

International Symposium on Epilepsy in Neurometabolic Diseases (ISENMD)

The 13th Annual Meeting of the Infantile Seizure Society (ISS)
The 14th Annual Meeting of the Taiwan Child Neurology Society

March 26-28, 2010 Taipei, Taiwan

Epilepsy in Neurometabolic Diseases

Venue:

Howard Plaza Hotel, Taipei, Taiwan

Host:



Taiwan Child Neurology Society (TCNS), Taiwan

Infantile Seizure Society (ISS), Japan

Co-Host:

China Medical University

Taipei Medical University

Department of Health, Taipei City Government

Supported by:

Taiwan Pediatric Association

Taiwan Epilepsy Society

Final Program and Abstract

Overview of Program

| March 26 Friday | March 27 Saturday | March 28 Sunday |
|---|--|---|
| | 07:30- Registration | 07:30- Registration |
| | 08:15-10:00 General and Aminoacidopathy O07 Raman Sankar (45 min) O08 Wang-Tso Lee (20 min) O09 Shigeo Kure (40 min) | 08:15-10:30 Mitochondrial Diseases O24 Jong Hee Chae (40 min) O25 Hsiu-Fen Lee (20 min) O26 Chitra Prasad (45 min) O27 Cheuk-Wing Fung (15 min) O28 Chee-Ming Teh (15 min) |
| | 10:00-10:20 Coffee Break | 10:30-11:15 Coffee Break & Poster Visit (2) |
| | 10:20-12:05 Aminoacidopathy O10 Asuri N. Prasad (45 min) O11 Jia-Wei Hou (30 min) O12 Dau-Ming Niu (30 min) | 11:15-12:15 Peroxisomal Disorders O29 Nobuyuki Shimozawa (40 min) O30 Jao-Shwann Liang (20 min) |
| 12:00- Registration | 12:25-13:10 Lunch Seminar (1) O13 Philip L. Pearl (45 min) | 12:20-13:30 Lunch Seminar (2) O31 Ki-Joong Kim (35 min) O32 Asuri N. Prasad (35 min) |
| 14:20-14:30 Opening Addresses | 13:10-14:50 Organic Acid & Urea Cycle Disorders O14 Seiji Yamaguchi (40 min) O15 Yue-Hua Zhang (30 min) O16 Wuh-Liang Hwu (30 min) | 13:30-15:10 Vitamin & Mineral Metabolic Disorders O33 Peter Baxter (45 min) O34 Shunsuke Ohtahara (40 min) O35 Pratibha Singhi (15 min) |
| 14:30-16:00 General O01 Ching-Shiang Chi (20 min) O02 Jiong Qin (30 min) O03 Joyce Y. Wu (40 min) | 14:50-15:35 Coffee Break & Poster Visit (1) | 15:10-15:30 Coffee Break |
| 16:00-16:20 Coffee Break | 15:35-18:00 Lipid Metabolism & Lysosomal Storage Diseases O17 Ingrid Tein (45 min) O18 Hiroyuki Ida (40 min) O19 Shyi-Jou Chen (20 min) O20 Ralph Z. Kern (40 min) | 15:30-17:00 Neurotransmitter Diseases & Miscellaneous O36 Philip L. Pearl (45 min) O37 Shinn-Fornng Peng (30 min) O38 Yoshiko Nomura (15 min) |
| 16:20-18:30 General O04 Yoshiyuki Suzuki (40 min) O05 Hans H. Goebel (45 min) O06 Robert A. Zimmerman (45 min) | 18:00-18:45 Cross-Strait Session O21 Ding-An Mao (15 min) O22 Hui Xiong (15 min) O23 Dar-Shong Lin (15 min) | 17:00-17:30 Discussion Summary |
| 18:30-18:50 Business Meeting (TCNS) | | 17:30-17:50 Closing Addresses Best Poster Award Ceremony |
| 19:30-21:00 Welcome Party | 19:30-21:30 Grand Social Party | 18:00-19:00 AOCNA Delegate Meeting |
| | | 19:30-21:30 Farewell Party (Invitees only) |



Contents



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Welcome Message

Cordial Welcome!

It is my great pleasure to invite any person in the world who are interested in the study of seizures in neonates, infants and young children to the forthcoming International Symposium on Epilepsy in Neurometabolic Diseases (ISENMD), Taipei, Taiwan, March 26-28, 2010. This Symposium constitutes the 13th Annual Meeting of the Infantile Seizure Society (ISS).



Remarkably, there are two key features which are worth to be notified. The one is its main theme chosen; modern sophisticated technological advances are clarifying various kinds of genetic/acquired neurometabolic derangements, rendering immature brain more susceptible to seizures. Metabolic approach is a new promising avenue of research in effectively elucidating the causation of epilepsy. Despite, such a comprehensive project as ISENMD, which will concentrate on causal relation between epilepsy and neurometabolic diseases, has been quite rare in the past.

Similarly conspicuous is the fact the ISENMD will be held in Taipei, Taiwan, one of the most prosperous Asian metropolis. Being peaceful and rich in cultural flavor and delicious cuisine, Taiwan is nicknamed as an Island of Dream.

ISENMD will be fully supported by the Taiwan Child Neurology Society. By attending the ISENMD, you will certainly be benefited professionally, but also you would be able to enjoy a rare humane experience in the dream island.

Yukio Fukuyama, M.D.

*Chairperson,
Infantile Seizure Society
Honorary President,
Asian & Oceanean Child Neurology Association*





Dear colleagues and friends,

On behalf of the Organizing Committee, I am very pleased to invite you to the 13th Annual Meeting of the Infantile Seizure Society and The International Symposium on Epilepsy in Neurometabolic Diseases (ISENMD) which will be held in Taipei, Taiwan, March 26-28, 2010.



Although each inborn error of metabolism is rare, in the aggregate they make a significant contribution to the causes of mental retardation, seizures, sudden infant death, and neurologic impairment. Inborn errors of metabolism result from a genetic deficiency in a metabolic pathway; signs and symptoms result from the accumulation of metabolites related to the pathway. The most common neurometabolic disorders to be considered are organic acidemias and aminoacidopathies followed by neuronal ceroid lipofuscinoses, urea cycle disorders, congenital lactic acidosis, peroxisomal disorders, and, less frequently, sphingolipidoses, mucopolysaccharidoses, glycoprotein degradation disorders and fatty acid oxidation disorders. The approach to diagnosis and management requires knowledge of the pathophysiology of the disorders and what laboratory analyses provide the best measure of clinical control. We believe that this symposium will be inspiring and very helpful to all participants as many famous and outstanding physicians in this field are invited from around the world. It is also a good opportunity to know the current views and progress of “Epilepsy in Neurometabolic Diseases”.

Taipei, the political, economic and recreational center of our country, is offering an array of significant cultural sights. The city is situated in a basin in northern Taiwan. With the exotic culture, breathtaking scenery, priceless art, the entire range of Chinese cuisine, and very hospitable people, it makes Taipei an ideal place for both business and leisure. Taipei also offers a wide range of other diversions – shopping malls, night clubs, live-music bars, quality hotels, and gourmet restaurants.

Howard Plaza Hotel is located near commercial and financial hubs in the prosperous east of Taipei city and serves Chinese cuisine and global culinary delights await the pleasure of our guests and offers luxurious accommodation and warm personalized service combined with all the comforts of home in the capital city.

Sincerely yours,

Ein-Yiao Shen, M.D.

President,

*Taiwan Child Neurology Society and International Symposium on Epilepsy
in Neurometabolic Diseases (ISENMD)*



Organization

Host Organization

Taiwan Child Neurology Society (TCNS), Taiwan; Infantile Seizure Society (ISS), Japan
(By last name alphabetical order)

Organizing Committee

| | | | | |
|---------------------------|----------------|-----------------|---------------|------------------|
| Congress President | Ein-Yiao Shen | | | |
| Secretary General | Kai-Ping Chang | | | |
| Treasurer | Shyi-Jou Chen | | | |
| Member | Ming-Yuh Chang | Wun-Tsong Chaou | Chu-Chin Chen | Ching-Shiang Chi |
| | Nan-Chang Chiu | I-Ching Chou | Pi-Chuan Fan | Che-Sheng Ho |
| | Kun-Long Hung | Yuh-Jyh Jong | Yung-Ting Kuo | Hsiu-Fen Lee |
| | Wang-Tso Lee | Kuang-Lin Lin | Ming-I Lin | Huei-Shyong Wang |
| | Geng-Chang Yeh | | | |
| Spokesperson | I-Ching Chou | | | |

Scientific Committee

| | | | | |
|-----------------------|------------------|---------------|------------------|------------------|
| Chairperson | Kun-Long Hung | | | |
| Co-Chairperson | Wang-Tso Lee | | | |
| Members | Kai-Ping Chang | Shyi-Jou Chen | Ching-Shiang Chi | Che-Sheng Ho |
| | Chao-Ching Huang | Yuh-Jyh Jong | Ein-Yiao Shen | Huei-Shyong Wang |
| | Geng-Chang Yeh | | | |

Advisory Committee

| | | | | |
|------------------------|-------------------|-----------------|------------------|--------------------|
| Supreme Advisor | Yukio Fukuyama | | | |
| Chairperson | Ching-Shiang Chi | | | |
| Co-Chairperson | Wun-Tsong Chaou | | | |
| Advisor | Yuan-Tsong Chen | Mei-Mei Ho | Yong-Seung Hwang | Toyojiro Matsuishi |
| | Shunsuke Ohtahara | Liu-Ching Shiao | Kenji Sugai | Yoshihiro Takeuchi |
| | Chang-Hai Tsai | Seiji Yamaguchi | Hitoshi Yamamoto | Pen-Jung Wang |
| | Xi-Ru Wu | | | |

Financial Committee

| | | | | |
|-----------------------|----------------|-------------|----------------|----------------|
| Chairperson | Shyi-Jou Chen | | | |
| Co-Chairperson | Ming-Yuh Chang | | | |
| Members | Yi-Yen Lee | Sung-Tse Li | Hung-Ying Tsai | Ann-Ching Wang |
| | Tai-Tong Wong | | | |

Exhibition Committee

| | | | | |
|-----------------------|-----------------|----------------|---------------|--------------|
| Chairperson | Yuh-Jyh Jong | | | |
| Co-Chairperson | Che-Sheng Ho | | | |
| Members | Ying-Chao Chang | Yung-Jung Chen | Yung-Ting Kuo | Wang-Tso Lee |
| | Ming-Liong Tso | | | |

Facility Committee

| | | | | |
|-----------------------|-----------------|-------------|------------|---------------|
| Chairperson | Ming-I Lin | | | |
| Co-Chairperson | Pi-Chuan Fan | | | |
| Members | Wen-Cheng Chang | Yu-Chia Kao | Yi-Pei Lin | Whey-Chen Sue |
| | Ming-Tao Yang | | | |

Publication Committee

| | | | | |
|-----------------------|-----------------|------------------|--------------|----------------|
| Chairperson | Geng-Chang Yeh | | | |
| Co-Chairperson | Yung-Ting Kuo | | | |
| Members | Hsaio-Feng Chou | Cheng-Hung Huang | Hsiu-Fen Lee | Hung-Tsai Liao |
| | Haung-Chi Lin | | | |

Social Committee

| | | | | |
|-----------------------|------------------|----------------|--------------|---------------|
| Chairperson | Huei-Shyong Wang | | | |
| Co-Chairperson | Kuang-Lin Lin | | | |
| Members | Chu-Chin Chen | Nan-Chang Chiu | I-Ching Chou | Ting-Rong Hsu |
| | Pen-Jung Wang | | | |



General Information

Date

March 26th (Fri.) – March 28th (Sun.), 2010

Secretariat Office

c/o K&A International Co., Ltd.

7F, No.249, Fuxing South Road, Section 1, Taipei, Taiwan

Tel: +886-2-2701-8768 Fax: +886-2-2702-2025

Email: isenmd2010@knaintl.com.tw

Website: www.isenmd2010taipei.org

Venue

Howard Plaza Hotel Taipei

No. 160, Jen-Ai Road, Sec. 3, Taipei, Taiwan

Location: B2, Banquet Hall I+II

Plenary Sessions

Location: B2, Banquet Hall I+II

Slides Preview Room & VIP Lounge

Opening Hours: March 26, 12:00-18:00

March 27-28, 07:30-18:00

Location: B2, Peony Room

TCNS Business Meeting

Date & Time: Friday, March 26, 18:30-18:50

Location: B2, Banquet Hall I+II

Lunch

Lunch will be served for participants during Lunch

Seminar on March 27 and March 28.

Official Language

English

Secretariat Office On-site

Opening Hours: March 26, 12:00-18:00

March 27-28, 07:30-18:00

Location: B2, Osmanthus & Balsam Room

Registration / Information Desk

Opening Hours: March 26, 12:00-18:00

March 27-28, 07:30-18:00

Location: Next to Exhibition Area

ISS & AOCNA Information Desk

Location: B2, in front of Lily and Jasmine Room

Sponsor Exhibitions

Opening Hours: March 26, 12:00-18:00

March 27-28, 07:30-18:00

Location: B2, Banquet Hall III, Lily, Jasmine, Hibiscus, Rose, Narcissus and Magnolia Room

AOCNA National Delegate Meeting

Date & Time: Sunday, March 28, 18:00-19:00

Location: 4F, Room 406

Official Certificate for Attendance and CME Points

An official certificate for attendance at the ISENMD will be delivered to all participants. To Japanese colleagues, authorized CME units will be rewarded by three societies as following CME Points.

| Society | Attendance | Authorship | |
|-------------------------------------|------------|------------|-----------|
| | | Presenter | Co-author |
| Japan Pediatric Society | 5u | 0u | 0u |
| Japan Epilepsy Society | 5u | 20u | 0u |
| Japanese Society of Child Neurology | 2u | 2u | 0u |

U = unit



Social Program

1. Welcome Party

Date & Time: Friday, March 26, 19:30-21:00

Location: B2, Banquet Hall I+II, Howard Plaza Hotel

Attire: Casual

* Voucher required to enter Welcome Party

2. Grand Social Party

Date & Time: Saturday, March 27, 19:30-21:30

Location: B2, Banquet Hall I+II, Howard Plaza Hotel

Attire: Smart Casual

* Participant Badge required to enter Grand Social Party

3. Farewell Party

Date & Time: Sunday, March 28, 19:30-21:30

Location: 3F, Cool Meeting Room, Grand Victoria Hotel

Attire: Casual

* By Invitation only. Shuttle buses will be provided between Victoria and Howard Plaza Hotel. Please meet at the Howard Plaza Hotel lobby at 18:50 for boarding.

Conference Excursion

(Complimentary for registered participants and accompanying persons)

Half Day Taipei City Tour (March 29)

Pick-up: 09:00 at Howard Plaza Hotel Lobby

Duration: 3 hrs

Tour Stops: Martyrs' Shrine → National Palace Museum
→ Chiang Kai-shek Memorial Hall → Chinese Temple
→ Presidential Office (Pass by) → Handicraft Center

Introduction: The tour takes you to the Martyrs' Shrine to see the impressive classical architecture, to the National Palace Museum to view priceless art treasures recording the 5,000-year history of Chinese culture, to the Chiang Kai-Shek Memorial Hall--an imposing Chinese-style monument to the late President-- and to Chinese temple to observe its religious activities.





Instructions for Oral Presentations

Preview Room Operation Hours

Opening Hours: March 26, 12:00-18:00

March 27-28, 07:30-18:00

Location: B2, Peony Room

1. All speakers are requested to strictly observe the allotted presentation time. Since the conference schedule is tight, session chairpersons will strictly enforce the timing. The staff will ring the bell for time-reminding. First bell suggests there will be 5 minutes left before presentation ends; the second bell will ring 3 minutes later.
2. It is required to use the laptop prepared by the conference for stable computer system connection. For any reason that you **MUST** use your own laptop, please inform the secretariat in advance.
3. The conference will have a laptop set up at the podium for all presenters. A remote control for changing the slides will be prepared; the presenter can control the slides on his/her own.
4. All presentation slides should be prepared by "Microsoft Office PowerPoint 2002" or above. **Kindly advise the secretariat, if your slides are prepared by "Microsoft Office PowerPoint 2007".**
5. Every speaker is requested to finish up an arrangement necessary for data projection **two hours** before the respective presentation at the latest, by contacting the staff of the Peony Room, located on B2. It is suggested you to save your final slides both in a CD-R and a USB flash memory and bring to the Preview Room.
6. If your slides are prepared by Mac system, the data may deform after its transfer to the Windows system. Please check and correct this possible deformation at the Preview Room.
7. Video tape presentation is not available. If you need to use video records, please transfer them to the computer in a digital form. **The projection does not support Full HD video mode**, please avoid this kind of file format. If you prepare to use a Mac laptop, please bring the **Apple DVI to VGA display adapter**. The connector of the projector is D-SUB, be sure the correct adapter is brought with you.
8. Standard microphone is prepared for all presenters, if you wish to use a pin-microphone or wireless one, or any other special equipment or need, please advise in advance for proper arrangement.
9. Please remind that the details of the oral presentations will be delivered over a network by audio/video streaming, thereby enabling closed-users to see and hear the audio and video files. In this data streaming, the majority of PC slides will be shown with synchronized oral presentations. It will contain almost all lectures and discussions presented at the ISENMD. In this regard, if you have any problems, or any PC slides that you want to delete from this data streaming, please contact the staff of Preview Room.

Instructions for Discussion

1. Active discussions from the floor are encouraged as far as the time is available.
2. All aspects of discussion session shall be ordered by due consideration of chairpersons.
3. Anyone who wishes to raise a question/discussion can raise their hands and wait for an order of chairpersons. To begin your discussion, please identify yourself first.



Instructions for Poster Presentations

Poster Presentation Operation Hours

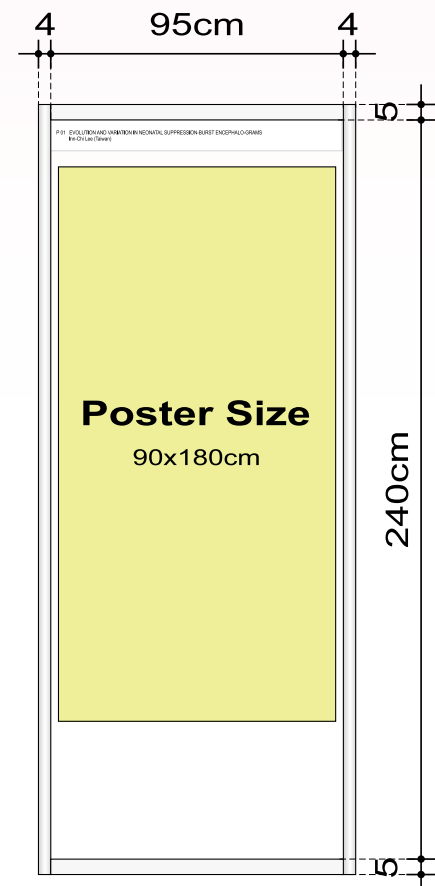
Mounting: March 26, 12:00-18:00

Exhibition: March 26, 14:20 to March 28, 17:30

Removal: Poster presenter may start take down the poster from 15:20-17:30 on March 28

Location: B2, Banquet Hall III

1. Necessary office supplies for mounting will be provided on-site. Staple guns are prohibited for mounting. Conference will provide free masking tape for all poster presenters.
2. In the event of posters not removed after 17:50 on March 28, 2010, the staff will remove them without further notice.
3. All poster board has a surface of 90 cm wide and 180 cm high. Top corner space will be used to place the poster number, pre-fixed by the Secretariat.
4. Poster judges will evaluate all posters during Coffee Break & Poster Visit (1) and (2), between 14:50 to 15:35 on March 27 and 10:30 to 11:15 on March 28, 2010. Presenters are suggested to be present at the site of respective posters for discussion during the two time period.
5. Conference will present poster award at the Closing Ceremony on March 28. We strongly encourage all poster presenters to stay on-site to receive the award and scholarship.



Poster Board Size

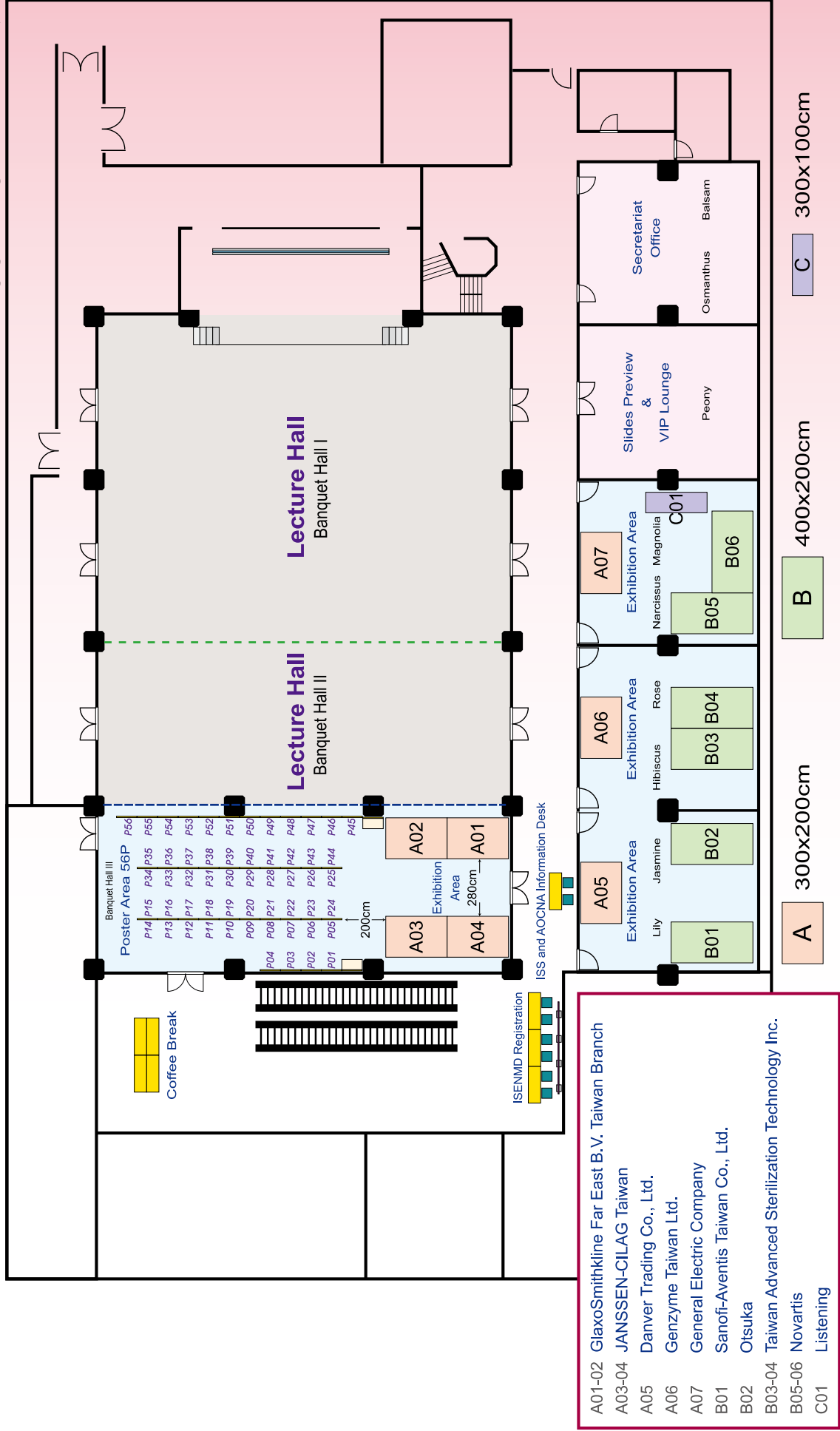
Floor Plan

Plenary Sessions: Banquet Hall I+II
Lunch Seminar: Banquet Hall I+II

Welcome Party: Banquet Hall I+II
Grand Social Party: Banquet Hall I+II

Howard Plaza Hotel Taipei

B2 Floor Plan S:1/250;cm





Program

Day 1, March 26 (Friday)

Opening Addresses 14:20-14:30

Yukio Fukuyama (Chairperson, Board of Councilor, ISS)

Ein-Yao Shen (President, ISENMD)

Session I Clinical and Neurophysiological Diagnoses of Neurometabolic Diseases 14:30 -16:00

Chairpersons: Shinichi Niijima (Tokyo, Japan)

Ein-Yao Shen (Taipei, Taiwan)

O 01 14:30 -14:50

NEUROMETABOLIC DISEASES IN TAIWAN

Ching-Shiang Chi (Taichung, Taiwan)

O 02 14:50 -15:20

THE NEUROLOGICAL MANIFESTATION OF INBORN ERRORS OF METABOLISM IN MAINLAND CHINA

Jiong Qin (Beijing, China)

O 03 15:20 -16:00

NEUROPHYSIOLOGICAL CHARACTERISTICS OF NEUROMETABOLIC DISEASES IN CHILDREN

Joyce Y. Wu (Los Angeles, USA)

Coffee Break 16:00 -16:20

Session II Molecular Basis, Neuropathology and Neuroimaging of Neurometabolic Diseases 16:20 -18:30

Chairpersons: Takao Takahashi (Tokyo, Japan)

Geng-Chang Yeh (Taipei, Taiwan)

O 04 16:20 -17:00

MOLECULAR BASIS OF METABOLIC ENCEPHALOPATHY - NEUROGENETIC DISEASES: FROM MOLECULE TO PATIENT

Yoshiyuki Suzuki (Tokyo, Japan)

O 05 17:00 -17:45

NEUROPATHOLOGY OF NEUROMETABOLIC DISEASES IN CHILDREN WITH EPILEPSY

Hans H. Goebel (Mainz, Germany)

O 06 17:45 -18:30

NEUROIMAGING PERSPECTIVES IN PEDIATRIC NEUROMETABOLIC DISEASES WITH EPILEPSY

Robert A. Zimmerman (Philadelphia, USA)

Business Meeting of Taiwan Child Neurology Society 18:30 - 18:50

Welcome Party 19:30 - 21:00

B2 Banquet Hall I+II Howard Plaza Hotel



Day 2, March 27 (Saturday)

Session III General and Aminoacidopathy

08:15 -10:00

Chairpersons: Yong-Seung Hwang (Seoul, Korea)
Raman Sankar (Los Angeles, USA)

O 07 08:15 - 09:00

CLINICAL PERSPECTIVES OF EPILEPSY AMONG NEUROMETABOLIC DISEASES IN CHILDREN

Raman Sankar (Los Angeles, USA)

O 08 09:00 - 09:20

AMINO ACID METABOLIC DISORDERS AND INFANTILE EPILEPSY

Wan-Tso Lee (Taipei, Taiwan)

O 09 09:20 -10:00

NON-KETOTIC HYPERGLYCEMIA

Shigeo Kure (Sendai, Japan)

Coffee Break

10:00 -10:20

Session IV Aminoacidopathy

10:20 -12:05

Chairpersons: Toyojiro Matsuishi (Kurume, Japan)
Nan-Chang Chiu (Taipei, Taiwan)

O 10 10:20 -11:05

METHYLENE TETRAHYDROFOLATE REDUCTASE (MTHFR) DEFECIENCY AND INFANTILE EPILEPSY

Asuri N. Prasad (London, Canada)

O 11 11:05 -11:35

MAPLE SYRUP URINE DISEASE AND INFANTILE EPILEPSY

Jia-Wei Hou (Taipei, Taiwan)

O 12 11:35 -12:05

LONG-TERM TREATMENT AND PROGNOSIS OF CHINESE PATIENTS WITH 6-PYRUVOYL-TETRAHYDROPTERIN SYNTHASE DEFICIENCY

Dau-Ming Niu (Taipei, Taiwan)

Lunch Seminar (1)

12:25-13:10

Chairperson: Kenji Sugai (Tokyo, Japan)
Sponsored by GlaxoSmithKline Far East B.V. Taiwan Branch

O 13 12:25 -13:10

TREATABLE METABOLIC EPILEPSIES: CASE STUDIES

Phillip L. Pearl (Washington DC, USA)



Session V Organic Acid and Urea Cycle Disorders

13:10 -14:50

Chairpersons: Yoshihiro Takeuchi (Shiga, Japan)
Yung-Ting Kuo (Taipei, Taiwan)

O 14 13:10 -13:50

HEAT STRESS AND ACUTE ENCEPHALOPATHY IN CHILDHOOD DUE TO INHERITED ORGANIC AND FATTY ACID DISORDERS

Seiji Yamaguchi (Shimane, Japan)

O 15 13:50 -14:20

METHYLMALONIC ACIDEMIA IN CHINA

Yue-Hua Zhang (Beijing, China)

O 16 14:20 -14:50

EPILEPSY IN UREA CYCLE DEFECTS

Wuh-Liang Hwu (Taipei, Taiwan)

Coffee Break and Poster Visit (1)

14:50-15:35

Session VI Lipid Metabolism and Lysosomal Storage Diseases

15:35 -18:00

Chairpersons: Geoffrey Wallace (Brisbane, Australia)
Huang-Tsung Kuo (Taichung, Taiwan)

O 17 15:35 -16:20

CARNITINE AND FATTY ACID OXIDATION DEFECTS IN INFANTILE EPILEPSY

Ingrid Tein (Toronto, Canada)

O 18 16:20 -17:00

NEUROLOGICAL ASPECTS OF LYSOSOMAL STORAGE DISEASES

Hiroyuki Ida (Tokyo, Japan)

O 19 17:00 -17:20

INFANTILE EPILEPSY IN LYSOSOMAL STORAGE DISEASES

Shyi-Jou Chen (Taipei, Taiwan)

O 20 17:20 -18:00

CNS PATHOLOGY IN LYSOSOMAL STORAGE DISEASES

Ralph Z. Kern (Toronto, Canada)

Cross-Strait Session

18:00-18:45

Chairpersons: Jiong Qin (Beijing, China)
Chao-Ching Huang (Tainan, Taiwan)

O 21 18:00 -18:15

EFFECTS OF GINKGO BILOBA EXTRACT AND PROGESTERONE ON EXPRESSION OF GLUCOCORTICOID RECEPTOR IN CORTEX OF THE RAT AFTER RECURRENT SEIZURES

Ding-An Mao (Changsha, China)



O 22 18:15 -18:30

CLINICAL ANALYSIS OF NIEMANN-PICK DISEASE TYPE C- 7 CASES

Hui Xiong (Beijing, China)

O 23 18:30-18:45

INTRACRANIAL GENE DELIVERY OF AAV-GALC VECTOR CORRECTS NEUROPATHOLOGY IN MURINE GLOBOID CELL LEUKODYSTROPHY

Dar-Shong Lin (Taipei, Taiwan)

Grand Social Party

19:30-21:30

B2 Banquet Hall I+II Howard Plaza Hotel

Day 3, March 28 (Sunday)

Session VII Mitochondrial Diseases

08:15 -10:30

Chairpersons: Veena Kalra (New Delhi, India)

Suad Al Yamani (Riyadh, Saudi Arabia)

O 24 08:15 -08:55

EPILEPSY WITH MITOCHONDRIAL DISEASES IN KOREA

Jong-Hee Chae (Seoul, Korea)

O 25 08:55 -09:15

EPILEPTIC SEIZURES IN INFANTS AND CHILDREN WITH MITOCHONDRIAL DISEASES IN TAIWAN

Hsiu-Fen Lee (Taichung, Taiwan)

O 26 09:15 -10:00

CONGENITAL LACTIC ACIDOSIS (PYRUVATE DEHYDROGENASE DEFICIENCY) AND EPILEPSY

Chitra Prasad (London, Canada)

O 27 10:00 -10:15

SPECTRUM OF MITOCHONDRIAL DISEASES IN A TERTIARY REFERRAL CENTRE IN HONG KONG

Cheuk-Wing Fung (Hong Kong, China)

O 28 10:15 -10:30

THE CHARACTERISTICS OF SEIZURES IN MALAYSIAN CHILDREN AND ADOLESCENTS WITH MELAS DUE TO A3243G MITOCHONDRIAL DNA MUTATION

Chee-Ming Teh (Kuala Lumpur, Malaysia)

Coffee Break and Poster Visit (2)

10:30-11:15

Session VIII Peroxisomal Disorders

11:15 -12:15

Chairpersons: Shinichi Hirose (Fukuoka, Japan)

Rei-Cheng Yang (Kaohsiung, Taiwan)



O 29 11:15 -11:55

CLINICAL FINDINGS AND DIAGNOSTIC FLOWCHART OF PEROXISOMAL DISEASES

Nobuyuki Shimozawa (Gifu, Japan)

O 30 11:55 -12:15

PEROXISOMAL DISORDERS AND EPILEPTIC SEIZURES

Jao-Shwann Liang (Taipei, Taiwan)

Lunch Seminar (2)

12:20-13:30

Chairpersons: Yoichi Sakakihara (Tokyo, Japan)

Yuh-Jyh Jong (Taipei, Taiwan)

Sponsored by Jassen-Cilag Taiwan

O 31 12:20 -12:55

LATEST FINDINGS IN PEDIATRIC EPILEPSY TREATMENT

Ki-Joong Kim (Seoul, Korea)

O 32 12:55 -13:30

MENKES DISEASE AND INFANTILE EPILEPSY

Asuri N. Prasad (London, Canada)

Session IX Vitamin and Mineral Metabolic Disorders

13:30 -15:10

Chairpersons: Aida Salonga (Manila, Philippines)

Huei-Shyong Wang (Taipei, Taiwan)

O 33 13:30 -14:15

PYRIDOXINE DEPENDENT AND RESPONSIVE SEIZURES

Peter Baxter (Sheffield, UK)

O 34 14:15 -14:55

CLINICAL EVALUATION OF PYRIDOXINE TREATMENT OF INTRACTABLE SEIZURES

Shunsuke Ohtahara (Okayama, Japan)

O 35 14:55 -15:10

EPILEPSY IN CHILDREN WITH BIOTINIDASE DEFICIENCY

Pratibha Singhi (Chandigarh, India)

Coffee Break 15:10 -15:30

Session X Neurotransmitter Diseases and Miscellaneous

15:30 -17:50

Chairpersons: Hitoshi Yamamoto (Kanagawa, Japan)

Ching-Shiang Chi (Taichung, Taiwan)

O 36 15:30 -16:15

SUCCINIC SEMIALDEHYDE DEHYDROGENASE (SSADH) DEFICIENCY AND EPILEPSY

Phillip L. Pearl (Washington DC, USA)



O 37 16:15 -16:45

NEUROIMAGE OF MONOAMINE METABOLIC DISORDERS

Shinn-Forng Peng (Taipei, Taiwan)

O 38 16:45 -17:00

PATHOPHYSIOLOGY OF EPILEPSY IN NEUROTRANSMITTER DISORDERS

Yoshiko Nomura (Tokyo, Japan)

Discussion Summary

17:00 -17:30

Chairpersons: Virginia Wong (Hong Kong, China)

Kun-Long Hung (Taipei, Taiwan)

Principal Discussers: Raman Sankar (Los Angeles, USA)

Asuri N. Prasad (London, Canada)

Closing Addresses and Best Poster Award Ceremony 17:30-17:50

Ein-Yao Shen (President, 13th Annual Meeting of ISS, 2010)

Shinichi Nijima (President, 14th Annual Meeting of ISS, 2011)

