Scientific Publications Compendium

2019·**2020**·2021

Nestlé HealthScience

Prologue

Welcome to the 4th issue of the Nestlé Health Science Scientific Publications Compendium.

Nestlé Health Science is a leader in the field of nutritional science, committed to redefining the management of health. As an innovative health science company, we strongly believe in leveraging and investing in leading-edge science in order to improve quality of life and provide clinical and health economic value. Our aim is to maximize the role of nutrition in empowering healthier lives.

This year Nestlé Health Science marks its 10-year anniversary. Since its creation, it has contributed to building solid scientific evidence of nutrition's role in supporting a healthy life and as an integrated part of disease management.

In 2020, Nestlé Health Science contributed to and supported a large number of scientific publications covering a broad spectrum of clinical conditions. The present booklet summarizes these publications. Also included are contributions from the scientific community which were not specifically sponsored by Nestlé Health Science but are also relevant within the field, as well as some recent related guidelines.

I would like to take the opportunity to thank all the experts involved in this work, namely scientists, healthcare professionals, institutions and Nestlé Health Science colleagues. Our meaningful scientific partnership will positively impact patients' and consumers' lives.

We do hope that you will find the compendium of great interest!

Best regards on behalf of the Nestlé Health Science Medical Affairs community,

Anette Järvi, R.D. Ph.D.

Global Head of Medical Affairs
Nestlé Health Science

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Design, quality, safety and efficacy of extensively hydrolyzed formula for management of cow's milk protein allergy: What are the challenges?

Nutten S, Schuh S, Dutter T, Heine RG, Kuslys M

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https://pubmed.ncbi.nlm.nih.gov/32711862/

One of the most common food allergies in young children is cow's milk protein allergy (CMPA). Guidelines favor that non-breastfed infants should be primarily fed with an extensively hydrolyzed formula (EHF).

However, there are some challenges that should be taken into account when designing and commercializing EHF: each manufacturing step needs managing in accordance with broad quality systems. Suppliers should be selected based on quality requirements to avoid cross-contamination of ingredients; manufacturing areas should be strictly defined as well as effective strategies to prevent accidental contamination by allergens. Also, hypoallergenic products should only be manufactured in dedicated manufacturing lines to prevent potential cross-contamination.

Each manufacturer has its own methods of enzymatic hydrolysis, heat treatment and ultrafiltration. EHF consist of a heterogeneous group of products with differences in various aspects, namely molecular weight profile of peptides, content of residual immunogenic cow's milk allergens and residual in-vitro allergenicity that may affect clinical efficacy and safety.

There is a need to develop guidelines for minimum technical and regulatory requirements (validated assays for ongoing quality control included) for these products because not all commercialized EHF have undergone laboratory and clinical trials.

The ultimate proof of efficacy and safety in infants and children with CMPA is evaluating new EHF products for their hypoallergenicity and ability to support children's growth through clinical trials.

Introduction of solid foods: Where advice on the introduction of complementary feeding and food allergen introduction meets

Meyer R

as planned for World Congress of Paediatric Gastroenterology, Hepatology and Nutrition (WCPGHAN) 2020

https://www.nestlehealthscience.com/newsroom/events/online-symposium-future-nutritional-strategies-for-food-allergy-prevention

There has been significant research, to establish dietary drivers associated with the development of food allergy. The timing and food allergen introduction have been researched extensively in context of allergy prevention and has informed international allergy societies in their guidance. Whilst all current guidelines support the World Health Organization in relation to breastfeeding there are some differences in guidelines on the advice on the introduction of complementary foods. This has been highlighted in a recent publication around the language of appropriate timing for the introduction of foods, with only 41.7% using the exact wording around the timing of complementary food. This study reflects well the challenges that face guideline bodies and therefore also clinicians; integrating research on allergy prevention, whilst supporting other guidelines on breast and complementary feeding. The differences between general guidelines and allergy specific guidelines are not only evident in the timing of complementary feeding but also the introduction of allergens. Although there is consensus between all guidelines, that no allergens should be delayed beyond 6 months, the early introduction (defined as 4-6 months) of peanut has been recommended for allergy prevention in high risk infants. Whilst the implementation of the advice in regard to the introduction of specific allergens may be feasible, the question of availability (including cost) and cultural acceptability of specific allergens needs to also be considered. Therefore, guidelines on complementary feeding, including allergen introduction, are as good as the practical implementation, by healthcare professionals taking country specific requirements into account, specific to their patient's needs.

Around the world in 20 min: making sense of allergy prevention Guidelines

Nadeau K

as planned for World Congress of Paediatric Gastroenterology, Hepatology and Nutrition (WCPGHAN) 2020

https://www.nestlehealthscience.com/newsroom/events/online-symposium-future-nutritional-strategies-for-food-allergy-prevention

Food allergy affects an estimated 8% of the global population, with evidence of increasing prevalence among children in developed countries. While the exact etiology of food allergy is unknown, research suggests a complex interaction between the immune system, rising susceptibility due to environmental factors, feeding habits, and genetics. Around the turn of the century, international guidelines pushed for delayed introduction of complementary allergenic foods to slow the rise. However, food allergy incidence continued to increase in developed countries despite widespread adoption of avoidance measures. Landmark studies, including PASTURE, LEAP, and EAT, have contradicted previous guidelines, demonstrating that early diversity, and early introduction of complementary foods, including allergenic ones, contribute to a reduced risk of developing a food allergy. Recent guidelines have reversed to now encourage early potential allergenic food introduction, between the ages of 4-6 months, both in healthy and infants at high risk for atopy. Guideline inconsistencies remain for the early introduction of peanut and egg, with countries adjusting recommendations based on cultural trends in peanut consumption, peanut allergy epidemiology, availability of IgE tests, and existing eczema and/or egg allergy. Oral tolerance appears to be antigen specific; emerging research explores the relationship between timing of allergenic food introduction, the value of multiprotein feeding at once, and food diversity on allergic diseases in a global population. Future prevention guidelines should reference emerging research to recommend a multiple food allergen approach and stress the value of early introduction with ongoing consistent inclusion of potential allergens during critical immune development.

It's all about diversity: foods, food groups and food allergens

Venter C

as planned for World Congress of Paediatric Gastroenterology, Hepatology and Nutrition (WCPGHAN) 2020

https://www.nestlehealthscience.com/newsroom/events/online-symposium-future-nutritional-strategies-for-food-allergy-prevention

The World Allergy Organization and the Institute of Medicine state that the prevalence of food allergies is rising dramatically. This increase is especially problematic in children, who are bearing the greatest burden of the disease. There is considerable interest in the effect of infant diversity on the prevention of allergic disease. A task force report from the European Academy of Asthma, Allergy and Immunology (EAACI), suggested that increased diet diversity may reduce the risk for allergy development via its effect on the microbiome, increased intake of nutrients related to allergy prevention, and by increased exposure to allergens. The report summarized 14 papers reporting the role of diet diversity on allergy outcomes. However, only one study reported on the association between diet diversity and food allergy outcomes, suggesting that increased diet diversity in infancy may reduce the risk of food allergy. Since this report, data from the Isle of Wight demonstrated that increased diet diversity in infancy significantly reduced food allergies over the first 10 years of life. This was true for diet diversity as defined by the World Health Organization, food diversity, allergen diversity and fruit and vegetable diversity. For every additional food introduced in the first year of life, and for each additional food allergen the odds of developing food allergy by age 10 years, were reduced by 11% and 33% respectively. There is no data on the effect of diet diversity in pregnancy or lactation on allergy prevention, but evidence are evolving in this field.

Extensively hydrolysed formula with two human milk oligosaccharides reduces rate of upper respiratory tract infections in infants with cow's milk allergy

Vandenplas Y, Zolnowska M, Berni Canani R, Ludman S, Tengelyi Z, Moreno Álvarez A, Goh A, Gosoniu ML, Tadi M, Heine R

European Academy of Allergy and Clinical Immunology (EAACI) Congress 2020
https://onlinelibrary.wiley.com/toc/13989995/2020/75/S109

• Background

This objective of this study was to evaluate if an extensively hydrolyzed formula (EHF) enriched with two human milk oligosaccharides (HMO) affects the rate of lower and upper respiratory infections (LRTI, URTI) during the first year of life.

• Methods

This study screened 200 infants with cow's milk protein allergy (CMPA) aged 0-6 months from 44 European sites. They were randomized to a tested formula, a whey-based EHF supplemented with 2'fucosyl-lactose and lacto-N-neotetraose, or a control formula, a currently marketed EHF (Althéra®), with no HMO. Milk protein free complementary feeding was initiated from 4-6 months. From enrolment to 12 months of age, carers documented adverse events and "events of interest." "Events of interest" were defined as the rate of LRTI and URTI. The rate of LRTI and URTI events per month was estimated, and the hazard ratio was calculated. The percentage of infants with at least one event was calculated for each group.

• Results

A total of 194 infants were randomized to the Test (n=97) or Control formula. The mean age was 3.2 ± 1.7 months (0.1-6.1 mo), 95 female and 99 male. The safety analysis set (SAS) included 190 infants (94 Test). In regard to the SAS, the fraction of babies with at least one LRTI was reduced by 33.6%, and URTI episodes reduced by 5.2%. There was a significant >40% reduction in the frequency of URTI episodes to 12 months of age.

Number of events/ infants	Test	Control
LRTI	24/13	29/20
URTI	60/39	94/42

• Conclusion

Extensively hydrolyzed formulas enriched with HMO are associated with a significant reduction in URTI frequency compared to non-supplemented formulas in infants with CMPA.

How to implement nutritional strategies for food allergy prevention

Carina V

European Academy of Allergy and Clinical Immunology (EAACI) Congress 2020
https://onlinelibrary.wiley.com/toc/13989995/2020/75/S109

The last two decades were essential for the evolution of guidelines for preventing food allergy. The definition of an infant at high risk of food allergy has changed from being based on a familial risk to an infant's own risk of developing a food allergy. Also, early food allergen introduction can be beneficial for the prevention of food allergies. More recently, guidance on when to introduce food allergens into the infant diet has progressed, following the LEAP and EAT studies' publication, which recommended no need to delay the active introduction of food allergens in the first year of life. This report aimed to summarize the current guidelines.

A systematic search of published literature found only one study that focused on the potential association of diet diversity and food allergy development. This study demonstrated that children with a more diverse diet during the first year of life have a lower prevalence of diagnosed food allergy until six years old. A study led by the author explored the relationship between four different diet diversity measures during infancy and food allergy development over the first ten years of life.

The study focused on the number of foods introduced over the first nine months of life and the number of food allergens introduced over the first 12 months. Food diversity at six months and food allergen diversity at 12 months significantly reduced the odds of food allergy over the first ten years of life.

An increased diet diversity in the first year of life is associated with reduced food allergy outcomes until six years of age, indicating that the microbiome is a possible mechanism for infant tolerance induction.

Human milk oligosaccharides for immune system development

Sprenger N

European Academy of Allergy and Clinical Immunology (EAACI) Congress 2020
https://onlinelibrary.wiley.com/toc/13989995/2020/75/S109

Human milk oligosaccharides (HMO) are the third most abundant solid component after lactose and lipids in breast milk. Two common HMO, 2'-fucosyllactose (2'-FL) and lacto-N-neotetraose (LNnT) have been the focus of clinical trials regarding the effects of HMO in infants. Some studies have identified that bifidobacterial strains found in breast milk, such as *Bifidobacterium longum*, may use HMO as a growth substrate. Specific HMO, including 2'-FL, improves the growth of bifidobacteria and their metabolic activity related to immune protection.

A multicentre trial included 175 healthy, full-term infants who were not breastfed and aged 0-14 days. They were randomized to receive regular infant formula supplemented with 2'-FL and LNnT (n=88) or a control formula (the same without HMO, n=87). The same study was also used to compare microbiota composition at three months of age with a breastfed reference group.

The supplemented formula was well tolerated and supported average growth in healthy infants for four months. It also showed that infants fed with the supplemented formula had significantly lower rates of parent-reported morbidities related to lower respiratory tract infections, especially bronchitis, and used fewer antibiotics and antipyretics for 12 months compared to control. Concerning microbiota, the composition in infants fed with the supplemented HMO-formula was closer to that of the breastfed reference group, mainly because of increases in *Bifidobacterium* simultaneous with decreases *Escherichia* and *Peptostreptococcaceae*.

The two HMO, 2'-FL and LNnT, help protect from lower respiratory tract infections and antibiotic use, probably due to their effects on early-life gut microbiome establishment and function.

New data on the benefits of human milk oligosaccharides in the management of cow's milk protein allergy

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European Academy of Allergy and Clinical Immunology (EAACI) Congress 2020
https://onlinelibrary.wiley.com/toc/13989995/2020/75/S109

The gold standard of infant nutrition is breast milk. It influences immune response and contains immunomodulatory ingredients, such as human milk oligosaccharides (HMO), which help develop the gut microbiome. This article aimed to report on studies that show the benefits of HMO in managing cow's milk protein allergy (CMPA).

This report includes the results of two clinical trials. The IVORY trial was a multicentre, randomized study that included 67 infants and children between 2 months and four years with CMPA. It compared an extensively hydrolyzed formula (EHF) without HMO with a newly modified EHF enriched with 2'-FL and LNnT. The CINNAMON trial was a double-blind, randomized, multicentre interventional study that compared the same formulas as the IVORY study. It evaluated if the newly modified EHF enriched with 2'-FL and LNnT supported normal growth and if it had beneficial effects on infection rates and related drug use in infants with CMPA.

The IVORY trial results showed that the supplemented formula met the American Academy of Pediatrics (AAP) criteria for hypoallergenicity, being tolerated by > 90% of participants. The CINNAMON trial showed that both groups showed a comparable weight gain per day at four months. Also, it demonstrated a significant reduction of 42% (p=0.003) in the frequency of upper respiratory tract infections episodes to 12 months of age in infants fed with the HMO-supplemented EHF compared to control EHF. The frequency of lower respiratory tract infections was reduced by 23% (p=0.61).

The reductions in the frequency of infections in CMPA have shown consistency with reduced respiratory infections in healthy babies fed with formulas supplemented with 2'-FL and LNnT since birth. These findings support the enrichment of infant formulas with the immunomodulatory components present in breast milk.

Prospective surveillance of an amino acid-based infant formula in infants with cow's milk protein allergy, in a routine clinical practice setting

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European Academy of Allergy and Clinical Immunology (EAACI) Congress 2020
https://onlinelibrary.wiley.com/toc/13989995/2020/75/S109

• Background

Cow's milk protein allergy (CMPA) is the most common food allergy in infants. Amino acid (AA) formulas are commonly used in the management of CMPA. The requisites for commercialization of AA formulas in the United States are defined by the American Academy of Pediatrics and include clinical documentation of infant growth and hypoallergenicity. This study's objective was to assess the safety and use of a hypoallergenic AA formula (HAA) in routine clinical practice settings. The primary endpoint was to evaluate the frequency and nature of infants' adverse events fed an AA formula. Secondary objectives were to describe demographics and clinical characteristics of infants fed an AA formula.

• Methods

This was a prospective, post-market surveillance study conducted during February 2017-May 2018 at 30 sites in the United States. Children diagnosed with CMPA, ≤ 12 months of age, > 37 weeks corrected gestation age at enrollment, and planned use of HAA were included. Participants were followed by their healthcare providers and data was collected for 4 months after enrollment or until formula discontinuation. Complementary food intake and HAA caregiver satisfaction were assessed at medical visits.

• Results

The study included 144 infants, 69% (n=100) with CMPA diagnosis. 84% of subjects with CMPA had severe CMPA, based on protocol criteria. Six serious adverse events were reported in 6 infants (3 with severe CMPA), all of them unrelated (5 of 6), or unlikely related (1 of 6) to HAA. A total of 125 adverse events were reported in 43 subjects (26 with severe CMA). Most adverse events were reported as unrelated (78%) or unlikely related (10%) to HAA; the 9% adverse events reported as probably related to HAA were emesis or constipation. No anaphylaxis events were reported. 71% had complementary food intake, including cereal, dairy, single fruit/vegetable, and animal protein. Twelve infants (12%) had a documented reaction to complementary foods. 82% of carers indicated satisfaction with the formula.

