On behalf of Nestlé Nutrition Institute Middle East, it is with great pleasure that we welcome you to the 6th NNI ME Symposium in Istanbul. Our goal is to contribute to the advancement of the medical community in the Middle East and Africa region and we are committed to supporting medical education initiatives in infant nutrition.

This educational forum features key clinical topics that will be presented by a group of renowned international and regional experts. The presentations will focus on a wide array of topics, including early programming, functional gastrointestinal disorders, the gut-brain-microbiota axis, and allergy prevention.

This forum will offer you an excellent opportunity to discuss issues related to your clinical practice with the faculty, encouraging a free-flowing exchange of ideas and practical solutions that are useful in improving patient outcomes.

We would like to extend our sincere gratitude for your participation and thank you for bringing your expertise to our gathering. We hope that this meeting will serve as an educational forum and effective tool for updating your knowledge and enhancing clinical value.

Yours sincerely,

Mohamed Salah
Chief Medical Officer
NNI MENA & WIN AfME
## Day 1: Friday 5th June / Chair: Prof. Ahmed El Beleidy

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# Agenda

**Day 2: Saturday 6th June / Chair: Prof. Robin Green**

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Today’s global health problems require that we manage the persistence of malnutrition and infectious diseases in some parts of the world as well as the epidemic of non-communicable diseases (NCDs) that has accompanied the social and economic development of nations. The double burden of under- and over-nutrition, in its various forms, affects those countries that contain the majority of the world’s population, with long-term health and major economic consequences.

It has become increasingly clear that prevention of the consequences of inadequate nutrition starts with conception. The development of stunting, cognitive deficits and cardiovascular disease due to early under-nutrition add to the burden of obesity and metabolic disease (including diabetes, cardiovascular disease and chronic immune problems), both of which start in early life.

Early nutrition is one of the most significant determinants of the immunologic and metabolic programming mechanisms that can modify all organ systems, leading to lifelong disease consequences. There is growing evidence that nutrition during gestation and the first 2 years of life (the first 1,000 days) is a critical “programming window” for future health. Gene expression can be modified in the early postnatal period, altering chronic disease risk through epigenetic mechanisms.

Interaction with various dietary and environmental proteins (including allergens) in the first 2 years of life, as well as interactions with environmental microbes – including the factors leading to the development of a specific gut microbiota – contribute to immune programming, which is associated with the development of chronic inflammatory diseases, particularly the broad range of paediatric and adult allergic conditions. Early diet also determines the metabolic responses of body tissues, and early growth. Early weight gain is a predictor of childhood obesity and its related negative consequences. High intake of energy and excessive intake of protein in early life contribute to the negative consequences of inadequate early nutrition.

Finally, food preferences and dietary habits are programmed in early life. High energy intake from foods with excessive sugar, protein and saturated fat and poor intake of fruit and vegetables, which are associated with obesity, appear to be set before 2 years of age. This, coupled with inappropriate feeding methods, from low breastfeeding rates to inappropriate bottle feeding and poor choices in weaning foods and feeding behaviours during weaning, all contribute to life-long diet patterns that make a mechanistic contribution to the NCD epidemic.

Early interventions to positively modify the factors that contribute to long-term disease are likely to be not only the most effective but also the least costly means of improving the health of future generations.
Early Programming
Professor Alan Lucas

This lecture will be a scientific adventure spanning a 38 year period of personal research on early nutrition and its later impact; and on the development of our counter-intuitive concept that accelerated early growth adversely programs cardiovascular risk and obesity – a concept that has major implications for breast feeding as a public health intervention and for the design of safer infant formulas.

Nutrient intake of the breast fed baby

Breast feeding medicine has recently developed as an evidence-based field with major and diverse implications for public health and clinical practice. However, only a few decades ago, this field often suffered from flawed science; and one good example was the flawed exploration of the dietary intake of the fully breast fed baby. The two important factors in breast milk that influence early growth are energy and protein, both of which were incorrectly researched resulting in misleading findings with major public health implications.

With regard to energy, in 1961 Macy reviewed 1500 publications on the composition of expressed breast milk; these and later analyses suggested the energy content of breast milk was 70-75 kcals/100ml. In 1977, I challenged those figures pointing out that because of the rise in fat content of breast milk during a feeding, obtaining representative samples of expressed milk was difficult. Instead, we used two novel approaches, one involving stable isotope probes, showing the energy content of the milk actually received by the baby (“suckled breast milk”) was only 57-61 kcals per 100ml. Breast milk fat – an important contributor to energy – was a massive 60% higher in expressed milk than in the milk received by the baby. Protein content of expressed breast milk was also previously over-estimated using methods suitable for cow’s milk that derive protein from nitrogen content – methods which erroneously count the high non-protein nitrogen in breast milk as protein.

Errors in estimating energy and protein intake of breast fed babies had little consequence until the 1970s when the new highly adapted formulas, modelled on breast milk composition, were introduced. To a large extent, because the expressed breast milk model was the wrong one, infant formulas contained inappropriately high energy and protein contents; and in consequence formula fed infants gained more weight and grew faster than those who were breast fed. In 1981 we showed formula fed babies had higher insulin levels even in the first week and speculated that this might have later consequences.

