The Hong Kong Society of Paediatric Endocrinology and Metabolism (HKSPEM) & The Hong Kong Society of Inborn Errors of Metabolism (HKSIEM)

A Proposal of Subspecialty Training Programme on
Paediatric Endocrinology and Metabolic Medicine (PEMM)

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Abbreviations:
PEM = Paediatric Endocrinology and Metabolism
HKSPEM = Hong Kong Society of Paediatric Endocrinology and Metabolism
IEM = Inborn Errors of Metabolism
HKSIEM = Hong Kong Society of Inborn Errors of Metabolism
IMD = Inherited Metabolic diseases
PEMM = Paediatric Endocrinology and Metabolic Medicine

Background and Introduction

Since the Hong Kong College of Paediatricians (HKCPaed) decided to look into the feasibility of developing and accrediting higher training of paediatric subspecialties in Hong Kong, the Hong Kong Society of Paediatric Endocrinology and Metabolism (HKSPEM) has been actively discussing the issue and preparing for subspecialty training programme on Paediatric Endocrinology and Metabolism (PEM). Paediatric Endocrinology and Metabolism has been practised in Hong Kong for more than 30 years. Paediatricians practising PEM have been organising diabetic camps for children and adolescents with diabetes till over decades. The Hong Kong Society of Paediatric Endocrinology and Metabolism (HKSPEM) was founded in 1996 with the objective of promoting the practice of PEM in Hong Kong. Patient support groups for diabetes were established in various hospitals and the Hong Kong Juvenile Diabetic Association (HKJDA) was founded in 2001. The HKJDA has been organizing educational activities and providing support to children and adolescents with diabetes and their families. It also participates actively in organizing diabetic camps in recent years.

A meeting on the future development of PEM was held in August 1999 in which council members of the HKSPEM, representatives of Paediatric Chief of Service (COS) of hospitals and all those interested were welcomed to participate. In the meeting, it was pointed out that there were a number of general paediatricians with special interest in PEM working in different hospitals but there was no structured subspecialty training programme in Hong Kong. It was agreed that subspecialty training programme on PEM was needed for future development of the subspecialty. The development of tertiary centers is generally welcomed for the provision of comprehensive training programme, improvement in the quality of care and co-ordination of collaborative research among regional hospitals etc. Response to a questionnaire for subspecialty development and accreditation was prepared and submitted to the HKCPaed in December 2002. Consensus was reached at that time that there would be one training programme on PEM with 3-4 training centres in Hong Kong. A training centre can be a single institution or a group of related establishments.

The Hong Kong Society of Inborn Errors of Metabolism (HKSIEM) was founded in 2004 by a group of clinicians, pathologists and geneticists to promote the study and management of IEM as the field of IEM has been rapidly expanding in recent years. The Hong Kong Mucopolysaccharidosis and Rare Genetic Diseases Mutual Aid Group was established in 2005 with an aim to support children with rare diseases and their families and has been advocating enzyme replacement therapy for lysosomal storage diseases. The Joshua Hellmann Foundation for Orphan Diseases was established in 2009 with the mission of advancing the awareness, diagnosis, treatment and research of orphan diseases. It also aims at improving the welfare of children with orphan diseases in Hong Kong.

Historically the HKPSEM focused on endocrine disorders while the HKSIEM focused more on IEM/IMD even though there is significant overlap in the personnel involved in both societies. A number of paediatric endocrinologists also take care of patients with IEM/IMD. Personnel who are currently involved in IEM are from a much more diverse background including not just paediatric

endocrinologists but also paediatric metabolic clinicians, paediatric neurologists, chemical pathologists, geneticists and others.

Upon commissioning of the Centre of Excellence in Paediatrics (CEP) to be opened in 2018, there is urgency for the provision of subspecialty training in HK. In 2012, the councils of the HKSPEM and HKSIEM reached the consensus of combining the training programmes on Paediatric Endocrinology and Inborn Errors of Metabolism together as one programme. Consensus that Inborn Errors of Metabolism be incorporated together with Paediatric Endocrinology as **Paediatric Endocrinology and Metabolic Medicine (PEMM)** was reached by paediatricians practising PEM and IEM based on the following main considerations: 1) as of current local clinical practice, a great proportion of IEM patients are looked after by paediatricians practicing PEM, 2) historically, IEM has been incorporated within the training syllabus of the Hong Kong College of Paediatricians under the Endocrinology and Metabolism section. IEM has also been included in the training curriculum of Endocrinology, Diabetes and Metabolism of the Hong Kong College of Physicians as well.

