NUTRICIA
LIFE-TRANSFORMING NUTRITION
METABOLICS

Global Nutricia Metabolics Expert Day

19th February 2025
Nutricia Research Centre
in Utrecht, the Netherlands

PROGRAM

Chair: Prof. Nikolas Boy, Consultant for Paediatric Metabolic Medicine and Child Neurology, University Children's Hospital in Heidelberg

09:15-09:45 **Registration**

09:45-09:55 **Welcome and introduction**

09:55-10:25 **Breastfeeding and IMDs: how to calculate optimal intake of human milk**
Prof. Dr. Isidro Vitoria Miñana, Pediatrician, Unit of Nutrition and Metabolopathies, University Hospital La Fe, Valencia, Spain

10:25-10:55 **Importance of body composition in adults with IMDs: An innovative approach**
Prof. Dr. Luis Miguel Luengo, Endocrinologist, Clinical Nutrition and Dietetics Unit Lead, Infanta Cristina Hospital, Badajoz, Spain

10:55-11:25 **Crucial role of l-carnitine in dietary management of intoxication type IMDs**
Prof. Jolanta Sykut-Cegielska, Metabolic Consultant, Inborn Errors of Metabolism and Paediatrics (DIEMP)
Institute of Mother and Child, Warsaw, Poland

11:25-11:40 **Break**

11:40-12:25 **GMP: from science to clinical experience**
Jessica Kopesky, Senior Clinical Dietitian, Genetics Clinic Children's Hospital of Wisconsin, USA

12:25:13:25 **Lunch**

13:25-13:40 **Oral poster presentation specially selected from abstract submissions:**
Evaluation of nutritional status in patients diagnosed with glutaric aciduria type I aged six and above
Dr. Fatma Derya Bulut, Metabolic Paediatrician, Department of Paediatric Metabolism, Cukurova University, Adana, Turkey

13:40-14:10 **Understanding how protein metabolism may help tyrosine control in alkaptonuria**
Dr. Clare Soulsby, AKU Dietitian, National Alkaptonuria Centre at the Royal Liverpool University Hospital, UK

14:10-14.40 **Optimising dietary management of MSUD across the patient journey**
Prof. Dr. A. Çiğdem Aktuğlu Zeybek, Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Pediatrics, Division of Nutrition and Metabolism, Istanbul

14:40-15:00 **Break**

15:00-15.30 **Long term outcomes in GA1: the Irish experience**
Prof. Ahmad Monavari, Metabolic Consultant, Paediatrician, National Centre of Inherited Metabolic Disorders, Children's Health Ireland, Temple Street, Dublin, Republic of Ireland

15:30-16:00 **Severe neurological crisis in adult patients with tyrosinemia type 1**
Prof. Tarekegn Hiwot, Metabolic Consultant, University of Birmingham Hospital, UK

16:00-16:10 **Closing remarks**
Chair

This event is intended for Healthcare professionals and the agenda maybe subject to change.

Prof. Dr. med. Nikolas Boy

Consultant for Paediatric Metabolic Medicine and Child Neurology, University Children's Hospital in Heidelberg

Prof. Dr. med. Nikolas Boy is a consultant for Paediatric Metabolic Medicine and Child Neurology at the University Children's Hospital in Heidelberg since 2009. After his specialization in Paediatrics in 2014, his clinical and scientific activities have focussed on metabolic medicine, specifically glutaric aciduria type 1 (GA1) and intoxication-type metabolic diseases. Since 2015 he is the coordinator of the GA1 guideline group and has coordinated two guideline revisions.

He is currently the head consultant of the metabolic ward. In 2019, he received his Venia Legendi for his postdoctoral thesis 'Clinical long-term outcome and success of therapy in glutaric aciduria type 1'. In 2023, he was nominated as an Adjunct Professor for Paediatrics by the Medical Faculty of the University of Heidelberg. His current main research activities comprise long-term outcome and disease.