Nutritional programming

In 1982, recognising that both term and preterm infants were fed on diets providing major variations in nutrient intake – such as breast milk versus formula; and taking account of animal evidence of over 80 years standing that experimentally altering early diet and growth influenced later health and lifespan, we embarked on a series of studies with experimental design (efficacy and safety trials based on the pharma model) to test if early
nutrition could programme long term health and development (the term “programming” was coined by Lucas in 1983). In all we have conducted 29 randomised trials with long term follow-up that demonstrate the programming of CVD risk, brain, bones and immune health experimentally in humans.

In preterm infants, in whom it was possible to randomly assign to donor breast milk or preterm formula, we generated the first experimental evidence, published from 2001, that those fed breast milk rather than formula in the neonatal period had, at age 16 years, lower: diastolic pressure, LDL:HDL cholesterol ratio, ApoB: ApoA ratio, insulin resistance, CRP levels and metabolic tendency to obesity. Parallel evidence from our trials starting in 1982 with random assignment of preterm infants to standard or high protein and energy formula showed the standard, lower protein and energy formula, that promoted slower growth, also improved later cardiovascular risk.

We found that in full term SGA infants, randomly assigned from the early 1990s to formulas with higher versus standard protein contents, those assigned to higher protein formula and who grew faster in infancy, had reduced later blood pressure and body fatness at 8 year follow-up.

Postnatal growth acceleration hypothesis

In 2004 Professor Singhal and I proposed the hypothesis, rooted in published observations; our trials in preterm and SGA term infants; and in extensive animal evidence, that accelerated early growth increased the risk of later cardiovascular disease and obesity. We proposed that the lower risk of cardiovascular disease and fatness, shown observationally by others in breast fed term infants and shown experimentally by us in breast milk fed preterm infants could be explained in terms of lower early growth rate with breast milk. Our postnatal growth acceleration hypothesis is supported by over 60 subsequent studies including randomised trials.

Implications

Our findings had two key implications. Firstly that breast feeding should now be viewed as an evidence-based intervention to reduce the population risk of cardiovascular disease and obesity. Secondly, it was imperative (and long overdue) that consideration should be given to the radical redesign of infant formulas so that they promoted more optimal growth similar to that of the healthy breast fed baby.

Formula design and cardiovascular risk

It is now clear that over 1500 papers on the composition of expressed breast milk up until the 1970s were indeed misleading - and misguided the development of highly adapted infant formulas from the 1970s onwards; and that our evidence on the composition of suckled breast milk published in the 1980s (and more recently confirmed by others) provided a more sound basis for infant formula composition. Unfortunately, up to the early
Early Programming (continuation)

Professor Alan Lucas

2000s, those who advised industry on whether or not to make such radical changes in formulas found the evidence counter-intuitive that reducing energy and protein in formulas could be beneficial and it is only now that a new revolution in formula design will likely emerge.

We believe our trial in preterm infants commencing in 1982 of term versus preterm formula, diets that differed in both protein and energy contents, was the first randomised trial to show that formulas with major differences in energy and protein content could influence later cardiovascular risk. And our trials on term SGA babies from 1993 were the first to show manipulation of protein content in a formula could influence later blood pressure and body fatness in full term infants. From the initiation of our first trial it took over 20 years to see the testing of formulas with modified macronutrient contents designed for healthy term infants to reduce later CVD or obesity risk by slowing early growth to a rate comparable with that of the breast fed infant.

A broader perspective

Few public health policies in nutrition can be determined on the basis of one class of outcome and evidence will be presented to show programming of the brain must also be considered as part of the safety of current proposed changes in formulas – indeed for preterm infants rapid growth takes precedent because of the extreme sensitivity of the brain at low gestation.

Conclusion

This adventure has been a fruitful one for understanding the public health importance of breast-feeding and for underpinning new improvements in formula feeding that will help to address decades of increased later morbidity in formula fed infants that related, at least in part, to past flawed breast-feeding research.
Protein Content in Infant Formula: When More is Not Better

Professor Carlos Lifschitz

Approximately 43 million children under 5 years old are overweight or obese, 80% of whom live in developing countries even though the prevalence of obesity in industrialized countries is about twice that of developing countries. Multiple, but not all, studies support the role of breastfeeding in the prevention of obesity. In a systematic review that included 29 studies, 28 showed that breastfeeding was a protective factor against becoming overweight or obese (pooled odds ratio 0.87).

For non-breastfed infants, research has shown that the protein content of formula may have long-lasting effects on body weight. A multicentre, double-blind, randomized controlled trial in Belgium, Germany, Italy, Poland and Spain compared the effects of a low-protein versus a high-protein infant formula, started from 2 months of age, on length, BMI and weight-for-length at 24 months. After adjusting for baseline status, BMI z-score and weight-for-length z-score were 0.23 and 0.20 greater, respectively, in the high-protein formula group than the low-protein formula group. There were no significant differences in length between the high-protein and low-protein groups. The growth pattern of the low-protein formula group was similar to that of the breastfed group.