The new combined subspecialty programme is titled **Paediatric Endocrinology and Metabolic Medicine (PEMM).** This proposal is based on previous discussions, taking into account the local setting and consensus among paediatricians practising PEM and IEM in Hong Kong with inputs and comments from external referees. The subspecialty training programme on PEMM outlined here aims to provide structured training to paediatricians who are interested in this subspecialty of paediatric endocrinology and metabolic medicine and dedicated to the care of patients with endocrine and inborn errors of metabolism/ inherited metabolic diseases.

Scope of the subspecialty

Paediatric Endocrinology and Metabolic Medicine (PEMM) is the branch of medicine concerned with the study and research of the diseases of the endocrine organs, disorders of hormone systems and their target organs as well as inherited metabolic diseases encompassing various inborn errors of metabolism. The subspecialty of Paediatric Endocrinology and Metabolic Medicine (PEMM) encompasses all aspects on the diagnosis, assessment and management of paediatric patients with endocrine and inherited metabolic disorders.

Objectives

The training programme intends to:

1. Provide a structured training curriculum and broad experience in paediatric endocrinology and metabolic medicine;
2. Ensure a thorough and up-to-date understanding of the normal physiology of the endocrine systems and metabolic pathways of the body;
3. Establish clearly defined standards of knowledge, skills and attitudes required to practise endocrinology and metabolic medicine at secondary and tertiary care levels
4. Improve the standard of care for children with complicated endocrine and inherited metabolic diseases;
5. Encourage critical thinking, self-learning and a commitment to continuing medical education in endocrinology and inherited metabolic diseases;
6. Promote research and facilitate the translation of research findings into clinical practice.

Structure

Subspecialty training in paediatric endocrinology and metabolic medicine is a 3-year full time programme. Candidates must have completed the basic paediatric training and passed the MRCPCH (HK) / Intermediate Examination recognised by the Hong Kong College of Paediatricians. During their 3 years of higher training in general paediatrics, they are eligible for commencing the subspecialty training for up to one year with the approval of the Subspecialty Board of PEMM.

The 3-year training programme on PEMM includes at least 24 months of core clinical training and 6 months of elective (non-core) clinical training either in Endocrinology or Metabolic Medicine. The core clinical training is a hospital-based training on paediatric endocrinology and metabolic medicine. The time spent in endocrinology and metabolic medicine should be roughly 12 months each during this two-year training period. Trainees should acquire knowledge and fully understand the etiology and pathophysiology of a disease in order to make informed decisions concerning the diagnosis and management of a patient. Clinical experience must involve patients in all categories of paediatric

endocrine or inherited metabolic diseases, both acute and chronic. This should consist of a minimum of 3 sessions of outpatient clinics per week including endocrinology, diabetes and inherited metabolic diseases, clinical meetings such as X-ray meetings, case discussions, joint laboratory/ clinical meetings, journal club, inpatient care, peri-operative management of pituitary, thyroid, adrenal and other endocrine diseases, acute management of metabolic decompensation, consultations, daily ward rounds and on emergency call duties. During the elective (non-core) clinical training, trainee may take either the stream in endocrinology or metabolic medicine. At least 6-12 months of training in an overseas institution (tertiary care centre) with a well recognised training programme subject to approval by the Subspecialty Board is highly recommended and encouraged. This enables trainees to gain sufficient breadth of exposure and experience. Some outpatient experience in an adult endocrine unit (e.g. a weekly clinic for 3- 6 months) is desirable but not essential.

Trainee must acquire knowledge in laboratory techniques, use of laboratory methods, interpretation of the results and recognise the limitations/ pitfalls in the interpretation of laboratory results. Practical experience in an endocrine and metabolic laboratory is highly desirable. Trainee should also be equipped with the ability to utilise current diagnostic procedures of paediatric endocrinology and metabolic medicine. Experience in research relevant to endocrinology and/ or metabolic medicine may be accredited for a maximum of 3-6 months. Obtaining the qualification of a postgraduate diploma or degree (e.g. MSc, MPhil, PhD or MD) related to endocrinology and/or metabolic medicine may also be recognised as completion of training for up to a maximum of 6 months subject to approval by the Subspecialty Board. Trainees are advised to undertake endocrine/ metabolic -related educational activities such as journal clubs or case discussions during periods of non clinical training.

