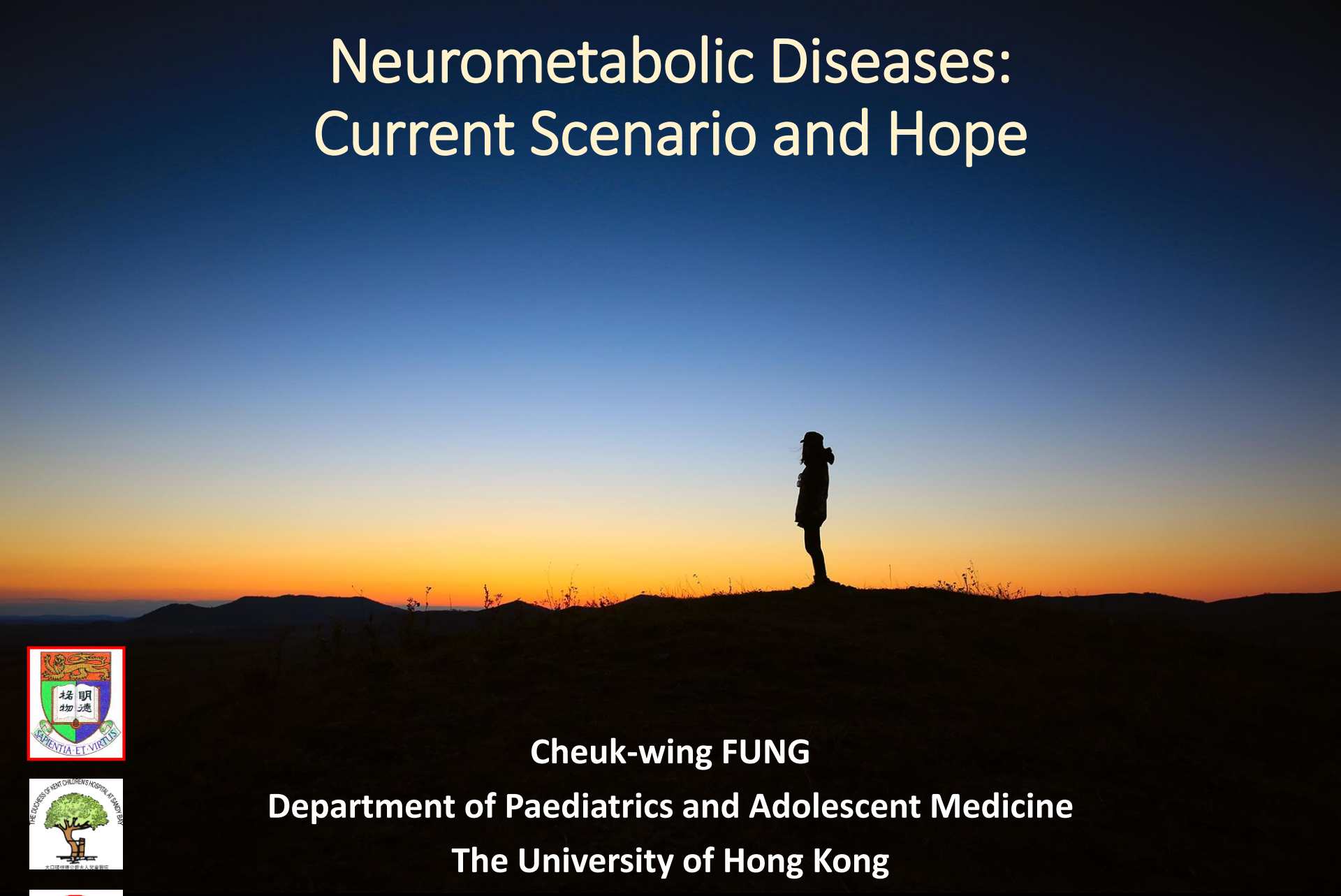
Neurometabolic Diseases: Current Scenario and Hope