Another randomized controlled trial in the UK showed that 28% more protein in the infant’s diet increased children’s body fat by 30% at 8 years of age. An observational study in Denmark assessed the association between protein intake at 9 months and weight, height and skin-fold thickness at 10 years. There was a positive association between protein intake and weight and height, but no association was observed for BMI and skin-fold thickness. Follow-up results of this cohort were recently published and concluded that infant formula with a lower protein content reduces BMI and obesity risk at school age. Avoidance of infant foods that provide excessive protein intake could contribute to a reduction in childhood obesity.

In conclusion, at the present time evidence exists that the only way to decrease the risk of overweight and obesity is preventing excessive weight gain during pregnancy and breastfeeding and, whenever breastfeeding is not possible, using a low-protein formula (1.8 g/100 Kcal).
The Gut-Brain-Microbiota Axis

Professor Flavia Indrio

There is a rapidly growing interest in the characterization of the human intestinal microbiota, its composition and its multilevel effects in normal and pathological conditions. In addition to local intestinal effects, it is now evident that there is a close and continuous relationship between the gut, the intestinal microbiota and the brain, in a bi-directional pathway. The so-called ‘gut-brain axis’ is thought to play a role in modulating several metabolic, endocrine, immune and even nervous processes, and has become a possible target for therapeutic interventions. There are promising data about the clinical benefit of probiotics administration for treating functional and organic diseases.
**Lactobacillus reuteri: What is the Evidence in 2015?**

Professor Hania Szajewska

Probiotics are increasingly being used in the paediatric population. They are often discussed as a whole, but the efficacy of each probiotic strain should be evaluated separately. One of the most-studied probiotics is *Lactobacillus reuteri* DSM 17938, a daughter strain of *L reuteri* ATCC 55730. The latter was originally isolated from the breastmilk of a Peruvian mother but was found to carry potentially transferable resistance traits for tetracycline and lincomycin, so was replaced by *L reuteri* DSM17938, a strain without unwanted plasmid-borne resistance. *L reuteri* DSM 17938 inhibits pathogen growth and modulates the immune system.

The aim of this study was to systematically evaluate the evidence about the effectiveness of *L reuteri* DSM 17938 for treating and preventing diseases in infants and children. MEDLINE and the Cochrane Library were searched, with no language restrictions, for relevant randomized controlled trials and meta-analyses.

It was found that the use of *L reuteri* DSM 17938 may be considered as an adjunct to rehydration in the management of acute gastroenteritis. There is evidence that *L reuteri* DSM 17938 is effective in reducing the incidence of diarrhoea in children attending daycare centres but no evidence of its effectiveness in preventing nosocomial diarrhoea in children. The administration of *L reuteri* DSM 17938 is likely to reduce crying time in infants with infantile colic in exclusively or predominantly breastfed infants.

Preliminary data suggest that *L reuteri* DSM 17938 may be effective in the prevention of some functional gastrointestinal disorders, such as colic and regurgitation. This innovative approach needs further evaluation by an independent research team. Preliminary evidence provides a rationale for further assessing the efficacy of *L reuteri* DSM 17938 for treating functional constipation or functional abdominal pain. There are no safety concerns with the use of *L reuteri* DSM 17938 in non-immunocompromised subjects. There are also data to support the safety of using *L reuteri* DSM 17938 in preterm infants; however, evidence in very low birth weight infants (<1000 g) is still limited.
Functional Gastrointestinal Disorders: The Possible Role of Probiotics

Professor Flavia Indrio

Functional gastrointestinal disorders (FGID) are defined as a variable combination of chronic or recurrent gastrointestinal symptoms not explained by structural or biochemical abnormalities. FGIDs in childhood are age-dependent, so the Rome Foundation established two different paediatric committees to identify the criteria for FGID diagnosis: the Infant/Toddler (up to 4 years) Committee and the Child/Adolescent (4 to 18 years) Committee.

Infantile colic, gastro-esophageal reflux and constipation are the most common FGIDs that lead to referral to a paediatrician during the first 6 months of life; they are often responsible for hospitalization, feeding changes, use of drugs, parental anxiety and loss of parental working days with relevant social consequences.

Although FGIDs have been considered to be self-limited processes, it has been shown that a low-grade mucosal inflammation and immune/motor alteration could be found in infants affected by colic, regurgitation and constipation. This early traumatic insult to the intestine may represent a risk factor for the development of irritable bowel syndrome and psychological problems later in life. Recent work indicates a crucial role of the intestinal microbiota in the pathogenesis of gastrointestinal disorders as in FGID, and there are many studies that target probiotic therapy for specific diseases such as colic, regurgitation and constipation. Probiotics could play a crucial role in the modulation of intestinal inflammation.