• Conclusion

A prospective surveillance program, outside of a controlled clinical trial indicated HAA use in infants with CMPA was safe and associated with high satisfaction of carers. Complementary food reactions were reported in 12% of infants with CMPA.

A randomized trial of the acceptability of a daily multi-allergen food supplement for infants

Holl J L, Bilaver LA, Finn DJ, Savio K

Pediatr Allergy Immunol. 2020 May;31(4):418-420.
https://pubmed.ncbi.nlm.nih.gov/32030829/

• Background

The protective benefits of early dietary introduction and consistent inclusion of allergenic foods in infant diets, including those infants at increased risk has been demonstrated with some recommendations encouraging early allergenic food introduction for all infants. Yet adherence to a multi-food dietary inclusion protocol can be difficult in infants and children.

• Methods

To evaluate the acceptability by parents and tolerability by infants of a daily, single-dose of a patented powdered food supplement (Spoonfulone™) containing 30mg of protein from each of the 16-commonly allergenic foods (peanut, soy, almond, cashew, hazelnut, pecan, pistachio, walnut, wheat, oat, milk, egg, cod, shrimp, salmon, and sesame).

Study Design: Blinded, randomized, controlled 28-day trial, recruited from a national, web-enabled research panel. Healthy full-term infants (in USA) aged 5-11 months (mean age 7-months) at enrollment, 50% female, without parent reported severe eczema or food allergy. Excluded were those ≥2 hospitalizations since birth, or a health condition lasting ≥3 months since birth. Convenience sample of 705 infants where households were randomized to 339 placebo; 366 food supplement. Parents were instructed to mix or sprinkle a single-dose packet of powder (food supplement or placebo) into a small amount of liquid, soft, or solid food and feed it to their infant once a day. Then observe their infant for 2-hours for any reaction/symptom and record in an online daily diary any symptom and any medication or medical care received for the symptom. For any reported symptom, a blinded investigator called the parent to confirm the timing of the symptom and to determine whether it was an IgE-type reaction.

• Results

Trial completion was equal for both arms (88%; 298 and 321, respectively), with 10% in each arm withdrawing (4 in both groups) or being withdrawn (37 and 41, respectively) due to non-compliance with recording in the daily diary. No infants were withdrawn due to any symptoms or reactions. There were 8803 food supplement and 8087 placebo ingestions. There was no significant difference between the groups in the proportion of any specific reported symptoms: supplement and placebo ingestions, 0.75% and 0.64%, respectively, had a reported symptom. No infant had any IgE-type reaction to the supplement or received any related prescribed medication or medical care.

• Conclusion

This trial suggests that feeding a single daily dose of a multiple allergenic protein blend food supplement to healthy infants, over a 28-day period, is accepted by parents, given the high trial completion rate. The absence of any reported IgE-type reactions or need for medication or medical care supports tolerability in infants. This is the first study to show acceptability by parents and tolerability by healthy infants of a daily serving of a powdered food supplement that includes the 16 most common allergenic food proteins. The results offer an acceptable and tolerable option to achieve early, consistent dietary exposure to potential food allergens in healthy infants.

An extensively hydrolysed formula supplemented with two human milk oligosaccharides (HMO) shapes the gut microbiome in infants with cow's milk protein allergy

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European Academy of Allergy and Clinical Immunology (EAACI) Congress 2020
https://onlinelibrary.wiley.com/toc/13989995/2020/75/S109

• Background

Human milk oligosaccharides (HMO) are the third-largest solid component of human milk (after fat and lactose) and may have benefits in shaping the intestinal microbiota's early development. The objective of this study was to evaluate the effects of an extensively hydrolyzed formula (EHF) supplemented with 2'fucosyl-lactose (2'FL) and lacto-N-neotetraose (LNnT) on the faecal microbiome in infants with cow's milk protein allergy (CMPA).

• Methods

This was a controlled, double-blind, randomized, multicenter, interventional study of two parallel extensively hydrolyzed formula-fed groups. One hundred thirty-two infants (0-6 months) with CMPA were randomized to a lactose-containing EHF, with or without 2'FL and LNnT until 12 months of age. The microbiome composition was profiled at baseline, 1, and 3 months from baseline, and 12 months of age. Stool samples with similar microbiome composition were grouped into five faecal community types (FCT) and tracked to analyse temporal development. Microbial richness and diversity were compared between groups. HMO effects on the microbiome were also compared.

• Results

Age strongly influenced microbiome development. The microbiome trajectories showed a typical temporal growth from "early" to "late" FCT and lower to higher alpha diversity. Between V1 to V3, due to the wide age range, significant differences were not apparent. However, significantly, at 12 months of age (V6), infants from the HMO group had a lower alpha diversity and were enriched in early-type FCT. Beta diversity was similar until 12 months of age, where it showed significant differences. Twelve taxa associated with HMO supplementation were identified, including the genus Bifidobacterium, most abundant at V1.

• Conclusion

Changes in diet and environmental exposures led to a different evolution of the gut microbiome. At 12 months, infants fed with an HMO-supplemented EHF had lower microbial diversity and reduced gut microbiota. This demonstrates that HMO supplementation of EHF may slow the premature shift towards an adult-type gut microbiome as observed in breastfed infants.

Mixed allergen protein introduction in infants with and without eczema: safety observations

Swanson WS, Wei A, Jeong D

European Academy of Allergy and Clinical Immunology (EAACI) Congress 2020
https://onlinelibrary.wiley.com/toc/13989995/2020/75/S109

• Background

Evidence shows that early introduction and sustained feeding of common food allergens can decrease food allergy risk. It is therefore important for parents of those infants with high risk of severe atopic dermatitis (AD) to adopt allergy prevention strategies. In practice, however, Pediatricians and parents remain cautious even though it is known that reaction severity increases with age, and infant reaction rates are low, reinforcing the early introduction approach. This sub analysis of data from a clinical study aimed to define the rate of allergic reactions on first feeding and during one year in infants ≤12 months with no risk and high risk of developing a food allergy.

• Methods

Children were equally randomized to one of 18 cohorts of different protein mixes (single, dual, and ten), with 25 participants similarly divided among age groups, feeding daily for one year. Single protein was sourced from either: egg, milk, peanut, shrimp, white fish, almond, hazelnut, walnut, or cashew. Double protein combinations sourced in equal parts by protein weight from peanut plus soy, shrimp plus crab, cod plus salmon, walnut plus pecan, or cashew plus pistachio. Multi protein in equal parts by protein weight from egg, milk, shrimp, salmon, almond, hazelnut, walnut, peanut, cashew, and wheat.

• Results

The study included 450 children; 190 of them were ≤12 months old. From this cohort, 148 (78%) reported having AD, and 97 (51%) had a family history of food allergy or atopic disease. Protein cohorts were randomly allocated to 180 children, ten were randomized to control. Across all cohorts, there were no allergic reactions in children with AD or those at high-risk. Mild skin rashes were reported in the control group (n=2, 20%) and the protein group (n=13, 3%). The multi-protein blends did not have more adverse events than the single or dual-protein blends or the control. There was no significant increase in allergic reaction rate for infants with eczema than those with no eczema.

• Conclusion

This study showed no difference in an allergic reaction rate after first feeding between infants with and without severe eczema neither in the active nor placebo arms. The early introduction of different food proteins in infants 4-12 months of age with AD was well-tolerated and safe, even with no prior testing to allergies. Important to note is that the data suggests eczematous babies are not at higher risk of developing anaphylaxis on first feeding, despite them being at a higher risk of developing a food allergy.

Growth and tolerance with an amino acid formula at a children's center: a two-year retrospective review

Hulsey A, Cekola P, Henrikson A, Reichert H, Cohen S, Araujo Torres K

North American Society For Pediatric Gastroenterology, Hepatology & Nutrition 2020; Abstract 195

https://journals.lww.com/jpgn/Citation/2020/11001/NASPGHAN_Annual_Meeting_Abstracts.1.aspx

• Background

The dietary management of cow's milk protein allergy (CMPA), multiple food allergies, food-allergy associated conditions, and severe malabsorption is accomplished with hypoallergenic amino acid formulas. Guidelines from the American Academy of Pediatrics (AAP) and the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) endorse amino acid-based formulas to children > 1-year-old who do not tolerate extensively hydrolyzed formulas or formulas containing non-related protein without cross-reactivity. This retrospective study's primary aim was to describe the practice of an amino acid formula in children at a rehabilitation hospital. Secondary endpoints included growth, the achievement of nutrition goals, feeding tolerance, and the use of gastrointestinal medication.

• Methods

This was a retrospective study that included 26 children (1-18 years old), residing or having resided in a children's hospital with a rehabilitation center who had received Alfamino® Junior (AAF), an amino acid formula. Results from 2018 were reviewed: data registered at 12 and 6 months before the switch to AAF, at the moment of the switch, and 6 and 12 months after switch.

• Results

Three participants were excluded due to insufficient data pre or post AAF. Baseline characteristics were recorded as per the table below. One child was supplemented with parenteral nutrition at all time points, whilst most others received received additional nutrients, most commonly protein and Vitamin D3. Children >1-year-old were mainly fed with amino acid formulas pre switch. At switch, 100% of calorie and 99% of protein goals were achieved and maintained a one-year post switch. Children had a consistent growth trajectory across age groups and all time points. Four children with a primary diagnosis of vomiting continued to report episodes during the retrospective 2-year review. There was a mean of 3-5 episodes of vomiting reported by 20 to 25% of participants during AAF consumption. The daily average number of stools ranged from 1.5 to 2.1, with consistently soft mean consistency. Six months after formula switch, 10% had a reduction of 1 or more GI medications, 12 months post switch, 31% had the same decline.

Mean age (years)	7.5 ± 5.4
Gender (n=23)	
Female	61% (n=14)
Male	39% (n=9)
Tube fed	100% (n=23)
G-tube placement	70% (n=16)
Primary diagnosis	
Gastrointestinal (atrophic gastritis, delayed GI motility, diarrhea, reflux, flatulence, gastroschisis, vomiting)	48% (n=11)
Atopic dermatitis	13% (n=3)
Feeding difficulties	13% (n=3)
Allergy (milk, soy, wheat, peanuts, eggs, red dye)	9% (n=2)
Other (DiGeorge syndrome, chronic transaminitis, FTT, metabolism disorder)	17% (n=4)

• Conclusion

After switching to an AAF formula and up to 1 year later, children continued to meet nutrition goals, had good tolerability and consistent growth. In addition, there was a reduction in the number of GI medication after switching to AAF.

Peptide-based formula versus standard-based polymeric formula for critically ill children: is it superior for patients' tolerance?

Ibrahim H, Mansour M, El Gendy YG

Arch Med Sci 2020; 16 (3): 592–596
https://pubmed.ncbi.nlm.nih.gov/32399107/

• Background

More than half of hospitalized children and 25-70% of critically ill children suffers from malnutrition. Critically ill children receive generally enteral tube feding. Although clinical advantages the use of peptide-based formulas is still debated. The objective of this study was to compare the effect on feeding tolerance of a peptide-based formula with a standard polymeric formula and its outcome among critically ill-children.

• Methods

This was a single blind case control study that included 180 randomly selected critically ill children in the pediatric intensive care unit (PICU) of Ain Shams University. Children were included into two groups: one received a standard polymeric formula (n=90), other received a 100% whey peptide-based formula, Peptamen Jr. Powder (n=90). At admission, all patients had their nutritional requirements, days to reach full enteral feeding, feeding intolerance symptoms and anthropometric measurements registered, along with their pediatric risk of mortality score. At discharge, length of PICU stay, occurrence of sepsis together with survival were analyzed as outcome measures.

• Results

Children who received a peptide-based formula had a significant decrease in feeding interruptions and abdominal distention ($p<0.000$), reached full enteral feeding faster (2.60 ± 0.74 days versus 5.36 ±1.00 days in children who received polymeric standard formula; $p<0.001$) and improved weight ($p<0.028$). Also, duration of sepsis was significantly shorter ($p<0.045$) but there was no difference in mortality between groups.

• Conclusion

Critically ill pediatric patients tolerated better the peptide-based formula compared to polymeric formula.

Caregivers' perceptions of real-food containing tube feeding: A Canadian survey

Boston M, Wile H

Can J Diet Pract Res. 2020 Jun 4:1-5

https://pubmed.ncbi.nlm.nih.gov/32495643/

• Background

There is an increased interest in real-food containing formulas, such as home-blenderized tube feeding (HBTF) and commercial real food-containing formulas (CRFCF) by caregivers of children who need tube feeding. The objective of this study was to understand their perception of both real food-based products.

• Methods

This study consisted of a 13-question online survey that asked participants about use of HBTF and CRFCF, beliefs about their choices and what resources guided their formula use. Participants were real-food caregivers users recruited from the Feeding Tube Awareness Foundation Facebook group.

• Results

The survey was completed by 41 caregivers, with children with a mean age of 7 years old. Generally, 54% (n=22) used HBTF, 34% (n=14) CRFCF and 12% (n=5) used both. The presence of whole foods, nutritional completeness and natural ingredients were most important for the majority of responders (70%, n=29). CRFCF users commented a lack of variety (53%, n=10) and high cost (47%, n=9). HBTF users manifested difficulty in preparation away from home (70%, n=19) and need for special blenders (56%, n=15). The majority of responders believed CRFCF are convenient (85%, n=35) and nutritionally consistent (61%, n=25), although with insufficient real food ingredients (63%, n=26). The most valued resource guiding formula use was social media (61%, n=25).

• Conclusion

Formulas nutritionally complete and made of whole foods are preferred by caregivers. commercial real-food based formula offers convenience and consistency.

Tolerance and acceptability of a new paediatric enteral tube feeding formula containing ingredients derived from food: A multicentre trial in the United Kingdom

Thornton-Wood C, Saduera S

J Neonatol Clin Pediatr 2020, 7: 050

https://www.heraldopenaccess.us/openaccess/tolerance-and-acceptability-of-a-new-paediatric-enteral-tube-feeding-formula-containing-ingredients-derived-from-food-a-multicentre-trial-in-the-united-kingdom

• Background

Children who require tube feeding are increasingly being fed with Homemade Blended Diets (HBD), however this practice has increased risks of tube occlusion and nutritional insufficiencies. Back in 2015, the British Dietetic Association published a "Practice toolkit liquidized food via gastrostomy tube", but they did not advise the administration of liquidized food via an enteral feeding tube. Recently, this publication was updated, empowering dietitians to feel supported upon recommendation of blenderized diets. The aim of this study was to assess the tolerance and acceptability of a new paediatric enteral tube feeding formula containing ingredients derived from real food.

• Methods

The study was designed according to UK Advisory Committee on Borderline Substances (ACBS) criteria to support submission for prescription usage in the National Health Service (NHS), it included 19 tube fed participants (1-14 years old), who were recruited from the NHS setting and under the care of a dietitian/doctor. A tube fed formula developed to address safety and nutritional needs (Isosource Junior Mix, Nestlé Health Science) was given to all participants for a week. Demographic and medical data, and gastrointestinal tolerance were registered. Stool type was measured using the Bristol Stool Charts.

• Results

Participants had different medical conditions. Some reported positive changes in stools, being firmer and less frequent. One child improved mood, eye contact and concentration. Two participants resolved reflux and had a gradual decrease in retching. One child experienced flatulence and bloating, possibly due to a former tube feed without fibre. No changes in weight were registered.

• Conclusion

The majority of participants tolerated well the new formula, with less gastrointestinal symptoms and positive changes in stool type.

Tolerance and acceptability of a low-calorie paediatric peptide enteral tube formula: a multicentre trial in the United Kingdom

Thornton-Wood C, Saduera S

J Neonatol Clin Pediatr 2020, 7: 049;

https://www.heraldopenaccess.us/openaccess/tolerance-and-acceptability-of-a-low-calorie-paediatric-peptide-enteral-tube-formula-a-multicentre-trial-in-the-united-kingdom

• Background

Up to 15% of the children with cerebral palsy (CP) require a low-calorie feed. The ESPGHAN working group recommends a formula low in fat and calories, high in fibre and replete with micronutrients for maintenance of enteral tube feeding after nutritional rehabilitation in neurological impaired children who are immobile. The objective of this study was to assess the tolerance and acceptability of a low-calorie paediatric whey peptide-based enteral formula.

