subjects were divided into two groups: control group (n=40) and NBO intervention group (n=65) which was presented NBO video before delivery, and NBO operation within 3 days postpartum. The number of NBO intervention is 6 times from 3 days to 42 days postpartum, once every week. The beginning time of milk secretion, frequency of breastfeeding and breastfeeding rate were recorded.

Results: (1) The HAMA scores in the NBO intervention group were lower than those of the control group within 15 days postpartum (p<0.05). There was no significant difference in the HAMA scores between the NBO intervention group and normal group within 42 days postpartum (p>0.05). (2) The beginning time of milk secretion in the NBO intervention group were earlier than those of the control group (p<0.05). The frequency ≥10 of breastfeeding within 24h in the first 3 day postpartum in the NBO intervention group was more than those of the control group (p<0.05). (3) Within 3, 15, 42 days postpartum, the rate of exclusive breastfeeding (58.5%, 61.5%, 63%) in the NBO intervention group were higher than those of the control group (37.5%, 35%, 40%), respectively (p<0.05).

Conclusions: NBO intervention could ameliorate maternal perinatal anxious symptoms, and further to improve exclusive breastfeeding rate.
Genetics and Genomics

131

RETA: An R package for whole exome and targeted region sequencing data analysis

Mengbiao Guo, Jing Yang, Yu-Lung Lau, Wanling Yang
The University of Hong Kong, Hong Kong

Background and Aims: Whole exome and targeted region sequencing play a major role in diagnoses of Mendelian diseases. However, currently analysis of these data involves using a number of different complex tools and understanding of the analysis results is no easy job. So here we aim to creating a user-friendly integrative analysis tool, and using R programming, we have developed an easy-to-use package, RETA, to provide a one-stop analysis for whole exome and targeted region sequencing data.

Methods: RETA presents analysis results as an interactive report with many visualization features. The report is divided into six sections: general QC, in-depth QC, candidate gene QC, structural variants, inheritance mode analysis and detailed figures for CNV and coverage analysis. General QC shows overall summary of the targeted regions and sequencing reads. In-depth QC includes IBD relationship check, consanguinity check and summary of sequencing coverage for targeted regions. Candidate gene QC reports low coverage or quality regions within the focused genes specified by the user. Structural variants section is for CNV analysis currently. Inheritance analysis provides a list of high quality variants that are consistent with the inheritance mode for e.g. autosomal dominant or recessive for families. Finally, the detailed figures for CNV context and low coverage regions are shown in the last section and users may click gene names and jump back and forth conveniently.

Results: The final results were presented in a well-organized interactive HTML file.

Conclusions: RETA should help researchers and medical professionals to analyze the huge amount clinical sequencing data with ease.

168

Impact of clinical geneticist’s analysis on the diagnostic process of whole exome sequencing: Experience from 104 families

Christopher CY Mak, Gordon KC Leung, Steven LC Pei, Kit-San Yeung, Mandy HY Tsang, Gary Mok, Brian HY Chung
Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong

Background and Aims: To evaluate the role of clinical geneticists in the diagnostic process and subsequent clinical utility of whole exome sequencing results.

Methods: 104 prospectively recruited patients with undetermined diagnoses had Whole exome sequencing (WES) performed by two laboratories, Genome Diagnostics Nijmegen (Nijmegen, Netherlands) and Ambry Genetics (Aliso Viejo, CA). Among them, 93% were children below the age of 18, and families were predominantly Chinese (94%). The WES result of each patient was comprehensively reviewed with incorporation of clinical and molecular data, review of literature and databases, segregation analysis, subsequent clinical investigations, functional studies, expert review and exome reanalysis. The subsequent changes in diagnosis and management was evaluated.

Results: Among the 104 patients, singleton WES was performed in 81 patients and trio-based WES in the remaining 23 families. Review by the clinical geneticist changed variant classification in 18 patients (17%) and variants were either promoted (n=10), demoted (n=5), or additional variants (n=3) were identified. For example, clinical review and discussion prompted reanalysis for variants in the FGD1 gene and a diagnosis of Aarskog-Scott syndrome (OMIM #305400) was identified. Overall the diagnostic yield was 40%, some of which involved recently discovered disease genes (e.g. PURA, DDX3X, WAC, PPP1CB, KMT2B). Recommendation in clinical management was made in 77% of the diagnosed patients after WES.

Conclusions: Comprehensive review of WES reports by the clinical geneticist can have substantial impact on the diagnostic yield of exome reports. Clinical geneticists have a unique advantage, as they have direct contact with the families, prior knowledge of the clinical background, and possess the skills in dysmorphic assessment and gestalt analysis which gives insights missed by the use of phenotypic keywords. We demonstrate that even when the clinical and exome teams are not co-located geographically, a good collaboration is still achievable by enhanced cross talk between institutions.

Acknowledgement: The study is supported by (i) SK Yee Medical Foundation and (ii) the Society for the Relief of Disabled Children.
genetic mutations identified by next generation sequencing in the ciprofloxacin-resistant nontyphoid Salmonella isolates in Taiwan

Shiuh-Bin Fang1,2,3, Wan-Hsuan Chou3, Ke-Chuan Wang4,5, Che-Mai Chang3, Lauderdale Tsai-Ling Yang5, Wei-Chiao Chang1
1Division of Pediatric Gastroenterology and Hepatology, Department of Pediatrics, Shuang Ho Hospital, Taipei Medical University, Taipei, Taiwan, 2Department of Pediatrics, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan, 4Master Program for Clinical Pharmacogenomics and Pharmacoproteomics, College of Pharmacy, Taipei Medical University, Taipei, Taiwan, 5National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, Zhunan, Taiwan

Background and Aims: The ciprofloxacin resistance rate in non-typhoidal Salmonella (NTS) has increased to 8% in non-specific serotypes of Salmonella. Our previous study using the next generation sequencing (NGS) identified 2 novel (parC g.1307delA and parE g.1031G>T) and 2 reported (gyrA g.248C>T and parC g.170C>G) genetic mutations in one NTS isolate from a pediatric patient in TMU-SHH. Thus, we conducted this study to investigate the incidences of these four mutational targets in the NTS clinical isolates from different areas in Taiwan.

Methods: A total of 39 ciprofloxacin-resistant NTS isolates were used in this study, including 34 NTS isolates from northern, middle, southern, and eastern Taiwan in the Taiwan Surveillance of Antibiotic Resistance (TSAR) from NHRI during 2010-2016 and 5 NTS isolates from TMU-SHH during 2012-2016, including the isolates with all 4 mutations as positive control. The 39 NTS isolates were cultured in LB broth at 225 rpm at 37°C for 18 hours. The bacterial genomic DNAs were purified for the mismatch amplification mutation assay (MAMA) PCR using the primers specific to the 4 genetic loci, and the amplified fragments were visualized using 1.3% agarose gel. Finally, the incidences of the individual 4 genetic mutations in the 39 isolates were obtained and expressed in percentage (%).

Results: We demonstrated that 11 among the 39 NTS isolates (28.2%) have at least one of the four genetic mutations. Single mutation was detected in 9 NTS isolates. Quadruple mutations were present in the other two NTS isolates. Quadruple mutations were confirmed in the NTS isolate as positive control. The known mutation gyrA g.248C>T occurred in 7 NTS isolates (17.9%), and the known mutation parC g.170C>G was found in 6 NTS isolates (15.4%). The novel mutation parE g.1031G>T was present in 3 NTS isolates (7.7 %), including the positive control, the other one coexistent with gyrA g.248C>T, and another one in single mutation (1/39, 2.6%). The deletional frameshift mutation parC g.1307delA was not identified in the additional 38 NTS isolates. gyrA g.248C>T was the most commonly seen but not the predominant genetic mutation. The novel genetic mutation parC g.1031G>T was found alone in one NTS isolate without coexistence of the other 3 genetic mutations related to ciprofloxacin resistance.

169
Blood cell type-specific Genome-Wide DNA methylation analysis of Chinese patients with early-onset Systemic Lupus Erythematosus identifies loss of DNA methylation in genes related to the type I interferon Pathway

KS Yeung1, T Mok2, S Choufani3, YL Lau1, R Weksberg2, BHY Chung1
1The University of Hong Kong, Hong Kong, Hong Kong, 2City University of Hong Kong, Hong Kong, 3Hospital for Sick Children Research Institute, Toronto, Canada

Background and Aims: Around 20% of Systemic Lupus Erythematosus (SLE) is diagnosed in children under 18. These children usually present with a severer disease than adult-onset patients. Since whole blood comprised of different immune cells, we aimed to identify the cell type-specific DNA methylation signatures of CD4+ T cells, CD8+ T cells, B cells, neutrophils and whole blood in individuals with SLE patients who presented before 18-years of age.

Methods: We compared the DNA methylation profiles of different blood cells for 16 Chinese SLE patients to that of 13 healthy controls using the Illumina HumanMethylationEPIC BeadChip. Data pre-processing was performed to remove cross-reactive probes, probes with SNPs at the target site, and probes from sex chromosomes. For each specific region, Wilcoxon rank-sum test was used for group comparisons, and false discovery rate was used for multiple testing corrections. Differentially methylated CpG sites were defined as CpG sites with an adjusted p-value <0.05 and a mean methylation change > 0.1.

Results: 775280 probes remained after data preprocessing and principal component analysis showed that samples clustered according to specific cell types rather than disease manifestation. Global changes of DNA methylation were not observed among different cell types. The number of differentially methylated CpG sites ranged from 46 to 169 in comparisons of different cell types, with more CpG sites showing hypomethylation than hypermethylation. Gene ontology analysis was performed for each cell type and revealed that in all the cell types examined, hypomethylated genes identified were overrepresented in the type I interferon pathway.

Conclusions: Our results suggest that the DNA methylation changes in different immune cells of SLE patients target the same biological pathway. As type I interferon has long been believed to be involved in the pathogenesis of SLE, our findings support the importance of an epigenetic mechanism in the dysregulation of type I interferon in SLE pathogenesis.

Acknowledgement: This work was supported by the General Research Fund (Ref: HKU 765513).
Conclusions: In this study, no single genetic mutation predominates in ciprofloxacin-resistant NTS isolates. For the first time, our NGS-identified novel genetic mutation paret g.1031G>T was detected in the ciprofloxacin-resistant NTS isolate without presence of the other genetic mutation. Further studies are warranted for validating the genetic epidemiology of all the genetic mutations related to ciprofloxacin resistance in NTS.

The development of a web-based tool generating graphical plots of functional domain with reported pathogenic variants, population variants and amino acid conservation as evidence for ACMG variant classification

Mullin Ho-Chung Yu, Brian Hon-Yin Chung

The University of Hong Kong, Hong Kong

Background and Aims: Despite American College of Medical Genetics and Genomics (ACMG) developed standards and guidance for the interpretation of sequence variants, there are lots of tedious and manual works to classify variants by using and interpreting typical types of variant evidence, e.g. population, computational and functional data. One of the classification rules is to locate whether the variants in a mutational hot spot and well-established functional domain. We aim to develop a publicly available tool to easily classify the variants by interpreting the graphical representations of mutation and functional data and facilitate easy clinical management by the graphical plots.

Methods: A web-based tool is to be developed by using HTML5 web technologies to link up with database of population data (gnomAD), protein sequence and functional information (UniProt), evolutionary conservation of amino/nucleic acid positions in a protein (ConSurf) and variant database (Clinvar). A series of graphical plots of functional domain with reported pathogenic variants, population variants and amino acid conservation for a region of a gene against the amino acid residue position will be generated based on the input of the gene and the variant position.

Results: Take an example of a variant p.Arg76 in SRY gene. After inputting SRY gene on the website, 3 graphical plots of SRY gene were generated and shown on the website. The first one is a plot of 204 residue sequence of SRY with a black horizontal line that HMG box shown by a box and above the line are shown positions of mutations of different syndrome represented by different symbols. The second one is shown with the ConSurf grade, ranging from 1 (minimum) to 9 (maximum), plotted by amino acid position. The third one is with the gnomAD missense variants plotted by position (x-axis) against allele frequency (y-axis). Based on the above information, it provides strong evidence to support variant, p.Arg76, as PM1.

Conclusion: The tool provides an easy and convenient way to generate strong evidence of a series of graphical plots for the classification and interpretation of the variants based on ACMG’s PM1 rule.

Acknowledgement: This work was supported by the Edward & Yolanda Wong Research Fund.

Genetic basis of chronic granulomatous disease in North India

Amit Rawat1, Madhubala Sharma2, Vignesh Pandiarajan2, Deepi Suri3, Anju Gupta3, Rakesh Pilania1, Jitendra Shandilya1, Shubham Goel1, Gurjit Kaur1, Ravinder Garg2, Kohsuke Imai1, Shigeaki Nonoyama2, Osamu Ohara4, Koon-Wing Chan5, Yu-Lung Lau6, Biman Saikia6, Ranjana Minz6, Surjit Singh2

1Pediatric Allergy and Immunology Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research Chandigarh, Chandigarh, India, 2Tokyo Medical and Dental University, Tokyo, Japan, 3Department of Pediatrics, National Defense Medical College, Saitama, Japan, 4Kazusa DNA Research Institute, Kisarazu, Chiba, Japan, 5Department of Pediatrics and Adolescent Medicine, Queen Mary Hospital, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong, 6Department of Immunopathology, Postgraduate Institute of Medical Education and Research Chandigarh, Chandigarh, India

Background and Aims: Chronic granulomatous disease (CGD) is a genetic defect in the phagocyte function resulting for mutations in genes encoding for different components of the NADPH oxidase system. Impairment of NADPH oxidase complex results in defective generation of superoxides in phagocytic cells and defective killing of intracellular pathogens. Mutations in five different genes namely CYBB, NCF1, CYBA, NCF2 and NCF2 encoding for gp91phox, p47phox, p22phox, p67phox and p40phox respectively are responsible for the clinical phenotype. X-linked recessive disease due to mutations in the CYBB gene is the commonest form of CGD reported from the USA, UK and Europe. However, autosomal recessive forms of CGD due to defects in NCF1, NCF2 and CYBA genes are more common in geographical locales with high rates of consanguinity such as the Middle East and North Africa. There are very few reports on the genetic basis of CGD from India. We report the genetic basis of 32 patients from our cohort of 50 patients with CGD.

Methods: We analyzed the molecular defects in our cohort of CGD patients, diagnosed and followed-up at the Pediatric Allergy and Immunology Unit, Advanced Pediatrics Centre, Postgraduate Institute of Medical Education and Research, Chandigarh. Fifty (50) cases of CGD were diagnosed over the past two decades. Diagnosis of CGD was made on the basis of nitroblue tetrazolium test, dihydrorhodamine test and NADPH oxidase component analysis by flow cytometry. Genetic mutation analysis was available for 32 patients. Mutational analysis was performed at our centre and centres in Japan and Hong Kong.

Results: Mutations in the CYBB gene were the commonest being detected in 17/32 patients (53%) in whom genetic analysis results were available. NCF1 gene mutations accounted for the largest proportion of autosomal recessive form of CGD, being present in 12/32 patients (37%). Mutations in the NCF2 gene were present in 3 patients. All patients with NCF1 gene mutations had a GT deletion
in Exon 2. Six of the 17 CYBB gene mutations were novel mutations. Prenatal diagnosis was performed in 6 families.

Conclusions: X-linked CGD with mutation in the CYBB gene was the commonest form of CGD (17 cases) in our cohort of 32 patients (53%) in whom genetic analysis results were available. However, AR CGD was also not uncommon present in 15 patients (47%). Novel mutations in the CYBB gene were also detected in our CGD cohort.

268
Application of whole exome sequencing in diagnosing movement disorders in Hong Kong

Jasmine LF Fung1, Mandy HY Tsang1, Gordon KC Leung2, Steven LC Pei1, Christopher CY Mak1, KS Yeung1, Mullin HC Yu1, Gary TK Mok2, Brian HY Chung1,2, CW Fung1,2

1Department of Paediatrics and Adolescent Medicine, The University of Hong Kong, Hong Kong, 2Duchess of Kent Children’s Hospital, Hong Kong

Background: Movement disorders (MD) are neurologic syndromes involving a variable combination of impaired voluntary movements, dysfunction of posture, abnormal voluntary movements and normal appearing movements at inappropriate or unintended times. It has been a challenge to make a molecular diagnosis for paediatric patients with MD because of their genetic and clinical heterogeneity. The aim of our study is to utilize whole-exome sequencing (WES) as an alternative or additional diagnostic tool for children with MD in Hong Kong.

Methods: This is an ongoing project with a target cohort of 100 patients. Paediatric patients up to 18-year-old with unexplained MD were recruited. They were either having active follow-up in clinics, or newly referred from other hospitals. WES and analysis were performed using in-house diagnostic pipeline in our department. First-tier screening was performed on a list of MD-associated genes, and second-tier analysis was open to the entire human exome. Validation of target mutations and segregation analysis were performed by Sanger sequencing.

Results: Out of the 15 patients recruited, we identified two pathogenic mutations in three patients (20%) (TGM6:p.L517W and ATP1A3:p.E944K); one patient with a likely pathogenic mutation (POLG:p.E944K); and one patient with a variant of uncertain clinical significance (KCND3:p.N639K). The patient with TGM6 mutation had a phenotype of hereditary spastic paraplegia (HSP) with distal amyotrophy and mild intellectual disability. The two patients with ATP1A3 mutation are siblings with CAPOS syndrome (Cerebellar ataxia, Areflexia, Pes cavus, Optic atrophy and Sensorineural hearing loss), and their mother with the same phenotype is being tested.

Discussion: In particular to TGM6 mutation, we had conflicting interpretation towards the previously reported TGM6:p.L517W. Despite the high allelic frequency in East-Asians(i.e. 0.0015), the mutation was revealed in multiple patients with suspected HSP, dystonia, spinocerebellar ataxia, or acute myeloid leukaemia, with a functional characterization supporting pathogenicity. We postulated that TGM6 is a pleiotropic gene causing multiple phenotypes. As there are asymptomatic individuals with TGM6 mutations (e.g. p.L517W), other genetic modifiers or environmental factors may contribute to the disease etiology.

Conclusions: The preliminary yield of WES in unexplained MD was 20%. Further analysis is on-going. However, due to the limitations in technology and current knowledge in genetics, careful judgement and interpretation on the pathogenicity of variants are necessary when performing WES in clinical settings.

Acknowledgements: We would like to thank The Society for the Relief of Disabled Children and The Edward and Yolanda Wong Fund for the support.

292
Mutations in PI3K-AKT-mTOR signaling pathway are the major cause of macrocephaly with developmental delay/autism

Winnie WY Tsao1, Kit-San Yeung1, Janice JK Ip1, Christopher CY Mak1, Gordon KC Leung2, Dingge Ying1, Steven LC Pei1, Wanling Yang1, Brian HY Chung1

1Department of Paediatrics & Adolescent Medicine, LKS Faculty of Medicine, University of Hong Kong, Hong Kong, 2Department of Radiology, Queen Mary Hospital, Hong Kong

Introduction: Macrocephaly is a common dysmorphic feature in children with developmental delay/autism. PTEN was the first gene identified in patients with developmental delay and macrocephaly. Since then, other genes in the PI3K-AKT-mTOR signaling pathway have also been reported in patients with macrocephaly and developmental delay/autism. In this study, we aim to characterize the mutation spectrum of patients with macrocephaly (head circumference ≥ +2 SD) and developmental delay/autism.

Methods: Whole-exome sequencing was performed for 21 patients with macrocephaly and developmental delay/autism, with the source of DNA either from blood, buccal mucosa or saliva. Germline mutations were validated by sanger sequencing, whereas somatic mutations were validated by droplet digital PCR.

Results: A total of 11 pathogenic mutations were identified in PTEN (n=5), PIK3CA (n=3), MTOR (n=1) and PPP2R5D (n=2) in ten patients, with one patient harboring biallelic PTEN mutations. Besides germline mutations, somatic mutations of PIK3CA were identified in two of the ten patients, which could be easily missed by testing on blood DNA. While nine mutations were de novo mutations, two mutations were inherited maternally but both of the parents did not have remarkable clinical history. MRI findings showed that polymicrogyria and periventricular white matter lesions were common in these patients.

Conclusion: Mutations in PI3K-AKT-mTOR signaling pathway are a major cause of macrocephaly with developmental delay/autism, which can be found in nearly half of the patients tested. Genetic testing is recommended for this group of patient because mutations in the PI3K pathway potentially increase the risk of cancer. Clinically it is hard to distinguish patients with germline mutations and somatic
mutations, therefore the use of buccal or saliva DNA is important to identify somatic mosaicsisms and to maximize diagnostic yield. We propose an umbrella term “mTOR pathway-related macrocephaly spectrum” to encompass patients with macrocephaly and developmental delay/autism who are associated with germline or somatic mutations of mTOR signaling pathway.

293

Comparing MEFV variants in Chinese and Moroccan patients with Familial Mediterranean fever

Chung-Yin Wong1, Koon-Wing Chan2, Barakat Abdelhamid3, Zineb Jouhadi4, Chun-Yin Chong5, Huawei Mao4, Pamela Pui-Wah Lee6, Yu-Lung Lau1,4

1Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong, 2Human Molecular Genetic Laboratory, Institut Pasteur du Maroc, Casablanca, Morocco, 3Pediatric Infectious Diseases Department, Ibn Rochd Children’s Hospital, Medical School University Hassan II, Casablanca, Morocco, 4Shenzhen Primary Immunodeficiency Diagnostic and Therapeutic Laboratory, The University of Hong Kong -Shenzhen Hospital, Shenzhen, China

Background: Familial Mediterranean fever (FMF) is defined as an autosomal recessive disease characterized by recurrent attacks of fever with serosal inflammation.

Aims: To compare the frequency and the spectrum of MEFV variations in Chinese and Moroccan patients clinically suspected of FMF.

Methods: Thirty-six males and 16 females who had symptoms of FMF were analyzed for their genomic sequences of all MEFV exons by PCR direct sequencing.

Results: MEFV variations associated with FMF were detected in 16 out of 23 Chinese patients. Thirteen out of 29 patients referred from Morocco were found to have MEFV variations.

E148Q and R202Q were the predominant variations in our Chinese and Moroccan patients respectively. E148Q was found in 8 Chinese patients (50%) and 2 Moroccan patients (15%) whereas R202Q was identified in 9 Moroccan patients (69%) and 2 Chinese patients (13%). Of the remaining 6 Chinese patients, 3 patients were carriers of the complex allele L110P-E148Q, 1 patient was a carrier of G304R and 1 patient each was a carrier of E148Q-R202Q or L110P-E148Q-I641F. Two novel variations were found in Moroccan patients, V620D and R133P which were unreported in HGMD professional and INFEVERS.

Conclusions: The identification of MEFV variations could facilitate FMF diagnosis. Genetic analysis revealed that the frequency of the variation was different across ethnic groups.

Acknowledgement: Hong Kong Society for the Relief of Disabled Children

785

ARHGAP18 is a novel gene under positive natural selection influences HbF levels in β-thalassemia

Yunyan He1, Jianming Luo1, Yang Chen2, Xiaoheng Zhou3, Shanjuan Yu1, Ling Jin3, Xuan Xiao4, Siyuan Jia5, Qiang Liu4

1Department of Paediatrics, The First Affiliated Hospital of Guangxi Medical University, Nanning, China, 2Guangxi Medical University, Nanning, China, 3Department of Paediatrics, the First Affiliated Hospital of Guangxi Technology University, Nanning, China, 4Department of Paediatrics Surgery, The First Affiliated Hospital of Guangxi Medical University, Nanning, China

Background and Aims: Foetal haemoglobin (HbF) plays a dominant role in ameliorating the morbidity and mortality of β-thalassemia. Better understand loci and genes involved HbF expression is beneficial for treatment for β-thalassemia major. However, many genes associated with HbF expression remain largely unknown.

Methods: In this study, we firstly explored large-scale data sets and examined the human genome for evidence of positive natural selection to screen out single nucleotide polymorphisms (SNPs). A genetic analysis of HbF levels was conducted in a Chinese cohort with β-thalassemia to confirm the result of bioinformatics assay. A total of 1,151 subjects with β-thalassemia were recruited.

Results: The results showed that the SNP rs11759328 in the ARHGAP18 gene was significantly associated with HbF levels (P=4.6×10-4). Secondly, determining that ARHGAP18 was highly expressed in the human K562 cell line, we used lentiviral-mediated small interfering RNA to knock down ARHGAP18 expression, then assessed cell proliferation and apoptosis using cell proliferation assays and flow cytometry, respectively. The downregulation of ARHGAP18 expression in K562 cells significantly increased the HBG1/2 expression and apoptosis, but proliferation was not significantly changed in vitro.

Conclusions: Our data suggest that the ARHGAP18 gene, which was located by the SNP rs11759328 with positive selection, plays a potential role in regulating HbF expression in β-thalassemia, may be a promising therapeutic target for β-thalassemia. Knockout studies of ARHGAP18 warrant further investigation into its aetiology in HbF.

Acknowledgement: This study was sponsored by the National Natural Science Foundation of China (No.81360093) and Guangxi Key Laboratory of Thalassemia Research (16-380-34). The authors would like to thank Professor Liang Rong (Department of Pediatrics-Neonatology, Baylor College of Medicine, Houston, Texas, USA) for helpful discussions regarding this manuscript.
Clinical and molecular studies in 203 Chinese patients with mitochondrial disorders

Dongxiao Li¹,², Yi Liu¹, Xiyuan Li¹, Ying Jin¹, Jinqing Song¹, Hezhi Fang³, Yao Zhang¹, Hui Dong¹, Yanling Yang¹

¹Peking University First Hospital, Beijing, China, ²Henan Children’s Hospital, Zhengzhou, China, ³Key Laboratory of Laboratory Medicine, Ministry of Education, Zhejiang Provincial Key Laboratory of Medical Genetics, College of Laboratory Medicine and Life Sciences, Wenzhou Medical University, Zhejiang, China

Background and Aims: Because of the complexity and heterogeneity of the phenotypes and genotypes, the diagnosis of mitochondrial disorders is difficult. We aimed to establish a comprehensive analysis method for the etiologic diagnosis and prenatal diagnosis of mitochondrial disorders.

Methods: 203 patients were enrolled in this study. PCR-RFLP and NGS were used to detect mtDNA and nDNA sequence. Pathogenic study was performed to confirm the pathogenicity of suspected mutations. Amniocytes mutation analysis was performed for families with definite gene diagnosis.

Results: Candidate pathogenic mutations were identified in 152 patients among 203 cases. The detection rate was 74.88%. Seventy-nine cases (51.97%) had mtDNA variations, while 73 cases (48.03%) had nDNA variations. The most common mtDNA mutation was m.3243A>G (44.30%). Ninety-two novel mutations in nDNA were identified. m.3243A>G is the most common mtDNA mutation. Two novel mtDNA mutations and 92 novel nDNA mutations were found, expanding mutation spectrum.

Conclusion: The m.3243A>G is the most common mtDNA mutation. Two novel mtDNA mutations and 92 novel nDNA mutations were found, expanding mutation spectrum. The pathogenicity of part NDUF53, AIFM1 and SERAC1 mutations was confirmed. Leigh or Leigh-like syndrome. Seventeen fetuses got precise prenatal diagnosis.

Search for congenital radioulnar synostosis causative gene and modeling in mouse

Xiaoling Jiang, Zhe Yuan, Yiqiang Li, Junpu Mei, Zhilin Xiao, Ting Tan, Huazhen Liu, Xiaoyun Lu, Hongwen Xu, Ya-ping Tang

Guangzhou Women and Children’s Medical Center, Guangzhou, China

Background and Aims: Congenital radio-ulnar synostosis (RUS, MIM:179300) is a rare disease characterized by congenital synostosis of the radius and ulna, which results in limited rotational movement of the forearm. The upper limb bud arises embryologically from the unsegmented...
body wall at 25-28 days, and the radius and ulna are initially connected and share a common perichondrium. Failure of segmentation during embryo development has been hypothesized as the cause of RUS. Further, an autosomal dominant inheritance pattern has been indicated based on RUS case report. However, the causative genes and underlying mechanisms of isolated RUS are still unknown. In this study, we performed whole genome sequencing (WGS) to search for candidate causative gene for RUS in a rare dizygotic-twin family, which comprises a girl with bilateral RUS, her normal twin-sister and healthy parents.

Methods: Genomic DNA were extracted and subjected WGS using HiSeq X10 (Illumina, San Diego, CA) sequencing system. Crispr/Cas9 technology was used to establish a novel knock-in mouse line harboring the exactly same mutation found in patient.

Results: WGS results revealed a de novo missense mutation in SLC04A1 gene, which locates adjacent to/in the protein trans-membrane region and may affects the transport of thyroid hormone (TH), rostaglandin and taurocholate. TH is well known for regulating development, growth and metabolism. SLC04A1 mutation in fetus may affect the transport of TH from maternal blood, or local cellular transportation of TH during embryogenesis, which in turn affects bone development and segmentation. As this hypothesis could only be firmly confirmed in an appropriate animal model, we are establishing a new knock-in model, which carries exactly the same patient-specific missense point mutation, to facilitate evaluation of the causative roles of the candidate SLC04A1 mutation in RUS.

Conclusions: We identified a novel SLC04A1 missense mutation in a rare RUS twin family case using WGS. To facilitate evaluation of the causative role of this candidate mutation in RUS, a new knock-in mouse model carrying this patient-specific mutation is under developing.

Identification and characterization of heart-specific enhancers in zebrafish genome

Feng Wang, Qiang Li, Yonghao Gui
Children’s hospital of Fudan University, Shanghai, China

Background and Aims: Enhancers are cis-acting DNA elements which are critical for precise patterns of gene expression during embryonic development. Indeed, one challenge toward understanding the function of genome is to identify the regulatory elements embedded in DNA sequences. Also, little information about how spatiotemporal patterns of gene expression driven by these elements is available. Here we apply a combined computational and experimental approach to discover heart-specific enhancers within zebrafish genome. After identification, we then uncover critical motifs within these enhancers from common features of transcription factor binding sequences. The aim of this research is to provide new insight into the gene regulatory network of heart development.

Methods: Comparative genomic analyses are effective and efficient tools to identify conserved non-coding elements (CNEs) which may act as potential candidates for enhancers. Based on literature and gene expression database, group of heart-specific/enriched genes were chosen as candidates for CNEs selection. Using website “ECRbrowser”, we screened CNEs between zebrafish genome and human genome. Then, a Tol2-based enhancer trap method was used to test enhancers in zebrafish. After identifying heart-specific enhancers, we later conducted de novo motif prediction algorithms to uncover top-ranked 6-nucleotide motifs that are significantly enriched in these enhancers. Finally, mutation motifs within selected heart-specific enhancers were carried out to determine whether these predicted motifs are critical for heart-specific enhancer activity.

Results: In this study, we chose a set of 83 CNEs near 32 heart-specific/enriched genes. Subsequently, we tested their ability to drive reporter gene GFP expression using a transient transgenic method. We found that 12% of tested CNEs exhibited heart-specific enhancer activity. Application of de novo motif prediction algorithms on a set of ten heart-specific enhancers revealed three top-ranked 6-nucleotide motifs that were significantly enriched in these enhancers. Experimental analyses of these motifs in zebrafish demonstrated that they are functionally critical for heart-specific enhancer activity.

Conclusions: Taking advantage of this combined computational and experimental method, we successfully discovered heart-specific enhancers within zebrafish genome. This efficient and practical approach can be adopted to other tissues of interests for enhancer trap screening. Moreover, characterization analyses and experimental validation revealed functional motifs that are important for gene-specific expression. Our results provide important resources for further analyses of regulatory network of heart development and function.

Identification and clinical Implications of novel MYO15A mutations in a non-consanguineous Chinese family

Tizhen Yan1,2, Ning Tang1,2, Zhetao Li1,2, Wugao Li1,2, Ren Cai1,2, Dingyuan Zeng1

1Department of Medical Genetics, Liuzhou Municipal Maternity and Child Healthcare Hospital, Liuzhou, China
2Key Laboratory of birth defects prevention and control, Liuzhou, China

Introduction: Autosomal recessive nonsyndromic hearing loss (ARNSHL) is a genetically heterogeneous sensorineural disorder, generally manifested with prelingual hearing loss and absence of other clinical manifestations. The aim of this study is to identify the pathogenic gene in a four-generation consanguineous Chinese family with ARNSHL.

Case Report: Two novel frame-shift mutations, c.5964+3G>A and c.7395+1G>A, in the myoxin Xva gene (MYO15A) was identified by exome sequencing and Sanger sequencing. The compound heterozygous MYO15A c.5964+3G>A and c.7395+1G>A variants co-segregated with the phenotypes in the ARNSHL family and was absent in one hundred normal controls. The variant was predicted to interfere with the formation of the Myoxin Xva-whirlin-Eps8 complex at the tip of stereocilia, which is indispensable for stereocilia elongation.
Learning Points: Our data suggest that the compound heterozygous MYO15A c.5964+3G>A and c.7395+1G>A variants might be the pathogenic mutation, and exome sequencing is a powerful molecular diagnostic strategy for ARNSHL, an extremely heterogeneous disorder. Our findings extend the mutation spectrum of the MYO15A gene and have important implications for genetic counseling for the family.

1867

The generation of embryonic stem cells with erythrocytic expression of marker genes

Guanheng Yang¹, Shaoqing Zhang², Qingfu Yi³, Yiwen Zhu¹, Yunhan Wang⁴, Yanan Chi⁵, Xiuli Gong¹, Xinying Gao¹, Haiyan Ma¹, Ji Ma³, Jingzhi Zhang¹, Fanyi Zeng¹,²

¹Shanghai Children’s Hospital, Shanghai, China, ²Shanghai Children’s Hospital, Shanghai Jiao Tong University, Shanghai, China, ³Institute of Medical Science, Shanghai Jiao Tong University, School of Medicine, Shanghai, China

Blood diseases, including sickle-cell anaemia and thalassemia that are characterized by aberrant versions of haemoglobin gene, are common in children. How do these diseases proceed, and how to treat these diseases are some of the most important questions to ask. The embryonic stem cells (ESCs) with specific marker genes (such as GFP) may be useful to study these issues. Herein, we aimed to establish the murine ES cell lines with erythrocytic expression of marker genes.

The GFP expression was driven by a human β-globin gene promoter, and the transgene was detected at generation F10 in metaphase chromosome with one integration site. Pluripotent tests of the ESCs were performed both in vivo and in vitro through studying genic expression at the mRNA level, and the formation of embryonic bodies and teratoma. Chimeric mice of HG ESCs were generated. Moreover, erythrocytes derived from HG ESCs had special erythrocytic expression of GFP. First of all, HG mice (A HS23-GFP transgenic mice line with erythroid-specific GFP expression) were produced by pronuclei microinjection. The GFP expression was driven by a human β-globin gene promoter, and the transgene was detected at generation F10 in metaphase chromosome with one integration site by FISH method. ESCs were derived using these HG mice blastocysts. Pluripotent tests of the ESCs were performed both in vivo and in vitro through studying genic expression at the mRNA level, and the formation of embryonic bodies and teratoma.

Chimeric mice of HG ESCs were generated. Pluripotent genotypes such as Sox2, Oct3/4 and Nanog were expressed. Embryo bodies were formed in vitro. Moreover, erythrocytes derived from HG ESCs had special GFP expression in the blood smear of the offspring of HG ESC chimera. HG ESCs also had the capacity of germline transmitted. Thus this dynamic cellular model system would be useful for the study of ESCs differentiation into hemopoietic stem cells, and specifically to evaluate ES cellular quality of differentiation into erythroid cells. This would also have implications of the safety and reliability of ESCs clinical applications.
pattern of protein expressions same as previous reports, related to leukemia. Of these, the decreased expression of ATPB was validated by western immunoblotting.