Driving a change of colonization during the first weeks of life by giving lactobacilli may promote an improvement in intestinal permeability, visceral sensitivity and mast cell density, and probiotic administration in a preventive way may represent a new strategy for preventing these conditions, at least in predisposed children.
Evaluation and Prevention of Childhood Obesity in the MENA Region

Professor Gamal Samy

ENGAGE: Establishing Nutritional Guidelines For Achieving Healthy Growth Parameters

Abnormal growth in infancy (as under- or over-weight) can affect cognitive functioning and impair the immune system, increasing liability for infections as well as having long-term effects such as obesity, hypertension, diabetes and coronary heart disease. Worldwide obesity has nearly doubled since 1980 and the WHO estimates that around one in three of the world’s adults is currently overweight, while nearly one in ten is obese. This trend is known as the new world syndrome.

Worldwide prevalence of overweight and obesity in infants and children is high and increasing in developed and developing countries. In 2013, 42 million children under the age of 5 years worldwide were overweight or obese. Infantile obesity, when an infant is above the normal weight for his age and height, is a serious medical condition, the medical consequences of which include: type 2 diabetes, cardiovascular diseases, hypertension, orthopaedic problems, mental disorders, underachievement in school and low self-esteem.

Although one of the most important measurable parameters for abnormal growth is the body mass index (BMI), weight for length is used in young infants instead because BMI is based on height, measured while standing, which no baby can do well enough to measure.

The overall goal of the ENGAGE study is to develop an evidence-based consensus statement addressing efforts in the MENAP region to combat abnormal growth parameters in infants in relation to nutritional intake, particularly protein intake, during the first year of life. The main objectives are to adapt existing recommendations to local conditions in order to decrease the incidence of abnormal growth parameters in the region, with the final aim of creating a consensus statement on early infant nutrition in order to decrease the incidence of abnormal infant growth. It is hoped that the statement will be incorporated within the governmental healthy infant programmes.

In order to create the consensus statement, a group of expert professors formulated a survey for healthcare providers. Its preliminary results will be presented.

In conclusion, infant obesity is common and strongly predicts obesity at 24 months and older. Until very recently, paediatricians have not focused on obesity in babies, but infant obesity does exist and can be diagnosed as early as 6 months of life. Plotting the growth parameters as weight, length at every visit is very important. Paediatricians should explain the situation to parents and remind them of the hazards of infant obesity to their child’s future health. Breastfeeding is associated with a reduced prevalence of obesity, although the evidence is still inconsistent and limited. Recent advances in the ability to manipulate infant formula composition by reducing its protein content and bringing its composition closer to that of breastmilk might help prevent the rapid weight gain observed in formula-fed infants.
Allergy Prediction and Prevention: A MENA Perspective
Professor Robin Green

ACURATE: MENA Consensus Group for the Prevention of Food Allergy in the Young

Allergic diseases are common throughout the world. In two Turkish studies in children, the prevalence of atopic dermatitis was documented to be between 2.8 and 4.9%. Even more distressing is the fact that allergic conditions are increasing around the world. Unfortunately, by the time an allergic condition has manifested in a child, opportunities for prevention are very limited. Therefore, primary prevention of sensitization and clinical disease, early in life, is a viable strategy.

In order to implement the numerous available allergy-prevention strategies and interventions, it is essential to predict children at risk. The only reliable tool that has stood the test of time is the 'atopy family history score'. This tool scores mothers, fathers and siblings with two points for a doctor-diagnosed allergic condition and one point for a suspected condition. Allergy prevention strategies are important for a new child in a family with two or more points.

Allergy prevention could then occur at three time-points. Firstly, a number of interventions are possible during pregnancy. These include the avoidance of cigarette smoke exposure, and probiotic and long-chain fatty acid supplements. The next stage for intervention is the first 4 months of life, when exclusive breastfeeding is best; if it is not possible, a hypoallergenic partially hydrolysed whey milk formula is a very useful alternative. The final stage for intervention occurs between 4 and 6 months of age in an infant, when intervention is designed to promote oral tolerance. Allergenic food exposure, healthy gut microbiota promotion and immunoregulatory strategies are beneficial.

Recent research has shown that attempts to predict allergy in newborns and then institute prevention measures are relatively unfamiliar to healthcare practitioners in the Middle East. Together we should promote this strategy and limit the risk of allergy in children.

The ACURATE working group consists of regional and international experts who are currently working to develop a tool to identify infants at high risk of allergy in the MENA region. This tool will be incorporated into a consensus manuscript for the prevention of allergy in high-risk infants in order to increase awareness of, and promote best clinical practice for, allergy prevention amongst healthcare professionals.
The goals of the ACT group are to develop an evidence-based consensus statement addressing the prophylaxis of infantile colic and other functional gastrointestinal diseases in children in the MENA region and to create regional MENA guidelines for the prevention, diagnosis and treatment of colic that can be disseminated and activated through other formats and activities.

In order to develop the guidelines, existing international guidelines will be reviewed in the context of regional epidemiology and regional diagnostic and therapeutic practice, to include the upcoming ESPGHAN guidelines and the upcoming ROME IV diagnostic criteria for functional gastrointestinal disorders. Literature searches will also be performed to identify available literature addressing colic across the region, to cover the topics of awareness, risk factors, prevention, prevalence, consultation rates, treatment and challenges.