Prof. Dr. Isidro Vitoria Miñana

Pediatrician, Unit of Nutrition and Metabolopathies, University Hospital La Fe, Valencia, Spain

Isidro Vitoria Miñana is an Emeritus Researcher of the Nutrition and Metabolopathies Unit at the Hospital La Fe Research Institute in Valencia, Spain. He holds an MD, with speciality in Paediatrics, a PhD in Medicine and a Bachelor's in Chemistry from the University of Valencia. Isidro has extensive teaching experience, having served as an Associate Lecturer in Public Health and Pediatrics at the University of Valencia and as a Lecturer in Pediatric Nutrition at the University of Granada. He has been the Head Physician of the Nutrition and Metabolopathies Unit at La Fe University Hospital in Valencia (2008-2022), and has extensive clinical experience as a pediatrician specializing in nutrition (1998-2008), and as a Pediatric Primary Care Practitioner (1992-1998).

He is the author of the book *"Entendiendo las metabolopatías. Una guía sencilla con ejemplos"*. Ed. Plataforma. Barcelona. 2020 and collaborates with associations of patients with IMDs, coordinates courses on IMDs for the Spanish Society for Study of Inborn Error of Metabolism (AECOM), and coordinates the Nutrition Working Group at AECOM.

His research focuses on a) optimization of enzyme replacement therapies, b) quality of life in IMDs, c) European Galactosemia Network register and d) nutritional status in patients with IEM of amino acids and proteins.

Summary of talk: Breastfeeding and IMDs: how to calculate optimal intake of human milk

Human milk (HM) provides nutritional benefits and can be used as an intact protein in IMD of amino acids and proteins (IMD-AA-P). We developed a spreadsheet to calculate the amounts of special formula (SF) without the "limiting AA" and HM required in these patients under 6 months of age, which was published in Nutrients (2023;15:3566). Based on this work, we designed a website that allows the calculation of the amount of SF and HM or infant formula. After entering the infant's weight and the "limiting" AA or intact protein requirement for the specific IMD, the website calculates the corresponding required volume of HM based on the AA concentration in HM. Next, the daily fluid intake (usually 150ml/kg/day) is calculated. The required daily volume of SF is the difference between the daily fluid intake value and the calculated volume of HM. The website allows you to calculate the required volume of extracted HM that may be needed for MSUD, MMA/PA or UCD. This tool has the advantages of versatility, speed and the ability to generate a report, but its recommendations are based on guidelines or relevant authors and experience is limited except in PKU. In any case, it is important to consider individual patient factors.

Prof. Dr. Luis Miguel Luengo Pérez

Endocrinologist, Clinical Nutrition and Dietetics Unit Lead, Infanta Cristina Hospital, Badajoz, Spain

Academic background: Luis M. Luengo has a background in Medicine (MD, 1997), Food Science and Technology (MSc, 2000), Medicine (PhD, 2003), Master in Basic and Clinical Human Nutrition (2001), Master in Medical and Clinical Management (2007), and Master in university teaching (2011)

1. *Clinical experience:* Dr. Luis Luengo has 27 years of experience as a physician; from 1998-2002 in Endocrinology and Nutrition, and since 2002, as head of the Clinical Nutrition and Dietetics Unit at University Hospital in Badajoz, Spain. He was trained in clinical nutrition at Hospital La Paz with Dr. Carmen Gómez-Candela (Madrid, Spain), and in inherited metabolic diseases (IMDs) with Dr. Mercedes Martínez-Pardo (Hospital Ramón y Cajal, Madrid, Spain), and with Júlio Rocha (Centro Hospitalar Lisboa Central, Portugal)
2. *Academic experience:* Luis M. Luengo has been a lecturer in Nutrition and Dietetics and in Endocrinology from 1999-2005, an associate professor from 2005-2020, and a full professor since 2020 at the Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, University of Extremadura, Spain
3. *Professional activity:* Luis M. Luengo is a member of several scientific societies, including the executive board of SEEN and SENBA. He is also a member of the adult and nutrition working groups of SSIEM and AECOM, participating in the leaflets about several IMDs for patients and families in Spain.
   He is the founder of the IMDs in adults working group in SEEN.