AOCNA Delegate Meeting

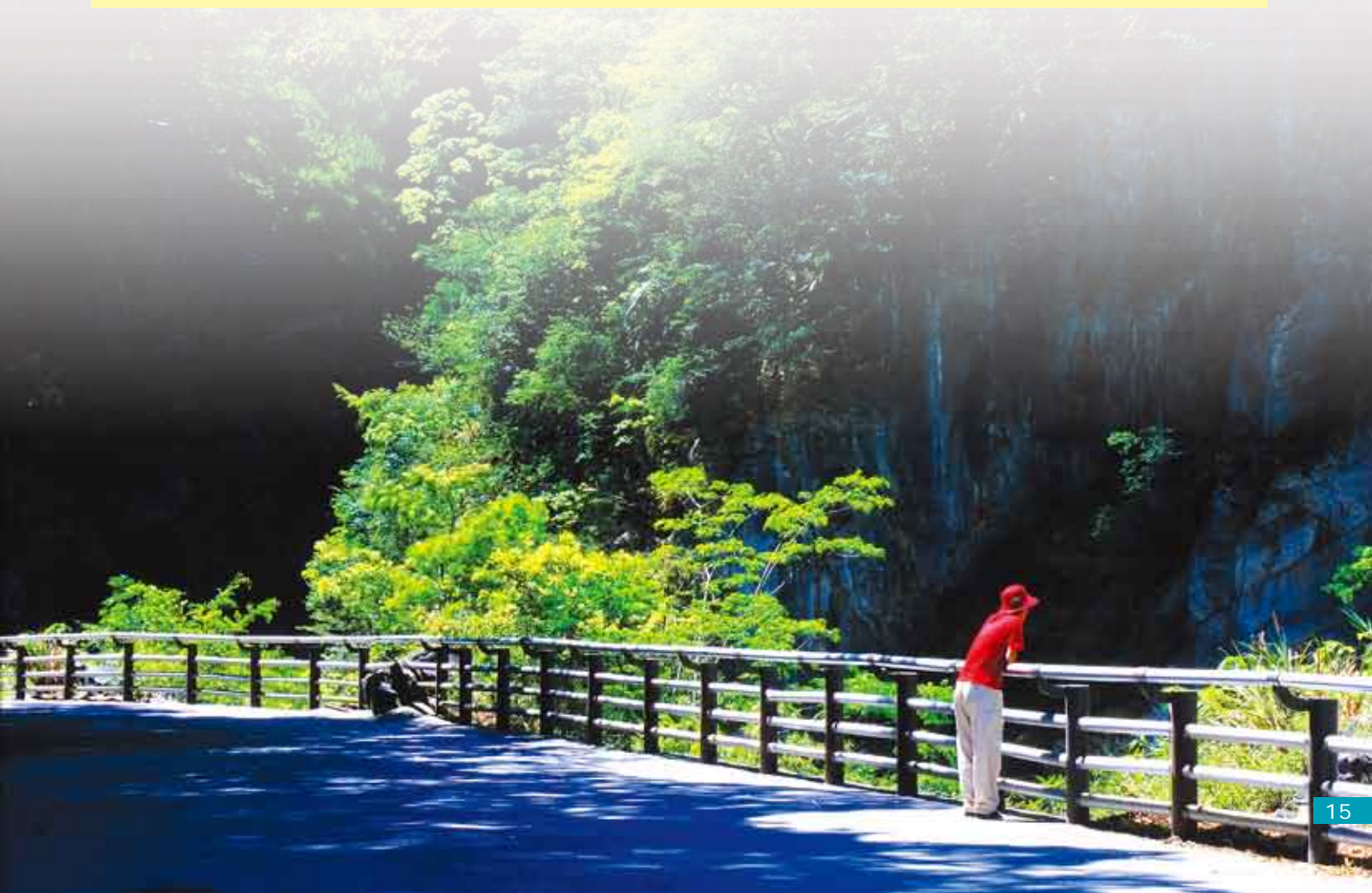
18:00 - 19:00

4F Rm406 Howard Plaza Hotel

Farewell Party (by invitation)

19:30-21:30

3F Grand Victoria Hotel





Poster Presentations List

GENERAL

P 01 EVOLUTION AND VARIATION IN NEONATAL SUPPRESSION-BURST ENCEPHALO GRAMS

Inn-Chi Lee (Taichung, Taiwan)

P 02 CLINICAL PRESENTATION AND LABORATORY PROFILE IN SUSPECTED CASES OF NEUROMETABOLIC DISORDERS: A PRELIMINARY REPORT FROM BANGLADESH

Naila Zaman Khan, SC Majumdar, Mustafa Mahbub, Selina Huo Banu, Mosiul Azam (Dhaka, Bangladesh)

P 03 INCIDENCE OF SEIZURE IN NEUROMETABOLIC DISEASES UNDER CURRENT NEWBORN SCREENING IN TAIWAN

Tzu-Ying Yang, Chung-Hao Wang, Ting-Rong Hsu, Cheng-Hung Huaung, Dau-Ming Niu, Kai-Ping Chang (Taipei, Taiwan)

AMINOACIDOPATHY

P 04 A CASE WITH NONKETOTIC HYPERGLYCINEMIA DIAGNOSED WITH NOVEL SCREENING METHODS —¹³C-GLYCINE BREATHING TEST AND MLPA METHOD

Hitomi Hino, Masaaki Ohta, Yuka Suzuki, Mitsumasa Fukuda, Shigeo Kure, Eiichi Ishii (Toon, Japan)

P 05 EFFECTS OF GLUTAMATE ON NEURAL PROGENITOR/STEM CELLS CULTURED IN VITRO

Tingsong Li, Li Jiang (Chongqing, China)

P 06 NON KETOTIC HYPERGLYCINEMIA IN 2 CHILDREN PRESENTING WITH SEIZURES

Shahnaz H. Ibrahim, Sarwari Arif (Karachi, Pakistan)

P 07 DRAMATIC RESPONSE TO DELAYED TREATMENT IN SEVERE 6-PYRUVOYL TETRAHYDROPTERIN SYNTHASE DEFICIENCY

Sau Wei Wong, Lai Choo Ong, LH Ngu, TT Liu (Kuala Lumpur, Malaysia)

ORGANIC ACADEMIA AND UREA CYCLE DEFECTS

P 08 GLUTARIC ACIDEMIA TYPE I REVEALED BY NEWBORN SCREENING PROGRAM IN TAIWAN: EXPERIENCE IN ONE MEDICAL CENTER

Cheng-Hung Huang, Ting-Rong Hsu, Dau-Ming Niu (Taipei, Taiwan)

P 09 CLINICAL ANALYSIS OF METHYLMALONIC ACIDEMIA IN 14 CASES

Li Gao, Yan-Ping Liu, Yan Wang, Su-Jing Xu, Nan-Nan Huang (Zhengzhou, China)



P 10 MUTATIONS ANALYSIS OF MMACHC GENE IN EIGHT PATIENTS WITH METHYLMALONIC ACIDEMIA AND HOMOCYSTEINEMIA

Shu-Li Chen, Jian-Xiang Liao, Cheng-Rong Li, Dong Cui, Peng-Qiang Wen, Quan Yuan, Yu-Hui Hu, Ping Song (Shenzhen, China)

P 11 THE PROGNOSIS OF THE EPILEPSY WITH ORGANIC ACIDEMIA

Takako Fujita, Yukiko Ihara, Yuko Tomonoh, Hiroshi Ideguchi, Takahito Inoue, Sawa Yasumoto, Shinichi Hirose (Fukuoka, Japan)

P 12 ELECTROENCEPHALOGRAM AND TRANSCRANIAL DOPPLER ULTRASONOGRAPHY IN NEONATAL CITRULLINEMIA

Inn-Chi Lee, Pen-Hua Su, Yung-Jung Chen, Jui-Ming Hu, Yan-Yan Ng, Jia-Yuh Chen (Taichung, Taiwan)

P 13 USING NEONATAL CONTINUOUS HAEMODIALYSIS TO PREVENT HYPERAMMONAEMIC ENCEPHALOPATHY

Ryutaro Kinoshita, Makoto Tsutsumi, Eiji Ohta, Masatoshi Nakamura, Hayato Matsumoto, Sawa Yasumoto, Yoshitugu Shirakawa, Shinichi Hirose (Fukuoka, Japan)

DEFECTS IN CARBOHYDRATE METABOLISM

P 14 A CASE OF GLYCOGEN STORAGE DISEASE SIMILAR TO MELAS

Young Ok Kim, Young Jun Son, Young Jong Woo, Si Un Lee, Eun Young Kim, Young Il Roh (Gwangju, Korea)

P 15 EFFECTIVENESS OF MODIFIED ATKINS DIET FOR 5 PATIENTS WITH GLUT1 DEFICIENCY SYNDROME

Yasushi Ito, Hirokazu Oguni, Susumu Ito, Miyako Oguni, Makiko Osawa (Tokyo, Japan)

P 16 WHITE MATTER ABNORMALITIES IN GLUT1 DEFICIENCY SYNDROME: A DIFFUSION TENSOR IMAGING STUDY WITH SPM

Tomohiko Nakata, Jun Natsume, Tatsuya Fukasawa, Yoshiteru Azuma, Tamiko Negoro, Keiko Yanagihara, Kazuyoshi Watanabe (Aichi, Japan)

P 17 FDG-PET IN GLUT1 DEFICIENCY SYNDROME: COMPARISON OF PATIENTS WITH AND WITHOUT DECREASED ERYTHROCYTE GLUCOSE UPTAKE

Jun Natsume, Yoshiteru Azuma, Hirokazu Kurahashi, Tomohiko Nakata, Naoko Ishihara, Akihisa Okumura, Keiko Yanagihara, Kazuyoshi Watanabe (Aichi, Japan)

P 18 WEST SYNDROME ASSOCIATED WITH NEONATAL HYPOGLYCEMIC BRAIN

Sawa Yasumoto, Noriko Nakamura, Yuko Tomonoh, Yukiko Ihara, Hiroshi Ideguchi, Takahito Inoue, Toshiko Mori, Shinichi Hirose (Fukuoka, Japan)



P 19 THREE AUTOPSY CASES OF UNIQUE BRAIN ANOMALY SUFFERING FROM REPETITIVE HYPOGLYCEMIC ATTACKS

Naho Miwa, Naoyuki Tanuma, Masaharu Hayashi (Tokyo, Japan)

P 20 GENOTYPIC PHENOTYPIC CHARACTERISTIC OF GALACTOSEMIA IN THE POST NEONATAL AGE IN INDIA

Harshuti Shah, Zachary Grinspan (Ahmedabad, India)

LIPID METABOLISM AND LYSOSOMAL STORAGE DISEASES

P 21 A CASE OF A CHILD WITH CARNITINE DEFICIENCY

Ung Ninh Thi (Hanoi, Viet Nam)

P 22 CLINICAL CHARACTERISTICS OF EPILEPSY WITH HUNTER SYNDROME

Kenjiro Kikuchi, Shin-ichiro Hamano, Reiko Koichihara, Tomotaka Oritsu, Manabu Tanaka, Motoyuki Minamitani, Hiroshi Mochizuki, Hiroyuki Ida (Saitama, Japan)

P 23 A GROSS DELETION OF ARYLSULFATASE B IDENTIFYING IN A TAIWANESE PATIENT WITH MUCOPOLYSACCHARIDOSIS TYPE VI

Wei-De Lin, Yu-Yuan Ke, Chung-Shing Wang, I-Ching Chou, Fuu-Jen Tsai (Taichung, Taiwan)

P 24 A METACHROMATIC LEUKODYSTROPHY (MLD) PATIENT'S LONG-TERM FOLLOW UP: NEUROLOGIC AND EXTRA- NEUROLOGIC COMPLICATIONS

Takahito Inoue, Michitaka Yonekura, Takako Fujita, Yukiko Ihara, Sawa Yasumoto, Shiho Kodama, Sachio Takashima, Shinichi Hirose (Fukuoka, Japan)

P 25 LATE-ONSET KRABBE'S DISEASE WITH HYPOPHOSPHATEMIC RICKETS AND FOCAL STATUS EPILEPTICUS

Derrick Wei-Shih Cha, Ee-Shien Tan, Fabian Kok-Peng Yap, Maureen Cleary (Singapore)

P 26 PROGRESSIVE MYOCLONUS EPILEPSY DUE TO GAUCHER DISEASE TYPE 3 WITHOUT HEPATOSPLENOMEGALY

Norimichi Higurashi, Shin-ichiro Hamano, Asako Tajima, Toya Ohashi, Hiroyuki Ida (Saitama, Japan)

P 27 A CASE OF TAY-SACHS DISEASE WITH CLUSTERS OF SUBCLINICAL SEIZURES

Motomasa Suzuki, Koichi Maruyama, Hirokazu Kurahashi, Toshiyuki Kumagai, Kazuyoshi Watanabe (Kasugai, Japan)

P 28 SERIAL MR IMAGING AND 1H-MR SPECTROSCOPY IN MONOZYGOTIC TWIN WITH MILD INFANTILE TAY - SACHS DISEASE

Asuka Iwai, Ryosuke Miura, Atsushi Terazawa, Reiko Ito, Koji Orii, Atsushi Imamura (Gifu, Japan)



P 29 LONG-TERM PROGNOSIS FOR A CASE OF NEURONAL CEROID-LIPOFUSCINOSIS WITH EPILEPSY AND SICK SINUS SYNDROME

Yukiko Ihara, Hiroshi Ideguchi, Takahito Inoue, Sawa Yasumoto, Shinichi Hirose, Yuko Tomonoh, Noriko Nakamura, Takako Fujita (Fukuoka, Japan)

MITOCHONDRIAL AND PEROXISOMAL DISORDERS

P 30 CLINICAL EVALUATION OF LEIGH ENCEPHALOPATHY IN 4 PEDIATRIC CASES

Reiko Koichihara, Shin-ichiro Hamano, Manabu Tanaka, Kenjiro Kikuchi, Tomotaka Oritsu, Motoyuki Minamitani (Saitama, Japan)

P 31 A CASE OF NEONATAL CONVULSION WITH PERSISTENT HYPERLACTATEMIA: LEIGH SYNDROME WITH HETEROPLASMIC MUTATION FOR MT-ND5 GENE

Bosco Chan, Kwok Yin Chan, Kin Cheong Yau, Kam Ming Au, Yuet Ping Yuen, CM Mak, PLS Chen, Che Kwan Ma (Hong Kong, China)

P 32 EPILEPSIES IN MELAS SYNDROME

Wen-Kan Feng, Kun-Long Hung, Jia-Woei Hou (Taipei, Taiwan)

P 33 FOCAL EPILEPSY AND MELAS IN A SINGAPORE PAEDIATRIC HOSPITAL

Wendy Kein-Meng Liew, Tchoyoson Lim, SKH Tay, DWS Chan (Singapore)

P 34 EPILEPSY IN METABOLIC MYOPATHY WITH RAGGED-RED FIBERS

Tai-Heng Chen, Wen-Chen Liang, Tze-Kiong Er, Yuh-Jyh Jong (Kaohsiung, Taiwan)

P 35 SEVERE MYOCLONIC SEIZURES IN PEROXISOMAL D-BIFUNCTIONAL PROTEIN DEFICIENCY

Mustafa Kılıç, Haluk Topaloğlu, Ayşegül Tokatlı, Ali Dursun, Serap Sivri, Turgay Çoşkun (Ankara, Turkey)

VITAMIN AND MINERAL METABOLIC DISORDERS

P 36 RAPID ESTIMATION OF THE EFFICACY OF ORAL PYRIDOXINE FOR WEST SYNDROME: INTRAVENOUS ADMINISTRATION OF PYRIDOXINE UNDER EEG MONITORING

Kenji Sugai, Hitoshi Sakuma, Hirofumi Komaki, Yoshiaki Saito, Eiji Nakagawa, Masayuki Sasaki (Tokyo, Japan)

P 37 A NORMAL PTH HYPOCALCEMIC NEONATAL CONVULSION REVEALING MATERNAL NORMOCALCEMIC HYPERPARATHYROIDISM

Lung-Chang Lin, Rei-Cheng Yang (Kaohsiung, Taiwan)

P 38 SEIZURE LIKE TREMORS OF 6 WILSON DISEASES IN TWO FAMILIES

Won Seop Kim, Keon Su Lee, Ho Jin Park (Cheongju, Korea)



P 39 EPILEPSY IN MENKES DISEASE

Muneaki Matsuo, Toshiyuki Maeda, Kazuya Sasaki, Katsunori Tsuhiya, Kousuke Tsuji, Yuhei Hamasaki (Saga, Japan)

P 40 LOW SERUM URIC ACID IS AN IMPORTANT EARLY CLUE TO THE DIAGNOSIS OF MOLYBDENUM COFACTOR DEFICIENCY AS THE CAUSE OF NEONATAL SEIZURES – A CASE REPORT

Hian-Tat Ong, Denise Li Meng Goh, Karen Lim (Singapore)

NEUROTRANSMITTER DISEASES

P 41 NATIONWIDE EPIDEMIOLOGICAL STUDY OF PEDIATRIC NEUROTRANSMITTER DISEASES IN JAPAN (1st REPORT)

Haruo Shintaku, Masaya Segawa, Mitsuhiro Kato, Shinji Saitoh, Shin-ichiro Hamano, Masaya Kubota, Jun Tohyama, Jun Natsume, Yoshihiro Maegaki, Toyojiro Matsuishi, Hideji Hattori, Shuhei Ide, Yasusi Itoh, Hiroki Fujioka, Yoshiko Nomura (Osaka, Japan)

P 42 AROMATIC L-AMINO ACID DECARBOXYLASE (AADC) DEFICIENCY: CLINICAL FEATURES AND FOLLOW-UP IN A CASE

Hueng-Chuen Fan, Wang-Tso Lee, Wuh-Liang Hwu, Ruey-Meei Wu, Shyi-Jou Chen (Taipei, Taiwan)

P 43 TWO CASES OF TYROSINE HYDROXYLASE (TH) DEFICIENCY MIMICKING IDIOPATHIC CEREBRAL PALSY AND EPILEPSY

Eric Kin Cheong Yau, Kwok Yin Chan, Bosco Chan, Hencher Lee, Chloe Mak, Ching Wan Lam, Albert Yan Wo Chan (Hong Kong, China)

P 44 A STUDY OF CEREBROSPINAL FLUID NEUROTRANSMITTERS ASSAY IN CHILDREN WITH UNDIAGNOSED NEUROLOGICAL DISEASES IN HONG KONG

Cheuk-Wing Fung, Grace Poon, Anne Kwok, Pik-To Cheung, Louis Low, Nenad Blau, Simon Siu, Chloe Mak, S Tam, Virginia Wong (Hong Kong, China)

MISCELLANEOUS

P 45 SLC25A13 GENE TARGETED MUTATION ANALYSIS IN DIRECT BILIRUBIN ELEVATED JAUNDICE PATIENTS

Shu-Li Chen, Jian-Xiang Liao, Peng-Qiang Wen, Guo-Bing Wang, Dong Cui, Quan Yuan, Ping Song, Yu-Hui Hu (Shenzhen, China)

P 46 EFFECTS OF PROGESTERONE ON EXPRESSIONS OF INTERLEUKIN-18 IN CEREBRAL CORTEX OF NEONATAL RATS WITH SEIZURE INDUCED WITH TRIFLUOROMETHYLETHYER

Ding-An Mao, Jun-Chao Chen, Tao Bo, Li-Qun Liu, Jian Li (Hunan, China)



P 47 CUSHING'S DISEASE WITH EPILEPSY: A ROLE OF OVERACTIVITY OF THE HPA SYSTEM

Mariko Maezawa, Youichi Doumoto, Kouichi Tamada, Masao Miyazaki, Satomi Sonoda, Satoshi Kimiya, Akiko Kamiishi, Hirohiko Ozaki (Kanagawa, Japan)

P 48 EVOLUTION OF EPILEPSY IN A CASE OF ADENYLOSUCCINATE LYASE DEFICIENCY: VIDEO-EEG AND RESPONSE TO TREATMENT

Jeremy Freeman, Michiel van Werkhoven, Joy Lee, John Duley, James Pitt (Victoria, Australia)

P 49 SEVERE INFANTILE SPASM FEMALE CASE WITH RETT SYNDROME LIKE PHENOTYPE

Kazuhiro Muramatsu, Noriko Sawaura, Yoko Urano, Yasunori Okada, Hirokazu Arakawa (Gunma, Japan)

P 50 THREE CASES OF INFANTILE CONVULSION CHOREOATHETOSIS SYNDROME (ICCA SYNDROME)

Bosco Chan, Kwok Yin Chan (Hong Kong, China)

P 51 THE CLINICAL AND LABORATORY FEATURE OF TWO CASES EPIDERMAL NEVUS SYNDROME

Zhihong Zhuo, Huaili Wang (Zhengzhou, China)

P 52 CLINICAL FEATURES OF BENIGN INFANTILE CONVULSIONS ASSOCIATED WITH MILD GASTROENTERITIS

Hui Xiong, Weiping Xiang (Tian Jin, China)

P 53 JUVENILE HUNTINGTON'S DISEASE WITH REPETITIVE STATUS EPILEPTICUS AND PERIODIC SHARP WAVE COMPLEXES ON EEG: A CASE REPORT

Ryutaro Kira, Natsumi Isobe, Yoshito Ishizaki, Hiroyuki Torisu, Masafumi Sanefuji, Toshiro Hara (Fukuoka, Japan)

P 54 THE EARLY CLINICAL PICTURE, NEUROPHYSIOLOGICAL AND MRI INVESTIGATIONS IN 4 PATIENTS WITH MONOCARBOXYLATE TRANSPORTER 8 (MCT8) DYSFUNCTION (ALLAN-HERNDON-DUDLEY SYNDROME)

Masaya Kubota, Reiko Horikawa, Hideki Hoshino, Hirofumi Kashii, Akiko Koyama, Mari Imamura, Ichiro Kuki, Nobuhiko Okamoto (Tokyo, Japan)

P 55 A CLINICAL OBSERVATION FOR THE EFFICACY AND SAFETY OF LEVETIRACETAM MONOTHERAPY IN CHILDREN WITH EPILEPSY

Zhi-Sheng Liu, Jia-Sheng Hu, Fang-Lin Wang, Ge-Fei Wu (Wuhan, China)

P 56 A CLINICAL ANALYSIS AND STUDY OF 120 CHILDREN WITH VIRAL ENCEPHALITIS

Fuyong Jiao, Jing Lin (Shaanxi, China)



Profile of Lecturers

001

Ching-Shiang Chi, M.D.

Present Position:

Vice Superintendent, Tung's Taichung Metroharbor Hospital, Taiwan

Associate Professor, National Yang Ming University, Taiwan

Associate Professor, Chung Shan Medical University, Taiwan

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Education and Appointments:

1. 1969-1975 National Defense Medical School
2. 1975-1979 Resident and Chief Resident, Department of Pediatrics, Taipei Veterans General Hospital
3. 1979-1983 Attending Physician, Department of Pediatrics, Taipei Veterans General Hospital
4. 1982-1983 Visiting Fellowship, Department of Neurology, College of Physicians and Surgeons at Presbyterian Hospital, New York City, USA

Selected Publications:

1. Chi CS Book: Childhood Epilepsy (In Chinese) 1985.
2. Chi CS, Mak SC, Shian WJ, Chen CH. Oral glucose lactate stimulation test in mitochondrial diseases. *Pediatr Neurol* 1992; 8:445-9.
3. Chi CS, Tsai CR, Chen LH, Lee HF, Mak BS, Yang SH, Wang TY, Shu SG, Chen CH. Maple syrup urine disease in the Austronesian aboriginal tribe Paiwan of Taiwan: a novel DBT (E2) gene 4.7 kb founder deletion caused by a nonhomologous recombination between LINE-1 and Alu and the carrier-frequency determination. *Eur J Hum Genet* 2003; 11:931-6.
4. Lee HF, Tsai CR, Chi CS, Chang TM, Lee HJ. Aromatic L-amino acid decarboxylase deficiency in Taiwan. *Eur J Ped Neurol* 2009; 13:135-40.
5. Lee HF, Tsai CR, Chi CS, Lee HJ, Chen CCC. Leigh syndrome: Clinical and neuroimaging follow-up. *Pediatr Neurol* 2009; 40:88-93.



O 02

Jiong Qin, M.D., Ph.D.

Present Position:

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Education:

1. 1979-1984 M.D. Beijing Medical University
2. 1984-1989 Ph.D. Resident & Fellow, Beijing Medical University First Hospital
3. 1989-1992 Child Neurology Advanced Training, Peking University First Hospital
4. 1998-1999 Invited Researcher, National Institute of Neuroscience, NCNP, Japan

Selected Publications:

1. Qin J. Pay much attention to the understanding and clinical research on comorbidities of epilepsy in children. *Zhonghua Er Ke Za Zhi* 2007; 45:561-3. (Chinese)
2. Qin J. Clinical research progress in childhood nervous diseases. *Chin J Pract Pediatr* 2007; 22:340-3. (Chinese)
3. Chen J, Qin J, Liu X, Han Y, Yang Z, Chang X, Ji X. Nitric oxide-mediated neuronal apoptosis in rats with recurrent febrile seizures through endoplasmic reticulum stress pathway. *Neurosci Lett* 2008; 443:134-9.
4. Zhang Y, Yang YL, Hasegawa Y, Yamaguchi S, Shi CY, Song JQ, Sayami S, Liu P, Yan R, Dong JH, Qin J. Prenatal diagnosis of methylmalonic aciduria by analysis of organic acids and total homocysteine in amniotic fluid. *Chin Med J (Engl)* 2008; 121:216-9.
5. Yang Z, Liu X, Qin J, Jiang Y. Neck myoclonia with absence seizures: report of 3 cases. *J Child Neurol* 2009; 24:1026-9.



Joyce Y. Wu, M.D.

Present Position:

Associate Clinical Professor, Department of Pediatric Neurology, David Geffen School of Medicine at UCLA, Los Angeles, USA

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Education:

1. 1986-1990 BS, University of California, Berkeley
2. 1990-1995 MD, New York University (NYU) School of Medicine, New York
3. 1995-1997 General Pediatrics Training, Boston City Hospital, Boston
4. 1997-2000 Neurology/Pediatric Neurology Training, Tufts Floating Hospital/New England Medical Center, Boston
5. 2000-2002 EEG/Epilepsy Training, UCLA Medical Center, Los Angeles

Appointments:

1. Director, Pediatric Clinical Neurophysiology
2. Director, Tuberous Sclerosis Complex Clinic at UCLA

Publications Highlights:

1. Wu JY, Sutherling WW, Koh S, Salamon N, Jonas R, Yudovin S, Sankar R, Shields WD, Mathern GW. Magnetic source imaging localizes epileptogenic zone in children with tuberous sclerosis complex. *Neurology* 2006; 66:1270-2.
2. Salamon N, Kung J, Shaw S, Koo J, Koh S, Wu JY, Lerner JT, Sankar R, Shields WD, Engel J Jr, Miyata H, Yong W, Vinters HV, Mathern GW. FDG-PET/MRI co-registration and DTI improve detection of cortical dysplasia in epilepsy patients. *Neurology* 2008; 71:1594-601.
3. Wu JY, Koh S, Sankar R, Mathern GW. Paroxysmal fast activity: an interictal scalp EEG marker of epileptogenesis in children. *Epilepsy Res* 2008; 82:101-8.
4. Lerner JT, Salamon N, Hauptman JS, Velasco TR, Hemb M, Wu JY, Sankar R, Shields WD, Engel J Jr, Fried I, Cepeda C, Andre VM, Levine MS, Miyata H, Yong WH, Vinters HV, Mathern GW. Assessment and surgical outcomes for mild type I and severe type II cortical dysplasia: a critical review and the UCLA experience. *Epilepsia* 2009; 50:1310-35.
5. Wu JY, Salamon N, Kirsch HE, Mantle MM, Nagarajan S, Aung M, Kurelowech L, Sankar R, Shields WD, Mathern GW. Noninvasive testing, early surgery and seizure freedom in tuberous sclerosis complex. *Neurology* 2010; 74:392-8.



O 04

Yoshiyuki Suzuki, M.D., Ph.D.

Present Position:

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Academic Appointments:

1. 1969-1971 Fellowship, University of Pennsylvania
2. 1971-1986 Faculty and Associate Professor, the University of Tokyo
3. 1986-1988 Director, Inherited Metabolic Disease, National Center of Neurology and Psychiatry
4. 1988-1999 Vice Director, the Tokyo Metropolitan Institute of Medical Science
5. 1999-2005 Professor and Director, Clinical Research Center, International University of Health and Welfare
6. 2005-2009 Professor, International University of Health and Welfare

Selected Publications:

1. Suzuki Y, Suzuki K. Krabbe's globoid leukodystrophy: deficiency of galactocerebrosidase in serum, leukocytes and fibroblasts. Science 1971; 171:73-5.
2. Oshima A, Tsuji A, Nagao Y, Sakuraba H, Suzuki Y. Cloning, sequencing, and expression of cDNA for human β -galactosidase. Biochem Biophys Res Commun 1988; 157:238-44.
3. Fn JQ, Ishii S, Asano N, Suzuki Y. Accelerated transport and maturation of lysosomal α -galactosidase A in Fabry lymphoblasts by an enzyme inhibitor. Nat Med 1999; 5:112-5.
4. Matsuda J, Suzuki O, Oshima A, Yamamoto Y, Noguchi A, Takimoto K, Itoh M, Matsuzaki Y, Yasuda Y, Ogawa S, Sakata Y, Nanba E, Higaki K, Ogawa Y, Tominaga L, Ohno K, Iwasaki H, Watanabe H, Brady RO, Suzuki Y. Chemical chaperone therapy for brain pathology in G_{M1}-gangliosidosis. Proc Natl Acad Sci 2003; 100:15912-7.
5. Suzuki Y, Nanba E, Matsuda J, Higaki K, Oshima A. β -galactosidase deficiency (β -galactosidase): G_{M1}-gangliosidosis and Morquio B disease. Valle D, Beaudet AL, Vogelstein B, Kinzler KW, Antonarakis SF, Ballabio A (eds): The online metabolic and molecular bases of inherited disease <<http://www.ommbid.com/>>, McGraw-Hill, New York, 2008, Chap 151, pp 1-101.



O 05

Hans H. Goebel, M.D.

Present Position:

Retired Chairmanship of the Department of Neuropathology, University Mainz Medical Centre of the Johannes Gutenberg University, Mainz, Germany

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Education and Appointments:

1. 1966-1968 Resident in Anatomic Pathology, Free University of Berlin, Germany
2. 1968-1973 Resident and Fellow in Neuropathology at New York University and Indiana University, USA
3. 1973-1983 Senior Staff Member and Professor of Neuropathology at the Department of Neuropathology, University of Göttingen, Germany
4. 1983-2005 Professor of Neuropathology and Head of the Department of Neuropathology, University Mainz Medical Centre of the Johannes Gutenberg University, Mainz, Germany

Selected Publications:

1. Goebel HH, Gerhard L, Kominami E, Haltia M. Neuronal ceroid-lipofuscinosis - late-infantile or Jansky-Bielschowsky type - revisited. Brain Pathol 1996; 6:225-8.
2. Goebel HH. Neurodegenerative diseases: biopsy diagnosis in children In: Garcia JH (ed). Neuropathology: the diagnostic approach. Mosby-Year Book Inc: St. Louis, 1997 pp. 581-635.
3. Goebel HH, Warlo IAP. Progress in desmin-related myopathies. J Child Neurol 2000; 15:565-72.
4. Goebel HH. Congenital myopathies in the new millennium. J Child Neurol 2005; 20:94-101.
5. Goebel HH, Muller HD. Protein aggregate myopathies. Semin Pediatr Neurol 2006; 13:96-103.



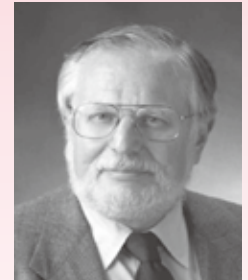
O 06

Robert A. Zimmerman, M.D.

Present Position:

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Education:

1. 1956-1960 BA, Temple University
2. 1960-1964 MD, Georgetown University School of Medicine (Summa Cum Laude)
3. 1964-1965 Intern in Medicine, Georgetown University Hospital, Washington, DC.
4. 1965-1969 Radiology Residency & Fellowship in Special Procedures, Hospital of the University of Pennsylvania, Philadelphia, PA

Professional Appointments:

1. 1972-1977 Assistant Professor, Department of Radiology, University of Pennsylvania School of Medicine
2. 1977-1981 Associate Professor, Department of Radiology and Neurosurgery, University of Pennsylvania School of Medicine
3. 1981- Professor, Department of Radiology, University of Pennsylvania School of Medicine

Selected Publications:

1. Wang ZH, Zimmerman RA. The value of proton MR spectroscopy in pediatric metabolic brain disease. AJNR 1997; 18:1872-9.
2. Wang ZJ, Zimmerman RA. Proton MR spectroscopy of pediatric brain metabolic disorders. Neuroimaging Clin N Am 1998; 8:781-807.
3. Chen CY, Zimmerman RA, Lee CC, Chen FH, Yuh YS, Hsiao HS. Neuroimaging findings in late infantile GM1 gangliosidosis. Am J Neuroradiol 1998; 19:1628-30.
4. Berry GT, Hunter JV, Wang Z, Dreha S, Mazur A, Brooks DG, Ning C, Zimmerman RA, Segal S. In vivo evidence of brain galactitol accumulation in an infant with galactosemia and encephalopathy. J Pediatr 2001; 138:260-2.
5. Jan W, Zimmerman RA, Wang ZJ, Berry GT, Kaplan PB, Kaye EM. MR diffusion imaging and MR spectroscopy of maple syrup urine disease during acute metabolic decompensation. Neuroradiology 2003; 45:393-9.



O 07

Raman Sankar, M.D., Ph.D.

Present Position:

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Education and Appointments:

1. 1986 MD, Tulane University School of Medicine
2. 1986-1987 Internship, Pediatrics, Childrens Hospital of Los Angeles
3. 1987-1988 Residency, Pediatrics, Childrens Hospital of Los Angeles
4. 1988-1989 Residency, Neurology, UCLA School of Medicine
5. 1989-1991 Fellowship, Pediatric Neurology, UCLA School of Medicine

Selected Publications:

1. Sankar R, Ramsay E, McKay A, Hulihan J, Wiegand F. CAPSS-311 Study Group. A multicenter, outpatient, open-label study to evaluate the dosing, effectiveness, and safety of topiramate as monotherapy in the treatment of epilepsy in clinical practice. *Epilepsy Behav* 2009; 15:506-12.
2. Caplan R, Levitt J, Siddarth P, Wu KN, Gurbani S, Sankar R, Shields WD. Frontal and temporal volumes in childhood absence epilepsy. *Epilepsia* 2009; 50:2466-72.
3. Rho JM, Sankar R. The ketogenic diet in a pill: is this possible? *Epilepsia*. 2008; 49 (Suppl 8):127-33. Review.
4. Glauser TA, Sankar R. Co-chairs of the Leadership in Epilepsy, Advocacy, and Development Faculty. Core elements of epilepsy diagnosis and management: expert consensus from the Leadership in Epilepsy, Advocacy, and Development (LEAD) Faculty. *Curr Med Res Opin* 2008; 24:3463-77.
5. Sankar R, Lerner JT. Teratogenicity of antiepileptic drugs: role of pharmacogenomics. *Int Rev Neurobiol* 2008; 83:215-25. Review.



Wang-Tso Lee, M.D., Ph.D.

Present Position:

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Education and Appointments:

1. 1991-1994 Resident, Department of Pediatrics, National Taiwan University Hospital, Taiwan
2. 1993-1996 Chief Resident and Clinical Fellow, Division of Child Neurology, Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
3. 1996- Attending Physician, Department of Pediatrics, National Taiwan University Hospital, Taiwan
4. 1999-2000 Neurology Research, Department of Neurology, Children's Hospital of Philadelphia, PA, USA
5. 2000 Visiting Scholar, Laboratory of Neuroscience, NIA, NIH, Baltimore, USA
Visiting Scholar, Division of Epilepsy, Department of Child Neurology, Hospital for Sick Children, Toronto, Canada

Selected Publications:

1. Chen PT, Young C, Lee WT, Wang PJ, Peng SS, Shen YZ. Early epileptic encephalopathy with suppression burst electroencephalographic pattern – an analysis of eight Taiwanese patients. Brain Dev 2001; 23: 715-20.
2. Chien YH, Hsu CC, Huang A, Chou SP, Lu FL, Lee WT, Hwu WL. Poor outcome for neonatal-type nonketotic hyperglycinemia treated with high-dose sodium benzoate and dextromethorphan. J Child Neurol 2001; 19, 39-42.
3. Liang JS, Lee WT, Hwu WL, Peng SS, Chu LW, Wang PJ, Shen YZ. Adrenoleukodystrophy: clinical analysis of 9 Taiwanese children. Acta Paediatr Taiwan 2004; 45:272-7.
4. Lee WT, Weng WC, Peng SF, Tzen KY. Neuroimaging findings in patients with pediatric neurotransmitter diseases. J Inherit Metab Dis 2009; 32:361-70.
5. Chien YH, Lin MI, Weng WC, Du JC, Lee WT. Dextromethorphan in the treatment of a case of early myoclonic encephalopathy evolving into migrating partial seizures in infancy. J Form Med Assoc 2010 (in press).



O 09

Shigeo Kure, M.D.