• Methods

The study was designed according to UK Advisory Committee on Borderline Substances (ACBS) criteria to support submission for prescription usage in the National Health Service (NHS), it included 9 children aged 1-11 years with neurological issues. They were given a new low-calorie enteral tube feed formula with fibre (Peptamen Junior 0.6 kcal/ml, Nestlé Health Science) during a week. Gastrointestinal tolerance and volume of formula intake were recorded.

• Results

The trial was completed by 7 children; one withdrew due to a minor increase in flatulence and another suspended the feed due to user error. All 7 children tolerated the low-calorie formula and their average daily formula intake was 1032 ml (600-1300 ml). One child, who was previously on a non-fibre containing feed has an increase in stool frequency (usually type 6) from 2 to 4 times per day and a slight increase in bloating and flatulence.

• Conclusion

Overall children with CP tolerated well the new low-calorie formula; This formula can help meet nutritional goals in children with CP who need low energy feeds.

Meeting nutritional needs of the enterally-fed child with neurological impairment

Minor G, Yamamoto S, Cekola P, Cohen SS, Huhmann MB, Krysmaru Araujo Torres K

Journal of Clinical Nutrition & Dietetics

https://clinical-nutrition.imedpub.com/meeting-nutritional-needs-of-the-enterally-fed-child-with-neurological-impairment.pdf

• Background

Developmental delay and neurological impairment in children are frequently associated with gastrointestinal disorders that interfere with oral food intake. Caregivers of tube-fed children look for more healthful alternative foods to be administered via feeding tube. The primary aim of this study was to evaluate meeting daily calorie goals. Secondary endpoints evaluated meeting protein-intake, formula intolerance, and quantification of adverse events.

• Methods

This was a prospective, observational study that included children requiring enteral tube feeding. Twenty-one children (1-13 years) receiving ≥90% of nutritional needs via gastrostomy tube, tolerant to enteral tube feeding pre-study were included. They received the study formula for seven days. This formula (1.0 kcal/mL) provided 15%, 34%, and 51% of calories from protein, fat, and carbohydrates, respectively, and contained ingredients from tomatoes, peas, green beans, peaches, chicken, and cranberry juice.

• Results

All children continued enteral tube feedings during the study. On average, 90% (n=18) of children met daily protein goals. Calorie goals were 90% achieved by 60% (n=12) of the children, and 90% (n=18) of the children achieved at least 70% of calorie goals. Of 160 feeding days, adverse events were only reported on five days and were determined as unrelated to unlikely related to study formula.

• Conclusion

The food-based enteral feeding formula tested was safe and convenient and nutritionally-balanced at the same time for children with neurological impairment and feeding disorders. Calorie and protein goals were reached with no intolerance and no reports of serious adverse events. This represents a practical, nutritionally complete, real-food option for enteral feedings in these children.

Development and alpha-testing of a decision aid about enteral feeding in children

Rivero MC, Moreno A, Rodríguez A, Vives I, Barreiro F, Herrero M, Jovani C, Lopez MA, Pérez-Lledó E, Sánchez-Valverde F, Tolín M, Layola M, Comellas M

ESPEN 2020

https://clinicalnutritionespen.com/article/S2405-4577(20)30691-4/fulltext

• Background

The choice of a nutrition strategy is very important in children who need enteral feeding. These options can be made using patient decision aids (PDA), which consist of clinical tools to help promote shared decision-making. The objective of this study was to develop and test a PDA for caregivers who are envisioning enteral tube feeding for their children.

• Methods

The rules of the International Patient Decision Aids Standards for generating a PDA were followed. They include: 1) Defining extension and design; 2) Creating a steering committee (4 pediatric gastroenterologists and 2 caregivers); 3) Identifying the needs and choices via a literature review and focus group (7 pediatricians and 6 caregivers); 4) designing a PDA prototype; and 5) α-testing to assess PDA comprehensibility, acceptability and feasibility using Design Support Acceptability Scale (6 pediatricians and 13 caregivers). This PDA will have a β-testing in real-life conditions.

• Results

There were 3 main parts of the PDA: 1) Informing in enteral feeding, options (start tube feeding or changing the route of administration) and caregivers experience; 2) Assessing preferences for clarification of values; and 3) summarizing preferences and questions for discussion with the physician. In regard to α-testing, most caregivers considered the information on enteral nutrition, feeding options or complication was presented in a good/excellent way (≥76.9%) and could help treatment decision making (84.6%). Some needed explanation on preferences (30.8%) or caregivers experience (50.0%). In regard to clinical practice, most clinician agreed that the PDA was useful (≥66.7% agreement in all items). These inputs were incorporated into the PDA.

• Conclusion

The developed PDA offers information on enteral feeding options for children and allows caregivers to elucidate and chose their choices. α-testing demonstrated that it constitutes a relevant and acceptable tool for caregivers and health care professionals to promote shared decision-making.

A prospective analysis of micronutrient status in quiescent inflammatory bowel disease

MacMaster MJ, Damianopoulou S, Thomson C, Talwar D, Stefanowicz F, Catchpole A, Gerasimidis K, Gaya DR

Clin Nutr. 2021 Jan;40(1):327-331.
https://pubmed.ncbi.nlm.nih.gov/32517876/

• Background

People with inflammatory bowel disease (IBD) should check micronutrients regularly, as reported in the ESPEN guidelines. The aim of this study was to explain the status of micronutrients of people with latent IBD and investigate if a micronutrient deficiency is relatable to a further relapse.

• Methods

This was a prospective study that included 93 participants with IBD in clinical remission [Harvey Bradshaw Index (HBI) 4 in Crohn's disease (CD) and a partial Mayo score <2 in ulcerative colitis (UC)]. blood samples were checked for 16 micronutrients and followed using the electronic patient records. A statistical test with survival analysis and Cox regression was used to assess the ability of micronutrient status to predict time to relapse.

• Results

54% of the participants (n = 50) were in biochemical remission, defined as a normal faecal calprotectin (< 250 mg/g), C-reactive protein (< 10 mg/L) and serum albumin (> 35 g/L). The following micronutrients deficiencies were found:

Vitamin D: 27 participants (29%); Zinc: 15 participants (16%); Vitamin B6: 13 participants (14%); Vitamin C: 12 participants (13%); Vitamin B12: 10 participants (11%); Folate: 7 participants (8%); Ferritin: 8 participants (9%); Copper: 4 participants (4%); Magnesium: 4 participants (4%); Selenium: 3 participants (3%).

A deficiency in zinc was predictive of a shorter time to relapse (HR: 6.9; 95%CI [1.9 to 26], p = 0.008); a sub-analysis showed that in people with CD, this effect was even more pronounced (p = 0.001).

• Conclusion

Participants with IBD in clinical remission had deficiencies for several nutrients. A significant association between zinc deficiency and time to subsequent relapse was found in people with CD, such finding needs to be further investigated.

Total and activity-induced energy expenditure measured during a year in children with inflammatory bowel disease in clinical remission remain lower than in healthy controls

Godin JP, Martin FP, Breton I, Schoepfer A, Nydegger A

Clinical Nutrition. 2020 Oct;39(10):3147-3152

https://pubmed.ncbi.nlm.nih.gov/32147199/

• Background

Malnutrition may be one of the causes of growth retardation in children with inflammatory bowel disease (IBD). There are still limited knowledge on total energy expenditure (TEE), active-induced energy expenditure (AEE) and physical activity in pediatric IBD, namely. The aim of this study was to evaluate TEE, resting energy expenditure (REE) and physical activity level in children with IBD (in remission) and healthy controls.

• Methods

The study included 21 children with IBD and 24 healthy controls. TEE was assessed using the doubly labelled water (DLW) method, REE using indirect calorimetry and physical activity level using the actigraph GT3Xþ. Predicted and measured REE and TEE values (using Schoefield and the actigraph GT3Xþ, respectively) were compared.

• Results

At baseline, mean ages were 14.8 ± 1.5 and 13.2 ± 2 years in children with IBD and in healthy control children, respectively. Children with IBD in remission had significantly lower measured TEEDLW ($p < 0.001$), REE corrected by FFM0.5, REE and AEE relatively to healthy children. Children with IBD had AEE of 17.5% of TEE and a significantly higher sedentary behaviour too.

• Conclusion

Children with IBD in clinical remission have reduced TEE and AEE, probably result of reduced moderate and vigorous physical activity level. This study also highlights that TEE may be predicted with the actigraph GT3Xþ in children with IBD at group level, although is highly variable at individual level.

This is a collaboration study between Nestlé Research and University Hospital of Lausanne, Switzerland, reporting that pediatric IBD patients in clinical remission still present deficit in energy compared to age-matched healthy population. These data suggest that providing a nutritional supplement to IBD children in remission would be beneficial to sustain remission, and support optimal growth and physical activity.

Dietary therapies induce rapid response and remission in pediatric patients with active Crohn's Disease

Sigall Boneh R, Van Limbergen J, Wine E, Assa A, Shaoul R, Milman P, Cohen S, Kori M, Peleg S, On A, Shamaly H, Abramas L, Levine A

Clinical Gastroenterology and Hepatology. 2020 Apr 14;S1542-3565(20)30487-0
https://pubmed.ncbi.nlm.nih.gov/32302709/

• Background

Children with Crohn's disease (CD) experience induction of remission with dietary therapies that exclude usual dietary elements known to triggers inflammation and dysbiosis, while re-exposure to these foods may provoke relapse of inflammation. The aim of this study was to evaluate if a short trial of dietary therapy, to identify patients with and without a rapid response or remission on the diet (DiRe), can be used to predict success or failure of long-term dietary therapy.

• Methods

Data from 73 children (mean age 14.2 ± 2.7 years) with mild to moderate CD from the multicenter randomized trial of the CD exclusion diet (CDED) were analyzed. These children had been randomly assigned to exclusive enteral nutrition (EEN, n =34) or to the CDED with partial (50%) enteral nutrition (n=39). They were assessed at baseline and at weeks 3 and 6 of the diet therapy. Inflammation was evaluated by C-reactive protein levels. Remission was defined as CD activity index score below 10 and response as a decrease in score of 12.5 points or clinical remission.

• Results

A DiRe was obtained by 82% of the patients in the CDED group and 85% of patients in the EEN group at week 3. Median C-reactive protein levels decreased from 24 mg/L at baseline to 5.0 mg/L at week 3 ($p < 0.001$). Those who entered remission at week 6, 94% (46/49) has a DiRe and 81% were already in clinical remission by week 3. The multivariable analysis showed that remission at week 3 increased odds of remission by week 6 (odds ratio, 6.37; 95% CI, 1.6-25; p=0.008), while poor compliance reduced odds of remission at week 6 (odds ratio, 0.75; 95% CI, 0.012-0,46; p=0.006).

• Conclusion

Dietary therapies (CDED and EEN) induce a rapid clinical response (by week 3) in pediatric patients with active CD. The data suggest that early response (at week3) with compliance can be a predictor of longer-term response to the diet.

A case-based approach to new directions in dietary therapy of Crohn's Disease: food for thought

Levine A, El-Matary W, Van Limbergen J

Nutrients 2020, 12, 880

https://pubmed.ncbi.nlm.nih.gov/32214055/

• Background

Crohn's disease may be caused by dysbiosis of the microbiome and other environmental factors, namely a link between immune activation and diet. The Crohn's disease exclusion diet (CDED) was shown to induce remission and improve inflammation children and young adults with mild to moderate CD.

The aim of this case-based narrative review was to discuss the use of CDED in CD patients with various clinical conditions.

• Methods

Different clinical cases of children with mild to moderate new onset Crohn's disease were analyzed and reviewed.

• Results

The CDED, with or without partial enteral nutrition (PEN) is a next-generation dietary therapy that was proved effective for induction of remission and reduction in inflammation, but with better tolerability and sustained remission than exclusive enteral nutrition.

This clinical case series reported that CDED can be an option as monotherapy, combination therapy with drugs, a rescue therapy in refractory patients and as an option for de-escalation from medical therapy.

• Conclusion

This new case-based review provides insights on the use of CDED+PEN in different treatment strategies

Dietary therapy may be more potent than previously thought. The authors believe that they should go beyond current goals with next generation modulating therapies at addressing the source of inflammation. The CDED shows promise in this field.

Dietary guidance from the International Organization for the Study of Inflammatory Bowel Diseases

Levine A, Rhodes JM, Lindsay JO, Abreu MT, Kamm MA, Gibson PR, Gasche C, Silverberg M, Mahadevan U, Boneh RS, Wine E, Damas OM, Syme G, Trakman GL, Yao CK, Stockhamer S, Hammami MB, Garces LC, Rogler G, Koutroubakis IE, Ananthakrishnan AN, McKeever L, Lewis JD

Clinical Gastroenterology and Hepatology 2020;18:1381–1392

https://pubmed.ncbi.nlm.nih.gov/32068150/

• Background

Crohn's disease (CD) and ulcerative colitis (UC) may be linked to environmental factors, such as diet, which may have an important role in pathogenesis and inflammation. The International Organization for the Study of Inflammatory Bowel Disease (IOIBD) prepared a dietary guidance for physicians, dietitians and patients, based on best available evidences.

• Methods

The IOIBD working group is composed of 12 members from 3 continents who met in March 2018 and selected 7 food groups, dietary components and 5 food additives as the most important to address for patient dietary guidance. Members reviewed the published literature for each chosen food or additive and prepared a concise document with overall recommendations and a narrative summary.

• Results

Dietary therapies based on exclusion of foods and replacement with nutritional formulas and/or a combination of both may induce remission in CD and UC.

• Conclusion

Although there is evidence that identifies potential harmful or beneficial dietary components, physicians and patients did not have guidance regarding which foods are safe, protective or deleterious. This document provides expert opinion regarding specific dietary components, food groups and food additives that should be increased or decreased from the diet of patients with CD, UC or other inflammatory bowel diseases to help control and prevent relapse. Among the dietary options assessed the IOIBD expert panel acknowledged the principles of CDED.

The medical management of paediatric Crohn's Disease: an ECCO-ESPGHAN Guideline update

van Rheenen P, Aloi M, Assa A, Bronsky J, Escher J, Fagerberg U, Gasparetto M, Gerasimidis K, Griffiths A, Henderson P, Koletzko S, Kolho KL, Levine A, van Limbergen J, Martin de Carpi FJ, Navas-López VM, Oliva S, de Ridder L, Russell RK, Shouval D, Spinelli A, Turner D, Wilson D, Wine E, Ruemmele FM

Journal of Crohn's and Colitis. 2020 Oct 7;jjaa161.

https://pubmed.ncbi.nlm.nih.gov/33026087/

• Background

Recent years have seen important advances in the care of children with Crohn's Disease (CD). Based on these new clinical evidencesthe objective of this work was to up-date the ECCO-ESPGHAN guideline on the medical management of children with CD.

• Methods

Ten working groups worked on 17 PICO-structured clinical questions (Patients, Intervention, Comparator and Outcome). A medical librarian performed a systematic literature search using MEDLINE, EMBASE and Cochrane Central databases, from January 1st, 1991 to March 19, 2019. Thirty draft statements were further refined and voted during a consensus meeting that occurred in Barcelona in October 2019. A total of 22 statements reached ≥80% and were reported in the present review.

• Results

The sooner patients at high risk of complicated disease course are identified, the better. This will prevent and reduce bowel damage. Children with perianal disease, stricturing or penetrating behaviour, or even severe growth retardation should be considered for antitumour necrosis factor (TNF) agents in combination with an immunomodulator as first line treatment. The consensus also recommends therapeutic drug monitoring to guide treatment changes over escalating anti-TNF dose or switching therapies on an empiric form. Patient with low-risk luminal CD should be induced with exclusive enteral nutrition (EEN), or with corticosteroids when EEN is not an option, and need immunomodulator-based maintenance therapy. Outcomes are better when there is a close monitoring of treatment response, with therapy adjustments when needed. Serial faecal calprotectin measurements or small bowel imaging are more consistent markers of treatment response than clinical scores alone.