Summary of talk: Importance of body composition in adults with IMDs: An innovative approach.

Body composition assessment has included anthropometry and some techniques, being Bioelectrical Impedance Analysis the most employed in clinic, but it is not always available.

GLIM criteria are recommended by ESPEN to diagnose malnutrition, and they include muscle mass assessment.

Nutritional ultrasound is a new tool to assess body composition, cheaper and more available, and it is useful in several clinical scenarios. For this, GLIM included nutritional ultrasound as a validated tool to assess muscle mass, with preference to anthropometry. Muscle thickness and cross-sectional area are the most recommended parameters for follow-up of muscle mass.

Functional performance is related to nutritional status, and this is why body composition assessment has to be complemented with functional evaluation to do a morphofunctional assessment of nutritional status. It must include strength, muscle mass (and quality), as well as functional ability.

Some IMDs (IMDs) have a known higher cardiovascular risk, but patients with other IMDs can increase their risk through excess adipose tissue. This is why cardiometabolic risk should be evaluated in adult patients with PKU and other IMDs. This morphofunctional assessment should include morphological and qualitative abdominal and muscle fat evaluation (muscle echogenicity) and, regarding function, at least, HOMA-IR, HDL/triglycerides, and PCR-us.

Prof. Jolanta Sykut-Cegielska

Metabolic Consultant, Inborn Errors of Metabolism and Paediatrics (DIEMP) Institute of Mother and Child, Warsaw, Poland

Jolanta Sykut-Cegielska, MD, PhD, Associate Professor at the Institute of Mother and Child in Warsaw, paediatrician, specialist in paediatric metabolic medicine, who for over 30 years has been dealing with inborn errors of metabolism. Currently, she is a Head of Department of Inborn Errors of Metabolism and Paediatrics at the Institute of Mother and Child. She was a President of the Board (currently Board member) of the Polish Society of Inborn Errors in Metabolism. She is a Corresponding Member for Poland and Hungary of the SSIEM (the Society for the Study of Inborn Errors of Metabolism). In the years 2006-2012 she was the national coordinator of the European network dedicated to rare diseases - ORPHANET Poland. She is also a member of the Coordinating Committee for the Treatment of Ultrarare Diseases and a member of the Council for Rare Diseases at the Ministry of Health. She is the editor-in-chief of a scientific journal the *Journal of Mother and Child*. She is the research supervisor of the Student Scientific Society of Paediatric Metabolic Medicine at the Medical University of Warsaw. Currently, she serves the third term as the National Consultant in the field of paediatric metabolic medicine. She cooperates with many local and international patient and parent organizations. She was awarded the *Angel of Medicine* in 2015, a prize given by patients and their families. She has published over 100 original articles in peer-reviewed journals.

Summary of talk: Crucial role of l-carnitine in dietary management of intoxication type IMDs

Carnitine is an essential water soluble molecule with many biological functions. It's endogenous synthesis (in 25%) in liver, kidney and brain is insufficient, so most of carnitine sources come form diet (mainly red meat). Carnitine homeostasis is maintained by balance between dietary intake, endogenous biosynthesis and and renal reabsorption. Plasma carnitine levels are age- and sex-dependent.

The main role of L-carnitine (metabolically active isoform) is shuttling long-chain fatty acids across mitochondrial membrane from the cytosol into the mitochondrial matrix for beta-oxidation. But in terms of treatment recommended in fatty acid oxidation disorders – in some of them supplementation of L-carnitine is controversial. Apart from many others biological functions, carnitine plays a crucial role in intermediary metabolism, particularly in inborn errors of metabolism presenting with intoxication syndrome, such as: methylmalonic, propionic, isovaleric acidurias and glutaric aciduria type 1, but also in maple syrup urine disease and urea cycle disorders. The therapeutic role of L-carnitine in above disease is to remove toxic metabolites that accumulate proximal to the enzymatic block and to restore free carnitine pool. Recent studies reveal that L-carnitine has also anti-inflammatory and anti-oxidative properties.