Present Position:

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Education and Appointments:

1. 1976-1982 Tohoku University School of Medicine
2. 1982-1984 Sendai City Hospital (Pediatrics)
3. 1984-1988 Tohoku University Graduate School (Medical Science)
4. 1989-2000 Assistant Professor in Medical Genetics, Tohoku University
5. 1998-2008 Associate Professor in Medical Genetics, Tohoku University
6. 2008- Associate Professor in Pediatrics, Tohoku University

Selected Publications:

1. Kure S, Kato K, Dinopoulos A, Gail C, deGrauw TJ, Christodoulou J, Bzduch V, Kalmancey R, Fekete G, Trojovský A, Plecko B, Breningstall G, Tohyama J, Aoki Y, Matsubara Y. Comprehensive mutation analysis of GLDC, AMT, and GCSH in nonketotic hyperglycinemia (glycine encephalopathy). *Hum Mutat* 2006; 27:343-52.
2. Kure S, Korman S, Kanno J, Narisawa A, Kubota M, Takayanagi T, Takayanagi M, Saito T, Matsui A, Kamada F, Aoki Y, Ohura T, Matsubara Y. Rapid diagnosis of glycine encephalopathy by ¹³C-glycine breath test. *Ann Neurol* 2006; 59:862-7.
3. Kanno J, Hutchin T, Narisawa A, Kamada F, Aoki Y, Matsubara Y, Kure S. Genomic deletion within GLDC is a major cause of nonketotic hyperglycinemia. *J Med Genet* 2007; 44:e69.
4. Oda M, Kure S, Sugawara T, Yamaguchi S, Kojima K, Shinka T, Sato K, Narisawa A, Matsubara Y, Omae T, Mizoi K, Kinouchi H. Direct correlation between ischemic injury and extracellular glycine concentration in mice with genetically altered of the glycine cleavage multienzyme system. *Stroke* 2007; 38:2157-64.
5. Kojima-Ishii K, Kure S, Ichinohe A, Shinka T, Narisawa A, Komatsuzaki S, Kanno J, Kamada F, Yoko Aoki Y, Yokoyama H, Oda M, Sugawara T, Mizoi K, Daiichiro Nakahara D, Matsubara Y. Model mice for mild-form glycine encephalopathy: behavioral and biochemical characterizations and efficacy of antagonists for glycine binding site of N-methyl D-aspartate receptor. *Pediatr Res* 2008; 64:228-33.



Asuri N. Prasad, M.D.

Present Position:

Associate Professor, Department of Pediatrics, Schulich School of Medicine & Dentistry, University of Western Ontario and Children's Hospital, London Health Sciences Centre, London, Canada

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Education:

1. 1987 Member, Royal College of Physicians of United Kingdom, UK
2. 1992 Specialist Certification Pediatrics, American Board of Pediatrics
3. 1995-1996 Clinical Fellow in Epilepsy and Electroencephalography, New England Medical Centre Hospitals (Tufts University)
4. 1996 Specialist Certification Neurology and Pediatric Neurology
Fellow, Royal College of Physicians and Surgeons of Canada, Canada
American Board of Psychiatry and Neurology

Appointments:

1. Member, Scientific Committee, & Pediatric Content Committee, American Epilepsy Society
2. Secretary, Canadian Association of Child Neurology
3. Director, Pediatric Epilepsy Monitoring Service

Selected Publications:

1. Funk CB, Prasad AN, Frosk P, Sauer S, Kolker S, Greenberg CR, Del Bigio MR. Neuropathological, biochemical and molecular findings in a glutaric acidemia type 1 cohort. Brain 2005; 128:711-22.
2. Prasad AN, Kaye EM, Alroy J. Reducing costs in the laboratory work up of neurometabolic disorders: electron microscopic examination of skin biopsy as a rapid diagnostic tool in the diagnosis of lysosomal storage disorders. J Child Neurol 1996; 11:301-8.
3. Prasad AN, Breen JC, Ampola MG, Rosman NP. Argininemia: a treatable genetic cause of progressive spastic diplegia simulating cerebral palsy - case reports and review of literature. J Child Neurol 1997; 12: 301-9.
4. Prasad AN, Bunzeluk K, Prasad C, Chodirker BN, Magnus KG, Greenberg CR. Agenesis of the corpus callosum and cerebral anomalies in inborn errors of metabolism. Congenit Anom (Kyoto). 2007; 47:125-35.
5. Prasad AN, Malinger G, Lerman-Sagie T. Primary disorders of metabolism and disturbed fetal brain development. Clin Perinatol 2009; 36:621-38.



O 11

Jia-Woei Hou, M.D., Ph.D.

Present Appointment:

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Education:

1. 1977-1984 MD, College of Medicine, National Taiwan University
2. 1993-1997 PhD, Institute of Medical Research, College of Medicine, National Taiwan University

Appointments:

1. 2000-2007 Chief, Center of the Child Health Research, Chang Gung Children's Hospital, Taoyuan, Taiwan
2. 2002-2009 Chief, Division of Medical Genetics and Endocrinology, Chang Gung Children's Hospital, Taoyuan, Taiwan
3. 2002-2009 Director, Center of Genetic Counseling, Chang Gung Memorial Hospital, Taoyuan, Taiwan
4. 2002-2009 Director, Department of Genetic Medicine, School of Medicine, Chang Gung University, Taoyuan, Taiwan

Selected Publications:

1. Hou JW. Chromosome 10q24.3-qter deletion associated with left-sided first branchial arch defect, diaphragmatic eventration, and duplicated renal pelvis. Am J Med Genet 2006; 140A:2241-4.
2. Hsu HF, Hou JW. Variable expressivity in Patau syndrome in not all related to trisomy 13 mosaicism. Am J Med Genet 2007; 143A:1739-48.
3. Hou JW. Rapidly progressive scoliosis after successful treatment for osteopenia in Costello syndrome. Am J Med Genet 2008; 146A:393-6.
4. Hou JW. Natural course of neonatal progeroid syndrome. Pediatr Neonatol 2009; 50:102-9.
5. Hou JW. Amelioration of hypophosphatemic rickets and osteoporosis with pamidronate and growth hormone in Lowe syndrome. J Formos Med Assoc 2009; 108:730-5.



O 12

Dau-Ming Niu, M.D., Ph.D.

Present Position:

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Appointments:

1. 1987-1992 Resident, Department of Pediatrics, Taipei Veterans General Hospital
2. 1992-1993 Chief Resident, Department of Pediatrics, Taipei Veterans General Hospital
3. 1993-1994 Clinical and Research Fellow, medical Genetic, National Taiwan University Hospital
4. 1994- Attending Staff, Department of Pediatrics, Taipei Veterans General Hospital
5. 2009- Director, Genetics Consultation Center, Taipei Veterans General Hospital

Selected Publications:

1. Niu DM, Hwang B, Hwang HW, Wang NH, Wu JY, Lee PC, Chien JC, Shieh RC, Chen YT. A common SCN5A polymorphism attenuates a severe cardiac phenotype caused by a nonsense SCN5A mutation in a Chinese family with an inherited cardiac conduction defect. J Med Genet 2006; 43:817-21.
2. Lee NC, Cheng LY, Liu TT, Hsiao KJ, Chiu PC, Niu DM. Long-term follow-up of Chinese patients who received delayed treatment for 6-pyruvoyl- tetrahydropterin synthase deficiency. Mol Genet Metab 2006; 87:128-34.
3. Liu KM, Liu TT, Lee NC, Cheng LY, Hsiao KJ, Niu DM. Long-term follow-up of Taiwanese Chinese patients treated early for 6-pyruvoyl-tetrahydropterin synthase deficiency. Arch Neurol 2008; 65:387-92.
4. Niu DM, Hsu JH, Chong KW, Huang CH, Lu YH, Kao CH, Yu HC, Lo MY, Jap TS. Six new mutations of the thyroglobulin gene discovered in Taiwanese children presenting with thyroid dysmorphogenesis. J Clin Endocrinol Metab 2009; 94:5045-52.
5. Lin HY, Chong KW, Hsu JH, Yu HC, Shih CC, Huang CH, Lin SJ, Chen CH, Chiang CC, Ho HJ, Lee PC, Kao CH, Cheng KH, Hsueh C, Niu DM. High incidence of the cardiac variant of Fabry disease revealed by newborn screening in the Taiwan Chinese population. Circulation (Cardiovasc Genet) 2009; 2:450-6.



O 13

O 36

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Present Position:

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Academic Appointments:

1. 1997-2002 Associate Professor of Pediatrics and Neurology, George Washington University
2. 2006 Visiting Associate Professor of Pediatrics, University of Virginia School of Medicine
3. 2009 Professor of Pediatrics and Neurology, George Washington University

Selected Publications:

1. Pearl PL, Shamim S, Theodore WH, Gibson KM, Forester K, Combs SE, Lewin D, Dustin I, Reeves-Tyer P, Jakobs C, Sato S. Polysomnographic abnormalities in SSADH deficiency. *Sleep* 2009; 32:1645-8.
2. Pearl PL, Gibson KM, Quezado Z, Dustin I, Taylor J, Trzcinski S, Schreiber J, Forester K, Reeves-Tyer P, Liew C, Shamim S, Herscovitch P, Carson RE, Butman JA, Jakobs C, Theodore WH. Decreased GABA-A binding on FMZ-PET in succinic semialdehyde dehydrogenase (SSADH) deficiency. *Neurology* 2009; 73:423-9.
3. Pearl PL: Neurological problems of jazz legends. *J Child Neurol* 2009; 24:1037-42.
4. Pearl PL: New treatment paradigms in neonatal seizures. *J Inherit Metab Dis* 2009; 32:204-13.
5. Pearl PL, Vezina LG, Saneto RP, McCarter R, Molloy-Wells E, Heffron A, Trzcinski S, McClintock WM, Conry JA, Elling NJ, Goodkin HP, Sotero de Menezes M, Ferri R, Gilles E, Kadom N, Gaillard WD: Cerebral MRI abnormalities associated with vigabatrin therapy. *Epilepsia* 2009; 50:184-94.



O 14

Seiji Yamaguchi, M.D., Ph.D.

Present Position:

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Education and Appointments:

1. 1975 MD, Gifu University School of Medicine
2. 1985 PhD, Gifu University
3. 1987-1993 Assistant Professor (Lecturer), Department of Pediatrics, Gifu University School of Medicine
4. 1993-2003 Professor, Department of Pediatrics, Shimane Medical University
5. 2003- Professor, Department of Pediatrics, Shimane University School of Medicine (University Integration)
6. 2005- Vice-director of Shimane University Hospital (Concurrent Post)

Selected Publications:

1. Yamaguchi S, Orii T, Suzuki Y, Maeda K, Oshima M, Hashimoto T. Newly identified forms of electron transfer flavoprotein deficiency in two patients with glutaric aciduria type II. *Pediatr Res* 1991; 29:60-3.
2. Yamaguchi S, Shimizu N, Orii T, Fukao T, Suzuki Y, Maeda K, Hashimoto T, Previs SF, Rinaldo P. Prenatal diagnosis and neonatal monitoring of a fetus with glutaric aciduria type II due to electron transfer flavoprotein (b-subunit) deficiency. *Pediatr Res* 1991; 30:439-43.
3. Yotsumoto Y, Hasegawa Y, Fukuda S, Kobayashi H, Endo M, Fukao T, Yamaguchi S. Clinical and molecular investigations of Japanese cases of glutaric acidemia type 2. *Mol Genet Metab* 2008; 94:61-7.
4. Yamaguchi S, Indo Y, Coates P, Hashimoto T, Tanaka K. Identification of very long chain acyl-CoA dehydrogenase deficiency in three patients previously diagnosed with long chain acyl-CoA dehydrogenase deficiency. *Pediatr Res* 1993; 34:111-3.
5. Li H, Fukuda S, Hasegawa Y, Hironori Kobayashi H, Purevsuren J, Mushimoto Y, Yamaguchi S. Effect of heat stress and bezafibrate on mitochondrial β -oxidation: comparison between cultured cells from normal and mitochondrial fatty acid oxidation disorder children using in vitro probe acylcarnitine profiling assay. *Brain Dev* 2009, in press.



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Yue-Hua Zhang M.D., Ph.D.

Present Position:

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Education:

1. 1993-1996 Post-Graduate School, Beijing Medical University, PhD Degree of Pediatric Neurology
2. 1987-1990 Xian Medical University, Master Degree of Pediatrics
3. 1980-1985 Xian Medical University, Bachelor Degree of Medical Science

Selected Publications:

1. Wang J, Zhang Y, Liang J, et al. CACNA1I is not associated with childhood absence epilepsy in the chinese han population. *Pediatr Neurol* 2006; 35:187-90.
2. Liang J, Zhang Y, Wang J, et al. New variants in CACNA1H gene associated with childhood absence epilepsy. *Neurosci Lett* 2006; 406:27-32.
3. Liang J, Zhang Y, Chen Y, et al. Common polymorphisms in the CACNA1H gene associated with childhood absence epilepsy in chinese han population. *Ann Human Genet* 2006; 71:325-35.
4. Sun H, Zhang Y, Liang J, et al. Seven novel mutations in Chinese patients with severe myoclonic epilepsy of infancy. *Epilepsia* 2008; 49:1104-7.
5. Sun H, Zhang Y, Liang J, et al. SCN1A, SCN1B and GABRG₂ gene mutation analysis in Chinese families with generalized epilepsy with febrile seizures plus. *J Hum Genet* 2008; 53:769-74.



O 16

Wuh-Liang Hwu, M.D., Ph.D.

Present Appointment:

Associated Professor, Department of Pediatrics, National Taiwan University Hospital

Director, Department of Medical Genetics, National Taiwan University Hospital

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Education:

1. 1976-1983 Medicine, College of Medicine, National Taiwan University,
2. 1991-1996 PhD Program, Institute of Molecular Medicine, College of Medicine, National Taiwan University

Selected Publications:

1. Chien YH, Chiang SC, Zhang XK, Keutzer J, Lee NC, Huang AC, Chen CA, Wu MH, Huang PH, Tsai FJ, Chen YT, Hwu WL. Early detection of Pompe disease by newborn screening is feasible: results from the Taiwan screening program. *Pediatrics* 2008; 122:e39-45.
2. Hwu WL, Chien YH, Lee NC, Chiang SC, Dobrovolny R, Huang AC, Yeh HY, Chao MC, Lin SJ, Kitagawa T, Desnick RJ, Hsu LW. Newborn screening for Fabry disease in Taiwan reveals a high incidence of the later-onset GLA mutation c.936+919G>A (IVS4+919G>A). *Hum Mutat* 2009; 30:1397-405.
3. Chien YH, Lee NC, Thurberg BL, Chiang SC, Zhang XK, Keutzer J, Huang AC, Wu MH, Huang PH, Tsai FJ, Chen YT, Hwu WL. Pompe disease in infants: improving the prognosis by newborn screening and early treatment. *Pediatrics* 2009; 124:e1116-25.
4. Lin HY, Lin SP, Chuang CK, Niu DM, Chen MR, Tsai FJ, Chao MC, Chiu PC, Lin SJ, Tsai LP, Hwu WL, Lin JL. Incidence of the mucopolysaccharidoses in Taiwan, 1984-2004. *Am J Med Genet A* 2009; 149A:960-4.
5. Chang KL, Hwu WL, Yeh HY, Lee NC, Chien YH. CCL18 as an alternative marker in Gaucher and Niemann-Pick disease with chitotriosidase deficiency. *Blood Cells Mol Dis* 2010; 44:38-40.



O 17

Ingrid Tein, M.D., BSc

Present Position:

Associate Professor of Pediatrics, Laboratory Medicine and Pathobiology, University of Toronto

Director, Neurometabolic Clinic, Investigational Unit, and Research Laboratory, Division of Neurology

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Education and Appointments:

1. 1976-1979 M.D. degree, University of Toronto, Ontario, Canada (Advanced standing program)
2. 1983-1986 Clinical Fellowship in Pediatric Neurology, including Chief Residency, HSC, Univ. Toronto
3. 1987-1990 Post-doctoral Research Fellowship in Neurometabolic Diseases: Fatty acid oxidation
4. 1987-1988 Fac. Medicine, Hopital Necker-Enfants Malades, Paris, France
5. 1988-1990 Columbia University, New York, USA

Selected Publications:

1. Lamhonwah AM, Olpin SE, Pollitt RJ, Vianey-Saban C, Divry P, Guffon N, Besley GTN, Onizuka R, De Meirleir LJ, Cvitanovic-Sojat L, Baric I, Dionisi-Vici C, Fumic K, Maradin M, Tein I. Novel OCTN2 mutations: no genotype-phenotype correlations. Early carnitine therapy prevents cardiomyopathy. Am J Med Genet 2002; 111:271-84.
2. Lamhonwah AM, Skaug J, Scherer SW, Tein I. A third human carnitine/organic cation transporter (OCTN3) as a candidate for the 5q31 Crohn's disease locus (IBD5). Biochem Biophys Res Commun 2003; 301: 98-101.
3. Lamhonwah AM, Tein I. Novel localization of OCTN1, an organic cation/carnitine transporter, to mammalian mitochondria. Biochem Biophys Res Commun 2006; 345:1315-25.
4. Lamhonwah AM, Hawkins C, Tam C, Wong J, Mai L, Tein I. Expression patterns of organic cation/carnitine transporter family in adult murine brain. Brain Dev 2008; 30:31-42.
5. Tein I, Elpeleg O., BenZe'ev B, Korman S, Lossos A, Lev D, Lerman-Sagie T, Leshinsky-Silver E, Vockley G, Berry G, Lamhonwah AM, Matern D, Roe C, Gregersen N. Short-chain acyl-CoA dehydrogenase gene mutation (c.319 C>T) presents with clinical heterogeneity and is candidate founder mutation in individuals of Ashkenazi Jewish origin. Mol Genet Metab 2008; 93:179-89.



O 18

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Education and Professional Appointments:

1. 1981 MD, Jikei University School of Medicine
2. 1983 Instructor, Department of Pediatrics, Jikei University School of Medicine
3. 1989 PhD, Jikei University School of Medicine
4. 1989-1992 Visiting Assistant Professor, Department of Pediatrics, Georgetown University Washington DC, USA
5. 1996 Assistant Professor, Department of Pediatrics, Jikei University School of Medicine, Tokyo, Japan
6. 2002 Associate Professor, Department of Pediatrics, Jikei University School of Medicine, Tokyo, Japan
7. 2008 Executive Chairman and Professor, Department of Pediatrics, Jikei University School of Medicine, Tokyo, Japan

Selected Publications:

1. Lin H, Sugimoto Y, Ohsaki Y, Ninomiya H, Oka A, Taniguchi M, Ida H, Eto Y, Ogawa S, Matsuzaki Y, Sawa M, Inoue T, Higaki K, Nanba E, Ohno K, Suzuki Y. N-octyl-beta-valienamine up-regulates activity of F213I mutant beta-glucosidase in cultured cells: a potential chemical chaperone therapy for Gaucher disease. *Biochim Biophys Acta* 2004; 1689:219-28.
2. Ohashi T, Iizuka S, Ida H, Eto Y. Reduced alpha-Gal A enzyme activity in Fabry fibroblast cells and Fabry mice tissues induced by serum from antibody positive patients with Fabry disease. *Mol Genet Metab* 2008; 94:313-8.
3. Okuyama T, Tanaka A, Suzuki Y, Ida H, Tanaka T, Cox GF, Eto Y, Orii T. Japan Elaprase Treatment (JET) study: idursulfase enzyme replacement therapy in adult patients with attenuated Hunter syndrome (Mucopolysaccharidosis II, MPS II). *Mol Genet Metab*. 2010; 99:18-25.
4. Tajima A, Ohashi T, Hamano S, Higurashi N, Ida H. Gaucher disease patient with myoclonus epilepsy and a novel mutation. *Pediatr Neurol* 2010; 42:65-8.
5. Ida H. Clinical issues of adult patients with genetic and metabolic disorders diagnosed in childhood. *Nippon Rinsho*. 2010; 68:19-25. (Japanese)



O 19

Shyi-Jou Chen, M.D., Ph.D.

Present Position:

Chief of Section of Neurology and Cardiology in Department of Pediatrics, Tri-Service General Hospital, Taipei, Taiwan

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Education:

1. 1984-1991 MD, National Defense Medical Center
2. 2001~2005 PhD, Institute of Medical Sciences, National Defense Medical Center

Academic Appointments:

1. 1993-1996 Resident of Pediatric in Tri-Service General Hospital
2. 1996-1998 Fellow of pediatric neurology in Veteran General Hospital
3. 1998- Pediatric neurologist and attending physician in Tri-Service General Hospital
4. 2006- Assistant Professor, Tri-Service General Hospital

Selected Publications:

1. Chen Shyi-Jou, Wang Yen-Lin, Kao Jen-Hsin, Wu Shu-Feng, Lao Wen-Tsong, Wu Chia-Cho, Tao Pao-Luh, Wang Chih-Chien, Chang Deh-Ming and Sytwu Huey-Kang. Decoy receptor 3 ameliorates experimental autoimmune encephalomyelitis by directly counteracting local inflammation and downregulating Th17 cells. *Mol Immunol* 2009; 47:567-74.
2. Lo Wen-Tsung, Tang Ching-Shen, Chen Shyi-Jou, Huang Ching-Feng, Tseng Min-Hua, Wang Chih-Chien. Panton-valentine leukocidin is associated with exacerbated skin manifestations and inflammatory response in children with community-associated staphylococcal scarlet fever. *Clin Infect Dis* 2009; 49:e69-75.
3. Chen Shyi-Jou, Hirose Shinichi. Current proceedings of febrile seizures and related epileptic syndromes in SCN1A: from beside to bench. *Medical Sciences* 2009; 29:167-72.
4. Fan HC, Wang AC, Lao CP, Chang KP, Chen SJ. Damage of cerebellar white matter due to carbon monoxide poisoning: a case report. *Am J Emerg Med* 2009; 27, 757.e5-757.e7.
5. Wu PC, Jiang JP, Wang CC, Chen SJ. A rare case of aplasia cutis congenita with refractory seizures. *Pediatr Neurol* 2008; 39:435-7.



O 20

Ralph Z. Kern, M.D.

Present Position:

General Manager Fabry Disease, Personalized Genetic Health, Genzyme Corporation, Cambridge, USA

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Education:

1. 1978-1982 MD, Queen's University, Ontario
2. 1982-1984 Internal Medicine, Mount Sinai Hospital, University of Toronto
3. 1984-1987 Neurology Resident, Montreal Neurological Institute, McGill University
4. 2003-2005 Masters of Health Administration, University of Toronto
5. 2007-2008 Research Fellow Pediatric Epilepsy, Hospital for Sick Children, University of Toronto

Appointments:

1. Medical Director, Genzyme Canada
2. Neurology Program Director, University of Toronto
3. Assistant Professor, Neurology, University of Toronto
4. Neurology Bioethics Coordinator, University of Toronto
5. Neurologist, University Health Network, Toronto, Ontario, Canada

Selected Publications:

1. Kern RZ, Brown AD. Disease adaptation may have decreased quality-of-life responsiveness in patients with chronic progressive disorders. J Clin Epidemiol 2004; 10:1033-9.
2. Goldszmidt E, Chettle C, Kern RZ, Downey K, Devito I, MacArthur A. The incidence and etiology of post partum headaches: prospective cohort study. Can J Anaesth 2005; 52:971-7.
3. Al-Afifi T, Kern RZ, Fehlings M. Cervical spondylotic myelopathy: clinical and MRI predictors of outcome after surgical intervention. J Neuroimaging 2007; 17:1-9.
4. Pronovost A, Kern RZ, Peng P. Telemedicine in the management of chronic pain: a cost analysis study. Can J Anesth 2009; 56:590-6.
5. Gerretsen P, Kern RZ. Reversible cerebral vasoconstriction syndrome: a thunderclap-headache associated condition. Curr Neurol Neurosci Rep 2009; 9:108-14.



O 21

Din-An Mao, M.D.

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Appointments:

1. 1983-1987 Assistant, Department of Pediatrics, The Second Affiliated Hospital, Xiangya Medical School
2. 1990-1994 Assistant Researcher, Laboratory of Pediatric Cardiovascular Disease, Xiangya Medical School
3. 1994-2000 Vice-professor, Department of Pediatrics, The Second Xiangya Hospital, Central South University

Selected Publications:

1. Bo Tao, Chen Yong, Mao Ding-An, et al. Long-term effects of recurrent seizures in neonate period on gamma-aminobutyric acid A receptor $\alpha 1$ and $\beta 2$ subunits expression in adult brain: experiment with rat. Natl Med J China 2007; 87:275-8.
2. Mao Ding-An, Liu Li-Qun, Bo Tao, et al. Effect of Ligustrazine on the expression of caspase-1 mRNA in the infant rats with brain injury following recurrent seizures. Chin J Emerg Med 2007; 16:406-9.
3. Mao Ding-An, Tan Chuan-Mei, Liu Li-Qun, et al. Effect and significance of Ginkgo biloba extract on the expression of caspase-3 in the infant rats with brain injury following recurrent seizures. Chin J TCM WM Crit Care 2008; 15:81-4.
4. Li Jian, Mao Ding-An, Bo Tao, et al. Gamma-aminobutyric acid A receptor gamma 2 subunit following Mg-free-induced seizures in cultured developing neurons. Neural Regeneration Research 2008; 3:1187-91.
5. Mao Ding-An, Wang Fang, Bo Tao, et al. Effects of recurrent neonatal seizures on expression of mineralocorticoid receptor and glucocorticoid receptor in the rat brain. Chin J Crit Care Med 2010; 30:40-4.



O 22

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Education and Appointments:

1. 1988-1993 BS, Beijing Medical University.
2. 1996-1999 MD-PhD, The First Hospital, Beijing Medical University
3. 2004-2006 Attending Doctor, Department of Pediatric, Beijing University First Hospital
4. 2006- Associate Chief Physician, Department of Pediatrics, Beijing University First Hospital
5. 2007- Associate Professor, Department of Pediatric, Beijing University First Hospital

Selected Publications:

1. Xiong H, Kobayashi K, Tachikawa M, et al. Molecular interaction between fukutin and POMGnT1 in the glycosylation pathway of α -dystroglycan. *Biochem Biophys Res Commun* 2006; 350:935-41.
2. Xiong H, Zhang YH, Zhou R, et al. Clinical features and management of multiple sclerosis in children. *Zhonghua Er Ke Za Zhi* 2007; 45:568-73.
3. Xiong Hui, Peng Jing, Zhang Yuehua, et al. Clinical diagnosis and therapy analysis of opsoclonus-myoclonus syndrome. *Zhonghua Er Ke Za Zhi* 2008; 46:570-3.
4. Xiong Hui, Wang Shuo, Kobayashi Kazuhiro, Jiang Yuwu, Wang Jingmin, Chang Xingzhi, Yuan Yun, Liu Jieyu, Toda Tatsushi, Fukuyama Yukio, Wu Xiru. Fukutin gene retrotransposal insertion in a non-Japanese Fukuyama Congenital Muscular Dystrophy (FCMD) patient. *Am J Med Genet A* 2009; 149A:2403-8.
5. Wang Shuo, Xiong Hui, Luo Jing, Chang Xing-Zhi, Yuan Yun, Wu Xi-Ru Clinical, molecular pathological and genetic analysis of a Chinese family with congenital muscular dystrophy type 1A, MDC1A. *ZhongHua Yixue Jiaoyu Za Zhi* 2010; 27:13-7.



O 23

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Present Position:

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Education:

1. 1983-1991 MD, Taipei Medical University
2. 1992-1995 Resident, Pediatrics, Mackay Memorial Hospital
3. 1995-1997 Fellowship, Genetics, Mackay Memorial Hospital
4. 2001-2002 Associated Researcher: Pediatric, Children Hospital of Philadelphia, USA
5. 2002-2004 Associated Researcher: Internal Medicine, Washington University, MO, USA

Appointments:

1. 1997- Attending Physician, Genetics, Department of Pediatrics, Mackay Memorial Hospital
2. 2006-2009 Principle Investigator, Funded by National Science Council
3. 2007~2008 Principle Investigator, Funded by Bureau of Health Promotion, department of Health

Selected Publications:

1. Lin SP, Chang JH, Lee-Chen GJ, Lin DS, Lin HY, Chuang CK. Detection of Hunter syndrome (mucopolysaccharidosis type II) in Taiwanese: biochemical and linkage studies of the iduronate-2-sulfatase gene defects in MPS II patients and carriers. Clin Chim Acta 2006; 369:29-34.
2. Chuang CK, Wang TJ, Yeung CY, Hsieh WS, Lin DS, Ho SC, Lin SP. Interference and blood sample preparation for a pyruvate enzymatic assay. Clin Biochem 2006; 39:74-7.
3. Chuang CK, Wang TJ, Yeung CY, Lin DS, Lin HY, Liu HL, Ho HT, Hsieh WS, Lin SP. A method for lactate and pyruvate determination in filter-paper dried blood spots. J Chromatogr A 2009; 1216:8947-52.
4. Lin D, Fantz CR, Levy B, Rafi MA, Vogler C, Wenger DA, Sands MS. AAV2/5 vector expressing galactocerebrosidase ameliorates CNS disease in the murine model of globoid-cell leukodystrophy more efficiently than AAV2. Mol Ther 2005; 12:422-30.
5. Lin D, Donsante A, Macauley S, Levy B, Vogler C, Sands MS. Central nervous system-directed AAV2/5-mediated gene therapy synergizes with bone marrow transplantation in the murine model of globoid-cell leukodystrophy. Mol Ther 2007; 15:44-52.



O 24

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Professional Appointments:

1. 1992-1993 Internship, Seoul National University Hospital
2. 1993-1997 Residency, Department of Pediatrics, Seoul National University Children's Hospital
3. 1997-1999 Clinical Fellow, Department of Pediatric Neurology, Seoul National University Children's Hospital
4. 1999-2000 Research Fellow, Department of Ultrastructural Research, NCNP, Japan
5. 2002 PhD, Seoul National University, College of Medicine, Seoul Korea
6. 2005-2006 Post Doc Fellow, Department of Neurology, College of Physician and Surgeon, Columbia University, New York, USA

Selected Publications:

1. Chae JH, Keem JS, Hwang H, Kim KJ, Hwang YS, Park JD, Cheon JE, Kim IO, Choe GY, Park SH. Merosin deficient congenital muscular dystrophy in Korea. Brain Dev 2009; 31:341-6.
2. Lim BC, Park JD, Hwang H, Kim KJ, Hwang YS, Cheon JE, Kim IO, Lee R, Moon HK, Chae JH. Mutation in ND subunits of complex I are an important genetic cause of childhood mitochondrial encephalopathy. J Child Neurol 2009; 24:828-32.
3. Koh KN, Lim BC, Park JD, Kim KJ, Kim SK, Wang KC, Hwang YS, Chae JH. Cerebellum can be a possible generator of progressive myoclonus. J Child Neurol 2009; Sep (Epub)
4. Chae JH, Lee JS, Kim KJ, Hwang YS, Hirano M. Biochemical and mutational analysis of Leigh syndrome in Korea. Brain Dev 2008; 30:387-90.
5. Chae JH, Lee JS, Hwang YS, Kim KJ, Tanji K, Bonilla E, Hirano M. A novel ND3 mitochondrial DNA mutation in three Korean children with basal ganglia lesions and complex I deficiency. Pediatr Res 2007; 61:622-4.



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Education and Academic Appointments:

1. 1989-1996 Kaohsiung Medical University
2. 1996-1999 Resident, Department of Pediatrics, Taichung Veterans General Hospital
3. 1999-2000 Chief Resident, Department of Pediatrics, Taichung Veterans General Hospital
4. 1999-2004 Fellowship of Pediatric Neurology, Taichung Veterans General Hospital
5. 2004-2007 Attending Physician, Department of Pediatrics, Taichung Veterans General Hospital

Selected Publications:

1. Lee HF, Mak SC, Wu FW, Chi CS, Huang SC. Zellweger syndrome: Report of one case. Acta Paediatr Tw 2001; 42:53-6.
2. Lee HF, Mak SC, Chi CS, Hung DZ. Hyperbaric oxygen for carbon monoxide poisoning-induced delayed neuropsychiatric sequelae. Chin Med J (Taipei) 2001; 64:310-4.
3. Lee HF, Mak BSC, Chi CS, Tsai CR, Chen CH, Shu SG. A novel mutation in neonatal isolated sulphite oxidase deficiency. Neuropediatrics 2002; 33:174-9.
4. Chi CS, Tsai CR, Chen LH, Lee HF, Mak BSC, Yang SH, Wang TY, Shu SG, Chen CH. Maple syrup urine disease in the Austronesian aboriginal tribe Paiwan of Taiwan: a novel DBT (E2) gene 4.7kb founder deletion caused by a nonhomologous recombination between LINE-1 and Alu and carrier-frequency determination. Eur J Hum Genet 2003; 11:931-6.
5. Chang TM, Chi CS, Tsai CR, Lee HF, Li MC. Paralytic ileus in MELAS with phenotypic features of MNGIE. Ped Neurol 2004; 31:374-7.



O 26

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Education:

Dr. Prasad is trained in pediatrics at the Post Graduate Institute for Medical Education and Research, Chandigarh India and at the Memorial University of Newfoundland, Canada. She received postdoctoral training in medical genetics and inborn errors of metabolism at Children's Hospital, Harvard Medical School, Boston. She has sub specialized in clinical and biochemical genetics (American College of Medical Genetics and Canadian College of Medical Genetics).

Selected Publications:

1. Prasad AN and Prasad C. Genetic aspects of human epilepsy. In Emery & Rimoin's Principles & Practice of Medical Genetics, 2006, 5th edition. Vol 3. Rimoin D, Connor JM, Pyeritz RE, Korf BR. (Eds) Churchill Livingstone Elsevier. Philadelphia. Pennsylvania. Chapter 122. 2676-702.
2. Prasad C, Rupar CA. Non-immune hydrops. Genetic and metabolic causes. Perinatology 2006; 8:164-74.
3. Prasad AN, Bunzeluk K, Prasad C, Chodirker BN, Magnus KG, Greenberg CR. Agenesis of the corpus callosum and cerebral anomalies in inborn errors of metabolism. Congenit Anom (Kyoto) 2007; 47:125-35.
4. Prasad C, Rosenblatt DS, Corley K, Cairney AE, Rupar CA Transcobalamin (TC) Deficiency. Potential cause of bone marrow failure in childhood. J Inherit Metab Dis 2008 Oct 29 (Epub ahead of print).
5. Yanofsky RA, Seshia SS, Dawson AJ, Stobart K, Greenberg CR, Booth FA, Prasad C, Del Bigio MR, Wrongemann JJ, Fike FM, Gatti RA. Ataxia-telangiectasia: atypical presentation and toxicity of cancer treatment. Can J Neuro Sci 2009; 36:462-7.



O 27

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Education:

1. 1995 MBBS, The University of Hong Kong
2. 1997-2000 Membership of Royal College of Physicians, London, UK
3. 2004 Fellowship of the Hong Kong College of Paediatricians
4. 2004 Fellowship of the Hong Kong Academy of Medicine

Appointments:

1. 2004- Member, the Society for the Study of Inborn Error of Metabolism
2. 2007- Council Member, the Hong Kong Epilepsy Society
3. 2008- Council Member, the Hong Kong Society for Inborn Error of Metabolism
4. 2008- Honorary Medical Consultant, the Joshua Hellmann Foundation for Orphan Diseases
5. 2009- Council Member, the Paediatric Neurology Association, Hong Kong

Selected Publications:

1. V Wong, CW Lam, CW Fung. Stiff child syndrome with mutation of DYT1 gene. *Neurology*. 2005; 8; 65:1465-6.
2. Yam WK, Ronen GM, Cherk SW, Rosenbaum P, Chan KY, Streiner DL, Cheng SW, Fung CW, Ho JC, Kwong KL, Ma LC, Ma DK, Tsui KW, Wong V, Wong TY. Health-related quality of life of children with epilepsy in Hong Kong: how does it compare with that of youth with epilepsy in Canada? *Epilepsy Behaviour* 2008; 12:419-26. Epub 2007 Dec 26.
3. Mak CM, Lam CW, Siu TS, Chan KY, Siu WK, Yeung WL, Hui J, Wong VC, Low LC, Ko CH, Fung CW, Chen SP, Yuen YP, Lee HC, Yau E, Chan B, Tong SF, Tam S, Chan YW. Biochemical and molecular characterization of tyrosine hydroxylase deficiency in Hong Kong Chinese. *Mol Genet Metab*. 2010; 99:431-3 .
4. HM Luk, D Ching, CW Fung, C Mak, V Wong. Arginase deficiency in a Chinese girl presenting as spastic diplegic cerebral palsy (in preparation).
5. CW Fung, S Siu, C Mak, PL Khong, G Poon, A Kwok, KY Wong, PT Cheung, L Low, S Tam, V Wong. Transaldolase deficiency – a novel leucodystrophy presenting with hepatosplenomegaly (submitted).