Conclusions: This study employed proteomic analysis to elucidate ATPB as a candidate biomarker of relapsed disease. Further validation study using an independent cohort is required to demonstrate clinical applicability of ATPB in the very high risk group of pediatric ALL.

Pediatric T-cell acute lymphoblastic leukemia (T-ALL); an integrated genetic and epigenetic analysis

Shunsuke Kimura1,2, Masafumi Seki3, Tomoko Kawai4, Kenichi Yoshida5, Tomoya Isobe6, Hiroo Ueno7, Hiromichi Suzuki8, Kentaro Ohki9, Toshikiho Imamura10, Nobutaka Kiyokawa11, Masao Kobayashi12, Katsuyoshi Koh13, Atsushi Manabe14, Akira Ohara15, Masashi Sanada16, Akira Oka17, Yasuhide Hayashi18, Satoru Miyano19, Kenichiro Hata11, Seishi Ogawa20, Junko Takita21

1Department of Pediatrics, The University of Tokyo, Tokyo, Japan, 2Department of Pediatrics, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan, 3Department of Maternal-Fetal Biology, National Center for Child Health and Development, Tokyo, Japan, 4Department of Pathology and Tumor Biology, Graduate School of Medicine, Kyoto, Japan, 5Department of Pediatric Hematology and Oncology Research, National Research Institute for Child Health and Development, Tokyo, Japan, 6Department of Pediatrics, Kyoto Prefectural University of Medicine, Graduate School of Medical Science, Kyoto, Japan, 7Department of Hematology and Oncology, Saitama Children’s Medical Center, Saitama, Japan, 8Department of Pediatrics, St. Luke’s International Hospital, Tokyo, Japan, 9Department of Pediatrics, Toho University, Tokyo, Japan, 10Clinical Research Center, National Hospital Organization Nagoya Medical Center, Nagoya, Japan, 11Gunma Children’s Medical Center, Maebashi, Japan, 12Human Genome Center Institute of Medical Science, The Genome Center of Tokyo, Tokyo, Japan

Background and Aims: Pediatric T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive hematologic malignancy accounting for 10% to 15% of newly diagnosed pediatric ALL cases. Although genetic basis of pediatric T-ALL has been well characterized by several reports including our recent research, no comprehensive study has yet explored the epigenetic profiles and their potential contribution to clinicopathological features of T-ALL.

Methods: To describe epigenetic landscape of T-ALL, we conducted methylation array analysis using illumina HumanMethylationEPIC array, whole transcriptome sequencing (WTS), and targeted-capture sequencing for 158 ALL-related genes in a cohort of 48 cases with T-ALL. Following analyses were performed using R (v3.3.0) and ChAMP package.

Results: After normalization, 3210 probes were selected to identify the most variable methylated probes, when a standard deviation of the beta-values across the samples was above 0.35. Unsupervised consensus clustering using selected 3210 probes clearly identified 4 distinct sample clusters. Combined analyses with expression and fusion data from WTS revealed that these 4 clusters were characterized by TAL1 fusions/high expression (M1 cluster; low methylation), high TLX1/TLX3 expression (M2 cluster; high methylation), PU.1 fusions (M3 cluster; intermediate methylation), and others (M4 cluster; intermediate methylation), respectively. PTEN and USP7 abnormalities were particularly enriched in M1 cluster and PHF6, DNMT2, and EZH2 mutations were frequently observed in M2 cluster, whereas all PU.1 fusions were clustered in M3. Differentially methylated probes showed that promoter regions of ALDH1A2 were significantly unmethylated in M1 cluster, which were consistent with high ALDH1A2 expression in M1 cluster. ALDH1A2 is one of the main downstream of TAL1, known as an enzyme that functions at the apex of the retinoic acid signaling pathway involved in cell proliferation and apoptosis. Furthermore, it should be noted that patients in M2 cluster showed excellent clinical outcome compared to other clusters (Log-Rank p = 0.03).

Conclusions: Based on the DNA methylation profiles, pediatric T-ALL is clustered into 4 distinct subtypes, which exhibited remarkable correlation with fusion gene status, gene expression patterns, genetic signatures, and clinical outcomes. Especially ALDH1A2 was significantly upregulated in M1 cluster, suggesting that activation of retinoic acid signaling pathway has a potential role in the pathogenesis of TAL1 related T-ALL. Although our cohort in the current study is very limited, our results suggested that the biological phenotype of T-ALL is mediated by both genetic and epigenetic regulations. Therefore, explorations for aberrant DNA methylation along with genetic alterations might be helpful for development a new therapeutic strategy for T-ALL.

Association of factor VIII and factor IX mutations, HLA class II, tumor necrosis factor-α and interleukin-10 on inhibitor development among Thai haemophilia A and B patients

Ampaiwan Chuanumsrit2, Werasak Sasanakul1, Nongnuch Sirachainan3, Praguywan Kadegasem4, Pakawan Wongwerawattanakoon5, Lalita Mahaklan1, Oytip Nathalang6

1Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, 2Division of Pediatric Nursing, Nursing Department, Faculty of Medicine Ramathibodi Hospital, Bangkok, Thailand, 3Graduate Program, Faculty of Allied Health Sciences, Thammasat University, Pathumthani, Thailand

Objectives: To investigate the association of factor VIII and IX mutations, HLA-DRB1, TNF-α and IL-10 influencing the
risk of inhibitor development among Thai patients with hemophilia A and B.

**Methods:** A total of 100 patients with hemophilia A (severe 84, moderate 16 cases) and 36 with hemophilia B with a mean age of 14.4 years were enrolled. All patients received on-demand treatment for episodic bleeding and home treatment for early bleeding. Plasma derived products of cryoprecipitate, cryoprecipitate-removed plasma, FFP, fresh dried plasma, heat-treated lyophilized cryoprecipitate and factor concentrate were given exclusively.

**Results:** The occurrence of high inhibitor among patients with severe hemophilia A was 29.7% (25/84). Factor VIII mutations were identified in 97% (97/100) including intron 22 inversion (n=53), large deletion (n=5), nonsense (n=23) and missense mutations (n=16). Eleven were novel. The risk of high inhibitor among patients with severe degree was found in intron 22 inversion, 34.7% (17/79); large deletion, 40% (2/5) and nonsense mutation, 25% (5/20) similar to other studies. However, neither of patients with missense mutation developed high inhibitor. Factor IX mutations were identified in all 36 studied patients including missense (n=24), nonsense (n=7), splicing site (n=3) and promoter (n=2). Seven were novel. Unfortunately, inhibitor was found in one patient with severe hemophilia B whose mutation was a point mutation at exon 2: c.223C>T, p.R75X. No significant difference among frequencies of HLA-DBR1*15, TNF-α-308A and IL-10-1082G alleles in hemophiliacs with and without inhibitor, was found.

**Conclusion:** Thai patients with severe hemophilia A receiving exclusively plasma-derived products of FFP, cryoprecipitate, and small amount of factor concentrates on episodic treatment plus home treatment for early bleeding episodes, possessed a 29.4% chance of high inhibitor. Factor VIII and factor IX mutations showed a significant contribution for inhibitor development. The HLA-DRB1*15, TNF-α-308A and at the IL-10-1082G were in hemophiliacs with and without inhibitor, was found.

**Results:** In total, 37 patients with hemophilia A (severe 33, moderate 4) were enrolled in the study. Altogether, 32 patients completed the study. Their mean (SD) age was 20.4 (6.9) years old. The mean (SD) incremental FVIII:C after receiving one unit of factor VIII concentrate per BW (kg) was 2.3% (0.5). The pharmacokinetics analysis revealed the half-life of F VIII:C at 12.7 hours. The efficacy of bleeding control among 42 episodes found in 18 patients was designated as excellent (n=1), good (n=39) and moderate (n=2). All patients required one dose of factor VIII concentrate at a mean dose (SD) of 10.9 (9.9) units/kg except 2 patients with moderate response requiring 2 and 3 doses, respectively. Neither of the patients required hospitalization. Adverse reactions of mild tightness of breath (n=1) and low grade fever (n=3) were found in 2 patients which were unrelated to the administered factor concentrate. No seroconversion related to HIV, hepatitis A, B and C viruses was found after a 3-month period.

**Conclusion:** Factor VIII concentrate produced by the National Blood Center, Thai Red Cross Society showed safety and efficacy in bleeding control among Thai hemophilia A patients with severe and moderate degrees.

**Integrated genetic and epigenetic analysis of neuroblastoma utilizing the open dataset**

Kentarō Watanabe, Shunsuke Kimura, Masafumi Seki, Tomoya Isobe, Tomoko Kawai, Mitsuteru Hiwatari, Kenichi Yoshida, Keisuke Kataoka, Yusuke Sato, Yoichi Fujii, Yuichi Shiraishi, Kenichi Chiba, Hiroko Tanaka, Akira Oka, Katsuyoshi Koh, Kenichiro Hata, Satoru Miyano, Seishi Ogawa, Junko Takita

**Objectives:** To study the safety and efficacy of factor VIII concentrate produced by the National Blood Center, Thai Red Cross Society among Thai patients with hemophilia A.

**Methods:** Previously-treated patients with hemophilia A for more than 150 days were enrolled in the study. After 5-day wash-out period, they received 500 units of locally-produced factor VIII concentrate. The vital signs and clinical manifestations were closely monitored before and at 1, 2 and 4 hours. Factor VIII clotting activity (FVIII:C) was determined before and 30 minutes after factor VIII concentrate administration. Then, 500 units of factor VIII concentrate twice weekly were prescribed as a low dose prophylaxis regimen for 3 months. In cases of any bleeding episodes, the patients received only locally-produced factor VIII concentrate. The infectious markers of HIV, hepatitis A, B and C viruses were screened before and after 3 months of factor VIII administration. Also, the pharmacokinetics of FVIII:C were studied among 10 patients.

**Results:** In total, 37 patients with hemophilia A (severe 33, moderate 4) were enrolled in the study. Altogether, 32 patients completed the study. Their mean (SD) age was 20.4 (6.9) years old. The mean (SD) incremental FVIII:C after receiving one unit of factor VIII concentrate per BW (kg) was 2.3% (0.5). The pharmacokinetics analysis revealed the half-life of F VIII:C at 12.7 hours. The efficacy of bleeding control among 42 episodes found in 18 patients was designated as excellent (n=1), good (n=39) and moderate (n=2). All patients required one dose of factor VIII concentrate at a mean dose (SD) of 10.9 (9.9) units/kg except 2 patients with moderate response requiring 2 and 3 doses, respectively. Neither of the patients required hospitalization. Adverse reactions of mild tightness of breath (n=1) and low grade fever (n=3) were found in 2 patients which were unrelated to the administered factor concentrate. No seroconversion related to HIV, hepatitis A, B and C viruses was found after a 3-month period.

**Conclusion:** Factor VIII concentrate produced by the National Blood Center, Thai Red Cross Society showed safety and efficacy in bleeding control among Thai hemophilia A patients with severe and moderate degrees.
often associated with a poor prognosis. Besides few known abnormalities such as ALK mutation and MYCN amplification, molecular features of NBL are still poorly understood. Many genetic/epigenetic datasets are currently available as open data, which are of use in the research of relatively rare pediatric tumors. We re-analyzed an open data, focusing on high-risk NBL to disclose whole picture of genetic/epigenetic basis of high-risk NBL.

Methods: We analyzed 94 samples with high-risk NBL from the open data of “TARGET NBL” from National Cancer Institute, which contains all the three-platform data: whole exome sequencing, RNA sequencing, and DNA methylation array analysis.

Results: Consensus clustering based on DNA methylation status revealed 5 distinct clusters, which were independent of the pathological findings. Instead, these clusters exhibited remarkable correlation with genetic lesions. Cluster 1 had lower frequency of copy number alterations and gene abnormalities compared to the other clusters. Cluster 2 was characterized by 11q deletion combined with 3p and 4p deletions. ATRX alterations were also enriched in this cluster. 11q deletion was relatively frequent in both Clusters 3 and 5, but 3p or 4p deletion was less common in these clusters. Clusters 3 and 5 were also characterized by hyperdiploid with frequency of around 80%. Among the 12 cases with ALK mutations, 5 cases were grouped into Cluster 3 and 4 cases with MYCN amplification were included in Cluster 4. Cluster 4 was strongly linked to MYCN amplification and 1p deletions without 11q and 4p deletions. Furthermore, consensus clustering of 51 samples with 11q deletion based on DNA methylation status revealed another 2 distinct clusters. Cluster A was strongly linked to 4p deletion. Event-free-survival of Cluster B was significantly worse than that of Cluster A (p = 0.00025).

Conclusions: further validation of these insights in additional cohort would be necessary, our results highlight the close relationship with DNA methylation and genetic alterations in high-risk NBL and revealed genetic/epigenetic catalogue of this disease.

181
Clinical features and treatment of oncologic emergencies

Yuichi Mitani, Mayumi Hangai, Moe Hidaka, Masafumi Seki, Mitsuteru Hiwatari, Akira Oka, Junko Takita
Department of Pediatrics, The University of Tokyo, Tokyo, Japan

Background and Aims: The survival rates of pediatric malignancies continue to improve over the past several decades. This dramatic increase in survival has been accomplished due to new therapeutic strategies and enhanced supportive care. On the other hand, the pediatric oncology patients may present with variety of life-threatening situations resulted from structural or functional compromise of the critical organs, leading to early cancer-related death. Thus, there is a need to better understand oncology emergency in pediatric cancers in order to optimize treatment strategy and further improve the survival rate. Here we report oncologic emergency cases for 8 years in our institute.

Methods: We retrospectively reviewed pediatric oncology cases in our institution from January 2009 to March 2017 and extracted by chief complaints or symptoms at the presentation. We defined eligible symptoms as airway obstruction, respiratory failure, shock and disturbance of consciousness. We investigated age, time to diagnosis from the first physician contacted, the primary lesions, examinations, treatments and outcomes.

[Results] In total 230 pediatric oncology cases were assessed, and 8 cases were identified as oncology emergency cases (3 neuroblastoma cases, 1 rhabdomyosarcoma case, 1 unclassifiable sarcoma case, 1 T-LBL/ALL case, 1 aplastic anemia case and 1 anaplastic ependymoma case). The median age at the diagnosis was 3.5 years (2 to 12 years). The median time to diagnosis was 0.75 months (7 days to 2 months), and 6 patients admitted to pediatric intensive care unit. Emergency surgery was needed in 3 cases, and emergency endotracheal intubation was performed in a case. All patients subsequently received chemotherapy. Currently, 5 cases are alive and 3 cases died, however there was no dying case in the acute phase.

Conclusion: For most pediatric cancers, prognosis generally depends on the biology of the tumor, however, time to diagnosis relates to outcome in pediatric oncologic emergency cases. With prompt recognition and treatment initiation in the emergency department involved by pediatric oncologists, surgeons, radiation oncologists and other medical specialists, lives can be saved and quality of life maintained.

197
Transcriptomic and epigenetic analyses of hepatoblastoma identify subgroups with different clinical and biological features

Masahiro Sekiguchi¹, Masafumi Seki¹, Tomoko Kawai², Tomoya Isobe¹, Misa Yoshida¹, Kenichi Yoshida³, Keisuke Kataoka³, Yusuke Sato², Yoichi Fujii¹, Noriko Hoshino¹, Yuichi Shiraiishi², Kenichi Chiba², Hiroko Tanaka², Ryota Souzaki³, Kentaro Watanabe¹, Yuki Arakawa⁷, Katsuyoshi Koh³, Yasuhide Hayashi³, Tomoaki Taguchi¹, Masashi Sanada³, Yukichi Tanaka¹, Satoru Miyano², Kenichiro Hata³, Seishi Ogawa³, Junko Takita¹

¹Department of Pediatrics, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, 2Department of Maternal-Fetal Biology, National Research Institute for Child Health and Development, Tokyo, Japan, 3Department of Pathology and Tumor Biology, School of Medicine, Kyoto University, Kyoto, Japan, 4Department of Pediatric Surgery, The University of Tokyo Hospital, Tokyo, Japan, 5Laboratory of DNA Information Analysis, Human Genome Center, Institute of Medical Science, The University of Tokyo, Tokyo, Japan, 6Department of Pediatric Surgery, Faculty of Medical Sciences, Kyushu University, Fukuoka, Japan, 7Department of Hematology/Oncology, Saitama Children’s Medical Center, Saitama, Japan, 8Japanese Red Cross Gunma Blood Center,
Background and Aims: Hepatoblastoma (HBL) is the most common pediatric liver tumor. Despite intensive multimodal therapy, the prognosis of high-risk HBL remains poor, and this underscores the importance of understanding HBL pathogenesis and developing novel therapeutic modalities. However, as the mutation rate in HBL is relatively low and molecular targets except for Wnt/beta-catenin pathway have not been established, our understanding of the molecular basis of HBL is still limited.

Methods: To obtain a comprehensive set of the molecular lesions in HBL, we performed methylation array analysis, single nucleotide polymorphism (SNP) array-based copy number (CN) analysis and RNA sequencing (RNA-seq) on 31 diagnostic biopsy samples of HBL.

Results: SNP array analysis showed frequent whole-arm CN gains in multiple chromosomes, especially in 1q, 2, 5, 6, 7, 8, 17q and 20. Uniparental disomy/trisomy (UPD/UPT) of chromosome 11p was observed in 6 cases (19%). Gene expression data obtained from RNA-seq showed upregulation of Wnt signaling pathway in HBL. Consensus clustering based on methylation data indicated the presence of 3 distinct clusters. Cluster 1 exhibited low expression of NQO1 (encoding a cytoplasmic reductase associated with detoxification pathways) with the promoter hypermethylation, and less frequent CN alterations. Patients with lower serum AFP levels at diagnosis were enriched in this cluster. Being consistent with low expression of NQO1, known as a poor prognostic factor in several kinds of tumors, patients in cluster 3 showed better survival rate, although not reaching statistical significance (log-rank test, p=0.07). In contrast, cluster 2 had 1q/2q gains. Cluster 3 was characterized by high hypomethylation. In addition, all but one case in cluster 2 had 1q/2q gains. Cluster 3 was characterized by high expression of GSTP1 (encoding a glutathione S-transferase, known as a poor prognostic factor) with the promoter hypomethylation and marked by low age at diagnosis. Intriguingly, cluster 3 included most of the cases with UPD/UPT of chromosome 11p.

Conclusions: Our integrated genome-wide study of HBL identified methylation subgroups well correlated with biological and clinical features. It may be useful for clinical risk stratification and searching for new molecular targets.
it an attractive adjuvant for transplantation and regenerative medicine applications. We aim to generate iPSCs from MSCs by genetically transducing a panel of stem cells transcription factors. We also would investigate whether the immunomodulatory effects of the reprogrammed MSCs can be retained.

Methods: MSCs isolated from human bone marrow were reprogrammed by Sendai virus-based delivery of Oct3/4, Sox2, Klf4, and c-Myc genes. Colonies of reprogrammed cells were expanded and selected following with characterizations of a panel of stem cells and neural cells markers including SSEA4, TRA1-60, Sox2, NANONG, OCT3/4, SOX1, PAX6, NESTIN and TU11 by using immuno-staining, qPCR and flow cytometry. The pluripotency was examined by embryoid body (EB) formation in vitro and teratoma formation in vivo. The immunomodulatory effect was evaluated by co-culture experiments of iPSCs derived-neural progenitor cells with human lymphocytes in vitro. CD3+ T cells stained with CFSE were selected and quantified after activation with specific surface markers CD69 or CD25.

Results and Conclusion: iPSCs were successfully generated from human MSCs. Human MSCs-derived iPSCs (hMSCS-iPSCs) expressed the same transcriptional factors and surface markers as those derived from human embryonic stem (ES) cells. hMSCs-iPSCS also formed embryoid bodies and teratoma, which showed the pluripotency of the cells. Neural progenitor cells derived from the hMSCS-iPSCS highly expressed PAX6, which is a key regulatory gene in brain development. In the co-culture system with lymphocytes, these neural progenitor cells showed lower CD3+ T cells activation and proliferation compared to those derived from ES cells. This may suggest an advantage of iPSCs with MSC origin. Nevertheless, it is necessary and essential to have further research on the underlying mechanisms and potential clinical applications of hMSCS-iPSCs.

Results: We found significant differences in plasma concentrations of some cytokines between the dust mite-induced asthma subjects and the healthy controls. The transcript levels of the SYK and PI3K genes were higher, while those of EGFR were lower in the former group. A down-expression of miRNA-27b-3p in the former group was found by microarray analysis. This was confirmed by qRT-PCR that found the miRNA-27b-3p transcripts that regulated the expression of SYK and EGFR were also significantly decreased (p<0.01) in the same group. This correlated with the finding that the transcripts of SYK and its downstream PI3K were decreased in miRNA-27b-3p transfected HBE, but were increased in HBE transfected with the inhibitor.

Conclusions: Our results indicate that the differential expression of the miRNAs in dust mite-induced pediatric asthma may regulate their target gene SYK and may have an impact on the PI3K-AKT pathway associated with the production of cytokines, leading to an asthma attack. These findings should add new insight into the pathogenesis of pediatric asthma.

386

SYK down-regulated by microRNA 27b-3p impacts on PI3K-AKT pathway in pediatric asthma induced by dust mites

Xiaoyan Dong1, Yudan Fang2, Qin Cai2, Min Lu1, Quan Lu1, Nanbert Zhong2

1Shanghai Children’s Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, 2Shanghai Institute of Medical Genetics, Shanghai Children’s Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

Background and Aim: The PI3K-AKT pathway is known to regulate cytokines in dust mite-induced pediatric asthma. However, the underlying molecular steps involved are not clear. In order to clarify further the molecular steps, this study investigated the expression of certain genes and the involvement of miRNAs in the PI3K-AKT pathway, which might affect the resultant cytokine-secretion.

Method: In-vivo and in-vitro ELISA, qRT-PCR and microarrays analyses were used in this study.

426

Novel mutations in patients with hereditary red blood cell membrane disorders using next-generation sequencing

Yunyan He1, Siyuan Jia2, Roma Kajal Dewan2, Ning Liao2

1Department of Paediatrics, The First Affiliated Hospital of Guangxi Medical University, Nanning, China, 2Guangxi Medical University, Nanning, China

Background and Aims: To identify the diagnosis and investigate genotype-phenotype relation of intractable hereditary red blood cell (RBC) membrane cases.

Methods: We have utilized next-generation sequencing (NGS) to provide a high-throughput, highly sensitive assay. Three unrelated families including 15 individuals were analyzed with a panel interrogating 600 genes of hematopathy disorders. Where possible, inheritance patterns of pathogenic mutations were determined by sequencing of other relatives.

Results: We found 2 novel mutations in ANK1 (Y216X and E142X) responsible for hereditary spherocytosis (HS), which were stop gain single nucleotide variants (SNV). Furthermore, novel SPTA1 mutation (H54P) has been identified which was a nonsynonymous SNV and associated with hereditary elliptocytosis (HE). In addition, patients who coexist with erythropoiesis gene mutations, showed a more severe disease phenotype.

Conclusions: NGS panel provides a fast and accurate method at a molecular diagnosis in patients with intractable hereditary RBC membrane disorders. An integrated approach of medical history, clinical and molecular test, and pedigree analysis, is beneficial to these patients and families.

Acknowledgement: This study was sponsored by the National Natural Science Foundation of China (No.81360093) and Guangxi Key Laboratory of Thalassemia Research (16-380-34). We would like to thank the staff in the First
The study of METTL3 and METTL14 expression in childhood ETV6/RUNX1-positive acute lymphoblastic leukemia

Congcong Sun1, Lixian Chang2, Shuai Zhu3, Chao Liu1, Jingliao Zhang1, Yang Lan1, Xiaoyan Chen1, Li Zhang1, Fang Liu1, Yumei Chen1, Xiaofan Zhu1

1Center for Pediatric Blood Disease, State Key Laboratory of Experimental Hematology, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences, and Peking Union Medical College, Tianjin, China, 2Center for Pediatric Blood Disease, State Key Laboratory of Experimental Hematology, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences, and Peking Union Medical College, Tianjin, China

Background and Aims: This study was aimed to explore the METTL3 and METTL14 expression in children with ETV6/ RUNX1 (E/R)-positive acute lymphoblastic leukemia (ALL) and investigate the relation between the METTL3 and METTL14 expression with clinical features.

Methods: This study included 37 newly diagnosed E/R-positive ALL children and 6 controls in Institute of Hematology and Blood Disease Hospital. The CD10+CD19+ cells were sorted by flow cytometry (FCM) and mRNA was extracted from these cells. Real-time fluorescent quantitative PCR was used to detect the expression level of METTL3 and METTL14.

Results: Among the 37 cases, 51.35% (n=19) were boys and 48.65% (n=18) were girls and the median age was 4.72 (1.72-11.99) years. Among the 6 controls, 50% (n=3) were boys and 50% (n=3) were girls and the median age was 5.24 (1.53-13.17) years. The expression level of METTL3 and METTL14 in E/R-positive ALL patients were lower than in controls (p<0.05). Although the difference of METTL3 and METTL14 expression level between the relapse patients with non-relapse patients did not have statistical significant (p=0.171, p=0.150), respectively, the two gene expression levels in relapse patients were lower than in non-relapse patients. At last, the METTL3 and METTL14 expression were not correlated with blast percentage, white blood cell count and the level of lactate dehydrogenase (LDH).

Conclusions: The expression level of METTL3 and METTL14 were much lower in E/R-positive ALL patients than in controls and much lower in relapse patients than in non-relapse patients. Thus, METTL3 and METTL14 may play an important role in the pathogenesis and relapse mechanism of pediatric E/R-positive ALL patients.

Development and application of a rapid multiplex molecular detection method of children leukemia fusion genes

Qian Chen, Zheng Hu, Yongjun Fang, Meiyun Kang

Children’s Hospital of Nanjing Medical University, Nanjing, China

Background and Aims: Fusion gene detecting is widely used in the diagnosis and treatment of leukemia. This study develops a rapid detecting method of eight common fusion genes in leukemia of children.

Methods: The approach need only one step RT-PCR mediated by universal primers after obtained total RNA from bone marrow specimens, then acquired the size of the amplified fragment after analyzed by capillary electrophoresis assay.
**Results:** A total of 122 patients with positive leukemia fusion genes were examined by this technique, 121 cases were detected successfully. Respectively, 21 cases were detected with CBRB-MYH11 fusion gene, 13 cases were detected with SIL-TAL1 fusion gene, 16 cases were detected with TEL-AML1 fusion gene, 16 cases were detected with E2A-PBX1 fusion gene, 15 cases were detected with PML-RARA fusion gene, 14 cases were detected with AML1-ETO fusion gene, 13 cases were detected with MLL-AF4 fusion gene, except for 1 case was not detected. This method proves to be with high accuracy and detection rate.

**Conclusion:** Therefore, one step multiple RT-PCR combining capillary electrophoresis analysis system can be used as an important tool for the clinical diagnosis, treatment and prognosis of pediatric leukemia.

**1335**

**Genetic variations of GWAS-identified genes and neuroblastoma susceptibility in Chinese children**

Jing He, Yan Zou, Ruizong Zhang, Huimin Xia  
Department of Pediatric Surgery, Guangzhou Institute of Pediatrics, Guangzhou Women and Children’s Medical Center, Guangzhou, China

**Background and Aims:** Neuroblastoma is one of the most commonly diagnosed solid cancers of the early childhood, in the development of which genetic factors may play an important role. Previous genome-wide association studies (GWAS) have identified nine genes associated with neuroblastoma susceptibility for Caucasians. With the purpose to find whether genetic variations in these genes are also associated with neuroblastoma susceptibility for Southern Chinese children, we genotyped 25 polymorphisms within these genes by Taqman method in 256 cases and 531 controls.

**Methods:** Odds ratios (ORs) and 95% confidence intervals (CIs) were used to evaluate the strength of the associations. Furthermore, we calculated the area under the receiver-operating characteristic curves (AUC) to assess which gene/genes may be better in the predictive neuroblastoma risk.

**Results:** We confirmed that CASC15 rs6939340 A>G, rs4712653 T>C, rs9295536 C>A, LIN28B rs221634 A>T, and LMO1 rs110419 A>G were associated with significantly altered neuroblastoma susceptibility. We also confirmed that rs6939340 A>G (G vs. A: OR=1.30, 95% CI=1.13-1.50) and rs110419 G>A (A vs. G: OR=1.37, 95% CI=1.19-1.58) were associated with an increased neuroblastoma risk for all subjects. We also found that the combination of CASC15, LIN28B, and LMO1 may be used to predict neuroblastoma risk (AUC=0.63, 95% CI=0.59-0.67).

**Conclusions:** Overall, we verified that five GWAS-identified polymorphisms were associated with neuroblastoma susceptibility in a Southern Chinese population, which needs further validation in larger sample size studies.

**1374**

**Novel GD2 aptamer selectively delivers cytotoxic agent to neuroblastoma tumor cells in vitro**

Liyu Zhang, Ying Yang, Haibin Wu, Yanmin Zhang  
Xi’an Children’s Hospital, Xi’an, China

**Background and Aims:** Chemotherapy is a major treatment for late stage Neuroblastoma (NB), but its efficacy is often limited by the adverse effects of cytotoxic agents. There is an urgent need to develop novel targeting therapy for NB. Aptamers are single-strand oligonucleotides that can bind to target molecules with high affinity and specificity because of its specific spatial structure. Aptamers possess distinctive advantages as targeting ligand: high affinity for binding to most molecules, limited synthesis cost, low-immunogenicity, and small size that allows it to penetrate solid tumors. Due to these advantages, aptamers have been employed as novel targeting ligands in tumor targeted therapy. Ganglioside GD2 exits in membrane of NB tumor cell is a promising target for targeted therapy, so far, however, GD2 aptamer has not been reported in literature. Since here in this project, we plan to develop a novel functional GD2 aptamer for NB targeted therapy.

**Methods:** GD2 aptamer was selected by SELEX technology from a random DNA library in vitro. This DNA library was 90-base in length. After each SELEX round, the flow cytometry was carried out to assess the enrichment of clones capable of targeting GD2 molecule. The binding specificities and affinities of GD2 aptamer were evaluated by flow cytometry. To detect whether GD2 aptamer could decrease the adverse effects of cytotoxic agents, an aptamer-doxorubicin complex (Apt-Dox) was formulated by intercalating doxorubicin into the DNA structure of GD2 aptamer. GD2+ NB cell line IMR32 and GD2- cell line EL4 were either incubated with Apt-Dox, free Dox, and PBS. Then the cell viabilities were assessed by MTS test.

**Results:** After the 9th SELEX round, the abundance of enrichment was the furthest. We tested 102 clones and found a clone showed relatively strong binding specificity to GD2, whereas had low binding to BSA. This clone was termed GGDL1. Further, the binding affinity of GGDL1 to GD2 was 56.98nM. The cell viability of GD2+ cell line IMR32 and GD2- cell line EL4 were either incubated with Apt-Dox, free Dox, and PBS. Then the cell viabilities were assessed by MTS test.

**Conclusions:** GD2 aptamer may have potential utility as a targeting ligand for selective delivery of cytotoxic agent to GD2-expressing NB tumor cells.

**1558**

**High frequency of NUDT15 variant among Chinese paediatric patients with acute lymphoblastic leukaemia in Hong Kong**

Wing-Kwan Leung¹, Felix Chi-Kin Wong², Yat-Ping Yuen³, Grace Kee-See Lam³, Vincent Lee¹, Chi-Kong Li³

Since here in this project, we plan to develop a novel functional GD2 aptamer for NB targeted therapy.

**Methods:** GD2 aptamer was selected by SELEX technology from a random DNA library in vitro. This DNA library was 90-base in length. After each SELEX round, the flow cytometry was carried out to assess the enrichment of clones capable of targeting GD2 molecule. The binding specificities and affinities of GD2 aptamer were evaluated by flow cytometry. To detect whether GD2 aptamer could decrease the adverse effects of cytotoxic agents, an aptamer-doxorubicin complex (Apt-Dox) was formulated by intercalating doxorubicin into the DNA structure of GD2 aptamer. GD2+ NB cell line IMR32 and GD2- cell line EL4 were either incubated with Apt-Dox, free Dox, and PBS. Then the cell viabilities were assessed by MTS test.

**Results:** After the 9th SELEX round, the abundance of enrichment was the furthest. We tested 102 clones and found a clone showed relatively strong binding specificity to GD2, whereas had low binding to BSA. This clone was termed GGDL1. Further, the binding affinity of GGDL1 to GD2 was 56.98nM. The cell viability of GD2+ cell line IMR32 treated with Apt-Dox was 30.8%, with free Dox was 28.9%. However, the cell viability of GD2- cell line EL4 treated with Apt-Dox was 87.9%, with free Dox was 36.7% (p<0.01).
Background: Thiopurine is an essential treatment of childhood acute lymphoblastic leukaemia (ALL). Thiopurine S-methyltransferase (TPMT) mutation is a well-known mutation affecting metabolism of thiopurine. Recently, a variant in NUDT15 gene [p.Arg139Cys(R139C)] is identified in Asian population with increased risk of thiopurine-induced leucopenia. We started screening for TPMT and NUDT15 mutation in Chinese ALL children to determine their prevalence.

Method: All new cases of paediatric ALL were screened for TPMT and NUDT15 variant in a tertiary referral centre in Hong Kong. Sanger sequencing of TPMT exons 5, 7 and 10 and NUDT15 exons 1 to 3 were performed.

Results: From August 2015 to June 2017, 45 Chinese children were screened with 28 male and 17 females. Among them, 42 subjects were treated with Chinese Children Cancer Group (CCCCG) ALL 2015 study and 3 infants were treated with inter-fant-ALL 2006 protocol. Thirteen subjects (28.8%) were found to carry NUDT15 variant, 11 being heterozygous (24.4%) and 2 (4.4%) were homozygous. The commonest variant was NUDT15 R139C (Haplotype *3) detected in 9 subjects. 4 had p.Gly17_Val18dup and p.Arg139Cys variant (Haplotype *2). 2 subjects (4.4%) were heterozygous for TPMT variant, 1 being double heterozygous with NUDT15 R139C variant. Among 42 subjects treated with CCCG ALL 2015 protocol, 33 had completed 8 weeks of consolidation therapy with 6-mercaptopurine (6MP) and methotrexate. 6MP starting dose is reduced in subjects with known TPMT or NUDT15 variants. 6MP would be withheld during severe leucopenia (WCC <1.5 or ANC <0.5). In subjects with wild-type NUDT15 and TMPT allele (n=22), median dose of 6MP given in consolidation therapy was 1380mg/m2 (range 987 mg/m2 to 1695 mg/m2) and it was 695 mg/m2 (range 254 mg/m2 to 846 mg/m2) in subjects with heterozygous NUDT15 variant (n=8). Two subjects with homozygous NUDT15 and double heterozygous NUDT15 and TMPT variants received 210 mg/m2 and 249 mg/m2 of 6MP, respectively. Despite the reduction of 6MP starting dose in subjects with NUDT15 or TMPT variants, 7 out of 11 (63.6%) subjects had severe leucopenia during consolidation therapy leading to interruption of 6MP and further dose reduction. In comparison, only 3 out of 22 subjects (13.6%) with wide type allele had 6MP interruption and dose reduction.

Conclusion: NUDT15 variant is occurring at high frequency among Chinese population in Hong Kong while TPMT variant is infrequently encountered. Screening for NUDT15 variant should be performed for all newly diagnosed Chinese ALL patients. Patients with NUDT15 and TPMT variant are susceptible to thiopurine side effects and prone to develop severe leucopenia.