• Conclusion

These guidelines support the medical treatment and long-term management of children and adolescents with CD. For the first time partial enteral nutrition (PEN) at 50% of daily energy was recommended for maintenance therapy. Also, although CD exclusion diet (CDED) is not yet part of these guidelines, it is described and mentioned as an option, which represents a potential for the future.

EEN yesterday and today ... CDED today and tomorrow

Herrador-López M, Martín-Masot R, Navas-López VM

Nutrients. 2020 Dec 10;12(12):3793

https://pubmed.ncbi.nlm.nih.gov/33322060/

• Background

Crohn's Disease (CD) is a chronic idiopathic inflammatory condition, with periods of inflammatory activity alternating with remission. Around 10-25% of all inflammatory bowel disease cases are diagnosed before 21 years old. The treatment of pediatric CD needs management of mucosal healing and optimization of growth, balanced with a proper bone health. The aim of this review was to highlight the role of enteral nutrition in the treatment of CD, especially the new dietary modalities, such as Crohn's Disease Exclusion Diet (CDED).

• Conclusion

The first line treatment of luminal CD is exclusive enteral nutrition (EEN), however its therapeutics mechanisms are still being investigated by studying the gut microbiota and other immune modulatory functions. New modalities of dietary treatment indicate there's a successful future for the nutritional management of CD. Among the diet options the CDED, acts on the triggers of inflammation and dysbiosis (by reducing dietary exposure to products that negatively affect microbiota) by increasing the time of clinical remission and promoting healthy lifestyle habits. The advances of CDED, which minimize the problems of EEN, has facilitated an improvement in the treatment of pediatric CD. It has shown to respond to a frequent demand by patients and their caregivers with respect to acceptability and compliance. The CDED is as effective as EEN to induce clinical and biochemical remission, but better than EEN with regards to tolerance and compliance. It is nutritionally balanced: the dietary fiber helps correct the bacterial dysbiosis that CD patients usually have. CDED constitutes a long-term strategy that may be used as monotherapy, as combination therapy, for de-escalation of drugs, and as a rescue therapy for refractory patients.

Narrowing the protein deficit gap in critically ill patients using a very high-protein enteral formula

ApSimon M, Johnston C, Winder B, Cohen SS, Hopkins B

Nutr Clin Pract. 2020 Jun;35(3):533-539.
https://pubmed.ncbi.nlm.nih.gov/32083356/

• Background

Patients with protein deficit admitted to intensive care unit (ICU), stay longer and have higher mortality rates. Studies have shown that meeting protein goals is more important than meeting energy targets and prevents harmful effects of overfeeding. The aim of this study was to assess whether a very-high protein (VHP) enteral nutrition (EN) formula provided adequate protein levels, without overfeeding in the first week of ICU stay.

• Methods

Forty patients admitted to ICU [average Acute Physiology and Chronic Health Evaluation II score of 20.1] in exclusive EN feeding for more than 5 days were included in a retrospective study. Twenty patients received standard EN, the remaining 20 received the VHPEN formula (1 kcal/mL, 37% protein). Investigators registered protein and energy prescribed/received, gastrointestinal tolerance and feeding interruptions.

• Results

Protein prescribed and received was significantly higher in the VHP group, compared to the standard EN group. Energy prescribed and received was similar between groups (table 1). There were no differences in gastrointestinal tolerance nor feeding interruptions.

	VHP group	Standard EN group	P value
Protein prescribed	135.5 g/d ± 22.9	111.4 g/d ± 25	0.003
Protein received	112.2 g/d ± 27.8	81.7 ± 16.7	0.002
Energy prescribed	1606 kcal/d ± 402	1893 kcal/d ± 341	0.101
Energy received	1520 kcal/d ± 346	1506 kcal/d ± 380	0.901

• Conclusion

ICU patients who were fed with a VHP formula had higher protein intake with no overfeeding nor need of modular protein in the first 5 days of exclusive EN.

Meeting calorie and protein needs in the critical care unit: a prospective observational pilot study

Yamamoto S, Allen K, Jones KR, Cohen SS, Reyes K, Huhmann MB

Nutr Metab Insights. 2020 Feb 26;13:1178638820905992.

https://pubmed.ncbi.nlm.nih.gov/32153344/

• Background

Poor clinical outcomes are usually related to inadequate calorie and protein intake during illness, however most critically ill patients are not properly fed with these nutrients. The aim of this study was to evaluate if an enteral formula with an adequate composition of protein and energy could help these patients' nutritional goals.

• Methods

This single center, prospective, observational study included 29 adults in an intensive care unit who needed enteral nutrition for, at least, 3 days. They were fed with an enteral formula high in calories and enzymatically hydrolyzed 100% whey peptide-based for up to 5 days. The primary outcome was the ability to achieve 50% of caloric goals within the first 3 days and the secondary outcome, the daily percentage of protein goals attained and gastrointestinal tolerance.

• Results

Four participants were excluded and 25 were included, 92% of them were on a mechanical ventilator and experienced organ failure. They were aged 55.5 ± 16.9 years-old and had a mean body mass index (BMI) of 27.9 ± 7.5 kg/m^2. During the first 3 days, the primary outcome was achieved in 78.9% of the participants and the secondary outcome in 73.7%. Globally, using the study formula, calorie goals were achieved by 75.0 ± 26.3% and protein goals by 69.3 ± 26.7%.

• Conclusion

More than half of the critically ill patients of this study exceeded 50% of caloric and protein goals using an enteral formula high in calories and enzymatically hydrolyzed 100% whey peptide based. No severe gastrointestinal intolerance was registered.

Effect of high-protein nutrition in critically ill patients: A retrospective cohort study

Suzuki G, Ichibayashi R, Yamamoto S, Serizawa H, Nakamichi Y, Watanabe M, Honda M

Clin Nutr ESPEN. 2020 Aug;38:111-117.
https://pubmed.ncbi.nlm.nih.gov/32690144/

• Background

The prognosis of patients in intensive care units is improved when they are given high-protein nutrition at an early stage, however this increases blood urea nitrogen (BUN). There are no studies on outcomes of protein intake neither on the clinical changes in blood urea nitrogen (BUN) in patients in intensive care units. The aim of this study was to assess the relation of high protein intake with outcomes and BUN and the clinical significance of the changes of BUN.

• Methods

This single-center retrospective study included 295 ICU patients who received enteral nutrition for at least 3 days, together with mechanical ventilation between 1 January 2016 and 30 September 2019. Exclusion criteria were age < 18-year, gastrointestinal disease, maintenance dialysis, renal replacement therapy after admission, kidney transplantation and death within 7 days after starting enteral nutrition. After exclusion criteria, 206 patients remained in the study, who were divided into those receiving > 1.2 g/kg/day of protein (n = 111, high-protein group) and those receiving ≤ 1.2 g/kg/day of protein (n = 95, non-high-protein group). Both groups were balanced by predisposition score matching. Primary endpoint was 28-mortality, and secondary endpoints were 90-day mortality, length of ICU stay, number of ventilator-free days in the first 28 days and changes in BUN.

• Results

28- and 90-day mortality was significantly lower in patients on the high-protein group. Changes in BUN were greater, including after propensity score matching.

• Conclusion

The provision of > 1.2 g/kg/day of protein may be related to lower mortality rates in tube-fed and ventilated patients. Also, although high protein may be related to higher BUN, the changes may not be adversely associated with outcomes.

Malnutrition prevalence on patients' admission at Nuestra Señora del Prado General Hospital, Talavera de la Reina

Milla M, López S, Alía M, Marín Guerrero AI, Blanco B

Nutrition Hospitalaria. 2021 Jan 18

https://pubmed.ncbi.nlm.nih.gov/33455405/

• Background

Malnutrition is a global problem, affecting hospitalized patients in particular, and influenced by eating habits and the presence of disease. The aim of this study was to determine the prevalence of the risk of malnutrition upon admission to the Nuestra Señora del Prado General Hospital in Talavera de la Reina (Spain).

• Methods

This was an observational, transversal and descriptive study that included patients from September 2017 to October 2018.They were nutritionally screened using the NRS-2002® test. Anthropometric and clinical data were registered for patients at nutritional risk (NRS-2002® score≥3). Malnutrition was diagnosed according to type and severity, and nutritional indications were recorded in the report to the clinician and kept until discharge.

• Results

From the 476 patients who took the NRS-2002® test upon admission, 137 were at risk of malnutrition. The average BMI was 24.6 kg/m^2. Nutritional supplementation was recommended to 78,4% of the patients and nutritional status (ICD-10) was registered to 82.1%. At discharge, more than 70% of these recommendations were missing.

• Conclusion

Upon admission, 28.8% of the patients were at risk of malnutrition or undernourished. It is fundamental to incorporate screening methods at admission to detect these conditions and implement nutritional interventions and the incorporation of trained health personnel.

Monitoring of the patient with home enteral nutrition by tube: nutritional status, quality of life and use of health resources (Seguimiento del paciente con nutrición enteral domiciliaria por sonda: estado nutricional, calidad de vida y uso de recursos sanitarios)

López Osorio N, Gómez Vázquez E, González Rodríguez M, Cao Sánchez MP, Ferreiro Fariña S, Blanco Naveira M, Garí Peris C, Cantón Blanco A, Martínez Olmos MA

SENPE 2020

https://www.nutricionhospitalaria.org/articles/03332/show#!

• Background

The aim of this study was to assess the nutritional state, the quality of life and need of health resources of patients with tube home enteral nutrition (HEN), before and after starting a monitoring programme by phone (NEXO®), complementary to usual care.

• Methods

This was an observational study in adult patients with tube HEN from a tertiary health area. Data registered included sociodemographic variables, nutritional status (MNA®), QoL (NutriQoL®) and use of health resources not related with the condition six months before and after the start of the monitoring programme.

• Results

The study included 43 patients (mean age 72.2; 53,5% female; average of 3,9 years of HEN). A total of 401 phone calls were registered, with 7,4% from the patient proactivity. Some patients were at risk of malnutrition, with no differences in the MNA® at 6 months follow up. The nutritional state was good, with no difference between assessments. The total cost of not programmed health resources was 6229,3€ and 4711,1€ in the months before and after monitoring, with savings of 1518,2€ due to less emergency needs.

• Conclusion

Telephone and close monitoring has helped patients maintain their nutritional state and quality of life and reduce not programmed resources related to HEN.

Reduction in healthcare utilization with transition to peptide-based diets in intolerant home enteral nutrition patients

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Nutr Clin Pract. 2020 Jun;35(3):487-494

https://pubmed.ncbi.nlm.nih.gov/32149433/

• Background

The prevalence of home enteral nutrition (HEN) continues to increase and can be a life-sustaining therapy in patients with a functional gastrointestinal (GI) tract who are unable to meet their nutrition needs by oral intake. Major clinical guidelines recommend initiating standard polymeric formulas (SPFs) unless special indications are present. Unfortunately, not all patients tolerate SPFs, especially in hospitalized critically ill patients. Intolerance of EN can be associated with significant morbidity and mortality, including symptoms of GI distress. An approach is to substitute the EN formula to include the use of peptide-based enteral formulas (PBDs). This study aimed at evaluating the tolerance of PBDs in patients at risk for malabsorption and the impact of transitioning to PBDs in patients who showed intolerance to SPFs.

• Methods

A retrospective review of electronic medical records (EMRs) was conducted, for patients who had research authorization and received PBDs as exclusive EN from January 1, 2016, to May 31, 2018. The sample was subdivided into 2 groups: (1) HEN-naïve patients who were started on PBDs directly and (2) patients who were transitioned to PBDs because of intolerance of SPFs. A total of 588 patients received HEN.

• Results

Forty-four percent of patients who were started on PBDs directly presented no symptoms of intolerance. The major symptoms of intolerance reported were nausea and vomiting (20%), diarrhea (15%), abdominal pain/cramping (8%), gas/bloating (6%), and abdominal distension (6%). In the switch group, the symptoms of intolerance significantly improved after transitioning to PBDs from SPFs. The frequency of nausea and vomiting improved from 42% to 22% ($P = 0.02$), diarrhea from 46% to 25% ($P = 0.002$), abdominal pain/cramping from 22% to 5% ($P = 0.01$), and abdominal distention from 9% to 2% ($P = 0.17$). Although only 21% of patients were symptom free while using SPFs, up to 49% of patients were symptom free with PBDs without any symptoms after being switched. A similar trend was also seen in the utilization of healthcare resources relating to HEN tolerance: mean number of phone calls (1.8 ± 1.6 to 1.1 ± 0.9, $P = 0.006$), mean number of emergency room visits (0.3 ± 0.6 to 0.09 ± 0.3, $P = 0.015$), and mean number of provider visits (1.3 ± 1.3 to 0.3 ± 0.5, $P < 0.0001$).

• Conclusion

The study showed that PBDs were well tolerated as the initial formula in patients at risk for malabsorption. Additionally, switching to PBDs in SPF-intolerant patients resulted in improved tolerance, as well as a reduction in healthcare utilization. Although PBDs may have increased cost compared with SPFs, these costs can be significantly outweighed by the cost of healthcare utilization. Prospective studies are necessary to confirm these findings in the HEN population and compare with other approaches, such as BTF.

Real-world evidence of treatment, tolerance, healthcare utilization, and costs among adult post-acute care patients receiving enteral peptide-based diets in the United States

LaVallee C, Seelam P, Balakrishnan S, Lowen C, Henrikson A, Kesting B, Perugini, M, Araujo Torres K

ASPEN 2020 Nutrition Science and Practice Conference Poster

https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Fjpen.1813&file=jpen1813-sup-0001-SuppMat.pdf/

• Background

Disease-related malnutrition/undernutrition can impair muscle strength, immunity, or wound healing, and is associated with a considerable economic burden. Standard ETF formulas contain complex nutrients, and some patients experience poor gastrointestinal tolerance, characterized by nausea, vomiting, bloating, constipation and diarrhea. Enteral tube feeding (ETF) is a medical nutrition therapy, typically initiated in a hospital setting, used to help meet nutritional requirements in patients who have inadequate volitional intake. Peptide-based (PB) ETF formulas have been shown to be well-tolerated in a post-acute care setting in patients with malabsorption. The objective of this study was to evaluate the real-world tolerance, healthcare utilization and cost of peptide based (PB) ETF in adults in the post-acute care setting.

• Methods

The study was conducted on a group of 1,022 adult patients that received Peptamen® formulas (wPBD) via ETF after hospital discharge, in the period from Q1-2013 to Q4-2017. Medical claims data were obtained in the post-acute care setting for up to one year after initiation of wPBDs, in the post-acute care setting, from the Decision Resources Group Real World Evidence Data Repository US database. A multivariate general linearized model, adjusted for age, gender, and Charlson Comorbidity Index score was used to estimate resource use costs. Considering study variables, means, standard deviations, and proportions were evaluated as univariate statistics.

• Results

Patients included had an average age of 47.5 years and 54% were female. Underlaying medical conditions affected the digestive system (42.2%), respiratory system (24.5%), circulatory system (20.3%), and nervous system (17.8%) or were endocrine nutritional and metabolic diseases (32.9%). The data showed a statistically significant improvement in tolerance after initiation of wPBD for all outcomes evaluated: nausea and vomiting, 288 (28.2%) vs 159 (15.6%), p<0.001; diarrhea, 262 (25.6%) vs 177 (17.3%), p<0.001; constipation 295 (28.9%) vs 215 (21.0%), p<0.001; abdominal distension, 144 (14.1%) vs 82 (8.0%), p<0.001; gastric residual, 78 (7.6%) vs 47 (4.6%), p=0.005. The percentage of patients experiencing one or multiple gastrointestinal intolerance events also declined after initiation of wPBD, with a corresponding increase in the percentage of patients experiencing no gastrointestinal intolerance events. 30, 90 and 180 days after initiating PB ETF, 42.6%, 56.9% and 66.4% of patients, respectively, had at least one inpatient visit recorded, while 99.8%, 100% and 100% respectively, recorded at least one outpatient visit. The modeled cost of inpatient, outpatient and emergency room visits (Table 1) show that of the total 180-day resource use costs of $ 7,050 per patient, 38% are attributable to inpatient visits, 56% to outpatient visits, and 6% to emergency room visits.