Jessica Kopesky

Senior Clinical Dietitian, Genetics Clinic Children's Hospital of Wisconsin, USA

Jessica Kopesky is a Senior Clinical Dietitian in the Genetics Clinic at Children's Wisconsin where she has enjoyed working with patients with inborn errors of metabolism, collaborating with providers across the state as a member of the Newborn Screening Metabolic Subcommittee, and participating as a research dietitian in multiple industry sponsored clinical trials since 2008. She earned her master's degree through Colorado State University in 2017 where her final project focused on the potential benefits of glycomacropeptide (GMP) compared to traditional amino acid based formulas in the management of PKU. In addition to her clinical role, she is actively involved in the Genetic Metabolic Dietitians International organization, in which she recently served as Co-Chair for the Technology Committee and Co-Chair for the Ad-Hoc Committee on Mentorship and is now serving on the board as President-Elect.

Summary of talk: GMP: from science to clinical experience

Take a walk through the journey of casein glycomacropeptide (CGMP) in the treatment of PKU and other inborn errors of metabolism. We'll briefly review the history and early science behind the development of CGMP, evaluate the current evidence supporting its safety and use in the treatment of PKU and tyrosinemia, discuss real patient cases to explore its clinical applications, and consider potential future developments.

Dr. Fatma Derya Bulut

Metabolic Paediatrician, Department of Paediatric Metabolism, Cukurova University, Adana, Turkey

Fatma Derya Bulut is Assistant Professor of Paediatric Metabolism and Nutrition at Çukurova University Medical Faculty. As a metabolic paediatrician, she specializes in the diagnosis and management of inherited metabolic disorders in both paediatric and adult patients. Her clinical and academic interests focus on advancing the understanding and treatment of rare metabolic disorders to improve patient outcomes.

Summary of talk: Evaluation of nutritional status in patients diagnosed with glutaric aciduria type I aged six and above

Co-Presenting Authors: Tuğçe Kartal[1], Süleyman Gönkek[1], Sema Uzunoğlu[1], Fatmanur Yavuz Alashqar[1], Ebru Çiçek Türköz[1], Nazmiye Tüzel Gündüz[1], Ezgi Burgaç[1], Fatma Derya Bulut[1], Deniz Kor[1], Halise Neslihan Önenli Mungan[1]

[1] Çukurova Üniversitesi Tıp Fakültesi, Çocuk Metabolizma ve Beslenme

Introduction: Glutaric aciduria type 1 (GA1) is an autosomal recessively-inherited metabolic disorder caused by the deficiency of glutaryl-CoA dehydrogenase enzyme. Early diagnosis through neonatal screening programs, combined with a lysine-restricted diet, carnitine supplementation, and intensified emergency management during catabolic crises, has been reported to significantly improve neurological outcomes. After the critical period of vulnerability to striatal damage (up to 6 years of age), dietary restrictions may be relaxed, although data on this matter are limited. Based on this premise, we aimed to evaluate the nutritional status of our GA1 patients aged six years and above.

Materials and Methods: The sociodemographic data, anthropometric measurements, biochemical parameters, and 3-day dietary intake records of 10 patients diagnosed with GA1 were evaluated.

Results: The mean age of the patients was 9.45±3.24 years, and 50% were male. All patients were diagnosed with prior clinical findings related to GA1 and had neurological sequelae. The mean body mass index (BMI) SDS was -1.69±2.56. Only one patient was being fed via a gastrostomy tube. The mean total energy intake of all patients was inadequate (1057.78±98.37 kcal/day). When evaluating macronutrient intake, 55.77±7.31% of energy intake was derived from carbohydrates, 12.22±3.41% from proteins, and 32±6.53% from fats. Adequate fibre intake was noted in only one patient. Calculation of micronutrient consumption revealed inadequate intake regarding recommended intake in paediatric age.