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Education:

1. 1996-2001 MBBS, University of Malaya (Honor)
2. 2005 Certificate for Membership of Royal College of Paediatrics and Child Health (MRCPCH), United Kingdom
3. 2007 Excellent service certificate by Malaysian Ministry Of Health

Appointments:

1. Member, Royal College of Paediatrics and Child Health, United Kingdom
2. Member, Malaysian Neuroscience Society
3. Member, Malaysian Paediatric Association



O 29

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Education:

1. 1976-1982 Gifu University School of Medicine
2. 1989 PhD, Gifu University

Appointments:

1. 1982-2004 Department of Pediatrics, Gifu University School of Medicine
2. 2000-2001 Department of Pediatric Laboratory Medicine, The Hospital for Sick Children, University of Toronto, Toronto, Canada
3. 2004- Division of Genomics Research, Life Science Research Center, Gifu University
4. 2006- Dean, Life Science Research Center, Gifu University

Selected Publications:

1. Shimosawa N, et al. A human gene responsible for Zellweger syndrome that affects peroxisome assembly. Science 1992; 255:1132-4.
2. Shimosawa N, et al. Nonsense and temperature-sensitive mutations in PEX13 are the cause of complementation group H of peroxisome biogenesis disorders. Hum Mol Genet 1999; 8:1077-83.
3. Shimosawa N, et al. Genetic heterogeneity of peroxisome biogenesis disorders among Japanese patients: evidence for a founder haplotype for the most common PEX10 gene mutation. Am J Med Genet 2003; 120A:40-3.
4. Shimosawa N, et al. Identification of a new complementation group of the peroxisome biogenesis disorders and PEX14 as the mutated gene. Hum Mutat 2004; 23:552-8.
5. Shimosawa N. Molecular and clinical aspects of peroxisomal diseases. J Inher Metab Dis 2007; 30:193-7.



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Education and Appointments:

1. 1997-2000 Resident, Department of Pediatrics, National Taiwan University Hospital
2. 2000-2002 Fellow in Pediatric Neurology, Department of Pediatrics, National Taiwan University Hospital
3. 2002-2004 Attending Physician of Pediatrics, National Taiwan University Hospital
4. 2004- Attending Physician of Pediatrics, Far Eastern Memorial Hospital
5. 2008-2009 Research Fellow, IREIIMS (International Research and Educational Institute for Integrated Medical Sciences), Tokyo Women's Medical University, Tokyo, Japan

Selected Publications:

1. Liang JS, Lee WT, Peng SS, Wang PJ, Shen YZ. Adrenoleukodystrophy: clinical analysis of 9 patients. *Acta Paediatr Taiwan* 2004; 45:272-7.
2. Chiu HC, Liang JS, Wang JS, Lu JF. Mutational analyses of Taiwanese kindred with X-linked adrenoleukodystrophy. *Pediatr Neurol* 2006; 35:250-6.
3. Liang JS, Shimojima K, Yamamoto T. Application of array-based comparative genome hybridization in children with developmental delay or mental retardation. *Pediatr Neonatol* 2008; 49:213-7. Review.
4. Liang JS, Chien YH, Hwu WL, Yeh SJ, Peng SF. Schizencephaly in LEOPARD syndrome. *Pediatr Neurol* 2009; 41:71-3.
5. Liang JS, Shimojima K, Ohno K, Sugiura C, Une Y, Ohno K, Yamamoto T. A newly recognized microdeletion syndrome of 2p15-16.1 manifesting moderate developmental delay, autistic behavior, short stature, microcephaly, and dysmorphic features: a new patient with 3.2-Mb deletion. *JMG* 2009; 46:645-7.



O 31

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Education and Training:

1. 1979-1985 MD, Seoul National University, College of Medicine
2. 1993-1995 PhD, Seoul National University Graduate School
3. 1989-1992 Residency, Department of Pediatrics, Seoul National University Children's Hospital
4. 1992-1993 Fellowship, Division of Pediatric Neurology, Department of Pediatrics, Seoul National University Children's Hospital
5. 1997-1998 Visiting Researcher, Center for Human Genetics, Comprehensive Epilepsy Center, Duke University Medical Center, Durham NC, USA

Appointments:

1. 1994-1996 Instructor, Department of Pediatrics, Seoul National University College of Medicine
2. 1996-2002 Assistant Professor, Department of Pediatrics, Seoul National University College of Medicine
3. 2002-2007 Associate Professor, Department of Pediatrics, Seoul National University College of Medicine

Selected Publications:

1. Chae JH, Lee JS, Kim KJ, Hwang YS, Bonilla D, Tanji K, Hirano M. A novel ND3 mitochondrial DNA mutation in three Korean children with basal ganglia lesions and complex I deficiency. *Pediatr Res* 2007; 61:622-4.
2. Chae JH, Kim KJ, Hwang YS, Ki CS, Kim JW. Identification of a novel DHCR7 mutation in a Korean patient with Smith-Lemli-Opitz syndrome. *J Child Neurol* 2007; 1297-1300.
3. Hwang H, Kim KJ. New antiepileptic drugs in pediatric epilepsy. *Brain Dev* 2008; 30:549-55.
4. Kim SK, Wang KC, Hwang YS, Kim KJ, Chae JH, Kim IO, Cho BK. Epilepsy surgery in children: outcomes and complications. *J Neurosurg Pediatr* 2008; 1:277-83.
5. Chae JH, Lee JS, Hwang H, Kim KJ, Hwang YS, Park JD, Cheon JE, Kim IO, Choe GY, Park SH. Merosin-deficient congenital muscular dystrophy in Korea. *Brain Dev* 2009; 31:341-6.



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Education:

1. 1975 BA, Cambridge University
2. 1978 MB BS, University College Hospital London
3. 1991 MD, Cambridge University
4. Diploma in Child Health, London
5. Membership/Fellowship of Royal Colleges of Physicians and of Paediatrics and Child Health (DCH; FRCP; FRCPCH)

Appointments:

1. 1986-1990 Lecturer / Honorary Senior Registrar, Children's Hospital, Sheffield
2. 1990-1993 Senior Registrar in Paediatric Neurology, Newcastle General Hospital

Selected Publications:

1. Baxter P. Pyridoxine dependent and pyridoxine responsive seizures. In: Baxter P, ed "Vitamin responsive conditions in paediatric neurology" International Review of Child Neurology Series. London: MacKeith Press 2001; 109-65.
2. Baxter P, Clarke A, Cross H, Harding B, Hicks E, Livingston J, Surtees R. Idiopathic catastrophic epileptic encephalopathy presenting with acute onset intractable status. *Seizure* 2003; 12:379-87.
3. Mills PB, Struys E, Jakobs C, Plecko B, Baxter P, Baumgartner M, Willemsen MA, Omran H, Tacke U, Uhlenberg B, Weschke B, Clayton PT. Mutations in antiquitin in individuals with pyridoxine-dependent seizures. *Nat Med* 2006; 12:307-9.
4. Crow YJ, Leitch A, Hayward BE, Garner A, Parmar R, Griffith E, Ali M, Semple C, Aicardi J, Babul-Hirji R, Baumann C, Baxter P, Bertini E, Chandler KE, Chitayat D, Cau D, Déry C, Fazzi E, Goizet C, King MD, Klepper J, Lacombe D, Lanzi G, Lyall H, Martínez-Frías ML, Mathieu M, McKeown C, Monier A, Oade Y, Quarrell OW, Rittey CD, Rogers RC, Sanchis A, Stephenson JBP, Tacke U, Till M, Tolmie JL, Tomlin P, Voit T, Weschke B, Woods CG, Lebon P, Bonthron DT, Ponting CP, Jackson AP. Mutations in each of the three Ribonuclease H2 subunits cause Aicardi Goutières syndrome and mimic congenital viral brain infection. *Nat Genet* 2006; 38:906-10.
5. Baxter PS, Rigby AS, Rotsaert MH, Wright I. Acquired microcephaly: causes, patterns, motor and IQ effects, and associated growth changes. *Pediatrics* 2009; 124:590-5.



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Education and Appointments:

1. 1956 MD, Okayama University Medical School
2. 1962 Instructor of Pediatrics
3. 1970 Assistant Professor of Pediatrics and Child Neurology
4. 1978 Associate Professor of Pediatrics and Child Neurology
5. 1979-1995 Professor and Chairman, Department of Child Neurology, Okayama University Medical School and Hospital
6. 1995-2003 Professor of Pediatrics and Child Neurology, Kibi International University Health Sciences School

Selected Publications:

1. Ohtahara S, Ohtsuka Y, Kobayashi K. Lennox-Gastaut syndrome: a new vista. *Psychiat Clin Neurosci* 1995; 49:179-83.
2. Ohtahara S, Yamatogi Y. Epileptic encephalopathies in early infancy with suppression burst. *J Clin Neurophysiol* 2003; 20:398-407.
3. Yamatogi Y, Ohtahara S. Severe epilepsy with multiple independent spike foci. *J Clin Neurophysiol* 2003; 20:442-8.
4. Ohtahara S, Yamatogi Y. Ohtahara syndrome: with special reference to its developmental aspects for differentiating from early myoclonic encephalopathy. *Epilepsy Res* 70S; 2006:58-67.
5. Ohtahara S, Yamatogi Y, Ohtsuka Y. Ohtahara syndrome. In: Engel J Jr, Pedley TA eds. *Epilepsy: a Comprehensive Textbook*. 2nd Ed. Philadelphia: Lippincott-Raven, 2008; 3:2303-11.



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Appointments and Experiences:

1. 1974-1978 Junior Resident, All India Institute of Medical Sciences, New Delhi
2. 1975-1976 Fellow, University of Southern California, Los Angeles, USA
3. 1978-1981 Lecturer and Consultant, JLN Medical College Ajmer, Rajasthan
4. 1981-1983 Lecturer and Consultant, University of the West Indies, Kingston, Jamaica
5. 1983-1985 Lecturer and Consultant, Postgraduate Institute of Medical Education and Research, Chandigarh
6. 1986-1988 Assistant Professor, Postgraduate Institute of Medical Education and Research, Chandigarh
7. 1988-1993 Associate Professor, Postgraduate Institute of Medical Education and Research, Chandigarh
8. 1993-2001 Additional Professor, Postgraduate Institute of Medical Education and Research, Chandigarh

Selected Publications:

1. Singhi P, Bansal A, Geeta P, Singhi S. Predictors of long term neurological outcome in bacterial meningitis. Indian J Pediatr 2007; 74:369-74.
2. Chinta SS, Malhi P, Singhi P, Prabhakar S. Clinical and psychosocial characteristics of children with nonepileptic seizures. Ann Indian Acad Neurol 2008; 11:159-63.
3. Sankar J, Singhi P, Bansal A, Ray P, Singhi S. Role of dexamethasone and oral glycerol in reducing hearing and neurological sequelae in children with bacterial meningitis. Indian Pediatr 2007; 44:649-56.
4. Singhi P, Singhi S. Neurocysticercosis in children. Indian J Pediatr 2009; 76:537-45.
5. Rajyadhyaksha S, Kalra V, Potharaju NR, Singhi P, Shah KN, Yardi N, Murthy JM, Desai M, Ursekar M, Hegde A, Kumaresan G, Aneja S, Udani V, Mani J, Naik N, Gupta R, Passi GR, Chattopadhyay A, Nathan J, Sankhe M, Udani S. (Expert Committee on Pediatric Epilepsy, Indian Academy of Pediatrics) Guidelines for diagnosis and management of childhood epilepsy. Indian Pediatr 2009; 46:681-98.



O 37

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1. 1984-1990 Department of Medicine, National Taiwan University
2. 1990-1991 Internship in National Taiwan University Hospital
3. 1998-1999 Research Fellow in the Department of Radiology, University of California in San Francisco, USA

Appointments:

1. 1995- Staff of Division of Pediatric Radiology, Department of Medical Imaging, National Taiwan University Hospital
2. 1998-2001 Instructor, Department of Medicine, Medical College, National Taiwan University
3. 2001-2007 Clinical Assistant Professor, Department of Medicine, Medical College, National Taiwan University
4. 2004- Chief of the Section of Pediatric Radiology, Department of Medical Imaging, National Taiwan University Hospital
5. 2007- Assistant Professor, Department of Radiology, Medical College, National Taiwan University

Selected Publications:

1. Chien YH, Peng SF, Wang TR, Hwu WL. Cranial magnetic resonance spectroscopy of tetrahydrobiopterin deficiency. Am J Neuroradiol 2002; 23:1055-8.
2. Peng SF, Tseng WY, Chien YH, Hwu WL, Liu HM. Diffusion tensor images in early-treated, chronic malignant phenylketonuric children-correlation with intelligence assessment. Am J Neuroradiol 2004; 25:1569-74.
3. Peng SF, Lee WT, Wang YH, Huang KM. Cerebral diffusion tensor images in children with tuberous sclerosis. Pediatr Radiol 2004; 34:387-92.
4. Chien YH, Lee NC, Peng SF, Hwu WL. Brain development in infantile-onset Pompe disease treated by enzyme replacement therapy. Pediatr Res 2006; 60:349-52.
5. Lee NJ, Chien YH, Peng SS, Huang AC, Liu TT, Wu ASH, Chen LC, Hsu LW, Tseng SC, Hwu WL. Brain damage by mild metabolic derangements in methylmalonic academia. Pediatr Neurol 2008; 39:325-9.



O 38

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Education and Appointments:

1. 1968-1970 Fellow in Pediatrics, Mayo Clinic, Rochester, USA
2. 1970-1971 Fellow in Pediatric Neurology, Children's Hospital of Washington DC, USA
3. 1971-1973 Staff in Department of Pediatrics, Yokohama City University School of Medicine, Yokohama, Japan
4. 1973-1975 Resident in Neurology, Georgetown University, Washington DC, USA

Selected Publications:

1. Nomura Y, Ikeuchi T, Tsuji S, Segawa M. Two phenotypes and anticipation observed in Japanese cases with early onset torsion dystonia (DYT1)-pathophysiological consideration. Brain Dev 2000; 22 Suppl 1; S92-101.
2. Nomura Y, Fukuda H, Terao Y, Hikosaka O, Segawa M. Abnormalities of voluntary saccades in Gilles de la Tourette's syndrome: pathophysiological consideration. Brain Dev 2003; 25 Suppl 1; S48-54.
3. Nomura Y, Segawa M. Natural history of Rett syndrome. J Child Neurol 2005; 20:764-8. Review.
4. Nomura Y. Disease entities with a temporary autistic phases; autistic features of Rett syndrome. In: Coleman M, ed. The neurology of autism. Oxford University Press, New York. 2005 pp.136-56.
5. Nomura Y, Hachimori K, Nagao Y, Segawa M, Kimura K, Segawa M. Childhood myasthenia gravis in Japan-clinical analysis of 184 cases at Segawa Neurological Clinic for Children for 30 years. Neuro-ophthalmology 2007; 31:201-5.



Abstracts

Oral Presentation (O 01-O 38)

A1-A38

Poster Presentation (P 01-P 56)

A39-A94

OVERVIEW OF EPILEPTIC SEIZURES IN NEUROMETABOLIC DISEASES

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Objectives: Metabolic disorders constitute an important cause of neurologic diseases. There are more than 10,000 well-recognized and characterized inherited disorders in human, many of which impact central nervous system function either directly or indirectly. Among them, nearly 200 disorders are associated with seizures or epilepsy. Here we reviewed epileptic seizures in children with neurometabolic diseases in Taiwan

Methods: From 1978 to October 2009, we collected children with neurometabolic diseases. The diagnosis was based on characteristic clinical features, metabolic survey, enzyme activities, tissue biopsies, genetic analysis, and specific MRI and MRS findings. We analyzed the epileptic seizures as well as electroencephalography (EEG) in these patients.

Results: Total 213 cases, aged from 1 day to 15 years, were enrolled. One hundred and four patients (104/213; 48.8%) presented with seizures, 57 out of 104 (54.8%) had seizures as an initial manifestation, 47 (45.2%) had seizures during the course of illness, 60 (57.7%) were refractory to antiepileptic drug therapy. With the seizure types, 65 patients (62.5%) had generalized seizures, including generalized tonic seizure, generalized tonic-clonic seizure, and myoclonic seizure, 18 (17.3%) had partial seizures, 17 (16.3%) had mixed seizure types, and four (3.8%) had epileptic syndromes. Eight cases were presented with pseudoseizures. The most common intractable seizures occurred in the heavy metals disorders (7/8; 87.5%), lysosomal storage disorders (7/9; 77.8%), and mitochondrial disorders (27/43; 62.8%). In our study, specific EEG features in neurometabolic disorders included comb-like rhythm, vanishing EEG, high voltage activity, marked photosensitivity, burst-suppression, and hypsarrhythmia.

Conclusion: Epileptic seizures or syndromes are often a part of the clinical picture of inherited neurometabolic disorders. Some patterns of clinical presentations and/or EEG findings may indicate underlying neurometabolic diseases. Thus, neurometabolic work-up has become an imperative for those patients with psychomotor retardation and /or intractable seizures.

INBORN ERRORS OF METABOLISM AND SEIZURES IN CHILDREN: AN OVERVIEW FROM CHINA

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Objectives: To briefly summarize the current status of researches on the inborn errors of metabolism (IEM), and the significance of such disorders in seizures of children in China.

Methods: Browse the main literature database of medicine in China in the past two decades, and retrospectively summarize the data of urinary metabolic analysis from an university based department of pediatrics in Beijing, to analyze the conditions of IEM in the practice of child neurology.

Results: The main disorders of IEM including most diseases in this field, including IEM involving organic acid, amino acid, fatty acid, and mitochondrial encephalopathy, etc. An eighteen-year study on phenylketonuria by China-Japan Friendship Hospital included totally 603 patients, with various patterns of seizures in 119 cases. Six single base mutations were detected in 18 unrelated northern Chinese BH4 deficiency families, and the mutations at nucleotides 259C-T and 286G-A were common mutations. The results from 29 late-treated patients with classical PKU indicate a well matched genotype and intellectual phenotype association in classical PKU patients. A 13 year data from Peking University First Hospital Department of Pediatrics included 16542 children, amongwhom 5210 were with seizures. IEMs were diagnosed in 2247 cases afterwards, including organic aciduria 489, aminoacidopathy 1586, and fatty acid disorders 172 cases.

Conclusion: IEMs are relatively common in the practice of child neurology. Many types of IEMs were reported in China. Seizures are fairly common features in the IEMs.

NEUROPHYSIOLOGICAL CHARACTERISTICS OF NEUROMETABOLIC DISEASES IN CHILDREN

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Dr. Wu will review the clinical neurophysiological characteristics of the various categories of neurometabolic disorders in children. This will include a comprehensive summary of the type, location, timeline, and incidence of the various abnormalities on a variety of clinical neurophysiologic tests, including evoked potential, surface EEG, electrocorticography and intracranial recording, and MEG.

MOLECULAR BASIS OF METABOLIC ENCEPHALOPATHY – NEUROGENETIC DISEASE: FROM MOLECULE TO PATIENT

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Child neurology started with clinical and pathological analysis of neurological diseases in children with brain damage, presenting with mental retardation, epileptic disorders and various somatic disabilities. Among them lysosomal diseases have been my major targets for scientific research. Recently new methods of biochemical analysis were developed, leading to discoveries of unexpected metabolic errors in neurodegenerative diseases. Gene analysis particularly has become a powerful tool for investigation of molecular events in individual patients with diseases of unknown etiology. At present almost 7,000 single gene disorders are listed in the McKusick's catalog of inherited diseases. Many of them present with progressive neurological manifestations caused by single gene mutations, resulting in loss of enzyme activity and diverse phenotypic manifestations. At present we can make diagnosis of patients and heterozygous carriers by gene mutation analysis. However, even with plenty of information about phenotypes and molecules in individual patients, we do not know much about pathogenesis of each disease, and treatment is not possible particularly for brain damage. In my research on the black box of human cells and tissues, I have been trying to elucidate the pathogenesis of Krabbe disease, GM1-gangliosidosis, galactosialidosis, and other neuronopathic lysosomal diseases. In this talk I will mainly focus on the therapeutic aspect of β -galactosidase deficiency disorders (β -galactosidosis) as a model experiment. I will briefly summarize our research data of diagnostic, pathogenetic, and therapeutic studies (chemical chaperone therapy). This experimental approach disclosed some new molecular events in disease cells and tissues. I hope to step up in the near future to human patients toward my final goal of molecular therapy of inherited brain disease.

THE NEUROPATHOLOGY OF EPILEPSY-RELATED NEUROMETABOLIC DISEASES

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Objectives: Neurometabolic diseases (NMD) are often hereditary, associated with epilepsy, especially myoclonus epilepsy and grand mal seizures. Most hereditary NMD belong to the single-organelle multi-organ disorders, encompassing lysosomal, peroxisomal, and mitochondrial conditions, of which lysosomal diseases are the best explored ones. Within the context of this presentation, the sphingolipidoses and the neuronal ceroid-lipofuscinoses (NCL) are the most important ones, among them sialidosis and late-infantile NCL which are associated with myoclonus epilepsy. It is the purpose of this review to present the neuropathology of epilepsy-related NMD.

Methods: Electron microscopy is a pivotal diagnostic technique recognizing lysosomal conditions, which may be divided into vacuolar and avacuolar forms. The nosography is based on biochemical (substrate) and molecular criteria.

Results: While there is an abundance of diverse ultrastructural features in lysosomal diseases, based on the diversity of intralysosomally stored biochemical substrates, peroxisomal diseases have a rather limited electron microscopic expression concerning the pathology of peroxisomes, best identified in liver and kidney rather than in the nervous system, and cholesterol needles in adrenoleukodystrophy. Among the emerging and rapidly expanding group of mitochondrial encephalomyopathies, MERRF (myoclonus epilepsy and ragged red fibres) is most prominent among the myoclonus epilepsies, but many other forms of mitochondrial encephalomyopathies are also associated with seizures. Another progressive myoclonus epilepsy is Lafora disease marked by polyglucosan inclusions in neurons, liver cells, and sweat gland epithelial cells.

Conclusion: NMD affect cerebral and non-cerebral tissues. The latter ones, e.g. skin, muscle, rectum, nerve, and blood lymphocytes are variably involved and require a differential diagnostic approach for an in-vivo recognition of an individual NMD.

NEUROIMAGING PERSPECTIVES IN PEDIATRIC NEUROMETABOLIC DISEASES

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The purpose of neuroimaging is to identify the presence or absence of abnormalities that help to identify a disease process, findings that when present, focus the differential diagnosis to one or more entities, and, when treatment is possible, allow for assessment of the effectiveness of therapy.

To this end, the armamentarium of the neuroimager has been constantly changing over the past two decades. Improvement in imaging techniques have occurred both in sequence design, e.g., FLAIR, diffusion imaging with ADC maps, diffusion tensor imaging with fractional anisotropy maps, as well as perfusion imaging with arterial spin labeling (ASL), as well as in the equipment used (1.5 Tesla to 3 Tesla, and even higher field strengths). Not only has MR imaging evolved, but so has magnetic resonance spectroscopy (MRS), with the development of multivoxel techniques (2D & 3D), improved short TE studies and identification of more metabolites.

The application of these imaging and spectroscopy techniques in conjunction with further advances in understanding the metabolism of diseases and their genetic origins has lead to improvements in specificity with which some neurometabolic diseases can be identified and followed.

This presentation deals with the overview of these developments from the view of the neuroradiologist in approaching the neurometabolic diseases as to the findings on MRI & MRS that are found in the gray matter, cortex and deep structures, and the white matter.

CLINICAL AND SCIENTIFIC PERSPECTIVES ON EPILEPSY AMONG NEUROMETABOLIC DISEASES IN CHILDREN

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This presentation will address questions of interest pertaining to areas of knowledge which are not advanced enough at present to provide very clear answers. A wealth of detail regarding specific metabolic aberrations, how new understanding of the biochemical pathways has facilitated diagnosis and treatment will be furnished by the distinguished experts gathered here. New knowledge about the involvement of specific genes will also be brought up to date. Nevertheless, it remains difficult to see clearly why a particular metabolic defect produces epilepsy. How do abnormal metabolites alter neuronal excitability? What is the present state of understanding as how an abnormal metabolic milieu can impact on neuronal migration, excitability, injury, survival, and plasticity to produce the myriad phenotypes we see in terms of epilepsy (this group's – including my own – biased focus) as well as the associated neurodevelopmental (cognitive and behavioral) problems?

Areas we shall attempt to explore include how a neurometabolic disorder may influence bioenergetics, mitochondrial function, and approaches to manipulating the metabolic milieu (such as the ketogenic diet). Metabolic defects may influence normal neurotransmitter (e.g. GABA) synthesis as well as abnormal neurotransmitter (e.g. GHB) synthesis. Even before the development of synapses, ambient GABA produces excitatory drive to neurons and controls migration. Some abnormal metabolites may produce excitotoxicity. A number of disorders may interfere with the functioning of Na-K-ATPase. Abnormal metabolites may contribute to inflammation. Is there a role for immunomodulation in treating children with neurometabolic disorders? Many questions, few answers, constituting a great recipe for this symposium to stimulate the generation of new hypotheses and catalyze novel clinical research.

AMINO ACID METABOLIC DISORDERS AND INFANTILE EPILEPSYWang-Tso Lee¹¹ Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan

Seizure is not an unusual clinical manifestation in children with disorders in amino acid metabolism. Neurological manifestations in patients with phenylketonuria usually appear insidiously. However, chronic exposure to elevated phenylalanine may result in microcephaly and seizures, including infantile spasms. Severe bipterin disorders may also present with developmental delay and seizures. For patients with maple syrup urine disease (MSUD), seizures commonly occur in neonatal stage. But in intermittent MSUD or thiamine-responsive MSUD, seizures usually develop in later stage. In glycine encephalopathy, seizures, like early myoclonic encephalopathy, are very common, and usually present in first weeks of life. However, for patients with late-onset glycine encephalopathy, the clinical presentations may be different, and seizures may be uncommon. In addition to these disorders, patients with sulfite oxidase deficiency, serine synthesis disorders, or GABA-related disorders (like SSADH deficiency) may also present with different types of seizures. Although seizures or epilepsy are common neurological manifestations for some kinds of amino acid-related metabolic disorders, involuntary movements, which are also common in these disorders, may also be mistaken to be seizures or epilepsy. Careful evaluation and correct diagnosis may avoid the unnecessary treatment in these patients.

NONKETOTIC HYPERGLYCINEMIA

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Nonketotic hyperglycinemia (NKH), also referred to as glycine encephalopathy, is an inborn error of metabolism characterized by accumulation of glycine in body fluids. Neonatal seizures, coma and profound hypotonia are typical presentations of typical NKH. In milder cases delayed psychomotor development and behavioral abnormality are main symptoms. NKH is caused by deficiency of glycine cleavage system (GCS), which consists of four individual proteins; P, T, and H-proteins (Tada et al., Tohoku J Exp Med, 1969).

In this presentation, I will talk about recent advances in study of NKH, which include, 1) mutation spectrum of NKH, 2) development of a novel enzymatic diagnosis and 3) pathophysiology: 1) GLDC mutations were identified in ~70% of the mutant alleles while the rest of the alleles carried AMT mutations. GCSL mutations cause Leigh syndrome, but not NKH. Mutation spectra of GLDC and AMT are heterogeneous (Kure et al., Hum Mutat, 2006). We established a detection system of genomic deletion within GLDC by multiplex-ligation probe amplification (MLPA) method, and found that 20~30% of NKH mutant allele have genomic deletions, in which multiple GLDC exons are involved (Kanno et al., J Med Gent, 2006). 2) We have developed the [1-13C]glycine breath test, which enabled us to evaluate the enzymatic activity of the GCS without risking liver biopsy (Kure et al, Ann Neurol, 2006). 3) Development of mice model of NKH revealed that overexcitation of the NMDA type glutamate receptor by high level of glycine is involved in the etiology of NKH (Kojima-Ishii, Pediatr Res, 2007). NKH is frequently associated with brain malformations such as microcephaly or hypogenesis of corpus callosum. The GCS is abundantly expressed in neural stem cells in fetal period (Ichinohe et al, Eur J Neurosci, 2004), which may explain the etiology of brain malformations associated with NKH.

METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) DEFICIENCY AND INFANTILE EPILEPSY

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Objectives: A recessively inherited defect leading to deficiency of the enzyme 5, 10-methylenetetrahydrofolate reductase (MTHFR) underlies one form of hyperhomocysteinemia. We describe the association of MTHFR deficiency and epilepsy, emphasizing the clinical neurobiological, biochemical, genetic, and therapeutic aspects.

Methods: Case Study and review of literature.

Results: A 9 year old female infant born to Caucasian non-consanguineous parents presented with infantile spasms and developmental regression in the first year. The biochemical profile of low plasma methionine (undetectable) and homocystinuria (234 μ moles/gm creatinine) suggested MTHFR deficiency. MTHFR assay in skin fibroblasts confirmed a severe deficiency (patient 0.92, control 13.3 \pm 4.6 nmole/mg/hr). Molecular genetic studies identified compound heterozygosity with R57Q and c1348+1g>a mutations. The c.1348+1g>a mutation is a novel mutation that removes a splice site at the end of exon 7 and introduces a premature stop codon that truncates the protein without exons 8-11. In addition, the patient was heterozygous for the common A222V polymorphism that is considered a risk factor for diseases that may be influenced by disruption of folate metabolism. CSF neurotransmitter analysis showed extremely low level of 5-methyl tetrahydrofolate of <5 (40-128 nmol/L). The course of epilepsy has been progressive and severe. Treatment protocols include; betaine, methionine, folic acid, and 5-methyltetrahydrofolate with questionable benefit. Epileptic seizures remain pharmacoresistant to antiepileptic medications singly and in combinations. Frequent bouts of status epilepticus have led to multiple hospitalizations, and neurosurgical interventions (corpus callosotomy, vagal nerve stimulation). At age 9 years, the patient remains severely impaired by vertebral compressive and limb fractures secondary to significant osteoporosis.

Conclusion: Severe MTHFR deficiency is an important diagnostic consideration in infantile epileptic encephalopathies. Genotype phenotype correlations will be explored in the light of biochemical and molecular genetic data. While early diagnosis and interventions are possible, future research needs to focus on developing effective treatment strategies for this complex disorder.

MAPLE SYRUP URINE DISEASE AND INFANTILE EPILEPSY

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Objectives: Maple syrup urine disease (MSUD) is an autosomal recessive aminoacidopathy secondary to an enzyme defect in the catabolic pathway of the branched-chain amino acids leucine, isoleucine, and valine. Accumulation of their corresponding keto-acids leads to encephalopathy if not treated in time. The clinical phenotypes with highlight on epilepsy patterns among patients with different forms of MSUD were analyzed.

Methods: The diagnosis of MSUD was made and classified by its pattern of signs and symptoms and the patients' clinical courses: classic type in three patients (2 boys and 1 girl), intermediate type in one boy, and thiamine-responsive type in one girl. Extensive investigations including tandem mass spectrometry, urine organic acids by chromatography-mass spectrometry, concentrations of plasma amino acids, urine dinitrophenylhydrazine test, electroencephalography (EEG), metabolic profile, DNA, and imaging studies were performed.

Results: Features of MSUD in early infancy include poor feeding, vomiting, dehydration, lethargy, hypotonia, ketoacidosis, and seizures. Epilepsy manifested as tonic peddling-like patterns with suppression-burst rhythms on EEG. Leukodystrophy was noted in well-controlled patients with classic MSUD. Zinc deficiency with acrodermatitis enteropathica-like skin lesions, increased lipid peroxidation and decreased antioxidant defenses were also noted in MSUD patients even after restrict diet control. Founder mutation of the E2 (DBT) gene was noted among certain population.

Conclusion: Although morbidities (such as seizures and encephalopathy) and mortality can almost be prevented with early diagnosis and appropriate treatment at presentation and during episodes of potential metabolic decompensation, additional biochemical disturbances (known or unknown) may play an important role in the pathogenesis of further nervous disorders.

THE LONG-TERM OUTCOMES OF THE TAIWANESE PATIENTS WITH 6-PYRUVOYL-TETRAHYDROPTERIN SYNTHASE DEFICIENCY BEFORE OR AFTER THE NEWBORN SCREENING

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Hyperphenylalaninemia is the most common inherited disorder of amino acid metabolism. It is caused by a deficiency of phenylalanine hydroxylase (PKU) or tetrahydrobiopterin (BH4), an important cofactor involved in the biogenic syntheses of tyrosine, L-DOPA, 5- hydroxytryptophan (5-HTP), nitric oxide, and glycerol. Apart from the classical PKU phenotype, deficiency of BH4 is often accompanied by seizures and various extrapyramidal neurological symptoms, such as truncal hypotonia, increased limb tone, postural instability, hypokinesia, choreatic or dystonic limb movements, gait difficulties, hypersalivation, swallowing difficulties, etc, due to impaired synthesis of catecholamines and serotonin. 6-pyruvoyl-tetrahydropterin synthase (PTPS) deficiency is the most predominant type of BH4 deficiency. Reports of the long-term treatment of PTPS deficiency are few. A considerable proportion of patients experience adverse outcomes, despite the detection of PTPS by newborn screening and early initiation of treatment. In Taiwan, PTPS deficiency is the cause of approximately one-third of all cases of HPA. The prevalence of PTPS deficiency in this country (1/100,000) is considerably higher than in Caucasian populations (1/1,000,000). This provides us an opportunity to observe the treatment outcome of this form of illness within a single medical center. In this study, we reviewed the characteristics of 8 PTPS-deficient patients with delayed treatment and 12 patents with early treatment. The relationships among clinical manifestations, biochemical findings, genotypes, and long-term outcomes were analyzed. For the patients with delayed treatment, most of them suffered from severe psychomotor, as in a vegetative-like state before treatment. After the long-term BH4 (2 and 4 mg/kg) and neurotransmitters (L-dopa: 10 to 15 mg/kg/day, 5-HTTP: 3-5mg/kg/day) replacements, all patients have remarkable improvements gradually after 15 years follow-up (final FIQ score was 62.8±13.06). For the patients with early treatment, the average FIQ score was 96.7 ±9.7 (range 86-119), considerably higher than previously reported.

TREATABLE METABOLIC EPILEPSIES: CASE STUDIES

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A selected group of eminently treatable but otherwise catastrophic epileptic encephalopathies will be highlighted. These epilepsies represent a vexing clinical challenge because a sufficiently low diagnostic threshold must be maintained for rare and esoteric diseases. Pyridoxine (vitamin B6) dependency is the prototype and recently identified as antiquitin deficiency involving lysine degradation. Urinary pipecolic acid is a valuable laboratory aid in addition to the standard concomitant administration of 100 mg IV during EEG. CSF monoamine metabolic analysis will show a characteristic pattern analogous to aromatic aminoacid decarboxylase deficiency. Empirical discontinuation of therapy as a diagnostic maneuver is inadvisable, and the diagnosis must be re-suspected even in initial treatment failures. The enigmatic folinic acid dependency is allelic to pyridoxine dependency, and patients may respond to either or both therapies. Pyridoxal-5-phosphate dependency is a newly recognized variant which is due to pyridox(am)ine oxidase deficiency and requires supplementation with the biologically active form of pyridoxine. Newborn screening may lead to a misdiagnosis of PKU whereas an infant presenting with seizures may have a biopterin-responsive hyperphenylalaninemia. Dihydropteridine reductase deficiency additionally requires folinic acid which may result in resolution of basal ganglia calcifications. Cerebral folate deficiency, also treatable with folinic acid, is associated with decreased CSF 5-methyltetrahydrofolate with normal peripheral folate levels. Seizures (including infantile spasms or myoclonic) may be the sole feature in biotinidase deficiency, which is not universally covered in newborn screening. Glucose transporter 1 deficiency has an enlarging phenotype, requires CSF analysis for hypoglycorrhachia, and is treatable with the ketogenic diet, offering an alternative metabolic fuel to glucose. A neonate presenting with seizures and diabetes may have a potassium-regulated ATP channelopathy of pancreas and brain, DEND (developmental disorder, epilepsy, neonatal diabetes) whereas the hyperglycemia is corrected by insulin but a profound encephalopathy will result if treatment is not instead a sulfonylurea. In contrast, congenital hyperinsulinism with hyperammonemia (HI/HA), a mutation of glutamate dehydrogenase, is associated with generalized epilepsy and learning disabilities, and is treated with diazoxide and protein restriction. Serine biosynthesis disorders are treatable with combined L-serine and glycine but otherwise result in microcephaly and epilepsy. Creatine synthesis disorders feature intellectual disability and epilepsy, may be diagnosed with abnormal guanidinoacetic acid (GAA) levels in urine or plasma (or MR spectroscopy), and respond to creatine and ornithine supplementation and arginine restriction. Benzodiazepines appear to have an ameliorative role in hyperekplexia, an epilepsy mimicker due to mutations in the glycine inhibitory receptor or transport system associated with sudden death.