Training Syllabus

At the completion of training, trainees should demonstrate competencies and ability in the following aspects as a subspecialist in paediatric endocrinology and metabolic medicine

1. To acquire knowledge and experience in the underlying pathological and biochemical changes, clinical symptoms, investigations and management of the following:

1.1 Endocrine disorders

A) Disorders of growth and development including

- Intrauterine growth retardation
- Failure to thrive
- Skeletal dysplasias
- Chromosomal abnormalities and growth problems caused by Turner Syndrome, Noonan Syndrome, SHOX gene disorders, Prader Willi Syndrome and Silver Russell Syndrome
- Genetic short stature
- Constitutional delay in growth and puberty

- Growth hormone and IGF-1 deficiency and resistant states
- Delayed puberty
- Premature thelarche
- Premature adrenarche
- Pubertal gynaecomastia
- Precocious Puberty
- Excess growth and tall stature

B) Disorders of the thyroid gland and thyroid metabolism including
- Hypothyroidism,
- Hyperthyroidism,
- Goitre
- Thyroid cancer

C) Disorders of the adrenal gland including
- Congenital adrenal hyperplasia
- Addison's disease/hypoadrenalism
- Phaeochromocytoma
- Multiple endocrine neoplasia syndromes
- Cushing's syndrome
- Hypoaldosteronism
- Hyperaldosteronism

D) Disorder of the pituitary and hypothalamus including
- Craniopharyngioma, intracranial germ cell tumours and other pituitary tumours
- Congenital hypopituitarism and associated genotypes
- Hypothalamic syndromes
- Pituitary hormone replacement (acute and chronic)
- Diabetes Insipidus
- Syndrome of inappropriate antidiuretic hormone
- Treatment of hypernatremia and hyponatremia
- Hyperprolactinaemia

E) Disorders of sexual development including
- Assessment of ambiguous external genitalia
- Disorders of steroidogenesis
- Disorders of gonadal determination and differentiation
- Disorders of androgen action
- Counselling of parents and patients
- Leading multidisciplinary team in management and understanding the ethics behind it

F) Disorders of the reproductive system
- Female hypogonadism
- Male hypogonadism
- Adolescent menstrual disorders

G) Disorders of bone and mineral metabolism including
- Hypercalcaemia
- Hypocalcaemia
- Parathyroid diseases
- Disorders related to vitamin D metabolism
- Disorders of bone mineralization and metabolism
- Osteroporosis and chronic steroid use
- Osteogenesis imperfecta
- Bisphosphonate therapy

H) Follow up of adverse endocrine effects of childhood malignancy (growth and weight, puberty and bone density)

1.2 Diabetes and related disorders
- Type 1 diabetes mellitus
- Type 2 diabetes melltius
- Other types of diabetes including maturity onset diabetes of the young (MODY), neonatal diabetes and diabetes associated with endocrinopathies and genetic syndromes
- Role of nutrition, exercise and pharmacological management including insulin pump therapy
- Inpatient care of diabetic emergencies including diabetic ketoacidosis and hypoglycaemia
- Complications of diabetes including ophthalmic, renal, vascular and neurological
- Obesity and metabolic syndrome
- Lipid disorders

1.3 Inherited metabolic diseases (Inborn Errors of Metabolism)
- Disorders of aminoacid and peptide metabolism
  (Phenylketonuria, homocystinuria, MSUD, etc)
- Disorders of organic acid metabolism
  (Propionic acidaemia, methylmalonic acidaemia, isovaleric acidaemia etc)
- Hyperammonaemia and urea cycle disorders
- Disorders of carbohydrate metabolism
  (Glycogen storage disease, galactosaemia, fructosaemia, etc)
- Disorders of fatty acid oxidation (MCAD, LCHAD, etc)
- Disorders of ketone body metabolism
- Lysosomal storage disorders (MPS, Pompe disease, Fabry disease etc)