Discussion and Conclusion: Although the frequency of neurological crises, which cause sequelae, decreases after six years of age in GA1 patients, controlled protein intake by avoiding lysine-rich foods and ensuring adequate energy intake to support normal growth and development remain essential. However, problems such as hypotonia, movement disorders and swallowing dysfunction often lead to malnutrition in these patients. Since none of the patients were diagnosed through newborn screening, all had neurological complications which may lead to insufficient energy and micronutrient intake. We present our cases to emphasize the importance of continued dietary management in GA1 patients beyond the age of six.

Dr. Clare Soulsby

AKU Dietitian,
National Alkaptonuria Centre, Royal Liverpool University Hospital, UK

Clare has 35 years' experience as a dietitian gaining her BSc in Dietetics in 1989, MRes in 1995 and PhD in 2005. She has worked in a variety of clinical and academic roles.
Clinical experience: until 2022 Clare worked mainly in nutritional support roles in critical care, liver disease and intestinal failure.
In 2022 she made the big change to metabolic dietetics and took up her post at the National Alkaptonuria Centre at the Royal Liverpool Hospital.
Academic experience: Clare worked as a lecturer on Dietetic programs in Finders University (South Australia), University of North London and University of Chester. She also worked as a research assistant at Barts and the London Medical School where she gained her PhD.
Professional activity: Clare has been a co-author of the "estimating nutritional requirements" section of the PENG Pocket Guide, a publication used by UK dietitians to estimate requirements in patients requiring nutritional support. For the last 2 editions of the Pocket Guide, Clare has been the lead author on protein requirements for adults.

Summary of talk: Understanding how protein metabolism may help tyrosine control in alkaptonuria
In the UK, dietary management of Alkaptonuria (AKU) in patients taking Nitisinone focuses on limiting dietary protein to the minimum safe level of 0.75-0.83g/kg/day. Clare will talk about the dietary strategies used at the UK National Alkaptonuria Centre including how an understanding of protein metabolism may help maintain lean body mass and manage serum tyrosine levels. Clare will also present some practical tips on how to manage tyrosinaemia in AKU.

Prof. Dr. A. Çiğdem Aktuğlu Zeybek

Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Pediatrics, Division of Nutrition and Metabolism, Istanbul

Prof. Dr. Ayşe Çiğdem Aktuğlu Zeybek is a professor at Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, where her focus is pediatric nutrition and metabolism disorders. Since earning her medical degree from the same institution in 1995 and her subsequent rise to professorship in 2020, Prof. Zeybek has dedicated her career to the study and treatment of inherited metabolic diseases. Her expertise encompasses organic acidemias and amino acid-related disorders, areas in which she has contributed significantly through both clinical practice and research. Prof. Zeybek is respected for her practical approach to these complex conditions, which involves developing and refining treatment protocols that are now widely recognized within the medical community in Turkiye and internationally.
Prof. Zeybek is also an active academic mentor, guiding postgraduate students through their research projects. These projects often focus on new dietary management strategies and treatment options for pediatric metabolic disorders, contributing to the broader field of pediatric healthcare.

Her role extends beyond national boundaries through her active memberships in several professional organizations. She is the General Secretary of the Turkish Pediatric Association and a member of the Turkish Pediatric Nutrition and Metabolism Association, Society For The Study of Inborn Errors of Metabolism and The International Society for Neonatal Screening. Through these roles, she plays a critical part in shaping policies and clinical guidelines that advance pediatric healthcare in Turkiye.
Her research interests include innovative treatments for organic acidemias, the management of dietary therapies in rare metabolic disorders, and the impact of nutrition on pediatric health outcomes. Prof. Zeybek has also led several national projects investigating the prevalence of rare metabolic conditions and has authored numerous articles in high-impact international journals, helping to enhance the quality of life for children with metabolic disorders.
Through her teaching, research, and professional service, Prof. Dr. Ayşe Çiğdem Aktuğlu Zeybek continues to influence the fields of pediatric nutrition and metabolism, advocating for comprehensive approaches to treatment that benefit patients and their families.