HEAT STRESS AND ACUTE ENCEPHALOPATHY IN CHILDHOOD DUE TO INHERITED ORGANIC AND FATTY ACID DISORDERS

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Objectives: Hyperpyrexia in childhood occasionally triggers some serious febrile illnesses such as febrile convulsions, deliria, or acute encephalopathies including influenza-associated encephalopathy (IAE). On the other hand, it is known that aspirin also potentially causes Reye encephalopathy. It was reported that hyperpyrexia might be responsible for impaired fatty acid oxidation (FAO) in IAE. We investigated the effect of heat stress or some drugs that might be related to encephalopathy on FAO.

Methods: Cell lines from 15 cases of FAO disorders including CPT2 deficiency, VLCAD deficiency, MTP deficiency or MCAD deficiency as well as 6 controls were examined for acylcarnitine (AC) profiles by the in vitro probe assay using MS/MS. The AC profiles in cells cultured at 37°C and 41°C were compared in the presence or absence of some drugs.

Results and Discussions: 1) Heat stress (at 41°C compared with at 37°C) increased acetylcarnitine (C2), which reflects the production of acetyl-CoA in all cells from FAO disorders and controls. It is suggested that heat stress generally facilitates FAO. 2) In controls and MCAD deficiency, ACs from the short to long-chain species decreased. 3) In long-chain FAO disorders including CPT2- VLCAD- MTP-deficiencies, long-chain ACs (at least C16) significantly increased. 4) In glutaric acidemia type 2 (GA2), which is caused by a defect of ETF or ETF-DH and results in multiple acyl-CoA dehydrogenation deficiency, the short- to medium-chain ACs (C4 to C10) decreased at 41°C, while the long-chain ACs (C12 to C16) significantly increased. These findings indicate that heat stress might inhibit long-chain FAO. Patients with impaired FAO may be more vulnerable to heat stress. 5) Palmitate loading in the presence of aspirin showed an elevation of C12. 6) Bezafibrate, one of the hyperlipidemic drugs, improved long-chain FAO defects. It may be concluded that some acute encephalopathy in childhood is related to temporarily or congenitally impaired FAO.

EPILEPSY IN CHILDREN WITH METHYLMALONIC ACADEMIA

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Objectives: To summarize the clinical features of epilepsy in children with methylmalonic academia (MMA)

Methods: In the past 13 years, children with unknown cause of mental retardation, seizures, motor deficit, recurrent vomiting, metabolic acidosis or lethargy were screened by urine organic acid analysis (gas chromatography-mass spectrometry, GC-MS). The medical records of hospitalized MMA patients associated with epilepsy were retrospectively reviewed.

Results: 489 patients with organic academia (3.0%) were confirmed in 16542 screened children. 291 of 489 patients with organic academia were diagnosed with MMA (59.5%). Some MMA patients combined with homocysteinemia. 62 of 291 MMA patients were hospitalized. 26 of 62 hospitalized patients associated with epilepsy (41.9%). Seizure onset age was from 8 days to 11 years. Partial seizures were presented in 17, generalized tonic-clonic seizures in 3, tonic seizures in 4, myoclonic seizures in 3 and infantile spasm in one. Five patients had two or more seizure types. Eight patients had a history of status epilepticus (30.8%). Four hours Video-EEG was done in 18 patients with epilepsy. Seizures were recorded in 9 patients. 18 of 26 MMA patients with epilepsy were further classified, 17 with cobalamin C disease (65.4%) and one with partial mutase deficiency (mut-). Vitamin B12-responsive patients had good outcome compared with vitamin B12-nonresponsive patients.

Conclusion: Epilepsy is a common symptom of patients with MMA. Partial seizures is common than other seizure types. Status epilepticus is not rare. When children with unknown cause of epilepsy combined with other symptoms of central nervous system, GC-MS should be investigated for the further diagnosis.

EPILEPSY IN UREA CYCLE DEFECTS

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Objectives: Urea cycle disorders (UCDs) are caused by the deficiency of one of the urea cycle enzymes. The primary manifestation of UCDs is hyperammonemia. Hyperammonemia is toxic to the brain and affects consciousness level rapidly. Seizure can be part of the clinical manifestations when brain edema occurs.

Methods: Patients with UCDs in the National Taiwan University Hospital were reviewed. Clinical manifestations including symptoms and age of onset were analyzed.

Results: In NTUH record, ornithine transcarbamylase (OTC) deficiency is the most common UCD. Both infants, children and adults, females and males patients were diagnosed. Cases of carbamoyl phosphate synthase deficiency were also found. Two cases of adult-onset citrullinemia II were detected because of hyperammonemia. There are other diseases that secondary hyperammonemia can be prominent. Those diseases include carnitine uptake defect and methylmalonic acidemia. Seizure was rare in these cases.

Conclusion: Patients with severe deficiency of the urea cycle enzymes have symptoms during neonatal period. Other patients may have first symptoms at ages ranging from infancy to adulthood. Fluid therapy needs to be cautious, supplying ample energy but without aggravating brain edema. UCDs, when properly managed, rarely present seizure.

CARNITINE AND FATTY ACID OXIDATION DEFECTS IN INFANTILE EPILEPSY

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Objective: To determine the risk factors for infantile epilepsy in primary and secondary disorders of fatty acid oxidation (FAO) and the indications for L-carnitine (Cn) supplementation.

Background: Primary FAO disorders are an important group of diseases because they are potentially rapidly fatal and source of major morbidity. They may present with recurrent hypoglycemic hypoketotic encephalopathy or Reye-like syndrome, seizures, and developmental delay. All 23 known conditions are autosomal-recessive. Early recognition and prompt institution of therapy and appropriate preventive measures may be life saving, significantly decreasing long-term morbidity, particularly with respect to seizures and CNS sequelae. Fatty acids serve 3 major functions. First, partial oxidation of fatty acids by liver produces ketones which are an important auxiliary fuel for brain to spare glucose oxidation and proteolysis during prolonged fasting. Second, fatty acids serve as a major fuel for skeletal and cardiac muscle. Resting and exercising muscle (mild to moderate prolonged exercise), depend primarily on FAO. Third, high rates of hepatic gluconeogenesis and ureagenesis needed for maintaining fasting homeostasis are sustained by the production of ATP, reducing equivalents, and metabolic intermediates derived from FAO. FAO is also important in shivering thermogenesis and during acute infections. In the medium- and long-chain defects, there is a risk for hypoketotic, hypoglycemic coma during fasting or infections with secondary cerebral injury and seizures. In short-chain acyl-CoA dehydrogenase (SCAD) deficiency, cerebral injury and seizures are more likely related to accumulation of short-chain fatty acid metabolites, such as ethylmalonic acid which may be neurotoxic by inhibiting mitochondrial CK, increasing lipid and protein oxidation products, decreasing glutathione, and inhibiting electron transport chain activity at Complexes I and III leading to decreased ATP and excessive oxidative stress.

L-Cn is an essential cofactor for long-chain FAO. Cn also modulates the intramitochondrial acyl-CoA/CoA sulfhydryl ratio, providing cells with a critical source of free CoA for operation of essential CoA requiring processes such as the citric acid cycle, pyruvate oxidation, etc. The role of the Cn system is to maintain homeostasis in the acyl-CoA pools of the cell, keeping the acyl-CoA/CoA pool constant even under conditions of very high acyl-CoA turnover. Cn also provides a shuttle mechanism for acyl groups between mitochondria, peroxisomes and microsomes and is therefore essential in complex lipid-synthetic and –breakdown pathways. Cn also has a detoxifying role in trapping potentially toxic acyl-CoA metabolites, that may increase during acute metabolic crises, and serves as an antioxidant.

Methods: A literature review was conducted including recommendations from a consensus statement by a North American panel of neurologists and metabolic experts on Cn therapy in childhood epilepsy.

Results and Conclusions: In primary FAO disorders, the essential indication for Cn therapy is the Cn uptake (OCTN2) defect, characterized by Cn-responsive cardiomyopathy and very low plasma and tissue Cn (<5% normal). In the OCTN2 defect, high-dose oral Cn at 100 mg/kg/day in four divided daily doses is critical and life-saving, significantly reversing the pathology in this otherwise progressive and lethal disease. In intramitochondrial β -oxidation defects with secondary Cn deficiency, the results of Cn therapy have been highly variable and insufficiently evaluated. Cn has been given to limit the intracellular concentrations of potentially toxic acyl-CoA intermediates within the cell through transesterification and to liberate CoA which is a critical intracellular cofactor. However, there has been no objective study to prove that Cn has had a beneficial effect. There is also evidence to suggest that Cn may have deleterious effects in long-chain FAO disorders in which there is an accumulation of long-chain acyl-CoAs, which become long-chain acylcarnitines which in excess may have membranotoxic and arrhythmogenic effects and thus warrant further study. In secondary FAO disorders, intravenous L-Cn is clearly indicated for valproate (VPA)-induced hepatotoxicity, overdose, and other acute metabolic crises associated with Cn deficiency. Oral L-Cn is strongly suggested for the following groups as well: patients with certain secondary Cn-deficiency syndromes, symptomatic VPA-associated hyperammonemia, multiple risk factors for VPA hepatotoxicity, or renal-associated syndromes; infants and young children on VPA; patients with epilepsy on the ketogenic diet who have hypocarnitinemia; patients receiving dialysis; and premature infants who are receiving total parenteral nutrition.

NEUROLOGICAL ASPECTS OF LYSOSOMAL STORAGE DISEASES

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Lysosomal storage disease (LSD) is caused by loss of lysosomal enzyme activity and results in accumulation of substrates. As a result, cell dysfunction, biochemical and pathological abnormality occur and subsequently patients manifest clinical symptoms. Their manifestations are hepatosplenomegaly, bone deformity, joint stiffness, muscle weakness, neurological deterioration, convulsion and so on. When we focus on epilepsy LSDs show symptomatic epilepsy including progressive myoclonic epilepsy (PME). Autosomal recessively inherited PMEs include Lafora disease, Unverricht-Lundborg disease, the neural ceroid lipofuscinoses, type 1 sialidosis and Gaucher disease type 3. Almost all the autosomal recessively inherited PMEs are lysosomal storage disease except Lafora disease. I will present the clinical manifestations, pathophysiology and genes of PMEs related to LSDs in this lecture. And genotype/phenotype correlation and treatment of Gaucher disease type 3 with PME will be discussed.

INFANTILE EPILEPSY IN LYSOSOMAL STORAGE DISEASES

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Lysosomal storage disorders (LSD) are rare inborn errors of metabolism. The incidence of LSD is approximately 1 in 1500 to 7000 live births. To date, over forty diseases of LSD are illustrated. Some diseases of the LSD present with neuromuscular manifestations. Most often these manifestations include hypotonia or weakness. However, seizures are a common neurologic presentation in other LSD and often combined with variant degrees of neurologic deficit(s) and/or developmental regression.

Here we reviewed diseases of LSD presenting infantile epilepsy and associated neurologic problems, including diseases of (1) type III Gaucher disease, (2) neuronal ceroid lipofuscinoses (NCLs), (3) Sialidoses type II, (4) LSD with white matter involvement in terms of metachromatic leukodystrophy and Krabbe disease (globoid-cell leukodystrophy): the two most common leukodystrophies and demyelination in both the CNS and PNS, (5) GM1 and GM2 gangliosidosis, Niemann–Pick disease and Fabry disease. Currently, Infantile-onset symptomatic epilepsy syndrome caused by a homozygous loss-of-function mutation of GM3 synthase was reported.

Infantile spasms (IS), epilepsy with myoclonic seizures, progressive myoclonic epilepsies (PMEs), epilepsy with generalized tonic-clonic seizures, epilepsy with myoclonic-astatic seizures and epilepsy with (multi-)focal seizures are almost their epileptic manifestation.

We highlighted the characteristics of seizure and EEG in the correlated diseases of LSD.

CNS PATHOLOGY IN LYSOSOMAL STORAGE DISORDERS.

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Objectives: 1) Gain understanding of general principles of CNS pathology in LSDs. 2) Describe primary and secondary pathology in Fabry Disease. 3) Review pathogenesis of neuronopathic Gaucher Disease and link between Parkinson's Disease and glucocerebrosidase mutations. 4) Describe the animal model of late infantile onset Neuronal Ceroid Lipofuscinosis and potential treatment opportunities

Conclusion: The pathogenesis of CNS manifestations of LSDs involves a complex interplay between a primary biochemical abnormality, toxic and cytopathic cellular dysfunction, elaboration of toxic mediators, and secondary pathology. Interaction of LSD mutations and population susceptibility genes may link LSDs with other more prevalent neurodegenerative disorders. The challenge of CNS delivery of effective and timely intervention is highlighted in the CLN-2 animal model.

EFFECTS OF GINKGO BILOBA EXTRACT AND PROGESTERONE ON EXPRESSION OF GLUCOCORTICOID RECEPTOR IN CORTEX OF THE RAT AFTER RECURRENT SEIZURES

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Objectives: To investigate the expression of glucocorticoid receptor (GR) in the cortex of the infantile rats following recurrent seizures and the effects of Ginkgo biloba extract and progesterone on them, and discuss the relationship between GR and developing brain hurt and the protective mechanisms of Ginkgo biloba extract and progesterone on the brain injury.

Methods: 96 SD rats of 7-day-old were randomly divided into four groups: the control group, the seizure group, the Ginkgo biloba extract intervention group and the progesterone intervention group. Seizures in rats were induced by inhalant flurothyl daily in six consecutive days. Brain tissue was sampled at different time points (1d, 3d, 7d) in each group after last seizure. The expression of GR proteins in the cortex was detected by immunohistochemistry and Western blot methods.

Results: Western blot method was used in comparing the protein expression of GR among the three groups in cortex. In the control group, the expression of cytoplasmic GR protein was extensive, the older the more increased. The expression of cytoplasmic GR protein in the seizure group significantly decreased than those in the control group and the Ginkgo biloba extract intervention group on PN-15d and PN-19d ($P < 0.05$). Then the expression of cytoplasmic GR protein was no significant difference on PN-13d ($P > 0.05$). The expression of cortical cytoplasm of GR protein in the progesterone intervention group was significantly higher than those in the seizure group on PN-13d ($P < 0.05$). And on PN-15d, the expression of cytoplasmic GR protein in the seizure group was significantly decreased than those in the control group and the progesterone intervention group ($P < 0.05$), then the expression of cortical cytoplasm of GR protein was similar on PN-19d ($P > 0.05$). In immunohistochemistry method it showed that there were no significant differences in the expression GR in the cerebral cortex between the control group and the seizure group on ARS-1d (PN-13d) ($P > 0.05$). On ARS-3d (PN-15d) and ARS-7 d (PN-19d) they were significantly lower than the control group ($P < 0.05$). Comparing with the seizure group, the GR expressions in the cerebral cortex in the Ginkgo biloba extract intervention group were no significant difference between the two groups on PN-13d ($P > 0.05$). But on PN-15d and PN-19d they were significantly higher than the seizure group ($P < 0.05$). The GR expressions in the cerebral cortex in the progesterone intervention group were significantly higher than the seizure group on PN-13d and PN-15d. Between the two groups there was no significant difference ($P > 0.05$) on PN-19d.

Conclusion: Recurrent seizures in neonatal rats modify GR expression in the cortex of rats. This phenomenon raised the possibility that abnormal GR expression might play an important role in developmental brain injury. The increase of the abnormal levels of GR in the cortex is probably related to the protective effects of Ginkgo biloba extract and progesterone on the infantile brain injury induced by seizures.

CLINICAL ANALYSIS OF NIEMANN-PICK DISEASE TYPE C - 7 CASES

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Objectives: Clinical manifestations, biochemical profiles and follow-up of Niemann-Pick disease type C (NP-C) children were summarized and analyzed to improve its diagnosis and management.

Methods: Clinical information on features of 7 cases of NP-C inpatients being followed up from 2007 to 2009 were collected and analyzed. Bone marrow aspiration examination and acid sphingomyelinase activity assay were performed.

Results: Among the 7 cases, five were male and two were female. Six were classical type of NP-C, half of which were started at late infantile and half at juvenile, between 4 to 8 years old, and 2 of them were siblings. These 6 cases presented primarily with neurologic symptoms. They started to develop ataxia and dysarthria, followed by dementia, dysphagia, dystonia and seizures within a couple of years. Epilepsy occurred 1~4 years after the onset. Supranuclear vertical gaze palsy was found at the beginning. Four cases had gelastic cataplexy. The other one case was found with splenomegaly at 4 months old. Hypotonia and delay of developmental milestones became evident by the age of 12 months. She had epileptic seizure at the age of 7.5, then rapidly progressed to anarthric, pyramidal tract involvement and bedridden without supranuclear gaze palsy. Cranial MRI showed signs of leukodystrophy. Lipid profiles of all cases demonstrated reduced level of total cholesterol, LDL-C and HDL-C. Bone marrow aspirates revealed foamy storage cells and sea-blue histiocytes. However, acid sphingomyelinase activity was normal or mildly decreased.

Conclusion: NP-C is a rare autosomal recessive lysosomal storage disorder, whose clinical characteristics, biochemical and pathologic findings are different from type A and B. It has variant clinical features depending on the age at onset. Epilepsy and gelastic cataplexy are relatively common. Lipid profiles represent a biomarker of NP-C. Early diagnosis and genetic counseling should be emphasized in China.

INTRACRANIAL GENE DELIVERY OF AAV-GALC VECTOR CORRECTS NEUROPATHOLOGY IN MURINE GLOBOID CELL LEUKODYSTROPHY

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Objectives: Globoid cell leukodystrophy is a devastating, neurodegenerative lysosomal storage disease. It is an autosomal recessive disease caused by a deficiency of galactocerebrosidase (GALC). Affected infants present symptoms between 3 to 6 months of age, followed by loss of previously achieved milestone and rapid deterioration of motor function, with death usually occurring before 2 years of age. Currently no cure therapy is available. Twitcher mouse, a murine model of GLD, is used for evaluating novel intracranial AAV-mediated gene therapy.

Methods: We inoculated AAV2/5-GALC vector directly into the cortex, hippocampus and cerebellum of neonatal Twitcher mice and assayed the GALC activity, psychosine accumulation, demyelination, astrogliosis, and axonal degeneration in the CNS.

Results: AAV vectors were distributed globally in the cerebrum, brainstem, cerebellum and whole spinal cord in treated Twitcher. AAV-treated Twitcher had folds of normal GALC activity, greater reduced psychosine accumulation, abrogated astrogliosis, attenuated demyelination, and ameliorated axonal degeneration, resulting significantly extended lifespan up to 66 days compared to untreated Twitcher mice died around 38 days of age.

Conclusion: Intracranial delivery of AAV using axonal transportation resulted in the wide distribution of transgenic expression along the neuroaxis, correction of neuropathology and amelioration of phenotype in murine model of GLD. AAV has shown promise for the treatment of the CNS disease associated with lysosomal storage disease. Furthermore, this study provides a basis for a strategy of axonal transporting AAV- GALC globally to correct neuropathology as a possible means of GLD treatment.

EPILEPSY IN MITOCHONDRIAL DISEASE

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Epilepsies are group of heterogeneous clinical syndrome, which affect more than 50 million people. Particularly the incidence is high in children younger than 5 years of age.

In contrast with genetic epileptic syndrome, acquired epilepsy usually results from injury associated with episodes such as prolonged febrile seizures, status epilepticus, hypoxia or trauma. These initial insults result in complex molecular, biochemical and structural changes and eventually the development of spontaneous recurring seizures associated with neuronal cell death, which is referred to as epileptogenesis.

Mitochondrial diseases are clinically variable disorders caused by dysfunction of mitochondrial energy metabolism, which are also highly prevalent in children. Epileptic seizures are well known to be the one of the major presenting symptoms in some of the typical mitochondrial syndrome such as MERRF or MELAS. Mitochondria have critical cellular functions that influence neuronal excitability including production of ATP, fatty acid oxidation, control of apoptosis and necrosis, regulation of amino acid cycling, neurotransmitter biosynthesis, and regulation of cytosolic calcium homeostasis. Recently many clinical reports that suggest mitochondrial oxidative stress and dysfunction are key factors that not only result from seizures, but may also contribute epileptogenesis. There are some suggesting evidence; 1) Epilepsy frequently occurs with inherited mitochondrial syndromes, 2) Role of mitochondrial oxidative stress in lowering seizure threshold in mice with deficiency of mitochondrial antioxidant, 3) Occurrence of epilepsy in humans also increased with age with mitochondrial oxidative stress. However, Mitochondrial oxidative stress and dysfunction as causes or consequences of epileptic seizures are still not clear.

Here, neuronal cell death in epileptogenesis associated mitochondrial dysfunction and possible development of new drugs that reinforce the mitochondrial function or protection of mitochondrial dysfunction as an antiepileptic role will be discussed.

EPILEPTIC SEIZURES IN INFANTS AND CHILDREN WITH MITOCHONDRIAL DISEASES IN TAIWAN

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Objectives: Knowledge of mitochondria and the relationship of mitochondrial dysfunction to human diseases have evolved over the past century. Central nervous system (CNS) is frequently affected because it needs more ATPs to carry out cellular work. Here we report the epileptic seizures in infants and children with mitochondrial diseases in Taiwan.

Methods: From January 1983 to June 2009, 69 patients, 42 males and 27 females, diagnosed with mitochondrial diseases were classified into syndromic mitochondrial diseases (SMDs) and nonsyndromic mitochondrial diseases (NSMDs). The median age at the initial clinical presentation was 15 months (range, 1 month to 15 years). We analyzed the epileptic seizures in patients with mitochondrial diseases.

Results: Among the 69 recruited patients, 34 (49.3%) were classified as having SMDs and 35 (50.7%) were classified as having NSMDs. Forty-three patients (62.3%) presented with seizures, 20 had SMDs and 23 had NSMDs. Twenty out of 34 patients (58.8%) in the SMD group had seizures: 8 generalized seizures in terms of myoclonic and generalized tonic and/or clonic seizures, 7 focal seizures, 2 unclassified seizures, and 3 mixed seizure types. Twenty-three out of 35 patients (65.7%) in NSMD group had seizures: 10 generalized seizures, 7 focal seizures, 2 unclassified seizures, and 4 mixed seizure types. Sixty-three cases had done EEG: 10 normal EEG, 21 epileptiform discharges in terms of focal spikes, sharp waves or hypsarrhythmia, and 32 nonspecific findings, i.e. background slow or intermittent polymorphic slow waves. Thirty-five out of 43 cases (81.4%) with seizures had developmental delay (DD) or psychomotor retardation (PMR).

Conclusion: Epileptic seizures in pediatric patients with mitochondrial diseases were not uncommon. Most of them were refractory to antiepileptic drugs treatment and associated with DD and PMR.

CONGENITAL LACTIC ACIDOSIS (PYRUVATE DEHYDROGENASE DEFICIENCY) AND EPILEPSY

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Objectives: The pyruvate dehydrogenase complex (PDHc) is a mitochondrial multienzyme complex that provides the link between glycolysis and the tricarboxylic acid (TCA) cycle by catalyzing the conversion of pyruvate into acetyl-CoA. We examine the association of PDHc deficiency and neurological manifestations including epilepsy.

Methods: Case reports showing variable neurological phenotypes & review of literature.

Results: The diagnosis of PDHc deficiency was established in patient 1 born to consanguineous parents of Lebanese descent based on apneic episodes, elevated lactate of 22 (0.5-2.2 mmol/L), agenesis of corpus callosum, PDH E1 skin fibroblast enzyme activity 11% of normal and homozygous missense R36C mutation in PDHB gene (Mol Genet Metab 2008 Apr; 93(4):371-80). He is now 9 years old with microcephaly with some social interaction. The second patient is a 4 year old female born to non-consanguineous parents who presented with structural brain malformations detected on fetal ultrasound. Lactate levels remain 4-6 mmol/L. Cultured skin fibroblasts showed deficient PDH activity of 0.15 ± 0.02 (0.7-2.5 nmoles/min/mg protein) and a western blot with total PDHc antibody showed no E1 α or E1 β present. Patient 2 developed a variety of seizures of focal onset with secondary generalization. Brain MRI in the patient 2 showed callosal agenesis, generalized cortical and cerebellar atrophy, marked ventriculomegaly and mega cisterna magna.

Conclusion: PDHc deficiency illustrates the consequences of failure of energy metabolism in the prenatal period and infancy. Epilepsy is reported in a third of patients with PDHc deficiency. Epileptogenesis likely involves multiple mechanisms. A ketogenic diet bypasses the defect and provides acetyl-CoA directly to the tricarboxylic acid cycle and can ameliorate the metabolic lactic acidosis, however the neurological outcome remains poor in the majority. Genetic counseling should be provided to the families as inheritance can be either X-linked or autosomal recessive.

SPECTRUM OF MITOCHONDRIAL DISEASES IN A TERTIARY REFERRAL CENTRE IN HONG KONG

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Background: Disorders of the mitochondrial respiratory chain may present with various neurologic features, including encephalopathy, myopathy and hearing loss. Non-neurologic presentations occur in over 30% of paediatric patients. We review the clinical presentations of patients with mitochondrial diseases in our centre.

Methods: From 1995 to 2009, retrospective review of medical records revealed 22 patients with mitochondrial diseases (15 males and 7 females). The diagnosis of mitochondrial disease is either based on the clinical phenotype or the Mitochondrial Disease Criteria proposed by Morava et al as definite mitochondrial disorders. Respiratory chain enzymology was performed in Murdoch Childrens Research Institute, Australia. Genetic analysis was either performed in the former centre or locally.

Results: The age of presentation ranged from immediately after birth to 10 years of age. The most common clinical phenotype was Mitochondrial Encephalomyopathy, Lactic acidosis, and Stroke-like episodes (MELAS) (n=7, 32%). Only 2 carried the typical A3243 mutation. The second most common presentation was Leigh disease (LS) (n=6, 27%). Mutation in the SURF1 gene causing complex IV deficiency was found in 1 patient. A patient with Kearns-Sayre syndrome (KSS) and another with Pearson syndrome had a deletion in the mitochondrial DNA genome. One had Leber's Hereditary Optic Neuropathy (LHON). A patient who had mutation in the POLG gene presented with a spinocerebellar ataxia syndrome with intractable epilepsy. 2 patients with complex IV deficiency had a phenotype of encephalomyopathy with or without epilepsy. A patient with complex I deficiency presented with a multi-system disease including cataract, hearing impairment, global developmental delay, short stature and recurrent hypoglycaemia. 2 patients had an ill-defined phenotype. Both met the Mitochondrial Disease Criteria as definite mitochondrial disorders. One presented with a fatal cardiomyopathy and corneal opacity of neonatal onset. The other had a combination of global developmental delay with regression, intractable epilepsy, cortical visual impairment and generalized dystonia. Further biochemical and genetic analysis was in progress. Significant mortality was found among the cohort (n=7, 32%).

Conclusion: Mitochondrial oxidative phosphorylation defects form an important group of inborn error of metabolism causing significant morbidity and mortality in neurologically disabled children. High index of suspicion is necessary for a proper diagnosis including biochemical and genetic analysis.

THE CHARACTERISTICS OF SEIZURES IN MALAYSIAN CHILDREN AND ADOLESCENTS WITH MELAS DUE TO A3243G MITOCHONDRIAL DNA MUTATION

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Objectives: MELAS (mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes) is a well-recognized phenotype of mitochondrial disorder, with ~80% of cases resulted from A3243G mtDNA mutation. Seizure is a known associated problem but not well-described in literature. The aim of this article is to study the seizure characteristics in children / adolescents with MELAS.

Methods: This is a descriptive study. The medical records of all our patients with MELAS due to A3243G mtDNA mutation (confirmed by PCR technique) were reviewed.

Results: 11 out of 13 patients with MELAS had seizures. The mean age of presentation and diagnosis of MELAS was 6.5 and 9.6 years respectively. Half of them (n=6) had seizures as their initial symptom. Among those with seizures, 91% had complex partial seizures, 82% had generalized tonic-clonic seizures and 27% had simple partial seizures. Status epilepticus occurred in 3 patients. The interictal EEGs were all abnormal, showing focal, multi-focal or diffuse slowing. However, epileptiform discharges were only present in minority (n=2). During mean follow up of 3 years, 2 patients had only acute symptomatic seizures, 4 patients were seizure-free (for at least 6 months), 2 patients had infrequent seizures and 3 patients had intractable seizures. Most of the patients with better-controlled epilepsy were on benzodiazepine and lamotrigine, at times, combined with phenytoin.

Conclusion: Seizure is a common manifestation and complication in MELAS due to A3243G mtDNA mutation. Benzodiazepine and lamotrigine, at times, combined with phenytoin, seem efficacious for seizure-control in this group of patients.

CLINICAL FINDINGS AND DIAGNOSTIC FLOWCHART OF PEROXISOMAL DISEASES

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Peroxisomes are single-membrane lined organelles present in all eukaryotic cells and catalyzing a range of essential metabolic functions. Inborn errors of peroxisomal metabolism, an expanding group of genetic disorders in humans, have been divided into two groups with disorders of peroxisome biogenesis (PBD) and single peroxisomal enzyme deficiencies. PBD include Zellweger syndrome (ZS), neonatal adrenoleukodystrophy (NALD), infantile Refsum disease (IRD) and rhizomelic chondrodysplasia punctata (RCDP) type 1, all caused by a defect in PEX genes which encode peroxins, proteins necessary for peroxisome biogenesis and the import of peroxisomal matrix and membrane proteins. The peroxisomal matrix contains over 50 enzymes mainly related to lipid metabolism, of which ten single peroxisomal enzyme deficiencies have been identified. These include dysfunction of beta-oxidation enzyme, containing of X-linked adrenoleukodystrophy (ALD), acyl CoA oxidase deficiency, D-bifunctional protein deficiency, Sterol carrier protein 2 deficiency, and Rasemase deficiency, and deficient of plasmalogen synthesis, catalase deficiency, hyperoxaluria type 1 and classical Refsum disease. Furthermore, a novel phenotype similar to ZS caused by a contiguous deletion spanning the 5' ends of ALD gene and DXS1357E in Xq28 (CADD5) has been reported, therefore, we classify the peroxisomal diseases into three groups including contiguous gene syndrome.

We have been studying peroxisomal diseases for more than 20 years, as the only diagnostic center in Japan, and doing molecular analysis on PBD and their related disorders. We found the first responsible gene for PBD, PEX2 in 1992, and then PEX6 in 1996, PEX13 in 1999, PEX3 in 2000 and PEX14 in 2004, therefore, until now all 13 responsible genes have been identified.

We have developed the screening system of peroxisomal diseases, using GC/MS analysis of very long chain fatty acids, phytanic acids and plasmalogen, and identified many Japanese patients, using biochemical and molecular analysis: 43 patients with ZS, 3 with NALD, 3 with RCDP, 3 with acyl-CoA oxidase deficiency, 10 with D-bifunctional protein deficiency, 1 with CADD5 and over 100 patients and carriers with ALD. Hematopoietic stem cell transplantation (HSCT) is the only effective treatment for cerebral form of ALD, however, only one-third of patients with post-cerebral onset have undergone HSCT in Japan. Therefore, detection of pre-symptomatic patients by familiar analysis with enough genetic counseling is necessary.

Here I present the molecular and clinical aspects of peroxisomal diseases, and those screening and diagnostic system in Japan. We will develop these screen system of peroxisomal diseases also for other country in this opportunity.

PEROXISOMAL DISORDERS WITH INFANTILE SEIZURES

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Peroxisomes are organelles responsible for multiple metabolic pathways including the biosynthesis of plasmalogens and the β -oxidation of very-long-chain fatty acids (VLCFA). Lack of peroxisomes or dysfunction in any of their normal functions is the cellular basis for human peroxisomal disorders. Based on organelle structure and deficiencies, peroxisomal disorders can be subdivided into two major groups. In the first group, there is a defect in peroxisome biogenesis which is associated with either a generalized or multiple loss of peroxisomal functions. The peroxisome biogenesis disorders (PBDs) include Zellweger syndrome (ZS), neonatal adrenoleukodystrophy (NALD), and infantile Refsum disease (IRD). The differences among these disorders are continuous, with overlap between abnormalities. Seizures are present in approximately one-third of affected individuals in PBDs and occurred in neonatal period or infancy. Seizures may be difficult to control despite use of appropriate medication. The second group includes disorders resulting from the deficiency of a single peroxisomal enzyme. In the second group, although the peroxisome is intact and functioning, there is a defect in one enzymatic process. However, these disorders can be severely as those in which peroxisomal activity is nearly or completely absent. X-linked adrenoleukodystrophy (X-ALD) is the most common disorder in this group.

Peroxisomal disorder can involve other organs, but mainly the nervous system. In general, developmental delay, vision and hearing impairment are common in peroxisomal disorder patients. Generalized hypotonia is present in most severe cases. Epileptic seizures are also a common characteristic of patients with certain peroxisomal disorder. However, the incidence of peroxisomal diseases is low; the correct diagnosis needs special examinations, and the life span of affected patients is limited. These conditions make it difficult to conduct satisfactory clinical investigations in peroxisomal disorders. Peroxisomal disorders are heterogeneous disease group, with different degrees of severity. The characteristics of epileptic seizures in patients with different peroxisomal diseases should be clarified further.

LATEST FINDINGS IN PEDIATRIC EPILEPSY TREATMENT

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Antiepileptic drugs (AEDs) are the principal treatment modality for the patient with epilepsy regardless of the type of seizures or syndromes. New AEDs, introduced since 1993, provide more diverse options in the treatment of epilepsy. Despite the equivalent efficacy and better tolerability of these drugs, more than 25% of patients remain refractory to treatment. Moreover, the issues for pediatric patients are different from those for adults, and have not been addressed in the development and application of the new AEDs. In the past, choosing AEDs has mostly been dependent on the physician's personal knowledge and experience. Current trend is to choose AEDs based on the scientific evidence. Recently published evidence-based treatment guidelines have helped physicians to choose the most reasonable AED, although they cannot fully endorse new AEDs because of the lack of well-designed, randomized controlled trials.

Although much progress has been made in understanding the mechanisms of ketogenic diet (KD), how the KD works remains still elusive. Several recent publications support that the KD is superior to conventional AEDs in treating refractory epilepsy in infants and children (e.g. infantile spasms). However, to obtain scientific information on effective treatment strategies for catastrophic epilepsy syndromes in children, high-quality collaborative studies like patient registry program should be performed in the near future.

Increasing numbers of pediatric patients with intractable epilepsy are being considered for surgical treatment. The key elements of candidacy for epilepsy surgery include medically intractable and disabling epilepsy, localizable epileptogenic zone, and low postoperative risk. At the same time, following questions should be considered seriously before doing epilepsy surgery: what is the chance for seizure-freedom after surgery, what are the risks associated with surgery, and what will be the risk of not doing surgery?

MENKES DISEASE AND INFANTILE EPILEPSY

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Objectives: Menkes disease, an X linked recessive neurodegenerative disorder, results from a mutation in the gene coding for the copper transporting ATPase (ATP7a) leading to a systemic intracellular copper deficit. We describe the clinical presentation, and evolution of epilepsy in Menkes disease, with attention to diagnosis, genotype phenotype correlations and response to treatment interventions.