Introduction: Beta-ketothiolase Deficiency (BKD) is a metabolic disease affecting ketone body metabolism and isoleucine degradation. Clinically, it is characterized by intermittent ketoacidotic events that are frequently associated with febrile illness, gastroenteritis, poor feeding or prolonged fasting. Clinical symptoms vary widely, ranging from vomiting, tachypnea or lethargy to altered consciousness, seizures, coma or death. Diagnosis of BKD can be made by urinary organic acid analysis, plasma acylcarnitine profile, enzymatic analysis or mutational analysis of ACAT1 gene. It is a rare condition and its prevalence was estimated to be less than 1 in one-million newborns.

Case Report: We reported three unrelated Chinese patients who were presented to our hospital at age 12 to 24 months with similar history of fever and poor oral intake for 2-4 days before attending emergency department. All of them were noted to have labored breathing and two of them were intubated shortly after admission. They were all found to have severe metabolic acidosis (pH <7.1 and BE > -20) with significant ketosis. All three cases were subsequently confirmed to have BKD due to mutations in ACAT1 gene. Ketoacidosis in BKD can occur with normo-, hypo- or hyper-glycemia which could mimic other medical conditions such as ketogenic hypoglycemia or diabetic ketoacidosis. Such variations in blood glucose levels were also seen in our cases during the acute metabolic decompensation with ketoacidosis. BKD has been described as an IEM with good prognosis. Avoidance of prolonged fasting and modest dietary protein restriction usually lead to a favorable outcome. None of our cases had further ketoacidotic attacks.
Impaired cellular immunity correlates with severe respiratory syncytial virus, rotavirus and varicella-zoster virus infection among patients with primary immunodeficiency

Etsuro Nanishi¹, Hisanori Nishio¹, Takayuki Hoshina², Masataka Ishimura¹, Hidetoshi Takada¹,², Toshiro Hara¹,², Shouichi Ohga¹

¹Departments of Pediatrics, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, ²Department of Pediatrics, School of Medicine, University of Occupational and Environmental Health, Japan, Kitakyushu, Japan, ³Perinatal and Pediatric Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, ⁴Fukuoka Children’s Hospital, Fukuoka, Japan

Background and Aims: Patients with primary immunodeficiency diseases (PID) are highly susceptible to various microorganisms. Respiratory syncytial virus (RSV) is one of the most common pathogens of lower respiratory tract infections in childhood, and is considered to be highly pathogenic in PID patients. In 2013, the use of palivizumab in children with immunocompromised conditions were approved in Japan. However, no population-based studies have been performed to clarify the actual severity of RSV infections in PID patients. Similarly, the reports on rotavirus (RV), varicella-zoster virus (VZV) and influenza virus (IV) infection among PID patients are limited. The objective of this study was to reveal the clinical burden of these four infections among PID patients in Japan.

Methods: We conducted a nationwide survey by sending questionnaires to 898 hospitals with pediatric departments throughout Japan.

Results: Nine hundred ten PID patients from 621 hospitals were registered (response rate: 69.2%). Among them, 54 PID patients (58 episodes) were admitted for one of the 4 viral infections among PID patients in Japan.

Background and Aims: Invasive pulmonary aspergillosis (IPA) has been one of the major causes of mortality in immunocompromised patients. Therefore, early diagnosis and appropriate treatment could improve survival outcome. The gold standard in diagnosis IPA is histopathological examination of lung tissue; however, post-procedural bleeding limits the feasibility of lung biopsy. The European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and The National Institute of Allergy and Infectious Disease Mycoses Study Group (EORTC/MSG) defined definitions for IPA as proven, probable, and possible IPA. To our knowledge, there is limited data about validity of these definitions comparing to histopathological diagnosis of IPA, especially in pediatric population. The objective in this study was to validate of EORTC/MSG 2008 definition IPA, comparing to the gold standard of histopathological result, in pediatric population.

Methods: Histopathological examination of lung tissue of 1 month to 18 years old patients, with respiratory tract infection at the time obtaining biopsy/autopsy, between January 2006 to December 2016, were identified. Retrospective chart review for clinical characteristic, including underlying disease, immune status, diagnostic tests, treatment and outcome was done. IPA diagnosis was classified according to EORTC/MSG 2008 definition. Data was analyzed using SPSS 18 software.

Results: During the 10-year period, there were 256 histopathology of lung tissue, 58 of which suspected pulmonary infection. Fourteen (24%) was proven IPA by histopathology. Seven (50%), 7 (50%) and none were classified as probable, possible, and no IPA, respectively, by using EORTC/MSG 2008 definition. While, histopathological negative for IPA showed 14 (32%), 14 (32%) and 16 (36%) were classified as probable, possible, and no IPA, respectively. When compare probable/possible IPA to no IPA, we found that EORTC/MSG 2008 definition had 100% sensitivity, 36% specificity, 33% positive predictive value, and 100% negative predictive value in diagnosis of IPA.

Conclusion: Our study show the EORTC/MSG 2008 consensus definitions have a 100% sensitivity but low specificity for diagnosis of IPA.
The accuracy of Dengue NS1 antigen test for the early diagnosis of Dengue infection: A systematic review and meta analysis

Charles Likamto, Gloriosa Galindez

De Los Santos Medical Center, Metro Manila, Philippines

Background: Dengue Fever is a major international public health concern. There has been a dramatic global increase in the incidence of Dengue Fever (DF), DHF and DSS. There is thus, an urgent need for an affordable, time saving and convenient diagnostic test for the early diagnosis of Dengue. Dengue NS1 antigen was introduced before for the early diagnosis of Dengue. Several studies have been conducted to evaluate the accuracy of this tool.

Aims:

General: To determine the accuracy of Dengue NS1 Antigen test for the early diagnosis of dengue infection by systematic review and meta analysis.

Specific: To determine the Sensitivity and Specificity of Dengue NS1 antigen based on all literatures reviewed. To determine the PPV and NPV of Dengue NS1 antigen based on all literatures reviewed. To determine the likelihood ratio of Dengue NS1 antigen test based on all literatures reviewed. To determine the overall accuracy of Dengue NS1 antigen test based on all literatures reviewed.

Methods: Inclusion Criteria: Cross Sectional Studies using Dengue NS1 Antigen as an index test for the early diagnosis of Dengue infection.

Search Strategy: Electronic Searches were done using the library of the local references, Cochrane central Register of Controlled Trials, Pubmed, Elsevier, Google Scholar, NEJM and the reference lists of identified studies.

Data Extraction and Statistical Analysis: Two authors independently assessed the studies and extracted data from the studies. Data synthesis was carried out using Review Manager version 5.3.

Result: 5 Studies were included with a total of 1,976 serum samples. Results showed; Sensitivity: 63.5% (Mean), 59% (Median), 62% (Mode); Specificity: 98.6% (Mean), 97% (Median), 100% (Mode); PPV: 98.6% (Mean), 97% (Median), 100% (Mode); NPV: 48.4% (Mean), 55.9% (Median); LR+: 27.4 (Mean), 43.5 (Median); LR-: 0.36 (Mean), 0.37 (Median), 0.57 (Mode); and for overall accuracy the mean was 73.1%.

Conclusion: This meta-analysis implies that the Dengue NS1 antigen test can be used as a valid method and deserve inclusion in the diagnostic evaluation of early Dengue infection.

Cadherin-related family member 3 expression and their regulation in the human respiratory explant cultures

Kin-Pong Tao¹², Joseph Gar-Shun Tsun¹, Wai-Ming Lee¹, Ting-Fan Leung², John M Nicholls¹, Renee WY Chan¹²

¹Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong, ²The Chinese University of Hong Kong–University Medical Center Utrecht Joint Research Laboratory of Respiratory Virus and Immunobiology, Hong Kong, Biological Mimetics, Inc., Frederick, MD, USA, ³Department of Pathology, LKS Faculty of Medicine, The University of Hong Kong, Hong Kong

Background: Cadherin-related family member 3 (CDHR3) is identified as a susceptible gene for early childhood asthma with severe exacerbations in genome-wide association study published in 2014. In early 2015, the same transmembrane protein is found to be the cellular receptor for the human rhinovirus C (RV-C). Intriguingly, the HRV-C infection is the leading cause of childhood wheezing illnesses and asthma exacerbation. The rs6967330 in CDHR3 is one of the top SNPs identified and the tyrosine at position 529 is found to be more cell surface expression and yielded ten-fold more RV-C progeny viruses. This finding infers that factors that could induce an overexpression of CDHR3 at the cell surface might lead to a greater susceptibility of RV-C, therefore, a higher chance of wheezing or asthma exacerbation.

Aims: To examine the expression of CDHR3 in human respiratory epithelial cells upon the exposure to wheezing and asthma exacerbation associated risk factors, and its effect in alternating RV-C susceptibility.

Methods: Primary human bronchial and lung explant cultures were derived from bronchial and lung tissues of patients underwent resection in Prince of Wales Hospital. These epithelia were cultured in air-liquid interface cells were pre-incubated with Th2-cytokines, including interleukin(IL)-4, IL-5 and IL-13, aeroallergens including liposaccharides, dust mite extract cigarette smoke extract (CSE) and dexamethasone prior RVs infection. The CDHR3 expression and the RVs replication were monitored at 1, 24, 48 hours post infection.

Results: CDHR3 is highly expressed in the bronchial epithelia but not always in the alveolar epithelial cells. The pre-incubation of IL-5, CSE, liposaccharides and dexamethasone would enhance the CDHR3 expression on these respiratory epithelial cells. More importantly, both CSM and dexamethasone enhanced the replication of rhinovirus.

Conclusions: Cigarette smoke exposure might alter the CDHR3 expression in a way to enhance RV replication. The routine use of dexamethasone in the clinical management of patients with underlying respiratory diseases should be carefully evaluated.

Acknowledgement: CUHK Direct Grants 2015.1.055 to RWYC.
Background and Aims: Influenza imposes substantial healthcare burden in terms of hospitalisation and mortality in children, which can be prevented by vaccination. Influenza vaccination coverage varies widely among childhood populations worldwide, which has significant impact on herd immunity and usefulness of influenza vaccine. However, there is limited real-life data on influenza vaccine effectiveness (VE) in children. This study aimed to investigate clinical spectrum of influenza infection and VE in preventing influenza in Hong Kong children.

Methods: This prospective cohort study recruited children aged 2-12 years from 15 kindergartens and primary schools. Parents completed a questionnaire on subjects’ health status and history of influenza vaccination. Flocked nasopharyngeal swabs (NPSs) were collected at biweekly school visits during influenza seasons in 2014-15, and illness visits were arranged for children with influenza-like illness (ILI). Influenza A and B were detected and typed by polymerase chain reaction, and influenza immunity measured by haemagglutination inhibition (HAI).

Results: 623 children provided a total of 2,633 NPS samples. Two samples were obtained from 607 (97.4%) of subjects. Thirty-six (11.2%) subjects had influenza A or B in 2014 whereas all 19 (6.3%) subjects had influenza A in 2015. Seropositivity rates for A(H1N1)pdm09, A/H3N2, A/H3N2-Switzerland, B/Victoria-lineage and B/Yamagata-lineage were 92%, 91%, 68%, 49% and 85%, respectively. Ninety-nine subjects reported ILI and nine illness visits were arranged. Seasonal influenza vaccination was protective against ILI but not laboratory-confirmed influenza by surveillance. Influenza VE for ILI varied between 42.1 (10.5-63.1) % and 51.9 (24.5-70.1) % depending on the year of vaccination. Subgroup analyses showed higher VE for both ILI (70.9% vs 34.6%) and mild laboratory-confirmed influenza (44.0% vs -6.2%) in school-age children than preschoolers who were vaccinated within 12 months. HAI titres and seropositivity did not differ in subjects with and without ILI. Logistic regression confirmed protective effect of influenza vaccination against ILI. There was no reported transmission of influenza within subjects’ classes and household.

Conclusions: Mildly symptomatic influenza is common in children during influenza seasons. Seasonal influenza vaccination is effective against ILI but not mild influenza identified by surveillance. HAI titres do not appear to indicate protective immunity for childhood influenza.

Funding: Medical and Health Research Fund (Reference 13120422)
Effects of different immune and non-immune factors on CDHR3 expression in airway epithelial cells and Ex vivo bronchus culture

Ting-Fan Leung1, Kin-Pong Tao1, Joseph Gar-Shun Tsun1, Judith CW Mak2, Yu-Ping Song3, Agnes Sze-Yin Leung1, Renee Wan-Yi Chan1

1Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong, 2Department of Pharmacology and Pharmacy, The University of Hong Kong, Hong Kong

Background and Aims: Human rhinovirus C (HRV-C) infection was reported to be a major risk factor for asthma exacerbations and wheezing illnesses in children. This respiratory virus has not been widely studied because it was not culturable in standard cell culture until the recent identification of cadherin-related family member 3 (CDHR3) as its cellular receptor on airway epithelial cells. We hypothesized that cellular distribution of CDHR3 in the human airways was associated with host susceptibility to HRV-C infection. This study aimed to investigate changes in CDHR3 expression of the human respiratory epithelial cells upon exposure to asthma-related stimuli.

Methods: Both human alveolar type II epithelial cells (A549) and primary human nasopharyngeal epithelial cells were challenged with dexamethasone, lipopolysaccharide (LPS), and cigarette smoke medium (CSM). CDHR3 expression levels on these respiratory epithelial cells were determined at gene and protein levels using quantitative PCR and western blot. The localization of CDHR3 was detected by immunoflourescence staining. The effects of these stimuli on the susceptibility of respiratory epithelial cells to HRV-C infection were evaluated by the subsequent inoculation with HRV-C isolate. The replication kinetics of HRV-C was assessed by titrating the culture supernatant using CDHR3-expressing H1-HeLa cells.

Results: A 549 cells incubated with dexamethasone expressed 4-fold higher CDHR3 than control cells at 24 hours post treatment, while LPS induced 8-fold increase in CDHR3 at 48 hours post-treatment. Stimulation with 0.625% CSM upregulated CDHR3 expression by 5-fold and 150-fold at 24 and 48 hours following treatment, respectively. The effects of CSM on the human primary nasopharyngeal epithelial cell culture were consistent to those observed in A549 cells, although primary nasopharyngeal epithelial cells were less responsive to dexamethasone and LPS treatments. CDHR3 expression only increased 2-fold at 48 hours after these treatments.

Conclusions: The exposure of respiratory epithelial cells to asthma-related stimuli such as LPS and CSM can enhance CDHR3 expression. Interestingly, the incubation of these respiratory epithelial cells with dexamethasone, a corticosteroid useful for suppressing asthmatic airway inflammation, can also alter the expression of HRV-C receptor.

Funding: Direct Grants for Research (2015.1.055 and 2015.1.058) of CUHK

HIV coreceptor tropism in treatment-naive and treatment-experienced HIV-1 infected children and adolescents

Natt Arayapong3, Nopporrn Apiwattanakul4, Angsana Phuphuakrat2, Chonnemet Techasaensiri2

1Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, 2Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background and Aims: HIV-1 enters host cells by interaction with the envelope glycoprotein gp120 with CD4 molecule and coreceptor. The chemokine receptor 5 (CCR5) and chemokine receptor 4 (CXCR4) are usually the main coreceptors. Initially, the CCR5 antagonist, maraviroc, was approved for treatment-experienced adults infected with CCR5-using strains. However, CCR5 antagonists could be considered in the future as alternative drugs in HIV-1-infected children and adolescents who have virologic failure after standard treatment. Coreceptor tropism testing should be performed prior to initiation of therapy with CCR5 antagonists. HIV-1 coreceptor tropism varies among different HIV-1 subtypes. The majority of HIV-1 subtype in Thailand is CRF01_AE. To our knowledge, data on coreceptor tropism of HIV-1 CRF01_AE in children and adolescents are limited. We aim to evaluate the prevalence of coreceptor tropism in HIV-1-infected children and adolescents in Thailand.

Methods: HIV-1 infected patients, aged <20 years, who failed the standard ARV’s and had viral HIV-1 RNA >1000 copies/ml or who were treatment-naive were enrolled from September 2015 to February 2017. Plasma samples were collected for determining the HIV-1 coreceptor tropism by using genotypic testing methods. Coreceptor tropism was predicted base on V3 sequences using GENO2PHENO version 2.5 with a false positive rate of 5%.

Results: Fifty-two HIV-1 infected participants, aged 14.9 years (IQR 8.9-16.8) were recruited. The median CD4 cell count was 396 (IQR 72-630.25) cell/μL. HIV-1 RNA viral load was done in 47 (90.38%) patients and the median was 4.6 (IQR 3.8-5.3) log10 copies/ml. Thirty-nine patients (75%) had experience virological failure of the standard ART and had viral HIV-1 RNA >1000 copies/ml. Median number of antiretroviral regimens was 3 (IQR 2-4) in treatment failure group. Of the sequence obtained from the patients, 36 (69.2%) were subtype CRF01_AE, 7 (13.5%) were subtype A or AG, 6 (11.5%) were subtype B and 3 (5.8%) were subtype C based on V3 loop. Sixteen (30.8%, 95% CI 18.7-45.1) were classified as R5 virus that reflected the CCR5 antagonists was likely to be effective. Twenty-six (50%) were classified as X4 virus that reflected the drug was not likely to be effective and the drug might be useful in 10 (19.2%) of patients. CRF01_AE showed significantly associated with X4 virus compared with non-AE subtypes (61% vs 25%, respectively, P = 0.016). The Proportion of R5 viruses in treatment failure group were 28.2% compare with 38.5% in treatment naive group but no statistic significant.

Conclusions: In regions where HIV-1 CRF01_AE are predominant, the use of CCR5 antagonist must be considered with caution. Tropism testing should be performed whenever considering the use of the CCR5 antagonist.
Whole genome sequencing study of the enterovirus D68 detected in hospitalized children in Hong Kong with serious respiratory disease

Haichao Wang1, Zigui Chen2, Kin-Pong Tao2,3, Paul KS Chan4, Ting-Fan Leung2,3, Renee Wan-Yi Chan1,4

1Department of Paediatrics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, 2Department of Microbiology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, 3The Chinese University of Hong Kong–University Medical Center Utrecht Joint Research Laboratory of Respiratory Virus and Immunobiology, Hong Kong

Background: Human enterovirus 68 (EV-D68) has re-caught the public concern until it caused a nationwide outbreak among children from mid-August 2014 to January 2015 in the United States. This EV-D68 is associated with severe respiratory illness in children whom had asthma or a history of wheezing, with sporadic cases with acute flaccid myelitis in 2014. Since then, the laboratory confirmed case of EV-D68 has become low again. EV-D68 was first isolated in California, from four American children with respiratory illness. Its disease spectrum ranges from asymptomatic to severe respiratory complications and in rare instances, subsequent death. It belongs to the family Picornaviridae and the genus Enterovirus, a member of D species. In the US, there is a National Enterovirus Surveillance System since the 1960s, however, in Hong Kong, the surveillance system of such is lacking. In addition, the whole genome data of EV-D68 is limited. With the effort of screening through 6,800 nasopharyngeal aspirate (NPA) sample from September 2014 to December 2015 from in-patient under 17 years old were retrospectively examined. Samples which were PCR screened to be enterovirus positive were further genotyped by PCR of the VP4/VP2 region followed by Sanger sequencing. Nucleotide sequences with published EV-D68 sequences were aligned using Clustal Omega and phylogenetic trees were generated by MEGA software using the neighbor-joining method with a reliability with 1,000 bootstrap replications.

Results and Discussion: Within the 10,529 NPA collected from hospitalized children, 23.3% (n=2,457) of them were positive with an enterovirus in the regular diagnostic testing. 1,033 (42%) underwent genotyping and fifteen EV-D68 were identified followed by full genome sequencing. The EV-D68 viruses detected in the winter of 2015 showed high similarity with the published strains from Southern China, Taiwan and Japan during a similar study period.

Molecular detection and the whole genome sequencing of Echovirus serotypes identified in Hong Kong hospitalized children

Haichao Wang1, Kin Pang Tao1,2, Paul KS Chan3, Ellis KL Hon1,2, Ting-Fan Leung2,3, RWY Chan1,2

1Department of Paediatrics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, 2The Chinese University of Hong Kong–University Medical Center Utrecht Joint Research Laboratory of Respiratory Virus and Immunobiology, Hong Kong, 3Department of Microbiology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong

Background: Enteric cytopathic human orphan virus (Echo) virus is single-stranded positive sense RNA virus which was first isolated from the feces of asymptomatic children in the context of epidemiological studies of polioviruses in the 1950s. It can cause mild and self-limited disease but sporadically, it can cause a severe central nervous system infection, such as aseptic meningitis, encephalitis, paralysis. So far, there were no complete genome data of echovirus strains from Hong Kong’s isolates and in general, genomic data of such is limited. Echovirus has a genome of approximately 7.5 Kb. It belongs to the species Enterovirus B, genus Enterovirus of the Picornaviridae family, echoviruses include 33 serotypes and the genome consists of a 5’ untranslated region (UTR), structural polypeptide P1, nonstructural polypeptides P2 and P3, and a 3’ UTR.

Aim: By conducting the Enterovirus surveillance in the nasopharyngeal aspirate (NPA) obtained from hospitalized population below 17 years old, we would like to improve the understanding of the molecular epidemiology and evolution of echovirus serotypes in Hong Kong.

Methods: Retrospective NPA samples collected from September 2014 to December 2015 in the two major hospitals in the East New Territories from in-patient settings were screened. Genotyping of echovirus was carried out by using the PCR of the VP4/VP2 region followed by Sanger sequencing. When echovirus was screened positive, whole genome sequencing was performed and nucleotide sequences with published echovirus sequences were aligned using Clustal Omega and phylogenetic trees were generated by MEGA software using the neighbor-joining method with a reliability with 1,000 bootstrap replications.

Results and Conclusions: Within the 10,529 NPA collected from hospitalized children, 23.3% (n=2,457) of them were positive with an enterovirus in the regular diagnostic testing. One thousand and thirty-three (42%) underwent genotyping and ten echoviruses were identified followed by full genome sequencing. Six different echovirus serotypes, E6 (n=1), E9 (n=3), E16 (n=1), E18 (n=2), E25 (n=2), E3 (n=1), were detected using VP4/VP2 region specific PCR, whole genome sequencing was performed to get their complete genome data. This could indicate a wide range of echovirus serotypes circulating in Hong Kong. Our study contributed the first Hong Kong echovirus whole genome data to this research arena all over the world. Data from a variety of geographic areas promote the investigation on associations between variants and clinical symptoms.
408
Inhibition of microRNA155 alleviates lipopolysaccharide-induced kidney injury in mice

Yuqian Ren, Yun Cui, Xi Xiong, Chunxia Wang, Yucai Zhang
Department of Critical Care Medicine, Shanghai Children's Hospital, Shanghai Jiao Tong University, Shanghai, China

Background and Aims: Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Accumulated evidences suggest that microRNAs (miRNAs) are related with inflammation-associated diseases. The aim of this study is to investigate whether miR-155 is involved in lipopolysaccharide (LPS)-induced kidney injury, and to explore the underlying mechanisms.

Methods: Mice were intraperitoneally injected with LPS to construct endotoxemia mice model, and miR-155 inhibitor was injected via tail vein to suppress the expression of miR-155 in kidney.

Results: The results indicated that the expression of miR-155 was markedly increased in renal tissues of LPS-treated mice. And miR-155 inhibitor protected mice from LPS-induced kidney injury associated with the lower levels of TNF-α and IL-6 in renal tissues. Furthermore, inhibition of miR-155 increased the expression of suppressor of cytokine signaling 1 (SOCS1), a target gene of miR-155 and a negative regulator of Janus activated kinase (JAK)-signal transducer and activator of transcription (STAT) signaling pathway. Consistently, inhibition of miR-155 suppressed the expression of JAK2, STAT3 and phosphorylated STAT3 (p-STAT3).

Conclusions: All these results indicated that inhibition of miR-155 protects mice from LPS-induced kidney injury possibly through regulating SOCS1-JAK2/STAT signaling pathway, which suggested that miR-155 might be an important and potential target in developing therapy for preventing sepsis-associated kidney injury.

642
Serum inflammatory cytokine levels correlate with CD4+ T cells in hand-foot-mouth disease

Yan Li, Min Jiang, Yanyan Zhang, Wei Lin, Guangmin Nong
The First Affiliated Hospital of Guangxi Medical University, Nanning, China

Background and Aims: To investigate the correlation between the expression of proinflammatory and anti-inflammatory cytokines associated with CD4+ T cells and severity of disease and prognosis in severe hand, foot, and mouth disease to find out predict factors for further immunotherapy.

Methods: From January 2014 to January 2016, the serum of 433 cases of children with HFMD and divided into five groups: death group of 30 cases of death, survival group of 58 cases, severe group of 167 cases, mild group of 118 cases, subclinical infection group of 60 cases and 50 cases of normal control group were collected, IFN-α, IFN-β, IFN-γ, IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-18, IL-21, TNF-α, IL-1β, GM-CSF, TGF-β were measured by quantitative cytokines antibody microarray.

Results: Serum IFN-γ, IFN-α, IFN-β in children with death group significantly increased compare with severe group, the mild group, the recessive infection group increased compare with normal control group (p<0.05). Proinflammatory cytokine TNF-α, TNF-β, IL-6, IL-1, IL-2, IL-12 levels increased significantly both in death group and survival group compare with severe group, the mild group and normal control group (p<0.05). IL-18 and IL-8 levels significantly increased of the death group (p<0.05), IL-1β, IL-6, IL-8 levels higher in subclinical infection group than NC group (p<0.05). In the death group, anti-inflammatory cytokines of IL-10, TGF-β levels were high than survival group, severe group, mild group, the recessive infection group and normal control group (p<0.05). IL-4 levels increased in mild, recessive infection group and normal control group (P<0.05), but there was no significant difference between death group, survival group and severe group. The levels of GM-CSF, IL-21 of death group increased significantly compare with the severe group, the mild group, the recessive infection group and normal control group (p<0.05).

Conclusion: The proinflammatory cytokine and anti-inflammation cytokine levels are increased by disease severity, but the death group had higher IL-10 which reveal that compensatory anitflammation syndrome exist in severe hand, foot, and mouth disease.

999
Development and application of enterovirus 71 vaccine in China

Muhan Li, Gang Liu
Beijing Children's Hospital, Beijing, China

Background and Aims: Enterovirus 71 (EV71)-associated hand, foot and mouth disease (HFMD) causes significant morbidity and mortality, leads to some severe neurological complications, and poses a serious burden on the health of children and the public. Due to the lack of effective drug treatment, vaccine is the main method to control disease. This article summarizes EV71 vaccine research and evaluation, clinical trial and application since 2001 were reviewed and summarized.

Methods: Through document retrieval, all literatures related to EV71 vaccine research and evaluation, clinical trial and application since 2001 were reviewed and summarized.

Results: A total of 50 related literature were retrieved in the database. Varieties of EV71 vaccine are in research and development. At present, EV71 vaccine mainly includes inactivated whole vaccine, live attenuated vaccine, recombinant VP1 vaccine, VP1-based DNA vaccine, synthetic peptide vaccine and virus-like particle vaccine. Three inactivated vaccine in China have been completed phase III clinical trials. Among them, the vaccine developed by Chinese Academy of Medical Sciences and Sinovac Biotechnology Co., Ltd. have been approved on Dec.2015. The vaccine developed by Beijing Vigoo biological is undergoing
Background and Aims: Human neutrophil lipocalin (HNL) is a protein released from neutrophil granules and is regarded as a useful marker for discriminating acute bacterial and viral infections. The aim of this study was to explore its potential to monitor the effect of antibiotic treatment in patients with local bacterial infections.

Methods: Sera HNL were quantified in 40 healthy individuals and 105 patients confirmed with acute infections (30 with sepsis; 45 with local bacterial infections; 30 with viral infections). HNL levels were measured in all cases before antibiotic treatment, as well as 48 h and 72 h post antibiotic treatment for cases with local bacterial infections. Levels of serum CRP were measured at the same time for comparison.

Results: Prior to antibiotic treatment, serum HNL levels were significantly higher in patients with local bacterial infections than those with viral infections (p<0.001). After treatment for 48 h and 72 h, HNL levels declined rapidly as the infections went under control.

Conclusions: In summary, serum HNL may serve as a highly sensitive and specific early diagnostic marker for acute bacterial infections. Kinetic detection of HNL may monitor the efficacy of antibiotic treatment in patients with local bacterial infections.

A permit review process. Three vaccines have good safety, efficacy and immune response in each clinical trials. The rate of prevent infection EV71-associated HFMD infection is 90%-97.3%, severe case protection is 100%. After 1 year two-pin base immunization, inoculation of 1-pin boosted immunization could cause long-term protection of the disease.

Conclusions: The nucleotide and amino acid of RSV F protein, especially, in the antigenic sites area, were highly conserved except limited genetic variations. These results revealed that F protein remains the potential candidate for the development of vaccine and drug.
Blocking integrin CD11b inhibits LPS-induced HMGB1 release and translocation during sepsis

Huiting Zhou¹, Huan Gui¹, Ming Wu¹, Gang Li¹, Zhihui Zhao², Jian Wang¹
¹Institute for Pediatric Research, Affiliated Children’s Hospital, Soochow University, Suzhou, Jiangsu, China, ²Jiangsu Province Key Laboratory for Molecular and Medicine Biotechnology, College of Life Science, Nanjing Normal University, Nanjing, Jiangsu, China

Background and Aims: High mobility group box 1 (HMGB1), a chromatin-binding nuclear protein, plays a critical role in the generation and development of sepsis by acting as a key “late-phase” inflammatory mediator. Due to its unique secretion pattern and severe pro-inflammatory effect, HMGB1 has been recognized as an alarm in the regulation of immune response to infection and the pathophysiological process of sepsis and other autoimmune disease. Here, we investigate the role of integrin CD11b in HMGB1-mediated sepsis and LPS-induced HMGB1 release.

Methods: Firstly, the exact role of CD11b in sepsis was investigated in mouse CLP-induced sepsis model in vivo. The detailed molecular mechanisms of CD11b in LPS-induced HMGB1 release was forward to evaluate by Western blot, flow cytometry, immunocytochemical analysis and CoIP analysis in vitro.

Results: In CLP-induced septic model, antagonism of CD11b by using blocking antibody or pharmacological CD11b inhibitor could protect mice from septic death and inhibit the level of circulating HMGB1 but not TNF-α. Consistent with this, compared to wild-type mice, CD11b knockout (CD11b-/−) mice exhibited improved survival rate with decreased HMGB1 level in serum. Further study showed that pharmacological antagonism and genetic knockout/knockout of CD11b could hamper LPS-induced HMGB1 cytoplasmic translocation and active release from macrophages. To clarify the underlying mechanism of effect of CD11b-mediated HMGB1 inhibition, immunofluorescence microscopy and co-immunoprecipitation were carried out. As observed, CD11b knockdown blocked HMGB1 nucleo-cytoplasmic translocation both by hampering interaction with a nuclear export factor CRM1 and inhibiting phosphorylated modification of HMGB1 by cPKC.

Conclusions: Taken together, all results give us the direct evidence of antagonism of integrin CD11b could exert protection against sepsis and inhibit LPS-induced HMGB1 cytoplasmic translocation and active release by hampering interaction between HMGB1 with CRM1 and PKC. Our studies will help us to clarify that targets for CD11b could be an alternative therapeutic target of HMGB1-mediated endotoxemia and sepsis.

Utility and access of the rotavirus vaccine in introducing countries

Alice Abou-Nader, EAS Nelson
The Chinese University of Hong Kong, Hong Kong, Hong Kong

Background and Objectives: The third dose of the diphtheria, tetanus, pertussis (DTP) vaccine has been internationally recognized as a performance indicator providing insight into the utility and access of immunization services. Since 2006, the World Health Organization (WHO) has encouraged countries to adopt the rotavirus vaccine to protect children against severe diarrhea and death caused by dehydration. The rotavirus vaccine schedule would follow that of DTP, meaning that the same service performance indicators could be used and applied to the Rotavirus vaccine.

Methods: Reported 2016 vaccine coverage of the first and last dose of the DTP and rotavirus vaccine series were collected from the WHO/UNICEF Joint Reporting Form (JRF) for the 84 rotavirus vaccine introducing countries. Eighteen countries were excluded from the analysis for either having missing, incomplete, or inconsistent vaccine coverage data. The final number of countries included in the analysis was 66.

Results: Low-income countries (LICs) have the highest reported rotavirus vaccine coverages (for the first and last dose within the series) compared to the other income groups. High income countries (HICs), on the other hand, reported the highest DTP coverage values but had the lowest reported rotavirus vaccine rates, which contributed to having the highest percent difference (15%) between the reportage coverage rates of the two vaccines. As outliers, São Tome Principe, Zimbabwe, Senegal reported higher Rot1 coverage values than DTP1. A great majority (46/66, 70%) of rotavirus vaccine introducing countries have good utilization and access to the rotavirus vaccine while only 11% (7/66) scored poorly on these service indicators.

Conclusions: LICs and low-middle income countries (LMICs) have successfully integrated the rotavirus vaccine into their National Immunization Programs in comparison to HICs. There should be efforts geared towards improving rotavirus vaccine coverage in LICs. The seven poor performing countries (Greece, Guinea-Bissau, Haiti, Liberia, Marshall Islands, Micronesia, Venezuela) should be encouraged to decrease their immunization service gaps, utility and access of rotavirus vaccination, to better protect infants against life-threatening rotavirus infections.
Comparison of effects of bubble nasal continuous positive airway pressure and nasal continuous positive airway pressure for neonatal respiratory support

Xianxiao Shu¹,², Chao Chen¹, Jun Tang¹,²,³, Jing Shi¹, Hua Wang¹

¹West China Second University Hospital, Sichuan University, Chengdu, China, ²Key Laboratory of Obstetric & Gynecologic and Pediatric Diseases and Birth Defects of Ministry of Education, Sichuan University, Chengdu, China, ³West China School of Public Health, Sichuan University, Chengdu, China

Background and aims: To compare the effects and safety of bubble nasal continuous positive airway pressure (BNCPAP) and nasal continuous positive airway pressure (nCPAP) for neonatal respiratory support.

Methods: We retrospectively analyzed the data of the neonates who accepted BNCPAP or nCPAP treatment in the neonatal ward of West China Second University Hospital of Sichuan University during March 2016 and October 2016. Neonates were divided into BNCPAP group and nCPAP group according to the ventilation strategies. Demographics data of both groups were documented, including gender, birth weight (BW), gestational age (GA), underlying diseases, Apgar score, delivery pattern, as well as whether pulmonary surfactant (PS) was administrated. The outcome measures included: death, failure of intervention, and bronchopulmonary dysplasia (BPD). Multiple administration of PS, duration of respiratory support, days in hospital and retinopathy of prematurity (ROP) were also documented. The safety data were also analyzed. All the data were analyzed by SPSS 19.0.

Results: A total 47 infants were included in the nCPAP group and 60 infants in the BNCPAP group. There were more males in the nCPAP group (57.45% in the nCPAP group versus 31.67% in the BNCPAP group, p<0.05). While other demographics data were of no significant difference between two groups (p>0.05). Mortality rate in BNCPAP group and nCPAP group were of no significant difference (0.00% versus 2.13%, p>0.05); neither was rate of failure of intervention (0.87% versus 2.21%, p>0.05). The durations of respiratory support were of no significant difference in both groups (p>0.05). Meanwhile, rate of pneumothorax and/or pneumomediastinum were of no significant difference in both groups (p>0.05).

Conclusion: There is no evidence to support that significant difference of effects and safety is existed between BNCPAP and nCPAP for neonatal respiratory support. However, BNCPAP might be more suitable for neonatal transport system and/or basic hospitals with limited medical support ability because of its easy and cheap.
Attenuated SUMOylation of SIRT1 in premature neonates with bronchopulmonary dysplasia

Fengmei Tan, Wenbin Dong
Department of Neonatology, The Affiliated Hospital of Southwest Medical University, Luzhou, China

Background and Aims: To investigate the effects of hyperoxia on the expressions of small ubiquitin-related modifier (SUMO) and sirtuin 1 (SIRT1) proteins, and to examine interactions between these proteins in premature neonates with bronchopulmonary dysplasia (BPD).