Cheuk-wing FUNG

Department of Paediatrics and Adolescent Medicine

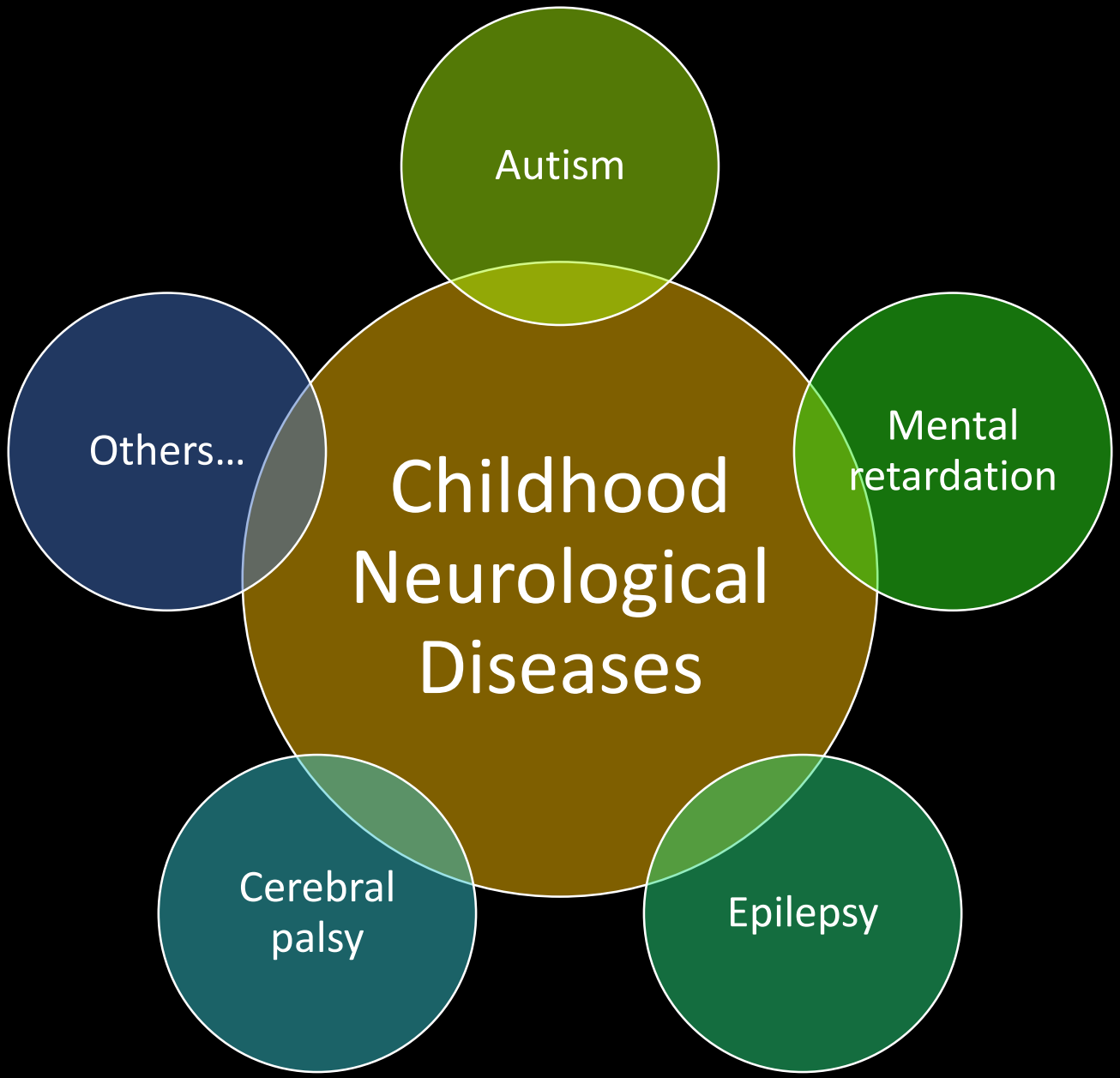
The University of Hong Kong

Queen Mary Hospital / Duchess of Kent Children's Hospital

Hong Kong

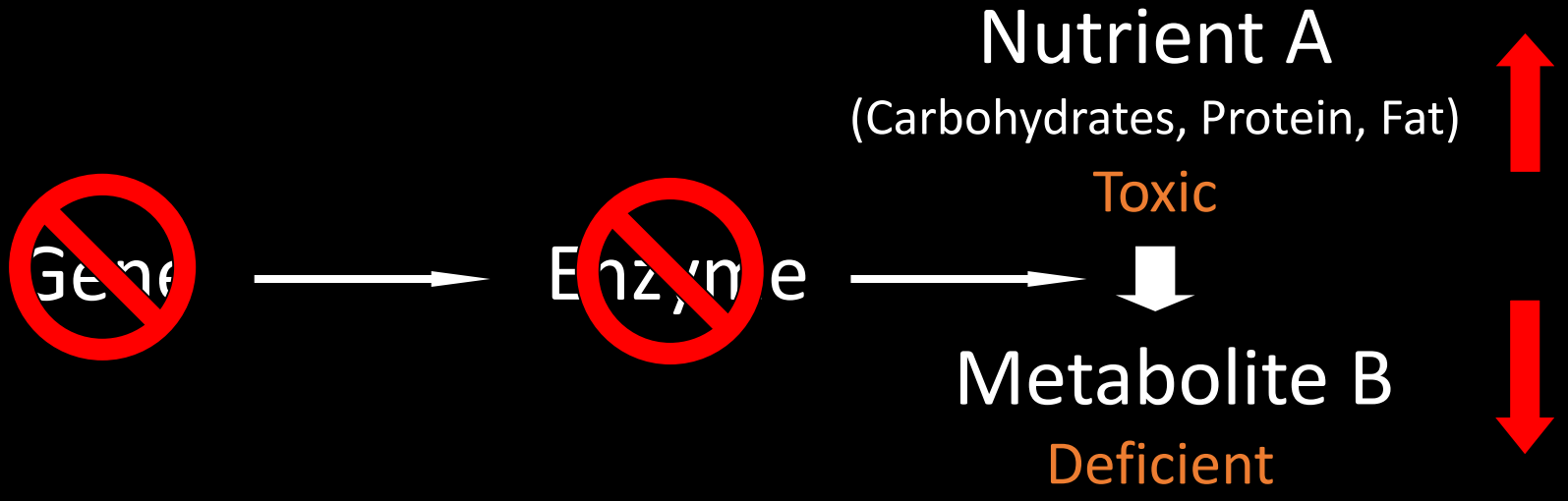
pexels.com

No cause, No cure……



Plasma amino acid: phenylalanine ***978***umol/L (Normal 30-75)

Inborn error of metabolism (IEM)



Neurometabolic Diseases:
IEM affecting nervous system

Incidence up to 1 in 591 to 6,370 i.e. at least 1,100 in Hong Kong

(Alfadhel et al 2016 Orphanet J Rare Dis)

Treatable Neurometabolic Disorders with Intellectual Disability
89 identified

(van Karnebeek et al 2014 Mol Metab Genet Metab)