- Peroxisomal disorders (Adrenoleucodystrophy, Zellweger syndrome, etc)
- Disorders of purine and pyrimidine metabolism
- Disorders of metal metabolism (Wilson disease, Menkes syndrome, etc)
- Congenital lactic acidoses and metabolic myopathies
- Mitochondrial muscle. liver, neurological disorders
- Porphyrias
- Disorders of cholesterol, sterol and bile acid metabolism
- Disorders of vitamin metabolism (biotin, cobalamin, etc)
- Defects of membrane transport (lysinuric protein intolerance, etc)
- Congenital disorders of glycosylation
- Defects of connective tissues

Trainees are not expected to have in depth knowledge of all inherited metabolic disorders but should be aware of:

A) The biochemical consequences of a primary enzyme block in a metabolic pathway and the way in which clinical and pathological signs may be produced.

B) The major categories, presentation, investigation, mechanisms of inheritance, scope of prenatal and newborn diagnosis, principles of treatment for the above metabolic disorders

C) Acquire the clinical skills necessary in the assessment and investigation of metabolic causes for the following clinical scenarios:

- Hypoglycemia
- Hyperammonaemia
- Metabolic acidosis
- Acute encephalopathy
- Neurological conditions including mental retardation, regression, fits, movement disorders, myopathy, etc
- Liver diseases including acute liver failure
- Hepatosplenomegaly
- Cardiomyopathy
- Eye diseases
- Nutritional status and growth
- Dysmorphic patients
- Skeletal disorders
- Skin disorders
- Renal disorders including Fanconi syndrome
- Muscle diseases

D) Acquire the technical skills (working in close collaboration with pathologist through joint

laboratory/ clinical meetings) in the interpretation of the following investigative tools in the diagnosis and long term monitoring of metabolic disorders including understanding the analytical, physiological and nutritional factors that can influence their results:

- Aminoacids
- Organic acids (including interpretation of GC/MS data)
- Ammonia
- Lactate, pyruvate
- Intermediary metabolites: glucose, FFA, lactate, ketones
- Carnitines and acylcarnitines
- Glycosaminoglycans
- Enzymes studies: specific and non-specific assays
- Neurotransmitter and biogenic amine metabolites in CSF and other fluids
- Lipids and lipoproteins
- Peroxisomal enzymes and metabolites (VLCFA, pristanoate, phytanate, etc)
- Purines and pyrimidines
- Vitamin, minerals and other nutrient analyses including copper and ceruloplasmin
- Cholesterol and other sterols
- Porphyrins, bilirubin and related compounds
- Experience of the use and interpretation of molecular genetic techniques
- Biopsies, their indications for, planning and interpretation of:
    - skin biopsy (for fibroblast culture)
    - liver biopsy
    - muscle biopsy (needle and open)
    - other biopsies

E) Acquire the management skills needed for inherited metabolic disorders

- Emergency management including the use of emergency lifesaving drugs and assess the indications for and the use of:
    - peritoneal dialysis
    - haemodialysis, haemofiltration and related techniques
    - intracranial pressure monitoring
    - assisted ventilation
- Long term management
    - Drug management with an understanding and experience of the drugs used for the treatment of metabolic disorders.
    - Dietary management (working in close collaboration with dieticians)
        - evaluate the nutritional intake and requirements of patients
        - principles and practice of daily protein prescription for patients on low protein diets
        - principles and practice of daily carbohydrate prescription for patients with Glycogen storage diseases

- principles and practice of daily fat and fatty acid composition of diet for patients with disorders of long chain fatty acid oxidation and for patients with mitochondrial OXPHOS disorders
- principles and practice of galactose and fructose free diets
- principles of diet for peroxisomal disorders including adrenoleukodystrophy
- emergency /crisis/sick day regimens

Perioperative management of patients with various inherited metabolic diseases like fatty acid oxidation disorders, urea cycle disorders, organic acidaemias and glycogen storage diseases etc.,

- Transplantation - the metabolic indications for and long term follow up of patients who have undergone liver transplantation, haematopoietic stem cell transplantation and renal transplantation
- Enzyme replacement therapy for lysosomal storage disorders - be familiar with local HK treatment policy and guidelines, understand the efficacy and need for ongoing monitoring
- Keep up to date with new and on the horizon treatment modalities e.g. gene therapy and its relevance to IEM

F) Understand the indication, changing practice, individual country's practice of newborn screening and how it affects the management of inherited metabolic diseases at a population level and be prepared to advocate and implement in the suitable and appropriate time frame

