A summary of the latest scientific news

Update: Nutrition issues

Risk of cow’s milk allergy
What makes breast milk healthy?
Effect of HMO proven
New perspectives for FGID
ESPGHAN recommendations for irritable bowel syndrome
Focus on consequences: Overweight
Premature babies: Nutrition and brain development
Paediatricians and artificial intelligence
Dear Readers

It is well known that functional gastrointestinal diseases do not generally have serious medical consequences. Not only do they account for a considerable part of daily practice, they are also always accompanied by a great deal of insecurity and worry on the part of parents. So it is not surprising that this topic is also a target of scientific investigation.

It is becoming increasingly clear that the composition of the child’s intestinal microbiome plays an important role here. Likewise, human milk oligosaccharides, HMO, evidently have an influence on the development or prevention of gastrointestinal diseases. It is likely that they contribute significantly to the protection of the child’s body. Since it became possible to supplement conventional baby food with HMO, this topic has become a very exciting one.

Childhood overweight and obesity are not diseases in the strict sense, but paediatricians and nutritionists are increasingly confronted with these problems. Can long-term consequential damage be avoided or at least limited through early intervention, targeted counselling and dietary change? Some interesting research results have been published recently on this topic, and we’d like to inform you about them in this update. Detailed presentations, studies and webinars can of course also be found on the Nestlé Nutrition Institute web portal.

I hope you find the articles helpful and informative – happy reading!

Dr. med. Mike Poßner
Medical Director Europe
Nestlé Nutrition Institute

Current guidelines recommend the use of an infant formula based on hydrolysed cow’s milk protein for non-breastfed infants from families with a history of atopy in order to reduce the risk of allergic manifestations until the introduction of complementary food.

However, a systematic review (Boyle et al., 2016) concluded that a preventive benefit of such infant formulas was not proven. This question of whether such a benefit exists – a highly important issue in practice – was thus surrounded by uncertainty. However, Boyle’s review also included studies that examined a combination of different interventions. In addition, the data collected and evaluated did not all meet the requirements of a meta-analysis.

In contrast to the work of Boyle et al., Szajewska et al. (2017) conducted a meta-analysis exclusively on studies with whey-based, partially hydrolysed formulas from a single manufacturer in clearly defined high-risk populations. This confirmed a reduction in allergic diseases, although this was not significant in every age group.

The Nutrition Commission of the DGKJ (German Society of Pediatrics and Adolescent Medicine) therefore sees no reason at present to change the valid recommendations. Similarly, the European Food Safety Authority (EFSA) and the revised European legislation on infant formulas adopted in 2016 provide for the assessment of allergy-preventive effects only separately for individual products, and not for a group of different foods.

Non- or non-exclusively breastfed babies whose parents or siblings are affected by an allergy should receive a hydrolysed infant formula with proven preventive effects for the first six months until the introduction of complementary food.

Nutrition Commission of the DGKJ, 2018
CoMiSS improves cow’s milk allergy (CMA) diagnosis

The protein in cow’s milk triggers a cow’s milk allergy (CMA) in about 2–5 percent of all babies. However, detection and diagnosis is often inaccurate or delayed because the symptoms are unspecific. The Cow’s Milk-related Symptom Score (CoMiSS), developed by international experts, is intended to improve awareness of this risk.

In India, a multicentre, long-term observational study carried out for four months on infants aged 0–24 months has now been conducted to evaluate the positive and negative predictive value of CoMiSS. A prepared questionnaire was used to record the CoMiSS information. Cow’s milk allergy (CMA) was documented by way of an oral provocation test or prick test.

83 children were included in the study, 51 of them had gastrointestinal complaints (61%), followed by respiratory (41%) and skin problems (33%). A CoMiSS score > 12 was found in 72.3 percent of the children and 84.3 percent had cow’s milk allergy (CMA) confirmed by the tests.

The positive and negative predictive values of CoMiSS were 93 and 33 percent, respectively.

Checking with CoMiSS may help predict cow’s milk allergy (CMA) in children < 2 years and support an early diagnosis. Prospective studies should further evaluate the usefulness of this tool.

Prasad R et al. 2018

Tolerance development in pHF formulas

Partially hydrolysed infant formulas (pHF) have a lower allergenicity. A randomised double-blind study was carried out in Japan in order to evaluate whether oral immunotherapy with pHF increases the tolerated milk quantity.

In the first phase, the 25 participants aged 1–9 years were randomly assigned either to the pHF group or to the eHF group, which instead received an extensively hydrolysed infant formula (eHF). In the second phase, all children received a pHF.

The primary endpoint was the change in sensitivity between the beginning and end of the first phase. Second endpoints were the changes between the beginning and end of the second phase, as well as casein-specific IgE, IgG4 and basophilic activation.

The result:

- The tolerance value between the beginning and end of the first phase was significantly increased in the pHF-pHF group (p = 0.048), but not in the eHF-pHF group.
- The values of the other phases did not change significantly.
- There was a significant decrease in casein-specific IgE antibody levels between the beginning and second phase in the eHF group (p = 0.014).
- No participant showed systemic allergic reactions that would have required adrenaline or systemic corticosteroid administration after ingestion of the formula.