Methods: Longitudinal case study and literature review

Results: A 2 month old male infant presented with focal seizures initially controlled with Phenobarbital. However, the seizures evolved over 2 months to infantile spasms. The diagnosis of Menkes disease was established on clinical grounds (hypotonia, failure to thrive, and kinky hair), and a biochemical profile of low copper (2.2, 3.9-17.3µmol/L), and ceruloplasmin (0.07, 0.21-0.51g/L). Magnetic resonance imaging (Brain) showed progressive atrophy of grey matter, ventriculomegaly, tortuous intracranial vasculature and white matter signal changes consistent with loss of myelin and axons. During the encephalopathic stage, significant lactic acidosis was noted (blood lactate (4.2, 0.5-2.2 mmol/L), CSF lactate (5.0 mmol/L) and the MR spectroscopy demonstrated intracerebral lactate accumulation. A pathogenic mutation c.1831G>T (p.E611X) in exon 7 of the ATPase gene was confirmed on DNA sequence analysis; his mother, maternal grandmother and aunt were shown to be a carrier for the same mutation. The mutation results in a premature stop codon and a truncated protein product. Treatment with copper chloride injections produced no demonstrable neurological improvement, but improved general health. Presently, his epilepsy is treatment resistant (tonic spasms and multifocal myoclonus), while the EEG shows background slowing and multifocal epileptiform activity.

Conclusion: The onset and evolution of epilepsy in Menkes disease is marked by different stages. Neurological manifestations are likely related to perturbations in copper dependent enzymatic pathways involved in neurotransmitter and energy metabolism. The early diagnosis and institution of copper supplementation has been shown to be beneficial particularly in patients with residual ATP7A activity.

PYRIDOXINE DEPENDENT AND RESPONSIVE SEIZURES

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With recent clinical, biochemical and genetic advances it is now becoming clear that pyridoxal phosphate (PLP) deficiency has a variety of aetiologies. With an antenatal onset, in neonates it causes a multisystem disorder including an encephalopathy which can be misdiagnosed as being due to birth asphyxia, other metabolic disorders such as glycine encephalopathy, structural abnormalities and/or intracranial haemorrhage. With a later onset infants and children mainly present with seizures, sometimes with a normal EEG. Seizures in some children without deficiency can also respond to PLP. Recent advances and the biochemical differential diagnosis will be discussed.

CLINICAL EVALUATION OF PYRIDOXINE TREATMENT OF EPILEPSY

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Clinical seizures related to vitamin B6 are inclusively called vitamin B6 related seizures. Formerly, these were grossly classified into B6 deficiency seizures and B6 dependent seizures. Both types of seizures are suppressed by administration of vitamin B6. I proposed the vitamin B6 responsive seizures as the third category of vitamin B6 related seizures.

Vitamin B6 responsive seizures will be outlined in this paper. This type of seizures, meeting neither the categories of vitamin B6 deficiency seizures nor B6 dependent seizures, decrease or disappear responding to high-dose vitamin B6 administration without co-medication of antiepileptic drugs. The ages of seizure onset are variable. Most of our cases had their seizure onset in the first year of life, though ranging widely from ages 3 months to 12 years. Etiologically, many cases are idiopathic, but some are symptomatic with apparent organic brain lesions. With responded seizure or epilepsy types, the majority is West syndrome, though including some others with Lennox-Gastaut syndrome, grand mal seizures or partial motor seizures.

The efficacy of vitamin B6 on epilepsy will also be mentioned, mainly high-dose vitamin B6 treatment on West syndrome proposed by us, precisely referring to its effect on 216 successive cases and their long-term prognosis.

Its overall efficacy rate on WS was 13.5%, particularly high as 32% in cryptogenic WS. Interestingly, it was also effective in WS with gross brain pathologies.

In 1960, we observed no abnormality in tryptophan load test in most cases of childhood epilepsy including WS and recognized 10-30mg/day of vitamin B6 exerting no efficacy on WS. Since then, trials escalating its dose to 50-100mg/day gradually increased responders. Finally, the fore-mentioned large-scale trial revealed a dramatic efficacy of high-dose vitamin B6 such as 100-400mg/day. Notably, responders showed excellent long-term prognosis without antiepileptic drugs, suggesting that this treatment should not be underestimated.

It is a clinical disadvantage that only trial discriminates effective cases.

Energetic studies, including molecular genetics, are required to predict efficacy of high dose vitamin B6 before administration.

EPILEPSY IN CHILDREN WITH BIOTINIDASE DEFICIENCY

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Objectives: To study the clinical and EEG features of seizures in children with biotinidase deficiency and their response to biotin therapy.

Methods: Seventeen consecutive patients with biotinidase deficiency registered in the neurodevelopmental clinic at the Postgraduate Institute of Medical Education and Research, Chandigarh between September 2004 to May 2009 were studied. Their medical records were reviewed and follow up was done to assess their response to biotin.

Results: The mean age at presentation was 14 months (range day 3 to 12 years) and the mean interval between presentation and diagnosis was 9.6 months. Developmental delay was noted in 52.9% cases and regression of milestones was noted in two. Seizures were the chief complaints in 15 children (88.2%). Myoclonic seizures were the predominant (53.3%) type. Only two children had dermatitis and alopecia. Microcephaly was seen in 6 cases and hypotonia in 29.4%. Serum biotinidase levels varied from 1 to 5 nmol/min/ml (Normal: ≥ 5 nmol/min/ml). EEG showed spikes and spike wave complexes in most cases. The main abnormalities on MRI brain were cortical atrophy, widening of CSF spaces and white matter hyperintensities. MRI Brain was normal in seven patients. Biotin, 10 mg/day, was started in all patients. The mean follow up period was 24.9 months. Two patients were lost to follow up and one patient died; 80% patients had seizure control and symptomatic relief following biotin therapy; 60% had some neurological sequelae.

Conclusion: Seizures are common in biotinidase deficiency; prompt initiation of biotin therapy can help early seizure control.

EPILEPTIC MECHANISMS IN SSADH DEFICIENCY, A DISORDER OF GABA METABOLISM

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Objectives: Succinic semialdehyde dehydrogenase (SSADH) deficiency is a GABA degradative defect associated with high endogenous levels of GABA and γ -hydroxybutyrate (GHB) in physiologic body fluids and brain parenchyma. Epilepsy affects approximately half of patients. The murine model is associated with a transition from absence to generalized convulsive seizures in the third week with ultimately fatal status epilepticus.

Methods: Characteristics of clinical seizures and EEG abnormalities are reported from a patient database. Electrocorticography, single cell electrophysiology, and radioligand binding studies are reported from murine null versus heterozygote and wild type genotypes.

Results: Generalized seizures predominate in the clinical condition, including tonic-clonic, atypical absence, and myoclonic. EEG discharges are typically generalized spike-wave and may include photosensitivity and ESES. GHB induces spike-wave discharges in homozygous null mice via GHB_R and GABAB_R-mediated mechanisms. These resemble absence seizures, and may be abolished by GABAB_R antagonists CGP 35348. Decreased binding of a GABA_AR antagonist ([³⁵S]TBPS) and GABAB_R antagonist (CGP54626) have been demonstrated in P19 and P14 null mice, respectively. Down regulation of GABA_A and GABAB receptor subunits is observed by P14, along with decreased input resistance and resting membrane potential in hippocampal neurons. GABAB mediated synaptic potentials and GABA_A mediated IPSPs are further reduced from P8-P14.

Conclusion: Generalized epilepsy and epileptiform EEG discharges are characteristic of human SSADH deficiency, an apparent paradox in this hyperGABA_Aergic disorder. Spontaneous, recurrent absence seizures appear in null mice by the third week of life, which may be induced by GHB and resolved with GABAB_R antagonists. Build-up of GHB in SSADH deficiency may cause early absence seizures through GABAB_R mediated activity. There is subsequent overuse dependent down regulation of GABA_A and GABAB receptor activity, which may be associated with hyperexcitability concomitant with the transition to generalized convulsive activity.

MAGNETIC RESONANCE IMAGING OF MONOAMINE METABOLIC DISORDERS

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Objectives: To share Taiwanese experience about MR image, MR spectroscopy and diffusion tensor image of monoamine-related disorders.

Methods: All patients and control subject received MR examinations using a 1.5-T echo-planar scanner (Sonata; Siemens, Erlangen, Germany). All MR examinations used a standard birdcage head coil in a 1.5-T MR system (Sonata; Siemens, Erlangen, Germany). At first, fast spin-echo (FSE) T2-weighted images (T2WIs) in the axial plane were obtained. Localized proton spectra were acquired using a short TE stimulated echo acquisition mode (STEAM) technique (TE= 10 ms). The 8-ml volumes of interest were localized in the brain parenchyma of interest. Diffusion tensor images were acquired with diffusion encoding gradients in six directions, i.e., {1, ±1, 0}, {0, ±1, 1}, {±1, 0, 1}, and diffusion sensitivity $b = 1500 \text{ s/mm}^2$.

Results: 1) Cerebral folate deficiency syndrome is a recently recognized cause of developmental delay, regression, and seizures. At least five distinct inherited disorders of folate transport and metabolism are known till now, and all of them cause systemic folate deficiency. Brain magnetic resonance (MR) imaging demonstrated hypomyelination, mild cerebellar atrophy and MR-based in vivo MR spectroscopy indicated a combined decrease of white-matter choline and myoinositol but mostly nonspecific changes at the basal ganglia. 2) Phenylketouria, Malignant phenylketonuria (MPKU), which results from a defect in the synthesis or metabolism of tetrahydrobiopterin (BH4), is a rare variant of an inborn error of amino acid metabolism. This study analyzed eight patients suffering from BH4 deficiency in a Taiwanese population identified by neonatal screening. Only one patient with seizure had signal changes at central white matters on MRI similar to those most prevalent in classical hyperphenylalaninemia. Lactate peaks were revealed on MRS in two patients who had lower IQ scores than the other patients. Besides, Myoinositol /Choline ratio was correlated positively with the average BH4 dosage ($p=0.027$, Correlation Coefficient=0.027). In addition, Choline/Creatine ratio was negatively correlated with the average 5-hydroxytryptophen dosage ($p= 0.035$, Correlation Coefficient=-0.742 respectively), which may be a useful indicator in the monitoring treatment. On magnetic resonance (MR) images of malignant PKU patients, hyperintense lesions are usually not shown at the periventricular white matter on T2-weighted images. Pathologic changes in the brain of untreated PKU patients were impaired myelination, gliosis and even white matter degeneration. However, substantial decrease in signal was observed in parietal-occipital central white matter in the fractional anisotropy and diffusion anisotropy maps. As compared with controls, patients with PKU had significantly lower fractional anisotropy in parietal-occipital central white matter. 3) Disorders of neurotransmitters, Aromatic L-amino acid decarboxylase (AADC) deficiency is an uncommon inherited neurometabolic disease. AADC deficiency is more prevalent in Taiwan than that in western countries. Because AADC is widely distributed in the brain parenchyma and participates in the synthesis of monoamines, deficiency of AADC will result in combined deficiency of dopamine, serotonin, and other catecholamines, and may lead to the abnormal development of the brain. In the AADC patients, the frontal horn was significantly widened than the controls ($p<0.01$), and the volume of caudate nucleus was also significantly smaller than that of controls ($p = 0.02$). The ratios of thickness of the splenium to that of the genu of corpus callosum were also significantly increased in patients with AADC deficiency ($p < 0.01$). For three patients with follow-up MR images, all revealed mesiotemporal atrophy, indicating mildly progressive cerebral atrophy. The evaluation of children with metabolic disorders is important but lengthy and time-consuming. Imaging examination including MR image, MR spectroscopy and diffusion tensor image, is part of the team work of neurometabolic evaluation.

Conclusion: The evaluation of children with metabolic disorders is important but lengthy and time-consuming. Imaging examination including MR image, MR spectroscopy and diffusion tensor image is part of the team work of neurometabolic evaluation.

PATHOPHYSIOLOGY OF EPILEPSY IN NEUROTRANSMITTER DISORDERS

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Objectives: Neurotransmitter disorders are known to cause movement disorders. Some neurotransmitter disorders, however, show epilepsy. Pathomechanism of the epilepsy of neurotransmitter disorders is discussed.

Methods: Personal 46 cases of gene proved Segawa disease, one recessive dihydropteridine reductase (DHPR) deficiency and one aromatic amino acid decarboxylase (AADC) deficiency case were evaluated. Two cases with recessive 6-pyruvoyl-tetrahydropterin synthase (PTPS) deficiency were reviewed.

Results: No cases with Segawa disease showed epilepsy. AADC, DHPR and PTPS deficiency cases developed epilepsy, and all resisted to various anticonvulsants. Levodopa was not effective for the epilepsy. The cases with epilepsy revealed mental retardation, muscle hypotonia and failure in locomotion. They revealed atonia of REM sleep into non REM sleep.

Discussion and Conclusion: Segawa disease is a dominantly inherited childhood onset dystonia caused by the mutation of GTP cyclohydrolase I gene. Psychomental development is normal, but occasionally develops depression. The pathophysiology is the non-progressive deficiency of the dopamine at the terminal of nigrostriatal dopamine neuron. The clinical course reflects the physiological age dependent decrement of the terminal dopamine. This does not affect any morphological changes or disturbances of higher cortical function. The recessive PTPS and DHPR deficiency involve the deficiency of serotonin activity besides that of dopamine in the terminal. The serotonin deficiency causes postural hypotonia and failure in locomotion. Leak out of atonia of REM sleep into non REM sleep reflects the deficiency of specific serotonin system involved in antigravity muscle and locomotion. These processes cause dysfunction of the pedunculopontine nucleus, and lead to the disturbances of nigrostriatal and ventro-tegmental dopamine neurons. These dopamine deficiencies in the developing brain induce the compensatory upward regulation of dopamine receptors. This causes the disinhibition of the thalamo-cortical pathway, and induces the epileptic spikes in the cortex, that is epilepsy. Early encouragement of locomotion is important for the management of this epilepsy.

EVOLUTION AND VARIATION IN NEONATAL SUPPRESSION-BURST ENECEPHALOGRAMS

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Objectives: Suppression-burst (SB) activity of electroencephalogram (EEG) in newborn is a pattern of high-amplitude and slow-waves discharges with or without spikes, being alternating with periods of minimal activity of low amplitude (less than 10 μ V). Although SB usually indicates a grave syndrome in neurodevelopment, the evolution of EEGs is varied and uncertain.

Patients and Methods: We study 5 newborns with SB EEGs, included varied etiologies, evolution of EEGs and associated change of seizures semiology. Five cases include a nonketotic hyperglycinemia (NKH), a severe hypoxia-ischemic encephalopathy (SHIE), a citrullinemia, an Aicardi's syndrome, and an Ohtahara syndrome with unidentified etiology.

Results: The bursting activities were asynchronously alternating appeared in both hemispheres except in one EIEE with synchronous SB. The follow-up periods were ranged from 6 months to 6 years. The longest period of suppression on EEGs was in SHIE. Continuous backgrounds of EEGs was reached at 15 days in citrullinemia, 3 months in EIEE and in Aicardi syndrome, and never to be continuous in SHIE and in NKH. Three cases being followed up over 2 years, myoclonic seizures still were prominent in both patients with NKH and SHIE, however, tonic seizures was predominant after 2-years in EIEE. EEGs after 2 years of age were changed to multi-focal independent spike foci in EIEE and frontal epileptic spike focus in NKH. Four cases have severe mental retardation except in one citrullinemia, in whom, almost was normal neurodevelopment at 6 months of age.

Conclusion: We conclude neonatal SB on EEGs have varied pattern of evolution on EEGs and clinical courses, depending on different etiologies. They have grave outcomes except those with treatable metabolic disorders.

CLINICAL PRESENTATION AND LABORATORY PROFILE IN SUSPECTED CASES OF NEUROMETABOLIC DISORDERS: A PRELIMINARY REPORT FROM BANGLADESH

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Background: Neurometabolic disorders in children may present at any age with a wide range of clinical manifestations. Unexplained or intractable seizure is one important association. Consanguinity, regression of development, sibling death are some other clues to suspect neurometabolic disorders when laboratory support is limited. Laboratory findings, however, provides the confirmatory diagnosis which is unavailable in Bangladesh.

Objective: To determine the association of consanguinity, regression of development, seizures, EEG findings and other laboratory investigations in children suspected to have neurometabolic disorders, to aid clinicians working in resource-poor countries.

Method: A retrospective analysis from the records of the patients suspected to have neurometabolic disorders in the Child Development and Neurology Unit, Dhaka Shishu Hospital, during the period of July 2007 to October 2009. Tandem Mass Spectrometry (TMS) was done through a private laboratory in New Delhi, India in most.

Results: Total 82 children were studied and the parents of 29 (35%) had history of consanguineous marriage. Seizure was associated with 64(78%) children and abnormal EEG findings recorded in 53(65%) . Plasma ammonia was measured in 54 cases and found increased in 34 (63%). Plasma lactate was examined in 53 cases and found high in 25 (31%). TMS was done in 77 (94%) children and abnormality found in 47/77(57%) cases. Serum biotinidase activity was advised for 31 children as per TMS result and measured in 18 children of which deficient activity was found in 10/18(56%); borderline in 4/18 (22%) and normal activity in 4/18 (22%) cases. Of three cases followed up with biotin supplementation all were found to be doing well neurologically.

Conclusion: Early suspicion by background history and clinical presentation followed by stepwise laboratory investigation is necessary to identify neurometabolic disorders. Early and appropriate intervention can reduce neurodisability in many situations. A central laboratory for determining NMDs is needed urgently in Bangladesh.

INCIDENCE OF SEIZURE IN NEUROMETABOLIC DISEASES UNDER CURRENT NEWBORN SCREENING IN TAIWAN

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Objectives: During the past, without adequate technique in diagnosis of neurometabolic disease, most of the children had developed vomiting, hypotonia, failure to thrive, seizure and eventually died in the very early of age. Since the use of tandem mass for screening the abnormal metabolites, we could early diagnose these diseases. As the consequence, fewer neurological manifestations had been presented in these children. We retrospectively review eight common neurometabolic diseases in Taiwan to find out the incidence of seizures in neurometabolic diseases.

Methods: We had screened the newborns in Taiwan since 2006 to 2009. Forty-nine newborns were diagnosed of phenylketonuria, homocystinuria, maple syrup urine disease, tyrosinemia, citrulinemia, glutaric aciduria type I (GA1) and methylmalonic academia. We investigated the incidences of seizure attack, neurologic deficits and the clinical prognosis in these newborns.

Results: In the 49 newborns, only one with GA1 had seizure. In addition, newborns of GA1 also had significant higher rate of neurological deficits and mortality than other diseases. Most of the patients under diet or medical control present with development delay, only a few have severe neurological problems.

Conclusion: Within these neurometabolic diseases, GA1 had significantly higher potential to develop seizure. Seizure could soon occur in infancy. Under early diagnosis and adequate treatment, few children had severe neurological deficit. However, developmental delay was still seen in these children.

A CASE WITH NONKETOTIC HYPERGLYCINEMIA DIAGNOSED WITH NOVEL SCREENING METHODS —¹³C-GLYCINE BREATHING TEST AND MLPA METHOD

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Introduction: Nonketotic hyperglycinemia (NKH) is an inborn metabolic disorder caused by the glycine cleavage system (GCS) deficiencies. The definitive diagnosis of NKH requires either measurement of GCS enzymatic activity or genetic analysis. Although most of the patients with NKH present with typical symptoms, definitive diagnosis in some cases is difficult because it requires invasive and time-consuming methods. Recently, rapid and non-invasive diagnostic techniques for NKH, ¹³C-glycine breathing test and multiplex-ligand-dependent probe amplification (MLPA) method have become available. We report a boy diagnosed as having NKH with novel diagnostic methods.

Case report: The boy was born at full-term after uncomplicated pregnancy. Due to progressive worsening of apnea, he required assisted ventilation at 2 days of age. He also showed marked hypotonia and frequent seizures, erratic myoclonus and tonic seizures. His clinical and electrophysiological features are compatible with early myoclonic encephalopathy. Blood and CSF amino acid analysis revealed elevated glycine levels, and ratio of CSF to plasma glycine with 0.118 (normal, <0.03). [¹³C-]glycine breath test showed decreased ¹³CO₂ excretion of 7.9% (normal, 24.1 ± 4.0%), which imply the reduced GCS activity. Mutational analysis of GLDC gene showed a compound heterozygosity; a missense mutation with 1382G>A resulting in amino acid change of R461Q, and a large deletion involving exons 1-25. Under the diagnosis of NKH, treatments with sodium benzoate and ketamine were initiated. He was successfully extubated at 45 days of age. He is now 10 months old with developmental mile stone of 5-6 months.

Discussion: Our patient was diagnosed as NKH with the enzymatic and genetic analysis. To provide longer-term and accurate prospective, we need to accumulate information of the genotype-phenotype correlations utilizing the fast and reliable testing.

EFFECTS OF GLUTAMATE ON NEURAL PROGENITOR/STEM CELLS CULTURED IN VITRO

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Objectives: To explore the effects of glutamate on the neural progenitor/stem cells (NPCs) in vitro.

Methods: Immunofluorescence and Western blot were used to detect the expression of NR1 on NPCs cultured in vitro; Calcium imaging by Fluo-3/AM and single channel recording were used to investigate the function of NMDA receptors in NPCs; The single NPC was obtained by mechanical dissociation and grown for 4 days in medium containing 30 μ M MK-801 and Glu at the different concentration of 50-1600 μ M, TUNEL staining positive cells and the level of lactic acid dehydrogenase (LDH) in culture medium were measured to evaluate the effects of Glu on NPCs' survival; The number and diameter of neurosphere were measured to evaluate the effects of Glu on NPCs' proliferation.

Results: The NR1 expression by immunofluorescence and western blot was positive. Calcium imaging showed the fluorescence intensity increased significantly after glutamate stimulation. Three types of currents were detected with the cell-attached recording: unipolar rectangular pulse discharge, flicking, burst and cluster. The level of LDH in the culture medium of 1600 μ M Glu group increased significantly compared with other groups. There was no great difference in diameter or apoptotic rate of neurospheres among each group. However, the number of neurospheres in 800 μ M Glu increased significantly than that in other groups.

Conclusion: NPCs express functional NMDA receptor; Calcium influx conducted by NMDA receptor activation may participate in the process that Glu promotes the proliferation of neural progenitor/stem cells.

NON KETOTIC HYPERGLYCINEMIA IN 2 CHILDREN PRESENTING WITH SEIZURES

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Inborn error of metabolism may present with a diverse spectrum of presentations varying from episodes of hypoglycemia, lethargy to full blown sepsis. Rarely may they present with subtle or obvious neurological manifestations ranging from seizure activity to encephalopathy.

We report two cases of Nonketotic Hyperglycinemia in infants who were born with an uneventful antenatal, perinatal course and developed lethargy, respiratory difficulty and seizures. Both infants had history of one sibling death in the early neonatal period. Biochemical markers revealed raised ammonia which responded to sodium benzoate treatment. Neuro-imaging was normal in both cases while one infant had pathological EEG suggestive of hypsarrythmia and infantile spasm.

Urine for organic acidemias was negative, while glycine levels in the plasma and CSF of both infants were high, with very high ratios conclusive of Nonketotic Hyperglycinemia.

Both the infants are alive at 2 years of age, on antiepileptic medications along with sodium benzoate for elevated levels of glycine

Both the children have significant global developmental delay with microcephaly.

DRAMATIC RESPONSE TO DELAYED TREATMENT IN SEVERE 6-PYRUVOYL TETRAHYDROPTERIN SYNTHASE DEFICIENCY

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Objectives: To describe the dramatic response to delayed treatment in a patient with severe 6-pyruvoyl tetrahydropterin synthase (PTPS) deficiency misdiagnosed to have cerebral palsy and epilepsy.

Methods: Case description.

Results: An 18 year-old boy previously diagnosed to have choreoathetoid cerebral palsy and epilepsy was assessed for recurrent 'status epilepticus'. These episodes consisted of prolonged head version, stiffening of limbs, hypersalivation and tongue protrusion with preserved consciousness. He was born term and had history of global developmental delay. He was wheelchair bound, had dysarthria, understood simple conversation and was almost totally dependent. He had frequent admissions to another hospital for 'status epilepticus', was treated as intractable epilepsy and was on three anti-epileptic drugs (AED). An episode of status dystonicus and features of parkinsonism were noted in clinic. Subsequent investigations confirmed diagnosis of PTPS deficiency (elevated serum phenylalanine, absent urinary biopterin, elevated urinary neopterin, low cerebrospinal fluid 5-hydroxyindoleacetic acid, homovanillic acid and biopterin and elevated neopterin levels). He was commenced on tetrahydrobiopterin, 5-hydroxytryptophan, l-dopa/carbidopa, pyridoxine and folate. He was later confirmed to have c.259C>T homozygous mutation of PTS gene, inherited from both parents. There was dramatic response to treatment; dystonia and parkinsonism resolved and he could walk within one month. Speech improved and he was able to read and write slowly. He continued to improve and could perform most activities of daily living independently. He is now 23 year-old, AED free and travels independently to attend cooking and handicraft classes in a training centre.

Conclusion: In PTPS deficiency, the global delay, dystonia and parkinsonism could masquerade as choreoathetoid cerebral palsy, whereas status dystonicus mimics seizures. Despite delayed diagnosis and treatment, a favourable response is still possible.

GLUTARIC ACIDEMIA TYPE I REVEALED BY NEWBORN SCREENING PROGRAM IN TAIWAN: EXPERIENCE IN ONE MEDICAL CENTER

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Objectives: To review 4 cases of glutaric academia type I (GA-1) revealed by newborn screening program. They were detected during 2006 to 2009, after glutaric academia type I was enrolled in Taiwan Newborn screening Program by 2 newborn screening centers.

Methods: We reviewed the initial C5DC level, serum aminoacids, urine organic acid data and the results of molecular study. We also examined the image data including brain echo and brain MRI. The prognosis and its relation with treatment were also assessed.

Results: The frequency of GA-1 based on newborn screening by MS/MS was 1/72534, which is lower than in Western country. The recall rate is 0.08%. Two cases of them suffered from nystagmus after birth, which was not reported in GA-1 patients in literature. Brain echo in all cases showed bilateral multiple subependymal cysts and ventricular septums. We did brain MRI for 2 cases in less than 2 weeks –old, these images all revealed symmetric widening of bilateral sylvian fissures and bilateral frontotemporal volume loss. One case suffered from severe dystonia due to inadequate treatment during acute episodes, in other cases developmental milestones were within normal range.

Conclusion: We revealed the frequency of GA-1, which is similar with previous report. Brain MRI in 2 neonates showed brain atrophy in very early stage, which suggested us that glutaric acid metabolites may cause prenatal damage in brain in GA-1 cases. Early and adequate treatments for GA-1 patients during acute episodes are very important and significantly related to their prognosis.

CLINICAL ANALYSIS OF METHYLMALONIC ACIDEMIA IN 14 CASES

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Objectives: To explore the clinical characteristics and treatment of methylmalonic acidemia (MMA) in earlier period and prognosis.

Methods: The clinical data of 14 patients with MMA diagnosed by gas chromatography-mass spectrometry (GC/MS) were analyzed to understand management and prognosis.

Results: The patients consisted of 10 males and 4 females, whose age of onset ranged from 0 to 3 months. The main clinical manifestations were developmental delay (8 cases), abnormal tonus of muscle (8 cases), vomiting and bucking (4 cases), convulsion (4 cases), lethargy (1 case), poor feeding (8 cases), dyspnea (1 case), hepatomegaly and jaundice (2 cases), anaemia, hyperammonemia and metabolic acidosis (2 cases), abnormal EEG (4 cases), etc. The laboratory findings showed remarkable elevation of urinary or blood methylmalonic acid concentration in all cases. Some abnormalities were shown by the brain MRI or CT in 14 cases and electrophysiologic study (ABR and AEP) in 7 cases. 14 cases received therapy of vitamin B12 and supplementation of carnitine with low protein diet. The follow-up was made for a period ranging from 3 months to 12 months, 4 cases recovered completely under medical therapy, in association with seizure freedom and MRI improvement.

Conclusion: The clinical manifestations of MMA are nonspecific. Gas chromatography-mass spectrometry (GC/MS) is an effective method to diagnose and identify methylmalonic acidemia. Early diagnosis and early treatment can help improve the prognosis obviously.

MUTATIONS ANALYSIS OF MMACHC GENE IN EIGHT PATIENTS WITH METHYLMALONIC ACIDEMIA AND HOMOCYSTEINEMIA

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Objectives: Methylmalonic acidemia complicated with homocystinemia, cblC type, is a disorder of vitamin B12 (cobalamin) metabolism caused by mutations in the MMACHC gene. Recently, more than 40 mutations have been found in other countries. But there were not many reports in China. Eight patients had been detected to identify the mutation types in this study.

Methods: Eight patients were diagnosed to methylmalonic acidemia with homocystinemia in our hospital. Gas chromatography-mass spectrometry (GC-MS) was used for urine organic acids analysis. Homocystinemia was found by serum total homocysteine determination using a fluorescence polarization immunoassay. Then, the coding region of MMACHC gene was screened by polymerase chain reaction (PCR) and DNA direct sequencing.

Results: They had markedly increased urine methylmalonic acid. Serum total homocysteine also multiplied 8~30 times in seven patients. Another patient who had been dead was not detected. However, they were determined cblC disease through gene diagnosis. In this study, six mutations were found in all patients, and four mutations were located in exon 4. Respectively, the six mutations were c.609G>A, c.482G>A, c.617G>A, c.365A>T, c.658_660delAAG and c.146_154delCCTTCCTGG. The c.609G>A is the most mutation, which was detected in 5 of 15 alleles. The c.482G>A was found in two late-onset patients.

Conclusion: It is common for methylmalonic acidemia with homocystinemia, cblC type in China. The clinical symptoms of patients are variety. In this study, MMACHC gene mutations were mostly in exon 4. The c.609G>A may be the hotspot mutation. The c.482G>A is probably related to late-onset patients. The c.658_660delAAG was only found in Chinese till now.

THE PROGNOSIS OF THE EPILEPSY WITH ORGANIC ACIDEMIA

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Objectives: As for clinical symptoms of congenital metabolic disease, there are various symptoms such as vomiting, headache, seizure, and the developmental delay. The report is few about the prognosis of epilepsy with congenital metabolic syndrome. Therefore, we report the prognosis of the organic acidemia in our hospital.

Methods: We experienced seven cases of organic acidemia and the clinical course and the prognosis of epilepsy were analysed in the cases with seizure.

Results: We experienced four methylmalonic acidemia, one propionic acidemia, one glutaric aciduria type II and one isovaleric acidemia. One case affected with seizure, two cases hypotonia/developmental delay and four cases vomiting/respiratory disturbance. Three cases had seizure problems; one being febrile seizure, the other two being epilepsy. Prognosis of epilepsy was good in both cases. They had various degrees of developmental delay.

Conclusions: The half of cases had seizure, but a few cases complicated epilepsy. The prognoses of epilepsy were good. It was suggested that early diagnosis and treatment of the metabolic diseases take part in preventing the complication of the epilepsy and poor prognosis.

ELECTROENCEPHALOGRAM AND TRANSCRANIAL DOPPLER ULTRASONOGRAPHY IN NEONATAL CITRULLINEMIA

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Objectives: We studied a first-reported case with genotype of argininosuccinate synthetase (ASS1) mutations, c.380G>A (p.R127Q)/ c.380G>A (p.R127Q) in two alleles by a series of electroencephalograms and real-time transcranial Doppler ultrasonography.

Patient and Methods: The newborn presented with status epilepticus and coma at 3 days old. The laboratory data showed hyperammonemia and marked lactic acidosis in the blood and cerebral spinal fluid.

Results: An electroencephalogram on day 3 showed severe suppression of cerebral activity and focal paroxysmal volleys of slow and sharp waves (< 1 Hz) over the left hemisphere, which returned to normal after blood exchange transfusion and peritoneal dialysis at 15 days of age. Real-time transcranial Doppler ultrasonography showed a brain edema at day 3, high peaked systolic and low diastolic flows in basal, anterior, and middle cerebral arteries, which registered lower systolic and higher diastolic flows immediately after a blood exchange transfusion. The resistance indices were significantly different (mean resistance indices of 0.58 vs. 0.37; P = 0.01).

Conclusion: Electroencephalogram and transcranial Doppler ultrasonography can be used to monitor the efficacy of a blood exchange transfusion at the metabolic crisis and neurological status, showed a significant improvement in blood flow after half a dozen full-volume blood-exchange transfusions.

USING NEONATAL CONTINUOUS HAEMODIALYSIS TO PREVENT HYPERAMMONAEMIC ENCEPHALOPATHY

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Objective: We record EEG and MRI findings for a hyperammonemia patient and report his neurological development.

Case report: The patient is a male born at 35 weeks with a low birth weight of 2,254g. On his second day after birth he was in poor condition and was hospitalized with apnea. Laboratory examinations showed hyperammonemia (NH₃ >2480ug/dl) and metabolic acidosis. GC/MS and MS/MS tests indicated his orotic acid was normal, an unexpected result when an organic acid metabolism disorder is suspected. Our diagnosis was CPS (carbamoyl phosphate synthetase) deficiency. After hospitalization, the patient began convulsing and we performed an EEG, which showed a suppression-burst pattern indicating a severe abnormality. As a treatment for hyperammonemia, we did an exchange blood transfusion, but it was ineffective. We then began continuous haemodialysis (CHD), and normalized the patient's ammoniacal value. After four days of CHD, there were no subsequent hyperammonemia attacks. One month later, a head MRI indicated no abnormalities; similarly, an EEG done at two months showed neither paroxysms nor suppression-bursts. At 18 months, the boy's neurological development was normal, without convulsions or EEG irregularities.

Conclusion: CHD is an effective treatment for neonatal metabolic disease presenting hyperammonemia. It is possible that EEG findings are improved when the ammoniacal value is controlled early and that this control leads to improved outcomes.

A CASE OF GLYCOGEN STORAGE DISEASE SIMILAR TO MELAS

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Objectives: Lactic acidosis with mental confusion in children who had failure to thrive and similar family history can resulted in suspicion of inherited disorders such as mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) and glycogen storage disease type Ia (GSD Ia).

Methods: A 12-year-old girl was admitted in stuporous mental state following dyspnea. Her height and weight were both below 3 percentile. Physical examination revealed hepatomegaly and multiple old bruise on lower extremities. Her older brother also had easy bruising tendency, frequent epistaxis, short stature and hepatomegaly.

Results: Laboratory exam in blood revealed increased lactate (over 12 mmol/L) and lactate versus pyruvate ratio (49.5); anemia; increased total/LDL-cholesterol (295/121 mg/dL) and triglyceride (1314 mg/dL); and uric acid (10.5 mg/dL) in addition to proteinuria. The brain CT showed bilateral multifocal calcifications in basal ganglia, thalami, cerebellum and cerebral subcortical white matter. Evaluation for her brother also showed similar abnormalities. Glucose-6-phosphatase catalase unit gene was analyzed in two sibilings, which showed the same heterozygous mutation (P178A and G222R).

Conclusion: We reported a case of GSD Ia in need of differential diagnosis with MELAS, because she had similar presenting findings with MELAS (encephalopathy, lactic acidosis, short stature, and basal ganglia calcification). But she and her brother had different characteristics from MELAS: hepatomegaly, easy bruise, frequent epistaxis, hyperuricemia, and marked increased level of triglyceride. She and her brother had got treatment of dietary therapy and allopurinol medication. And then, they were transferred to other hospital for liver transplantation.

EFFECTIVENESS OF MODIFIED ATKINS DIET FOR 5 PATIENTS WITH GLUT1 DEFICIENCY SYNDROME

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Objectives: Glucose transporter type 1 deficiency syndrome (GLUT1-DS) is a treatable metabolic encephalopathy resulting from impaired glucose transport into the brain. We investigated the effectiveness of modified Atkins diet (MAD) for 5 patients with GLUT1-DS.

Methods: MAD was tried for 5 male patients with GLUT1-DS. Ages at starting MAD ranged from 7y4m to 16y9m. Duration of MAD treatment ranged from 1 to 33 months (mean; 15 months). In two patients, MCT-ketogenic diet (2:1) was changed to MAD because the latter was less restricted in total proteins and calories. The seizure frequency, neurological status, EEG background activities were compared before and after the introduction of MAD. This study was approved by the Ethics Committee of Tokyo Women's Medical University and informed consent was obtained from all patients.

Results: All patients produced 2+ to 3+ urinary ketosis by ketostick test checking in the morning before breakfast. Epileptic seizures either decreased remarkably in number or ceased completely in all patients. The interictal EEG examination showed improvement of the background activity, and a disappearance of epileptic discharges. Although other neurological manifestations such as ataxia, spasticity, dysarthria and dystonia were not sufficiently improved, their aggravation mostly observed before meals disappeared after the introduction of MAD. Along with an increased vigilance level, motivation and cognitive function appeared to be better. There was no significant side effect.

