Transitional Care in Inborn Metabolic Diseases

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Disclosure

• I am serving the principle investigator of the rare disease registry program and the MPS virtual advisory board, sponsored by Genzyme
Inborn metabolic diseases

Rare
1:10,000 - 1:1,000,000

Diverse
>1000

Collectively
MANY
1/1000 live birth
Genetic Medicine Department, Westmead hospital
Serve the whole population in NSW (7.2M)
Close to 1000 patients in adult IEM service
Question: Do we have IEM patients around?

Question: Where are the older IEM patients now?
Difficult to know the exact incidence of IEM disease

The estimation is around 1 in 4000 live birth for classical IEM
Where are the older IEM patients now?

- A survey to paediatric units
  - Age 16 or above
  - Classical IEM
- PMH: 10 patients (age 17-26)
- QMH: ?20-30 patients
- PWH: 1
- KWH: Nil
  - (15 IEM patients in their registry, oldest one in early teens)
- PYH: Nil

? A lost generation of IEM in adolescence
Mak M. Chemical pathology analysis of inborn errors of metabolism for expanded newborn screening in Hong Kong. The University of Hong Kong. 2012. http://hdl.handle.net/10722/180075
The lost generation

- Delay diagnosis / under- diagnosis / mis-diagnosis
  - Improving with better laboratory support and clinical awareness
  - High risk screening
- Newborn screening
  - TMS
  - Many disease at one go
  - NBS not just bring new young patients but new families with affected members in different age groups
Who is looking after IEM patients

Paediatrics

Adult medicine

Expertise

Fear of transition

Training

Spectrum

Volume
Inborn metabolic diseases: trends in development

Growing older
- Advances in biochemical and molecular diagnosis
- New born screening program
- Early intervention
- Better treatment

Wide disease spectrum
- Late presentations
- Milder phenotype
- Continuous progression of disease related complications in later life

Better independence
- Compliance to lifelong treatments
- Occupation
- Pregnancy & reproduction

Coordinated service need
- New treatments
- Coordinated care provided by different subspecialties
- Long term outcome
- Researches
Transition needs

- Slow & progressive deterioration e.g. LSD
- Persistent disabling, no effective tx. e.g. Lesch-Nyhan disease
- Successful treatment, independent life e.g. PKU
- Benign childhood, late deterioration e.g. leukodystrophy
Dealing with women with IEM disease undergoing pregnancy

J Inherit Metab Dis 2006;29:311-316
Inborn metabolic diseases: trends in development

- Knowledge & skill, training
  - Diagnoses & management of disease / complications
  - Facilitate contact between patients & families
  - Coordinate holistic care

- Assess to emerging therapies
  - Adult IEM service

• 24 IEM service providers in UK
  • 22 general IEM
  • 2 LSD only

• General IEM
  • 6 provides combined adult and paediatric service
  • 2 provides adult only service
  • 5 provides separate adult & paediatric service with some coordination
  • 4 provides paediatric service only

• 46 doctors or 22.6 WTE

• Estimated only 57% IEM patients under these service providers

J Inhert Metab Dis
2006;29:667-676
Australia: designated adult IEM service only available in Sydney, Melbourne and Adelaide

- **Victoria**
  - Adult metabolic service Monash Medical Centre in mid 2009

- **NSW**
  - Adult metabolic service Westmead Hospital started in 2008, fully funded in 2010

- **Queensland**
  - No specific adult metabolic service
  - Adult patients requiring hospitalization admitted to an adult unit, metabolic clinician go around to provide consultations

- **SA**
  - Joint clinic in Royal Adelaide Hospital

- **WA**
  - No coordinated service
Training in IEM clinical service

• UK
  • Higher training in IEM fell in subspecialty of Metabolic Medicine recognized by the Joint Royal College of Physicians Training Board
  • Trainees from Chemical pathology or General internal medicine
  • IEM is one of the five clinical domains in Metabolic Medicine curriculum (with DM, Lipid disorders, nutrition and bone disease)
Training in IEM clinical service

• Australia
  • Advanced training in Clinical genetics under the Royal Australasian College of Physicians
  • Subspecialize in Metabolic Medicine in Clinical genetics