In children with cow’s milk allergy (CMA), tolerance to cow’s milk can certainly be improved with pHF formula compared to eHF formula.

Inoue C et al. 2018
Intestinal microbiome and HMO

Human milk oligosaccharides (HMO) are the third-largest solid component in breast milk after lactose and lipids. Around 200 different HMO have now been identified. In the milk of cows and other mammals they occur only in traces or do not occur at all. Some of their positive effects have been known for a long time. They seem to have a crucial influence on the colonisation of the intestinal microbiome of children.

What makes breast milk healthy?

The infant intestinal microbiome develops dynamically in the first weeks of life. The bacterial diversity increases with age, associated with changes in the composition of the microbiome. At the very beginning of life, the majority of newborns show a microbial structure consisting mainly of enterobacteriaceae. But within a few weeks, bifidobacteria dominate. At around 6 months and with the introduction of complementary foods, the composition approaches that of adults.

In caesarean section births, colonisation with bifidobacteria is significantly delayed. It was therefore thought that the mother’s vaginal microbiome was the source of the colonisation of the child’s microbiome. New studies show, however, that this proportion is relatively low, and that the mother’s intestinal microbiome is more important. In particular, bacteroids and bifidobacteria were the groups that were most clearly shared. However, this could only be observed with vaginal deliveries, not with caesarean deliveries.

The amounts of HMO in breast milk vary within the lactation period, e.g., shortly after birth the 2’FL content is very high, but then decreases. The milk group also plays a role. About 20 percent of breastfeeding mothers belong to the non-secretor group, which lacks the fucosyltransferase 2 gene (FUT2) of the secretors, resulting in a 2’FL deficiency.

This deficiency facilitates research into the health-promoting factors of HMO. For example, a prospective cohort study in Bangladesh with children who were exclusively breastfed up to 6 months showed that the offspring of non-secretor mothers had an increased risk of respiratory infections.

Sakwinska O, 2018

Section, secretor and intestinal microbiome

It is well known that the intestinal microbiome of newborn children does not develop as positively after a caesarean section as after a vaginal birth. However, it appears that certain human milk oligosaccharides (HMO) in breast milk can alleviate this disadvantage.

HMO are the third-largest solid component in breast milk. However, the composition of breast milk does not only vary during the lactation period, but also from mother to mother. The mother’s secretor genotype plays a special role here. Milk from secretor mothers contains 1-2-fucosylated HMO, which are absent in the milk of non-secretors.

Various bacterial strains in the child’s intestine have the capacity to utilise HMO. The differences in the composition of the infant intestinal microbiome of secretor (N=76) and non-secretor mothers (N=15) were investigated with regard to the delivery method. In vaginally born children there was no difference in the microbial composition...
The development of the microbiome from infant to toddler depends on a number of factors. However, until now, there had been no large multicentre study with many participants for the detailed characterisation of the microbiome in early childhood.

The present longitudinal study examined stool samples from 903 children (3–46 months) with 16S rRNA sequencing (n = 12,005) and metagenomic sequencing (n = 10,867) as part of the TEDDY study (The Environmental Determinants of Diabetes in the Young).

It emerged that the developing intestinal microbiome undergoes three distinctive phases: a development phase (3–14 months), a transition phase (15–30 months) and a stable phase (31–46 months). Breastfeeding, exclusively or partially, was the most significant factor associated with the infant microbiome. Breastfeeding was associated with higher levels of bifidobacterium species (B. breve and B. bifidum), and stopping breastfeeding led to faster maturation of the intestinal microbiome, characterised by the phylum firmicutes. The delivery method also has significant influence, characterised by higher levels of bacteroides species (especially B. fragilis) in vaginally born children. Bacteroids were also associated with increased intestinal diversity and faster maturation, regardless of delivery method. Environmental factors such as geographical location and household conditions (siblings, animals with fur) were also important covariates. An inserted case control analysis revealed subtle links between microbial taxonomy and the development of islet autoimmunity and type I diabetes.

Stewart CJ et al. 2018

Secretor – non-secretor?

- Secretor mothers have an active fucosyltransferase 2 (FUT2) gene. Approx. 80% of all women. Milk from secretor women is rich in 2’FL and other 1-2-fucosylated HMO.
- Non-secretor women lack the FUT gene, and their milk contains only very small amounts of 2’FL. Approx. 20% of all women.
- Lewis blood groups also seem to play a role in the quantity and structure of HMO.

These results show that maternal secretor status can be particularly influential in children with an already disturbed development of intestinal microbiota. These children could benefit from corrective supplementation.

Korpela K et al. 2018

Character of the microbiome in early childhood

Breastfeeding was associated with higher levels of bifidobacterium species (B. breve and B. bifidum), and stopping breastfeeding led to faster maturation of the intestinal microbiome, characterised by the phylum firmicutes. The delivery method also has significant influence, characterised by higher levels of bacteroides species (especially B. fragilis) in vaginally born children. Bacteroids were also associated with increased intestinal diversity and faster maturation, regardless of delivery method. Environmental factors such as geographical location and household conditions (siblings, animals with fur) were also important covariates. An inserted case control analysis revealed subtle links between microbial taxonomy and the development of islet autoimmunity and type I diabetes.