Methods: In this prospective study, peripheral blood mononuclear cells (PBMCs) were isolated from residual venous blood samples of 20 premature infants with BPD and 20 gender-matched premature infants without BPD (non-BPD group). Expressions of SUMO and SIRT1 proteins in PBMCs were assessed by Western blot analysis, and their interactions in PBMCs were detected by immunoprecipitation assay. Based on the fraction of inspired oxygen (FiO2) administered, neonates were divided into normal- (FiO2=21%), low- (21% <FiO2 <30%), medium- (30% ≤FiO2 <40%), and high-oxygen (FiO2 ≥40%) groups.

Results: Expression levels of SUMO1 and SUMO2/3 proteins in the normal-oxygen group were significantly lower than those in the medium- or high-oxygen groups, but were comparable to those in the low-oxygen group. SIRT1 expression in both the medium- and high-oxygen groups was significantly lower than that in the normal-oxygen group. In the BPD group, the expression of SIRT1 protein was lower, and its interaction with SUMO1 and SUMO2/3 was attenuated as compared to that in the non-BPD group.

Conclusion: Oxygen therapy Supplemental oxygen with FiO2 ≥30% was associated with upregulation of SUMO1 and SUMO2/3 expressions and downregulation of SIRT1 expression.

Urine biomarkers for monitoring renal function in premature infants

Yo Han Ahn1, Juyoung Lee2, Ji Young Chun1, Tae-Jung Sung1
1Hallym University Kangnam Sacred Heart Hospital, Seoul, Korea, Republic of, 2University Hospital, Incheon, Korea

Background and Aims: Premature infants are at high risk for acute kidney injury (AKI) from various causes. The serum creatinine level has limitations in evaluating the renal function of premature infants because neonatal serum creatinine reflects maternal levels at early postnatal period. Furthermore, it is difficult to repeat invasive blood sampling to monitor serum creatinine levels for them. The purpose of this study is to evaluate whether urine biomarkers can be used to monitor development of AKI in premature infants.

Methods: A prospective cohort study was conducted in premature infants born less than gestational age (GA) 37 weeks and admitted to the neonatal intensive care units of Kangnam Sacred Heart Hospital and Inha University Hospital. Urine biomarkers and serum creatinine were measured on postnatal day 1, 3, 5, 7, 10, and 14. Urine biomarkers include neutrophil-gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), interleukin-18 (IL-18), liver fatty acid binding protein (L-FABP), cystatin-C (CysC), osteopontin (OPN), and epidermal growth factor (EGF). AKI was classified using modified Acute Kidney Injury Network (AKIN) definition.

Results: A total of 83 infants were recruited. (male:female 1.4:1) Mean GA and birth weight was 30.5±3.0 weeks and 1514±549 g, respectively. AKIs occurred in 17 (20.5%) infants at mean age of 7.4±2.6 days. When classified using the modified AKIN definition, 9 (12.0%) infants were classified as the stage 1, 5 (6.0%) and 2 (2.4%) infants were classified as the stage 2 and 3, respectively. One (1.2%) infants died because of sepsis and AKI. Because AKI did not occur in infants born after GA 32 weeks, we compared demographic factors and urine biomarker between AKI and non-AKI groups under GA 32 weeks. There are no differences in baseline characteristics except GA in multivariate logistic regression analysis. Urine levels of NGAL, CysC, KIM-1, L-FABP and OPN were higher in AKI group than in non-AKI group before the onset of AKI. Urine levels of IL-8 were higher in AKI group than in non-AKI group at around the onset of AKI. Conversely, urine levels of EGF were lower in AKI group than in non-AKI group before the onset of AKI.

Conclusion: In this study on premature infants, though there was no demographic risk factor for AKI except GA, several urine biomarkers were significantly different between AKI and non-AKI groups. Urine biomarkers could be useful to monitor renal function and predict AKI development in premature infants.
Outcome predictors of children receiving continuous renal replacement therapy (CRRT)

Wun-Fung Hui, Winnie Kwai-Yu Chan
Department of Paediatrics, Queen Elizabeth Hospital, Hong Kong

Background and Aims: CRRT has been increasingly used as the modality of dialysis and renal support for acute kidney injury (AKI) and other non-renal conditions among critically ill children. Identification of prognostic factors can help to predict the outcome.

Methods: We retrospectively reviewed the medical records of patients below 18 years old who had received CRRT in either NICU or PICU of Queen Elizabeth Hospital from January 1998 to May 2017.

Results: Altogether 76 patients received 81 episodes of CRRT during the period. 55.6% were male and 25.9% were neonatal patients. The median (interquartile range) age was 6.0 (11.6) years for paediatric patients and 3.0 (12.5) days for neonatal patients. 76.5% of CRRT were performed for AKI-related indications including abnormal renal function, acidosis or electrolytes imbalance (91.9%), volume overload (56.5%) and removal of toxic substances (4.8%), whereas 23.5% of CRRT were performed for non-renal indications including metabolic disease (57.9%), sepsis (15.8%), medication intoxication (15.8%) and tumour lysis syndrome (10.5%). The overall mortality was 33.3% and the duration of ICU stay was 17 (30) days. 81.5% of survivors managed to stop CRRT but 18.5% remained dialysis-dependent. Besides, 54.5% of those who were off CRRT had impaired renal function. Multivariate analysis identified PRISM III score (Odds ratio [95% confidence interval] 1.14[1.03-1.25]) and pre-CRRT fluid overload (OR: 1.39 [1.10-1.77]) as independent predictors for mortality. Comparison of variables between survivors with and without renal recovery revealed that diagnosis of primary renal diseases (p<0.001), PRISM III score (p=0.047), pre-CRRT urine output (p=0.001) and baseline estimated glomerular filtration rate (p<0.001) were significant determinants of renal outcome.

Conclusion: Children required CRRT carried high mortality. 63% of survivors had impaired renal function or remained dialysis-dependent. PRISM III score and pre-CRRT fluid overload were independent predictors for mortality. Survivors with primary renal disease, lower PRISM III score and poorer baseline renal function carried worse renal prognosis.

Chronic intermittent hypoxia exposure induces kidney injury in growing rats

Xiao-Hong Cai¹, Neha Devi Poonit², Yi-Chun Zhang², Chu-Yuan ye², Hui-Lin Cai², Chen-Yi Yu¹, Ting Li⁴
¹The Second Affiliation Hospital and Yuying Children’s Hospital of Wenzhou Medical University, Wenzhou, China, ²The Second Affiliation Hospital and Yuying Children’s Hospital of Wenzhou Medical University, Wenzhou, China, ³Institute of Hypoxia Medicine, Wenzhou Medical University, Wenzhou, China

Objective: To examine the effect of chronic intermittent hypoxia (CIH) on the morphological changes in the kidney of growing rats and to explore the mechanisms underlying the CIH-induced renal damage.

Methods: 40 Sprague-Dawley rats were randomly divided into two groups: 2 and 4 weeks CIH groups (2IH, 4IH), and in the control group 2 and 4 weeks air stimulated groups (2C, 4C), with 10 rats in each group. Pathological changes of renal tissue were observed by HE staining, PAS staining and Masson staining. Real-time PCR method was used to detect the mRNA expression of HIF-1α, Cu/ZnSOD and MnSOD in renal tissue.

Results: (1) Intermittent hypoxia (IH) caused morphological damage in the kidney. Hypertrophy of epithelial cells in the kidney tubules and dilation in the glomeruli were observed under light microscope in HE and PAS stain, especially in 4IH group. Masson staining showed no significant fibrotic response in the IH groups. (2) Compared with the corresponding control groups, the levels of serum SOD were significantly lower in CIH groups, and especially in 4IH group. The mRNA expression of Cu/ZnSOD and MnSOD in CIH groups decreased significantly as compared to control groups. The mRNA levels of HIF-1α in the kidney were significantly higher in CIH groups than those in the corresponding control groups.

Conclusion: Oxidative stress played a critical role in renal damage by up-regulating HIF-1α transcription and down-regulating Cu/ZnSOD and MnSOD transcription after chronic intermittent hypoxia exposure in growing rats.
Pharmacokinetics of intravenous levetiracetam in Thai children

Suchawadee Horsuwan, Nuttawut Jenjirattithigarn, Chonlaphat Sukasem, Chaiyos Khongkhathitum, Ananit Visudtibhan, Luniya Thampratankul

Ramathibodi, Bangkok, Thailand

Background and Aims: Levetiracetam (LEV) is a new generation antiepileptic drug approved for partial onset and generalized seizures in adults and children aged over one month. Intravenous LEV, approved by the United States’ FDA in 2006, is an alternative when oral LEV is not feasible. Currently, LEV is frequently used in children with hepatic and/or cardiovascular problems and concerns over drug interaction. The recommended dosage varies from 20 to 50 mg/kg. Very limited information from pharmacokinetic studies of LEV infusions exists, particularly regarding children. This study is to determine pharmacokinetics (PK) of intravenous LEV in Thai children.

Method: This was a prospective study conducted in Thai children with clinical indication for IV LEV therapy aged between 1 month and 18 years old. Patients with glomerular filtration rate (GFR) <50 ml/min/1.73 m², severe cirrhosis and history of LEV allergy were excluded. Data collection included demographic data, underlying disease, seizure type and etiology, response and adverse effects, as well as GFR (revised Schwartz formula). All received LEV infusions of 30 mg/kg in 15 minutes. Plasma LEV levels, analyzed by LC-MS/MS, were measured at 0, 30, and 60 minutes, and 4, 8 and 12 hours after the loading dose. Pharmacokinetic parameters were determined using Kinetica 2.0 (Thermo Fisher Scientific, MA, USA) with non-compartmental model.

Results: 14 patients (50% male, mean age 115.6±14.9 months) were enrolled. Four patients received concomitant treatment with enzyme inducers, while another 4 patients received enzyme inhibitors. Notably, 3 patients had significantly prolonged half-life and delayed clearance when compared with the others. From these, two patients had sepsis and acute kidney injury, while the other had steroid resistant nephrotic syndrome. Their results were within normal range. Significant differences in gender, age group, or concomitant medication were found.

Conclusions: Pharmacokinetics of IV levetiracetam in these children revealed short half-life and rapid clearance. Patients with kidney problems had significantly prolonged half-life and slower clearance.
Application of Whole Exome Sequencing to Identify Genetic Causes of Syndromic Craniosynostosis

Yufei Xu1,2, Shouqing Sun2, Niu Li1,2, Tingting Yu1,2, Xiumin Wang3, Jian Wang1,2, Nan Bao2
1Department of Medical Genetics and Molecular Diagnostic Laboratory, Shanghai Children’s Medical Center; Shanghai Jiao Tong University School of Medicine, Shanghai 200127, China, 2Institute of Pediatric Translational Medicine, Shanghai Children’s Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200127, PR China, 3Department of Neurosurgery, Shanghai Children’s Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200127, China, 4Department of Endocrinology and Metabolism, Shanghai Children’s Medical Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200127, China

Background and Aims: Syndromic craniosynostoses are a group of multiple conditions with high heterogeneity. To identify and analyze causative genetic variants in 9 unrelated family pedigrees mainly manifested as syndromic craniosynostosis without pre-existing clinical diagnoses.

Methods: We reviewed the relevant medical information of the study subjects. Whole exome sequencing was performed in the probands and relevant variants were verified with Sanger sequencing and parental background. Bioinformatics analysis was used to evaluate the potential pathogenicity through evolutionary conservation alignment, multi-predication, and variants classification according to the criteria recommended by the American College of Medical Genetics and Genomics.

Results: We shared the strategies of interpreting the genetic results and the results revealed 9 variants in four different genes: TWIST1, FGFR2, IFT122 and SMC1A. Five (5) of the 9 variants have been identified previously, while 4 variants including three missense mutations (c.628C>T, c.3385C>T in IFT122 gene, c.3581A>G in SMC1A gene) and a frameshift mutation (c.434dupA in TWIST1 gene) were novel or extremely rare and have not been previously reported.

Conclusions: Our study not only expanded genotype-phenotype correlations, but also confirmed the underlying causative variations of syndromic craniosynostoses, and emphasized the importance of genetic testing applied in patients with syndromic craniosynostoses.

Aberrant expression of histone homocysteinylation: Implications for neural tube defects

Qin Zhang, Ting Zhang, Baoling Bai
Capital Institute of Pediatrics, Beijing, China

Background and Aims: Neural tube defects (NTDs) are serious congenital malformations. A superphysical maternal homocysteine (Hcy) level increases the risk of NTDs, but the mechanism behind this remains elusive. Previous studies have shown that cellular one-carbon metabolism (associated with NTDs) can function to directly affect histone modification and consequently plays a critical role in early embryogenesis in particular. Therefore, we hypothesized that cellular Hcy, inter-metabolites within the one-carbon metabolism, that modifies histones and aberrant histone homocysteinylation due to the disturbance of one-carbon metabolism are involved in the failure of neural tube closure (NTC).

Methods: Mass spectrometry was used to identify the new histone homocysteinylation in human fetal brain and neural stem cell; Immunoblot was used to validate the histone homocysteinylation; Hcy and HTL treatment were used to find if Hcy and HTL can regulate the level of histone homocysteinylation in neural stem cell; ChiP-seq and RNA-seq were used to find the genes regulated by histone homocysteinylation; Human NTDs and normal controls were used to test out hypothesis.

Results: In total, 39 histone homocysteinylation sites were identified in human embryonic brain tissue by QE-HF mass spectrometry. Then, the conservatism and extent of histone Hcy and H3K79Hcy were evaluated using specific anti-KHcy antibody and anti-H3K79Hcy antibody. Higher expression levels of histone Hcy and H3K79Hcy were detected, while the cellular Hcy levels were increased. ChIP-seq analysis revealed that histone H3K79Hcy bound to neural development-related genes participating in developmentally controlled processes, namely, nervous system development, generation of neurons, and neurogenesis. Combining with data from RNA-seq, our results showed that H3K79Hcy regulated the expression of selected NTC-related genes including Cecr2, Smarca4, and Dnmt3b. Lastly, in human NTDs, the decreased expression of Cecr2, Smarca4, and Dnmt3b was also detected in brain tissues with high levels of Hcy and H3K79Hcy.

Conclusions: Collectively, our results suggest that high levels of Hcy may contribute to the onset of NTDs through the upregulation of histone H3K79Hcy, leading to a decreased level of expression of selected NTC-related genes.
A randomized controlled study and valuation of children with cerebral palsy by mind acupuncture

Zhenhuan Liu¹, Yan-Chao Qi², Yong Zhao¹
¹Cerebral Palsy Rehabilitation Center of Nanhai Maternity and Children Hospital Affiliated to Guangzhou University of Chinese Medicine, Foshan, China,
²Guangzhou Cancer Hospital Guangdong, Guangzhou, China

Objective: To investigate the effects of clearing the Governor Vessel and refreshing the mind needling in neural development and remediation of children with cerebral palsy.

Methods: 200 cases of children with cerebral palsy were randomly divided into the treatment group (n=100) and the control group (n=100). The treatment group was given the combined therapy of acupuncture and rehabilitation training, and the chosen acupoints were 13 points of the Governor Vessel, Shenshu (BL 23), Taixi (KI 3), Yanglingquan (GB 34), Zusani (ST 36) and Sanyinjiao (SP 6), and points of refreshing the mind were also selected, which included puncturing Shenling (GV 24) toward Qianding (GV 21), puncturing Qianding (GV 21) toward Baihui (GV 20), puncturing Baihui (GV 20) toward Naohu (GV 17) and Sishencong (Ex-HN 1). The control group was only treated with rehabilitation training. A contrastive analysis of the therapeutic effect of acupuncture combined with rehabilitation training and pure rehabilitation training was made after a treatment course of 3 months. The Gross Motor Function Measure (GMFM) and Beijing Gesell Developmental Scale were adopted to assess the neural development and rehabilitation outcomes of the two groups. In addition, skull CT/MRI was adopted to evaluate the plerosis of injured cerebral nerve after treatment.

Results: The total effective rate in treatment group was 87%, significantly higher than the 55% in the control group (p<0.01). The improving and curing rates presented by skull CT/MRI in the treatment group were higher than the control group (p<0.01).

Conclusions: Clearing the Governor Vessel and refreshing the mind Needling could accelerate the recovery of injured brain nerve and the reconstruction of brain function. The acupuncture therapy could ameliorate both the motor development and cognitive development. On the other hand, the forward curative effect of acupuncture combined with rehabilitation training was significantly better than the pure rehabilitation training.

Experimental study of lentiviral vector-mediated ephrinb2 gene transfection rat bone marrow mesenchymal stem cells

Min Zhu, Yu Hua, Yue Zhang, Jian Tang, Xiaoke Zhao, Senjie Du
Department of Neurology and Rehabilitation, Nanjing, China

Background and Aims: To culture and identify rat bone marrow-derived mesenchymal stem cells, to detect the over-expression and morphological changes after ephrinb2 gene transfection to BMSCs and study the effect of Ephb4/ephrinB2 on rat bone marrow mesenchymal stem cells (BMSCs) in vitro.

Methods: The simple adherent method was adopted in isolating and culturing experiments of bone marrow mesenchymal stem cells (BMSCs). The inverted microscope was used to observe cells. Expression of BMSCs marker antigen was examined by flow cytometry. Lentivirus carrying ephrinb2 infected BMSCs (MOI=10) and (MOI=100), using qPCR and Western blot to detect ephrinb2 after transfection, detect the mRNA and protein’s expression. Morphological changes of BMSCs after differentiation was observed. In 28 days, the cell differentiation was determined by microtubule-associated protein 2 (MAP2), CD133 and Nestin immunofluorescent staining. For migration assay, Transwell assay was used to detect the ability of cell migration. The migration rate was assessed to study the role of Ephb4/Ephrinb2 pathway in the stem cells migration by transwell chambers. The expression of Grb4, Jnk and C-jun protein in Ephb4 / ephrinB2 reverse signal pathway were detected by Western blot.

Results: The morphological characteristics of major of the BMSCs were unified into polygonal or fusiform, germinated into a spiral shape. The BMSCs were successfully isolated, since flow cytometry results showed that rat BMSCs CD90 and CD29 positive, CD34 and CD45 negative. We confirmed exogenous ephrinb2 expression in ephrinb2-BMSCs by qPCR and Western blot.3 days after ephrinb2 gene transfection, BMSCs cell body began to shrink, refraction enhanced cell protrusions, and differentiate into the typical neuron-like cell. RT-PCR and Western blot detection of Nestin positive expression. In 15 days, expression levels of MAP2, CD133 and Nestin in the low and high concentration transfected group were significantly higher than those in the negative control group (p<0.05). Transwell assay showed the number of transmembrane cells in the low and high concentration transfected group were obviously higher compared to non-transfected group and negative control group (p<0.05). Western blot analysis showed that the expression of Grb4, Jnk and C-jun protein of were increased.

Conclusion: The simple adherent method was a feasible way to isolate, culture and purify BMSCs successfully. It laid foundation for later experimental procedures of this research. Lentiviral-mediated ephrinb2 can efficiently infect BMSCs, and differentiate into neuron-like cells. EphB4/ephrinB2 pathway can play the role of migration in bone marrow mesenchymal stem cells.
Association between maternal dietary diversity and nutritional status of under two years age children: Results from a case-control study in an urban care setting of Dhaka

Mahamudul Hasan, Munirul Islam, Ahshanul Haque, Nuzhat Choudhury, Tahmeed Ahmed
International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh

Background: Mothers have the prime responsibility of selecting, preparing, and serving nutritious foods to support their children. However, the diets of mothers are often overlooked along with potential impact of poor diet on health and nutrition of both mother and their children.

Objectives: Objective of this study was to identify association between maternal dietary diversity and nutritional status of under-2 years old children attending a diarrhoeal disease treatment hospital in Dhaka, Bangladesh.

Methods: This study was a hospital-based age and sex matched case-control study conducted among under-2 years old children attending the short-stay unit of Dhaka Hospital of icddr,b from November 2016 to February 2017. Stunted children, having a length-for-age z-score (LAZ) < -2 were selected as cases. Controls were defined as children who were not wasted or underweight (weight-for-height and weight-for-age z score ≥ -2) and have LAZ ≥ -1. Maternal dietary diversity was assessed using Guidelines for Minimum Dietary Diversity for Women (MDD-W) where mothers were asked about their recall of consumption of ten defined food groups on the previous day of the interview (24-hour recall). After collecting all the data, they were analysed using STATA software for Windows (version 13).

Results: Total 296 children (148 cases and 148 controls) were enrolled in this study. Each group comprised of 91 (61%) male and 57 (39%) female children. Mean length-for-age Z-score score was -2.71±0.51 in stunted children and -0.13±0.72 in non-stunted children. Regarding dietary diversity, about 58% mothers of case children consumed less than 5 food group on the previous day of the interview and this proportion was lower in control mothers (45%). Minimum dietary diversity score for mothers was 4.23±1.92 in cases and 4.89±1.80 in controls. Individual food groups like pulses, milk or milk like products, eggs and vitamin A rich fruits intake was higher in control mothers than cases. The risk of stunting was evident in both the unadjusted and adjusted analysis for women who consumed less than 5 food groups during 24 hr recall period. Children whose mothers consumed less than 5 food groups were 1.7 times more likely to be stunted than their counterparts (aOR=1.69, 95% CI= 1.02-2.83, p-value 0.04). Other variables (maternal illiteracy, monthly family income of less than 11480 BDT, absence of bank account and unimproved sanitation) which were found associated during bivariate analysis, did not show any significant relationship with child stunting in logistic regression analysis.

Conclusion: As no single food contains all necessary nutrients, diversity in dietary sources is needed to ensure a balanced and healthy diet for mothers, and for improved nutritional status of children.

Effect of environmental enteric dysfunction on zinc (Zn) absorption from different Zn doses in micronutrient powder: Findings from an absorption study in Peri-urban Slum of Dhaka, Bangladesh

International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh, University of Colorado, Denver, Denver, USA

Background and Aims: Environmental enteric dysfunction (EED) alters gut integrity and is suspected to impair absorption of micronutrients, including zinc (Zn), due to abnormal small bowel mucosa. Interventions with micronutrient powders (MNP) containing 5mg Zn have not yielded positive Zn sensitive outcomes. Zn requirements need to be better quantified in the context of EED to maximize the impact of preventive interventions. The aim of the study was to compare Zn absorption across a wide range of MNP Zn doses in young children at risk of EED.

Methods: Bangladeshi children aged 18-24 months old, living in a peri-urban slum, with and without EED (by urinary lactulose-mannitol excretion ratio test) were randomized to MNP with 0, 5, 10, or 15 mg (10 subjects/EED group/dose) of Zn. Outcomes by EED status included fractional Zn absorption (FAZ) from MNP meal plus from MNP unfortified meals, measured with stable isotopes by urine dual isotope tracer ratio method; total dietary Zn intake (TDZ, mg/d) measured by duplicate diet collections; and total absorbed Zn (TAZ, mg/d) measured by FAZ x TDZ. TAZ data were applied to saturation response model (SRM), and to Estimated Physiologic Requirement (EPR, = 0.74 mg/d).

Results: A total of 73 children aged between 18-24 months completed the study and comprised the analyzable sample. Mean±SD age of the participants was 19±2 months and 50% were male. Approximately 47% of subjects had EED diagnosed as lactulose-mannitol ratio being ≥ 0.09. Mean excretion ratio for EED and non EED groups were 0.211 ± 0.16 and 0.057 ± 0.02 respectively (p<0.05). Mean TAZ for MNP dose 0mg, 5mg, 10mg and 15mg was 0.5±0.3, 0.5±0.3, 0.8±0.4, and 1.0±0.4, respectively (p<0.05), with no significant difference in TAZ when segregated by EED status. Absorption followed SRM pattern but the curves of both groups were lower at all MNP doses than the curve for healthy 9 month old breastfed U.S. infants (Krebs et al, AJCN, 2012). The latter group reached the EPR with <5 mg/d Zn intake, while for current study participants, only mean TAZ for 10 and 15 mg MNP doses exceeded the EPR.
Impact of nutritional supplements on cognitive development of children in developing countries: A meta-analysis

Patrick Ip 1, Frederick Ho 1, Nirmala Rao 1, Jin Sun 2, Mary Young 3, Chun-Bong Chow 1, Winnie Tso 1, Kam-Lun Hon 4

1The University of Hong Kong, Hong Kong, 2The Education University of Hong Kong, Hong Kong, 3China Development Research Fund, Beijing, China, 4The Chinese University of Hong Kong

Background and Aims: Nutritional supplements may be important on cognition but the evidence is heterogeneous. This meta-analysis aimed (1) to determine whether nutritional supplements provided to pregnant women or young children could improve cognitive development of children in developing countries, and (2) to explore how supplementation characteristics could improve children's cognitive outcomes.

Methods: This meta-analysis examined nutritional supplementation studies in 9 electronic databases and 13 specialist websites. Experimental studies were included if they were published from 1992 to 2016, were conducted in developing countries, had nutritional supplementation for pregnant women or children aged ≤8, and reported effect sizes on cognitive outcomes. Interventions with confounded components, such as stimulation and parenting, were excluded.

Results: 67 interventions (48 studies) for 29814 children in 20 developing countries were evaluated. Childhood nutritional supplementation could improve children’s cognitive development (d 0.08, 95% CI 0.03–0.13) and nutritional supplementation could improve children’s from 20 developing countries were evaluated. Childhood nutritional supplementation should target pregnancy women in the first trimester for better cognitive benefits.

Conclusions: In conclusion, childhood nutritional supplementation was beneficial to cognitive development but could be optimised by providing multiple nutrients; antenatal supplementation should target pregnancy women in the first trimester for better cognitive benefits.

Analysis of energy intake in very-low-birth-weight infants during NICU

Fang-Wen Hu, Qing-Ya Tang

Department of Clinical Nutrition, Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China

Background and Aims: Very-low-birth-weight infants (VLBW, <1500g) need a high energy intake to achieve intrauterine growth rate. Our aim was to analysis the energy, protein, lipid intake in VLBWI during NICU, to find and improve the deficiency of clinical nutrition support.

Methods: This’s a retrospective survey. We collected the clinical data of the hospitalized VLBWI in Xin Hua Hospital in Shanghai between 1 October 2012 and 31 December 2016. The nutritional status and energy, protein, lipid intake were analyzed.

Results: A total of 128 VLBWI accepted both enteral and parenteral nutrition (EN, PN) support was selected.
Respirology

A new interpretation of overnight pulse oximetry to diagnose moderate to severe childhood obstructive sleep apnea

Siriporn Warapongmanupong,
Aroonwan Preutthipan
Ramathibodi Hospital, Faculty of Medicine, Mahidol University, Bangkok, Thailand

Background and Aims: Pulse oximetry (PO) has been used relatively most often as an alternative test to polysomnography (PSG), which was expensive and not widely available. Three clusters of desaturation on PO trend graph (POTG) were found to have 97% positive predictive value. Since 2012, the American Academy of Sleep Medicine has changed PSG scoring rules. It was unknown whether POTG is still useful or there is any other interpretation method. We aimed to determine the accuracy of 3 desaturation clusters to diagnose moderate to severe OSA as compared to PSG and to find a new simple interpretation of PO to diagnose moderate to severe OSA, which was considered to be suitable candidates for adenotonsillectomy.

Methods: We recruited consecutive snoring children with adenotonsillar hypertrophy, aged 1-15 years, referred for PSG at Ramathibodi Hospital from January 2013- August 2014. They were monitored with Masimo® pulse oximeter while performing PSG. Apnea-hypopnea index (AHI) >5 per hour of sleep was defined as moderate to severe OSA. POTG were created by Masimo® Trend-Com Graph software program and number of desaturation clusters were determined. Other parameters of SpO₂ data including minimum, maximum, mean, median, skewness, kurtosis and standard deviation (SD) were calculated automatically from the software. All of them were analyzed to identify the most useful diagnostic one.

Results: Among 166 children, 103 (62%) were male. Mean age was 6.2±2.7 years, range 2-15 years. Ninety-one (54%) were diagnosed with moderate to severe OSA by PSG. Three clusters of desaturation on POTG provided a positive predictive value of 92.3%, an accuracy of 62%, a sensitivity of 28%, a specificity of 97.5% and an area under ROC curve (AUC) of 0.629. Among all parameters, SD of SpO₂ was found to be the most promising one. The SD of SpO₂ ≥ 1.3 provided a positive predictive value of 93.9%, an accuracy of 62.7%, a sensitivity of 34%, a specificity of 97.3% and an area under ROC curve (AUC) of 0.646 for diagnosis of moderate to severe OSA patients.

Conclusions: SD of overnight PO can be used as an initial test for snoring children. It yields good diagnostic performance compared with determination of desaturation cluster numbers on POTG but the calculation of SD of SpO₂ is much easier, less time consuming and least likely to generate interpersonal disagreement on interpretation.

Acknowledgements: This work was supported by grant from Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.
Long-term changes in spirometric and airway inflammatory parameters in asthmatic children

Ting-Fan Leung1, Agnes Sze-Yin Leung4, Man-Fung Tang1, Wilson Wai-San Tam5, Yu-Ping Song1, Jennifer Wing-Ki Yau1, Hing-Yee Sy1
1Department of Paediatrics, The Chinese University of Hong Kong, Hong Kong, 2Alice Lee Centre for Nursing Studies, National University of Singapore, Singapore

Background and Aims: Asthma is caused by complex interactions between many predisposition genes and early-life and environmental factors. A proportion of asthmatic children had decreased lung function with time. On the other hand, there is limited longitudinal data as well as the genetic influences on lung function growth of asthmatic children. This study characterised the pattern of and explored determinants for changes in spirometric indices among Chinese asthmatic children.

Methods: 186 Chinese asthmatic children aged 6-12 years were recruited from paediatric allergy clinic of our university-affiliated teaching hospital. These patients were prospectively followed by the same paediatrician for five years. Pre-bronchodilator spirometry was recorded at baseline and then annually. Genomic DNA from these patients was genotyped for single-nucleotide polymorphisms (SNPs) on major asthma loci by TaqMan genotyping assays. Generalised estimating equation was used to analyse longitudinal changes in these lung function outcomes.

Results: The mean (SD) age of patients at baseline was 9.7 (1.9) years, and 117 (63%) of them were male. Twenty-nine percent had passive smoking and 54% ever received inhaled corticosteroid (ICS) treatment during follow-up. Adjusting for age and presence of upper respiratory infection within 2 weeks before visits, we found significant decline in FVC of 1% per year, and significant increase in FEV1/FVC and FEF25-75 of 1.5% and 3.7% per year respectively. Male patients had 4.8% higher FEV1 and 6.9% higher FEV1/FVC than females in any single year. However, there was no significant gender disparity in longitudinal changes for FEV1 and FEV1/FVC. Patients treated with ICS had 4.0% lower FEV1 and 3.1% lower FEV1/FVC than those without ICS, but the former group had increased FEV1 and less rapid FVC decline over time. Among asthmatics, there was no association between lung function growth and passive smoking. Rs1342326 of IL33 was associated with FEV1, FVC, FEV1/FVC and FEF25-75. Rs2305480 of GSDMB was associated with FEV1/FVC.

Conclusions: Chinese schoolchildren with asthma have significant annual decrease in FVC and increase in FEV1/FVC and FEF25-75. Boys with asthma had higher FEV1 than females. ICS-treated asthmatics have lower baseline lung function but improved lung function growth. IL33 may be a candidate gene for longitudinal changes in several spirometric indices among Chinese children with asthma.

Funding: Research Committee’s One-off Funding for Research (3132910), CUHK
Balloon dilatation in management of central airway stenosis in children

ShangZhi Wu1, KangKang Zhang2, YuNeng Lin3, JiaXing Xu4, ZhanHang Huang2, QingYun Xu2, ChangHao Zhong2, Shi Yue Li3, DeHui Chen4
1Department of Pediatrics, First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China,
2Guangzhou Medical University, Guangzhou, China,
3Guangzhou Institute of Respiratory Disease, Guangzhou, China

Background and Aims: To access the clinical efficacy and safety of balloon dilatation of central airway stenosis in children.

Methods: Retrospective analysis 49 cases of central airway stenosis in children, who were classified into 2 groups, balloon dilatation and non-balloon dilatation, to assess the etiology of central airway stenosis and evaluate the optimal indications, efficacy and safety of bronchoscopic interventional therapy.

Results: Among the 49 cases of central airway stenosis diagnosed by bronchoscopy, 12 cases (24.5%) were associated with severe pneumonia, followed by primary pulmonary tuberculosis with or without tracheobronchial tuberculosis (22.4%,11/49), stenosis after tracheal intubation (22.4%,11/49), congenital tracheal stenosis (22.4%,11/49), stenosis by compression (4.1%,2), traumatic stenosis (4.1%,2). According to the pathology of the stenosis, these cases were divided into two types: 30 (61%) cases were muscular stenosis and 19 (39%) cases were non-muscular stenosis. The response rate was 82% (14/17). The location of stenosis in 49 patients included: 14 cases (28.6%) in upper trachea, 9 cases (18.4%) in lower tracheal stenosis, 15 cases (30.6%) in left main bronchus, 7 cases (14.3%) in right main bronchus and 2 cases (4.0%) in right middle bronchus. Group of balloon dilatation had apparent hypoxia (p<0.05). The symptoms of cough, wheezing and shortness of breath were relieved after using balloon dilatation. Expansion of the airway before and after treatment the average diameter stenosis was (2.5±1.3), (4.7±0.8) mm (p<0.01). Due to Intraperitoneal transient hypoxemia. Most patients got improved after more oxygen inhalation. Two cases (4.1%) had postoperative laryngeal wheezing and shortness of breath.

Conclusions: Children of central airway stenosis with severe hypoxia was effective using Bronchoscopic balloon dilatation, compared with dyspnea, hypoxia and other serious clinical signs caused by central airway stenosis, and bronchoscopic balloon dilatation was safe and feasible.

Clinical applications of impulse oscillometry in asthma management after exacerbation in preschool children

Yong Feng, Yunxiao Shang
Department of Pediatrics, Shengjing Hospital of China Medical University, Shenyang, Liaoning, China

Background and Aims: Determination of the values of specific physiologic tests has not been well studied in long-term asthma management in preschool children. We sought to determine the utility of impulse oscillometry in a long-term management in preschool children after asthma exacerbation.

Methods: 40 outpatients, aged 3 to 5 years old, with mild-to-moderate asthma exacerbation from Shengjing Hospital of China Medical University were enrolled. The impulse oscillometry was performed immediately after enrollment (T0). And then during 24 weeks of therapy with inhaled corticosteroid, which were adjusted according to GINA report, impulse oscillometry was performed at 4 (T1), 12 (T2) and 24 (T3) weeks separately for every children. The differences of resistance at 5Hz (R5), resistance at 20Hz (R20), resonant frequency (Fres) and low frequency integrated reactance from 5Hz to Fres (AX), among four visits were measured by repeated-measures analysis.

Results: For the 40 children, 26 were boys, the average age was 3.68±0.58 years old, the weight was 17.74±3.17 kg and the height was 103.95±6.49 cm. R5 was 1.27±0.33, 1.12±0.26, 1.01±0.26 and 0.89±0.24 kPa/L/s at T0, T1, T2 and T3 separately and the differences were significant when compared in pairs. R20 was 0.77±0.19, 0.67±0.16, 0.66±0.16 and 0.59±0.15 kPa/L/s separately, and the differences were significant except between T1 and T2. R5-R20 was 0.50±0.24, 0.45±0.18, 0.35±0.19 and 0.30±0.20 kPa/L/s separately, and the differences were significant except between T0 and T1. The Fres was 25.38±6.91, 22.70±3.19, 21.41±2.40 and 20.13±2.69 Hz separately, and the differences were significant. The AX was 4.29±1.91, 3.23±1.33, 2.48±1.28 and 1.81±0.90 kPa/L separately, and the differences were significant.