2 Skills:

- Perform a comprehensive physical examination and medical history relevant to the endocrine and metabolic problem
- Use of laboratory tests and screening of endocrine/ inherited metabolic disorders
- Understanding of the principles and practice of hormone assay methods and molecular biology techniques
- Interpretation of results of hormonal assays in basal, stimulated and suppressed states
- Use and interpretation of radiographic imaging and radio-isotopic scanning in the diagnosis and management of endocrine/ inherited metabolic disorders

3. Attitudes

- Ability to provide adequate information, appropriate support and counselling to patients and families with chronic endocrin / inherited metabolic diseases
- Appreciation of patients' perception of health, concerns and the impact of the disease on the patient and family
- Ability to lead a multi-disciplinary team in the care of patients with complex endocrine or

inherited metabolic disorders

- Understanding of the importance of communication among health care providers
- Ability to liaise with adult endocrinologists/metabolic physicians to provide transition care
- Ability to liaise with colleagues in Primary and Secondary Care Paediatrics for the provision of high quality health care
- Ability to promote and to advance the health and well-being of individual patients, communities and populations

4. Managerial

- Ability to contribute to the effectiveness and efficiency of services in a health care organisation
- Ability to identify problem areas and improve service outcomes
- Ability in administrative issues including assigning duty rotations and organizing teaching programmes/ meetings
- Recognizing the importance of fair allocations of healthcare resources and budget control.
- Ability to inspire or enlighten others to share the vision, mission and goals of the organisation

5. Academic/Research

- Acquire knowledge in statistical methodologies, epidemiological principles and evidence-based medicine
- Critically appraise sources of medical information
- Conduct clinical audits
- Acquire knowledge of principles in clinical research and reporting
- Contribute to the development of new knowledge in endocrinology/ metabolic medicine through research
- Ability to conduct teaching and presentations on research

6. Professional

- Understand the principles of medical ethics related to patient care and research
- Exhibit appropriate professional behaviours in practice, including honesty, integrity, commitment, compassion, respect and altruism
- Recognise the principles and limitations of patient confidentiality as defined by professional practice standards and the law
- Undertake continuing professional development

Requirements for Training Institutions

A training centre can be a single institution or a group of related establishments with each component considered as a unit. The Subspecialty Board will determine the duration of subspecialty training accredited to a unit which is dependent on the clinical activity load, case mix, allied health and other support and the number of accredited subspecialty trainers working in that unit.

A training centre must provide adequate experience in all fields of endocrinology and metabolic medicine including emergency care, inpatient service and outpatient specialist care. The quantity and quality of activities must be sufficient to provide adequate experience and exposure for a trainee.

The centre must have easy access and close relationships with other relevant specialists such as paediatric intensive care, nuclear medicine, imaging facilities, surgery, neurosurgery, gynaecology and laboratory facilities. Supportive service provided by dietitians, diabetic nurse educators, podiatrists, social workers, psychologists and others who may contribute to the quality of care of patients with endocrine or inherited metabolic diseases is essential for accreditation.

The training centre must provide in-service and continuing medical education/ continuing professional development in that subspecialty in the form of regular journal club, grand rounds, seminars, X-ray meetings and case audit meetings in accordance with College/ Academy Guidelines. Regular audits of clinical activities in the subspecialty must be performed.

The centre must provide evidence of ongoing clinical research. Basic textbooks in endocrinology and metabolic medicine should be easily available and there should be easy access to a comprehensive reference library either in paper or electronic format.

A trainer can supervise no more than two trainees either in the Subspecialty Training Programme or in the Higher Training Programme in Paediatrics and no more than three trainees at any one time. A subspecialty trainee should receive supervised training in at least two but not more than four accredited training centres. An individual trainee should be under the supervision of at least 2 accredited trainers during the 3-year subspecialty training programme. Accreditation of training centres will be undertaken by the Hong Kong College of Paediatricians every 5 years.

Requirement for Subspecialty Board

The subspecialty is supervised by a Subspecialty Board which is under the supervision of the Director of Subspecialty Boards of the Hong Kong College of Paediatricians and is represented by the Hong Kong College of Paediatricians at the Academy.