Stewart CJ et al. 2018
Review: HMO supplementation

Preclinical research has shown that HMO – and especially 2'-fucosyllactose (2'-FL) – are more than prebiotics and have numerous functions, including immune, intestinal and cognitive benefits.

Until now, breast milk was the only possible source of HMO. Now the most common HMO in breast milk, 2'-FL, is able to be synthesised – in a form structurally identical to the 2'-FL found in breast milk – and is available in some infant foods. Data from Allied & Complementary Medicine™, Analytical Abstracts, BIOSIS Previews®, Embase®, EMCare®, FSTA®; MEDLINE® and ToxFile® were evaluated for this review.

Here is a summary of the main study results with these 2'-FL supplemented infant formulas:

- Most studies investigated supplemented standard foods based on intact milk protein, one study evaluated a partially hydrolysed whey-based diet.
- A common finding of all the studies was that the added 2'-FL was safe, well tolerated and absorbed and excreted in a similar way to that in breast milk.
- Formulas supplemented with 2'-FL supported the immune system and the intestine.
- The examined formulas demonstrated fewer respiratory infections reported by parents, and improved symptoms of food intolerance.
- In composition and function, they are more similar to breast milk than conventional baby foods.

Tolerance of HMO supplementation

A prospective, controlled and double-blind randomised multicentre study investigated the tolerability of oligosaccharide-supplemented infant formula in healthy, mature infants.

The examination began 8 days after birth and lasted 28 days. The participants were randomly assigned to an intervention group (group 1, n = 35) and a control group (group 2, n = 30). Both groups exclusively received infant formulas, group 1 a formula supplemented with oligosaccharides (HMO: 0.2 g/L 2'-FL and short-chain fructooligosaccharide 2.0 g scFOS/L), group 2 a formula without oligosaccharides. A reference group was exclusively breastfed (reference, n = 36).

Results:

- No differences between the groups in stool consistency, amount and frequency of food intake, anthropometric data, spitting up frequency.
- Infant formula supplemented with 2'-FL and scFOS is safe and well tolerated.

Kajzer J, Oliver J, Marriage B 2016

HMO supplementation for “sensitive” babies

Studies on HMO-supplemented infant formulas have shown good tolerability and reduced occurrence of intestinal and respiratory symptoms. An as-yet-unpublished clinical feeding study investigated the effect on so-called sensitive children.

The prospective multicentre study included 59 healthy and mature but sensitive children. “Sensitive” was defined as having been described as “very fussy” or “extremely fussy” in a questionnaire for the past 3 days. Observation began at 7–42 days after birth, and the examination lasted 28 days. The participants received a partially hydrolysed whey-based infant formula supplemented with oligosaccharides (HMO: 0.2 g/L 2'-FL and short-chain fructooligosaccharides: 1.8 g scFOS/L).

Results:

- The observed symptoms included: fussiness, gassiness, crying episodes, spitting up frequency.
- 63.8% experienced an improvement in symptoms after one day.
- Decline in colic: 22% less on day 1, 30% less on day 2, 33% less in a week, 40% less after 28 days.
- Normal growth.

Reverri EJ et al. 2018

Abbott Nutrition, 2018 - unpublished
“We are at a turning point in HMO research.”

An interview with Dipl.-Ing. Dr. techn. Barbara Petschacher, Institute of Biotechnology and Biochemical Engineering at Graz University of Technology and acib – Austrian Centre of Industrial Biotechnology

Dr. Petschacher, human milk oligosaccharides, HMO, seem to be a particularly important component of breast milk?

In addition to important nutrients such as carbohydrates, fats and proteins, breast milk also contains indigestible complex sugars with special health-promoting effects for newborn babies. These are called human milk oligosaccharides. All HMO combined are present in breast milk at concentrations of 10–15 g/L on average. After milk sugar and fat, they make up the third largest solid component of breast milk in terms of quantity, if water is not counted.

What are HMO and how are they composed?

HMO are oligosaccharides, often with complex structures. Around 200 individual HMO structures have been identified so far. The five basic building blocks of HMO are the simple sugars glucose, galactose, N-acetylglucosamine, the sialic acid N-acety neuraminic acid and fucose. All HMO structures are made up of these. HMO are formed in the mammary gland. There, further sugar building blocks such as N-acetylglucosamine and galactose are attached to lactose with the aid of enzymes, so-called glycosyltransferases. The sugars are linked to each other in different ways to form branched and unbranched oligosaccharides. Sialic acid or fucose is attached to the ends of some of the chains. The simplest fucosylated HMO is 2'-fucosyllactose. Of all HMO, 2'-fucosyllactose is the most common, accounting for around 30% by mass of the HMO produced.

But the concentration and composition are not the same for all women?

On the one hand, the concentration of HMO changes during the lactation period. The concentration is highest in the colostrum, at 20–25 g/L, and the total HMO concentration decreases during the following months. However, recent studies show that individual HMO can also increase over time.

Another important difference between individual breastfeeding mothers has to do with genetics. Some women lack some of the enzymes to form special sugar linkages. So-called non-secretor mothers, for example, cannot form the linkage between fucose and lactose present in 2’-fucosyllactose. Others lack the enzymes for 3’-fucosyl compounds – these women are called Lewis negative. In addition to the effect on the composition of HMO, the same sugar structures are also missing from these women’s red blood cells, so they also differ in Lewis blood group characteristics.