Prof. Dr. A. Çiğdem Aktuğlu Zeybek

Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Department of Pediatrics, Division of Nutrition and Metabolism, Istanbul

Summary of talk: Optimising dietary management of MSUD across the patient journey

Maple Syrup Urine Disease (MSUD) is a rare metabolic disorder caused by a deficiency in branched-chain α-keto acid dehydrogenase, leading to the accumulation of leucine, isoleucine, and valine. Without proper management, MSUD can result in neurological impairment and metabolic crises. Early diagnosis through newborn screening is essential for initiating dietary intervention and preventing complications.

Dietary management is the cornerstone of treatment, requiring adjustments across life stages. In the newborn period, metabolic stability is maintained with BCAA-free formulas and controlled breastmilk or formula intake. During complementary feeding and infancy, low-protein foods must be carefully introduced to ensure proper growth while preventing amino acid imbalances. School-age children face challenges with social eating, necessitating structured meal planning and education. Adolescents are at risk of dietary non-compliance, emphasizing the need for self-monitoring tools and support. Pregnancy requires meticulous metabolic control due to increased protein demands and the risk of decompensation. Emergency protocols help prevent metabolic crises during illness. While future treatments, including gene therapy, enzyme replacement, and liver transplantation, may provide alternatives, long-term MSUD management today depends primarily on dietary therapy, requiring a personalized, multidisciplinary approach to optimize metabolic control and patient outcomes.

Prof. Ahmad Monavari

Metabolic Consultant, Paediatrician, National Centre of Inherited Metabolic Disorders, Children's Health Ireland, Temple Street, Dublin, Republic of Ireland

Prof. Monavari has more than 20 years experience in Inherited Metabolic Disorders in Ireland, the United Kingdom and Canada. He has been a permanent consultant in The National Centre for Inherited Metabolic Disorders (NCIMD) for more than 10 years. He is the Clinical Director of the NCIMD. Prof. Monavari is President and co-founder of the Irish Society of Inherited Metabolic Disorders (ISIMD).

Prof. Monavari is interested in all Inherited Metabolic Disorders. His clinical and research interests include Glutaric Aciduria, Urea Cycle Defects, and Maple Syrup Urine Disease (MSUD).

Summary of talk: Long term outcomes in GA1: the Irish experience

Glutaric Aciduria type 1 (GA1) is a rare neurometabolic disorder that can lead to encephalopathic crises and severe dystonic movement disorders. Adherence to strict dietary restrictions, in particular a diet low in lysine, carnitine supplementation and emergency treatment in pre-symptomatic patients diagnosed by high-risk screen (HRS) or newborn screen (NBS) leads to a favourable outcome.

We present clinical and biochemical characteristics and long-term data of Irish patients up to 40 years of age. Sixteen patients present clinically: median age at diagnosis of one year. Eighteen patients on high-risk screen and newborn screening: median age at diagnosis, four days.

Clinical events occurred after six years of age were unused but happened.

So, we support the recommendation for diet, carnitine supplementation, as well as emergency treatment for life.

Prof. Tarekegn Hiwot

Metabolic Consultant,
University of Birmingham Hospital, UK

Tarekegn Hiwot is Consultant in Inherited Metabolic Disorders and honorary professor at the University Hospital of Birmingham. He established and led the adult regional metabolic service along the national Lysosomal Storage Disorders (LSD) and Alström syndrome service based in Birmingham. Prof Hiwot main research interest focuses on monogenic obesity and insulin resistance, Fabry cardiomyopathy, small molecules related disorders and disease specific registry. Prof Hiwot has published more than 100 peer reviewed manuscripts in the journals such as NEJM, Nature, BMJ and Diabetes.

Summary of talk: Severe neurological crisis in adult patients with Tyrosinemia type 1

Tyrosinemia type 1 is an inherited metabolic disorder, if untreated, life expectancy rarely extends beyond 3 years. Since the introduction of 2-(2-nitro-4-trifluoro-methylbenzyol)-1,3 cyclohexanedione (NTBC) as a treatment in 1992, the natural history of the disease has transformed, with almost all early treated patients surviving to adulthood. This medical success story relies on parents' and patients' perseverance in adhering to treatment which includes lifelong medication and natural dietary protein restriction, in conjunction with tyrosine- and phenylalanine-free protein substitutes. Failure to adhere to their treatment, for some patients, leads to life threating neurological crises.