Conclusions: In preschool children, with the management of asthma after exacerbation, lung function assessed by impulse oscillometry improved in different degrees. R5, Fres and AX may reflect the ongoing improvements. Assessment of respiratory mechanics over time with oscillometry might offer useful insights into the response of asthmatic preschool children to therapy. Further studies should focus on longer term of management and the relationship between impulse oscillometry and airway inflammations.
Attenuation of acute lung injury by upregulating SP-B expression via pulmonary epithelial cell specific knockdown of NAMPT

Lei Wu², Guangliang Bi², Shuiqing Ye³
¹Changsha Central Hospital, Changsha, China, ²Nanfang Medical University, Guangzhou, China, ³UMKC, Kansas City, USA

Rationale: Our preliminary study found that pulmonary epithelial cell specific knockdown of Nampt gene could attenuate LPS induced acute lung injury (ALI) in mice. Since pulmonary epithelial cell expressed SP-B plays a significant role in normal lung physiology and its downregulation was implicated in the pathogenesis of ALI, we intended to investigate whether therapeutic effect of epithelial cell specific knockdown of Nampt on ALI is in part due to its upregulation of SP-B expression to shed some light on the underlying molecular mechanisms in order to further develop a new NAMPT based therapeutic modality to ALI.

Methods: Four groups of C57BL/6J male mice, 8-12 weeks old [(1) wild type, (2) lung epithelial cell specific Nampt knockdown (Nampt⁵⁺⁻) mice prepared in our lab by crossing Nampt gene exon2 floxed mice with mice expressing Cre in lung Clara cells, (3) wild type mice + intratracheally delivered Ad- SPC-Nampt-antisense scFv for 72 h, (4) wild type mice + intratracheally delivered Ad- SPC-Nampt-scFv, an adenovirus based and SPC promoter driven anti-Nampt single chain variable fragment antibody, for 72 h] were intratracheally administered with LPS (2 mg/kg) or PBS for 24 h before their bronchoalveolar lavage (BAL) and lung tissues were harvested for various assays. In vitro, A549 cells and H441 cells had been transfected with pCAGGS vector only, pCAGGS-NAMPT cDNA, pCAGGS NAMPT H247E, scRNA or NAMPTsiRNA or treated with pharmacological inhibitors for 48 h plus additional 6 h with or without LPS or TNFa treatment before their SP-B mRNA or protein levels were quantified.

Results: Nampt⁵⁺⁻ mice or mice receiving the Ad- SPC-Nampt-scFv treatment exhibited attenuated ALI (lung injury score: 4.10?1.11 vs 7.20?0.89, n=6 per group, p<0.01 or 5.71?1.23 vs 8.50?1.12, n=5 per group, p<0.01, respectively) and significantly increased their BAL SP-B expressions over their controls. Down regulation of NAMPT expression by either NAMPT siRNA or FK866, a NAMPT enzymatic inhibitor, increased the expression of SP-B at a basal level as well as rescued the TNF-α or LPS mediated inhibition of SP-B expression while overexpression of NAMPT inhibited SP-B expression in human A549 cells or H441 cells. NAMPT H247E like NAMPT wild type similarly inhibited SP-B expression. The JNK inhibitor abolishes NAMPT’s effect on SPB expression.

Conclusion: Lung epithelial cell-specific knockdown of Nampt gene expression significantly attenuated LPS induced ALI in part via its upregulation of SP-B expression through its nonenzymatic functions and JNK pathway.
Silencing of Pin1 suppresses oxidative stress-induced apoptosis of A549 cells

Shuai Zhao, Wenbin Dong, Chan Zhang, Xiaoping Lei, Lan Kang
Department of Neonatology, the Affiliated Hospital of Southwest Medical University, Iuzhou, China

Background: The peptidyl prolyl cis/trans isomerase (Pin1) has attracted considerable interest as an inhibitor of tumor cell targets. Pin1 is important in the oxidative stress pathway. We hypothesize that inhibition of Pin1 expression might dampen hyperoxic lung injury. Moreover, the mechanism responsible for this process is poorly understood.

Objective: We aimed to explore the role of Pin1 in the oxidative stress-signaling pathway and apoptosis in hyperoxia-exposed A549 cells.

Methods: The gene sequences were cloned into the pLenR-GPH-shRNA lentiviral vector, which was selected by Gene bank searches. The pLenR-GPH-shRNA and lentiviral vector packaging plasmid mix were cotransfected into 293T cells to package lentiviral particles. Culture virus supernatant was harvested, and then the virus titer was determined by serial dilution assay. A549 cells were transduced with the constructed lentiviral vectors, and real-time polymerase chain reaction (qPCR) and Western blot were used to evaluate Pin1 expression. The study is divided into a control group, a hyperoxia group, an A549-Pin1shRNA hyperoxia group. Its expression. Both qPCR and Western blot demonstrated downregulation of Pin1 expression in A549 cells. Cells apoptosis was detected by flow cytometry (FC) after 24 hrs, the expression of XIAP (X-linked inhibitor of apoptosis protein) and Caspase-9 were detected by immunohistochemistry. The production of ROS (reactive oxygen species), and cell mitochondria membrane potential (△Ψm) were determined by fluorescence microscopy.

Results: We established an A549-Pin1shRNA and inhibited expression. Both qPCR and Western blot demonstrated downregulation of Pin1 expression in A549 cells. In the A549-Pin1shRNA hyperoxia group, we found dampened oxidative stress.

Conclusion: Pin1 mediates the oxidative stress-induced signal pathway in hyperoxia-exposed A549 cells.

Loss of Thy-1 from myofibroblasts in progressive pulmonary fibrosis and reversibility of myofibroblast phenotype with soluble Thy-1

Min Jiang¹, Simon S. Wong², Ceonne Kim², Edward Connors², Celia R. Espinoza², James S. Hagood²
¹The First Affiliated Hospital of Guangxi medical university, Guangxi, China, ²University of California San Diego, San Diego, USA

Background: Previous studies have demonstrated Thy-1 expression decreases in aging lungs, and is silenced in fibroblastic foci associated with idiopathic pulmonary fibrosis (IPF). Repeat-dose intratracheal bleomycin (Bleo.) administration in mice results in progressive fibrosis, unlike the self-resolving fibrosis seen in the more widely used single-dose Bleo. model. In this study, we utilized a repetitive lung injury mouse model to determine whether progresive, non-resolving fibrosis is associated with Thy-1 loss in lung fibroblasts, and to what extent soluble Thy-1 (sThy-1) reverses myofibroblast differentiation in vitro.

Methods: Progressive lung fibrosis was induced in Col-GFP mice (6-8 weeks old) by 1 unit/kg Bleo. or saline (control) instilled intratracheally (IT) every 12 days for four doses. Single dose injection mouse model were instilled IT with 4 unit/kg Bleo. Thy-1 expression and fibrotic tissue remodeling were evaluated at 4 weeks and 8 weeks after final instillation by qPCR and immunofluorescence staining. Normal human fibroblasts were treated with TGFβ1 to monitor myofibroblast differentiation, the ability of a sThy-1 fusion protein (sThy-1-Fc) or mutated constructs of soluble human Thy-1-Fc (sThy-1 RLE) inhibit myofibroblast differentiation were determined by measuring expression of fibrotic genes both in transcriptional and protein levels.

Results: Using a repetitive lung injury mouse model and a traditional single dose model of intratracheal injection of Bleo., we show that Col-1A1, Col-III gene expression and collagen I deposition are reduced at 8 weeks after single dose Bleo. injection. No significant change in Thy1 gene expression was observed at 4 or 8 weeks post single dose Bleo administration. However, repetitive Bleo. instillation induced persistent fibrosis as assessed by Col-1A1, Col-III gene expression and immunofluorescence staining to detect collagen I and αSMA levels. Furthermore, Thy-1 gene expression significantly decreased at 8 weeks. Histological examination with IF confirmed that Thy-1 noticeably was down regulated in GFP-expressing myofibroblastic regions at 4 weeks, and that no significant recovery occurred at 8 weeks. By administrating sThy-1, ACTA2 and Col-1A1 gene and protein expression were significantly decreased after 1000 ng/mL sThy-1-Fc treatment when compared with sThy-1 RLE and controls.

Conclusion: Single-dose Bleo.-induced lung injury promotes reversible lung fibrosis associated with decreased myofibroblasts and recovery of Thy-1 expression, while repetitive lung injury induces progressive, non-resolving lung fibrosis associated with sustained silencing of Thy-1 expression in myofibroblasts. sThy-1 partially reverses differentiation of senescent human lung myofibroblasts, and the effect of sThy-1 requires the RLD integrin-binding motif. (Supported by NIH R01 HL111169-01A1).
Effect and mechanism of PM2.5 on airway inflammation in asthmatic mice

Meizheng Zhan, Weihui Ma, Leping Ye
The Second Affiliated Hospital and Yuying Children’s Hospital of Wenzhou Medical University, Wenzhou, China

Background and Aims: To explore the effect of fine particulate matter (PM2.5) on airway inflammation in normal and asthmatic mice as well as the regulation of PM2.5 on the expression of 11βHSD1 and 11βHSD2 in lung, and to investigate the preliminary mechanisms of PM2.5 for promoting inflammation.

Methods: 42 BALB/c mice were randomly divided into six groups (n=7): normal control group (NC), PM2.5 low-dose group (NP1) (3.5 mg/kg), PM2.5 high-dose group (NP2) (10 mg/kg), asthmatic group (AC), Asthma + PM2.5 low-dose group (AP1), asthma + PM2.5 high-dose group (AP2). Mice model of allergic asthma and PM2.5 exposure was established respectively. All animals were sacrificed for leukocyte count, HE staining and BALF ELISA kit detection. Real-time quantitative PCR and Western Blot method were applied to observe effect of PM2.5 on 11βHSD1 and 11βHSD2 mRNA and protein expression.

Results: (1) BALF lymphocyte count and proportion, eosinophil count and proportion of NP2, AC, AP1, AP2 groups are higher than the control group and the difference was significant. The number of eosinophils in AP2 group was higher than that in AC group and AP1 group (p<0.01). (2) The levels of IL-4 and IL-5 in BALF of AP1 group and AP2 group were higher than those in normal group (p<0.05). The concentration of IFN-γ in BALF of AP1 and AP2 groups was lower than that of normal group (p<0.01).The concentration of IL-4 and IL-5 in AP2 group were significantly higher than those in AP group. The concentration of IFN-γ in AP2 group was lower than that of AC group and AP group (p<0.05). (3) The expression of 11βHSD1 mRNA in NP2 group was higher than that in NP1 group. The expression level of 11βHSD1 mRNA in AP2 group was lower than that in normal group (p<0.01). The expression of 11βHSD2 mRNA in NP2 group and AP2 group was higher than that in normal control group. Compared with the AP1 group and normal group, the expression of 11βHSD2 in AP2 group was increased (p<0.05).

Conclusions: PM2.5 promote the immune response of Th2 cells and leading to the airway Th1/Th2 immune imbalance. PM2.5 can upregulate the 11βHSD1 level in lung tissue of normal mice. High dose PM2.5 down regulate the expression of 11βHSD1 in asthmatic mice. PM2.5 can upregulate the level of 11βHSD2 in lung tissue of normal and asthmatic mice.

Epigallocatechin gallate ameliorates airway inflammation by inducing regulatory T cells in an asthmatic mouse model

Nan Yang, Yunxiao Shang
Department of Pediatrics, Shengjing Hospital of China Medical University, Shenyang, Liaoning, China

Objective: Epigallocatechin gallate (EGCG) is a polyphenol that is found in green tea that has been shown to ameliorate airway inflammation in an ovalbumin-sensitized asthmatic mouse model. The purpose of this study was to investigate whether the immunomodulatory and anti-inflammatory effects of EGCG by enhancing the regulatory T cell (Treg) in this model.

Methods: Female BALB/c mice were sensitized and challenged with ovalbumin by intraperitoneal injection. EGCG was administered to asthmatic mice intraperitoneally one hour before each OVA challenge. Airway hyperresponsiveness (AHR) was measured, and lung inflammatory infiltrates were assessed by hematoxylin and eosin (HE) staining. Serum OVA-specific IgE level and Interleukin-10 (IL-10) levels in the bronchoalveolar lavage fluid (BALF), serum, and splenocyte culture supernatants were measured by ELISA. Flow cytometry was used to assess the effects of EGCG on the number of CD4+CD25+Foxp3+Treg cells in the splenocytes and real-time PCR was used to measure the expression of Forkhead box P3 (Foxp3) mRNA in the lung tissue.

Results: The results showed that administration of EGCG significantly decreased AHR and OVA specific IgE in the serum, increased IL-10 levels in the BALF, serum, and splenocyte culture supernatant, and the number of CD4+CD25+Foxp3+Treg cells in the splenocytes in asthmatic mice. Administration of EGCG also ameliorated airway inflammation and eosinophil infiltration in asthmatic mice. These results suggested that EGCG likely ameliorated OVA-induced airway inflammation by increasing the production of IL-10, the number of CD4+CD25+Foxp3+Treg cells and expression of Foxp3 mRNA in the lung tissue.

Conclusions: EGCG could be an effective agent for treating asthma by inducing regulatory T cells to ameliorate airway inflammation.
Rheumatology

18

Adult outcome of juvenile idiopathic arthritis: A nationwide population retrospective cohort study in Taiwan

Su Boon Yong1, Jing-Yang Huang2, Jeng-Yuan Chiou3, James Cheng-Chung Wei4

1Division of Pediatric Allergy, Immunology and Rheumatology, Department of Pediatrics, Show Chwan Memorial Hospital, Changhua, Taiwan, 2Department of Medical Research, Chung Shan Medical University Hospital, Taichung, Taiwan, 3School of Health Policy and Management, Chung Shan Medical University, Taichung, Taiwan, 4Division of Allergy, Immunology and Rheumatology, Chung Shan Medical University Hospital; Institute of Medicine, Taiwan

Background: This population-based case-control study investigated the development of juvenile idiopathic arthritis (JIA) and the subsequent risks of developing rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), psoriatic arthritis, ankylosing spondylitis (AS), and Sjogren’s disease in adulthood.

Methods: We analyzed data from 107,433 children born between 1990 and 1997 to identify those with JIA. We then retrospectively followed them up until December 2013 to observe the occurrence of autoimmune diseases. There were 262 patients with JIA diagnosed between 2000 and 2012, and 107,171 controls. For those with JIA, the hazard ratios and percentage of developing adult autoimmune diseases were calculated. The hazard ratios were further stratified by age of JIA diagnosis (3-5 years, 6-10 years, and 10-15 years). Cox proportional regression models were used to compare the adjusted hazard ratios (aHR) of adult-onset autoimmune diseases among the study subgroups.

Results: The subsequent risks of RA, SLE, AS, psoriatic arthritis, and Sjogren’s disease in adulthood were increased in the originally JIA group. The incidence rates (per 105 person months) were 83.56 (95% confidence interval [CI], 44.96-155.29), 16.61(4.15-66.40), 58.39(27.83-122.49), and 33.26 (12.48-88.61) for RA, SLE, AS, and psoriasis, respectively. The adjusted hazard ratios (aHR) were 29.597 for any autoimmune disease (95% CI, 21.145-41.426), 129.518 for RA (70.185-239.012), 10.007 for SLE (3.189-31.402), 49.624 for AS (29.699-82.917), and 8.199 for psoriasis (2.618-25.675). The highest risk of adult-onset RA was in JIA patients who were first diagnosed at age 3-5 years old.

Conclusions: Children with JIA were at increased risk of developing RA, SLE, AS, psoriatic arthritis, and Sjogren’s disease in adulthood. The increased risk was associated with the cumulative effect of concurrent rheumatologic diseases. Further study to investigate the role of JIA in the development of adult-onset rheumatic diseases is warranted.

133

The incidence and risk factors of recurrent HSP in children: estimation using a 16-year comprehensive nationwide database

Wei-Te Lei
Mackay Memorial Hospital, Hsinchu City, Taiwan

Background: The recurrence rate of Henoch-Scholein Purpura (HSP) was shown ranged from 2.7% to 30% in previous studies. The average interval between the first and second episode varied. Few studies have explored the incidence and risk factors of recurrent HSP.

Methods: This retrospective cohort study used a 16-year nationwide database to analyze the incidence of recurrent HSP. Patients with HSP were identified. Associated risk factors for the recurrence of HSP were explored. Kaplan-Meier and Cox regression model were performed for the analyses.

Results: From 1996 to 2013, of the 2,886,836 persons from the NHIRD database, 1002 patients under 18 years old were identified that had HSP. Among them, 164 had more than 2 times of HSP. The recurrent rate of HSP was 16.4%. The incidence of recurrent HSP was 7.5 per 100 person-years. At the end of the 16-year cohort, 83.6% of patients who had first HSP remained free from secondary HSP. The average time interval between the first and second HSP was 9.2 months; and was 6.4 months between the second and the third HSP. After adjusting for demographic parameters, comorbidities and socioeconomic status, recurrent HSP occurred more among patients with renal involvement (adjusted hazard ratio=2.41, 95%CI, 1.64-3.54, p<0.001), steroid therapy more than 10 days (adjusted hazard ratio=8.13, 95%CI, 2.51-26.36, p<0.001), and allergic rhinitis (adjusted hazard ratio=1.63, 95%CI, 1.06-2.50, p=0.026).

Conclusion: The annual incidence of recurrent HSP was not high. However, children with underlying allergic rhinitis, presented with renal involvement and had steroid treatment more than 10 days should be notified the possibility of recurrence and should be followed up for at least 9 months.
Influence of photoirradiation on the measurement of direct bilirubin by the vanadic acid method

Shohei Kawamoto, Hitoshi Okada, Susumu Itoh, Miyo Ozaki, Kohichiro Nii, Masashiro Sugino, Takeo Kondo, Sonoko Kondo, Saneyuki Yasuda, Takashi Kusaka

Introduction: Our team has been conducting research on bilirubin with emphasis on bilirubin photoisomers (BPs) in neonatal hyperbilirubinemia. (ZZ)-Bilirubin is photochemically converted into various water-soluble BPs. This mechanism is utilized for phototherapy. The standard laboratory test sometimes detects high direct bilirubin (DB) levels in neonates after phototherapy. Several methods of DB measurement are affected by BPs, but it is not known whether BPs affect the vanadic acid (VA) method, which is commonly used in Japan.

Objectives: To elucidate the involvement of BPs in DB measurements by the VA method after photoirradiation in vitro.

Methods: DB levels were measured before and after 15-s or 60-min blue light-emitting-diode photoirradiation of bilirubin/albumin mixtures. The VA method determines the DB level from the difference in absorbance at 450nm between the time of mixing a tartrate buffer with a sample (point A) and the time of adding a VA solution to the resulting mixture (point B). BPs were measured by high-performance-liquid-chromatography (HPLC) method reported by Itoh et al. (J Chromatogr A 1999). HPLC chromatograms were recorded at 455nm to measure BPs at point A and point B. The measurement was repeated five times in each session.

Results: The DB level increased by 0.37 mg/dL after 15-s photoirradiation and by 1.12 mg/dL after 60-min photoradiation compared with before photoirradiation. Before photoirradiation, BPs were not detected and only (ZZ)-bilirubin was detected at both point A and point B. After 15-s photoirradiation, (ZE)-bilirubin and (ZZ)-bilirubin were detected at point A, while only (ZZ)-bilirubin was detected at point B. After 60-min photoirradiation, (EE)-cyclobilirubin, (EZ)-cyclobilirubin, (ZE)-bilirubin, (EZ)-bilirubin and (ZZ)-bilirubin were detected at point A, while only (ZZ)-bilirubin was detected at point B.

Discussion: The VA method calculates the DB level from the difference in absorbance between before and after addition of VA; this difference increased after photoirradiation. Before photoirradiation, only (ZZ)-bilirubin was observed at both point A and point B, and not converted into BPs. Therefore, the increase in DB after photodark of the VA method included BPs.

Conclusion: After photoirradiation, DB values calculated by the VA method include BPs.

A scoping review of injury outcome indicators: Implications for injury surveillance

Tim MH Li, Keith TS Tung, Zi-Qi Kok, Patrick Ip, Wilfred HS Wong, Chun-Bong Chow

Department of Paediatrics & Adolescent Medicine, the University of Hong Kong, Hong Kong

Background and Aims: The aim of this review is to identify and scope injury outcome indicators for injury surveillance.

Methods: Literature search was conducted to identify existing injury outcome indicators using academic databases including Web of Science, PubMed, and ProQuest, and hand searching by Google Scholar. The method of this scoping review is an iterative process of search and analysis. After three rounds of review, researchers identified that saturation had occurred and stopped the searching process. Forty-seven search queries were generated to achieve a representative sample of the distribution of an evidence base across the topic area in this study. The searching process was outlined for identification of possible aspects of search terms which could contribute to more relevant results upon expansion of further literature search.

Results: Upon analysis of 142 articles, a total of 52 indicators were identified and were classified into four domains: in-hospital performance (17 indicators), functional/psychological outcomes (18 indicators), biological/physiological outcomes (9 indicators), and long-term impacts (7 indicators). There were injury severity definitions that were common across injury types. A synthesis of the findings and their significances in each domain were described.

Conclusions: Findings suggested that the list of injury outcome indicators in this review can serve as a set of indicators for different countries to extract their relevant set of indicators. A set of existing indicators relevant to a region is of particular importance for injury surveillance.
Selection of endotracheal tube cuff for children with congenital heart disease based on an ultrasound-based linear regression formula

Kan Zhang, Jijian Zheng, Hualin Chen, Yiqi Chen, Jie Bai, Mazhong Zhang

Department of Anesthesiology Shanghai Children’s Medical Center, Shanghai, China

Background and Aims: The use of empirical age-based formula to determine the endotracheal tube (ETT) size has been reformed after the introduction of ultrasound technology. However, it remains to be discovered whether an ultrasonography-based formula used to determine the subglottic transverse diameter for the selection of an appropriate ETT cuff for children with normal heart anatomy is useful for children with congenital heart disease (CHD).

Methods: A regression formula for predicting the subglottic diameter (SGD_{ultra}) was established after assessing 60 children \( \leq 8 \) years without CHD. The formula was validated on a group of 60 children with CHD. We selected the ETT cuff based on the SGD determined by ultrasound (SGD_{ultra}). Subsequently, the fit of the ETT cuff in 60 children who underwent cardiosurgery was examined via air leak test. The maximum allowed difference between the SGD predicted using the formula and the ETT cuff size that fit was 0.2 mm. The agreement among and accuracy of SGD_{ultra}, SGD_{formula} and the ETT used in children with CHD was analyzed.

Results: For children without CHD, we adopted a linear regression formula, given by SGD_{formula}(mm) = 0.4*age + 5.3. For children with CHD, we adopted an allometric formula, given by SGD_{formula}(mm) = 5.4*age^{0.18}. A stronger agreement existed between SGD_{ultra} and ETT compared to that between SGD_{formula} and ETT, and bias was 0.21 mm (95% confidence band, -0.59 to 1.01 mm) and -0.00 cm (-0.79 to 0.84 mm), respectively. Furthermore, for the CHD group, the ultrasound-based method yielded a 78% (47/60) success rate, while the formula-based method permitted an appropriate selection of ETT in only 32% (19/60) of subjects (P=0.00).

Conclusion: Our analysis shows that the allometric equation is ideal for children with CHD, and the linear regression equation is best suited for children without CHD. SGD_{ultra} was more accurately able to predict the ETT size for children awaiting cardiovascular surgery, while the linear regression equation was better for predicting the relationship between age and SGD.
Protective effect of nasal mucosa on PM$_{2.5}$-induced lung injury in mice

Jieqiong Liang, Yingxia Lu, Qinglong Gu

Capital Institute of Pediatrics affiliated Children’s Hospital, Beijing, China

**Object:** The purpose of this study was to explore whether the nasal mucosa can protect the PM$_{2.5}$-induced lung injury in mice.

**Methods:** The study was carried out in BALB/C mice. 40 mice were randomly divided into four groups, including normal control group (NC group), nebulized by normal saline group (NS group), nebulized by PM$_{2.5}$ suspension group (PS group) and nebulized by PM$_{2.5}$ suspension with blocked nose group (PB group). Mice in NS, PS and PB groups were treated by nebulization, lasting for 40 minutes once a day, for total 14 times with an interval of 24 hours. All animals were sacrificed after the last nebulization within 24 hours, then bronchoalveolar lavage fluid (BALF) was collected at the same time. The levels of acidic phosphatase (ACP), alkaline phosphatase (AKP), lactate dehydrogenase (LDH) and the levels of IL-6, TNF-α, IL-1β in BALF were examined. Pathological of lung and nasal mucosa were also observed meanwhile. The data were analyzed by SPSS 20.0.

**Results:** (1) After nebulization, the increase of mice weight in PS group was lower than that of NC group (p=0.041), while that of PB group was the least among all the groups (p<0.05). (2) Lung and nasal mucosa histopathology: lung histopathology demonstrated that inflammatory changes in different degrees were observed in some animals, along with lymphocytic infiltration, lung inflation, wall thickening, pulmonary interstitial hyperplasia and increased edema and lung consolidation. Quantitative scores were used to compare pathological manifestations conveniently. The scores of PB, PS, NS, NC were 11.90±1.79, 9.90±2.07, 7.20±1.55, 5.70±1.16 respectively. The scores of pathological injury of PB group were higher than those of the other three groups (p<0.05). The nasal mucosa of mice had no obvious manifestation of inflammation. (3) Comparison of the levels of enzymes and cytokines in BALF: The levels of ACP and LDH in PB group and PS group were higher than those in NC and NS groups respectively (p<0.05). And furthermore, the level of LDH in PB group was higher than that in PS group (p<0.05). (4) Comparison of the levels of inflammatory cytokines in BALF: The levels of IL-6 and IL-1β in PB group and PS group were higher than those of NC group and NS group (p<0.05). In addition, the level of IL-6 in PB group was higher than PS group.

**Conclusion:** (1) PM$_{2.5}$ inhalation can be involved in the lung inflammatory response. (2) Nasal breathing may alleviate PM$_{2.5}$-induced lung injuries than mouth breathing.
Adolescent Health

40 Philippines Eating Attitudes Among K7-K11 Students Using Eating Attitude Test-26 in Both Private and Public Schools in Quezon City, Philippines Melisa Intan, Gloriosa Galindez

38 Taiwan Global investigation of B cell immune repertoire in Kawasaki diseaseLien-Hung Huang, Sung-Chou Li, Cheng-Tsung Pan, Ying-Hsien Huang, Fu-Chen Huang, Weng-Shin Lin, Ho-Chang Kuo

123 Japan Parental Internet Use and Lifestyle Factors as Correlates of Screen Time of Children in Japan: Results from the Super Shokoku School (SSS) ProjectMasaki Yamada, Michikazu Sekine, Takashi Tatsuse

50 Japan Tonsillar Histopathology of Kawasaki Disease Presenting the Retropharyngeal lymphadenopathySeigo Okada, Yuki Kobayashi-Fujisawa, Atsunori Oga, Takashi Furuta, Kenzo Ikemoto, Hironori Fujii, Yassufumi Sakata, Yasuo Shioshi, Shunji Hasegawa, Takeshi Kusuda, Hiroshi Ito, Hiroshi Yamashita, Shouichi Ohga

165 Thailand Psychosocial Functioning Among Lesbian, Gay, Bisexual, and Queer (LGBQ) Youths in Northern ThailandNonglak Boonchooduang, Orawan Louthrenoo


203 Thailand Cyberbullying and Emotional-Behavioral Functioning Among Northern Thai AdolescentsOrawan Louthrenoo, Nonglak Boonchooduang

100 Taiwan The Association Between Body Height and Total Immunglobulin (IgE) LevelsLiu-Hui Li, Ho-Chang Kuo

204 Thailand Relationships Between Smoking, Alcohol Consumption, and Dietary Habits in Northern Thai AdolescentsNarueporn Likhitweerawong, Nonglak Boonchooduang, Orawan Louthrenoo

245 Hong Kong A Case-cohort Study on the Psychosocial Properties of Obese AdolescentsRobert Pa-Yee Loung, Iris Yee-Man Poon, Susan Ching-Shan Fung, Winnie Kwai-Yu Chan, Winnie Wing-Yee Tie

252 Hong Kong Chinese medical students’ knowledge, attitude, and practice towards Human papillomavirus (HPV) vaccination and their intention to recommend the vaccineAnthony Liu, Frederick Ho, Lily Chan, Joanne Ng, Sophia Li, Ko Ling Chan, Godfrey Chan, Ting-Fan Leung, Patrick Ip

126 Taiwan Different Classification of CVID Patients using B-cell SubsetsReza Yazdani, Robabeh Seify, Miazdak Ganjalikhani Hakemi, Nima Rezei, Asghar Aghamohammadi

127 Iran The Incidence of Asthma and Allergic Diseases in a Cohort of Patients with Common Variable ImmunodeficiencyReza Yazdani, Amin Heydari, Hassan Abolhassani, Asghar Aghamohammadi, IranReza Yazdani, Amin Heydari, Hassan Abolhassani, Asghar Aghamohammadi

1507 Japan Possibility of discrimination of plural personae in one body using non-linear regression analysisSung Kim, Masaki Ryosyo, Keichirou Yoneyama, Shinch Sakamoto, Urara Fukuchi, Keizo Sao, Hoyojin Lee, Toshioka Sawaguchi

153 India Abbreviated Plasmapheresis with High Dose Immunosuppression in Anti Complement Factor H Antibody Hemolytic Uremic Syndrome: Report of Twelve Cases From Tertiary Care Centre in North-West IndiaRakesh Kumar Pilania1, Karalongin Tiewsoh, Ankur Kumar Jindal, Armit Rawat, Rekha Hans, Raja Ramchandan, Deepthi Suri, Anju Gupta

10 Taiwan M1 and M2 macrophage mRNA expression profiles in patients with Kawasaki diseaseMindy Guo, Kai-Sheng Hsieh, Mao-Hung Lo, Ying-Hsien Huang, Ling-Sai Chang, Ho-Chang Kuo Taiwan

158 Taiwan Allergen Detection and Analysis in Eastern Taiwan Are-Ahtong-Hwa jan

35 Hong Kong A Novel Case of Systemic Delayed-type Hypersensitivity to Local AnestheticsJaime Rosa Duque, Patrick CY Chong, Yu-Lung Lau, Marco HK Ho

161 Hong Kong Severe Recalcitrant Eczema in A Child with Heterozygous FLG Gene Null Mutation and Heterozygous STAT6 Missense MutationGilbert T Chua, Pamela Pui-Wah Lee, Brian Hon-Yin Chung, Chun-Yin Chang, Marco Hok-Kung Ho, Yu-Lung Lau

Allergy & Immunology

10 Taiwan M1 and M2 macrophage mRNA expression profiles in patients with Kawasaki diseaseMindy Guo, Kai-Sheng Hsieh, Mao-Hung Lo, Ying-Hsien Huang, Ling-Sai Chang, Ho-Chang Kuo Taiwan

158 Taiwan Allergen Detection and Analysis in Eastern Taiwan Are-Ahtong-Hwa jan

35 Hong Kong A Novel Case of Systemic Delayed-type Hypersensitivity to Local AnestheticsJaime Rosa Duque, Patrick CY Chong, Yu-Lung Lau, Marco HK Ho

161 Hong Kong Severe Recalcitrant Eczema in A Child with Heterozygous FLG Gene Null Mutation and Heterozygous STAT6 Missense MutationGilbert T Chua, Pamela Pui-Wah Lee, Brian Hon-Yin Chung, Chun-Yin Chang, Marco Hok-Kung Ho, Yu-Lung Lau
Combined analysis revealed a modestly negative correlation between DNA methylation and gene expression and showed S100A family played important roles in the pathogenesis in Kawasaki disease.