HMO are evidently also responsible for the antimicrobial and immunomodulating effect of breast milk.

What does a different HMO composition mean for your children?

Non-secretor mothers can produce almost no 2’-fucosyllactose. Their milk therefore contains about one third less HMO than that of secretor mothers. No difference could be observed in the growth and development of children of secretor and non-secretor mothers in a study observing the first 4 months. However, another study has shown that in children born via caesarean section to breastfeeding non-secretor mothers, the bacterial population in the child’s intestines differed from that of naturally born children, while the bacterial population of children of breastfeeding secretor mothers was much more similar to that of naturally born children.

What are the main effects of HMO on the infant?

HMO have various effects on the health of the child, some of which have not yet been fully researched. One of these is their prebiotic effect. Since HMO are not digested by humans, they reach the large intestine and serve as nutrition for the intestinal microbiome. They promote the reproduction of certain health-promoting bacteria such as Bifidobacterium longum subs. infantis and other bifidobacteria in the child’s intestinal microbiome. They thus contribute to the formation of healthy intestinal flora, which in turn is important for protection against diseases such as inflammation or metabolic disorders, as well as strengthening the intestinal barrier function.

Another effect of HMO is that they directly support defence against pathogenic germs. Like red blood cells, human intestinal epithelial cells also carry sugar chains on their surface, which have the same structures as free HMO. Pathogenic bacteria use these sugar structures as docking sites to attach themselves to the body. However, if HMO are also present in the intestine at the same time, pathogenic bacteria cannot recognise whether they are sugar structures on a cell or free sugars and will also bind to HMO. Since HMO are present in free form, however, the pathogens bound to them are excreted.

HMO are also at least partly responsible for the antimicrobial and immunomodulating effect of breast milk. This is confirmed by a growing number of studies. Finally, studies in animal models even show a positive influence on brain development.

In view of these serious advantages, why have infant formulas supplemented with HMO only become available now?

Today we are indeed at a turning point in HMO research. For the first time, fermentative processes can be used to produce large quantities of some of these healthy sugars without having to rely on breast milk as a raw material. Now broad impact studies can be conducted with the most common HMO.

One study showed that an infant formula containing 2’-fucosyllactose and LNnT had no negative effect on the development of infants. A first clinical study on HMO-supplemented breast milk substitutes showed positive effects such as less waking up at night and less colic in children born by caesarean section. Parents also reported less bronchitis and other respiratory infections, and a two-fold decrease in the need for antibiotics. The intestinal microbiome of the children receiving such supplemented food was more similar to that of breastfed children.
Irritable bowel syndrome (IBS) and functional abdominal pain (FAP) are the most common functional gastrointestinal disorders. The role of probiotics in these cases is well documented, but there are noteworthy differences.

The etiology seems similar in infants and older children. They have a genetic predisposition, a higher incidence of previous diseases, or psychological factors are involved. IBS and FAP are often triggered by an infection. It should be noted that these patients show altered visceral sensitivity or hypersensitivity that is part of the gut-brain axis.

The problem for every treating physician is the question of diagnosis, because the lack of suitable biomarkers has led to the development of different criteria. The latest Rome IV recommendations highlight the importance of a positive rather than a negative diagnosis. There are various pharmaceutical treatment strategies, but reliable studies are lacking.

There are also nutritional recommendations. The FODMAP diet (= “Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols”) was the subject of a randomised controlled clinical trial (RCT) with 33 children who showed an improvement in symptoms as adolescents.

There are 10 RCTs on the efficiency of probiotics, with a total of 745 children. They evaluated a total of 4 probiotic strains: LGG, Lactobacillus reuteri DSM 17938. The exact definition of the strains is important. The studies on LGG showed effects primarily in the case of IBS, while those on L reuteri showed more effects on FAP. The frequency and severity of the pain decreased significantly in each case.

However, the effect of the placebos used for comparison should also be emphasised, as they also brought a significant reduction in pain in the studies. In almost half of the patients, the placebo was sufficient to improve the situation.

Summary:
- Probiotics differ in their effects.
- Only strains that have been tested for clinical applications should be recommended.
- For positive diagnoses with IBS or FAP, the following should be considered:
  - LGG more suitable for IBS
  - L. reuteri DSM 17938 more suitable for FAP

Do probiotics bring relief?
**Risk factor**

**cow’s milk allergy (CMA)?**

The influence and prevalence of cow’s milk allergy (CMA) in functional gastrointestinal disorders (FGID) are suspected but still unclear. The present study is intended to update the current understanding of the relationship between cow’s milk allergy (CMA) and functional abdominal pain in children.

In the literature studied, cow’s milk allergy (CMA) is considered a triggering or coexistent factor for a wide range of FGIDs in infants and young children. However, data on food allergies as a trigger are limited.

**ESPGHAN: Irritable bowel syndrome**

Growing evidence for the necessity of increased attention to nutrition and possible diets in children with irritable bowel syndrome (IBS).

An ESPGHAN working group therefore tried to define nutrition recommendations on the basis of the current evidence and to develop a helpful guideline for those doctors and nutritionists who are involved in the care of child IBS patients.