• Conclusion

The diet was associated with a reduction in all gastrointestinal intolerance events. All patients reported at least one outpatient visit and the inhospital visits were less frequent. Outpatient visits represented most healthcare costs, with a small percentage of emergency room visits.

High protein intake after subarachnoid hemorrhage improves ingestion function and temporal muscle volume

Onodera H, Mogamiya T, Mori M, Matsushima S, Sase T, Nakamura H, Sakakibara Y

ESPEN2020

https://espencongress.com/wp-content/uploads/2020/09/ESPEN-2020-Programme-for-ON-DEMAND-eposters-and-LB-v3.pdf

• Background

The clinical significance in ingestion function of the development of atrophy in the temporal muscle of patients with subarachnoid hemorrhage is not clear. This study's objective was to assess if temporal muscle volume (TMV) is related to the ingestion in SAH patients and examine predictors in temporal muscle atrophy.

• Methods

This was a retrospective, single-center study that included 60 SAH patients who received enteral nutrition in their acute phase from 2009 to 2019.TMV was measured on admission and week two by automatic segmentation of CT images. According to the TMV change, patients were divided into two groups: atrophied group (n=24), with patients with more than 20% reduction of TMV, and maintained group (n=36), with patients with less reduction. The food intake level scale (FILS) 7-9 at week two defined as a good oral intake, and the modified Rankin Scale (mRS) 0–2 at discharge is defined as a good prognosis. Also, protein intake on day four was collected.

• Results

The maintained group had a better ingestion function and mRS than the atrophied group. Good oral intake and good mRS were significantly affected by maintaining TMV at week 2, based on the univariate logistic analysis. Also, multivariable regression analysis revealed that protein intake on day four was significantly affected the TMV maintenance.

	Atrophied group (n=24)	Maintained group (n=36)	P-value
FILS 7-9 after 2 weeks, n (%)	8 (33.3%)	22 (61.1%)	0.064
mRS 0-2 at discharge, n (%)	11 (45.8%)	26 (72.2%)	0.058

• Conclusion

High-protein intake in the acute stage of SAH may contribute to improving the ingestion function and the maintenance of temporal muscle.

The selection of enteral nutrition in stroke influence on in-hospital infection control and hospital cost

Onodera H, Mogamiya T, Matsushima S, Kawaguchi K, Sase T, Nakamura H, Sakakibara Y

International Stroke Conference 2020

https://aha.scientificposters.com/epsAbstractAHA.cfm?id=1ç

• Background

People who suffer from stroke may have an unfavorable functional outcome after common complications, such as infection. It is known that nutritional intervention reduces the risk of postoperative infections; however, differences in products' outcomes are not clear. This study aimed to investigate if the selection of enteral nutrition in the acute phase of stroke patients may help control infections and hospital costs.

• Methods

This study was a retrospective analysis in a Japanese center and included 50 stroke patients who received enteral nutrition from April 2017 to March 2019. Patients were divided into two groups, Group 1 (n=25) who were on general nutrition of 1.0 kcal/mL, and Group 2 (n=25), who started with a high protein whey peptide-digested liquid diet (1.5 kcal/mL) and were switched to a liquid diet with highly fermentable fiber after four days. Data registered included length of hospital stay, days of antibiotic use, severe infection (including methicillin-resistant *Staphylococcus aureus*, extended-spectrum β-lactamase producing *Enterobacteriaceae*, and *Clostridium difficile*).

• Results

Both groups had similar baseline characteristics. The mean length of hospital stay was also equivalent (48.0 vs. 47.8 days). Group 1 used antibiotics for longer than group 2 (16.5 vs. 11.3 days). Serious infections were also more prevalent in group 1 (6 cases vs. 4 cases). Total hospital costs were lower in Group 2, with an average of 500 USD/patient less than Group 1 patients.

• Conclusion

The choice of enteral nutrition in stroke patients in the acute phase affects the risk of in-hospital infections and hospital costs.

Effect of high-protein nutrition in critically ill patients: a retrospective cohort study

Suzuki G, Ichibayashi R, Yamamoto S, Serizawa H, Nakamichi Y, Watanabe M, Honda M

Clinical Nutrition ESPEN 2020 Aug;38:111-117

https://pubmed.ncbi.nlm.nih.gov/32690144/

• Background

Patients in intensive care units (ICUs) may see their prognosis improved with an early provision of high-protein nutrition. However, high protein intake increases blood urea nitrogen (BUN). There is a gap in studies that compare changes in BUN and outcomes according to protein intake. This study aimed to research the relation of high protein intake with outcomes and BUN and evaluate the clinical significance of changes of BUN.

• Methods

This single-center retrospective cohort study occurred between 1 January 2016 and 30 September 2019 and assessed 295 ICU patients who received enteral nutrition for at least three days while on mechanical ventilation. Exclusion criteria included age < 18 years old, gastrointestinal disease, maintenance dialysis, renal replacement therapy after admission, kidney transplantation, and death with seven days.

• Results

A total of 206 patients were included. They were divided into two groups: those receiving >1.2 g/kg/day of protein (high protein group, n=111) and those receiving ≤1.2 g/kg/day (non-high protein group, n=95). Groups were balanced according to propensity score matching. The primary endpoint was 28-day mortality, and the secondary endpoints were 90-day mortality, length of ICU stay, number of ventilator-free days in the first 28 days, and changes in BUN. The high protein group had significantly lower 28- and 90-day mortality and significantly better changes in BUN.

• Conclusion

Although BUN changes may not be associated with outcomes, the provision of >1.2 g/kg/day of protein may be associated with lower mortality in these patients.

Value of nutrition support therapy: impact on clinical and economic outcomes in the United States

Tyler R, Barrocas A, Guenter P, Araujo Torres K, Bechtold ML, Chan LN, Collier B, Collins NA, Evans DC, Godamunne K, Hamilton C, Hernandez BJD, Mirtallo JM, Nadeau WJ, Partridge J, Perugini M, Valladares A, and the ASPEN Value Project Scientific Advisory Council

JPEN J Parenter Enteral Nutr. 2020 Mar;44(3):395-406.

https://pubmed.ncbi.nlm.nih.gov/31994761/

• Background

Nutrition therapy may represent an improvement in patient outcomes and reduction of costs in the United States. The aim of this study was to seek for evidence and to analyze claims to appreciate the financial and quality impact of nutrition support therapy on high-priority therapeutic conditions.

• Methods

This project was divided in two different tasks: Task 1 consisted of a review of literature from 2013 to 2018 to identify evidence of clinical and economic impact of nutrition therapy on patient outcomes across 13 therapeutic areas; Task 2, an analytic claims modeling was performed using the sample dataset of Medicare Parts A and B claims. Medicare beneficiaries diagnosed in 5 therapeutic areas (sepsis, gastrointestinal cancer, hospital-acquired infections, surgical complications and pancreatitis) were identified in the studies from Task 1, and their care costs were assessed based on nutrition intervention.

• Results

From 1099 initial publications, 43 articles met the criteria, with 8 of them using the Medicare claims modeling. One example of the modeling consisted on the savings of $52 million/year if an advanced enteral nutrition formula was used in a sepsis population. The total projected annual cost savings from the 5 selected therapeutic areas was $580 million.

• Conclusion

Medicare spending can be reduced by millions of dollars every year if nutrition support therapy is optimized across different therapeutic areas. These results also confirm the evidence-based value proposition of timely nutrition support to improve clinical outcomes with substantial savings.

Preoperative oral immunonutrition in gastrointestinal surgical patients: How the tumour microenvironment can be modified

D'Ignazio A, Kabata P, Ambrosio MR, Polom K, Marano L, Spagnoli L, Ongaro A, Pieretti L, Marrelli D, Biviano I, Roviello F

Clin Nutr ESPEN. 2020 Aug;38:153-159.
https://pubmed.ncbi.nlm.nih.gov/32690150/

• Background

Surgical resection is the main treatment for the majority of gastrointestinal cancers. However, different factors may influence its final outcome, such as malnutrition. The aim of this study was to assess the impact of enteral immunonutrition on the cell-mediated immune response in the microenvironment of gastrointestinal cancers.

• Methods

This was a prospective pilot study that compared the immunophenotypic structure of the immune cells before (biopsy) and after (surgical sample) the administration of enteral immunonutrition in 16 patients with the same structure in 8 patients who received regular diet. Antibodies tested included CD4, CD8, PD-1, FOX-P3, CD68, CC163, CD80, CD21, CD56 and PD-L1. Samples of non-tumor tissue from sleeve-gastrectomy were used as non-neoplastic control.

• Results

Treated patients showed a modulation of the immune response with higher number of cytotoxic and helper T-cells in the surgical sample compared to the biopsy sample, and lower number of lymphocytes presenting an exhausted (double positive CD8 and PD-1 lymphocytes) and regulatory (double positive CD4 and FOX-P3 lymphocytes) phenotype. Also, a M1 polarization was noticed with a lower number of CD163 positive macrophages and the inhibition of the PD-1/PD-L1 pathway in treated patients.

• Conclusion

Immunonutrition has shown impact on the tumoral tissues of gastric and colorectal cancer, with activation of the inflammatory pathway, in regards to humoral and cellular response.

Nutritional status according to the mini nutritional assessment (MNA)® as potential prognostic factor for health and treatment outcomes in patients with cancer – a systematic review

Torbahn G, Strauss T, Sieber CC, Kiesswetter E, Volkert D

BMC Cancer. 2020 Jun 26;20(1):594.
https://pubmed.ncbi.nlm.nih.gov/32586289/

• Background

The Mini Nutritional Assessment (MNA®) is a questionnaire used to validate the nutritional status of patients with cancer. Cancer patients with malnutrition have poorer outcomes. The objective of this study was to assess the result of the MNA® in older patients with cancer.

• Methods

This study analyzed four databases regarding MNA® and reported outcomes. Two reviewers searched for this information on titles/abstracts and full-texts and classified the risk of bias in an independent way.

• Results

Although numerous variations between patient and study characteristics were found in 56 studies, the risk of malnutrition assessed by MNA® predicted significantly a higher risk of mortality / poor overall survival (22/27 studies), shorter progression-free survival / time to progression (3/5 studies), treatment maintenance (5/8 studies) and health-related quality of life (2/2 studies), but did not predict treatment toxicity / complications (1/7 studies) or functional status / decline (1/3 studies). Other outcomes, such as length of hospital stay (2 studies), falls, fatigue and unplanned hospital admissions (1 study each) had no results reported. The risk of bias as considered moderate to high.

• Conclusion

The MNA® was found to predict mortality / survival, cancer progression, treatment maintenance and health-related quality of life, but did not predict adverse treatment outcomes and functional status / decline in patients with cancer. Due to the high risk of bias, there is a need of more studies.

Unmet needs in clinical nutrition in oncology: a multinational analysis of real-world evidence

Caccialanza R, Goldwasser F, Marschal O, Ottery F, Schiefke I, Tilleul P, Zalcman G, Pedrazzoli P

Ther Adv Med Oncol. 2020 Feb 14;12:1758835919899852.
https://pubmed.ncbi.nlm.nih.gov/32110247/

• Background

There is a lack in the understanding of cancer-related malnutrition and the use of clinical nutrition (CN). The aim of this analysis was to explore the relation between diagnosis and treatment frequency of malnutrition in a multinational questionnaire to detect unmet needs in the care of cancer patients.

• Methods

Three administrative healthcare datasets from France (n = 570,727), Germany (n = 4,642) and Italy (n = 58,468) were retrospectively analyzed regarding different aspects: data from France described frequency and timing of malnutrition diagnosis in patients with gastrointestinal cancer. Data from Germany described home parenteral nutrition (HPN) use in patients with stage III/IV cancers. Italian data analyzed metastatic with CN, metastatic without CN and patients without metastatic disease.

• Results

77% of the French patients had no malnutrition diagnosis, 13% were diagnosed with malnutrition after hospitalization and 10% had a malnutrition diagnosis at first hospitalization. In Germany, 16% of the patients received HPN, and the mean to starting HPN was 3 months before death. In Italy, 8.4% of metastatic cancer patients received CN, with an average time between metastasis diagnosis and first CN being 6.6 months. The average time between first CN and death was 3.5 months.

• Conclusions

Cancer-related malnutrition is under-recognized and undertreated. Clinical nutrition is usually prescribed as a last resource nutrition before death or is not prescribed. The adequate use of CN is still challenging, and current practice does not help taking conclusions regarding optimal use for patients at nutritional risk. It is very important to generate awareness on malnutrition and clinical and economic benefits of CN.

Post-discharge oral nutritional supplements with dietary advice in patients at nutritional risk after surgery for gastric cancer: A randomized clinical trial

Meng Q, Tan S, Jiang Y, Han J, Xi Q, Zhuang Q, Wu G

Clin Nutr. 2021 Jan;40(1):40-46.
https://pubmed.ncbi.nlm.nih.gov/32563598/

• Background

Patients with gastric cancer subject to surgery often suffer from malnutrition after hospital discharge, which is related to negative outcomes. There is a gap in information concerning the impact of post-discharge nutritional interventions. The objective of this study was to assess the impact of oral nutritional supplements (ONS) with dietary advice compared with dietary advice alone on post-discharge nutritional outcomes, such as body mass index (BMI), skeletal muscle index (SMI), sarcopenia, chemotherapy tolerance, 90-day readmission rate and quality of life in patients at nutritional risk after gastric cancer surgery.

• Methods

This was a prospective, single-center, open-label, non-blinded, and randomized controlled trial, with 353 patients subject to surgery for gastric cancer and at nutritional risk. They were randomly assigned to receive either ONS with dietary advice or dietary advice alone for 3 months after discharge. Primary endpoints included nutritional outcomes and sarcopenia prevalence, and secondary endpoints included chemotherapy tolerance, 90-day readmission rate and quality of life.

• Results

The study was completed by 337 patients, with 171 in the ONS group and 166 in the control group. The average daily intake of ONS was 370 mL in the intervention group. Three months later, patients in the intervention group had significantly less weight loss and higher BMI and SMI than those in the control group. Sarcopenia incidence was significantly lower in the ONS group. The number of patients who underwent postoperative chemotherapy was similar in both groups, however, those on ONS had significantly less chemotherapy modifications (delay, dose reduction or termination). 90-day readmission rate had no significant differences. Also, patients who received ONS referred significantly less fatigue and appetite loss, but there were no significant differences in the other outcomes.

• Conclusion

Oral nutrition supplements on post-discharge after gastric cancer surgery improved nutritional outcomes, skeletal muscle maintenance, chemotherapy tolerance and some quality of life variables, which supports the introduction of ONS to these patients.

Impact of oral nutritional supplements in post-discharge patients at nutritional risk following colorectal cancer surgery: A randomized clinical trial

Tan S, Meng Q, Jian Y, Zhuang Q, Xi Q, Xu J, Zhao J, Sui X, Wu G

Clin Nutr. 2021 Jan;40(1):47-53.

https://pubmed.ncbi.nlm.nih.gov/32563599/

• Background

Clinical nutrition guidelines endorse the use of adequate nutritional support therapy for surgical cancer patients at risk of malnutrition during hospital stay and following discharge. Former studies have only focused on patients during hospital stay, which sets a gap in evidence supporting the same recommendations for post-discharge patients after cancer surgery, especially those who underwent gastrointestinal cancer surgery and are at high risk of malnutrition. The aim of this study was to evaluate the impact of oral nutritional supplements (ONS) in post-discharge patients at nutritional risk following colorectal cancer surgery.

• Methods

Post-discharge patients who had been subject to colorectal cancer surgery were randomized to receive ONS with dietary advice or dietary advice alone for 3 months. Primary endpoints were nutritional outcomes and sarcopenia prevalence, and secondary outcomes were 90-day readmission rate, chemotherapy tolerance and quality of life.

• Results

The trial was completed by 212 patients (105 in the ONS group). Mean ONS daily intake was 410 mL. After 3 months of intervention, the ONS group has a significantly higher skeletal muscle index, but no significant differences between the two groups were registered in weight, weight loss, body mass index, serum albumin and hemoglobin. Also, the ONS group had significantly lower sarcopenia prevalence. There was no difference in 90-day readmission rate. Chemotherapy modifications (delay, dose reduction or termination) were significantly reduced in the ONS group, however ONS had no impact on quality of life.