Kawasaki Disease and Cyclic Neutropenia in Two Siblings: A Rare Association

The Risks between Allergic Disorders and Vegetarian Diet in Childhood

IL33 Plays a Positive Role in the Interaction between Alternative Activated Macrophage and Regulatory T Cells

Clinical, Molecular and Immunological Characterization of Five LRBA Deficiency in China

A study of allergenic proteins which are susceptible to cow milk protein allergen in different formulas

Changes of fecal sIgA and intestinal barrier function in children with different type of Henoch-Schonlein purpura

Activation of NLRP3 Inflammasome Bridges Innate Immune Recognition of Toll-like Receptors to Induction of Adaptive Th and Th17 Response

Changes of eosinophils in Kawasaki Disease and their Association with Coronary Artery Lesions Formation

All Submitted Abstracts with QR codes

Taiwan
Korea
India
Taiwan
Hong Kong
Hong Kong
Hong Kong
China
China
China
China
China
China
China
Japan
China
Hong Kong
Taiwan
Cardiology
<table>
<thead>
<tr>
<th>Page</th>
<th>Country</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>Japan</td>
<td>Effectiveness of biphasic cuirass ventilation on protein-losing enteropathy and plastic bronchiolitis in a patient with failing Fontan circulation</td>
<td>Seigo Okada, Jun Muneuchi, Yusaku Nogatomo, Kaori Nonaka, Chiaki Iida, Hiromitsu Shirouzu, Ryoei Matsuoka, Mamie Watanabe, Kunitaka Joo</td>
</tr>
<tr>
<td>69</td>
<td>Japan</td>
<td>Right ventricular performance after surgical closure of ventricular septal defect</td>
<td>Yuichiro Hashida, Hitoshi Uemasu, Shinai Sakata, Yoichi Mino, Susumu Kanakaki</td>
</tr>
<tr>
<td>80</td>
<td>Japan</td>
<td>An impact of aggressive surgical interventions in individuals with trisomy18; For achieving home medical care</td>
<td>Chiaki Iida, Jun Muneuchi, Mamie Watanabe, Yuichiro Sugitani, Yusaku Nogatomo, Seigo Okada, Hiromitsu Shirouzu, Naoki Kawaguchi, Ryoei Matsuoka</td>
</tr>
<tr>
<td>88</td>
<td>Taiwan</td>
<td>Maternal age are associated with coronary artery lesion formation in Kawasaki Disease</td>
<td>Chiaki Iida, Jun Muneuchi, Mamie Watanabe</td>
</tr>
<tr>
<td>212</td>
<td>Japan</td>
<td>Assessment of Biological Characteristics for Angiogenesis in Aorto-Pulmonary Collateral Artery Model Rat with Left Pulmonary Artery ligation under Hypoxia environment</td>
<td>Reiji Ito, Takashi Urashima, Miki Itohisa, Kenji Yoshida, Takuma Mori, Masatoshi Iijima, Tatsuya Ando, Hiroyuki Ida</td>
</tr>
<tr>
<td>228</td>
<td>Japan</td>
<td>Pulmonary arterial resistance and compliance in Down syndrome</td>
<td>Yuka Matsushita, Jun Muneuchi, Yuka Inoue-Kawatoko, Seigo Okada, Naoki Kawaguchi, Hiromitsu Shirouzu, Chiaki Iida, Yuichiro Sugitani, Mamie Watanabe</td>
</tr>
<tr>
<td>277</td>
<td>Japan</td>
<td>Validation of the Pediatric Index of Mortality (PIM) Score in Kawasaki Disease</td>
<td>Yuki Matsushita, Yuka Inoue-Kawatoko, Seigo Okada, Naoki Kawaguchi, Hiromitsu Shirouzu, Chiaki Iida, Yuichiro Sugitani, Mamie Watanabe</td>
</tr>
<tr>
<td>295</td>
<td>Thailand</td>
<td>How Do We Manage Unresectable Cardiac Tumor in Children?</td>
<td>Phoomipoom Katanyuwong, Piya Samarnkatiwat, Alisa Limswan</td>
</tr>
<tr>
<td>374</td>
<td>China</td>
<td>Peptidomic analysis of maternal serum to identify biomarker candidates for prenatal diagnosis of Tetralogy of Fallot</td>
<td>Bin Zhuang, Shuping Han, Zhangbin Yu</td>
</tr>
<tr>
<td>802</td>
<td>China</td>
<td>Clinical features and prognosis in cases of neonatal Cardiomyopathy</td>
<td>Guo Xiaolin, Zhao Zhankui, Li</td>
</tr>
<tr>
<td>1266</td>
<td>China</td>
<td>Postoperative Pulmonary Vein Stenosis in Scimitar Syndrome: A Case Report and Literature Survey</td>
<td>Hailing Song, Jiaming Wang</td>
</tr>
<tr>
<td>1339</td>
<td>China</td>
<td>Left atrial appendage inversion: A rare intracavitary atrial mass in a cardiac postoperative child</td>
<td>Jingying Ye, Jiangen Yu, Qiang Shu</td>
</tr>
<tr>
<td>1392</td>
<td>China</td>
<td>Diagnosis of the therapeutic strategies to congenital coronary artery fistula in children</td>
<td>Lin Hu, Shu-Shui Wang, Yu-Jen Li, Guo-hong Zeng, Zhu-Wei Zeng, Li Zhang</td>
</tr>
<tr>
<td>1592</td>
<td>China</td>
<td>MIR-22 May Suppress Fibrogenesis By Targeting TGF</td>
<td>Yuan Hong, Xichuang Chen, Jianlin Ye</td>
</tr>
<tr>
<td>1621</td>
<td>China</td>
<td>Prenatal Diagnosis of Absent Pulmonary Valve Syndrome by Fetal Echocardiogram in children</td>
<td>Yi Ai, Wei Pan</td>
</tr>
<tr>
<td>1687</td>
<td>China</td>
<td>Clinical Features of Ten Patients with Catecholaminergic Polymorphic Ventricular Tachycardia</td>
<td>Zhen Chen, Yue Yuan, Lu Gao, Wei Shao, Lang Cui, Qirui Li</td>
</tr>
<tr>
<td>1716</td>
<td>China</td>
<td>Hippo Pathway Transcription Factor TEAD4 Gene Promotor Region Rs10431346 is Closely Related to Susceptibility to Congenital Heart Disease in the Chinese Han Population</td>
<td>Liu Yonghao, Gui</td>
</tr>
<tr>
<td>1747</td>
<td>China</td>
<td>Research on health education clinical pathway table application in interventional therapy for children with congenital heart disease</td>
<td>Xiao Zhirong</td>
</tr>
<tr>
<td>1784</td>
<td>China</td>
<td>Clinical analysis of 430 cases of Kawasaki disease and related risk factors of coronary artery lesion</td>
<td>Hong-Hong Guo, Xian-Min Wang, Ya-Heng Yu, Ting-Ting Chen</td>
</tr>
<tr>
<td>1899</td>
<td>China</td>
<td>Early Diagnosis of Hutchinson-Gilford Progeria Syndrome with LMNA Mutation</td>
<td>Yang Zhou, Zhe Xu, Lin Ma</td>
</tr>
</tbody>
</table>

**Dermatology**
Drug Reaction with Eosinophilia and Systemic Symptoms Complicated by Hemophagocytic Syndrome
Zhou Yang, Ying Liu, Xin Xiang, Zigang Xu

The initial experience of treatment of Kasabach-Merritt syndrome with vincristine combined glucocorticoid in infant
Yuanyuan Xiao, Zigang Xu, Zhe Xu

Autosomal recessive hyper-IgE syndrome in two brothers of a Chinese family: a novel DOCK8 mutation identification and literature review
Shan Wang, Wenjun Mou, Lin Ma, Jingang Gui

Kaposiform Hemangioendothelioma with Kasabach-Merritt Phenomenon: A Case Report
Qing Feng, Li Li, Lin Ma

Pediatric Atrophic dermatofibrosarcoma protuberans: a case report
Ying Liu, Lin Ma

Desensitization of steroid phobia and encouragement of steroid acceptability on quality of life in childhood eczema
Jasmine WS Yu, Kathy YY Chan, Ellis KL Hon

Skin involvement in four cases of X-linked chronic granulomatous disease
Zhaoyang Wang, Zigang Xu, Jianxin He, Xin Xiang, Lin Ma, Zhaoyang Wang, Xiang He, Xin Xiang, Lin Ma

The Application of Propranolol in the Treatment of Kaposiform Hemangioendothelioma and Tufted Angioma
Li Wei, Li Li, Lin Ma

Behavior problems in children with language disorders
Xirui Ma, Yiwen Zhang

Genetic and neurobehavioral profile of the SHANK3 gene deficiency children in China
Chunxue Liu, Bingrui Zhou, Chun-chun Hu, Chunyang Wang, Qiong Xu, Xiu Xu

Analysis of Risk Factors and Prevalence of Attention Deficit Hyperactivity Disorder Among Elementary School Students in Liuzhou City
Honghui Li, Yu Zhang, Dingyuan Zeng, Zheng Nong

Factors Affecting Motor Skills Outcome in Young Children with Biliary Atresia Pre and Post Liver Transplantation
Celeste Yang, Ashwaniya Ramkumar, Marion Aw, Quak Seng Hock, S. Venkatesh Karthik, Evelyn Law

Non-Monosymptomatic Enuresis is Strongly Associated with Attention Deficit Hyperactivity Disorder in Chinese Children
Sharon Wong, Winnie Chan, Yu-Ki Lee, Michael Yiu

Neurocognitive Outcomes in Late Preterms, Early Terms and Full Term Infants
Daryl Yeo, Taufeeq Wahab, Sherlyyn Chan, Evelyn Law

Summer treatment program for children with ADHD: Efficacy comparison between 2 weeks STP and 1 week STP
Yushiro Yamashita, Koutaro Yuge, Shinichiro Nagamitsu, Hisayoshi Okamura, Akiko Mukasa, Masumi Inagaki

The Developmental and Neurocognitive Problems in Children with Brain Tumours Prior To/Without Radiotherapy in Hong Kong
Winnie WY Tso, Stephen Ky Liu, Anthony PY Liu, Brian YT Ip, Godfrey CF Chan

Genetic and neurobehavioral profile of the SHANK3 gene deficiency children in China
Chunxue Liu, Bingrui Zhou, Chun-chun Hu, Chunyang Wang, Qiong Xu, Xiu Xu

Factors Affecting Cognitive and Language Skills of Very Young Children with Biliary Atresia Pre and Post Liver Transplantation
Celeste Yang, Ashwaniya Ramkumar, Marion Aw, Quak Seng Hock, S. Venkatesh Karthik, Evelyn Law

Early-onset type 2 DM in a non-obese girl born small for gestational age (SGA)
Youngsoon Cha, Bum Suk Jung

A case of non-androgen secreting adrenocortical carcinoma in preadolescence
Hirko Narumi, Shunji Hasegawa, Kazuyuki Waki, Ken Fukuda, Yuji Ohanishi, Takuya Ichimura, Yosuke Fujimoto, Shunsaku Katsura, Hiroo Kawamoto, Eiji Ikeda, Satoshi Okada, Shouichi Ohga
<table>
<thead>
<tr>
<th>Page</th>
<th>Country</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>95</td>
<td>Hong Kong</td>
<td>Homozygous Mutation of AGPAT Gene Causing Type Congenital Generalized Lipodystrophy</td>
<td>SMY Wong, CM Mak, YK Chong, WM But</td>
</tr>
<tr>
<td>178</td>
<td>Indonesia</td>
<td>Graves Disease in A 16 Years Old Female: A Case Report</td>
<td>Ni Wayan Yuliandari, I Made Arimbawa</td>
</tr>
<tr>
<td>184</td>
<td>Hong Kong</td>
<td>A Rare Cause of Short Stature Due to WISP Gene Mutation</td>
<td>Shirley Man-Yee Wong, Jasmine Chow, Wai-Man But</td>
</tr>
<tr>
<td>193</td>
<td>Japan</td>
<td>A case of secondary hyperparathyroidism of neonate with severe skeletal demineralization and persistent respiratory distress</td>
<td>Sumie Yamashita, Chie Nabeysama, Koji Motokura, Hiroshi Mizumoto, Daisuke Hata</td>
</tr>
<tr>
<td>230</td>
<td>Hong Kong</td>
<td>Bone Health Among Boys with Duchenne Muscular Dystrophy Before and After Initiation of Glucocorticoids</td>
<td>Yuet-Ling Tung, Sophelia Hoi-Shan Chan</td>
</tr>
<tr>
<td>562</td>
<td>China</td>
<td>Novel compound heterozygous variants in the LHCGR gene</td>
<td>Yufei Xu, Yulin Chen, Niu Li, Xuyun Hu, Guoqiang Li, Yi Ding, Juan Li, Yiping Shen, Xilumin Wang, Jiang Wang</td>
</tr>
<tr>
<td>586</td>
<td>China</td>
<td>Protective effect and mechanism of exendin-4 on type 1 diabetes mice induced by STZ Qiang Li, Aimei Miao</td>
<td></td>
</tr>
<tr>
<td>89</td>
<td>Japan</td>
<td>A Case of pediatric traditional serrated adenoma in years-old boy resected by endoscopic submucosal dissection</td>
<td>Ami Inoue, Sonoko Kondo, Yoko Todotama, Tani Mari, Yimnom Hitun, Makato Arioka, Kanako Irie, Kiochiro Nii, Noriko Fuke, Takayuki Wakabayashi, Takeo Kondo, Kaori Kayano, Ikiko Kato, Yukiko Konishi, Sae Nishio, Takashi Iwase, Hitoshi Okada, Takashi Kusaka</td>
</tr>
<tr>
<td>103</td>
<td>Philippines</td>
<td>A Meta Analysis on the Efficacy and Safety of Folic Acid as an Adjunct to the Treatment of Acute Diarrhea in Children</td>
<td>April Joy Sarte, Felizardo Goitco</td>
</tr>
<tr>
<td>125</td>
<td>Japan</td>
<td>A 2-year-old patient with difficult-to-diagnose very early onset inflammatory bowel disease effectively treated with infliximab</td>
<td>Kenji Fukushima, Jun Murakami, Naomi Kuranobu, Susumu Kanak</td>
</tr>
<tr>
<td>130</td>
<td>Malaysia</td>
<td>Childhood Inflammatory Bowel Disease in Malaysia: a single-centre study</td>
<td>Way Seh Lee, Chun Wei Tee, Ruey Terng Ng</td>
</tr>
<tr>
<td>135</td>
<td>Japan</td>
<td>Quantitative analysis of meconium microbiota in healthy term infants indicates delayed colonization of Lactobacillus after cesarean delivery</td>
<td>Yuichiro Yamashita, Ravinder Nagpal, Hirokazu Tsuji, Takuya Takahashi, Kazunari Kawashima, Satoru Nagata, Koji Nomoto</td>
</tr>
<tr>
<td>141</td>
<td>Thailand</td>
<td>Etiology and outcome of pediatric acute liver failure</td>
<td>Songpon Getsuwong, Suporn Treepongkaruna, Pornthep Tanpowpong, Chatmanee Lertudomphonwanit, Thipwimon Tim-Aroon, Duangrudee Wattanasirichaiagoon</td>
</tr>
<tr>
<td>142</td>
<td>Thailand</td>
<td>A surviving child from acute liver failure after the ingestion of Cassia occidentalis seed</td>
<td>Songpon Getsuwong, Pornthep Tanpowpong, Satariya Trakulsrichai, Suporn Treepongkaruna</td>
</tr>
<tr>
<td>156</td>
<td>Thailand</td>
<td>Value of the ICD-10 Code for Identifying Cases with Biliary Atresia</td>
<td>Pornthep Tanpowpong, Chatmanee Lertudomphonwanit, Pornpimol Phuapect, Suporn Treepongkaruna</td>
</tr>
<tr>
<td>172</td>
<td>Japan</td>
<td>Strangulative-ileus for primary small bowel volvulus in ten years old boy</td>
<td>A review of 15 cases in Japanese school-aged children</td>
</tr>
<tr>
<td>227</td>
<td>Taiwan</td>
<td>Structural alterations of retinal pigment epithelium in patients with Usher syndrome</td>
<td>Shih-Hsi Song, Tzee-Chung Wu, Ching-Feng Huang</td>
</tr>
<tr>
<td>25</td>
<td>Hong Kong</td>
<td>Paediatric inflammatory bowel diseases in Hong Kong: A single-center analysis of 11-year data</td>
<td>Yung-Yung Ho, Chung-Mo Chow</td>
</tr>
<tr>
<td>71</td>
<td>Taiwan</td>
<td>Endoscopic Polypectomy of the Large Juvenile Polypl For</td>
<td>Recurrent Colocolonic Intussusception and Severe Iron-deficiency Anemia in A Child</td>
</tr>
<tr>
<td>Country</td>
<td>Abstract Title</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>----------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>Over-the-scope clip (OTSC) treatment for massive bleeding from a 4-year-old boy's duodenal ulcer Takao Kondo, Sonoko Kondo, Aki Inoue, Yoko Tadatomo, Makoto Arioka, Kanako Irie, Koichiro Nii, Takeshi Ikeda, Yuuki Matsuda, Noriko Nishiyama, Hideki Kobara, Hiroto Mori, Hitoshi Okada, Takashi Kusaka</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Effects of living related liver transplantation on rare genetic cholestatic liver diseases in children of China: a single center experience Xinbao Xie, Conghuan Shen, Jianshe Wang, Yi Lu</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Effects of living related liver transplantation for end-stage liver disease caused by cerebral organoids in children Xinbao Xie, Conghuan Shen, Jianshe Wang, Yi Lu</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Determination and value of vasoactive intestinal peptide, substance P, 5-hydroxytryptamine in children with He-noch-Schonlein purpura Yongkun Huang, Wei Li, Jiang Duan, Jingjing Xiong, Hongwei Hu, Mei Liu, Li Zhi Zhang</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>The relationship between antibiotic resistance and the virulence genes cagA and vacA of Helicobacter pylori clinical isolates Qin Dan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Analysis of Curative Effect of Wei-Chang-An-Wan in the Treatment of Children with Functional Abdominal Pain Runkai Yin, Rui Qin Zhao, Xiaoming Wang, Ge Lan Bai, Hai Yan Fu, Hai Hua Li, Chun Lan Yin, Wei Na Shi, Yi Li Liu, Li Juan Cheng</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Clinical analysis of pre-and postoperative high-resolution manometry in the evaluation of achalasia with POEM in children Hanhua Zhang, Hong-Bin Yang, Xiao-Xia Ren, Yi Chen, Ying Fang</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Efficacy of endoscopic radial incision (ERI) for esophageal stenosis in children Ying Fang, Xiao-Xia Ren, Hong-Bin Yang, Yi Chen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Chronic diarrhea: etiology, clinical feature, diagnosis strategy Yanan Han, Hong-Bin Yang, Xiao-Xia Ren, Hong Li, Ying Fang</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>(-)-Epigallocatechin-3-Gallate enhances poly I: C-induced interferon-1 production and inhibits HCV replication in hepatocytes Ting Zhang, Yi Hong, Jiali Liang, Xi Wang, Wenhe Ho</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Clinical analysis of 10 cases of children with eosinophilic gastroenteritis Xiao-Xia Ren, Hong-Bin Yang, Ku-Ku Ge, Yi Chen, Ying Fang</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Long-term effect of Endoscopic longitudinally cut transverse suture operation in Gastric antrum cicatricial stenosis after huge ulcer in children Ying Fang, Hong-Bin Yang, Xiao-Xia Ren, Tian-Jiao Gao, Ku-Ku Ge</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Infliximab corrects gut microbial dysbiosis of pediatric patients with Crohn's disease, but is underpowered to enrich multiple SCFA-producing bacteria Ting Zhang, Yizhong Wang, Hui Hu, Yongmei Xiao, Dan Li, Guangjun Yu</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Prevalence of malnutrition and risk of undernutrition in hospitalized children with liver disease Ting Zhang, Ronghua Yu, Yizhong Wang, Yongmei Xiao, Dan Li</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>Functional Analysis of Synonymous and Intronic Variants Identified in ABCB11 of Progressive Intrahepatic Cholestatic Children with Low ~glutamyltransferaseNeng-Li Wang, Jian-She Wang</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Philippines</td>
<td>The Effect of Probiotics in Reducing the Common Cold in Filipino Kindergarten Children in Public and Private Schools Aged Four to Six Years</td>
<td>Lany Lim, Rowena Therese Rome-rica, Ann Marie Tan-Ting, Francis Dimalanta</td>
<td></td>
</tr>
<tr>
<td>Taiwan</td>
<td>Caregiver's Assessment Skills and Children's Asthma Status Jia-Yi Peng, Shiaw-Ling Wang, Yu-Ting Hung, Hui-Chien Lai, Su-Boon Yong, Min-Tsung Lee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Philippines</td>
<td>Factors Affecting Compliance to the Expanded Program of Immunization of Children 2 Years Old and Below in Barangay Tabing -Ilog, Marilao, BulacanRomeo Barangan, Carolina Marian</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hong Kong</td>
<td>Parental involvement in primary school education: its relationship with children's academic performance and psychosocial competence through engaging children with school Rosa Sze-Man Wong, Frederick Ho, Wilfred Wong, Patrick Ip</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
High Venous Lactate Concentration Observed in Early Infant with Normal Acid-Base Balance. Masakazu Kinoshita, Junji Kamizono, Kotaro Ichikawa.

Current Status of Acute Otitis Media in Children with Fever. Hongmei Shan, Li Zhao.

Analysis on Factors Affecting Pediatric Outpatient Sedation. Huangquan Qu.

First reported the Association of Alagille Syndrome and total anomalous pulmonary venous connection. Zeng Hanshi, Wang Bi, Zhong Jing, Sun Yunxia.

A Minimally Invasive Biparietal Skull Expansion for Infants and Young with Sagittal Synostosis. Tian Jia Liu, Shuo Gu.


A Look Into Academic Productivity and Quality of Clinical Research by Pediatric Residents Within the Pediatric Residency Training Program Anchored on the Five Star Qualities. Jennie Wong, Marian Alsasua.


Deciphering the biological importance of TSPY1 through generating Tspyl1-/- mice by CRISPR. Lei Peng.

Identifying Genetic Hypomethylation and Upregulation of Matrix Metalloproteinase 9 in Patients with Kawasaki Disease. Yuan-Ting Chuang, HN Cheung, Heidi Iu, SMT Leung, Betty But, CC Shek.

Hyperammonaemia in a girl who inherited an ornithine transcarbamylase (OTC) gene mutation from her asymptomatic father. Jasmine Chow, HH Cheung, Heidi Iu, SMT Leung, Betty But, CC Shek.


Smith Lemli Optiz syndrome in Chinese. Mei-Tik Leung, Jacqueline Sit, Ho-Ning Cheung, Yan-Ping Iu, Winnie Chan, Chi-Chung Shek.

Congenital Nephrogenic Diabetes Insipidus: Challenges in Diagnosis and Implications For Affected Families. Mei-Tik Leung, Jacqueline Sit, Ho-Ning Cheung, Yan-Ping Iu, Winnie Chan, Chi-Chung Shek.


The Association Between GATA1 Mutations in Down Syndrome Newborns and Transient Abnormal Myelopoiesis. Kanokporn Chukua, Chayanont Netsawang, Kittipoom Padungthai, Thanthich Ketthkham, Pacharapan Surapolchai, Kittiwon Rujrueangrit.

Application of prenatal genetic testing in screening of congenital renal tubular acidosis high risk fetus. Lanjun Shuai.
Targeted gene capture and next-generation sequencing technologies uncovers candidate mutations of deafness genes in Chinese Cohort with hereditary non-syndromic hearing loss. Xiaohui Wu

Hypokalemic Periodic Paralysis: A Case Series. Jiaxiu Yan

Eleven Novel Mutations in Six Chinese Patients with Thalassemia. Yupeng Liu, Yao Zhang, Yanling Yang

A Chinese Boy with Geleophysic Dysplasia and Two Compound Heterozygous Mutations of ADAMTSL2. Juan Huang

Point Mutation in Two Chinese Nephronophthisis Pedigree: NPHP1 Whole Heterozygous Deletion Compounds with A Mutation. Ying Mo, Haiyan Wang, Ting Liu, Min Li, Liangzhong Sun

Optical Mosaicism By Do Buccal Cell FISH on 45,X0 Patients. Lei Zheng, Bi Yi, Xue Chen, You-Sheng Yan, Sheng-Ju Hao, Shibo Li

Identification of A Novel Germline Mutation of PIGA in A Chinese Family with Multiple Congenital Anomalies Hypotonia-seizures Syndrome 2 (MCAH52) via exome sequencing. Dong Zhou, Huawei Xin, Junli Yang, Qingci Zhuo, Wen Li, Fang Luo, Jinghui Zhang, Liangqiang Guo, Dan Bi, Xiaoyang Huang

The Value of Detecting Mosaicism By Do Buccal Cell FISH on 45,X0 Patients. Xiaohui Li, Li Xiong, Yue Huang, Hui Guo, Kun Xia, Yu Zhang, Dingyuan Zeng

The Autism Clinical and Genetic Resources in Guangxi. Huamu Chen, Hongrong Lin, Zhihui Yue, Haiyan Wang, Yan Yang, Ren Cai, Ning Tang

Detecting Novel Gene Mutations in Usher Syndrome Families. Tohid Shirzad

A Novel Insertion Mutation in the ATP7A Gene Associated with Delayed Infantile Onset of Menkes Disease. Tian Yan, Wuguo Li, Xiangrong Tang, Zhetao Li, Lin Wang, Lian Mo, Jiwei Huang, Yan Yang, Ren Cai, Ning Tang

First Report of a Chinese Boy Carrying a Novel -thalassemia Mutation IVS-I-129 (HBB c.93-2A>T). Yan Yang, Yinghong Lu, Juan Huang

Whole Exome Sequencing Identifies Two Novel MARVELD2 Frameshift Mutations as a Cause of Autosomal Recessive Nonsyndromic Hearing Loss in a Chinese Family. Tian Yan, Ren Cai, Ning Tang, Wuguo Li, Zhetao Li, Xiangrong Tang, Jingwen Li, Dingyuan Zeng

Chinese Family with Multiple Congenital Anomalies Hypotonia-seizures Syndrome 2 (MCAH52) via exome sequencing. Dong Zhou, Huawei Xin, Junli Yang, Qingci Zhuo, Wen Li, Fang Luo, Jinghui Zhang, Liangqiang Guo, Dan Bi, Xiaoyang Huang

Knowledge, attitudes and practice towards thalassemia prevention among parents of Bangladeshi thalassemic children: Correlation with educational and financial status. Tahura Sarabon

Cross-infection of CREEPP and KRAS mutations in a relapsed pediatric high hyperdiploid acute lymphoblastic leukemia. jun-ichi Ueyama, keisuke Okuno, Hitosi Sano, Naohiro Yoneda, Susumu Konzaki, Mizuka Miki, Shohei Eto, Yusuke Imanaka, Youko Mizokuchi, Masao Kobayashi, Takahisa Hanada, Hiromu Narasaki, Kanae Sasaki,bara, Takehiro Matubara, Akira Shimada


Novel Wasp Mutation in a 3 Months Old Boy with Wiskott-Aldrich Syndrome. Nguyen Lien Anh Phan, Minh Tuan Nguyen

Toxic epidermal necrolysis in a child six months post hematopoietic stem cell transplantation. Utako Oba, Hiroshi Yamada, Souichir Suendo, Yusuke Nakamura, Akiko Ito, Yukata Hatano, Nobuyoshi Itanaga, Kouti Chihoisha, Yukih Koga, Shouchi Ohga, Kenji Ibara

Knowledge, attitudes and practice towards thalassemia prevention among parents of Bangladeshi thalassemic children: Correlation with educational and financial status. Tahura Sarabon

Thalassemic Periodic Paralysis: A Case Series. Xiaohui Li, Guohua Wang, Chaoying Yan

China

Japan

Bangladesh

Japan

Vietnam

Haematology & Oncology

All Submitted Abstracts with QR codes

All Submitted Abstracts with QR codes
The Impact of the Individual Parameters of disseminated intravascular coagulation (DIC) Score on Clinical Outcomes in Pediatric Intensive Care Unit (PICU)
Rungrote Natesirinilkul, Wirapad Kadungkamnu, Sanit Reungrongrat, Suphara Manowong, Sujitra Inthapaen

Successful Treatment of Pediatric AML Harboring FUR-ERG Fusion Gene
Hitoshi Sano, Naohiro Yoneda, Keisuke Okuno, Jun-ichi Ueyama, Susumu Kanazaki

Soluble Transferrin Receptor (STfR), Ferritin, and STfR/LOG Ferritin Index in Hospitalized Children: A Pilot Study
Jetniphat Khamyuang

The Establishment of abcb4:EGFP Transgenic Zebrafish for Multidrug Resistance
Congjie Sun, Zhixu He, Liping Shu

Novel Germline DICE1 Mutations in Chinese Children with Pleuropulmonary blastoma (PPB)
Marcus Kwong-Lam Fung, Anthony Pak-Yin Liu, Gordon Ko-Chun Leung, Christopher Chun-Yu Mak, Xiaofeng My, Brian Hon-Yin Chung, Godfrey Chi-Fung Chan

A Novel \(\beta\)-globin Chain Deletion with TINF Mutation Caused Chronic Severe Anemia
Leiwen Peng, Yiping Zhu

Effects of Vinblastine on the expression of tumor resistance gene abcb4 in Zebrafish
Rong-ying HU, Zhi-xu HE, Li-ping SHU

Cost-effectiveness of iron chelators for \(\beta\)-thalassemia major: a systematic review
Li, Lingli Zhang, Min Chen, Yang-zong Suolang, Guoqian He, Linan Zeng

A Novel PCKR Gene Mutation Identified Using Advanced Molecular Techniques
Yunyan He, Jianming Luo, Yonghong Lei, Siyuan Jia, Ning Liao

A Study of Parathyroid Function in Chinese Paediatric Patients with Thalassemia
Yunyan He, Ping Chen, Siyuan Jia, Ning Liao

Febrile neutropenia in children with acute lymphoblastic leukemia during induction therapy
Zixian Cong, Chao Liu, Li Zhang, Yumei Chen, Xiaofan Zhu

The relationship between the CYP3A5 genetic polymorphism and susceptibility to childhood acute leukemia
Zixian Wang, Jiaqiang Qian, Haixia Zhou, Yuan Li

Successful Treatment of Pediatric AML Harboring FUR-ERG Fusion Gene
Hitoshi Sano, Naohiro Yoneda, Keisuke Okuno, Jun-ichi Ueyama, Susumu Kanazaki

The relationship between the CYP3A5 genetic polymorphism and susceptibility to childhood acute leukemia
Zixian Wang, Jiaqiang Qian, Haixia Zhou, Yuan Li

Efficacy of Combined Transperineal (TP) and Transabdominal (TA) Ultrasonography in Diagnosis and Follow-up of Vaginal Malignancies
Xuzhen Yang, Jingjing Ye, Jin Yu

Efficacy of ultrasonography in diagnosis in neonatal adrenal neuroblastoma
Yu, Jingjing Ye, Xizhen Yang

A novel synthetic compound bismuth zinc citrate could potentially reduce cisplatin induced toxicity without compromising the anticancer effect through enhanced expression of metallothioninein and GSH
Shing Chan, Hongzhe Sun, Yifan Hong, Nancy Kwan Man, John Nicholls, Godfrey Chi-Fung Chan

Prevalence, Onset Time and Related Factors For Speech Impairment in Childhood Cancer Survivors
Oi-Yan Yiu, Hing-Sang Wong, Godfrey Chi-Fung Chan

A 20-year retrospective review on outcomes and morbidities of survivors of Haemoglobin Bart’s Hydrops Fetalis Syndrome in Hong Kong
Wilson Chan, Alex Leung, Chung-Wing Luk, Rever Li4, Alvin Ling5, Shau-Yin Ha

Clinical Characteristics and Prognostic Factors of Epstein-Barr Virus-Associated Hemophagocytic Lymphohistiocytosis in Children
Honghao Ma, Rui Zhang, Li Zhang, Hongyun Lian, Dong Wang, Yunze Zhao

Group-based Trajectory Modelling of Hb Increasing Among Nutritional Anemic Infants in Rural Areas of North China: A Before-And-After Study with Concurrent Control
Shuyi Zhang, Fang Wang, Ting Zhang

Neurological Complications in Chinese Children Undergoing Hematopoietic Stem Cell Transplantation (HSCT)
Yuen-Kwan Mak, Daniel Ko-Leung Cheuk, Pamela Pui-Wah Lee, Alan Kwok-Shing Chiang, Shau-Yin Ha, Godfrey Chi-Fung Chan, Anthony Pak-Yin Liu
**Inborn Errors of Metabolism**

221 Hong Kong
Cobalamin C Disease Presenting as Haemolytic Uremic Syndrome in a Chinese Newborn
Anna Lin, Shuk-Ching Chong, Dawn Fong-Chu Tang, Stephanie Ho, Eric Lap-Kay Law, Liz Yuet-Ping Yuen, Joannie Hui

329 China
A Compound Heterozygous Variant of COG6Gene in A Chinese Patient with Deficiency of Subunit 6 of the Conserved Oligomeric Golgi Complex (COG6-CDG)Guoqiang Li, Xuyun Hu, Yufei Xu, Jian Wang

579 China
Prenatal genetic counseling and prenatal Diagnosis for inherited metabolic disease in high-risk families: 4 Years of Experience in a Single Center
Duan Li, Dongzhi Li, Huiying Sheng, Xiaoyuan Zhao, Xi Yin, Zhongcai Liu, Yunting Lin, Yonglan Huang, Li Liu

701 China
Neonatal-onset carbamoyl phosphate synthetase I deficiency: a case report
Xiaoyan Yang, Jin Shi, Xianxiao Shu, Jun Tang, Dezh Mu

1099 China
Phenotypes and Genotypes of 52 Chinese Patients with Propionic Acidemia
Le Wang, Mengchuan Zhao, Haixia Li, Yanling Yang

1104 China
Four Chinese Children with Congenital Generalized Lipodystrophy and Novel Mutations of BSCL and AGPAT2 Genes
Yi Liu, Xiyuan Li, Yuan Ding, Ying Jin, Jinqing Song, Yao Zhang, Haixia Li, Yanling Yang

175 Japan
Streptococcus pyogenes Infective Endocarditis in Children: Two Cases report and Review of the Literature
Makoto Yokouchi, Naoki Tanigawa, Teppei Okawa, Takashi Matsuzaka, Kiyotaka Takefuji, Tsuise Nobeishima, Mami Nakayashiro, Tsutomu Matsumura

240 Hong Kong
Detection of Multiple Respiratory Pathogens in Paediatric Oncology Patients
Ting-Fan Leung, Lai-Yin Tse, Karry Lei-Ka Ngai, Chi-Kong Li, Frankie Wai-Tsoi Cheng, Matthew Ming-Kong Shing, Paul Kay-Shueung Chan

309 China
The Effect of Pre-pregnancy MCMV Infection on Normal and LPS Stimulated Mice and Their Offspring
Huy Huang, Yuan Huang, Di Ma, Yuanyuan Lu, Feng Fang

331 China
Epidemiological analysis of human bocavirus in hospitalized children with acute respiratory tract infection in Guangzhou
Yong Cai, De-Hui Chen, Wen-Kuan Liu, Qun Wang, Xiaowen Chen, Rong Zhou

**Infectious Diseases**

221 Hong Kong
A study of the roles of interleukin-17A on macrophage functions in response to mycobacteria infection
William Ling, John Pong, Vicky Wang, Godfrey Chan, James Li

329 China
Association of TIM-3, PD-1, LAG-3, and CTLA-4 Polymorphisms with Hand, Foot, and Mouth Disease in Pediatric Patients Complicated with Enterovirus 71 Infection
Yan Li, Min Jiang, Yanyan Zhang, Wei Lin, Guangmin Nong

382 China
Epidemiological analysis of human metapneumovirus in hospitalized children with acute respiratory tract infection in Guangzhou
Yong Cai, De-Hui Chen, Wen-Kuan Liu, Qun Wang, Xiaowen Chen, Rong Zhou

435 Korea
Serotype and Genotype Distribution of Group B Streptococcus Isolated From Invasive Infections in Korean Infants From 2006 to 2016
Hye-Kyung Cho, Byung Wook Eun, Soo Han Choi, Hye Jung Cho, Dong Woo Son

454 China
The Molecular Epidemiology and Clinical Manifestations of Adenovirus in Hospitalized Children with Respiratory Infections
Le Wang, Mengchuan Zhao, Zhishan Feng, Guixia Li

464 China
Mycoplasma pneumoniae is not only an infectious agent but also an allergen for certain individuals
Qing Ye, Shiqiang Shang

544 China
The Role of Neutrophils in Lung Injury after Mycoplasma pneumoniae Infection
Shuang Shi, Deyu Zhao

586 Hong Kong
Community-acquired Pseudomonas Aeruginosa Bacteremia in Previously Healthy Children: A Case Report and Review of the Literature
Qing Wei, Guang-Min Nong, Min Jiang

591 China
Association of polymorphisms in interleukin-12/interferon-gamma pathway genes with susceptibility to enterovirus 71-infected hand, foot, and mouth disease
Yan Zhang, Min Jiang, Yan Li, Wei Lin, Jing Liu, Guangmin Nong

657 China
Chronic active Epstein-barr virus infection as the initial symptom in a Janus kinase 3 deficiency child and literature review
Linqing Zhong, Wei Wang, Mingsheng Ma, Lijian Gou, Xiaoyan Tang, Hongmei Song
662. China
Changes of T-lymphocyte Subsets, D-Dimer and immuno-
globulin in Mycoplasma Pneumonia Children and its Signifi-
cance
Cheng-zhong Zheng, Li Hao

53. Philippines
The Effects of Delivery Room Temperature on Thermoregu-
lation among Term Newborn Infants Delivered via Normal
Spontaneous Delivery and Cesarean Section in a Private
Tertiary Hospital in the Philippines
Cynthia Katerine Hanil, Violeta Valderrama, Aurora Gloria Libadia

670. China
Viral Etiology of Hospitalized Children with Acute Lower
Respiratory Tract Infection at a Single Center in Beijing
Yue Tang, Hong Cui

58. Japan
Edaravone As Adjuvant Therapy of Hypothermia in Neonatal
Hypoxic-ischemic Piglet Model
Yasunori Nakao, Takayuki Wakabayashi, Wataru Jinno, Satoshi Yamata, Makoto Nakamura, Kosuke Koyano, Saneyuki
Yasuda, Takashi Kusaka

766. China
A Comparative Study of Southwest Chinese HIV-Exposed
Infants’ Growth Parameters relative to Chinese and World
Health Organization (WHO) Standards
Jiang Chen, Yu Zhang, Bo Wang, Dingyu Zeng, Xuemei Huang, Chokechai
Rongkavil, Eric McGrath

64. Philippines
Factors Affecting Adequacy of Breastmilk Supply During Hos-
pital Stay Among Mothers Who Delivered At De Los Santos
Medical Center
Maria Lydwina Lausane, Gloriosa Galindez

1055. China
The Level of Antibodies Against Bordetella Pertussis in Serum
of Children in Shanghai
Xiao Yuan

73. Japan
Impact of Multiple Pregnancies Resulting From Medically
Assisted Conception on Regional Neonatal Intensive Care
Units in Japan
Shigeki Koshida, Kentaro Takahashi

1234. China
Effects of Autophagy on Myocardial Damage in Neonatal Rats
with Sepsis
Zhongqiang Liu, Dezhi Mu

77. Indonesia
The Impact of Infection Control Training in Increasing Survival
Rate of ELBW in Papua
Windhi Kresnawati, Lily Randjan