An international group of 20 experts on child IBS took part in an iterative consensus process following a call by the ESPGHAN. A total of 53 formal recommendations and 47 practice points were endorsed with an approval rate of at least 80 percent, covering the following topics: Evaluation of nutrition; nutrition as primary therapy for childhood IBS; need for macronutrients; trace elements, minerals and vitamins; pro- and prebiotics; special dietary restrictions; dietary supplements and the risk of IBS. **Miela E et al. Publish Ahead of Print**

**New Rome IV criteria**

Symptom-based diagnostic criteria for functional gastrointestinal disorders (FGIDs) were first presented at an international gastroenterology congress in Rome in 1988. In 1999, with Rome II, specific standardised criteria for FGIDs in children were presented for the first time.

Rome IV introduced a new definition of FGIDs as “disorders of gut-brain interaction” (DGBI). In recent years it has been recognised that mutual gut-brain interactions play an important role in the onset of symptoms.

In addition, the previous recommendations were examined and partially revised. The main changes concern infant colics:

The well-known Wessel criteria are no longer valid (Continuous crying > 3 hours/day on at least 3 days in the last week).

New Rome IV diagnostic criteria for infant colic:

- Age <5 months when the symptoms begin and disappear.
- Recurrent extended periods of crying, restlessness or irritability that occur without apparent cause and cannot be prevented or eliminated by parents/caregivers.
- No signs of failure to thrive, fever or disease.

Recommendations for the parents:

- Gentle massages can stimulate digestion and help to relieve stomach pain.
- Keep the child’s room dark and play soothing background noises such as the sound of the sea and soft music.
- A warm bath or hot-water bottle can calm the baby.
- It may help to wrap the baby in a towel or carry it on your body.
- Promising new treatment method: Lactobacillus reuteri DSM 17938. **Koppen IJN, 2018**

**1: Multifactorial pathophysiology of FGIDs**

Mucosal inflammation

Genetics

Psychological factors

Intestinal microbiome

Diet

Functional gastrointestinal disorders

Pensabene L et al. 2018

Updated nutrition issues
HMO structures influence NEC risk

Differences in the composition of human milk oligosaccharides (HMO) in breast milk may explain why some premature infants develop necrotising enterocolitis (NEC) even though they were exclusively breastfed.

The concentration of 15 dominant HMO in breast milk was measured during the neonatal phase, and it was investigated how their levels correlated with NEC, sepsis and growth in premature infants of extremely low birth weight (ELBW < 1000 g) fed exclusively on breast milk. Milk was collected from 91 mothers of 106 infants on days 14 and 28 after birth, as well as in the 36th postmenstrual week. The HMO were investigated using high-performance anion exchange chromatography with pulsed amperometric detection.

The diversity of HMO and the levels of lacto-N-difucohexaose I were lower among the mothers of NEC cases than among the mothers of non-NEC cases at all times. Lacto-N-difucohexaose I is produced only by secretor and Lewis-positive mothers.

There were also significant but inconsistent correlations between 3'-sialyllactose and 6'-sialyllactose with proven sepsis. Significant but weak correlations were found between different HMO and growth rates.

The authors conclude that differences in HMO composition in breast milk from different mothers are an important factor in why exclusively breast-fed ELBW premature infants can develop NEC.

Wejryd E et al. 2018

Probiotics improve growth of children with ELBW

Probiotics appear to reduce nutritional intolerance and the risk of necrotising enterocolitis in premature infants with a birth weight > 1000 g. But for extremely low birth weight (ELBW) infants this development is still questionable.

The study investigated whether oral supplementation with the bacterium Lactobacillus reuteri DSM 17938 can improve tolerance of enteral food intake and growth rates at ELBW <1000 g.

The randomised, double-blind, placebo-controlled study included 134 ELBW infants who were born before the 28th week of pregnancy. Daily supplementation with L. reuteri (1.25 x 10^8 bacteria/day) or placebo began within the first 3 days of life and lasted until the calculated 36th week of pregnancy.

Primary outcome was the feeding tolerance and secondary outcome was the growth rate, calculated as Z-score.

Feeding tolerance was similar in the probiotics and placebo groups. The time to complete enteral nutrition was 15 days in both groups. The Z-score of the head circumference from birth until the 28th day of life decreased in both groups, but decreased less in the group who received L. reuteri compared with the placebo group.

For other growth parameters, the two study groups were similar again. Lactobacillus reuteri therefore did not reduce the time until complete enteral nutrition in ELBW infants. But the supplemented children showed a better head growth rate in the first month of life.

Wejryd E et al. 2019

Deficiency despite enrichment

Sufficient energy and protein intake are important factors for the healthy growth of premature babies. One study investigated the relationship between nutritional practices and energy/protein intake during the transition from parenteral to enteral nutrition.

The retrospective analysis included 115 premature infants with very low birth weight (VLBW). The changes in protein and energy intake were examined in 5 phases: phase 1 (0% enteral); phase 2 (> 0, ≤ 3.3% enteral); phase 3 (> 3.3, ≤ 66.7% enteral); phase 4 (> 66.7, < 100% enteral); phase 5 (100% enteral).