Conclusion: As compared to the conventional ketogenic diet, MAD is less restrictive to the total protein and calories, and palatable. The effectiveness of MAD was comparable to that of conventional one. Therefore, MAD is very acceptable for patients and their family to continue for a long time.

WHITE MATTER ABNORMALITIES IN GLUT1 DEFICIENCY SYNDROME: A DIFFUSION TENSOR IMAGING STUDY WITH SPM

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Objectives: GLUT1-DS (glucose transporter type 1 deficiency syndrome) is a disorder of brain energy metabolism and leads to seizures with infantile onset, a movement disorder, mental impairment. Although neuroimaging is considered uninformative in GLUT1-DS, some case reports have indicated its white matter abnormalities. We attempted to determine whether diffusion tensor imaging (DTI) can detect fine white matter abnormalities in a patient with GLUT1-DS.

Methods: We studied a 3-year-old girl who exhibited seizure at 2 months of age and was diagnosed GLUT1-DS at 3 years of age based on her clinical features, hypoglycorrachia and reduced erythrocyte glucose uptake. Fractional anisotropy (FA) map was created from DTI and compared with those from 10 normal controls by using statistical parametric mapping (SPM). A significant cluster was defined as a cluster with a height $p=0.005$ and an extent threshold 50 voxels.

Results: This patient showed delayed myelination on T2-weighted images at 12 months of age and high T2-signal of left parietal subcortical white matter at the age of 3 years. Analysis with FA map revealed decreased FA values in bilateral posterior limbs of internal capsules, deep white matter lesion around lateral cerebral ventricles and genu of corpus callosum.

Conclusion: Analysis with FA map pointed out white matter abnormalities that conventional MRI images failed to detect. This finding suggests that a disorder of brain energy metabolism may relate to white matter abnormalities in the structure or myelination extending beyond the conventional MRI-visible lesion.

FDG-PET IN GLUT1 DEFICIENCY SYNDROME: COMPARISON OF PATIENTS WITH AND WITHOUT DECREASED ERYTHROCYTE GLUCOSE UPTAKE

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Objectives: Glucose transporter type 1 deficiency syndrome (Glut1-DS) is diagnosed by reduced CSF glucose level (hypoglycorrachia) and impaired glucose uptake into erythrocytes. However, we have experienced patients with hypoglycorrachia and normal erythrocyte glucose uptake. We performed FDG-PET in patients with hypoglycorrachia, and compared the PET in patients with and without decreased erythrocyte glucose uptake to assess the difference of metabolic patterns in these two conditions.

Methods: We studied 5 patients with hypoglycorrachia, who were suspected to have Glut1-DS. Erythrocyte glucose uptake was reduced in 3 of 5 patients. We divided the patients into 2 groups: patients with decreased erythrocyte glucose uptake (Group 1) and patients with normal erythrocyte glucose uptake (Group 2). FDG-PET was performed and analysis was carried out using SPM to compare the PET image of each patient with 11 controls. A significant cluster was defined as a cluster with a height $p = 0.001$ and an extent threshold 100.

Results: Decreased uptake in bilateral thalami was observed in all patients of Group 1 and one of two patients in Group 2. Relatively increased uptake in bilateral basal ganglia was seen in all patients of Group 1 and Group 2. Cortical abnormalities were variable.

Conclusion: Similar cerebral glucose uptake pattern was seen in patients with or without decreased erythrocyte glucose uptake. It suggests that patients without decreased erythrocyte glucose uptake may also have deficiency of Glut1 in central nervous system.

WEST SYNDROME ASSOCIATED WITH NEONATAL HYPOGLYCEMIC BRAIN INJURY

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Objectives: We herein report a case of West syndrome associated with neonatal hypoglycemic brain injury.

Methods: We report the clinical features of a 9-month-old boy and analyze his MRI and EEG findings since neonatal period.

Results: Clinical features show the patient born from a mother with toxemia at term. One day after birth, he suffered from neonatal seizures and intractable hypoglycemia (<10mg/dl), caused by hyperinsulinemia. It took over 24 hours to normalize blood glucose. From birth to the age of 9 months, he developed psychomotor retardation with visual disturbances. After that, he suffered from tonic spasms which appeared daily in a series. When the patient was two weeks old, MRI showed T2 prolongation in the white matter of bilateral parieto-occipital lobes. EEG showed hypsarrythmia with occipital paroxysms. Clonazepam combined with zonisamide was effective for tonic spasms and improved his psychomotor development. However epileptic seizures increased after he was 1 year old and EEG findings worsened. His family did not want the ACTH therapy and gabapentin was added on the previous medication. At two year of age, he had left severe psychomotor retardation, though clinical seizures had decreased.

Conclusion: Burns et al (2008) reported twelve patients developed epilepsy caused by neonatal hypoglycemic brain injury. Three cases of them had infantile spasms. Severe neonatal symptomatic hypoglycemia with cerebral lesions is a risk factor for West syndrome.

THREE AUTOPSY CASES OF UNIQUE BRAIN ANOMALY SUFFERING FROM REPETITIVE HYPOGLYCEMIC ATTACKS

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Objectives: In the patients with developmental brain disorders, attacks of hypoglycemia (HG), indiscernible from epileptic seizures, can occur in the absence of pancreas disorders and congenital metabolic errors occasionally. In order to clarify pathogenesis of such HG attack, we examined three autopsy cases of unique brain anomaly showing repetitive HG attacks.

Methods: Case 1 of diffuse cortical dysplasia, a 42-year-old male, developed generalized convulsion in infancy, and suffered from repetitive HG attacks between the ages of 27 and 38. Endocrine and metabolic tests failed to demonstrate abnormalities. Case 2 of megalencephaly and hydrocephalus, a 4-year-old boy, had a reduced subcutaneous adipose tissue, growth failure and frequent HG attacks. He lacked epileptic seizures, and endocrine and metabolic tests failed to demonstrate abnormalities. Case 3 of Arima syndrome with molar tooth sign on MRI, an 11-year-old female, suffered from renal failure at 9 years, but she did not show epileptic seizures. She developed HG attacks before death, which vanished after replacement of carnitine.

Results: Three cases demonstrated no abnormalities in the pancreas, liver, endocrine organs including the hypophysis or hypothalamus at autopsy, although the pancreas was not examined in case 3.

Conclusion: HG seemed to be caused by the reduction of carnitine in case 3. On the other hand, the cause of HG was not determined even by pathological analysis in cases 1 and 2. Interestingly HG attacks occurred for a limited period in case 1. The further immunohistochemical study will be performed in the pancreas, endocrine organs and hypothalamus in cases 1 and 2.

GENOTYPIC PHENOTYPIC CHARACTERISTIC OF GALACTOSEMIA IN THE POST NEONATAL AGE IN INDIA

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Summary: Classical Galactosemia is an inborn error of metabolism, which manifests in neonatal age group. Treatment with galactose free diet in neonatal age group, leads to symptom free outcome. In developing countries, lack of compulsory neonatal screening programme and lack of awareness leads to delay in diagnosis resulting in permanent neurological handicap

Abstract: Classical Galactosemia is an inborn error of galactose metabolism caused by a deficiency of the enzyme Galactose-1-phosphate uridyl transferase leading to significant neurological impairment. In Indian population, incidence, phenotypic characteristics are less known. The present study shows the current phenotypes in Indian population with striking findings because of delayed diagnosis associated with neurological impairment. They were followed up for one year or more with galactose free diet. We describe a cohort of 21 patients diagnosed by assay of galactose -1-phosphate uridyl transferase. Age at diagnosis was 6 months to 14 years with male preponderance. 20 patients demonstrated delay in developing motor milestones. 18 had hypotonia and 2 had hypertonia. 4 had extra pyramidal movements. 13 patients failed to develop language, 5 had dysarthria. 9 patients had epilepsy. 9 patients had neurobehavioral problems, 16 patients had a history of prolonged neonatal jaundice with or without sepsis. Of 7 patients who underwent MRI, five had abnormalities. The EEG tracings of 9 patients showed epileptiform abnormalities. Of 18 patients convinced for identifying mutation, 14 were diagnosed to have identifiable mutation. 9 patients were identified of having LA variant of GALT enzyme and rest were durate variant. All patients of galactosemia maintained on galactose free diet were followed for 1 year or more but there was no significant neurological improvement. Our observation reminds us of the severe consequences of treatable metabolic disorders due to delayed diagnosis and futility of galactose free diet for neurological outcome once the damage has set in.

A CASE OF A CHILD WITH CARNITINE DEFICIENCY

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Objective: To report a case of carnitine deficiency in a girl aged 26 months.

Methods: Case study.

Results: A 26-month girl is the second child with a past history of preterm 38 weeks gestation, 2200 gram at birth. The first child boy is also preterm and development delay. Patient presented with developmental delay, central nervous system dysfunction, hypotonia, and progressive proximal weakness. Metabolic decompensation was triggered by viral illness with rigid neck, right orbicularis weakness, hyperreflexia, failure to thrive. Cerebrospinal fluid biochemistry, microbiology and cytology, and MRI of the brain were normal. Other laboratory findings included: glycemia 4,6mol/L, lactic acid 4 mmol/L, NH₃ 110Mmol/L, LDH 361 u/L, AST: 43U/L, and ALT: 27U/L. Tandem mass spectrometry analyses showed a decrease in free carnitine. Total acylcarnitine was also decreased. 3-OH isobutyrate was elevated slightly, and glycerol and glycerate were also elevated. Metabolic decompensation was progressive with apnea and coma.

Conclusion: A girl of carnitine deficiency with onset at early 26 months presented with encephalopathy, myopathy with motor delay.

CLINICAL CHARACTERISTICS OF EPILEPSY WITH HUNTER SYNDROME

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Objectives: There are few reports concerning epilepsy in Hunter syndrome. The aim is to evaluate the clinical characteristics of epilepsy in Hunter syndrome.

Methods: The study included 17 patients with Hunter syndrome. We divided the patients into two groups: epilepsy group (4 patients) and non-epilepsy group (13 patients). Two groups were compared about clinical manifestations, and we described the clinical course of epilepsy in epilepsy group.

Results: Mental retardation was found in three of four patients (75%) in epilepsy group, whereas in 5 of 13 (46.2%) in non-epilepsy group, but there was no statistical difference ($p=0.24$). The ratio of using wheeled chair in epilepsy group was higher than in non-epilepsy group ($p<0.05$). There were no differences about cardiac manifestation, respiratory disability, deafness. Patients of the epilepsy group had seizures at the age of 13.1 ± 3.3 (average \pm SD) years old, and they had died at the age of 17.5 ± 1.8 (average \pm SD) years old. Three of them had tonic seizures which were controlled well by within 2 anticonvulsants, but one had refractory myoclonic seizure. Abnormal MRI findings were not observed except hydrocephalus.

Conclusion: The frequency of epilepsy in Hunter syndrome was higher than previous reports, and was associated with using wheeled chair. We could not found the relationship between epilepsy in Hunter syndrome and mental retardation. Epileptic seizures in the patients with Hunter syndrome were tended to be controlled by a few anticonvulsants.

A GROSS DELETION OF ARYLSULFATASE B IDENTIFYING IN A TAIWANESE PATIENT WITH MUCOPOLYSACCHARIDOSIS TYPE VI

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Objectives: Mucopolysaccharidosis type VI (MPS VI; Maroteaux-Lamy syndrome) is an autosomal recessive lysosomal storage disease induced by a deficiency of the enzyme N-acetylgalactosamine-4-sulfatase (arylsulfatase B, ARSB). The deficiency of ARSB leads to an accumulation of dermatan sulfate (DS) in lysosomes and gross excretion in the urine. The diagnosis is usually made in early childhood when organomegaly, corneal clouding, coarse features, enlarged tongue, frequent respiratory illness or otitis media, and joint stiffness are all apparent. Other complications include hearing loss, chronic respiratory tract infections, sleep apnea, pulmonary hypertension, hydrocephalus, rapid-onset blindness, and cardiac valve insufficiency or stenosis. In this study, an unusual ARSB gene deletion mutation type in a Taiwanese MPS VI patient was demonstrated.

Methods: To validate the patient's type of MPS, urine mucopolysaccharide was defined by two-dimensional electrophoresis and leukocyte ARSB activity was determined by fluorogenic assay. One MPS VI Taiwanese patient was investigated. Direct sequencing was used to identify any mutation in the patient's ARSB gene. Total RNA isolated from the patient's blood sample and performed reverse transcription-polymerase chain reactions (RT-PCR) to identify exon deletion.

Results: Abnormal excretion of DS and low leukocyte ARSB activity was observed in the urine sample of the patient studied. No mutation was found after direct sequencing of her ARSB gene except exon 4 region which could not be amplified by PCR. The result of RT-PCR revealed that her exon 4 of ARSB was deleted mutation in mRNA level.

Conclusion: The results of this study suggest that an unusual ARSB gene mutation exist in Taiwanese MPS VI patients. Therefore, ARSB gene profiling may be useful in genetic counseling for families affected by MPS VI.

A METACHROMATIC LEUKODYSTROPHY (MLD) PATIENT'S LONG-TERM FOLLOW UP: NEUROLOGIC AND EXTRA- NEUROLOGIC COMPLICATIONS

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Objectives: To describe complications in a metachromatic leukodystrophy (MLD) patient's long-term follow up. Background: MLD is a demyelinating genetic disorder characterized by the absence of the enzyme arylsulfatase A (ASA); this absence causes the toxin sulfatide to accumulate in the cells, especially in the nervous system. We report here on an MLD patient receiving home care.

Case: The patient is a 12 year old girl who developed status epilepticus (diagnosed by brain imaging and ASA measurement); at age four, she began having convulsive attacks which caused psycho-motor deterioration. During the next year, she presented progressive difficulty in walking and developed leg stiffness; she was unable to sit or stand. In addition, she developed hypertonia, and this gradually affected her respiratory system, gastroesophageal reflux and nutritional intake. For the next five years, a slowly progressing visual impairment and auditory and speech disorders made communication difficult. At age ten, she was in a vegetative state and was given emergency surgical treatment to puncture her tumorous gallbladder and remove fluids from it. She died two years later at age 12. Death was caused by an intestinal obstruction which resulted from the developing tumors in the gallbladder and by multiple organ dysfunction.

Results: Convulsive attacks, hypertonia, and gallbladder involvement (neurologic and extra-neurologic complications) in an MLD patient's long-term follow up not only increased the suffering of patient, but also added to the burden of caregiver, particularly by causing repeated hospitalization and discharge.

Conclusion: Convulsive attacks, hypertonia and gallbladder involvement in MLD cause serious problems and should be recognized as important MLD complications. For the convulsive attacks and hypertonia, early stage drug therapy is indispensable and early surgical treatment is essential for the gallbladder involvement, as later, invasive procedures, endanger the weakened patient. These therapeutic procedures will contribute to an improved quality of living for the MLD patient.

LATE-ONSET KRABBE'S DISEASE WITH HYPOPHOSPHATEMIC RICKETS AND FOCAL STATUS EPILEPTICUS

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Objectives: Krabbe's disease is a lysosomal storage disorder with neurological regression and leukodystrophy on MRI brain. The late-onset variant is rarer (10-15%) and has a clinically heterogenous phenotype. We report a child with late-onset Krabbe's disease and hypophosphatemic rickets who developed focal status epilepticus and subsequent focal epilepsy.

Methods: This is a retrospective case report.

Results: We describe a child with underlying hypophosphatemic rickets who presented aged 6 years old with progressive motor and cognitive regression. Magnetic resonance imaging of the brain showed leukodystrophy and analysis of galactosylceramidase GALC supportive of Krabbe's disease.

Conclusion: Late-onset Krabbe's disease and hypophosphatemic rickets are individually rare. This is the first description of a patient with both clinical entities. Focal status epilepticus and seizures are recognised in Krabbe's disease and can be medically intractable.

PROGRESSIVE MYOCLONUS EPILEPSY DUE TO GAUCHER DISEASE TYPE 3 WITHOUT HEPATOSPLENOMEGALY

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Objectives: Gaucher disease type 3 (GD3) is characterized by progressive myoclonus epilepsy and prominent hepatosplenomegaly. GD3 without hepatosplenomegaly has been rarely reported.

Methods: To extend phenotypic spectrum of GD3, we report a female patient with GD3 who did not present hepatosplenomegaly.

Results: This patient was born to nonconsanguineous parents suffered a convulsion at age one year. EEG and brain CT showed normal results. Her growth and psychomotor development were normal before onset of typical absence seizures at age five years six months. Although absences disappeared on multiple antiepileptic agents at age seven years 11 months, diffuse spike-waves and focal (poly-)spikes frequently appeared on interictal EEG. Generalized tonic-clonic seizures developed at age nine, and action tremor, ataxia, erratic myoclonus, and ophthalmoplegia at 12. These symptoms were progressively aggravated. Somatosensory evoked potential test at age 14 showed giant reactions. Although neither hepatosplenomegaly nor cherry-red spot were noted, lipid-accumulated bone-marrow macrophages were identified at age 16. Detailed examinations revealed reduction of leukocyte beta-glucosidase activity (less than 17 percent of normal control) and missense mutations in each allele of beta-glucosidase gene. One mutation, N188S, had been previously reported as a causative mutation for GD3, despite 67 percent of residual enzyme activity. The other was a novel mutation, G199D, later revealed to be null mutation. Even when she was admitted to our hospital at age 18 because of aggravation of seizures, hepatosplenomegaly was not observed.

Conclusion: It is of clinical importance to consider GD3 when patients present progressive myoclonus epilepsy even without hepatosplenomegaly.

A CASE OF TAY-SACHS DISEASE WITH CLUSTERS OF SUBCLINICAL SEIZURES

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Background: We report a 22-month-old boy with Tay-Sachs disease, who showed clusters of electrical seizures without clinical manifestation. Although seizures almost invariably occur after 1-year-of-age in patients with Tay-Sachs disease, clusters of subclinical seizures have not been reported.

Case report: He appeared normal at birth. He visited our hospital because of developmental delay when he was 15 months old. Physical examination revealed hypotonia, loss of head control, exaggerated startle response to sound. His hypotonia progressed and his fundus examination revealed cherry red spot. His cranial MRI showed high intensity in the bilateral basal ganglia, irregular high intensity area in bilateral thalamus and high intensity areas in deep white matter on T2-weighted imaging. He was diagnosed with Tay-Sachs disease because of deficiency of hexosaminidase A (20.1 nmol/mg P/hr, normal range of 153-371 nmol/mg P/hr). He developed the first febrile seizure at 13-month-old-of-age and the first afebrile seizure at 16-months-old-of-age. Seizures were characterized by twitchings of eyelids and clonic movements of limbs lasting for about 30 seconds. Phenobarbital was started. His EEG at 19-month-old showed repetitive bilateral anterior-temporal spikes without ictal discharges. His EEG at 22-month-old revealed ictal discharges of rhythmic sharp wave bursts originating from the left frontal/anterior-temporal or posterior-temporal region. Although some of ictal discharges were associated with staring eyes with eyelid twitchings, most of them were electrical seizures without clinical manifestations. The dosage of phenobarbital was increased.

Conclusions: We presented the first report of a patient with Tay-Sachs disease with clusters of subclinical seizures. Although it remains unknown whether electrical seizures without clinical manifestations are common in patients with Tay-Sachs disease, it can be useful to record EEG to detect subclinical seizures, even if they do not display any apparent clinical seizures.

SERIAL MR IMAGING AND 1H-MR SPECTROSCOPY IN MONOZYGOTIC TWIN WITH MILD INFANTILE TAY - SACHS DISEASE

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Objectives: Tay-Sachs disease is an autosomal recessive neurodegenerative disorder of ganglioside metabolism with a deficiency of hexosaminidase A (Hex A), an enzyme involved in the metabolism of gangliosides, causes an accumulation of GM2 ganglioside in neurons and impairment of neuronal function. We have performed serial MR imaging (MRI) and 1H-MR Spectroscopy (1H-MRS) in monozygotic siblings with early onset Tay-Sachs disease manifesting a mild phenotype, and discuss the evaluation of neuronal damage in these two cases.

Cases: Five-year-old monozygotic female twin who neurological deterioration and visual agnosia were appeared at 2 years of age. Biochemical measurements of lysosomal enzyme activity with leucocytes showed decreased Hex A in them, therefore, they were diagnosed as having infantile Tay-Sachs disease. The sister showed similar slowly progressive clinical symptoms and deterioration; however the younger sister also demonstrated intractable seizure in the right leg. Head circumference was not enlarged in them. MRI demonstrated bilateral hyperintense signal changes in the periventricular white matter on T2-weighted and FLAIR weighted images, however no signal changes in the basal ganglia in either twin. The ratio of N-acetylaspartate (NAA)/creatine (Cr) was decreased in the both white matter lesions and corpus striatum. The lactate peak was seen in left basal ganglia of the younger sister. Serial MRI and 1H-MRS were performed at three times, 2, 3 and 4 years of age, respectively. Brain atrophy was progressed and the ratio of NAA/Cr was gradually decreased in the twin. They were bed-ridden at 30 months; however they need neither tracheotomy nor hospitalization, even now. They had a putative Gln390Pro mutation; however another mutation had not been identified in Hex A gene.

Conclusion: Changes in metabolites on 1H-MRS were closely linked to the clinical features of the twin. Serial study by 1H-MRS is useful for the metabolic evaluation of neuronal tissue in children with Tay-Sachs disease.

LONG-TERM PROGNOSIS FOR A CASE OF NEURONAL CEROID-LIPOFUSCINOSIS WITH EPILEPSY AND SICK SINUS SYNDROME

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Objectives: We report a rare case of juvenile neuronal ceroid-lipofuscinosis (JNCL, CLN3) with epilepsy and sick sinus syndrome (SSS) to show that NCL lipopigment accumulates within neurons and other cells, suggesting a multisystemic distribution. NCL is characterized by progressive loss of vision, seizures, and loss of cognitive and motor functions, but it is rarely associated with arrhythmia, SSS.

Case report: The patient is a 33-year-old male with a history of visual disturbances beginning when he was six. At that age, his bilateral optic nerves showed atrophy and he had chronic seizures and myoclonus. At eight, he began antiepileptic drug treatments. His EEG showed irregular diffuse high voltage spikes and waves; his head MRI revealed diffuse high intensity areas in the bilateral insular cortex, and ventricles marked by diffuse dilatation. Skin and muscle biopsy revealed variations in fiber size and increased acid phosphatase positive granules. We diagnosed ceroid-lipofuscinosis. The patient also showed progressive mental retardation and retrogression. At 24, his face was pallid and he suffered from loss of appetite, consciousness disturbances, and bradycardia. An ECG showed complete A-V block and sinus bradycardia; echocardiography showed his wall motion was not asynergic, and that there were no organic changes. We performed emergency pacing and pacemaker implantation. After that, he had no cardiac problems, but he is unable to communicate and cannot perform daily tasks without assistance now.

Conclusion: Hoffman IL et al. (2001) reported a heart pathology revealed at autopsy by myocardial and valvular storage of lipopigments which were observed histologically and confirmed ultrastructurally. We suggest a similar mechanism (valvular storage of lipopigments) as the origin of our patient's SSS mechanism.

CLINICAL EVALUATION OF LEIGH ENCEPHALOPATHY IN 4 PEDIATRIC CASES

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Objectives: To report clinical and imaging characteristics of phenotype of epilepsy, EEG and neuroradiological findings in Leigh syndrome diagnosed in early childhood.

Methods: We reviewed the clinical, EEG and neuroradiological features of the patients diagnosed with Leigh syndrome in Saitama Children's Medical Center from 2003 to 2009.

Results: The 4 children (1 male and 3 female) were enrolled in this period. The mean age of onset was 6.25 months (range: 4-8months). They are diagnosed by clinical criteria based on the combination of neurological features and elevated lactic concentration with characteristic MRI features in basal ganglia. The 8993T>G mtDNA mutation was detected in two patients. Epilepsy was observed in three patients. Two of them demonstrated infantile spasms with hypsarrhythmia with focal epileptic discharge on EEG and their brain MRI showed signal changes on bilateral lenticular nucleus and brain stem. One case showed signal changes on subcortical gray matter of frontal and occipital lobes in MRI and hypoperfusion of frontal lobe in SPECT. Another case without infantile spasms showed partial and myoclonic seizures with thalamus signal changes on MRI without basal ganglia abnormalities.

Discussion: Previous reports suggested an important role of focal cortex, lenticular nucleus and brain stem in pathogenesis of infantile spasm through their PET results. In our study, the patients with infantile spasms demonstrated abnormal MRI signal changes on lenticular nucleus and brain stem, and their focal cortical lesions were also suggested from the results of EEG, MRI or SPECT.

A CASE OF NEONATAL CONVULSION WITH PERSISTENT HYPERLACTATEMIA: LEIGH SYNDROME WITH HETEROPLASMIC MUTATION FOR MT-ND5 GENE

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Case History: A 19-day-old full term baby girl who was previously well was admitted to neonatal unit because of convulsion. Physical examination was unremarkable. Investigations included sepsis screening, CT brain and EEG were normal. She was noted to have persistent metabolic acidosis and hyperlactatemia with serum lactate level over 7mmol/L. CSF lactate was 4.6mmol/L and lactate-to-pyruvate ratio was elevated to 35. Clinically there was no recurrence of seizure and the patient was neurologically normal until 5 months of age, she developed poor suck, generalized hypotonia and developmental delay. At 7 months, she had bilateral ptosis, nystagmus and ophthalmoplegia. MRI brain / MR spectroscopy showed symmetrical abnormal signals in brainstem and internal capsule. The presence of high lactate peak was suggestive of mitochondrial encephalopathy. Leigh syndrome was suspected based on clinical, biochemical and radiological findings. She was treated with mitochondrial cocktail therapies including riboflavin, thiamine, coenzyme Q10, ascorbic acid and levocarnitine. Muscle biopsy was refused by her parents. She was then referred for genetic analysis in particular searching for mitochondrial disorders. A stepwise approach targeting the common mutations was adopted. Initial study for hotspot mutations in mitochondrial DNA including nucleotides of m.8993T>G or C, m.3243A>G, m.8344A>G by PCR-restriction enzyme study were negative. Subsequent mutation screening for PHDA1 (pyruvate dehydrogenase E1A), PC (pyruvate caboxylase) and SURF-1 genes (for Leigh Syndrome) by PCR-direct sequencing was also negative. Heteroplasmic mutation for MT-ND5 gene at m.13094T>C (p.Val253Ala) was detected and confirmed by PCR-direct sequencing, PCR-restriction enzyme study and amplification refractory mutation system (ARMS). It was also recently reported to be the disease-causing mutation in a patient with mitochondrial encephalomyopathy (reference 1), and the pathogenic effect of this mutation on complex I activity has been demonstrated. She was found to have downhill clinical course despite medical treatments with persistent elevated serum and CSF lactate level. At 11 months, she developed apnea and had central hypoventilation and was now ventilator-dependent. CT brain performed at 12 months showed disease progression, with symmetrical hypodense lesions over bilateral thalami and midbrain and evolving cerebral atrophy.

Conclusion: Neonatal convulsion with persistent elevated serum lactate level is highly suggestive of primary neurometabolic disorder. Stepwise approach in the investigations of this patient confirms the diagnosis of mitochondrial disorder. This is the first reported case of Leigh syndrome with MT-ND5 gene mutation identified in our locality.

Reference: 1. Valente et al. Biochim Biophys Acta. 2009;1792:791-5

EPILEPSIES IN MELAS SYNDROME

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Objectives: Neurologic signs such as seizures, muscle weakness, headache with vomiting are often leading to the diagnostic workup for the mitochondrial encephalopathies. Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) is a disease characterized by recurrent headache and epilepsy. The onset of symptoms has been referred to as stroke-like episodes that caused by mitochondrial dysfunction in small cerebral blood vessels. This study is performed to define the clinical features including the epilepsy occurring in MELAS patients in a medical center in Taiwan.

Methods: Retrospective review of six patients with diagnosis of MELAS was conducted with clinical, neuroradiologic, biochemical and electrophysiologic analysis.

Results: By biochemical studies, all of the patients had lactic acid elevation during glucose loading test. MELAS was suspected initially when MRI revealed abnormal signal intensity at cortex or basal ganglion that revealed cerebral atrophy and infarction. Genetic testing from peripheral blood confirmed an A3243G transition in 4 patients and T3291C transition in one patient. Seizures occurred in 4 cases (66%) and mean age of onset was seven years. We also evaluated EEG for 5 patients included 4 seizure cases and one non-seizure case. Their EEGs showed focal or multifocal epileptiform activities and regional cortical dysfunction in four cases (80%) including the non-seizure one. Besides seizures, there were recurrent headache and vomiting in two cases (33%) and muscle weakness in one case as the early manifestations. Other features revealed short stature and failure to thrive (66%), visual field defect (50%), cognitive impairment (66%), and cardiac involvement (33%).

Conclusion: This study emphasizes that epileptic seizures are common in MELAS but not the earliest presenting sign. However EEG studies usually showed abnormal results as focal or multi-focal spikes and cortical dysfunction. Epileptic seizure in MELAS seems difficult to control leading to frequent attacks in some patients.

FOCAL EPILEPSY AND MELAS IN A SINGAPORE PAEDIATRIC HOSPITAL

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Objectives: Mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) is characterized by sudden onset of stroke-like episodes, usually presenting before the age of 20, and accompanied by migraine-like headaches, seizures, cognitive decline and progressive deafness. It is caused by mitochondrial DNA mutations, the most common being A3243G. Seizures may be generalized or focal. We report 2 patients with MELAS and their seizure semiology, neuroimaging and EEG findings.

Methods: We retrospectively studied cases of MELAS in a tertiary paediatric hospital. Data on diagnosis, clinical signs and symptoms, electroencephalogram (EEG) and anti-epileptic medications were collected and analyzed.

Results: Two patients, both females aged 8 years and 10 years old respectively, with MELAS were identified. One patient presented with headache, unsteady gait and vomiting. The other presented with recurrent episodes of encephalopathy with ataxia, dysphasia and visual hallucinations. Both developed focal seizures and one had non-convulsive focal status epilepticus. Comparison of EEG and MRI findings showed concordance between the seizure foci and the stroke-like lesions. Both patients required anti-epileptic medications to control seizures.

Conclusion: Initial seizures in MELAS occur during acute decompensations and often have focal semiology. Later multifocal symptomatic epilepsy develops in association with accumulating chronic structural lesions in the brain. Focal seizures show correlation between electrographic abnormalities and lesions on MRI brain and respond well to anticonvulsant therapy. Non-convulsive focal status epilepticus can occur in MELAS.

EPILEPSY IN METABOLIC MYOPATHY WITH RAGGED-RED FIBERS

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Objectives: Mitochondrial disorders (MDs) consist of a heterogeneous group of multisystem disorders. The pictures of metabolic myopathy, as lipid accumulation or ragged-red fibers (RRF), are common in MDs because the muscle is highly dependent on oxidative metabolism; however, concomitances of epilepsy are rare. We reviewed the epilepsy occurring in patients with muscle biopsy presenting suggestive of metabolic myopathy in MDs.

Methods: We retrospectively reviewed muscle biopsies from patients with clinical pictures of metabolic myopathy, followed from 1986 to 2009 in Kaohsiung Medical University Hospital. Clinical histories of epilepsy and electroencephalography (EEG) were reviewed; furthermore, neuroimaging, metabolic surveys, serum creatine kinase (CK) level, and genetic analysis have been performed in several cases.

Results: We enrolled ten patients, aged 10-33 years (male : female = 2 : 8), whose muscle biopsies revealed lipid accumulation and RRF. Their CK level ranged from 2,000 to 31,000 IU/L. Seven patients had epilepsy associated with epileptogenic EEG findings and five of them had abnormal neuroimaging. All seven epileptic patients were finally diagnosed mitochondrial encephalomyopathy confirmed by genetic analysis: three of them were myoclonus epilepsy with RRF (MERRF) with A8344G mtDNA mutation and four were mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) with one had rare mtDNA 3271T>C mutation and three had mtDNA 3243A>G mutation. Three patients without epilepsy were diagnosed multiple acyl-CoA dehydrogenase deficiency (MADD) with mutations at electron-transferring-flavoprotein dehydrogenase (ETFDH) gene.

Conclusion: In addition to mitochondrial encephalomyopathy, rare metabolic myopathies, such as MADD, might share the common myopathic pictures of lipid accumulation and RRF. Especially in those with no epileptic phenotypes and no proved mitochondrial genetic defect, MADD should be put in the list of differential diagnosis since its hotspot mutations (p.A84T) in Taiwanese can be readily identified recently.

SEVERE MYOCLONIC SEIZURES IN PEROXISOMAL D-BIFUNCTIONAL PROTEIN DEFICIENCY

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Objectives: D-bifunctional protein deficiency is a disorder of peroxisomal fatty acid beta-oxidation. It is a severe metabolic disease with early loss. Refractory seizures is common. It is amongst the single enzyme defects of the peroxisomal disorders. We present two young infants and one neonate with the condition

Methods: We have recently seen 3 cases, ages varying between 7 days and 6 months.

Results: All three babies had the common features of severe hypotonia, dysmorphic appearance with high forehead, high-arched palate, enlarged fontanel, long philtrum, epicanthal folds, hypertelorism, macrocephaly, retrognathia, and low-set ears. There was liver and spleen enlargement, early encephalopathy, and resistant epilepsy. Seizures showed short duration generalized pattern in the younger two. The six month old infant clearly presented with myoclonic fits resembling to infantile spasms (video presentation). EEGs were consistent with the seizure types. Burst suppression was a cardinal finding. Cranial MRIs demonstrated widespread polymicrogyria in all. VLCFA were elevated. Fibroblast culture denoted deficiency of the D-bifunctional protein. Our cases expired soon after the diagnosis without gaining any developmental milestones.

Conclusion: Infantile spasms may be encountered in peroxisomal disorders apart from the other more frequently seen seizure forms.

RAPID ESTIMATION OF THE EFFICACY OF ORAL PYRIDOXINE FOR WEST SYNDROME: INTRAVENOUS ADMINISTRATION OF PYRIDOXINE UNDER EEG MONITORING

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Objectives: Some patients with West syndrome (WS) respond to pyridoxine (V.B6), however, it is unknown how long the patients should take it to judge its efficacy, and it often causes vomiting and liver dysfunction. We studied on the rapid estimation of its efficacy for WS.

Methods: Thirty-five patients with WS were given intravenous administration (IV) of V.B6. IV V.B6 was done by approximately 10 mg/kg every 5 minutes to prevent vomiting, up to a total of 30-50 mg/kg, and EEG were recorded for every 5 minutes (min) before IV V.B6, just after IV, and 15 min, 30min, 45 min, and 60 min. after IV. Following this evaluation, V.B6, 30-50 mg/kg, was orally given to the patients. Twenty out of 35 patients, 5 cryptogenic and 15 symptomatic cases, completed both IV and oral administration of V.B6.

Results: By IV V.B6, hypsarrhythmia on EEG completely disappeared and did not recur within 30 min after IV (IV-Good) in 4 cases, transiently disappeared but recurred in 15 min (IV-Fair) in 4 cases, and did not disappear (IV-Poor) in 12 cases. Infantile spasms disappeared in three cases of IV-Good by oral V.B6 at 30-40 mg/kg. These three cases were symptomatic, including lissencephaly, porencephaly caused by intracranial hemorrhage, and tuberous sclerosis. Infantile spasms decreased by >50% in another one case of IV-Good with microcephaly and cerebral palsy. Oral V.B6 was ineffective in all IV-Good and IV-Poor patients.

Conclusion: IV V.B6 under EEG monitoring can rapidly estimate the efficacy of oral V.B6 for WS.