• Hong Kong
  • Proposed to incorporate IEM training in the coming Paediatric subspecialty Paediatric Endocrinology and Metabolic Medicine under Hong Kong College of Paediatricians
Adult inborn metabolic disease services

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Disorders seen in adult IEM services from an international multi-centre survey

- Aminoacidopathy: 39%
- Lysosomal: 23%
- Mitochondrial: 16%
- Peroxisomal: 5%
- Glycogen storage: 7%
- Fatty acid oxidation: 4%
- Mucopolysaccharides: 2%
- Porphyrias: 2%
- Vitamin and cofactor: 2%

JIMD Rep. 2015 Oct 9
Adult inborn metabolic disease services

More than 40% were diagnosed in adult age, notable examples were mitochondrial disease and Fabry disease.

JIMD Rep.2015 Oct 9
Adult inborn metabolic disease services

- Mitochondrial: 31%
- LSD: 39%
- AA/CHO/FAO: 13%
- FAP: 11%
- Others: 6%

54 patients under PMH adult IEM registry
# PMH adult IEM registry

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Adult inborn metabolic service in Princess Margaret Hospital

• July 2012, HAHO discussed on enzyme replacement therapy (ERT) arrangement for adult patients

• In the task force meeting, participating paediatricians and adult physicians all agreed that ERT only involved a few suitable patients, while the broader aspects of continuous medical care for other inborn metabolic diseases should not be overlooked.

• It was proposed to develop inborn metabolic service in adult medical units of QMH/PWH/QEH and PMH, taking care of both ERT and non-ERT related inborn metabolic diseases
Adult inborn metabolic service in Princess Margaret Hospital

- Hospital management in Princess Margaret Hospital supported the establishment of adult IEM centre to serve KWC patients
- Started adult IEM clinic in Nov 2012
  - Initially a joint clinic with paediatrician -> adult physician 2015
  - Bimonthly -> Monthly 2016
- 2014 Princess Margaret Hospital became the only designated adult ERT treatment centre for LSD patients in HK
- Inborn metabolic disease service training
  - 2013 Charles Dent Metabolic Unit, Queen sq. London
  - 2015 Genetic medicine department, Westmead Hospital, Sydney
Enzyme replacement therapy: a structured service driven by money concerns

• We started the first enzyme replacement therapy for a lady with late onset Pompe disease in 2011
• Since 2014, PMH started to assist ERT assessment and applications for patients from other clusters
• All newly started ERTs were managed in PMH
Enzyme replacement therapy: a structured service driven by money concerns

- Enzyme therapy: un ultra-expensive therapy with modest benefit
  - Alglucosidase alfa (myozyme): $3.2M / y
  - Agalsidase beta (fabrazyme): $1.2M / y for a 50kg person

- Who & When to treat
  - International guidelines
    - Very similar guidelines from different countries
    - Many unanswered questions, lack of consensus with good scientific evidence to put down in guidelines to govern the clinical practice
  - Individualized
    - Genotype, prognosis
Enzyme replacement therapy: longitudinal data is very important to optimize the use of ERT

Centralized management provides a window for longitudinal follow-up on asymptomatic and mild symptomatic patients and such information would be very helpful in deciding the best use of enzyme therapy.
An evolving transitional care model for inborn metabolic disease in Princess Margaret Hospital

- Quick preview on scheduled outpatients
- Review lab parameters, drugs & dietary plan
- Decide the treatment goal and follow up
- Combined IEM case conference
- Adult physician
- Chemical pathologist
- Dietitian
- Paediatrician
- In-depth review of paed patients planned for transition
- Topic review on the disease pathophysiology and management
- Work out the transition schedule & tx plan
An evolving transitional care model for inborn metabolic disease in Princess Margaret Hospital

- International connections
- Under development
  - Individualized crisis management protocols to combat metabolic decompensation
  - Multidisciplinary expertise
- Future
  - New drug trials
  - Pregnancy registry
    - Coordinated management for IEM pregnancy, from pre-conception to post-partum
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From Westmead Hospital
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HKSIEEM Council members

Expert Panel on ERT for LSD

PMH Clinical Research Centre

PMH Ambulatory Care Centre