Regional guidelines need to be rigorous from a scientific perspective and to follow best practice based on clinical evidence, while stopping harmful practices that are based on customs that have no supporting evidence.

Accordingly, a six-question survey of healthcare professionals from across the region will also be conducted in order to understand prevalence and treatment practices that will inform the guidelines development:

1. What percentage of infants aged between 0–4 months presenting each month are diagnosed with colic?
2. What are the main tools used to diagnose infantile colic? (e.g. clinical, blood tests, instrumental.)
3. What are the major lines of treatment used?
4. Which existing treatments do mothers come to consultation with?
5. Do you suggest changing milk formulas in formula-fed infants diagnosed with colic?
6. Do you suggest changing feeding in breastfed infants diagnosed with colic?
Iron for the Brain
Dr Mohamad Miqdady

This talk will provide advanced understanding of several aspects of the importance of iron in the brain development of infants and young children.

Micronutrient deficiency is a common problem, estimated to affect around 10–20% of children. According to the WHO, the most common micronutrient deficiencies are iron, vitamin D, zinc and iodine. These deficiencies happen throughout the world with variable frequencies. Iron is the single most common deficiency worldwide.

There is an established association between iron deficiency at young age and negative effects on neurodevelopment, IQ and cognitive abilities. It is alarming to learn, as shown by several researchers, that some of these effects may be irreversible even after the iron deficiency has been treated. Therefore, prevention by providing a balanced diet that is rich in micronutrients in early childhood is of extreme importance. Providing a balanced diet for growing children is challenging to most caregivers.

Practicing paediatricians and healthcare providers should address this issue during well-baby check-ups as well as during ill visits. The American Academy of Pediatrics has published clear recommendations about prevention and screening. It states clearly the importance of iron-rich complementary foods for all infants, and obviously more so in preterm infants. The AAP recommendations and relevant studies and meta-analyses will be discussed in greater detail.
There is clear evidence that the phenotype of the human can be affected by epigenetic factors. Behaviour and cognition can be influenced by nutrition and the environment.

We know that low socioeconomic status as well as toxic environment have negative effects on vocabulary growth and neurobiological stress hormones, which may lead to delinquency. Neuro-imaging studies using perfusion and metabolism assessment show striking differences between the brains of children raised in a toxic environment and those of normal children.

Nutrition also plays a role in cognition. Exclusive breastfeeding for at least 4 to 6 months has been proven to improve IQ. There is a trend towards improved cognition with early administration of docosahexaenoic acid (DHA) in infancy. However, this has not yet been proved and more studies are needed. Iron deficiency definitely impacts neurodevelopment and seems to have a long-lasting effect. Proteins may also play a role, as protein deficiency has been shown to induce neuronal and axonal distortion.

The above statements show that brain plasticity is a reality. The brain is shaped early in life and the window of opportunity – the so-called ‘first 1000 days’ – is the period when sensory pathways and language as well as cognitive function start to grow and develop. The beneficial effects of both a rich environment and adequate nutrition are proven to lead to better cognition and behaviour later in life.
Nutritional Management of Premature Infants

Professor Ekhard Ziegler

Premature infants have very high nutrient needs that must be met in order to avoid postnatal growth failure. The food of choice, mother’s milk, does not provide nutrients in the necessary quantities, so additional nutrients must be provided, which is most commonly done by adding fortifiers to human milk. Parenteral administration of nutrients is often necessary because the infant’s gastrointestinal tract is too immature to absorb all the nutrients. In addition, the immature gastrointestinal tract is prone to necrotizing enterocolitis, making it necessary to proceed very slowly and cautiously.

Nutritional support of premature infants is provided during several successive phases. During the immediate neonatal period, nutrients are provided parenterally in amounts that allow the infant to continue in an anabolic state. While parenteral nutrition is provided, small amounts of milk are introduced into the stomach of the baby via feeding tubes (intestinal priming). This helps the immature gut to make the necessary transition to a more mature functional state that is characterized, among other things, by improved motility and more rapid gastric emptying. As motility matures, the amount of milk can be increased and parenteral nutrition can gradually be phased out. During this transition period, the goal is to maintain total nutrient intake at adequate levels.

When full feedings are reached, parenteral nutrition can be discontinued. Now the baby receives all its nutrients from human milk plus fortifier. Because of concerns about excessively high protein intake, the protein content of fortifiers has traditionally been kept low; only recently has the protein content been increased. Fortified human milk provides all the nutrients needed by the infant in approximately adequate amounts. When human milk is not available, special formulas for premature infants suffice.

At the time of discharge, the nutrient needs of premature infants remain higher than those of full-term infants. Consequently, before discharge, special post-discharge formulas are introduced, which are continued for several months after discharge. Infants receiving fortified human milk receive partial fortification for some time after discharge.
Allergic diseases affect more than 150 million Europeans and more than one billion people worldwide. According to the latest press release of the EAACI (April 2015), the prevalence of allergic diseases is expected to reach 4 billion by the 2050s. Children are especially affected: today, every third child in Europe suffers from an allergy, and up to 40% of children in Australia and New Zealand are affected by allergic disorders at some time during their lives (ASCIA 2013). To fight the allergy epidemic has therefore become a principal target, especially for paediatric allergologists.