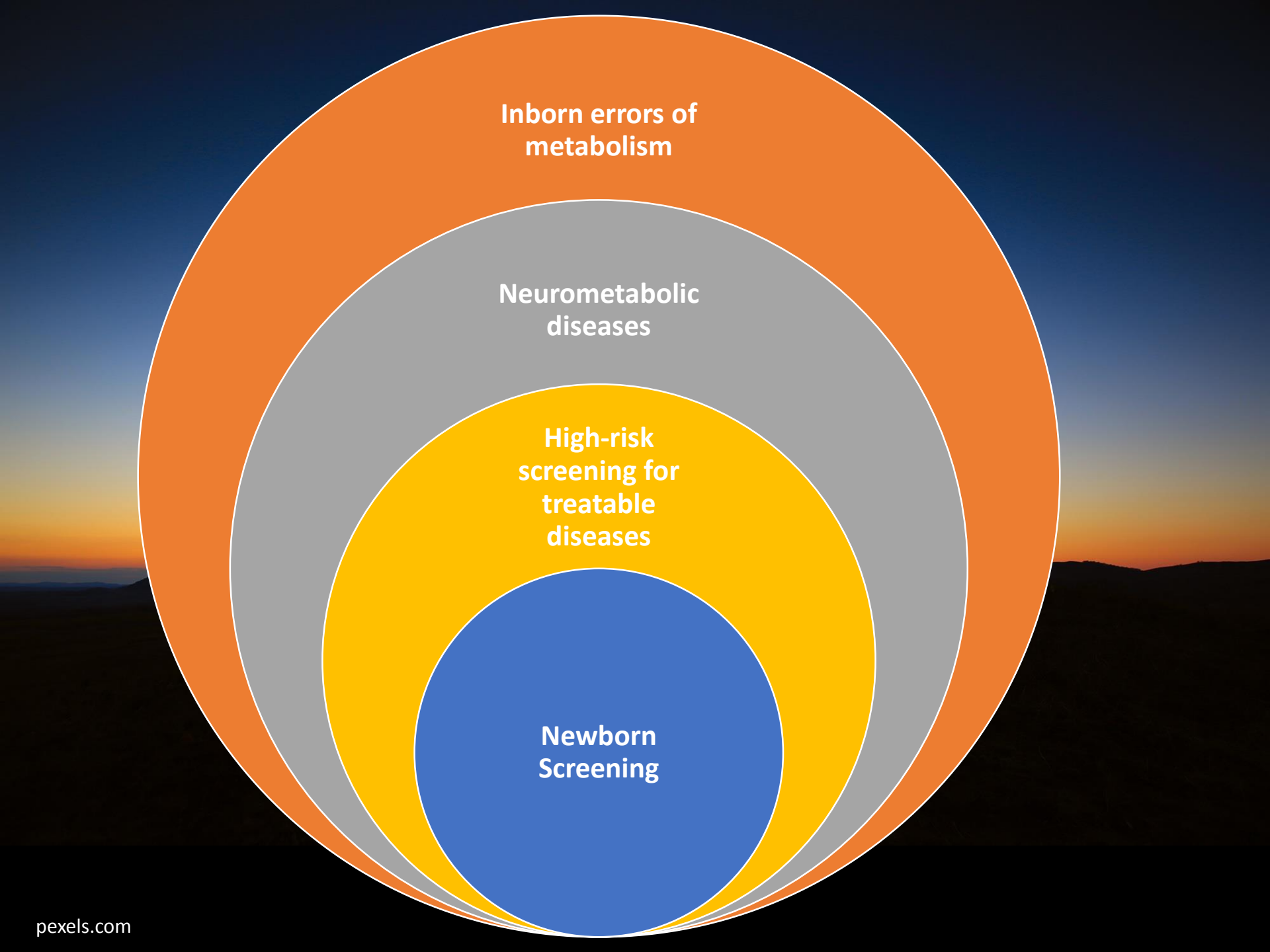
- ***Amino acid metabolism***
  - Dihydrofolate reductase deficiency
  - Hyperornithinaemia, Hyperammonaemia, and Homocitrullinuria (HHH) syndrome
  - Late onset Non-Ketotic Hyperglycinaemia
  - Phenylketonuria
  - Serine Deficiency syndromes
  - Tyrosinaemia type II
- ***Glucose transport and regulation***
  - Glucose transporter deficiency syndrome
  - Hyperinsulinism Hyperammonaemia syndrome
- ***Lysosomes***
  - α – Mannosidosis
  - Aspartylglucosaminuria
  - Gaucher Disease type III
  - Niem
  - Late c
  - Muco
- ***Neurotransm***
  - Biopt
  - Succi
  - Tyrosi
  - Vesicu
- ***Cholesterol a***
  - Cerebrotendinous xanthomatosis
  - Smith-Lemli-Opitz syndrome
  - Sterol-C4-methyl oxidase–like deficiency
- ***Fatty aldehydes***
  - Sjogren Larsson syndrome
- ***Creatine Deficiency syndromes***
- ***Hyperhomocysteine***
  - Cobalamin C, D, E, F, G deficiency
  - Homocystinuria
  - Late onset Methylenetetrahydrofolate Reductase deficiency
- ***Purine / Pyrimidine***
  - Lesch-Nyhan syndrome
  - Pyrimidine 5-Nucleotidase Superactivity

- ***Organic acids***
  - 3-Methylcrotonyl Glycinuria
  - 3-Methylglutaconic Aciduria type I
  - β – Ketothiolase deficiency
  - Cobalamin A / B deficiency
  - Ethylmalonic Encephalopathy
  - Late onset Glutaric Aciduria type I
  - Glutaric Acidaemia type II
  - 3-Hydroxy-3-Methylglutaryl-CoA Lyase deficiency
  - 2-Methyl-3-Hydroxybutyryl-CoA Dehydrogenase deficiency
  - Late onset Isovaleric Acidaemia
  - Maple Syrup Urine disease
  - Late onset Methylmalonic Aciduria
  - Mitochondrial 3-Hydroxy-3-Methylglutaryl-CoA Synthase Deficiency
  - Late onset Proprionic Acidaemia
  - Succinyl-CoA-Oxoacid CoA Transferase Deficiency
- ***Urea cycle***
  - Citrullinaemia type II