The Subspecialty Boards is responsible for

1. Setting the accreditation guidelines for the training programme of paediatric endocrinology and metabolic medicine
2. Accreditation of the subspecialty programme
3. Setting the criteria for accreditation of training modules (one module is defined as a 6-month period) within the training programme
4. Accreditation of an institution for the duration and type of training allowed

5. Accreditation of Subspecialty Training Programme Director and Subspecialty Trainers
6. Ensuring a high standard of practice in that subspecialty comparable to that in centres overseas by arranging peer reviews of the proposed Subspecialty Training Programme
7. Appointment of examiners and organisation of subspecialty board examinations
8. The administration, organisation and validation of continuing medical education / continuing professional development (CME/CPD) which must be fulfilled by all Fellows in paediatric endocrinology and metabolic medicine within the CME requirements of the Hong Kong College of Paediatrcians.

The composition of the Subspecialty Board should include six Fellows

1. Five Fellows in the subspecialty of paediatric endocrinology and metabolic medicine from University, Hospital Authority and private sector
2. One Fellow, not from the subspecialty appointed by the College Council
3. The Chairman of the Subspecialty Board will be elected by the Subspecialty Board members and appointed by the College Council.

Requirements for Subspecialty Training Programme Director

The Subspecialty Programme Director should:

1. Be a Fellow of the College in the subspecialty
2. Have at least 10 years of experience of good practice excluding the training period in the subspecialty
3. Be actively involved in teaching as evidenced by teaching of postgraduates in the subspecialty
4. Be actively participating in clinical audits and establishment of management guidelines
5. Be active in research with a track record in scientific publications
6. Participate and fulfill the continuing medical education / continuing professional development requirements of paediatric endocrinology and metabolic medicine
7. Have local or international standing in paediatric endocrinology and or metabolic medicine as evidenced by membership of learned societies, invitations for lectures and participation in local and international meetings / organisations
8. Be in full-time employment in an accredited institution and spend more that 50% of his / her activities in the practice of paediatric endocrinology and or metabolic medicine
9. Be re-accredited once every 3 years.

Requirement of Subspecialty Trainers

The Subspecialty Trainer should:

1. Be a Fellow of the Subspecialty of the Hong Kong College of Paediatricians
2. Have at least 3 years of experience of good practice excluding the training period. This rule will

be exempted in the first three years after the establishment of a new subspecialty.

3. Be actively involved in teaching, research and clinical service in paediatric endocrinology and metabolic medicine
4. Be in full-time employment in an accredited institution and spend more than 50% of his / her activities in the practice of paediatric endocrinology and or metabolic medicine
5. Participate and fulfill the continuing medical education / continuing professional development requirement of paediatric endocrinology and metabolic medicine
6. Be re-accredited once every 3 years.

Assessment and Exit Examination

The training programme for the trainee should be worked out by accredited subspecialty trainer in accordance with the trainee's own interests and available facilities of the institution. The plan should be submitted to the Accreditation Committee, Programme Director and the Subspecialty Board for approval. The application for subspecialty training and possession of certificate of Intermediate Examination or equivalent should normally be submitted at the end of the first year of Higher Training in General Paediatrics. The trainee admitted into a subspecialty training programme must undergo full-time subspecialty training. Regular review every 6 months will be required to allow for flexibility and early identification of problems or deficiencies. Annual assessment should be undertaken to state competencies achieved and to monitor progress within the teaching programme. Trainees should keep a written record of patients seen by them, procedures conducted, therapeutic interventions and follow-up in a logbook which should be kept up-to-date and endorsed by his/her trainer. The logbook should also contain information on educational activities, training received and problems encountered.

The trainee should attend and provide evidence of attendance at local and/or international endocrine and metabolic medicine meetings or training courses at least once per year. At least two presentations at meetings are required. In addition, trainee should actively participate and provide evidence of participation in at least one audit project.

Trainee should submit 2 dissertations on scientific papers relevant to endocrinology / metabolic medicine for assessment of which at least one is accepted for publication in an international or local journal upon completion of subspecialty training. The trainee should be prepared to discuss the dissertations in detail during a viva examination which will be held upon completion of subspecialty training. The competence and ability in various aspects of the trainee as a specialist in paediatric endocrinology and metabolic medicine will be assessed during the viva examination. Trainees who successfully pass the Portfolio assessment and Viva examination will be conferred Fellowship in the subspecialty of paediatric endocrinology and metabolic medicine.