Because the risk of allergy is determined by the interaction between genetic and environmental factors, decreasing allergy-provoking environmental influences is the goal for early intervention. Several interventional strategies have been tested, such as allergen avoidance (food/house dust mite); dietary intervention with vitamin D, omega-3 fatty acids or others; bacterial products (pro- and prebiotics); allergen immunotherapy (grass pollen, house dust mite); and drugs (anti-viral, cytokines, steroids); all have different results. Of the available strategies for primary allergy prevention, early nutritional intervention has become one of the most successful approaches.

For newborns at high risk of the development of allergic diseases, defined as having at least one first-degree relative with a history of allergy (mother, father or biological sibling), and who cannot exclusively breastfeed for the first 4 months of life, it has been shown that feeding certain hydrolysate infant formulas significantly reduces the risk of allergy, mainly atopic eczema, before school age. The findings from the German Infant Nutritional Intervention study (GINI), which investigated the allergy-preventive effect of three different hydrolysate formulas (a partial whey hydrolysate [pHF-W], an extensively hydrolysed whey [eHF-W] and an extensively hydrolysed caseine formula [eHF- C]) and a regular cow’s milk formula in children at high risk, clearly demonstrated that the two formulas pHF-W and eHF-C, but not eHF-W, significantly reduced the risk for atopic eczema up to the age of 10 years by between 35% and 45% compared with regular cow’s milk formula.

These results are of clinical importance because atopic eczema is not only the most frequent skin disease in early childhood but also lowers the quality of life of the child and the whole family to a great extent. These data are also important for the practical use of hydrolysates, because they show that the preventive effect of hydrolysates is not only dependent on the degree of hydrolysation, the molecular weight profile or the protein source (whey or casein), but also on the method by which epitopes with tolerogenic properties are created. Because the processing is different for each formula, only those hydrolysates that have shown to be efficacious in controlled clinical trials should be used for allergy prevention.
Guidelines for Allergy Prevention

Professor Yvan Vandenplas

Cow’s milk protein allergy (CMPA) is the most common food allergy in infants. All guidelines recommend exclusive breastfeeding up to the age of 4 to 6 months for all infants, without any dietary restrictions for the mother. There is no evidence that modification of maternal diet during pregnancy or lactation has a protective effect against allergy in at-risk infants; furthermore, a modified diet may create nutritional deficiencies in the lactating mother and infant. The introduction of solids should not be postponed; delay has been related to a higher incidence of allergy, as shown for peanuts.

Infants who are not exclusively breastfed and who are at risk of allergy should receive a prevention diet. At-risk infants are identified on the basis of a family history of one or more immediate family members (father, mother, brother or sister) with a history of atopic disease (CMPA, food allergy, atopic dermatitis, asthma, eczema). While some guidelines recommend partial hydrolysates, others do not differentiate between partial and extensive hydrolysates. Prevention should last for 4 to 6 months. Soy formula is not indicated for prevention. Non-cow’s-milk-based hydrolysates are also not recommended because these formulas may fail to introduce development of tolerance.

Owing to the difficulties in some regions in assessing the risk for allergy prenatally, where exclusive breastfeeding is impossible all infants should receive a hydrolysate for prevention of allergy until their risk has been assessed by a healthcare provider. All guidelines recommend using only those hydrolysates for which there is evidence of benefit.

According to today’s knowledge, hydrolysates in prevention should be restricted to at-risk infants because the metabolism of hydrolysed proteins has been insufficiently studied.
BIOGRAPHIES
Ahmed El Beleidy

Following his appointment as professor of paediatrics, Ahmed El Beleidy became head of the Paediatric Intensive Care Unit at the Cairo University Children's Hospital in 2011, and is currently the elected head of the Paediatric Department at Cairo University.

After graduating from the Kasr El Aini School of Medicine in 1978, Professor El Beleidy joined the Paediatric Department of Cairo University as a paediatric resident, where he later obtained an MSc and an MD in paediatrics.

Professor El Beleidy’s research interests include childhood nutrition, paediatric critical care, paediatric allergy, vaccinology and antimicrobial therapy. He is currently a member of the Egyptian Medical Association, the Pediatric Medical Association and the Egyptian Society for Neonatal and Preterm Care.
Jose (Pepe) Saavedra was born and raised in Peru. Following his medical training, as a fellow at the Nutrition Research Institute in Lima he began research on the dietary management of chronic diarrhoeal disease. Part of this time was spent working as a primary physician and studying diarrheal disease and malabsorption in the Amazon. Professor Saavedra received his medical degree from Universidad Peruana Cayetano Heredia, and his residency in pediatrics at State University of New York-Downstate Medical Center. He then went on to complete his fellowship in gastroenterology, hepatology and nutrition at the Johns Hopkins University School of Medicine, and then founded and developed the Johns Hopkins Children's Nutrition Center, which he directed for 10 years.