A NORMAL PTH HYPOCALCEMIC NEONATAL CONVULSION REVEALING MATERNAL NORMOCALCEMIC HYPERPARATHYROIDISM

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Neonatal hypocalcemia is an important cause of neonatal convulsion. We reported a rare case of normal PTH hypocalcemic neonatal convulsion with maternal normocalcemic hyperparathyroidism who had severe seizures after ten-day-old. The laboratory investigations at diagnosis showed as followings: blood sugar 53 mg/dl, WBC 8,100/ μ L, Hb 14.9 g/dl, total calcium (Ca) 4.6 mg/dl (reference value, 8.4-10.2), magnesium (Mg) 1.6 mg/dl (reference value, 1.8-2.5), phosphorus 11.3 mg/dl (reference value, 2.5-4.6), ionized Ca 2.05 mg/dl (reference value, 4.0-5.5), alkaline-phosphatase (ALP) 301 IU/L (reference value, 145-420), sodium 138 m mol/L (reference value, 136-145), potassium 4.0 m mol/L (reference value, 3.5-5.1), lactate 1.4 m mol/L (reference value, 0.5-2.2), ammonia 50 μ g/dl (reference value < 70), 25-OH-D 4.3 ng/ml (reference value, 5.30-27.7), 1,25-(OH)-D 33.8 pg/ml (reference value, 1.67-17.3), parathyroid hormone (PTH) 26.78 pg/ml (reference value, 11-62). The blood biochemistry study was performed at the same time in his mother, although she did not show any clinical manifestations. Results demonstrated as followings: serum total calcium 9.5 mg/dl, Mg 2.1 mg/dl, phosphorus 3.3 mg/dl, PTH 91.74 pg/ml. Since elevated PTH level was observed in his mother, neonatal hypocalcemia with maternal hyperparathyroidism was diagnosed. After calcium gluconate supply, the seizure stopped. He was on 1,25-(OH) D 0.125 μ g, and calcium carbonate 1000 mg therapy for six months and then stopped medication. Thereafter, he was free of any symptoms for 3 months with normocalcemia (ionized Ca 5.29 mg/dl). It is important to screen maternal calcium, and PTH levels in unexplained late neonatal hypocalcemia.

SEIZURE LIKE TREMORS OF 6 WILSON DISEASES IN TWO FAMILIES

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Objectives: Wilson disease is an autosomal recessive disorder with a genetic mutation recently localized on chromosomal 13. The primary defect is impaired biliary excretion of copper, leading to its accumulation in the liver, brain, and other tissue (kidney, eye, etc.).

Methods: We have experienced 6 cases of Wilson disease developed in 2 families.

Results: In all patients, Kayser-Fleischer ring, mild elevated SGOT/SGPT with negative HBsAg, decreased serum ceruloplasmin and elevated 24hours urine copper are observed, and neurologic symptoms are noted in 2 cases. Other familial members are negative in laboratory test for Wilson disease. In 2 cases, they had seizure like tremors and acute fulminant hepatitis developed in one, so he died despite of aggressive management such as D-penicillamine, albumin and pyridoxine administration, and intravenous hyperalimentation. In other case, tremors and laboratory findings are improved after carbamazepine, D-penicillamine and pyridoxine administration.

Conclusion: We experienced seizure like tremors with Wilson disease in 2 families.

EPILEPSY IN MENKES DISEASE

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Objectives: To characterize the epilepsy in Menkes disease.

Methods: Based on clinical charts, we retrospectively analyzed the clinical features of four patients with Menkes disease.

Results: Three of the four patients had their initial seizures before the age of six months (two months to six months). One patient received early copper treatment (within two weeks of age) and had his first seizure at eleven months. The initial seizures were infantile spasms (two cases), generalized clonic seizures, and tonic seizures. Brief tonic seizures and myoclonus were the main seizure type after the late infancy. One patient had prolonged breath holding spells which caused cardiac arrest twice. The diagnosis of Menkes disease was delayed in two patients (two months and seven months after the initial seizures). The initial EEG showed posterior predominant polyspikes and polyspike-waves in two cases, hypsarrhythmia, and diffuse irregular high-voltage slow bursts with spikes. The MRI/MRA findings showed diffuse brain atrophy and tortuous vessels. Subdural hematoma was detected on either CT or MRI in two cases. ACTH was not used because of the risk of subdural hemorrhage and infection. Partial seizure control was obtained after late infancy in all patients. Although zonisamide was effective, two out of three patients who used zonisamide developed urolithiasis.

Conclusion: The risk of intracranial hemorrhage and urolithiasis should be carefully taken into consideration when treating patients with epilepsy in Menkes disease.

LOW SERUM URIC ACID IS AN IMPORTANT EARLY CLUE TO THE DIAGNOSIS OF MOLYBDENUM COFACTOR DEFICIENCY AS THE CAUSE OF NEONATAL SEIZURES – A CASE REPORT

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Objectives: Neonates with refractory seizures and epileptic encephalopathy as a result of molybdenum cofactor deficiency are often reported to have poor prognosis, with early demise or severe global developmental delay. Abnormally low serum uric acid is an important early clue towards the diagnosis of this condition as the neurometabolic workup to determine the cause of neonatal seizures is often extensive and time-consuming.

Methods: A female neonate, who is the second child of non-consanguineous parents, presented with neonatal seizures and encephalopathy at day 2 of life. She had metabolic acidosis due to the refractory seizures, which recurred almost hourly. The neonatal electroencephalogram (EEG) showed diffuse low voltage record ($<20\mu\text{V}$) punctuated only by frequent EEG seizures, which only responded transiently to repeated intravenous boluses of phenobarbitone (PB) and later midazolam infusion. There was no benefit from two doses of intravenous pyridoxine 50mg, as well as megadoses of vitamin cocktail, coenzyme Q and carnithine supplements. Early investigations quickly excluded central nervous system infection and cerebral malformation as the cause. While awaiting the results of more extensive neurometabolic studies sent overseas, the only clue was the abnormally low serum uric acid level of less than $30\mu\text{mol/L}$ (below the detection limit of the assay).

Results: The neonate passed away on day 14 due to the refractory seizures. The diagnosis was confirmed soon after from the markedly raised ratio of S-sulphocysteine to creatinine in the urine, and the presence of peaks of S-sulphocysteine in the plasma and cerebrospinal fluid aminogram.

Conclusion: Serum uric acid is an easy but important test in the workup of neonatal epileptic encephalopathy towards the diagnosis of molybdenum cofactor deficiency. Early diagnosis may allow a trial of therapeutic dietary intervention with restriction of methionine and supplementation of cysteine. Nevertheless, the age of presentation remains the most important prognostic factor.

NATIONWIDE EPIDEMIOLOGICAL STUDY OF PEDIATRIC NEUROTRANSMITTER DISEASES IN JAPAN (1ST REPORT)

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Objectives: Pediatric neurotransmitter disease (PND) is a relatively new concept in medical science. PNDs, which are induced by genetic disorders that affect the regulation of neurotransmitters in children, include dopamine-/serotonin-related diseases and GABA-related diseases. Left untreated, PNDs can lead to severely compromised neurological function in patients. However, diagnosing these diseases has been difficult. Thus, it is assumed that many of those patients were not diagnosed accurately and they did not receive appropriate treatments. We investigated the numbers and the distributions of patients with these diseases in Japan.

Methods: We sent a questionnaire to pediatricians or neurologists of 1622 Japanese hospitals in 2009. The data were analyzed statistically.

Results: We received replies from 60.3% of those hospitals (969 of 1608 hospitals). Fourteen hospitals were excluded from this study because they had no pediatrician or neurologist. In dopamine-/serotonin-related diseases, 116 patients of Segawa disease (autosomal dominant guanosine triphosphate cyclohydrolase I (GTPCH) deficiency) were reported from 44 hospitals. Those patients were in every 10 region of Japan. The prevalence rate of Segawa disease was calculated as 0.96 patients/ million. Three patients of aromatic-L-amino acid decarboxylase (AADC) deficiency, another dopamine-/serotonin-related PND, were also reported from 2 hospitals. No patient with tyrosine hydroxylase (TH) deficiency or sepiapterin reductase (SR) deficiency was reported in this study. In GABA-related disease, 3 patients of succinic semialdehyde dehydrogenase (SSADH) deficiency were reported from 3 hospitals.

Conclusion: The prevalence rate of Segawa disease in this study was similar to that of a previous report by Nyggard et al. in 1993 (0.5-1.0 patients/ million). This is the first report of a nationwide epidemiological investigation of PND in Japan.

AROMATIC L-AMINO ACID DECARBOXYLASE (AADC) DEFICIENCY: CLINICAL FEATURES AND FOLLOW-UP IN A CASE

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Objectives: Aromatic L-aminoacid decarboxylase (AADC) deficiency is a neurotransmitter defect leading to a combined deficiency of catecholamines and serotonin. Affected individuals are usually detected in infancy due to severe developmental delay, oculogyric crises and extrapyramidal movements. In the beginning, all these clinical symptoms are hard to differentiate from neonatal or infantile seizure. In the end, no patient can achieve a complete recovery from neurological symptoms.

Methods: We report an AADC deficiency case of male infant presented with limbs involuntary movement, developmental delay, muscular hypotonia, dystonia, oculogyric crises, sleep disturbance and additional extraneurological symptoms. The results of EEG, brain MRI, and repeated newborn screens and CSF study were all negative. Analysis of CSF biogenic amines, including HVA, 5-HIAA, and DOPA proved AADC deficiency at his age of one year. His dystonia and oculogyric crisis had partial response to the treatment with L-Dopa, bromocriptine, and MAO inhibitors.

Results: The level of CSF catecholamine metabolites (HVA and 5-HIAA) were nondetectable and DOPA was elevated. Motor fatiguability, dystonia and sleep pattern partially improved with the use of L-dopa, bromocriptine, and MAO-I.

Conclusion: Only the levels of CSF catecholamine metabolites and DOPA can confirm the diagnosis of AADC deficiency, and the prognosis is usually grave. Medications including L-dopa, bromocriptine, and MAO-I are of limited benefit to this case.

TWO CASES OF TYROSINE HYDROXYLASE (TH) DEFICIENCY MIMICKING IDIOPATHIC CEREBRAL PALSY AND EPILEPSY

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Objectives: Cerebrospinal fluid (CSF) neurotransmitter analysis and molecular genetic studies revealed TH deficiency as the underlying cause of two children with developmental delay and suspected epilepsy.

Methods: Case report.

Results: Patient 1 presented with hypotonia and global developmental delay at 3-month-old and subsequently developed intermittent convergent squint and prolonged limbs dystonia without impairment in consciousness. Examination revealed truncal hypotonia but spastic limbs and brisk tendon reflexes. She was wheelchair-bound and could not communicate verbally. Blood tests including creatine kinase, ammonia, lactate/pyruvate and urine for amino acids/organic acids were normal. Nerve conduction study/electromyography, muscle biopsy and brain MRI showed no abnormality. Electroencephalogram performed during dystonic attack revealed no epileptiform activity. At 10-year-old, CSF study revealed very low homovanillic acid (HVA), low 5-hydroxyindoleacetic acid (5-HIAA), reduced HVA/HIAA ratio and normal neopterin, biopterin and 3-O-methyldopa levels. Diagnosis was further confirmed with mutational analysis of TH gene showing compound heterozygous mutation (p.G216S and p.G377R). Complete resolution of dystonic attack/intermittent squint with improvement in fine motor functions and speech were achieved after levodopa (2.3mg/kg/day). Patient 2, with uneventful perinatal history, was noted to have hypotonia since 3-month-old and later with repeated generalised dystonia and eye staring. Examinations revealed truncal hypotonia, limbs dystonia and hyperreflexia. Extensive investigations including brain MRI again showed no abnormality. Therapy with levodopa (2.9mg/kg/day) resulted in marked reduction in dystonic attack, improvement in voluntary hand functions and speech. The diagnosis was confirmed by genetic test (p.G263R and c.1163+5G>C) at 11-year-old.

Conclusion: TH, which catalyses the hydroxylation of L-tyrosine to L-Dopa, is the rate-limiting step in catecholamines synthesis. Broad spectrum of symptoms including developmental delay, hypotonia, rigidity, abnormal posturing and involuntary eye movement with variable severity was reported in patient with TH deficiency. Our patients were misdiagnosed as idiopathic cerebral palsy and epilepsy initially. Significant improvement in neurological symptoms and developmental achievement were noted after levodopa.

A STUDY OF CEREBROSPINAL FLUID NEUROTRANSMITTERS ASSAY IN CHILDREN WITH UNDIAGNOSED NEUROLOGICAL DISEASES IN HONG KONG

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Background: Paediatric neurotransmitter diseases (PND) are a group of disorders with a wide clinical spectrum of presentations including neonatal seizures, unexplained movement disorders such as dystonia, rigidity or ataxia, eye abnormalities including oculogyric crises, convergence spasm, ptosis or other intermittent ocular movement abnormalities, and autonomic symptoms like sweating, temperature instability, hypoglycaemia and hypothermia.

Method: From 2004 to 2009, 114 children, aged 2 days to 33 years, with undiagnosed neurological diseases underwent lumbar puncture. Patients had symptoms more than or equal to one of the followings: movement disorders, mental retardation / cognitive decline, epilepsy and spasticity which might be suggestive of disorders of bipterin, catecholamine and serotonin metabolism or cerebral folate deficiency. Extensive workup was unrevealing which included neuroimaging, cytogenetic studies, preliminary blood and urine for metabolic investigations. From 2004 to 2007, cerebrospinal fluid (CSF) was sent to the Division of Clinical Chemistry and Biochemistry, University Children's Hospital Zurich, Switzerland for neurotransmitters assay. From 2007 onwards, the analysis was performed in the Division of Clinical Biochemistry, Queen Mary Hospital, Hong Kong.

Results: The presenting features of our cohort included various combination of clinical symptoms such as dystonia / rigidity, epilepsy which could be intractable, cognitive regression, global developmental delay / mental retardation, oculogyric crises, spasticity and hypotonia. 10 patients (8.8%) had abnormal neurotransmitters profile compatible with 6-pyruvoyl-tetrahydropterin synthase (PTPS) deficiency (n=5), tyrosine hydroxylase (TH) deficiency (n=2), idiopathic cerebral folate deficiency (CFD) (n=2), aromatic L-amino decarboxylase deficiency (AADC) deficiency (n=1). Ultimate diagnosis was confirmed by genetic study in all patients with PTPS deficiency, TH deficiency and AADC deficiency. 2 patients with CFD showed elevated autoantibodies against folate receptor (FR) confirming the diagnosis. Treatment was commenced in all 10 patients. 1 patient with PTPS deficiency revealed complete resolution of a parkinsonism state after replacement with tetrahydrobiopterin and L-dopa with normal intelligence. Another patient with PTPS deficiency only showed resolution of hyperphenylalaninaemia biochemically without obvious clinical improvement with significant generalized dystonia and moderate mental retardation. The remaining 3 patients with PTPS deficiency showed no neurological signs but with mild learning problem. One patient with TH deficiency demonstrated marked improvement in her dystonia and oculogyric crises after treatment with L-dopa and significant developmental progress. Another patient with TH deficiency did not reveal definite improvement and developed drug-induced dyskinesia. The child with CFD showed no more regression in cognitive and motor functions after replacement with folinic acid. His younger brother, who was nearly asymptomatic except mild spasticity over both lower limbs, did not have further deterioration in neurological functions after treatment. The patient with AADC deficiency was just started on bromocriptine and vitamin B6 treatment.

Conclusion: PND, a group of potentially treatable neurometabolic diseases, should be considered in any child with unexplained neurological symptoms including movement disorder, cognitive regression, oculogyric crises and spasticity. Early identification and treatment will improve morbidity and mortality.

SLC25A13 GENE TARGETED MUTATION ANALYSIS IN DIRECT BILIRUBIN ELEVATED JAUNDICE PATIENTS

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Objectives: In order to confirm how many neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD) in direct bilirubin elevated jaundice patients.

Methods: Applied PCR and PCR-RFLP to analyze SLC25A13 gene hotspot mutation, including 851del4、1638ins23、IVS6 + 5G>A、IVS16ins3kb and IVS11 + 1G>A in 44 direct bilirubin elevated jaundice patients.

Results: In the present study, we have identified 9 NICCD in 44 direct bilirubin elevated jaundice patients. The ratio is 20.5%. 5 patients were 851del4 heterozygotes, 2 patients were 851del4 homozygotes and 2 patients were heterozygote of 1638ins23/ IVS6 + 5G>A. The major mutation type was 851del4 which accounted for 69.2% (9/13) in total mutation. 1638ins23 and IVS6+5>A accounted for 15.4% (2/13). IVS16ins3kb and IVS11 + 1G>A were not detected.

Conclusion: NICCD is very common in direct bilirubin elevated jaundice patients.

EFFECTS OF PROGESTERONE ON EXPRESSIONS OF INTERLEUKIN-18 IN CEREBRAL CORTEX OF NEONATAL RATS WITH SEIZURE INDUCED WITH TRIFLUOROMETHYLETHER

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Objectives: To investigate the effects of recurrent seizures on interleukin-18 expressions in immature and mature rat cerebral cortex; By giving progesterone, investigate the change of interleukin-18 in cerebral cortex of neonatal rat which was submitted to recurrent seizures, to determine whether progesterone protects the neurons from the damage of seizures by the change of interleukin-18.

Methods: 96 7-day-old(PN-7d) Sprague-Dawley rats were divided randomly into three groups: The first group was a control group of rats grown naturally. the second group was the seizure group, the rats were administered chemoconvulsant drug Trifluoromethyl ether (one time per day, the convulsion sustained for 30 min.) in this group. The third group was the intervention group; rats of this group were administered progesterone(16mg/kg) after given trifluoromethyl ether; ARS-13d, ARS-15 days, ARS-19 days, PN-75 days later, the rats were killed and their brains processed for localization of neuron plasma antigen. The expression of interleukin-18 protein in the cortex were detected by immunohistochemistry and Western-blot methods on ARS-1d(PN-13d), ARS-3d(PN-15d), ARS-7d(PN-19d) and PN-75d.

Results: ① IL-18 could be detected in the endochylema of rats cerebral cortex. The results of immunohistochemistry indicated: Compared with the control groups, the expression of IL-18 was significantly higher in the seizure groups ($P<0.05$). The level of IL-18 in seizure groups rise on ARS-1d, and the level of IL-18 reached the peak on ARS-7d, then declined. But on the PN-75d the expression of IL-18 in the seizure groups also more than control groups. The intervention groups (rats were given progesterone), compared with the seizure groups, the expression of IL-18 in cortex was significantly reduced ($P<0.05$). ② The results of Western-blot methods: The expression of IL-18 in cerebral cortex on the ARS-1d and ARS-3d couldn't be detected, on the ARS-7d and PN-75d. Compared the seizure groups with control group, the levels of IL-18 in the seizure groups significantly higher ($P<0.05$). Compared the seizure groups with the intervention groups, the levels of IL-18 were significantly reduced in the latter ($P<0.05$).

Conclusion: Recurrent seizures in neonatal rats raise the expression of IL-18 in cerebral cortex of rats. The progesterone could reduce the levels of IL-18 in cerebral cortex of the seizure rats. This phenomenon indicates progesterone could have anti-inflammatory effect on seizure severity. Progesterone can protect brain from injury induced by seizures in the infant rats.

CUSHING'S DISEASE WITH EPILEPSY: A ROLE OF OVERACTIVITY OF THE HPA SYSTEM

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Objectives: Epilepsy can induce hypercortisolism. We report a ACTH-dependent Cushing's syndrome with epilepsy and discuss the role of GABAergic systems and overactivity of the HPA systems.

Methods: We report a patient who followed up more than five years as epilepsy combined with Cushing's disease.

Results: A 24-year-old woman with EEG abnormality (diffuse 2.5-3c/s spike and wave, duration: more than 7 seconds) was referred to Ise Keiyu Hospital. She had unconscious episodes twice and already diagnosed as Cushing's disease. She had been born to non-consanguineous, healthy parents and weighed 2720g at 39 weeks gestation. Development was delayed and her IQ test at 24 years of age was 20. She already tried carbamazepine by the other hospital but failed. MRI finding showed the remarkable dilatation of posterior horn of the lateral ventricles. Her BMI shows 31.1 recently. Before the initiation of AEDs, we respected mother's opinion and selected zonisamide as treatment for her epilepsy. After the therapy of ZNS, her QOL had been well .

Conclusion: Epilepsy can induce hypercortisolism secondary to altered temporolimbic modulation of the hypothalamopituitary secretion of ACTH. (Herzog AG. 1998) We would like to discuss overactivity of the HPA , GABAergic systems and NMDA-antagonistic systems about epilepsy with Cushing's disease.

EVOLUTION OF EPILEPSY IN A CASE OF ADENYLOSUCCINATE LYASE DEFICIENCY: VIDEO-EEG AND RESPONSE TO TREATMENT

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Adenylosuccinate lyase (ADSL) deficiency is a rare disorder of the purine biosynthesis pathway associated with epilepsy, intellectual impairment and autism. Epilepsy syndromes reported in ADSL deficiency include early infantile epileptic encephalopathy, West syndrome and symptomatic epilepsy with both focal and generalized seizure types. We describe a boy with this disorder in whom focal seizures developed in the first week of life, then evolved into infantile spasms at 3 months. Treatment with high dose oral prednisolone, phenobarbitone and topiramate was ineffective, but vigabatrin was effective from 7 months until 12 months of age, when episodes of tonic upgaze associated with electroclinical absences manifest and were controlled by treatment with sodium valproate. Video-EEG findings at 3 and 12 months of age are presented.

Suspicion of ADSL deficiency was raised at 3 months of age when urine metabolic screening by tandem mass spectrometry showed elevated levels of succinyladenosine (S-Ado). Purine concentrations measured by HPLC confirmed increased levels of S-Ado and succinylaminoimidazole carboxamide riboside (SAICAr) in urine. The patient was given a trial of oral S-adenosylmethionine (SAME) to act as an adenosine donor from 5 months of age. However, levels of S-Ado and SAICAr in urine did not change and there was no clinical response to SAME treatment over 20 months. At 30 months of age he has the development of a 10-month-old infant and there are some features of autism. His epilepsy is well controlled with sodium valproate alone.

A FEMALE CASE OF SEVERE INFANTILE SPASMS WITH RETT SYNDROME-LIKE PHENOTYPE

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Objective: To assess the clinical characteristics of early onset severe infantile spasms with Rett syndrome-like phenotype.

Case: The patient, a 16-month-old female, started developing infantile spasms at age of 3 months. The spasms were considered to be atypical for first 6 months, because spasms did not occur in clusters and frequency was very low. She showed stereotypic midline hand movements and could not develop purposeful her hand skills at age of 7 months. Her development began to regress at age of 9 months. Furthermore, her parents had noticed several symptoms such as poor smile, loss of head control or reaching ability and loss of eye contact. She developed recurrent generalize tonic seizures at age of 11 months and was admitted to hospital for seizure control.

Results: Since her EEG showed generalized changes in forms of multiple spikes and slow waves, similar to hypsarrhythmia, anticonvulsant agents, VPA, VitB6 and NZP were administrated. However, her EEG was worsened, and she was transferred to our hospital for ACTH therapy. ACTH therapy was very effective, and resulted in amelioration of spasms and disappearance of hypsarrhythmic pattern. However, she again developed spasms after 1 month, and EEG was worsened. Since therapy with ZNS, CZP and CLB was not effective, we administrated ACTH again along with VitB6 and TPM.

Conclusion: She showed refractory infantile spasms and symptoms associated with Rett syndrome-like phenotype. Recently, X-linked cyclin-dependent kinase-like 5 (*CDKL5*) gene mutations have been reported in patients with neurodevelopmental disorders characterized by infantile spasms, psychomotor impairment, and Rett syndrome-like phenotype. In future we intend to analyze *CDKL5* gene in this case.

THREE CASES OF INFANTILE CONVULSION CHOREOATHETOSIS SYNDROME (ICCA SYNDROME)

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Objectives: Infantile convulsion choreoathetosis (ICCA) syndrome is a clinical entity derived from the association between benign infantile convulsion and the subsequent development of paroxysmal dyskinesia. We report our cohort of patients with ICCA syndrome and study their clinical characteristics.

Methods: We retrospectively reviewed our patients with the diagnosis of paroxysmal kinesigenic dyskinesia (PKD) and history of infantile convulsion that were followed up at our department over a five-year period.

Results: Three male Chinese patients were identified. Two patients had onset of infantile convulsions at four months of age, and one at nine months. All patients presented with generalized tonic-clonic seizures and had good response to phenobarbitone. Electroencephalograms showed no ictal discharges. Medications were stopped at age of three and there were no recurrence of seizure attacks. All patients had normal psychomotor developments and attended normal schools. The mean age of onset of PKD was 8.7 years (range 7-11 years). Two had positive family history of PKD. They all had good responses to low dose carbamazepine (100mg daily).

Discussion: Benign infantile convulsion is a seizure disorder occurring in the infancy period, usually 3 to 12 months after birth. It is inherited as an autosomal dominant trait with incomplete penetrance and phenotype variability. Linkage of the ICCA syndrome to the pericentromeric region of chromosome 16 has been reported in previous studies including Chinese and Japanese families. Despite the existence of several genetic foci, the search for the PKD or ICCA gene is hampered by the complicated genomic architecture of the highly duplicated DNA sequences. Patients with this syndrome have normal psychomotor developments and favourable outcomes. PKD is a rare but benign neurological disorder which is commonly being misdiagnosed or overlooked. We report our cohort of Chinese patients with benign infantile convulsions with subsequent development of paroxysmal kinesigenic dyskinesia. The history of benign infantile convulsion, together with the higher male preponderance rate and positive family history of PKD should alert both physicians and parents about the potential development of PKD.

THE CLINICAL AND LABORATORY FEATURE OF TWO CASES EPIDERMAL NEVUS SYNDROME

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Objectives: To study the clinical feature of epidermal nevus syndrome and improve the recognition to this disease.

Methods: Clinical, radiological and histopathological data of two children were analyzed, and literature was reviewed.

Results: Two patients both had typical epidermal nevus with abnormality of cerebral radiology, and associated to mental retardation, epilepsy, language and movement retardation. One of the two patients was combined to ocular tumor. All of these appeared at birth or soon after birth. Histopathological analysis of biopsy specimens obtained from the epidermal nevus revealed squamate epidermis papilliform proliferation.

Conclusion: The disease may affect every other organ system exclusive cutaneous lesion, including the central nervous system, and influence severely mental and life quality of patients. Early diagnosis and therapy can help improve the life quality.

CLINICAL FEATURES OF BENIGN INFANTILE CONVULSIONS ASSOCIATED WITH MILD GASTROENTERITIS

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Objectives: Clinical manifestations and outcomes of hospitalized children with afebrile seizures following mild gastroenteritis were evaluated and analyzed.

Methods: A retrospective study and a follow-up over 12 months were conducted on patients who were admitted to our hospital during November 2006~November 2008, who were diagnosed as mild rotavirus gastroenteritis with afebrile seizure but without previous seizure disorders or family history of febrile convulsion or epilepsy, dehydration, electrolyte imbalances or hypoglycemia.

Results: Out of the 31 patients, 17 were male and 14 were female. The age at the disease onset ranged from 8 months old to 29 months old (mean, 14 months). Six patients (19.4%) reported two or more episodes of seizures. All patients suffered from seizures, generalized tonic clonic seizure lasting 0.5 ~2 min, after 24~68 hours of onset of GI symptoms. No status epilepticus was observed. Neurological examination showed normal. Only 3 of the 28 patients showed abnormal interictal electroencephalogram (EEG) findings with a little more slow wave, which reverted to normal during follow-up. Cranial imaging, blood biochemical profiles and cerebrospinal fluid (CSF) testing did not show any abnormalitis in any of the cases. No antiepileptic medications were prescribed as the seizures stopped spontaneously. Rotavirus antigen test was positive in 25(80.6%) children. During the follow-up, all displayed normal psychomotor development without recurrence of seizures.

Conclusion: Benign infantile convulsions associated with mild gastroenteritis (BICE) has the following clinical features: most children occur at the age of 1-2 years old; The convulsions usually happen at the first several days after the onset in a generalized type; No significant changes in blood biochemical profiles, CSF, brain imaging and interictal EEG; Antiepileptic medication may not be necessary after seizure cessation.

JUVENILE HUNTINGTON'S DISEASE WITH REPETITIVE STATUS EPILEPTICUS AND PERIODIC SHARP WAVE COMPLEXES ON EEG: A CASE REPORT

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Objectives: Juvenile Huntington disease (JHD) is defined as having an age of onset of younger than 20 years. The clinical symptoms of JHD are different from that of adult-onset HD. Adult HD usually presents with chorea and personality changes, whereas juvenile HD is far less common and presents with parkinsonism, dystonia, dementia, and seizures. We describe a patient with juvenile HD presenting rapid regression after repetitive status epilepticus and periodic sharp wave complexes (PSWC) on EEG.

Case report: The patient was a 14-year-old woman. Her father had died of HD. Her developmental milestones were normal until the onset of JHD. At the age of 5 years, she fell down on many occasions. Brain MRI showed bilateral atrophy of caudate and putamen. We performed the genetic study for HD and found a CAG trinucleotide repeat expansion of 95-100 repeats. She had afebrile seizures at the age of 8 years. Anticonvulsant therapy was started. Thereafter, abnormal neurological signs including intellectual decline and involuntary movements gradually developed. Epileptic seizures frequently occurred. EEG showed continuous generalized high voltage spike and wave complexes. When she was 13 years old, two episodes of status epilepticus occurred at a 6-month interval. After the episodes, she developed severe mental regression and was in a semi-comatose state. EEG revealed lower voltage of background activity and continuous PSWC.

Conclusion: The EEG of JHD are known to show bursts of (poly-)spike and wave, focal epileptic discharges, and diffuse intermittent delta waves. To our knowledge, there have been no reports of PSWC associated with JHD. The periodic EEG pattern might be an indication of diffuse cerebral impairment in a severe type of JHD.

THE EARLY CLINICAL PICTURE, NEUROPHYSIOLOGICAL AND MRI INVESTIGATIONS IN 4 PATIENTS WITH MONOCARBOXYLATE TRANSPORTER 8 (MCT8) DYSFUNCTION (ALLAN–HERNDON–DUDLEY SYNDROME)

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Objectives: To delineate the early clinical, neurophysiological and neuroimaging aspects in patients with monocarboxylate transporter 8 (MCT8) dysfunction (Allan–Herndon–Dudley syndrome).

Patients and Methods: Four patients with Allan–Herndon–Dudley syndrome (genetically proven) were included in this study. The mean age was 1 year and 11 months. All patients showed high free triiodothyronine (T3) and low free T4 levels in serum. They showed no seizure. L-T4 treatment has been unsuccessful for modifying neurological symptoms. Neurological examination, electroencephalography (EEG), evoked potentials (somatosensory evoked potentials (median nerve SEP), auditory brainstem responses (ABR) and visual evoked potentials (VEP)) and MRI (T1WI, T2WI and FLAIR sequences) were performed at around 1 year of age.

Results: Inadequate head control, marked truncal hypotonia, persistent primitive reflexes, rigid extremities with dyskinetic postures and severe mental delay were observed in all patients. Delayed N20 (the first cortical potential of the primary sensory cortex) in SEP, delayed wave I in ABR and unclear P100 deflection in VEP were evident. All patients' MRI showed hypomyelination and thin corpus callosum. In EEG study, no paroxysmal discharge was observed.

Conclusion: All the findings obtained by clinical, neurophysiological and MRI studies seem to reflect the delayed myelination and the early neuronal dysfunction in the cerebrum and the brainstem. The neuronal localization of MCT8 in brain regions critically involved in motor control and mental development. The correlation between detailed clinical phenotypes and longitudinal neurophysiological findings should be followed.

A CLINICAL OBSERVATION FOR THE EFFICACY AND SAFETY OF LEVETIRACETAM MONOTHERAPY IN CHILDREN WITH EPILEPSY

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Objectives: To evaluate the efficacy and safety of levetiracetam (LEV) monotherapy in children with epilepsy.

Methods: Forty-one children (M 26, F 15) with epilepsy between the ages of 7 months and 13 years were treated with LEV as monotherapy. These patients were from Neurology Department of Wuhan Children's Hospital in 2007-2009. The starting dosage of LEV was 8.9-18.6mg/kg per day of tablet twice daily, and its objective dosage was 15.3-45.8mg/kg per day of tablet twice daily in children with epilepsy. This LEV monotherapy was investigated by a self-controlled and open-label research, and the follow-up period ranged from 6 months to 2 years.

Results: The effective rate (at least 50% reduction in seizures) was found in 68.3% (28/41), with 39.0% (16/41) achieving seizure freedom in LEV monotherapy of children with epilepsy. Thirteen patients (31.7%) had poor efficacy (less than 50% reduction in seizures) in reduction of seizures, with seven patients (17.1%) discontinuing LEV monotherapy due to either an inadequate seizure control or aggravated seizures. Fifteen patients (36.6%) had the therapy-related adverse events in LEV monotherapy of children with epilepsy, including gastrointestinal dysfunction, dizziness, somnolence and irritability, etc. The adverse effects appeared in 2-4 weeks of early LEV therapy and were spontaneously disappeared in 1 week to 1 month of continuing therapy.

Conclusion: The LEV monotherapy is effective and safe for the control of partial and generalized seizures in children with epilepsy. LEV appears to be a broad-spectrum, first-line anti-epileptic drug in treatment of children with epilepsy.

A CLINICAL ANALYSIS AND STUDY OF 120 CHILDREN WITH VIRAL ENCEPHALITIS

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Objectives: To explore the characteristics and the treatments of the viral encephalitis.

Methods: A total of 120 patients, clinically diagnosed with Encephalitis in the pediatric wards, between July 2001 and September 2007. The independent variables defined for each patient were age, sex, clinical symptoms, seizure type, presence of SE or refractory status epilepticus (RSE), initial electroencephalogram (EEG) finding, neuroimaging study, cerebrospinal fluid (CSF) and outcome.

Results: Between July 2001 and September 2007, there were 120 encephalitis patients. The male to female ratio was 1.6:1. The most common symptoms were fever (100%), upper respiratory symptoms (65.5%) and altered level of consciousness (35.2%). The initial seizure type was categorized as focal (21.5%), generalized (37.2%), primary focal and secondary generalized (39.4%). Abnormal EEGs were 76.2 %. Six cases died, and 24 cases developed epilepsy and/or neurologic deficits.

Conclusion: Our results support that appropriate symptomatic therapy and support, especially for treating convulsions, and traditional Chinese medicine should be recommended to reduce the mortality and improving.

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| 2004 | Neuronal Migration Disorders and Childhood Epilepsies (ISNMD) | Battaglia GS, Crino PB, Curatolo P, Golden JA, Granata T, Guerrini R, Leventer RJ, Mochida GH, Otsubo H, Woermann FG | Journal of Child Neurology 2005; 27(2): 79-140. |
| 2005 | Epileptic Syndromes in Infancy and Early Childhood (ISES) | Andermann F, Berg AT, Capovilla G, Craiu D, De Vivo DC, Engel J Jr, Fejerman N, Hirsch E, Kasteleijn-Nolst Trenite DGA, Kim DW, Lee WL, Lux AL, Moshe SL, Nordli DR Jr, O'Regan ME, Plouin P, Sankar R, Scheffer I, Scher MS, Specchio N, Wolf P. | Epilepsy Research 2006; 60 Suppl 1: S1-S279 |
| 2006 | Status Epilepticus in Infants and Young Children (ISSS) | Banu S, Fusco L, Kalra V, Lee JS, Lux AL, Neville B, Otsubo H, Sankar R, Shinner S, Specchio N, Wasterlain CG | Acta Neurologica Scandinavica Supplement 2007; Vol 115; Suppl 186: 5-86 |
| 2007 | Biology of Seizure Susceptibility (ISBSS) | Arzimanoglou A, Baram TZ, Curatolo P, Goldin AL, Jozwiak S, Mochida GH, Moshe SL, Otsubo H, Prasad A, Sarnat HB, Schridde U, Staley KJ, Swann JW | Takahashi T, Fukuyama Y, eds. Biology of Seizure Susceptibility in Developing Brain. Progress in Epileptic Disorders, Vol 6. Montrouge: John Libbey Eurotext. 2008: 232 pp |
| 2008 | Febrile Seizures and Related Conditions (ISFS) | Baram TZ, Chang YC, Heida JG, Kaila K, Kubek MJ, Neville BGR, Nordli D, Scheffer IE, Shinnar S, Vestergaard M | Brain & Development, Part 1: 2009; 31(5): 358-404 Part 2: 2010; 32(1): 33-77 |
| 2009 | Epilepsy in Autism Spectrum Disorders and Related Conditions (ISEASD) | Brooks-Kayal A, Chae JH, Deonna T, Dibbens LM, Parmeggiani A, Saemundsen E, Tuchman R, Wong V, Zappella M | Brain & Development 2010 (in preparation) |
| 2010 | Epilepsy in Neurometabolic Diseases (ISENMD) | Baxter P, Chae JH, Goebel H, Kern R, Kim KJ, Pearl P, Prasad AN, Prasad C, Qin J, Sankar R, Tein I, Wu J, Zhang YH, Zimmerman R, +9 Taiwanese, +6 Japanese | Brain & Development 2011 (in preparation) |

Notes

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