• Conclusion

The use of ONS may help reduce skeletal muscle loss and sarcopenia prevalence, as well as improve chemotherapy tolerance, compared to dietary advice alone in post-discharge patients at nutritional risk following colorectal cancer surgery, which supports the importance of ONS in these patients.

Specific quality of life assessment by the Nutriqol® Questionnaire among patients receiving home enteral nutrition

Campos RZ, Colomar Ferrer MT, Ruiz López RM, Sanchís Cortés MP, Urgelés Planella JR

JPEN J Parenter Enteral Nutr. 2020 May 27

https://pubmed.ncbi.nlm.nih.gov/32459026/

• Background

Quality of life (QoL) may be affected by Home enteral nutrition (HEN), either tube feeding or oral supplementation. It is important to assess the factors that affect QoL to identify conditions related with HEN. The objective of this study was to measure if the NutriQoL® questionnaire is suitable for evaluating the QoL and factors that impact patients receiving HEN.

• Methods

The NutriQoL® and SF-12 questionnaires were completed by 78 patients on HEN during their routine visits to nutrition service at the hospital.

• Results

Table 1: Patient characteristics

	NutriQoL® at recruitment	SF-12 at recruitment
Patients receiving HEN: Cancer (90%) Oral supplements (58%) Tube feeding (42%)	66 ± 14	40 ± 9

There was a positive correlation between NutriQoL® and SF-12 scores. NutriQoL® were dependent of the HEN type (oral vs. tube), age and sex, and the absence of secondary effects (table 2). The second visit showed significant improvements in NutriQoL® results.

Table 2: Correlation analysis between NutriQoL Scores, SF-12 Scores and Patients' Characteristics

Correlation factors (ρ)	Visit 1 (n = 78)			Visit 2 (n = 64)		
	NutriQoL					
	FF-AVD	VS	Total	FF-AVD	VS	Total
MCS12	0.317**	0.217	0.322**	0.156	0.063	0.154
PCS12	0.336**	0.271*	0.359**	0.290*	0.214	0.307*
SF-12	0.474**	0.396**	0.503**	0.270*	0.162	0.279*
Sex (male vs. female)	-0.095	-0.005	-0.094	0.128	0.033	0.112
Age	-0.121	-0.044	-0.113	-0.057	-0.181	-0.086
Underlying disease (cancer vs. other)	0.251*	0.016	0.214	0.276*	-0.062	0.216
HEN type (oral vs. tube)	-0.364**	-0.495**	-0.434**	-0.578**	-0.397**	-0.596**
HEN experience (with vs. without)	-0.091	-0.108	-0.103	-0.075	-0.169	-0.106
HEN complications (some vs. any)	-0.264*	-0.219	-0.281*	-0.290*	-0.072	-2.75*
Body weight	-0.41	-0.42	-0.61	-0.34	0.061	-0.007
BMI	-0.037	-0.051	-0.063	0.015	0.042	0.036
Questionnaires answering (patient vs. caregiver)	-0.029	-0.023	-0.024	0.054	-0.118	0.005

FF-AVD, physical functioning and activities of daily living; VS, social life aspects; Total, quality of life associated to enteral nutrition; MCS12, mental component summary scale from the SF12 questionnaire; PCS12, physical component summary scale and SF-12, total score for general quality of life scale; HEN, home enteral nutrition; BMI, body mass index. Spearman's correlation test. *p < 0.05; **p < 0.001.

• Conclusion

The NutriQoL® questionnaire identified problems that affect the QoL of patients on HEN, while the SF-12 did not. QoL is affected by the route of HEN and the occurrence of complications. Therefore, the NutriQoL® is a useful tool to check factors that influence negatively the QoL of patients on HEN.

Assessment of the systemic enzyme therapy effect on immune responses in urogenital chlamydia infection

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Urologiia. 2020 Sep;(4):36-44.
https://pubmed.ncbi.nlm.nih.gov/32351061/

• Background

Chlamydial infection is considered the leading etiological agent of pelvic inflammatory diseases, which negatively influences reproductive health, secondary infertility, ectopic and aborted pregnancy, and in males epididymitis and prostatitis. This study aimed to evaluate the severity of immunological disorders and antibacterial therapy's effectiveness combined with systemic enzyme therapy in patients with urogenital chlamydial infection (UGCI).

• Methods

In this open comparative prospective research 84 patients with identified UGCI were included. They were divided in two groups, where group 1 (n=42) received antibiotic therapy with doxycycline monohydrate for 10 days, 100 mg, 2 times a day (the first dose of 200 mg) at regular intervals (daily dose of 200 mg, course in total 2.0 g) in combination with Phlogenzym[1], 3 tablets, 2 times a day for 14 days. Group 2 (n=42) received only doxycycline monohydrate therapy, at the same doses as in group 1. The activity of immune responses was assessed by the blood serum level of cytokines (γ-INF, IL-1β, -4, -6), circulating immune complexes (CIC), lactoferrin (LF), and α2-macroglobulin in all patients.

• Results

CIC, IL-1β, -4, -6, LF, and α2-macroglobulin levels in all participants with UGCI were significantly higher than those of a reference group (n=32 healthy participants), and γ-INF was lower. 97.6% of the patients with UGCI who received complex therapy with antibiotics and Phlogenzym had a clinical and microbiological cure, confirmed by PCR done 1.5 and 3 months after completion of treatment, compared to 78.6% of those who received only antibiotics (statistically significant, p=0.007). The activity of Th-2 type cellular response of immunity in participants with UGCI treated with systemic enzyme therapy decreased.

• Conclusion

By confirming that one of the pathogenetic mechanisms of UGCI is the imbalance of the cytokine profile, a new approach for treatment, namely complementing eradicative antibacterial therapy with systemic enzyme therapy to correct systemic immunological disorders, has been substantiated.

[1]*Oral enzyme combination with 90 mg Bromelain, 48 mg Trypsin, 100 mg Rutosid.*

Systemic enzymotherapy in treatment of women with chronic recurrent bacterial cystitis

Kuzmenko AV, Kuzmenko VV, Gyaurgiev TA

Urologiia. 2020 Apr;(2):35-40.
https://pubmed.ncbi.nlm.nih.gov/32351061/

• Background

Antibacterial drugs are used to treat infections and inflammatory diseases, including lower urinary tract infections (LUTI). Due to the overuse of antibiotics, their efficacy is decreasing with time. Until new antibiotics are developed, there is a need to create alternative therapy regimens and methods. One of the promising treatments for LUTI is systemic enzyme therapy, which has shown efficacy in other diseases. This study aimed to assess the treatment of women with chronic recurrent bacterial cystitis using systemic enzyme therapy on top of standard antibiotic therapy.

• Methods

Women with chronic recurrent bacterial cystitis in the acute stage between 19 and 45 were examined and treated. They were randomized into two groups, where group 1 (n=30) was prescribed standard antibiotic therapy, and group 2 (n=30) received Phlogenzym[2] along with standard antibiotic treatment. Treatment efficacy was assessed on the 1st, 7th, and 14th day by analysis of symptoms (according to data of urination diaries), evaluation of the intensity of pain sensations, laboratory tests (CRP, IL-6, IL-1β, TNFα). Relapse frequency was estimated in both groups for the time period of six months after treatment.

• Results

In both groups, normalized parameters were observed by day 14. Nevertheless, women from the group receiving systemic enzyme therapy had a more rapid relief of the inflammatory process statistically significant already by day 7 which was defined by a decrease in urination frequency, urgency, nocturia, and in the severity of inflammatory changes in blood and urine. Follow-up revealed fewer relapses on women receiving systemic enzyme therapy (4 vs. 9).

• Conclusion

These results show that systemic enzyme therapy is beneficial as an add-on treatment to LUTI, accelerating dysuric symptoms and pain relief. It also reduced relapses in women with chronic recurrent bacterial cystitis.

[2]*Oral enzyme combination with 90 mg Bromelain, 48 mg Trypsin, 100 mg Rutosid*

Effects of exercise and enzyme therapy in early occupational carpal tunnel syndrome: A preliminary study

Ziddková V, Nakládalová M, Štjpánek L

Biomed Res Int. 2019 Jan 23;2019:8720493
https://pubmed.ncbi.nlm.nih.gov/30809548/

• Background

The prevalence of occupational carpal tunnel syndrome (CTS) has increased in the Czech Republic. It is mainly due to upper extremity overuse and is recognized as an occupational disease. This study's objective was to evaluate the effects of exercise techniques and oral enzyme therapy in automotive plant workers with diagnosed CTS.

• Methods

This was an observational study that included 45 participants who worked in the automotive plant assembly line and revealed incipient CTS in a nerve conduction study. Participants were allocated into three groups: a group that practiced exercise techniques (n=15), a group that received oral enzyme therapy (n=16), and a control group (n=14). Data regarding symptoms and median nerve parameters (sensory conduction velocity and distal motor latency) were registered before and after nine weeks.

• Results

There was a statistically significant decrease in the total score for symptoms in both exercise and enzyme therapy groups compared to the control group. After a 9-week observation period, the exercise and therapy groups showed a significant increase in sensory conduction velocity. A significant shortening of the distal motor latency was observed in the enzyme therapy group.

• Conclusion

These results demonstrate that both exercise and oral enzyme therapies are efficient in incipient CTS. They may also be recommended for preventing more severe CTS.

Comparison of structured nutrition therapy for ramadan with standard care in type 2 diabetes patients

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Nutrients 2020, 12, 813

https://pubmed.ncbi.nlm.nih.gov/32204476/

• Background

Type 2 diabetes (T2D) management includes structured nutrition therapy (NT), however its effects during Ramadan fasting are still unknown. The aim of this study was to assess the effect of a structured NT program in people with T2D during Ramadan.

• Methods

An 8-week, parallel, non-randomized, patients' preference design study was conducted in 64 participants with T2D. Participants were asked to choose between structured NT (Structured Ramadan NT, sRNT) or standard care (SC). The sRNYT group received a nutrition plan focused on Ramadan, which included a diabetes-specific formula, whereas the SC group received standard nutrition care. Clinical outcomes and quality of life (QoL) were study outcomes. Results were statistically analyzed.

• Results

Baseline characteristics were similar for all participants. 38 participants (63%) chose sRNT as preferred group. At the end of 8 weeks, results were as follow:

	sRNT group	SC group	p value
Fasting plasma glucose	-0.9 ± 0.3 mmol/L	0.2 ± 0.3 mmol/L	$p < 0.05$
Triglycerides	-0.21 ± 0.08 mmol/L	0.2 ± 0.17 mmol/L	$p < 0.05$
Self-monitoring glucose at pre-dawn	6.9 mmol/L	7.8 mmol/L	$p < 0.05$
Self-monitoring glucose at pre-bedtime	7.6 mmol/L	8.6 mmol/L	$p < 0.05$

Additionally, the HbA1c levels decreased significantly in the sNRT group (-0.72 ± 0.16 %, $p < 0.001$), but not in the SC group (-0.35 ± 0.24 %, $p = 0.155$), and there was improvement in the QoL and satisfaction scores in the sRNT group.

• Conclusion

A structured NT regimen for Ramadan for people with T2D is benefic and feasible, as shown by the improvement in clinical outcomes and QoL.

Monoacylglycerol form of omega-3s improves its bioavailability in humans compared to other forms

Cuenoud B, Rochat I, Gosoniu ML, Dupuis L, Berk E, Jaudszus A, Mainz JG, Hafen G, Beaumont M, Cruz-Hernandez C

Nutrients. 2020 Apr 7;12(4):1014

https://pubmed.ncbi.nlm.nih.gov/32272659/

• Background

Cardiovascular health is among the numerous benefits attributed to omega-3 fatty acids (OM3). The clinical efficacy and bioavailability however is influenced by numerous factors, including form, food matrix effects (especially the lipid content of the diet), and metabolic capacity. This study aims to demonstrate that a "pre-digested" omega-3 formulation (OM3-sn-1(3)-monoacylglycerol, OM3-MAG) has a significantly greater absorption at high therapeutic doses (2.9 g/day), compared to the most common OM-3-ethyl ester form (OM3-TAG, 3.1 g/day) and similar profile to other pre-digested OM3-fee fatty acids (OM3-FFA, 3.2 g/day) of similar structure.

• Methods

Three clinical trials were conducted. Clinical trial A was a randomized, controlled, acute, open trial in healthy adults. The study design included a three-arm crossover design with a 6-day wash out period between each period. The three study groups were: (1) OM3-MAG, (2) OM3-ethyl ester, (3) OM3-FFA. Each product was given as a single dose once daily. Clinical trial B was a randomized, acute, single blind, pharmacokinetic study with obese or overweight subjects. This trial followed a two-arm crossover design with a 7–10 day washout period between each intervention period. The two study groups included: (1) OM3-TAG and (2) OM3-MAG in which each subject on day 1 received 9 capsules of the study product after an overnight fast. Clinical trial C was a two-arm parallel, randomized, controlled trial in subjects with cystic fibrosis and exocrine pancreatic insufficiency. The two study groups were: (1) OM3-TAG and (2) OM3-MAG in which each subject ingested 4 to 8 capsules per day for 12 weeks.

• Results

Both forms of pre-digested OM3-MAG and OM3-FFA resulted in a similar increase in OM3 blood level compared to OM3-TAG supplements in obese subjects (1.2 g/day) following a low fat diet and in children with cystic fibrosis (1.0 g/day).

• Conclusion

Both forms of pre-digested OM3-MAG and OM3-FFA are successfully absorbed and re-incorporated effectively into triacylglycerols inside the enterocytes. The pre-digested OM3-MAG might deliver a more efficient therapy in severe cardiovascular conditions where high doses of OM3 are required and a low-fat diet is indicated.

Feasibility of a very low calorie diet to achieve a sustainable 10% weight loss in patients with nonalcoholic fatty liver disease

Scragg J, Avery L, Cassidy S, Taylor G, Haigh L, Boyle M, Trenell MI, Anstee QM, McPherson S, Hallsworth K

Clinical and Translational Gastroenterology. 2020 Sep;11(9):e00231
https://pubmed.ncbi.nlm.nih.gov/33094956/

• Background

Nonalcoholic fatty liver disease (NAFLD) is the most common liver condition worldwide. There is no pharmacological treatment available for NAFLD. The primary treatment recommended is a weight loss goal of ≥10% of body weight; however, few patients can achieve this reduction with standard dietary interventions. The objective of this study was to assess if a very low-calorie diet (VLCD) is an acceptable and feasible treatment to achieve and maintain a ≥10% weight loss in patients with clinically significant NAFLD.

• Methods

For this study, patients with clinically significant NAFLD were recruited to follow a VLCD (800 kcal/day) using meal replacement products. The key outcomes assessed at baseline, post-VLCD, and at the 9-month follow-up included anthropometrics, blood tests (liver and metabolic), liver stiffness, and cardiovascular disease risk using QRISK2.

• Results

A total of 30 patients were enrolled of which 27 (90%) completed the VLCD intervention, and 20 (67%) were retained at the 9-month follow-up. Overall, the VLCD was an acceptable and feasible treatment option for patients with NAFLD. The intention-to-treat analysis showed that 34% of patients achieved and maintained ≥10% weight loss, 51% achieved ≥7% weight loss, and 68% achieved ≥5% weight loss at the 9-month follow-up. Additionally, those that completed the VLCD, liver health (liver enzymes and liver stiffness), cardiovascular disease risk (blood pressure and QRISK2), metabolic health (fasting glucose, HbA1c, and insulin), and body composition had improved significantly at the 9-month follow-up.

• Conclusion

VLCD may be an alternative treatment option for some patients with NAFLD to achieve and maintain a ≥10% weight loss, leading to improved liver health, cardiovascular risk, and quality of life.

Implementation of a very low-calorie diet program into the pre-operative model of care for obese general elective surgery patients: Outcomes of a feasibility randomized control trial

Hollis G, Franz R, Bauer J, Bell J

Nutr Diet. 2020 Nov;77(5):490-498

https://pubmed.ncbi.nlm.nih.gov/32067341/

• Background

Obesity is a risk factor for adverse post-surgical outcomes, such as wound infection, intra-operative blood loss and increased length of stay. Very low-calorie diets (VLCDs) may represent an effective short-term intervention for adults with obesity. The objective of this study was to determine the feasibility of implementing a VLCD weight loss program as a pre-operative model for individuals with obesity undergoing elective general surgery.