Professor Saavedra currently holds joint appointments in the Johns Hopkins School of Medicine and the Johns Hopkins Bloomberg School of Public Health. He is a fellow of the American Academy of Pediatrics. His academic and clinical work has focused on nutritional management of intestinal dysfunction and preventive nutritional strategies. Professor Saavedra carried out seminal work in the area of probiotics in paediatric populations and has an extensive record of publications in nutrition, particularly in the area of intestinal microbiota, immunity and effects on long-term health. Professor Saavedra continues to be clinically active, following his long-term patients at the Johns Hopkins Children's Center.

Currently, Professor Saavedra is global chief medical officer for Nestlé Nutrition. Over the past 10 years he has expanded the scientific innovation of Nestlé Nutrition. He has also enhanced the educational and research activities of Nestlé with a focus on infant health.

Professor Saavedra is chair of the board of the Nestle Nutrition Institute.
Alan Lucas

Alan Lucas founded the MRC Child Nutrition Research Centre at the Institute of Child Health in London, where he is now professor of paediatric nutrition. This is the largest centre of its type in Europe devoted to the impact of infant and child nutrition on health. Professor Lucas’ work on nutrition spans the period from foetal life to adolescence, although he has a particular interest in the programming effects of very early nutrition on long-term health and development. He has around 400 publications in the field and has received a number of awards for his work.
Carlos Lifschitz

Carlos Lifschitz is a consultant in paediatric gastroenterology at the Hospital Italiano in Buenos Aires, Argentina. He obtained his medical degree at the University of Buenos Aires in 1973, and has held residencies in paediatrics at North Shore University Hospital in New York and Buenos Aires Children’s Hospital.

Professor Lifschitz has held research fellowships at Baylor College of Medicine in Texas and Copenhagen University Hospital, and his previous academic appointments include associate professor at the Children’s Nutrition Research Center in the Department of Pediatrics at Baylor College of Medicine.
Flavia Indrio is currently senior consultant in paediatric gastroenterology in the Department of Paediatrics at the University of Bari, Italy. She teaches on a paediatric gastroenterology course for residents at the University of Bari’s School of Medicine, and is a member of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition Committee and various Italian societies including Pediatrics, Pediatric Gastroenterology and Neonatology.

Professor Indrio is president of the scientific board for the Continuous Medical Education of Family Paediatricians, and has been awarded the Ivan Casas Prize for research on probiotics. She is also a scientific coordinator of a research group studying functional gastrointestinal disorders in the Middle East and North Africa region.
Hania Szajewska

Hania Szajewska, MD, is professor and chair of the Department of Paediatrics at the Medical University of Warsaw. Since March 2014, she has been editor-in-chief (Europe) of the Journal of Pediatric Gastroenterology and Nutrition.

Professor Szajewska has broad interests in paediatric nutrition but her research focuses on probiotics and prebiotics, the effects of early dietary interventions on later outcomes, acute and chronic diarrhoeal diseases and coeliac disease. She is or has been actively involved in several European Union-funded projects (e.g., PREVENTCD; NUTRIMENTHE; EarlyNutrition) and is an enthusiastic advocate for the practice of evidence-based medicine.

Professor Szajewska served as a member of the Council of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and, more recently, as the general secretary of ESPGHAN. She also served as member and secretary of the ESPGHAN Committee on Nutrition. Currently, she is co-chair of the ESPGHAN Working Group on Probiotics and Prebiotics and chair of the ESPGHAN Working Group on Outcomes in Nutrition Trials.

Professor Szajewska has written more than 200 publications and 25 book chapters. (Citations 5144; Hirsch index 43 – Web of Science, February 2015.)
Robin J Green is director of paediatric services and paediatric pulmonology, paediatric intensive care and allergy services at the Steve Biko Academic Hospital, Pretoria. He is a full professor in the Department of Paediatrics and Child Health within the School of Medicine at the University of Pretoria. He holds a PhD and a DSc, and is a fellow of the Royal College of Physicians and past president of the College of Paediatricians of South Africa. He is also immediate past chairman of the Allergy Society of South Africa. The National Research Foundation rates him as an established researcher, specialising in paediatric pulmonology.
Gamal Samy

Gamal Samy Aly Mahmoud is professor of paediatrics and neonatology at Ani Shams University in Cairo. He is also president of the Egyptian Society for Neonatal and Preterm Care and vice president of the Egyptian Association of Paediatrics.

Professor Samy is editor-in-chief of the *Egyptian Journal of Neonatology* and associate editor of the *Egyptian Journal of Paediatric Allergy and Immunology*. He serves on the editorial boards of the *Journal of Perinatology* and the *International Journal of Neonatal Perinatal Medicine*.

His board memberships include the Egyptian Society of Paediatric Allergy and Immunology, the Arab Union of Paediatrics Societies and the International Academy of Neonatology. He is also a World Health Organization consultant on the International Committee of Vaccine Safety and Monitoring.
Aiman Rahmani

Aiman Rahmani is chair of the Department of Paediatrics and senior consultant in neonatology at Tawam Hospital, a major academic medical centre for the Emirate of Abu Dhabi and the UAE. He is also the regional director of the hospital’s Neonatal Resuscitation Programme, medical director of the Paediatric Service Line council of the Abu Dhabi Health Service Company and is appointed clinical professor of paediatrics at UAE University.