Result:

In phases 2 and 3, those children who received enriched food received less protein than those who did not (-1.1 and -0.3 g/kg/d, respectively, P < .001). However, this negative connection was no longer observed after dietary practice was adapted. Despite the higher enteral protein content during phases 2 and 3 (0.3 and 0.8 g/kg/d, P < .001, respectively), children with early enrichment received less protein parenterally than those without (-1.4 and -1.1 g/kg/d, P < .001, respectively). Similar patterns were observed for energy intake. During phases 3 and 4, protein intake decreased.

Paradoxically, premature infants received less protein and energy on days with early enrichment. It can be assumed that this is because clinicians failed to observe easily accessible data showing a link between diet and overall nutrition of VLBW infants.

Falciglia GH et al. 2018
Update on nutrition issues

Power food for the brain

The progress that has been made in the treatment of premature babies is impressive. But it has also led to new challenges, such as the question of providing optimal energy supply to the brain through an appropriate diet.

The energy requirements of the growing brain are very high. The smallest premature babies need an intake of 120–130 kcal/kg/day. For comparison: a Tour de France winner needs about 100 kcal/kg/day for the most strenuous routes! The greatest need for energy is in the brain, so it is easy to understand how even small deficits can endanger the healthy brain development of the premature baby.

The development of the human brain is particularly rapid during the 3rd trimester of pregnancy and early childhood. Between the 24th week of pregnancy and the 2nd year of life, babies gain about 90 percent of their brain size. During this time, a series of neuro-anatomical development processes must take place.

At least five interrelated mechanisms connect nutrition and brain growth:

- Food for the tissue substrate: Macro- and micronutrients
- Energy to keep the system moving: Carbohydrates, lipids, proteins
- Signalling and growth factors: Energy, branched-chain amino acids
- Influences on gene expression: Folate, B12, iron, choline etc.
- Prevention of diseases: Breast milk reduces NEC and sepsis. And anything that reduces NEC and sepsis improves brain growth.

In the first days and weeks, parenteral nutrition (PE) is the only reliable means of providing very small premature babies with appropriate macronutrients. Insufficient care is associated with significant developmental disorders. And yet there are no clinical trials that show that PE leads to improved outcomes for the brain.

Other forms of nutrition could affect the brain:

Mother’s own milk: The strongest data on the association between the diet of premature infants and later brain outcome support the use of the mother’s milk. Unfortunately, however, most mothers are not able to cover 100% of the premature baby’s needs. Ways to supplement breast milk need to be discussed.

Donor milk: A Canadian study (n = 363; mean birth weight 996 g; 27th week of pregnancy) compared the effect of donor milk and infant formula on neurodevelopment and found no improvement.

Nutritional supplementation of breast milk: 14 studies (n = 1071) show a small increase in weight and/or length. But none of the studies show a benefit to the long-term outcome.

Special nutrient interventions: There have been studies on specific nutrients such as DHA or iodine, but there is little data on recommended amounts and most studies take little account of the cognitive outcome.

Observational studies point to the importance of breastfeeding even after hospital discharge, despite the associated slower weight gain.

Embleton N 2018
Children and adolescents of mothers with normal body weight and healthy lifestyle habits have an up to 75 percent lower risk of developing obesity. This is the conclusion of a large observational study by the Harvard T.H. Chan School of Public Health in America. Around 17,000 mothers and their 24,000 children (9–18 years) took part in the GUTS (Growing Up Today Study) project. The children’s body mass index (BMI) was determined and their diet and lifestyle were recorded with questionnaires.

1,282 (≈ 5.3%) of the children developed obesity in the following 5 years (BMI > 30). However, a healthy lifestyle of the mother evidently leads to a significant reduction in the risk of obesity. The risk was lowest when the mothers fulfilled the following conditions: normal body weight, regular exercise, non-smoker, moderate alcohol consumption and a „healthy“ diet with lots of fruit, vegetables and whole grains. A body weight in the normal range alone reduced the risk by 56 percent. Age, origin, medical history and social background played no role. The child’s lifestyle also had no demonstrable influence. The mother’s lifestyle thus seems to decisively influence the nutritional and exercise habits of the offspring. The authors therefore stress the importance of informing and training parents on this subject.

Dhana K et al. 2018

Childhood overweight is a worldwide problem. Recent research suggests that the intestinal microbiome plays a crucial and potentially causal role in the development of overweight.

A Norwegian prospective study (n = 165) investigated the early childhood intestinal microbiome on days 4, 10, 30, 120, 365 and 730 and the association with BMI Z-scores at 12 years of age. The study provides first indications that the intestinal microbiome at the age of 2 provides helpful information to identify adolescents at risk of becoming overweight at an early stage. This could enable more targeted early prevention.

Stanislawski MA et al. 2018
Stressed mother – overweight child?