ase I deficiency
se deficiency
e deficiency

tic Acid and

  - Wilson disease
  - Aceruloplasminaemia
  - Menkes disease / Occipital Horn syndrome
  - Hypermanganesaemia with dystonia, polycythaemia and cirrhosis syndrome
  - Mental retardation, enteropathy, deafness, neuropathy, ichthyosis, keratodermia syndrome
- ***Vitamins / Co-factors***
  - Brown–Vialetto–Van Laere/Fazio Londe syndrome
  - Biotinidase / Holocarboxylase Synthetase deficiency
  - Biotin-responsive Basal Ganglia disease
  - Carbonic anhydrase VA deficiency
  - Cerebral Folate Receptor – α deficiency
  - Congenital Intrinsic Factor deficiency
  - Imerslund-Grasbeck syndrome
  - Molybdenum Cofactor deficiency type A
  - Pyridoxine Dependent epilepsy
  - Thiamine Responsive Encephalopathy
- ***Peroxisomes***
  - X-linked adrenoleukodystrophy


Inborn errors of metabolism
Neurometabolic diseases
High-risk screening for treatable diseases
Newborn Screening
pexels.com

Common views about neurometabolic diseases…

pexels.com

Since 2004

Co… …n

Endocrine / … …al Genetics

DIAGNOSIS

MANAGEMEN…

Service

Research

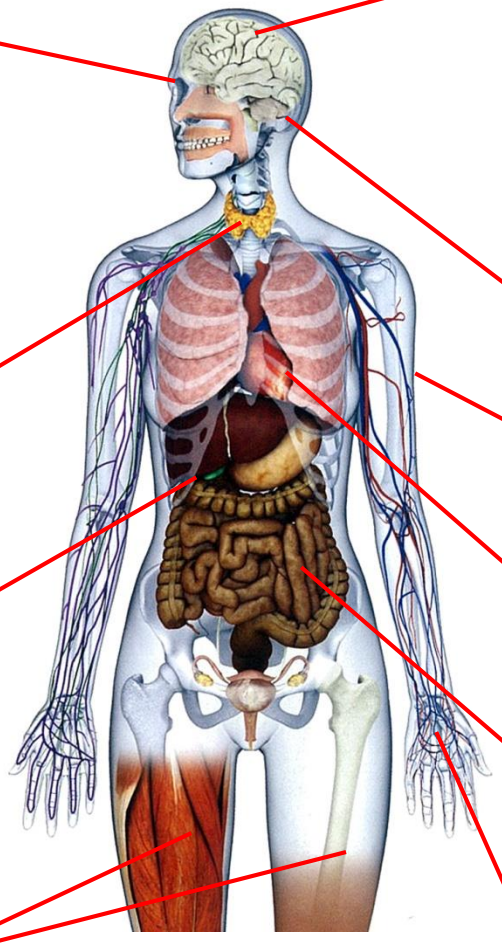
Gastroe… …spiratory

ENT … …thalmology

Dietitics | Optometry | Audiology | Physiotherapy | Nursing

Medical Social worker | Occupational therapy | Speech therapy | Clinical psychology

Mostly Untreatable…..



Eye
- Optic neuropathy
- Retinitis pigmentosa
- Ptosis / oculomotor defect
- Cataracts

Endocrine
- Hypothyroidism
- Diabetes
- Hypoparathyroidism

Kidneys, liver
- Renal tubular dysfunction
- Nephrotic syndrome
- Hepatic dysfunction / failure

Muscle, growth
- Myopathy, exercise intolerance, neuropathy
- Failure to thrive, short statue

Brain
- Stroke
- Neurodegeneration
- Developmental delay
- Epilepsy
- Movement disorder

Hearing
- Deaf

Skin
- Lipomatosis

Heart
- Arrhythmia
- Cardiomyopathy

Gastrointestinal
- Dysmotility
- Pancreatic dysfunction

Blood
- Sideroblastic anaemia
- Pancytopenia

Haas et al 2007 Pediatrics

Missions in the next 10 years

- Transitional care √
- Serving adult patients √
- Novel treatment discovery √
- Paediatric palliative care √
- Novel disease discovery √
- Patient registries and support groups