1261. China
Research of Continuous Blood Purification in the Treatment
of Children with Severe Hand, Foot and Mouth Disease
Cao, Hailing Song, Meixian Xu

81. Bangladesh
Role of oral Paracetamol in the treatment of Patent Ductus
Arteriosus in comparison to oral Indomethacin
Liton Saha, Md. Mahbubul Hoque, Rubina Younas

1543. China
The application of a single-tube multiplex RT-PCR assay for
the detection of 13 common respiratory pathogens in chil-
dren with acute respiratory tract infection
Mengchuan Zhao, Zhishan Feng, Guixia Li, Le Wang

99. Korea
A Newborn with severe hydrocephalus and myelomeningo-
cele associated with maternal antiepileptic medication
Soo Kyung Nang, Yujoung Lee

1696. Hong Kong
Development of System Using Routine Surveillance Data to Esti-
mate Influenza Vaccine Effectiveness for Hospitalised Hong Kong
Children
Karene Ho, Ting Yeung, Ching-Ching Chan, Paul Kay-
Sheung Chan, David Shu-Yan Lam, Philip Chak-On Sham, Yau-Sun
You, Wei-Hung Chan, Wo-Keung Chiu, Kwok-Leung Ng, Daniel
Kwok-Keung Ng, Iris Mei-Ching Chan, Edmund Anthony S Nelson

8. Bangladesh
Slow vs Rapid Enteral Feeding Advancement in Preterm Low
Birth Weight Infants: a Randomized Controlled Trial, in Dhaka
Shishu (Children) Hospital
Liton Saha, Md. Mahbubul Hoque, Rubina Younas

101. Japan
Neonatal outcomes of infants with birth weight of 500 g or
less from the Neonatal Research Network of Japan
Hiroki Inoue, Kazuaki Yasuoka, Yoshihiro Kusuda, Masakazu
Kurihara, Takaharu Matsusaka, Tomoaki
Taguchi, Shouichi Ohga

32. Indonesia
Modified Breastmilk Fortification for Preterm Babies in Limit-
ed Resources Area
Windhi Kresnawati, Lia Froulna, Ranawati Rohiswanto

129. Japan
A neonate with brain abscess and meningitis caused by
Citrobacter koseri
Hiroki Inoue, Eiji Ohta, Yasuhiro Onda, Toshikazu Nii, Atsushi Iishi, Tatsuki Miyamoto, Takashi
Setoue, Masatoshi Nakamura, Shinichi Hirose
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>150</td>
<td>The Effect of Oral Propranolol in Preventing the Progression of Early Stages of Retinopathy of Prematurity: A Meta-Analysis</td>
<td>Jeffrey Lappay, Kristal An Agrupis, Leonilla Dans, Rezli Mo Bautista</td>
</tr>
<tr>
<td>216</td>
<td>Tracheal Agenesis with Laryngeal Atresia Keiichiro Toma, Toshihumi Yodoshii, Ryuichi Genkawa, Tomoko Mokiya</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>246</td>
<td>Neonatal Haemochromatosis: 2 Case Reports Jacqueline Hung, Yuet-Yee Chee, Mabel Sia-Chun Wong, Rosanna Ming-Sum Wong</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>248</td>
<td>Usefulness of lung ultrasonography in neonatal respiratory disorder Tadashi Hiyodawaka, Ayaka Aki, Tsuro Kikumoto, Takeya Ota</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>416</td>
<td>Prematurity Due to Congenital Brucellosis Zhao Menghua, Zhang Bing, Zhang Aimin, Zhong Li</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>530</td>
<td>Clinical Analysis of Extremely and Very Low Birth Weight Infants Born from Assisted Reproductive Technologies Cong An, Qian Zhang</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>532</td>
<td>Analysis of Factors Related to Death of Infants with Extremely and Very Low Birth Weight After Assisted Reproductive Technology Cong An, Qian Zhang</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>540</td>
<td>Drug-induced Liver Failure and Hemophagocytic Syndrome in a Premature Infant Cong An, Qian Zhang, Zanyang Shi, Fengxia Mao, Li Wang</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>702</td>
<td>Analysis of nosocomial infection in neonatal ward Xiaoyan Yang, Jun Tang, Yanling Hu, Jing Zhao, Yanxia Shou, Chao Chen, Jing Shi</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>715</td>
<td>A pilot control study of methylxanthine for the treatment of apnea of prematurity: based on therapeutic drug monitoring Xiaoyan Yang, Zhimei Jiang, Yue Ma, Jing Shi, Xianxiao Shou, Jun Tang, Dezhi Mu</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>719</td>
<td>Pharmacokinetics of caffeine citrate in Chinese neonates with apnea of prematurity: a pilot study with sparse data Xiaoyan Yang, Zhimei Jiang, Yue Ma, Jing Shi, Xianxiao Shou, Jun Tang, Dezhi Mu</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>720</td>
<td>Role of adenosine receptor polymorphisms on individual preterm infant response to caffeine therapy: a preliminary study Xiaoyan Yang, Z., Xianxiao Shou, Jing Shi, Jun Tang, Dezhi Mu</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>720</td>
<td>Role of adenosine receptor polymorphisms on individual preterm infant response to caffeine therapy: a preliminary study Xiaoyan Yang, Z., Xianxiao Shou, Jing Shi, Jun Tang, Dezhi Mu</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>752</td>
<td>Prevalence and Determinants of Folic Acid Supplement Use Among Pregnancy Planning Couples and Early Pregnancy Women: A Cross-sectional Study in Shanghai, China</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>879</td>
<td>Risk factors for necrotizing enterocolitis in very preterm infants: a case-control study</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>880</td>
<td>Associations between Neonatal Serum Bilirubin and Childhood Obesity in Term Infants</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>888</td>
<td>SIRT Signaling Pathway Mediated the Effect of Budesonide and Poractan Alfa on Preventing Bronchopulmonary Dysplasia Fengling Du, Wenbin Dong, Qingping Li, Xiaoqing Lei, Xuesong Zhai, Shuai Zhao, Chan Zhang</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>1136</td>
<td>The Changes of SIRT1 Signaling Pathway in Peripheral Blood Mononuclear Cells and the Correlation with Bronchopulmonary Dysplasia after Oxygen Exposure in Preterm Infants Xingling Liu, Wenbin Dong</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>1139</td>
<td>Relative Factors Associated with the Deterioration of Necrotizing Enterocolitis in Small for Gestational Age Neonates Li-juan Luo, Wenbin Dong, Lingping Zhang, Xiaoqing Lei</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
<tr>
<td>1242</td>
<td>Bronchopulmonary Dysplasia-Pathogenesis and Treatment Asfia Banu Pasha, Guy-Ping Zhou</td>
<td>Jing Shi, Jun Tang, Dezhi Mu</td>
</tr>
</tbody>
</table>
China
Psychometric Evaluation of Three Pain Assessment Scales in Ventilated Neonates
Xiaozhi Huang, Li Li, Jun Zhou, Fang He, Chunxia Zhong, Bin Wang

China
Postnatal Development of Th1,Th17 Cell in Very Preterm Infants
Li-Ya Ma, Rui Chen, Ping Zhou

China
Non-invasive Micro Plastic technology of Auricular Deformities Correction in Newborns: A Retrospective Analysis of 48 Cases
Xuhua Fang, Jie Chen

China
Effects of Fentanyl For Acute Pain Control and Neuroprotection in Very Preterm Newborns on Mechanical Ventilation
Jie Qiu, Li Zhao, Yun Feng, Jing-Han Zhang, Yang Yang, Rui Cheng

China
Vascular Factors Associated with Bronchopulmonary Dysplasia in Preterm Infants
Hui Wu, Tongyan Han, Xinli Wang, Zailing Li, Xiaomei Tong, Meihua Piao

China
The comparison of serum ion between preterm respiratory distress syndrome and transient tachypnea of newborn during the first week after birth
Tongyan Han, Ziyuan Liu, Shaojun Liu, Hui Wu, Xiaomei Tong, Meihua Piao

China
Retrospective Analysis of Neonatal Blood Transfusion in a Chinese Hospital
Hong Zhao, Haijuan Wang, Jingxian Chen, Siqi Zhuang, Xiaoyu Li, Muxue Yu, Yijuan Li

China
Clinical Features and Prognosis of Neonatal Bacterial Meningitis in 56 Cases
Kailin Zhao, Jindu Guo, Zhanhui Li

China
Fetal and Neonatal Outcome in Rhesus Hemolytic Disease Managed with Intrauterine Transfusion: 16-Year Experience in A Tertiary Referral Hospital in Southern China
Wenxu Pan, Yuefang Huang, Jingxian Chen, Siqi Zhuang, Xiaoyu Li, Muxue Yu, Yijuan Li

China
The Role of Notch Effector Gene Hes1 Down-regulation in a Mouse Biliary Atresia Model
Zefeng Lin, Ruizhong Zhang, Yan Chen, Ming Fu, Huiling Lin, Huimin Xia

China
Effect of Human amnion mesenchymal stem cells on Expression of Integrin-beta1 in Hippocampus of Neonatal Rats with Hypoxic Ischemic Brain Damage
Jianlu Wu

China
Novel role for angioptietin 1 and 2 in vascular smooth muscle cell biology
Danyang Chen, Wenjun Ma, Gentile Lash

China
Expression of IL-1beta and its receptors in first trimester decidua and placenta
Fen Ning, Danyang Chen, Huishu Liu, Gentile Lash

China
Retrospective Analysis of 2362 Cases of Neonatal Asphyxia
Jian Wang, Qingqing Lin

China
Population Pharmacokinetics and Dosing Individualization of Vancomycin in Neonates and Young Infants
Jianlu Wu, Lijing Xia, Lin Zhu, Guangfei Wang, Zhiding Li

China
The Role of UGT1A1 Gene Variation on Clinical Etiology-unknown Neonatal Hyperbilirubinemia
LiFei Yang, Jing Li, Jian Wang, Meng Wei, LiQing Xu, Rui Hu, WeiWei Guo

China
Retrospective Analysis of Neonatal Asphyxia
Jian Wang, Qingqing Lin

China
Population Pharmacokinetics and Dosing Individualization of Vancomycin in Neonates and Young Infants
Yewei Chen, Jinmiao Lu, LiQing Xu, Rui Hu, WeiWei Guo

China
The Impact of Uridinediphosphate Glucuronosyl Transferase 1A1 (UGT1A1) Gene Variation on Clinical Etiology-unknown Neonatal Hyperbilirubinemia
LiFei Yang, Jing Li, Jian Wang, Meng Wei, LiQing Xu, Rui Hu, WeiWei Guo

Philippines
The Use of Trimethoprim-Sulfamethoxazole As Antibiotic Prophylaxis For the Prevention of Recurrent Urinary Tract Infections and Renal Scarring in Pediatric Vesicoureteral Reflux Patients: A Meta-Analysis of Randomized Controlled Trials
Kristal An Agrupis, Jeffrey Lappay, Eric Aragon, Leonila Dans

Japan
Genital Organ Anomalies in Female Pediatric Patients with Congenital Anomalies of the Kidney and Urinary Tract
Takatsugu Kanda, Naoya Morisada, Kiyonobu Ichizuka, Hiroko Chikamoto, Yuka Aoki, Kenichiro Miura, Kazumoto Iijima, Motoshi Hattori
59 Japan Assessment of Urinary Liver-type Fatty Acid-binding Protein After Hematopoietic Stem Cell Transplant: Four Case Reports Daisuke Matsuoka, Yoshihiko Hidaka, Takanori Tsukahara, Kazutoshi Komori, Daisuke Morita, Yozo Nakazawa

70 Hong Kong An Extreme Case of Posterior Reversible Encephalopathy Syndrome [PRES] or A New Clinical Entity Wing-In Yarn, Ngoc-Man Chan, Sunny Tse, Winnie Kwai-Yu Chan

78 Hong Kong Cimetidine-induced Acute Interstitial Nephritis: An Uncommon But Important Complication Wun Fung Hui, Wing Hung Lau, Winnie Kwai Yu Chan

152 Hong Kong The Challenges of Congenital Cystic Hygroma to Neonatal Kidneys CI Kuok, WF Hui, KO Chang, WKY Chan

177 Hong Kong Continuous Renal Replacement Therapy (CRRT) in Infants and Neonates Wun Fung Hui, Winnie Kwai Yu Chan

1559 China The effect of AG490 on JAK-STAT pathway on balance of Th17/Treg and podocyte in Adriamycin Nephrosis Sprague Dawley rat Yu Hui Wu, Xiao Shan Shao, Yu Hong Li, Xin Hui Jiang

1442 China The effects of RNA interference IL-17 gene on significance of Th17/Treg and podocyte in Adriamycin Nephrosis Sprague Dawley rat Yu Hui Wu, Xiao Shan Shao, Yu Hong Li, Xin Hui Jiang

1449 China Characteristics analysis of ambulatory blood pressure in 408 children with kidney diseases during 5 years in a single-center Bei Ying, Xiao Shan Shao, Yu Hong Li, Hai Xia Xu

1558 China Study on the relationship between urinary tract infection and vesicoureteral reflux in children Xin Hui Jiang, Xiao Shan Shao, Yu Hong Li, Hai Xia Xu

1518 China Interfering of IL-17 prevent primary glomerular disease progression in adriamycin nephrosis rats Yu-Hui Wu, Xiao-Shan Shao, Yu-Hong Li, Bei Ying

1699 China High-through gene sequencing and analysis aid differential diagnosis of Alport syndrome Shuo Wang, Zhu Tan, Ying Zhao, Peng Hao, Jianjun Xie

1700 China Diagnostic and therapeutic regimens for comorbidity of nephrotic syndrome and neuroblastoma: One case report Shuo Wang, Zhu Tan, Ying Zhao, Peng Hao, Jianjun Xie, Jian-Ping Huang, Hong-Xia Li, Li-Ying Zhang, Jianjun Xie

1701 China Clinico-pathological features and effective management of secondary steroid-resistant nephrotic syndrome in childhood: report of three cases Shuo Wang, He-Zhen Hu, Yu Qi, Ying Liu, Hai-Yan Gao, Jianjun Xie

Indonesia Factors influencing Treatment Response in Children with Epilepsy in Cipto Mangunkusumo National General Hospital Lady Aurora, RA Setyo Handryastuti, Regina Putri Apriza, Prinnisa Almanda Jonardi
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>45</td>
<td>Association Between Types of Epilepsy Based on ILAE 1989 Classification System with EEG Recording and Child Development in RSUPN Cipto Mangunkusumo</td>
<td>Regina Putri Apriza, RA Setya Handrastuti, Lady Aurora, Prinnisa Almanda Jonardi</td>
<td>Indonesia</td>
</tr>
<tr>
<td>79</td>
<td>Correlation between Febrile Seizure, Family History, and Imaging with ILAE 1989 Epilepsy Classification in Pediatric Patient in RSUPN Cipto Mangunkusumo</td>
<td>Regina Putri Apriza, RA Setya Handrastuti, Lady Aurora</td>
<td>Indonesia</td>
</tr>
<tr>
<td>79</td>
<td>Arsenic Poisoning-related Neuropathy Mimics Guillain-Barre Syndrome (GBS)</td>
<td>Kit-Yan Leung, Guan Yuet-Wong, Eric KC You, Sui-Fun Ng</td>
<td>Hong Kong</td>
</tr>
<tr>
<td>96</td>
<td>Early administration of vitamin B1/B6 and L-carnitine prevents the second attack of acute encephalopathy with biphasic seizures and late reduced diffusion</td>
<td>Kana Okazaki, Masaya Kubota, Hiroshi Terashima, Akira Ishiguro, Hirofumi Kashii</td>
<td>Japan</td>
</tr>
<tr>
<td>96</td>
<td>Migraine in Children and Adolescents with Tourette’s syndrome/Tics: A Population-based Cohort Study in Taiwan</td>
<td>Yang Yun-Hua, Lee Chuan-Pin, Yang Yao-Hsu, Chen Kai-Hua, McIntyre Roger S., Lee Yeno0, Chen Vincent Chin-Hung</td>
<td>Taiwan</td>
</tr>
<tr>
<td>176</td>
<td>Afebrile seizure in infancy associated with overconsumption of Ginkgo biloba seeds</td>
<td>Shigenobu Ishida, Shunsuke Kimura, Ayako Sakurai, Sunji Igarashi, Shosuke Sunami</td>
<td>Japan</td>
</tr>
<tr>
<td>195</td>
<td>Paediatric Status Epilepticus Treatment: A Qualitative Systematic Review of Regional/ National Guidelines 2010-2017</td>
<td>Cheuk Chung Au, Robert Tasker</td>
<td>Hong Kong</td>
</tr>
<tr>
<td>217</td>
<td>Multi-dimensional Impact of Paediatric Neuromuscular Disorders on Parents and Families</td>
<td>Yee-Ting Ip, Rui Liang, Sophelia Hoi-Shan Chan</td>
<td>Hong Kong</td>
</tr>
<tr>
<td>219</td>
<td>Effective Treatment of Quinidine in A Novel KCNT1 Mutation Associated Epileptic Encephalopathy: the First Case in Thailand</td>
<td>Wattanasiriwita, Thipwimol Tim-Arono, Duangrudee Wattanasiriwita, Chaisri Khongkhatthiboon</td>
<td>Thailand</td>
</tr>
<tr>
<td>229</td>
<td>Clinical Utility of A Non-Invasive and Easily Measured Index For Evaluation of Calf Muscles in Children with Walking Disabilities</td>
<td>Kenji Shin, Junko Nakayama, Tomohiro Nakayama, Haruka Oguro, Nobuaki Iwasaki</td>
<td>Japan</td>
</tr>
<tr>
<td>249</td>
<td>Efficacy of ketogenic diet according to pathogenic monogenic mutations in children with epileptic encephalopathies</td>
<td>Se Hee Kim, Seung Tae Lee, Hoon-Chul Kang, Joon Soo Lee, Jong Rak Choi, Heung Dong Kim</td>
<td>Korea</td>
</tr>
<tr>
<td>289</td>
<td>Quality of Management for headache in a Pediatric Emergency Population : blood pressure measurement and history interview</td>
<td>Kinumo Hirata, Junji Kamizono, Masano Amamoto, Kotaro Ichikawa</td>
<td>Japan</td>
</tr>
<tr>
<td>302</td>
<td>Neuromuscular involvement in children with mitochondrial disease: a single centre experience</td>
<td>Annie TG Chiu, Richard Rodenburg, Virginia CN Wong, Jan Smeitink</td>
<td>Hong Kong</td>
</tr>
<tr>
<td>392</td>
<td>Neuroprotective effect of Vitamin E and vitamin C by inhibiting autophagy of the epileptic rat hippocampus</td>
<td>Yi Qu, Fengyan Zhao, Rong Luo, Dezhi Mu</td>
<td>China</td>
</tr>
<tr>
<td>492</td>
<td>mir-96 attenuates status epilepticus-induced brain injury by directly targeting Atg16L1</td>
<td>Yi Qu, Fengyan Zhao, Rong Luo, Dezhi Mu</td>
<td>China</td>
</tr>
<tr>
<td>513</td>
<td>Muscle strength and pulmonary function in Duchenne Muscular Dystrophy</td>
<td>Sophelia Hoi-shan Chan, Rui Liang, Alice Chiu, Shuk Kuen Christy Chau, Wilfred Wong, So Lun Lee</td>
<td>Hong Kong</td>
</tr>
<tr>
<td>562</td>
<td>Calcification in cortex and other cerebral parenchyma affects pharmacoresistant epilepsy in tuberous sclerosis</td>
<td>Meng-Na Zhang, Ling-Yu Pang, Shu-Fang Ma, Meng-Jia Liu, Yang-Yang Wang, Lu-Lu Huang, Qian Lu, Shu-Fang Guo, Yang Gao, Guxia Zhang, Yu-Tian Liu, Xiu-Yu Shi, Li-Ping Zou</td>
<td>China</td>
</tr>
<tr>
<td>585</td>
<td>Early onset brain calcification is a risk factor for hypocalcemia after calcium supplement treatment in children with parathyroid disorders</td>
<td>Meng-Jia Liu, Jiu-Wei Li, Xiu-Yu Shi, Lin-Yan Hu, Li-Ping Zou</td>
<td>China</td>
</tr>
<tr>
<td>589</td>
<td>Rapamycin /sirolimus improves the behavior of an 8-year-old boy with nonsyndromic autism spectrum disorder</td>
<td>Lin-Yan Hu, Xiao-Fan Yang, Xiu-Yu Shi, Meng-Jia Liu, Li-Ping Zou</td>
<td>China</td>
</tr>
<tr>
<td>596</td>
<td>Alteration in gene expression after neural differentiation of rat mesenchymal stem cells by Salvia miltiorrhiza optimized protocol</td>
<td>Lin-Yan Hu, Xiao-Fan Yang, Xiu-Yu Shi, Meng-Jia Liu, Li-Ping Zou</td>
<td>China</td>
</tr>
</tbody>
</table>
All Submitted Abstracts with QR codes

661  China
Comparative retention rates of antiepileptic drugs in BECTS patients
Xiao-Jun Su, Meng-Jia Liu, Xiu-Yu Shi, Lin-yan Hu, Li-Ping Zou

664  China
Intermittent oral levetiracetam reduced recurrence of febrile seizure accompanied with epileptiform discharge: a pilot study
Lin-Yan Hu, Xiu-Yu Shi, Hui Li, Meng-Na Zhang, Shu-Fang Ma, Li-Ping Zou

667  China
Anti-N-methyl-D-aspartate Receptor Encephalitis with Severe Autonomic Dysfunctions in a Male Toddler: A Case Report
Li-Ying Liu, Li-Ping Zou, Ling-Yu Pang, Xiu-Yu Shi

671  China
POSS Scale can alert the occurrence of Posterior reversible encephalopathy syndrome
Li-Ying Liu, Li-Ping Zou, Ling-Yu Pang, Xiu-Yu Shi, Shu-Fang Ma

674  China
The clinical outcome of adjuvant therapy with verapamil on Dravet syndrome: a pilot study
Meng-Na Zhang, Xiao-Jun Su, Xiu-Yu Shi, Li-Ying Liu, Yang-Yang Wang, Li-Ping Zou

684  China
Homozygous ARHGEF2 Mutation Causes Intellectual Disability and Midbrain-hindbrain Malformation
Hao Hu, Ethiraj Ravindran, Hans-Hilger Ropers, Thomas F.

707  China
Rare mutation of POLG Gene in Chinese Han Ethnicity
Kunfang Yang, Chunmei Wang, Yongchen Yang, Hongyi Cheng, Yuanfeng Zhang, Linyi Meng, Simei Wang, Yanfen Lu, Jiaming Xi, Qin Lu, Jianjun Huang, Hong Zhang, Yucai Chen

710  China
Reversible splenial lesion syndrome in children
Wen-Xiong Chen

711  China
Recurrent meningitis in a boy with X-linked agammaglobulinaemia due to BTK gene mutation
Yan-Jun Gao, Si-Do Yang, Ke-Lu Zheng

712  China
Biomarkers of epilepsy: intensive review
Ahmed Arafat, Yin Fei

713  China
MiRNAs and Epilepsy, An outlook on the future: Review
Ahmed Arafat, Yin Fei

714  China
Inhibition of Huw1 Affects Apoptosis and Autophagy under Rat Cortex Neuron Oxygen-Glucose Deprivation/Reperfusion
Guoqian He, Yiping Zhu, Wenming Xu

715  China
LncRNA sequencing and ceRNA network analysis of Neonatal Rats following status epilepticus
Gan, Yi Qu, Fengyan Zhao, Rong Luo, Daxi Mu

1063  China
Long noncoding RNAs interfere with mitochondrial function in Down Syndrome
Kia-Jun Qiu, Yan-Na Liu, Zhao-Rui Ren, Jing-Bin Yan

1112  China
A Novel PANK2 Mutation in A 9-year-old Chinese Girl with Pantothenate Kinase-Associated Neurodegeneration
Tizhen Yan, Manxiang Zhou, Ren Cai, Renxiu Huang

1121  Hong Kong
Optimizing Function: 20-Years Review of Seating Service for Children with Spinal Muscular Atrophy
Kennis WY Ha, Mike WW Kwan, Sophelia HS Chan, Evelyn YL Kuong

1122  Korea
Cylinder Pump is More Effective in Administration of Pediatric Dose Dopamine Compared to Syringe Pump
Eunkyoung Kim, Seongjoo Park, Sunghee Han, Jinwoo Park, Cheong Lim

1131  China
Capture and Verification of Pathogenic Potassium Channel Gene in Genetic Epilepsy with Febrile Seizures Plus
Huafang Zou, Lin-Gan Wang, Jingwen Zhang, Muqing Zhuo, Yuxin Zhang, Xiaolu Zeng, Qiongxiang Zhai

1132  China
Nursing & Allied Health

1237  China
Inhibition of Huw1 Affects Apoptosis and Autophagy under Rat Cortex Neuron Oxygen-Glucose Deprivation/Reperfusion
Guoqian He, Yiping Zhu, Wenming Xu

1293  China
LncRNA sequencing and ceRNA network analysis of Neonatal Rats following status epilepticus
Gan, Yi Qu, Fengyan Zhao, Rong Luo, Daxi Mu

1544  China
Homozgyous ARHGEF2 Mutation Causes Intellectual Disability and Midbrain-hindbrain Malformation
Hao Hu, Ethiraj Ravindran, Hans-Hilger Ropers, Thomas F.

1728  Japan
A nationwide survey of pediatric acquired demyelinating syndromes in Japan
Takada-Yamaguchi, Hiroyuki Torisu, Ryutaro Kira, Yasunari Sakai, Yoshiho Ishizaki, Masayuki Sanefuji, Toshiro Hara, Shouichi Ohga

1740  Hong Kong
Miller Fisher Syndrome in Pediatric Population in Hong Kong
Wing-Ki Chan, Eric Kin-Cheong Yau, Sui Fun Ng, Sophelia Hoi-Shan Chan, Eva Lai-Wah Fung, Ling Kwong, Chi-Ho Tsang, Shun-Ping Wu, Louis Che-Kwan Ma Chun-Hung Ko

1843  China
A Novel PANK2 Mutation in A 9-year-old Chinese Girl with Pantothenate Kinase-Associated Neurodegeneration
Tizhen Yan, Manxiang Zhou, Ren Cai, Renxiu Huang

1883  China
Capture and Verification of Pathogenic Potassium Channel Gene in Genetic Epilepsy with Febrile Seizures Plus
Zhou, Lin-Gan Wang, Jingwen Zhang, Muqing Zhuo, Yuxin Zhang, Xiaolu Zeng, Qiongxiang Zhai

205  Hong Kong
Optimizing Function: 20-Years Review of Seating Service for Children with Spinal Muscular Atrophy
Kennis WY Ha, Mike WW Kwan, Sophelia HS Chan, Evelyn YL Kuong, Wang Chow
<table>
<thead>
<tr>
<th>Page</th>
<th>Country</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>82</td>
<td>Hong Kong</td>
<td>Promoting Healthy Eating in A School-Report of A Pilot Study</td>
<td>Sophie SF Leung, Albert Lee, Ruth Chan, Clare Yu, Rita Sung</td>
</tr>
<tr>
<td>83</td>
<td>Hong Kong</td>
<td>Promoting Healthy Eating in A Clinic Setting - Preliminary Report</td>
<td>Sophie SF Leung</td>
</tr>
<tr>
<td>97</td>
<td>Philippines</td>
<td>Caregiver Awareness of Food Calorie Information and Recommended Energy and Nutrient Intake (RENI) for Filipinos in Outpatient Department of Fe Del Mundo Medical Center</td>
<td>Theresia Umboh, Elsie Locson</td>
</tr>
<tr>
<td>139</td>
<td>Malaysia</td>
<td>Childhood feeding behaviours and difficulties in Malaysia</td>
<td>Way-Seah Lee, Chun-Wei Tee, Aaron Tan, Hon-Kit Cheang, Lucy Lum, Marion Aw</td>
</tr>
<tr>
<td>1702</td>
<td>China</td>
<td>Sudden death of two brothers due to very long-chain acyl-CoA dehydrogenase deficiency</td>
<td>Wang, Shuxiang Chen, Dongxia Li, Yi Liu, Ying Jin, Jinjing Song, Yao Zhang, Yanling Yang</td>
</tr>
<tr>
<td>23</td>
<td>Hong Kong</td>
<td>What Do Hong Kong Chinese Parents of Children with Asthma Tell Us? A Qualitative Descriptive Study</td>
<td>Yuen-Yu Chong, Doris Leung, Yim-Wah Mak, Shu-Yan Lam</td>
</tr>
<tr>
<td>194</td>
<td>Japan</td>
<td>A case of infant with prolonged severe respiratory failure after ARDS caused by allergy to soybean in amino acid-based formula</td>
<td>Masashiro Sugino, Noriko Fuke, Aya Hashimoto, Shinji Nakamura, Kosuke Koyano, Saneyuki Yasuda, Takashi Kusaka</td>
</tr>
<tr>
<td>324</td>
<td>China</td>
<td>A case report of cystic fibrosis in child identified by sweat and gene tests</td>
<td>Yong Cai, Dehui Chen, Shanghui Wu, Qiyun Xu, Qun Wang, Chengyun Lu, Yongxia Lei, Zhiying Yao, Wenkuan Liu, Qingsi Zeng</td>
</tr>
<tr>
<td>415</td>
<td>China</td>
<td>Diagnostic Value of Transbronchial Lung Biopsy in Pediatric Interstitial Lung Disease</td>
<td>Dehui Chen, Towen Zhang, Yuneng Lin</td>
</tr>
<tr>
<td>514</td>
<td>China</td>
<td>Clinical Analysis of Five Cases of Mycoplasma Pneumoniae Pneumonia with Fever Spontaneous Remission in Children</td>
<td>Qing Wei, Guang-Min Nong, Xiao-Bo Zhong, Xun Chen</td>
</tr>
<tr>
<td>538</td>
<td>China</td>
<td>Influence of Long-term Middle and Low Dose Inhaled Corticosteroids on the Prepubertal Growth of Children with Mild to Moderate Asthma</td>
<td>Fang, Lili Zhong, Meiting Tao, Han Huang</td>
</tr>
<tr>
<td>584</td>
<td>China</td>
<td>Mycoplasma pneumoniae23S rRNA A2063G mutation does not influence chest radiography features in children with pneumonia</td>
<td>Deyu Zhao, Huan Deng</td>
</tr>
<tr>
<td>632</td>
<td>China</td>
<td>Relationship Between Single RSV/HRV Infection and Expression of IFN-γ in Children</td>
<td>Meiting Tao, Yaping Xie, Lili Zhong, Han Huang</td>
</tr>
<tr>
<td>684</td>
<td>China</td>
<td>Extraluminal Use of the SF Arndt Endobronchial Blocker in Infant &lt;2 Years</td>
<td>Ting Xiao</td>
</tr>
<tr>
<td>757</td>
<td>China</td>
<td>The protective effect of resveratrol in respiratory system</td>
<td>Xiaodan Zhu, Wenzhong Dong</td>
</tr>
<tr>
<td>822</td>
<td>China</td>
<td>Detection of TXB2 in Children with Mycoplasma Pneumoniae Pneumonia and Its Relationship with Airway Mucus</td>
<td>Kuiyang Wang</td>
</tr>
<tr>
<td>854</td>
<td>China</td>
<td>Detection of H3-D-3 in Children with Refractory Mycoplasma Pneumonia and its Significance</td>
<td>Xiufang Wang</td>
</tr>
<tr>
<td>864</td>
<td>China</td>
<td>MicroRNA-223 Inhibits the Extracellular Matrix Deposition of Airway Smooth Muscle Cell Via PI3K/Akt Pathway By Targeting IGF-1R</td>
<td>Li, Qun Feng, Lu, Hao-xiang Gu, Bei-rong Wu</td>
</tr>
<tr>
<td>980</td>
<td>China</td>
<td>Analysis of cognitive status about nebulize therapy in Children with wheezing disease at home</td>
<td>Ai-Qiu Li, Qun-Feng Lu, Hao-xiang Gu, Bei-rong Wu</td>
</tr>
<tr>
<td>1027</td>
<td>China</td>
<td>The Correlation Between Main Caregiver Burden and Life Quality of Asthmatic Children</td>
<td>Ai-Qiu Li, Ying-Li Jiang, Xiao-Yan Dong, Min Lu</td>
</tr>
</tbody>
</table>
China
A Case Control Study of Serum Vitamin A and E Levels in Children with Obstructive Sleep Apnea Hypopnea Syndrome in Hunan Province
Xiaojuan Lin, Shuqin Qian, Lili Zhong, Xiaofang Ding, Yin Peng

China
Clinical Efficacy of Nebulization of Budesonide Combined with Ambroxol in the Treatment of Infants with Aspiration Pneumonia
Qionghua Chen, JIngyang Zheng, YIntao Lin, Li'e Zeng, Yanyan Liu, Chunyan Lin, Tan Zhang

China
The efficacy of bacterial lysate (bronchovaxom) in the acute phase of respiratory tract infection
Yuna Chang, Xiaohua Han

China
A Multicenter Preliminary Study of the Effect of Recombinant Human Interferon βb Treatment of Infants Hospitalized with Lower Respiratory Infection on Subsequent Wheezing
Guo-cheng Zhang, Lihua Yang, Xin Sun, Dongliang Xu, Changfian Liu, Lin Zhao, Zhuhua An, Jing Chen, Jianmin Xiong, Xue Xue, Bing Wei, Yanqi Su, Xiao Rong, Hui Shan, Chengpu Wang, Chenggang Wu, Xiaodong Rens, Haiming Yu, Li Liao, Shaofeng Song, Lusheng Huang, Jinfeng Liu, Hong Cao, Yujun Wang, Yi Xin

China
A Correlation Analysis Study of the Level of Serum 25-hydroxyvitamin D in Children with Bronchial Asthma
Qionghua Chen, Lang Chen

Hong Kong
Clinical Features and Disease Progression in Different Subgroups of Juvenile Idiopathic Arthritis
Asfia Banu Pasha, Guo-Ping Zhou

India
Kikuchi-Fujimoto Disease: A Great Mimicker
Sandesh Guleria, Rakesh Pilania, Vignesh Pandiarajan, Deepthi Suri, Surjit Singh

Indonesia
Recurrence of Kawasaki Disease in Indonesia: a Retrospective Study
Sandes Guleria, Ankur Jindal, Deepti Suri, Surjit Singh

Hong Kong
Raynaud’s Phenomenon and Acute Ischemic Foot - the Challenge in Early Identification and Management
Wing-Lum Cheung, Roanna Hoi-Man Yeung, Kin-Sun Tse, Winnie Kwai-Yu Chan

China
Neonatal-onset Multisystem Inflammatory Disease (NOMID) Due to A New Sequence Variant c.1568T>A of NLRP3 Gene in An Asian Infant
Grace Chiang, Miriam Weinstein, Ronald Laxer

China
Circulation Changes of Chemerin, Omentin-1 and Adiponectin in Acute Juvenile Idiopathic Arthritis
Xinyan Zhang, Huiling Lu

Hong Kong
Circulation Changes of Ceruloplasmin in the Acute Juvenile Idiopathic Arthritis
Xinyan Zhang, Huiling Lu