Can maternal stress affect the development of weight problems in children? The results of a study by the Helmholtz Centre for Environmental Research (UFZ) suggest that this is the case. Infants seem to suffer more often from overweight when their mothers found the first year of the baby’s life very stressful. Girls seem particularly affected. These are the results of a study carried out on almost 500 mothers and their children. The BMI of the children was determined each year and compared with standard value curves. The mothers were asked to use questionnaires to document their emotional life, recording fears, tension, worries and distress, but also satisfaction. The data thus obtained were used to compare the subjectively perceived stress of the mother during pregnancy and the first two years of the baby’s life with the baby’s weight development between the ages of one and five years. According to the study, mothers who were stressed in the first year of their baby’s life were more likely to have overweight children than more relaxed women. Incidentally, girls were more overweight than boys, and it is suspected that they are more likely to react with cravings.

In contrast, the mother’s life situation during pregnancy, and also in the 2nd year of the child’s life, had no influence on the child’s weight. The first year of life thus seems to be a particularly sensitive phase for the child’s weight development. The authors therefore urge that mothers be supported in their everyday lives, especially in the first months after birth, and that they be protected from excessive stress.

Leppert B et al. 2018

Milk against metabolic syndrome

A recent study recommends milk consumption to combat the risk of metabolic syndrome in overweight children in America. The recommended amount of at least two glasses of any type of milk per day can lower insulin levels, an indicator of better control of blood sugar.

Michael Yafi from the University of Texas Health Science Center at Houston (UTHealth) comes to this conclusion after evaluating a study with 353 participants (3–18 years of age). An earlier study had already shown sufficient milk consumption in adults to have a similar positive effect. Yafi also stresses that only one tenth of young people would drink the recommended amount.

Consumption in the USA has declined massively in recent decades, with children and adolescents in particular consuming less than one cup of milk a day. Parents increasingly perceive milk as something bad, explains Mona Eissen, who is in charge of the study. But they should be encouraging their children to drink milk instead.

Metabolic syndrome is defined as the presence of at least 3 of these 5 factors, which increase the risk of diabetes, heart disease and stroke: High blood sugar levels, high triglyceride levels, high blood pressure, an excess of abdominal fat and low levels of “good” cholesterol.

Lecture by Michael Yafi 2018
Overweight and its effects

Overweight in your teens – heart problems in your twenties

People who are already overweight as an adolescent often show increased blood pressure and a strained heart as a young adult. This observation was made during a recent study at the University of Bristol.

Data from more than 3,000 young participants (17 years old) were collected and evaluated, including blood pressure, heart rate and BMI. At the age of 21, MRI scans were used to determine heart size and certain parameters of heart function in about 400 of the participants.

Teenagers who had already weighed too much at the age of 17 showed increased blood pressure at the age of 21, and tended to have an enlarged left ventricle. This indicates organ damage to the muscle and is a harbinger of cardiovascular diseases later in life.

No elevated heart rate values were recorded. The enlargement of the heart was probably due solely to the increase in stroke volume.

The carotid artery was also not thickened in these cases. Obesity in adolescents therefore apparently initially only affects the heart, with atherosclerosis not occurring until later on in life.

Wade KH et al. 2018

Early childhood influences weight problems later on

A study by the University of Leipzig tracked the weight development of more than 51,000 children from birth to teenage age using BMI values. The conclusion: Children who already weigh too much at pre-school age usually remain overweight during adolescence.

Almost 90 percent of children who were overweight at the age of three remained overweight as adolescents. About half of the adolescents already had a too high body weight at the age of five. In contrast, most teenagers of normal weight also had a normal weight in their childhood. These developments were independent of gender.

The data showed that the weight of overweight and obese adolescents increased most significantly between two and six years of age. Thereafter, the BMI continued to rise and the extent of obesity continued to increase. However, not every overweight adult was already overweight as a child – many factors can play a role here. However, if overweight develops in early childhood, it usually persists.

Geserick M et al. 2018

Education makes you slim!

Health inequalities between families with different levels of education are greater than expected. In a direct comparison, the educational influences of the family have significantly greater effects on child health than, for example, differences in income. There is also evidence that disadvantaged children are at increased risk.

These are the most important results of the Children and Youth Report commissioned by the German health insurance company DAK-Gesundheit. For the report, the University of Bielefeld evaluated data from almost 600,000 children and 430,000 parents from 2016.

The differences depending on the educational status of the parents are apparent when it comes to obesity: Children of parents without educational qualifications are up to 2.5 times more likely to be affected by obesity between the ages of five and nine than the children of academic parents. Out of 1,000 children of parents with poor education, 52 are pathologically overweight. For children of academics, the equivalent figure is only 15 out of 1,000.

The situation is similar for dental caries – the number of cases increases by up to 2.8 times based on education level. Children of parents without educational qualifications are 45 percent more likely to be affected if they have developmental disorders such as speech and language problems. A similar picture can be seen in behavioral disorders such as attention deficit hyperactivity disorder (ADHD), with a difference of 44 percent.

The study also shows the influence of the socio-economic family background on the type of health care provided: Children of parents with poor education have up to 68 percent more hospital stays and receive up to 43 percent more medication than children of parents with a high level of education.

Storm A (ed.): Children and Youth Report 2018
The German Nutrition Society has reviewed and updated the reference values for the intake of folate.

The daily recommended intake for adolescents and adults is still 300 micrograms. The reference values have also remained the same for pregnant women (550 µg) and breastfeeding women (450 µg), who have an increased need. Women who want to or could become pregnant are advised to take 400 micrograms of synthetic folic acid per day in addition to a folate-rich diet in order to reduce the risk of neural tube defects in the embryo.