Notes

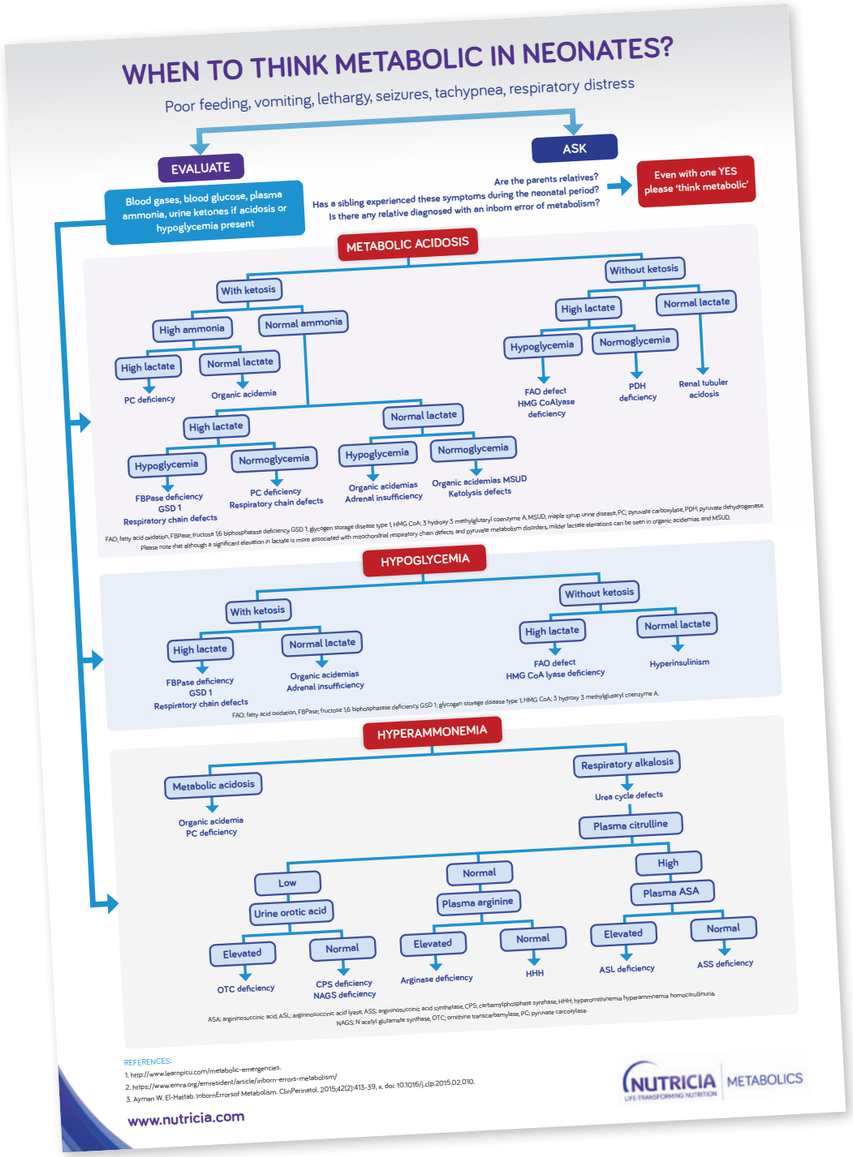
Notes

Early Diagnosis Algorithm

A tool to facilitate prompt diagnosis odf an Inherited Metabolic Disorder (IMD) created for the intensive care units in countries where expanded new born screening programmes may not be really available.

- Early diagnosis and intervention can help optimise patient outcomes
- If you suspect an IMD, the patient should be referred to an expert centre without delay

SCAN TO VIEW THE DOCUMENT




NUTRICIA
LIFE-TRANSFORMING NUTRITION
METABOLICS