India
MEFV M694V mutation has a role in susceptibility to ankylosing spondylitis
Asfia Banu Pasha, Guo-Ping Zhou
<table>
<thead>
<tr>
<th>Author Names</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABOUABAKER Samira</td>
<td>64, 31</td>
</tr>
<tr>
<td>ABOU-NADER Alice</td>
<td>170</td>
</tr>
<tr>
<td>AHMED Tahmeed</td>
<td>95, 59</td>
</tr>
<tr>
<td>AHN Yo Han</td>
<td>172</td>
</tr>
<tr>
<td>AMORNPRASITPOL Kittituch</td>
<td>114</td>
</tr>
<tr>
<td>AN Yunfei</td>
<td>100</td>
</tr>
<tr>
<td>ANANTASIT Nattachai</td>
<td>163</td>
</tr>
<tr>
<td>ARAYAPONG Nat</td>
<td>166</td>
</tr>
<tr>
<td>ARDY Ariana</td>
<td>143</td>
</tr>
<tr>
<td>BENJAPONPITAK Suwat</td>
<td>52</td>
</tr>
<tr>
<td>CAI Xiao-Hong</td>
<td>173</td>
</tr>
<tr>
<td>CAMPANA Dairo</td>
<td>68</td>
</tr>
<tr>
<td>CHAN Chok Wan</td>
<td>65</td>
</tr>
<tr>
<td>CHAN Edward KL</td>
<td>61</td>
</tr>
<tr>
<td>CHAN Godfrey CF</td>
<td>70, 43</td>
</tr>
<tr>
<td>CHAN Jacky Chun-kit</td>
<td>92</td>
</tr>
<tr>
<td>CHAN James Chun-Yip</td>
<td>128</td>
</tr>
<tr>
<td>CHAN Kate Ching-ching</td>
<td>89</td>
</tr>
<tr>
<td>CHAN Renee Wan-Yi</td>
<td>164, 77</td>
</tr>
<tr>
<td>CHAN Sophelia Hoi-shan</td>
<td>81</td>
</tr>
<tr>
<td>CHANG Mei-Hwei</td>
<td>58, 35</td>
</tr>
<tr>
<td>CHANG Ling-Sai</td>
<td>129</td>
</tr>
<tr>
<td>CHEN Biyuan</td>
<td>134</td>
</tr>
<tr>
<td>CHEN Cheng</td>
<td>188</td>
</tr>
<tr>
<td>CHEN Feng</td>
<td>174</td>
</tr>
<tr>
<td>CHEN Qian</td>
<td>160</td>
</tr>
<tr>
<td>CHEN Wen-Xiong</td>
<td>135</td>
</tr>
<tr>
<td>CHEN Xiangpeng</td>
<td>169</td>
</tr>
<tr>
<td>CHEN Xun</td>
<td>137</td>
</tr>
<tr>
<td>CHEN Yulin</td>
<td>152</td>
</tr>
<tr>
<td>CHENG Jack</td>
<td>87</td>
</tr>
<tr>
<td>CHENG Qi</td>
<td>119</td>
</tr>
<tr>
<td>CHEONG Kai Ning</td>
<td>38</td>
</tr>
<tr>
<td>CHEUNG Yiu Fai</td>
<td>55</td>
</tr>
<tr>
<td>CHIANG Alan KS</td>
<td>69</td>
</tr>
<tr>
<td>CHIANG Grace Pui-king</td>
<td>90</td>
</tr>
<tr>
<td>CHIONG Rachel Shi-hui</td>
<td>131</td>
</tr>
<tr>
<td>CHONG Yuen-yu</td>
<td>118</td>
</tr>
<tr>
<td>CHOW Ching Pang</td>
<td>82</td>
</tr>
<tr>
<td>CHOW Chun Bong</td>
<td>34</td>
</tr>
<tr>
<td>CHUA Gilbert T</td>
<td>145</td>
</tr>
<tr>
<td>CHUNGSURIMIT Ampaiwan</td>
<td>155</td>
</tr>
<tr>
<td>CHUNG Brain Hon-yin</td>
<td>67</td>
</tr>
<tr>
<td>CHUNG Thomas Wai-hung</td>
<td>61</td>
</tr>
<tr>
<td>COLE Theresa</td>
<td>48</td>
</tr>
<tr>
<td>COVERDALE Gill</td>
<td>93</td>
</tr>
<tr>
<td>DAI Siyu</td>
<td>143</td>
</tr>
<tr>
<td>DAYAL Rajeshwar</td>
<td>70</td>
</tr>
<tr>
<td>DENG Ruixia</td>
<td>158</td>
</tr>
<tr>
<td>DHOUHADEL Bhim Gopal</td>
<td>76</td>
</tr>
<tr>
<td>DING Yuan</td>
<td>101</td>
</tr>
<tr>
<td>DJER Mulyadi</td>
<td>55</td>
</tr>
<tr>
<td>DONG Xiaoyan</td>
<td>129</td>
</tr>
<tr>
<td>FANG Fang</td>
<td>101</td>
</tr>
<tr>
<td>FANG Shiu-Bin</td>
<td>174</td>
</tr>
<tr>
<td>FANG Ying</td>
<td>160</td>
</tr>
<tr>
<td>FENG Yong</td>
<td>135</td>
</tr>
<tr>
<td>FENG Cheuk Wing</td>
<td>169</td>
</tr>
<tr>
<td>FENG Eva Lai-wa</td>
<td>137</td>
</tr>
<tr>
<td>GARCIA-CAZORLA Angela</td>
<td>87</td>
</tr>
<tr>
<td>GONZALEZ Maria</td>
<td>119</td>
</tr>
<tr>
<td>GU Qinglong</td>
<td>38</td>
</tr>
<tr>
<td>GUO Mengbiao</td>
<td>55</td>
</tr>
<tr>
<td>GUO Mindy</td>
<td>69</td>
</tr>
<tr>
<td>GUO Yong</td>
<td>90</td>
</tr>
<tr>
<td>HAQUE Qareen</td>
<td>131</td>
</tr>
<tr>
<td>HASAN Mahamudul</td>
<td>118</td>
</tr>
<tr>
<td>HE Jing</td>
<td>82</td>
</tr>
<tr>
<td>HE Yunyan</td>
<td>159</td>
</tr>
<tr>
<td>HO Frederick Ka-Wing</td>
<td>60</td>
</tr>
<tr>
<td>HO Marco Hok-kung</td>
<td>145</td>
</tr>
<tr>
<td>HO Federick</td>
<td>178, 144</td>
</tr>
<tr>
<td>HO Tsz Wai</td>
<td>67</td>
</tr>
<tr>
<td>HON Ellis</td>
<td>61</td>
</tr>
<tr>
<td>HOQUE Mahbubul</td>
<td>49</td>
</tr>
<tr>
<td>HORSUWAN Suchawadee</td>
<td>93</td>
</tr>
<tr>
<td>HU Fang-wen</td>
<td>143</td>
</tr>
<tr>
<td>HU Chijun</td>
<td>70</td>
</tr>
<tr>
<td>HU Hongwei</td>
<td>158</td>
</tr>
<tr>
<td>HUANG Chiung-Hui</td>
<td>76</td>
</tr>
<tr>
<td>HUANG Yongkun</td>
<td>101</td>
</tr>
<tr>
<td>HUI Wun Fung</td>
<td>55</td>
</tr>
<tr>
<td>HWARGN Gwen</td>
<td>159</td>
</tr>
<tr>
<td>IP Patrick</td>
<td>125</td>
</tr>
<tr>
<td>ISHIWADA Naruhiro</td>
<td>178, 132</td>
</tr>
<tr>
<td>JIANG Min</td>
<td>107</td>
</tr>
<tr>
<td>JIANG Xiaoling</td>
<td>139, 138</td>
</tr>
<tr>
<td>JIANG Yuan</td>
<td>181</td>
</tr>
<tr>
<td>JIN Yuting</td>
<td>81</td>
</tr>
<tr>
<td>JONG Yuh Jh</td>
<td>83</td>
</tr>
<tr>
<td>KAO Jun-Kai</td>
<td>150</td>
</tr>
<tr>
<td>KAWAMOTO Shohi</td>
<td>56</td>
</tr>
<tr>
<td>KIMURA Shunsuke</td>
<td>188</td>
</tr>
<tr>
<td>KINNEY Sharon Bridget</td>
<td>147</td>
</tr>
<tr>
<td>KIRKWOOD Carl</td>
<td>109</td>
</tr>
<tr>
<td>KOBAYASHI Masaru</td>
<td>178</td>
</tr>
<tr>
<td>KOHN Donald B</td>
<td>160</td>
</tr>
<tr>
<td>KU Cheng-Iung</td>
<td>177</td>
</tr>
<tr>
<td>KUBOTA Yasuo</td>
<td>161</td>
</tr>
<tr>
<td>KUI Lin</td>
<td>151</td>
</tr>
<tr>
<td>KUNG Charmaine Jing-Sum</td>
<td>62</td>
</tr>
<tr>
<td>KWOK Sit-Yee</td>
<td>53</td>
</tr>
<tr>
<td>LAM Hugh simon Hung-san</td>
<td>132</td>
</tr>
<tr>
<td>LAM Janice Ki-Pui</td>
<td>162</td>
</tr>
<tr>
<td>LAU Yu Lung</td>
<td>56, 90, 46, 39, 54</td>
</tr>
<tr>
<td>LEE Bee Wah</td>
<td>78</td>
</tr>
<tr>
<td>LEE Billie Suk-yin</td>
<td>174</td>
</tr>
<tr>
<td>LEE Pamela</td>
<td>178</td>
</tr>
<tr>
<td>LEE So Lun</td>
<td>126</td>
</tr>
<tr>
<td>LEE Way-Seah</td>
<td>146</td>
</tr>
<tr>
<td>LEE Wen-I</td>
<td>128</td>
</tr>
<tr>
<td>LEI Wei Te</td>
<td>146</td>
</tr>
<tr>
<td>LEUNG Agnes Sze-yin</td>
<td>173</td>
</tr>
<tr>
<td>LEUNG Ming</td>
<td>115</td>
</tr>
<tr>
<td>LEUNG Ting Fan</td>
<td>60</td>
</tr>
<tr>
<td>LEUNG Tomcy SF</td>
<td>74</td>
</tr>
<tr>
<td>LEUNG Wing</td>
<td>183</td>
</tr>
<tr>
<td>LEUNG Wing Kwan</td>
<td>152</td>
</tr>
<tr>
<td>LI Albert Martin</td>
<td>136</td>
</tr>
<tr>
<td>LI Chunyang</td>
<td>169</td>
</tr>
<tr>
<td>LI Dongxiao</td>
<td>80</td>
</tr>
<tr>
<td>LI Jade Wing-sum</td>
<td>124</td>
</tr>
<tr>
<td>LI Muhan</td>
<td>186</td>
</tr>
<tr>
<td>LI Yan</td>
<td>155</td>
</tr>
<tr>
<td>LI Chi-Kong</td>
<td>92</td>
</tr>
<tr>
<td>LI Fei</td>
<td>72</td>
</tr>
<tr>
<td>LI Tim MH</td>
<td>125</td>
</tr>
<tr>
<td>LJANG Jieqiong</td>
<td>160</td>
</tr>
<tr>
<td>LIAO Ning</td>
<td>177</td>
</tr>
<tr>
<td>LIKAMTO Charles</td>
<td>161</td>
</tr>
<tr>
<td>LIN Zefeng</td>
<td>141</td>
</tr>
<tr>
<td>LIN Tzou-Yien</td>
<td>126</td>
</tr>
<tr>
<td>LINN Kyaw</td>
<td>71</td>
</tr>
<tr>
<td>LIU Chuxue</td>
<td>133, 106</td>
</tr>
<tr>
<td>LIU Jian</td>
<td>124</td>
</tr>
<tr>
<td>LIU Lian</td>
<td>103</td>
</tr>
<tr>
<td>LIU Xian</td>
<td>135</td>
</tr>
<tr>
<td>LIU Xiaojuan</td>
<td>136</td>
</tr>
<tr>
<td>LIU Zhenhuan</td>
<td>176</td>
</tr>
<tr>
<td>LO Ivan Fai-man</td>
<td>67</td>
</tr>
<tr>
<td>LO MO Ao-Hung</td>
<td>109</td>
</tr>
<tr>
<td>LOU Jingan</td>
<td>139</td>
</tr>
<tr>
<td>LOUng Robert Po Yee</td>
<td>122</td>
</tr>
<tr>
<td>LUI Dorothy Sze-ting</td>
<td>144</td>
</tr>
<tr>
<td>LUK David Chi-kong</td>
<td>56</td>
</tr>
<tr>
<td>LUK Dik Wai Anderson</td>
<td>66</td>
</tr>
<tr>
<td>LUK Ho Ming</td>
<td>60</td>
</tr>
<tr>
<td>LUNG David Christopher</td>
<td>40</td>
</tr>
<tr>
<td>LUNAO Xiaoping</td>
<td>91</td>
</tr>
<tr>
<td>LUO Youyou</td>
<td>68</td>
</tr>
<tr>
<td>MA Mingshen</td>
<td>88</td>
</tr>
<tr>
<td>MAK Christopher CY</td>
<td>132</td>
</tr>
<tr>
<td>MANUYAKORN Wiparat</td>
<td>152</td>
</tr>
<tr>
<td>MAO Hua-wei</td>
<td>118</td>
</tr>
<tr>
<td>MATSUBARA Yoichi</td>
<td>168</td>
</tr>
<tr>
<td>67</td>
<td>36</td>
</tr>
<tr>
<td>Name</td>
<td>Score</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------</td>
</tr>
<tr>
<td>MEYERS Tammy</td>
<td>71</td>
</tr>
<tr>
<td>MITANI Yuichi</td>
<td>157</td>
</tr>
<tr>
<td>MIURA Kenichiro</td>
<td>144</td>
</tr>
<tr>
<td>MIZUNO Yumi</td>
<td>102</td>
</tr>
<tr>
<td>MIZUTANI Makoto</td>
<td>116</td>
</tr>
<tr>
<td>MONDAL Prasenjit</td>
<td>177</td>
</tr>
<tr>
<td>MORIO Tomohiro</td>
<td>49</td>
</tr>
<tr>
<td>MOSTAFA Ishita</td>
<td>117</td>
</tr>
<tr>
<td>MUNEUCHI Jun</td>
<td>130</td>
</tr>
<tr>
<td>MURATA Kenji</td>
<td>98</td>
</tr>
<tr>
<td>NAKAGAWARA Akira</td>
<td>69</td>
</tr>
<tr>
<td>NANISHI Etsuro</td>
<td>163</td>
</tr>
<tr>
<td>NELSON Tony</td>
<td>73</td>
</tr>
<tr>
<td>Ni Kei</td>
<td>123</td>
</tr>
<tr>
<td>NISHIO Hisanori</td>
<td>163</td>
</tr>
<tr>
<td>NUZHAT Sharika</td>
<td>177</td>
</tr>
<tr>
<td>OCHS Hans</td>
<td>51</td>
</tr>
<tr>
<td>ONOE Yasuhiro</td>
<td>187</td>
</tr>
<tr>
<td>OUCHI Kazunobu</td>
<td>74</td>
</tr>
<tr>
<td>PEI Steven LC</td>
<td>110</td>
</tr>
<tr>
<td>POON Grace Wing-kit</td>
<td>78</td>
</tr>
<tr>
<td>RAO Nirmala</td>
<td>64</td>
</tr>
<tr>
<td>RAWAT Amit</td>
<td>149</td>
</tr>
<tr>
<td>REN Xiao-xia</td>
<td>142</td>
</tr>
<tr>
<td>REN Yuqian</td>
<td>168</td>
</tr>
<tr>
<td>RERKSWATTAVORN Chaiwat</td>
<td>154</td>
</tr>
<tr>
<td>RIVERA Genesis</td>
<td>37</td>
</tr>
<tr>
<td>ROTENBERG Alexander</td>
<td>84</td>
</tr>
<tr>
<td>SAWAGUCHI Toshiko</td>
<td>122</td>
</tr>
<tr>
<td>SEGGER Reinhard</td>
<td>52</td>
</tr>
<tr>
<td>SEKIGUCHI Masahiro</td>
<td>157</td>
</tr>
</tbody>
</table>
Invasive meningococcal disease can cause DEATH within 24 hours.

Why RISK babies’ lives? Provide EARLIER protection for every future smile!
Infanrix hexa™ is the only 6-in-1 vaccine in Hong Kong with...

Key Safety Information

- Infanrix hexa™ is intended for use in children 6 weeks to 36 months of age.
- Very common adverse events (≥1/10): appetite lost, irritability, crying abnormal, restlessness, pain, redness, local swelling at the injection site (≤50mm), fever ≥38°C, fatigue.

References:

1. Very common adverse events (≥1/10): appetite lost, irritability, crying abnormal, restlessness, pain, redness, local swelling at the injection site (≤50mm), fever ≥38°C, fatigue.
2. Infanrix hexa™ is the only 6-in-1 vaccine in Hong Kong with...
3. the longest documented immunogenicity against all vaccine antigens for up to 7 years (and hepatitis B for up to 11 years).13-14
4. the widest approved coadministration options 4-5
5. over 10 years of clinical experience and over 135 million doses distributed worldwide 4-5,15-17

For adverse events reporting, please call GlaxoSmithKline Limited at 9046 2498.
Key Safety Information

- Very common adverse events (≥1/10): appetite lost, irritability, crying abnormal, restlessness, nervousness, sleepiness, abnormal crying, grunting, rubbing face, irritability, agitation, drowsiness, restlessness, hyperactivity, crying, somnolence, convulsions (with or without fever), collapse or shock-like state (hypotonic-hyporesponsiveness episode)
- Common adverse events (1/100 to <1/10): apnoea
- For adverse events reporting, please call GlaxoSmithKline Limited at 9046 2498.


References:
At Amgen, biologic medicines are rooted in quality and nurtured by reliability

Robust quality control and a reliable supply are every bit as important as scientific innovation.

For more than 30 years, Amgen has poured commitment, passion, and a drive for perfection into every medicine we make.

So you can turn to Amgen for the biologic medicines that matter so much to your patients’ treatment...for generations to come.

To learn more about Amgen’s commitment to consistent quality and reliable supply, visit biotechnologybyamgen.com
REVOLADE is the first and only once-daily oral TPO receptor agonist available for second-line use in paediatric patients with chronic ITP.

Significantly increased platelet counts

Significantly more patients achieved sustained platelet counts with REVOLADE vs control

Reduced the relative incidence of bleeding by 49% from baseline, vs 20% for control

Allowed patients to reduce or discontinue use of concomitant ITP medications, primarily corticosteroids

Generally well tolerated compared to control

Once-daily oral therapy

REVOLADE™ (eltrombopag olamine)

References:
2. Full prescribing information for Hong Kong.
For patients with IVIg therapy needs

Privigen®: 10% liquid IVIg

Simple
Sophisticated
Safe*

*Please refer to reverse page for further safety information
Refer to reverse page for Privigen® abbreviated product information

References:
2. CSL Behring, Hong Kong Privigen® Package Insert, November 2012.

CSL Behring is committed to protecting the privacy of all individuals it deals with. Additional information on how CSL Behring safeguards your privacy can be found at http://www.cslbehring.com/privacy.

**Hong Kong Privigen Abbreviated Product Information**

**Privigen®**
Human normal immunoglobulin, solution for infusion (10%).

**Indication:**
Replacement therapy in primary immunodeficiency syndromes (PID), myeloma or chronic lymphocytic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections, and children with congenital AIDS and recurrent infections. Immunomodulation in immune thrombocytopenic purpura (ITP) in children or adults at high risk of bleeding or prior to surgical interventions to correct the platelet count, Guillain-Barré syndrome, Kawasaki disease. Allogeneic bone marrow transplantation.

**Dosage:**
Dosage regimen is dependent on the indication. In replacement therapy the dosage may be individualised depending on pharmacokinetic and clinical response.

**Method of use:**
Privigen should be infused intravenously. Initial infusion at rate of 0.3 ml/kg bw/hr for 30 minutes. If well tolerated, the infusion rate can be gradually increased to 4.8 ml/kg bw/hr. Maximum rate is 7.2 ml/kg bw/hr.

**Adverse effects:**
Adverse reactions may include cold shivers, headache, fever, vomiting, allergic reactions, nausea, joint pain, low blood pressure and mild backache. Rare adverse reactions include hypersensitivity reactions, anaphylactic shock, temporary skin reaction and haemolytic reactions.

**Contraindications:**
Hypersensitivity to the active substance or excipient and homologous immunoglobulins. Hyperprolinaemia.

**Precautions:**
Certain severe adverse reactions may be related to rate of infusion. In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. Caution for hypersensitivity, haemolytic anaemia, aseptic meningitis syndrome, thromboembolism and acute renal failure.

@2016 CSL Behring Asia Pacific Limited

4205 - 4208, AIA Tower, 183 Electric Road, North Point, Hong Kong

PVG-HK-2016003

Date of preparation: April 2016

Before prescribing, please review the approved Hong Kong Package Insert.
Simple
- Ready-to-use 10% liquid human immunoglobulin for intravenous use (IVIg)
  - No warming or reconstitution necessary, saving preparation time and minimizing product waste
- 36-month room temperature (up to 25°C) storage
  - Saves refrigeration space

Sophisticated
- L-Proline-stabilized IVIg therapy
  - Contains no sugar (eg, sucrose or maltose)
  - Compared with other stabilizers, L-proline demonstrated better stabilizing activity and reduced dimer formation
  - L-Proline also reduces IgG aggregation, minimizes fragmentation, and prevents solution discoloration
- Appropriate for a broad range of patient types
  - IgA ≤25 mcg/mL
  - IgG purity ≥98%

Safe
In a clinical trial for primary immunodeficiency syndromes, the proportion of Privigen® infusions with temporally associated adverse events was 0.21, below the limit of 0.4 set by the USA Food and Drug Administration (FDA); 97% of adverse events were non-serious; 95% of 1,038 infusions were administered without premedication
- The most common adverse reactions (observed in >5% of subjects) were headache, fatigue, nausea, chills, back pain, pain, vomiting, pyrexia, sinusitis, cough, diarrhea and stomach discomfort

Before prescribing, please review the approved Hong Kong Package Insert.

Hong Kong Privigen Abbreviated Product Information
Privigen® Human normal immunoglobulin, solution for infusion (10%). Indication: Replacement therapy in primary immunodeficiency syndromes (PID), myeloma or chronic lymphocytic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections, and children with congenital AIDS and recurrent infections. Immunomodulation in immune thrombocytopenic purpura (ITP) in children or adults at high risk of bleeding or prior to surgical interventions to correct the platelet count, Guillain-Barré syndrome, Kawasaki disease. Allogeneic bone marrow transplantation. Dosage: Dosage regimen is dependent on the indication. In replacement therapy the dosage may be individualised depending on pharmacokinetic and clinical response.
Method of use: Privigen should be infused intravenously. Initial infusion at rate of 0.3 ml/kg bw/hr for 30 minutes. If well tolerated, the infusion rate can be gradually increased to 4.8 ml/kg bw/hr. Maximum rate is 7.2 ml/kg bw/hr. Adverse effects: Adverse reactions may include cold shivers, headache, fever, vomiting, allergic reactions, nausea, joint pain, low blood pressure and mild backache. Rare adverse reactions include hypersensitivity reactions, anaphylactic shock, temporary skin reaction and haemolytic reactions. Contraindications: Hypersensitivity to the active substance or excipient and homologous immunoglobulins. Precautions: Certain severe adverse reactions may be related to rate of infusion. In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. Caution for hypersensitivity, haemolytic anaemia, aseptic meningitis syndrome, thromboembolism and acute renal failure.

CSL Behring is committed to protecting the privacy of all individuals it deals with. Additional information on how CSL Behring safeguards your privacy can be found at http://www.cslbehring.com/privacy.

References:
2. CSL Behring, Hong Kong Privigen® Package Insert, November 2012.
Soliris (eculizumab) significantly reduces haemolysis – the underlying cause of progressive morbidities and mortality in Paroxysmal Nocturnal Haemoglobinuria (PNH) 1-3

- 86% reduction in haemolysis (as measured by LDH) 1
- 92% reduction in thrombotic events observed with Soliris 4
  - 94% reduction in thrombotic event rate in patients receiving antithrombotics 4
- 94% of patients had either maintained or improved kidney function 5
- 73% reduction in transfusions across patient populations 1
- Survival comparable to an age- and sex-matched normal population in a retrospective analysis 6
- Adverse drug reactions were mostly mild to moderate in severity 7

IN PATIENTS WITH aHUS, SOLIRIS:

- Inhibits complement-mediated TMA 1
- Protects vital organs against the risk of TMA 2
- Soliris therapy resulted in rapid and sustained reduction of complement-mediated haemolytic activity 2
- Ongoing Soliris treatment resulted in significant and continued improvement in renal function 2

Early intervention with Soliris in aHUS is vital in maximising clinical benefit 2

References:
7. Hong Kong Prescribing Information.
NOW AVAILABLE IN HONG KONG

1 vaccine to help protect against 4 childhood diseases

Help prevent measles, mumps, rubella, and varicella with ProQuad

The Only MMRV vaccine Approved By The US FDA & EMA

Make ProQuad a part of your practice

Selected Safety Information

Indications:
- ProQuad® is indicated for simultaneous vaccination against measles, mumps, rubella, and varicella in individuals from 15 months of age.
- ProQuad® can be administered to children from 8 months of age under special circumstances.

Contraindications:
- History of hypersensitivity to any varicella vaccine or measles, mumps, or rubella vaccine, to any of the excipients, or to neomycin, which may be present as trace residues.
- Blood dyscrasias, leukemias, lymphomas of any type, or other malignant neoplasms affecting the haematopoietic and lymphatic system.
- Current immunosuppressive therapy (including high doses of corticosteroids).
- ProQuad® is not contraindicated in individuals who are known to have been previously infected with human cytomegalovirus (e.g., for atheroma prophylaxis or replacement therapy).
- Severe humoral or cellular (primary or acquired) immunodeficiency (e.g., severe combined immunodeficiency, agammaglobulinemia and AIDS, or symptoms of HIV infection or an age-specific CD4<sub>+</sub> lymphocyte percentage ≤ 10%) children below 12 months CD4<sub>+</sub> ≥ 20%; children between 12-35 months: CD4<sub>+</sub> ≥ 20%; children between 36-59 months: CD4<sub>+</sub> ≥ 15%.
- In severely immunocompromised individuals (heterologous vaccine with measles-containing vaccine, measles inclusion body encephalitis, measles virus infection have been reported).
- Family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential vaccine recipient is demonstrated.
- Active untreated tuberculosis. Children under treatment for tuberculosis have not experienced exacerbation of the disease when immunized with live measles virus vaccine. No studies have been reported to date on the effect of treatment on the immune response to other vaccines.
- ProQuad® should not be used in patients with a history of a severe, immediate hypersensitivity reaction to any component of ProQuad®.
- ProQuad® may not result in protection in all vaccine recipients.

Vaccine recipients should avoid use of salicylates for 6 weeks after vaccination.

Adverse events:
- The adverse effects most frequently reported were as follows: injection-site reactions including redness, swelling or bruising; fever (≥39.4°C rectal equivalent); irritability; rash (including measles-like rash) and contacts infected with varicella; all were as high-risk individuals (immunosuppressed/individuals' prior vaccination status without documented positive history, vaccination or laboratory evidence of prior infection; neonates infants of mothers without documented positive history of varicella or laboratory evidence of prior infection) susceptible to varicella.
- This vaccine should be given subcutaneously to individuals with thrombocytopenia or any coagulation disorder because bleeding may occur following an intramuscular administration in these individuals.

In the 5- to 12-day timeframe after the administration of the first dose of quadrivalent measles, mumps, rubella and varicella vaccines in children, an increased risk of febrile seizure was observed compared to concomitant administration of measles, mumps, rubella and varicella vaccines.

Before prescribing, please consult the full prescribing information.
ILARIS® – a treatment for patients with frequent gouty arthritis attacks who cannot be managed with standard-of-care medication\(^1\)^\(^2\)

**ILARIS®** is also indicated for Cryopyrin-Associated Periodic Syndromes (CAPS) and Systemic Juvenile Idiopathic Arthritis (SJIA).\(^1\)^\(^2\)

For further information, please consult full prescribing information.

---

**References:**
**FIRST CHOICE**

**WELL-TRUSTED RA TREATMENT**

**OVER 8 YEARS CONFIDENCE**
with >860,000 patients treated

**THE TRUSTED MONOTHERAPY**
To show comparable efficacy to combination therapy

**LOCAL REGISTRY DATA**
most frequent biologics currently used for RA

**PORTUGUESE REGISTRY DATA**
higher remission rate vs. anti-TNFs

---

*Both ACTEMRA monotherapy and ACTEMRA combination therapy (with additional DMARDs) led to meaningful clinical and radiographic responses that could be maintained and, in some cases, improved upon in the first year of treatment. No major overall difference was observed in the ACT-RAY trial.**

APLAR: Asia Pacific League of Associations for Rheumatology; DMARDs: disease-modifying antirheumatic drugs; EULAR: European League Against Rheumatism; IV: intravenous; RA: rheumatoid arthritis; SC: subcutaneous; TNF: tumor necrosis factor.

References:

**Abbreviated Prescribing Information**

**ACTEMRA® (tocilizumab)**

Indications: Treatment of severe active rheumatoid arthritis in adults who are not responsive to or intolerant of treatment with MTX or who have responded inadequately to previous MTX therapy and who are candidates for combination therapy with MTX and a biologic DMARD. Treatment of severe active rheumatoid arthritis in pediatric patients 2 years of age and older who have responded inadequately to previous MTX therapy and who are candidates for combination therapy with MTX and a biologic DMARD. Treatment of rheumatoid arthritis in adult patients with active ankylosing spondylitis who have had an inadequate response to or intolerance to previous treatment with traditional disease-modifying antirheumatic drugs (DMARDs) and who are candidates for combination therapy with MTX and a biologic DMARD. Treatment of active ankylosing spondylitis in adult patients with active ankylosing spondylitis who have had an inadequate response to or intolerance to previous treatment with traditional DMARDs and who are candidates for combination therapy with MTX and a biologic DMARD. Treatment of active ankylosing spondylitis in pediatric patients aged ≥ 5 years with active ankylosing spondylitis who have had an inadequate response to or intolerance to previous treatment with traditional DMARDs and who are candidates for combination therapy with MTX and a biologic DMARD. Treatment of active ankylosing spondylitis in pediatric patients aged ≥ 2 years with active ankylosing spondylitis who have had an inadequate response to or intolerance to previous treatment with traditional DMARDs and who are candidates for combination therapy with MTX and a biologic DMARD. Treatment of active ankylosing spondylitis in pediatric patients aged ≥ 2 years with active ankylosing spondylitis who have had an inadequate response to or intolerance to previous treatment with traditional DMARDs and who are candidates for combination therapy with MTX and a biologic DMARD.

**How to use ACTEMRA® (tocilizumab)**

ACTEMRA® (tocilizumab) is supplied as a lyophilized powder for reconstitution with 3 ml of滅 fluid. After reconstitution, ACTEMRA® (tocilizumab) solution contains 20 mg/mL to be used immediately after reconstitution. ACTEMRA® (tocilizumab) administration may be repeated as long as the patient shows adequate response and no signs of toxicity attributable to ACTEMRA® (tocilizumab).

**Contraindications**

ACTEMRA® (tocilizumab) should not be used in patients with severe infections or in patients with a history of severe infections, progressive multifocal leukoencephalopathy, and with active malignancies (except basal cell carcinoma). ACTEMRA® (tocilizumab) should not be used in patients with active opportunistic infections (e.g., tuberculosis, histoplasmosis, or pneumocystis). ACTEMRA® (tocilizumab) should not be used in patients with active, severe active herpes zoster infection.

**Warnings and Precautions**

ACTEMRA® (tocilizumab) should not be used in patients with active infections, including tuberculosis, fungal, or viral infections. ACTEMRA® (tocilizumab) should not be used in patients with active, severe active herpes zoster infection. ACTEMRA® (tocilizumab) should not be used in patients with a history of severe infections, progressive multifocal leukoencephalopathy, and with active malignancies.

**Adverse Reactions**

The most common (≥ 5%) adverse reactions associated with ACTEMRA® (tocilizumab) use in rheumatoid arthritis patients were: infections (29%), nasopharyngitis (18%), pyrexia (14%), skin infections (13%), and respiratory tract infections (11%). The most common (≥ 5%) adverse reactions associated with ACTEMRA® (tocilizumab) use in ankylosing spondylitis patients were: infections (32%), nasopharyngitis (16%), skin infections (13%), and respiratory tract infections (10%).

**Patients and Healthcare Providers**

ACTEMRA® (tocilizumab) is recommended for use in patients who are candidates for combination therapy with MTX and a biologic DMARD. This summary describes important aspects of the prescribing information for ACTEMRA® (tocilizumab) and does not include all the information that is important to the use of this medicine. For complete and detailed information, please see the full Prescribing Information for ACTEMRA® (tocilizumab).
Our development programmes focus on the potential of autologous ex-vivo lentiviral gene therapy to restore normal gene function in primary immune deficiencies including ADA-SCID (adenosine deaminase severe combined immunodeficiency) and in inherited metabolic disorders such as MPS-IIIA (or Sanfilippo syndrome type A).

Learn more on our programs:
info@orchard-tx.com
www.orchard-tx.com
Our development programmes focus on the potential of autologous ex-vivo lentiviral gene therapy to restore normal gene function in primary immune deficiencies including ADA-SCID (adenosine deaminase severe combined immunodeficiency) and in inherited metabolic disorders such as MPS-IIIA (or Sanfilippo syndrome type A).

Learn more on our programs:
info@orchard-tx.com
www.orchard-tx.com

Bringing transformative gene therapy to life

Orchard Therapeutics is proud to support the 13th Congress of Asian Society for Pediatric Research

---

Head Shape Assessment by Certified Orthotists

- measure and evaluate babies’ head
- advise on re-positioning & stretches
- Specialists in Cranial Remoulding Helmet Therapy
  (corrects babies’ flat head, most effective at age 4-8 months)

Before

After

Call us (852) 3596 6123 for an appointment
www.flatheadbaby.com.hk

Suite 12-06, 12/F Albion Plaza
2-6 Granville Road, Tsim Sha Tsui, Kowloon

---

Orthopaedia
Private Paediatric Orthotic Centre
dedicated in treating babies with
Flat Head Syndrome (Plagiocephaly)
Acknowledgements

The 13th Congress of Asian Society for Pediatric Research organizers gratefully acknowledge sponsorship of the following

**Gold Plus**

GlaxoSmithKline Limited (and Lunch Symposium)

**Silver**

Pfizer Corporation Hong Kong Ltd. (and Lunch Symposium)

**Bronze**

Alexion Pharmaceuticals

CSL Behring Asia Pacific Ltd.

Merck Sharp & Dohme (Asia) Ltd.

Novartis Pharmaceuticals (HK) Ltd. (for 2 Bronze)

Roche Hong Kong Ltd.

Orchard Therapeutics Ltd.

(in alphabetical order)

**Others**

AMGEN

MEDA

MEINTECH

ORTHOPAEDIA

SANOFI PASTEUR
The 13th Congress of Asian Society for Pediatric Research
6-8 October 2017

Hosted by:
Hong Kong College of Paediatricians

Sponsors:

Asia Pacific Society for Immunodeficiencies

Paediatric Neurology Association of Hong Kong

Chinese Pediatric Society

ROTA Council

Hong Kong College of Paediatric Nursing

The Hong Kong Paediatric Haematology and Oncology Study Group

Hong Kong Paediatric & Adolescent Dermatology Society

The Hong Kong Society of Child Neurology and Developmental Paediatrics

Viva-Asia Blood and Marrow Transplant (VABMT) Consortium

Supported by:
- Hong Kong Neonatal Society
- Hong Kong Paediatric Nephrology Society
- Hong Kong Paediatric Nurses Association
- Hong Kong Society for Adolescent Health
- Hong Kong Society of Paediatric Cardiology
- Hong Kong Society of Paediatric Endocrinology and Metabolism
- Hong Kong Society of Paediatric Respirology and Allergy
- Macau Pediatric Society
- The Hong Kong Society for Paediatric Rheumatology
- The Hong Kong Society of Paediatric Gastroenterology