Professor Rahmani’s research interests include the pulmonary physiology of the newborn and neonatal nutrition. His current research projects are focused on the treatment of hypoxic ischaemic injury in infants and weight gain in neonates with very low birth weight in intensive care. He is also a regional principal investigator in the Global Kernicterus Registry.

Amongst other awards and honours, Professor Rahmani won the 8th Sheikh Hamdan Award for Medical Sciences and has been awarded an Excellence in Teaching Award by the College of Medicine and Health Science at UAE University.
Mohamad Miqdady

Mohamad Miqdady is American Board certified in paediatric gastroenterology, hepatology and nutrition. He is chief of the Paediatric, Gastrointestinal, Hepatology & Nutrition Division at Sheikh Khalifa Medical City (SKMC) in UAE. He is also adjunct staff at Cleveland Clinic, Ohio, USA.

Dr Miqdady completed his fellowship in paediatric gastroenterology at Baylor College of Medicine and Texas Children’s Hospital in Houston, Texas, USA. He held the position of assistant professor at Jordan University of Science and Technology for 6 years prior to joining SKMC.

His main research interests include feeding difficulties, picky eating, obesity, procedural sedation, allergic gastrointestinal disorders and coeliac disease. He has several publications and has authored book chapters as well as writing for www.uptodate.com. He serves on the editorial board of a number of journals including Gastroenterology & Hepatology.
Joseph Haddad

Joseph Haddad is currently professor of paediatrics at Saint George University Hospital in Beirut. He has acted as editor-in-chief for the *Journal of the Arab Forum of Neonatology* and as a member of the editorial boards of the *Journal Médical Libanais*, the *Journal de Medicine Perinatale* and the *Turkish Journal of Perinatology*.

His has undertaken research on the cholinergic system in sudden infant death syndrome, cerebral blood flow in the newborn, imaging of the brain in the neonate and the perinatal origin of adult diseases. He has published over 70 research papers, and has chaired seminars, congresses and symposia.

Professor Haddad is president of the Union of Mediterranean and Middle East Paediatric Societies, and vice president of the Association des Pédiatres de Langue Française.
Ekhard Ziegler

Ekhard Ziegler is a professor of paediatrics at the University of Iowa, USA. He received his medical education and paediatric training from Medical School, University of Innsbruck, Innsbruck, Austria. Professor Ziegler has conducted research on various aspects of the nutrition of normal infants as well as pre-term infants.

Professor Ziegler has been a member of the executive committee of ISRHML (International Society for Research in Human Milk and Lactation) since 2011, and is a member of various societies including The Nutrition Society, American Pediatric Society and American College of Nutrition. He has also been granted the Nutrition Award by the American Academy of Pediatrics. Professor Ziegler is an honorary member of the American Dietetic Association and the European Milk Banking Association.

He has published several articles and has authored more than five books.
Andrea von Berg

Andrea von Berg has worked in the field of paediatric allergology and pulmonology since 1984: first at the University of Bonn, Germany, and then, since 1988, in the Children’s Department of the Marien-Hospital Wesel, Germany. Her scientific interest has always been the prevention and treatment of allergic diseases in children. She has performed more than 80 studies in epidemiology and genetics, as well as clinical studies in the diagnostics and pharmacotherapy of allergic diseases in children.

Professor von Berg collaborates with numerous national and international research institutions and has more than 190 publications in peer-reviewed journals. Her h-index is 34 and her citation index 5874. She is a member of several paediatric and allergologic societies and acts as a reviewer for their journals.

Professor von Berg is coordinator of the large multicentre German Infant Nutritional Intervention Study, GINI, which she initiated with Professor Dietrich Berdel in 1995. In 1998, Professor von Berg founded the Research Institute for the Prevention of Asthma and Allergic Diseases in Childhood at the Marien-Hospital Wesel; she remained its director until she retired at the end of 2013. Since then, she has worked for the Institute as honorary director. Professor von Berg received the paediatric allergology award of the Society of Pediatric Allergology (GPA).
Yvan Vandenplas

Yvan Vandenplas is head of the Department of Pediatrics at the Academic Hospital of the Free University of Brussels. He is a paediatric gastroenterologist with a special interest in gastro-esophageal reflux and nutrition, as well as being an expert in prebiotics and probiotics in paediatric nutrition.

Professor Vandenplas has published over 250 papers in international peer-reviewed journals and has given over 500 lectures at international meetings. He has written chapters on gastro-esophageal reflux, probiotics and prebiotics in many pediatric textbooks.

Professor Vandenplas is a reviewer for many journals and is a member of the editorial board of several journals, including the World Journal of Gastroenterology, the Journal of Paediatric Gastroenterology and Nutrition, Nutrition, Current Nutrition and Food Science, Current Nutrition Reviews and Current Pediatric Reviews.