• Methods

This was a prospective, randomized, controlled study conducted in 46 adults with obesity undergoing elective general surgery at a tertiary hospital outpatient clinic. Subjects were randomized to one of two arms: the intervention arm consisting of an 8-week VLCD program using Optifast (Nestle Health, Germany) or to standard of care which consisted of generic information on healthy eating. The primary objective of this study was feasibility which was assessed through demand, practicality, integration and acceptability measures. Data was collected at baseline, week 8- and 30-days post-surgery.

• Results

Study participants consisted of 17 males and 29 females, mean age of 51.6 years, and a body mass index (BMI) ≥ 30 kg/m^2. Among subjects who completed the study, those in the intervention group compared to the control group had a higher mean weight loss (-6.5 vs. +0.15 kg; p ≤ 0.001), greater reduction in waist circumference (–6.11 vs +1.36 cm; P = 0.003), and significantly greater increase in quality of life (P < 0.001). Also the weight reduction occurred without a significant loss of muscle mass, measured by bioelectrical impedance analysis.

• Conclusions

The use of a VLCD program as a pre-operative model in individuals with obesity undergoing elected general surgery resulted in rapid and clinically meaningful weight loss without an excessive loss of muscle mass and an improved quality of life.

Differences in treatment response to a total diet replacement intervention versus a food-based intervention: A secondary analysis of the OPTIWIN trial

Ard JD, Lewis KH, Cohen SS, Rothberg AE, Coburn SL, Loper J, Matarese L, Pories WJ, Periman S

Obesity and Science Practice. 2020 Aug 11;6(6):605-614
https://pubmed.ncbi.nlm.nih.gov/33354339/

• Background

Not all people who engage in a weight loss program lose the same amount of weight. This study aimed to determine if response rates to a total diet replacement (TDR) differed from those of a calorie-restricted, food-based (FB) diet.

• Methods

This study analyzed data from OPTIWIN, a 12-month multicenter, multi-phase(a 26 week active weight loss phase followed by a weight maintenance phase) trial in adults with a BMI of 30-55 kg/m^2. The OPTIWIN trial included 330 participants who were randomized to either the OPTIFAST program (OP) or a FB diet. Treatment non-responders were defined as subjects who lost < 3% of initial weight at either 6 or 12 months.

• Results

At one year, the OP group had 76% of responders (n = 103), compared to 57% (n = 78) in the FB diet group. The between group differences for the OP and FB groups were similar for odds of treatment response at 12 months among subjects who were non-responders at 3 months (p = 0.64). Response status was significantly associated with race, type 2 diabetes and previous weight loss attempts. OP responders had higher meal plan adherence and non-caloric fluid intake compared to FB responders.

• Conclusion

Early response to treatment is more likely to be sustained with a TDR compared to a food-based diet. Nevertheless, individual and treatment level factors appear to influence early treatment response to behavioural interventions for weight reduction.

Weight change in participants completing meal replacement program is related to level of engagement

Loper J, Lewis KH, Rothberg A, Auriemma A, Coburn SL, Cohen SS, Matarese L, Pories WJ, Jiang X, Periman S, Ard JD

Obesity Week Conference 2020 - The Obesity Society

https://tos.planion.com/Web.User/AbstractDet?ACCOUNT=TOS&ABSID=23619&CONF=OW2020&ssoOverride=OFF&CKEY=

• Background

The weight loss efficacy of a meal replacement program compared to a reduced-calorie food-based plan (FB) was previously demonstrated in the OPTIWIN study, a modified Diabetes Prevention Program. The intervention in the OPTIWIN study included clinic visits with a medical provider and dietitian as well as behavioral and lifestyle group sessions. The aim of this study analysis was to examine attendance at clinic and group visits in relation to amount of weight loss.

• Methods

The OPTIWIN study included 273 participants, aged 18-70 years old, with a BMI of 30-55 kg/m^2. Subjects were randomized to either the OPTIFAST® program (OP, n = 135) or FB plan (n = 138) for 26 weeks for weight loss, followed by a one-year weight maintenance phase. Relative weight change (RWC,%) was measured by percent of attendance at clinic (n=41 OP, 16 FB) and group (52 for both groups) visits to week 52. RWC from baseline to week 52 between groups was compared using repeated measures multivariable linear models.

• Results

RWC between group differences were similar for those who completed > 50% (n=100 for OP; 99 for FB) and > 75% of clinic visits (n=90 for OP; 85 for FB). For subjects who attended > 50% group visits, RWC was -16.0% for OP (n = 62) and -8.6% for FB (n = 53). For subjects who attended > 75% visits, RWC was -18.5% (OP, n = 35) and -11.2% (FB, n = 23). When analyzed together, those with > 75% attendance at clinic and group visits (n = 35 for OP; 19 for FB) had -18.9% and -11.5% RWC (p = 0.0008) whereas RWC was -5.8% for OP and -3.6% for FB (p=0.39) among those who attended < 75% of clinic and < 50% of group visits (n=19 for OP; n=18 for FB).

• Conclusion

The results of this analysis demonstrate the importance of attending both individual clinic visits and group sessions as part of a medically supervised weight management program. Moreover, group visits may represent a key for successful weight loss. Participants in the OP group that had a high attendance of both individual and group sessions had a significantly greater RWC by week 52 compared to those in the FB group.

Attitudes and approaches to use of meal replacement products among healthcare professionals in management of excess weight

Maston G, Franklin J, Gibson AA, Manson E, Hocking S, Sainsbury A, Markovic TP

Behavioral sciences. 2020 Sep 7;10(9):136

https://pubmed.ncbi.nlm.nih.gov/32906702/

• Background

One of the options for the management of obesity is meal replacement product-based diets, however, they are underutilized by Health Care Professionals (HCPs). The primary objective of this study was to explore the attitudes and prescribing patters of meal replacement products (MRPs) among HCPs. Qualitative and quantitative methods were used to identify potential barriers to MRP prescription and use in the management of overweight and obesity.

• Methods

A total of 330 HCPs working in weight management across Australia received an online survey, and 197 (65%) completed it.

• Results

From respondents, over 70% of HCPs had prescribed meal replacement products currently or in the past. However, only a median of 7% of patients seeking weight management treatment have been prescribed a MRP diet. Some of the barriers to meal replacement products prescription include challenges with patient non-compliance, perceived poor long-term weight loss durability and safety concerns regarding use of these products as a total meal replacement program. Perceived risk of weight cycling and its potential negative psychological impact were the key safety concerns identified. This study also reported that prescription of MRPs was 66% more likely to occur among HCPs that had formal training, compared to those who did not.

• Conclusion

The potential barriers to prescription of meal replacement products are primarily safety concerns. Formal training may help increase the prescription of these diets, which suggests that after HCPs have a comprehensive understanding of the products and their evidence, their use is likely to be increased.

The impact of the use of glycomacropeptide on satiety and dietary intake in phenylketonuria

Daly A, Evans S, Pinto A, Jackson R, Ashmore C, Rocha JC, MacDonald A

Nutrients 2020 Sep 4;12(9):2704.

https://pubmed.ncbi.nlm.nih.gov/32899700/

• Background

Protein increases secretion of gastrointestinal hormones and diet-induced thermogenesis, while being the most satiating macronutrient. Phenylketonuria (PKU) restricts natural protein intake, with about 80% of intake being from a synthetic source, which may alter satiety response. Satiety may be enhanced by casein glycomacropeptide (CGMP-AA), a carbohydrate containing peptide and alternative protein substitute (PS) to amino acids (AA), by mechanism of its bioactive properties. The objective of this study was to assess the effect of both amino acid based PS (AA) and CGMP AA when given as a sole source of PS (cGMP100) and a combination of CGMP-AA and AA PS (cGMP50) on satiety, weight and body mass index (BMI).

• Methods

This was a three-year longitudinal, prospective study with 48 children with PKU. Median ages were 9.2 years for CGMP100 group (n = 13), 7.3 years for CGMP50 group (n = 16), and 11.1 years for AA group (n = 19). Every three months, semi-quantitative dietary assessments and anthropometry (weight, height and BMI) were assessed.

• Results

The contribution of macronutrient to total energy intake from protein, carbohydrate and fat was similar within groups. After adjusting for age and gender, there were no apparent difference in energy intake, weight, BMI, incidence of overweight or obesity between groups.

• Conclusion

This three year study did not show an indication to support a relationship between cGMP and satiety, which is a complex multi-system process that is not fully understood.

Preliminary investigation to review if a glycomacropeptide compared to L-amino acid protein substitute alters the pre- and postprandial amino acid profile in children with phenylketonuria

Daly A, Evans S, Pinto A, Jackson R, Ashmore C, Rocha JC, MacDonald A

Nutrients. 2020 Aug 14;12(8):2443.

https://pubmed.ncbi.nlm.nih.gov/32823853/

• Background

Protein substitutes are an essential source of synthetic protein in the dietary management of phenylketonuria (PKU). These are either based on solely amino acids without phenylalanine (Phe-free AA) or based on casein glycomacropeptide (cGMP) with added amino acids. cGMP may slow the rate of amino acid (AA) absorption when compared with traditional Phe-free AA, improving nitrogen utilization, decreasing urea production and modifying insulin response. The aim of this study was to compare pre and postprandial AA concentrations in children with PKU, when taking one of protein substitute (Phe-free AA, CGMP-AA1 or CGMP-AA2).

• Methods

The study included 43 children (24 boys), with a median age of 9 years-old (5-16 years). CGMP-AA1 was given to 11 children, CGMP-AA2 to 18 children and 14 Phe-free AA. Quantitative AA was assessed in blood samples at 2 timepoints on one day.: early morning fasting preprandial and 2 hours postprandial. Children had a breakfast with 20 g protein equivalent from protein substitute post fasting blood sample.

• Results

All three protein substitutes yielded a significant increase in postprandial AA for all individual AAs. The AA composition of the three different protein substitutes led to higher postprandial AA histidine, leucine and tyrosine in CGMP-AA2 compared to CGMP-AA1, and leucine, threonine and tyrosine higher in GCMP-AA2 compared to Phe-free AA.

• Conclusion

The AA composition of CGMP-AA had an influence in 2 hour postprandial AA composition in children with PKU, which suggests that a protein substitute derived from CGMP-AA may be comparably absorbed to Phe-free AA.

Decanoic acid inhibits mTORC1 activity independent of glucose and insulin signaling

Warren E, Dooves S, Lugarà E, Damstra-Oddy J, Schaf J, Heine V, Walker M, Williams R

Proc Natl Acad Sci U S A. 2020 Sep 22;117(38):23617-23625

https//pubmed.ncbi.nlm.nih.gov/32879008/

• Background

The activity of the mechanistic target of rapamycin complex 1 (mTORC1) signaling pathway is thought to be reduced under low-glucose and low-insulin conditions associated with use of the classical (long chain fatty acid) ketogenic diet. This can lead to a range of positive medical and health-related effects. The aim of this study was to assess if mTORC1 signaling can also be reduced by decanoic acid, which is a key component of the medium-chain triglyceride (MCT) ketogenic diet.

• Methods

The effect of decanoic acid on mTORC1 activity was measured by phosphorylation of eukaryotic translation initiation factor 4Ebinding protein 1 (4E-BP1), initially using a tractable cellular model, *Dictyostelium discoideum*, and then through translation to an *ex vivo* rat hippocampus model and in astrocytes derived from in healthy individuals and patients with tuberous sclerosis complex (TSC).

• Results

Decanoic acid was shown to reduce mTORC1 activity in *Dictyostelium* in the absence of insulin and in high glucose conditions. This effect was shown to be dependent on a ubiquitin regulatory X domain-containing protein mediating inhibition of a conserved AAA ATPase, p97, which is a homolog of the human transitional endoplasmic reticulum ATPase (VCP/p97) protein. This insulin- and low glucose-independent effect of decanoic acid on reducing mTORC1 activity was confirmed in *ex vivo* rat hippocampal slices, and in astrocytes from healthy individuals and patients with tuberous sclerosis complex (TSC) mutations.

• Conclusion

This study demonstrates that decanoic acid decreases mTORC1 activity in the absence of insulin and under high glucose conditions in a different model systems and in human derived astrocytes. Thus, diets high in decanoic acid may provide a new approach to down-regulate mTORC1 signaling in health and disease treatment.

Use of ketogenic diet therapy in infants with epilepsy: A systematic review and meta-analysis

Lyons L, Schoeler N, Langan D, Cross H

Epilepsia. 2020 Jun;61(6):1261-1281
https://pubmed.ncbi.nlm.nih.gov/32452537/

• Background

Children and adults with drug-resistant epilepsy may benefit from ketogenic diet therapy (KDT). KDT is a group of high-fat, low-carbohydrate diets. There is a gap in knowledge on the efficacy of KDT in infants. The objective of this study was to systematically review studies that have reported on response to KDT in infants with epilepsy.

• Methods

A systematic literature search was executed and included reports with seizure frequency data for at least one infant younger than 2 years old, treated with KDT for one month or more. Data extracted from the studies included proportion of infants achieving ≥ 50% seizure reduction, seizure-freedom rates, retention rates, and reported side effects. Meta-analyses were performed using a random effects model, and subgroup analyses were executed to assess possible study heterogeneity.

• Results

The final analysis included 33 studies, with a total of 534 infants with efficacy data. Two studies were randomized controlled trials, 31 were uncontrolled cohort studies. All studies were classified as low quality. Meta-analyses of uncontrolled studies estimate 59% of infants reached ≥ 50% seizure reduction and 33% of infants achieved seizure freedom. Retention rates ranged between 27% and 84% at 24 and 3 months, respectively. The most commonly reported side effects were dyslipidemia (12%), vomiting (6%), constipation (4%), gastroesophageal reflux (4%), and diarrhea (4%).

• Conclusion

This study concludes that KDT is tolerable and safe and can work as an effective treatment option for infants with drug-resistant epilepsy. The lack of high-quality studies focusing on infants with drug-resistant epilepsy confirms the need to confirm the effectiveness, safety, and tolerability of KDT in this age group in a randomized controlled trial.

Ketogenic diet therapy in infants with epilepsy

Schoeler NE, Cross JH

Paediatrics and Child Health

https://www.sciencedirect.com/science/article/abs/pii/S1751722220301220

• Background

Epilepsy affects 0.5 – 1% of children, 25% of which are drug resistant. This lack of seizure control in infants has an impact on their developmental outcomes with an elevated burden on NHS services. There is a lack of studies regarding optimal treatment in infants with drug-resistant epilepsy. The objective of this article was to outline the basics on use of ketogenic diet therapy (KDT) in infants (< 2 years-old) with epilepsy.

• Methods

This occasional review summarizes the basics on use of ketogenic diet therapy in infants with epilepsy, including a history of dietary treatment, evidence for efficacy in infants, patient selection and clinical and dietetic management.

• Results

The first report of infants < 2 years treated with KDT dates 2001, where 17 of 31 became seizure-free or had > 50% seizure reduction, with a good tolerance. In 2016, a study compared the Modified Atkin's Diet with KDT, with 53% of infants on KDT becoming seizure-free and 59% achieving seizure reduction at 3 months. Another study from 2019 showed that 62% of the infants with West syndrome on KDT achieved seizure remission at 28 days.

• Conclusion

Ketogenic diet therapy has shown to be an effective non-pharmacological treatment option for individuals with drug-resistant epilepsy and reports of its use in infants have increased recently. An overview of clinical and dietetic management of infants on ketogenic diet therapy is presented herein.

Potassium citrate supplementation with ketogenic dietary therapy for drug-resistant epilepsy

Schoeler NE

Developmental Medicine & Child Neurology. 2020 Jan;62(1):8.
https://pubmed.ncbi.nlm.nih.gov/31777958/

• Background

Drug-resistant epilepsy may be treated with ketogenic diets (high-fat, low-carbohydrate, moderate protein). These diets have shown efficacy in reducing seizure frequency in 40% of patients with epilepsy.