Folate refers to the various forms of a water-soluble vitamin which is indispensable for human health. The synthetically produced form of the vitamin is called “folic acid”. Deficiency can primarily affect growth and cell division, which may result in anaemia.

The reference value can easily be reached with folate-rich foods such as green vegetables, especially spinach and salad. Tomatoes, pulses, nuts, oranges, sprouts, wheat germ, wholemeal products, potatoes, eggs and liver also contain plenty of folate.

A high intake of folic acid from fortified foods or vitamin preparations can be harmful in contrast to a high intake of folate.

The European Food Safety Authority (EFSA) has indicated a tolerable daily upper intake level of 200 to 800 µg of folic acid for children and adolescents aged 1 to 17 years. For adults, a tolerable upper intake level of 1000 µg per day applies.

A folic acid intake permanently above these values increases the risk of adverse effects.

German Nutrition Society 2018
Bundesgesundheitsblatt 2017

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Risk of malnutrition due to cow’s milk allergy (CMA)?

Children on a cow’s milk exclusion diet (CME) are at risk of nutrient deficiencies. However, meaningful data on biomarkers for micronutrients in this group has so far been largely lacking.

A cross-sectional study included 75 children (<2 years, average 9 months) with a cow’s milk allergy (CMA). The status of the micronutrients was determined by blood sampling, complementary food was defined as all solid and liquid food other than breast milk and was checked with a 3-day nutrition diary. The results were analysed according to three types of nutrition:

- Mainly breastfed
- Partially breastfed
- Not breastfed

The children had an average age of 9 months, and the status of micronutrients was within the normal range for all of them. There was no significant difference between the three groups except for B12:

- The risk of B12 deficiency was high in the predominantly breastfed children. The introduction of complementary food was associated with an improved B12 status.

Iron, zinc and vitamin D deficiency were identified in all three nutritional groups.

Complementary food should be introduced between the 4th and 6th months.

Vitamin D should be supplemented to ensure adequate intake.

Kvammen JA et al. 2018

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Federal Research Institute for Child Nutrition Opened in Germany

The Institute for Child Nutrition was opened in February by the German Federal Ministry of Food and Agriculture with a scientific symposium in Karlsruhe. The interdisciplinary institute was tasked with improving and expanding the knowledge base for the nutrition of children and adolescents. It consists of two research areas – one for natural sciences, one for social sciences – and is intended to investigate how the complex interaction of social, psychological and physiological influencing factors shapes children’s eating and drinking habits. Among other things, the Institute of Child Nutrition deals with the relationship between the diet and weight of pregnant women and the state of their children’s health later on. According to Regina Ensenauer, paediatrician and head of the institute, the origins of nutrition-related illnesses often can be traced back to pregnancy.
Diagnostic methods based on artificial intelligence (AI) techniques and learning systems have already proven effective in image-based diagnoses. A solution seems to have been found for the analysis of complex health data — at least in China.

An innovative new program can retrieve various and extensive electronic health data and extract clinically relevant information from it using an automated natural language program. 101.6 million records from 1,262,559 paediatric patient visits were analysed for training and validation. This AI diagnosis model was first tasked with determining which organ systems were affected. Its accuracy was between 85 percent for gastrointestinal and 98 percent for neuropsychiatric diseases. The next step was to make specific diagnoses. Here, too, the results were very accurate and were between 83 and 97 percent.

The second part of the study was a comparison with conventional medical diagnoses in 11,926 patients. 2 groups included physicians with less than 8 years of professional experience, 3 groups were made up of more experienced colleagues. The result was astounding: The accuracy demonstrated by the AI was often higher than that of the junior doctors. This applied to common diseases such as influenza or the hand, foot, and mouth diseases common in the Far East, but also to dangerous or life-threatening diseases such as acute asthma attacks or meningitis.

However, the authors view AI — for now? — as not as competition, but as a source of support, for example for quick preliminary clarification. It also remains to be seen whether electronic paediatricians will be able to inspire as much confidence as their human colleagues.


2. Irschenberg Paediatric Meeting

For many years, the Nestlé Nutrition Institute (NNI) has been organising training events on current issues in infant nutrition.

In 2017, an NNI training event for established paediatricians was successfully held at various locations in Germany, based on the topic “Compact nutritional knowledge for paediatric and youth practices”.

After receiving very positive feedback, the “Second Irschenberg Paediatric Meeting” took place on 17 November 2018, organised jointly by bvkJ Oberbayern, PädNetz Oberbayern Südost and the Nestlé Nutrition Institute.

The event was recognised by the Bavarian Medical Association with 4 training credit points.

The event, which was attended by around 60 interested paediatricians, focused on intensive dialogue with experts on practice-relevant topics and exchange between colleagues. In focus: Influence of early childhood nutrition on the microbiome, current research and recommendations on nut allergy as well as opportunities and benefits of telemedicine. Experts from the region gave lectures on questions and approaches on the topics of unexplained anaemia and care of children with bronchopulmonary dysplasia.

Information, dates and registrations for a 3rd Irschenberg Paediatric Meeting and other training courses for paediatricians can be found on the homepage of the Nestlé Nutrition Institute Germany.