Ketogenic diets increase circulating ketone bodies and therefore are associated with an increase of the acidic milieu of the body, which may have consequences such as nephrolithiasis, nephrocalcinosis and bone mineral density loss. The use of oral citrate supplementation as an alkalizing agent may be offered to prevent and treat metabolic acidosis, especially when the diet is followed alongside carbonic anhydrase inhibitors (topiramate, zonisamide or acetazolamide).

This commentary is based on the work of Bjurulf et al, who found that none of 22 participants on a ketogenic diet for epilepsy and receiving potassium citrate supplementation developed metabolic acidosis, compared to 10 out of 29 who did not receive supplementation. Supplementation with potassium citrate did not affect serum beta-hydroxybutyrate concentrations nor 7-month efficacy rates.

• Conclusion

Being a controversial issue, this study provides reassurance that supplementation with potassium citrate does not affect ketogenic diet efficacy, although a higher median age at diet start may have influenced the results, probably due to different ketogenic ratios and acidic load per unit of body weight.

Further studies are needed to clarify if citrate supplementation should be used for all people initiating a ketogenic diet or just for those with higher risk of complications related to metabolic acidosis. Also, it is important to understand if prophylactic supplementation effects long-term efficacy rates, as this would bring insights to the mechanisms of action of ketogenic diets.

Home delivery service of low protein foods in inherited metabolic disorders: Does it help?

MacDonald A, Pinto A, Evans S, Ashmore C, MacDonald J, Daly A

Molecular Genetics and Metabolism Reports; 2019 Mar 22;19:100466

https://pubmed.ncbi.nlm.nih.gov/30963029/

• Background

The usual method of people with inherited metabolic disorders (IMD) who require low protein (LP) diets assessing special LP foods in the UK was through pharmacies dispensing (until 2010). Lately, we've assisted to the introduction of home delivery services, however the effectiveness of these services is not known. The objective of this study was to assess the effectiveness and safety of patient home delivery services for LP foods during 12 months in people with IMD who require a LP diet.

• Methods

This was a prospective, longitudinal, observational study that included 58 patients. Patients or their carers could choose between 2 home delivery services (Homeward® and Vitaflo at Home®), as well as the access to primary care pharmacy services. The home delivery services provided a limited range of LP foods. A member of the IMD dietetic team visited patients 4 times for one year. Each visit was comprised of a 20-multiple choice and open questions regarding their experience with LP foods. Researchers also verified stocks, assessed expiration date and suitability of home storage of LP food.

• Results

For 1 year, 95% of carers used their local pharmacy, 93% Homeward® and 78% Vitaflo at Home® to get their LP foods. 71% of the carers used two home delivery services and 29% used only one. Each household only stored a median of 6 (range 0-22) different LP foods. Generally, 45% of the carers related problems with their prescriptions. 30% received at least one incorrect prescription when using their pharmact, 6% errors with Homeward® and 2% with Vitaflo at Home®. The reception of LP foods had a bigger delay in pharmacies (49%), compared with 11% from Homeward® and 8% with Vitaflo at Home®.

• Conclusion

This is a complex system, with inaccuracies and inefficiencies occurring with home delivery services and pharmacies. Nevertheless, less errors and delays occur with home delivery services. To ensure a better treatment for IMD patients and less burden on NHS resources, this study suggests that metabolic dietitians prescribe LP foods.

A randomized clinical trial on the acute therapeutic effect of TRPA1 and TRPM8 agonists in patients with oropharyngea dysphagia

Tomsen N, Alvarez-Berdugo D, Rofes L, Ortega O, Arreola V, Nascimento W, Martin A, Cabib C, Bolivar-Prados M, Mundet L, Legrand C, Clavé P, Michlig S

Neurogastroenterol Motil. 2020 Jun;32(6):e13821

https://pubmed.ncbi.nlm.nih.gov/32064725/

• Background

Oropharyngeal dysphagia (OD) is an elderly condition, with up 51% prevalence among institutionalized older people. More than choosing compensatory strategies to treat OD, active treatments that improve swallowing are being investigated. The objective of this study was to evaluate the effect of TRPA1/M8 agonists in improving swallowing in people with OD.

• Methods

This three-arm, quadruple-blind, randomized study included 58 participants with OD due to age, stroke or neurodegenerative disease. Investigators assessed swallowing safety, efficacy and its kinematics by videofluoroscopy (VFS), during the swallow of a 182 ± 2 mPa.s viscosity nectar thickened with xanthan gum supplemented with (a) 756.6 µmol/L cinnamaldehyde and 70 µmol/L zinc (CIN-Zn) (TRPA1 agonists), (b) 1.6 mmol/L citral (CIT) (TRPA1 agonist), or (c) 1.6 mmol/L citral and 1.3 mmol/L isopulegol (CIT-ISO) (TRPA1 and TRPM8 agonists). They used electroencephalography to evaluate effects on pharyngeal event-related potentials (ERP).

• Results

No significant adverse events were observed, and investigators related that TRPA1 stimulation with CIN-Zn or CIT reduced time to laryngeal vestibule closure (CIN-Zn P = 0.001, CIT P = 0.023) and upper sphincter opening (CIN-Zn P = 0.007, CIT P = 0.035). Also, they noticed that CIN-Zn reduced the penetration-aspiration scale score (P = 0.009), increased the prevalence of safe swallows (P = 0.041) and reduced the latency of the P2 peak of the ERT. There weren't positive effects on biomechanics nor neurophysiology due to CIT-ISO.

• Conclusion

These results are a basis for the development of new treatments for OD using TRPA1 agonists, as TRPA1 stimulation with CIN-Zn or CIT improved the swallow response, with CIN-Zn having a significant improvement in cortical activation and safety of swallow.

Texture-modified diet for improving the management of oropharyngeal dysphagia in nursing home residents: an expert review

Ballesteros-Pomar MD, Cherubini A, Keller H, Lam P, Rolland Y, Simmons SF

J Nutr Health Aging. 2020;24(6):576-581

https://pubmed.ncbi.nlm.nih.gov/32510109/

• Background

Long-stay nursing home residents who are prescribed texture-modified diets (TMDs) are also at high risk of worsening oropharyngeal dysphagia (OD), malnutrition, dehydration, aspiration pneumonia and OD-associated mortality, lower quality of life, and increased economic burden. This manuscript aimed to offer evidence and recommendations for these residents.

• Methods

Nestlé Health Science subsidized a first virtual meeting with all the authors. They debated on unmet needs and subsequent recommendations for OD management. OD is frequent in nursing home residents and is the incapacity of safe swallowing and is therefore associated with several multimorbidities. Complications of OD can be prevented with the use of TMDs.

• Results

This study describes expert opinion and evidence-informed recommendations for the better nutritional management of OD. It emphasizes practice gaps between evidence-based management of OD and real-world patterns, such as inadequate dietary provision and insufficient staff training. It also described the unmet need for OD screening and improvements in therapeutic diets.

• Conclusion

The opinions, results, and recommendations detailed are those of the authors and independent of any funding sources. There is a lack of empirical evidence for OD management. Some of the approaches and interventions described as “best-practice” require extensive efficacy testing before changes in guidelines are implemented.

The risk of penetration–aspiration related to residue in the pharynx

Steele CM, Peladeau-Pigeon M, Barrett E, Wolkina TS

Am J Speech-Lang Pat

https://www.researchgate.net/publication/342544030_The_Risk_of_Penetration-Aspiration_Related_to_Residue_in_the_Pharynx

• Background

Evidence suggests that the 75th and 95th percentiles for pharyngeal residue on swallows of thin liquids are 1% and 3% (C2-4)2, respectively, for healthy adults under 60. This study explores how pharyngeal residue below versus above these values before a swallow may predict penetration-aspiration.

• Methods

This was a retrospective analysis of previous research data from 305 adults at risk for dysphagia. They were requested to swallow six thin boluses and three mildly, moderately, and extremely thick barium in videofluoroscopy. For each swallow, pre swallow residue in%(C2-4)2 and Penetration-Aspiration Scale (PAS) scores were measured. The classification of swallows as follows: (a) "clean baseline" (with no pre swallow residue), (b) "clearing" swallows of residue with no new material added, or (c) swallows of "additional material" plus pre swallow residue. Frequencies of PAS scores of ≥3 were compared across swallow type by consistency according to residue severity.

• Results

The data set included 2,541 clean baselines, 209 clearing, and 1,722 swallows of additional material.

Frequency of PAS scores ≥3	Thin and mildly thick liquids	Moderately/ extremely thick liquids
Clean baseline swallows	5%	1%
0/640 (0%)	37/356 (10.4%)	<0.001
4.35 (271)	5.73 (45)	<0.001
6.61 (110)	6.80 (63)	<0.001

Compared to clean baseline swallows, the odds of penetration-aspiration on thin liquids increased 4.60-fold above the 1% threshold and 4.20-fold above the 3% threshold. PAS scores of ≥3 did not occur with clearing swallows of moderately/extremely thick liquids. Lower frequencies of above-threshold pre swallow residue were seen for swallows of additional material than for clearing swallows. According to consistency, compared to clean baseline swallows, the odds of PAS scores of ≥ 3 on swallows of other material increased ≥ 1.86-fold above the 1% threshold and ≥ 2.15- fold above the 3% threshold.

• Conclusion

These results suggest that a pharyngeal residue threshold of 1% (C2-4)2 is a meaningful cut-point to define increase risk of penetration-aspiration on a subsequent swallow.

Supplementation with whey protein, omega-3 fatty acids and polyphenols combined with electrical muscle stimulation increases muscle strength in elderly adults with limited mobility: A randomized controlled trial

Boutry-Regard C, Vinyes-Parés G, Breuillé D, Moritani T

Nutrients 2020, 12, 1866.
https://pubmed.ncbi.nlm.nih.gov/32585837/

• Background

Sarcopenia due to age affects skeletal muscle in a progressive and generalized way. The aim of this study was to assess the effects of both electrical muscle stimulation (EMS) and whey-based nutritional supplement (with or without polyphenols and fish oil-derived omega-3 fatty acids) on muscle size and function.

• Methods

The study included 41 elderly participants (33 women, 8 men) with mobility limitations who lived by their own. For 12 weeks, all participants received 2 sessions of EMS every week and were randomly assigned to an isocaloric drink and capsules. The change in knee extension strength was assessed.

n = 12	Carbohydrate + placebo capsules (CHO)
n = 15	Whey protein isolate + placebo capsules (WPI)
n = 10	Whey protein isolate + bioactives (BIO) capsules with omega-3 fatty acids, rutin and curcumin

• Results

Knee extension strength was significantly improved in the WPI + BIO group by 13% and gait speed was improved by 8% compared to CHO, while WPI alone did not provide a significant benefit over CHO.

• Conclusion

The combination of EMS and WPI + BIO capsules supplementation may be considered a new method for sarcopenia, although more studies are needed.

Can nutrition support healthy cognitive ageing and reduce dementia risk?

Jennings A, Cunnane SC, Minihane AM

BMJ. 2020 Jun 26;369:m2269

https://pubmed.ncbi.nlm.nih.gov/32591407/

• Background

Alzheimer's disease is one of the main forms of dementia. Up to 50 million people in the entire world have dementia, and this number is expected to triple until 2050. Up to two thirds of cases of dementia are women. Although there is no treatment available yet, high income countries, where people have more years of education and a better cardiovascular health have shown that dementia sets up later in life.

It has been shown that a better eating behavior can help reduce the risk and prevalence of dementia: one of the challenges of ageing is the chronic deficit in brain glucose uptake, for energy production. Glucose uptake declines with age; however, it has been shown that brain ketone uptake is normal during ageing, mild cognitive impairment and Alzheimer's disease. Ketones are the second most important source of energy to the brain, which can effectively replace glucose when dietary carbohydrates are limited.

Recent studies have shown that brain energy rescue with ketones is related to improved cognitive outcomes in mild cognitive impairment and Alzheimer's disease. It was also shown that ketogenic interventions may modify the course of the disease because the accumulation of dementia-associated proteins can be partially blocked by ketogenic supplements. These cognitive outcomes with ketogenic outcomes may be a result of a better insulin sensitivity and be improved by exercise.

• Conclusion

Changes to dietary patterns and foods are a promise for a better cognition, however there is a need for more randomized controlled studies to support the prospective evidence, establish efficacy and effect size as well as to inform public health policy, with the development of dietary guidelines specifically focuses on prevention of dementia or improving mild cognitive decline.

A ketogenic drink improves cognition in mild cognitive impairment: Results of a 6-month RCT

Fortier M, Castellano CA, St-Pierre V, Myette-Côté E, Langlois F, Roy M, Morin MC, Bocti C, Fulop T, Godin JP, Delannoy C, Cuenoud B, Cunnane SC

Alzheimers Dement. 2020 Oct 26.

https://pubmed.ncbi.nlm.nih.gov/33103819/

• Background

Ketones may improve cognition in mild cognitive impairment (MCI) by counteracting impaired brain glucose metabolism. The main objective of this study was to report the complete cognitive outcomes of the BENEFIC trial.

• Methods

This was a 6-month randomized, placebo-controlled trial that evaluated cognition, plasma ketone response, and metabolic profile before and six months after supplementation with a ketogenic drink containing medium-chain triglyceride (ketogenic medium-chain triglyceride [kMCT]; 15 g twice/day; n=39) or placebo (n=44).

• Results

Participants from the kMCT group had significant improvements in free and cued recall, verbal fluency, Boston Naming Test, and the Trail Making Test, compared to placebo. Plasma ketones were also positively correlated to some cognitive outcomes. Plasma metabolic profile and ketone response were unchanged.

• Conclusion

The kMCT drink enhanced cognitive outcomes in MCI, due to the increase in blood ketone level. Improved cognitive outcomes in MCI as the increased availability of ketones significantly improved brain energy supply. This includes clinical proof of improving memory, word recall, thinking speed and multitasking.

Sarcopenia: Potential interventions for a newly recognized disease

Gomez Cabrera MC, Viña J

Regulatory focus

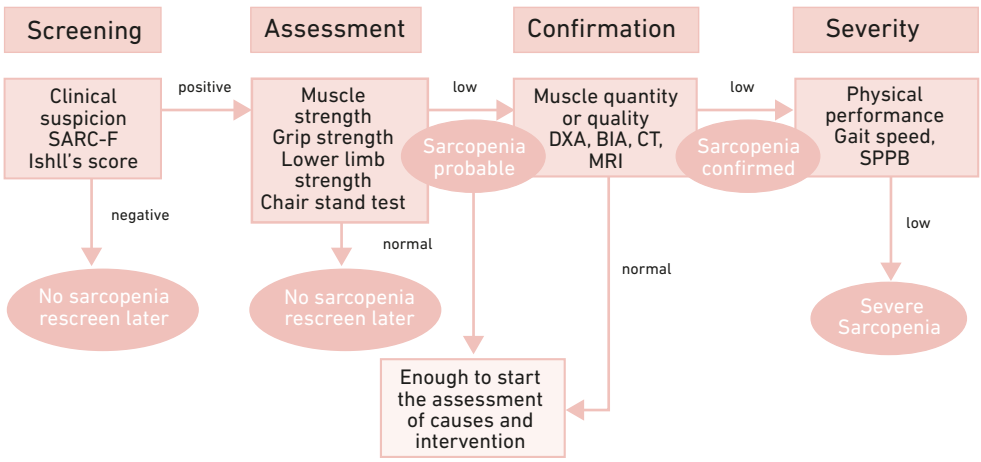
https://www.raps.org/news-and-articles/news-articles/2020/6/sarcopenia-potential-interventions-for-a-newly-rec

• Background

Sarcopenia is a newly recognized skeletal muscle disease. Low muscle mass is the principal characteristic of sarcopenia because it is often reduced to a great extent during aging and muscle strength is superior to muscle mass in predicting adverse outcomes. Malnutrition is also an important factor in sarcopenia and is prevalent in older people, especially those institutionalized or hospitalized.

Sarcopenia is considered primary when it is age-related and no other specific cause is evident, and secondary when causal factors are evident (physical inactivity, poor nutrition, a systemic disease or a neurological disorder). It can be further classified in acute, when it lasts for less than six months and is associated with an injury or illness, and chronic when lasts longer than six months and is related to a progressive condition.

Sarcopenia diagnosis involves the measurement of a combination of muscle strength, muscle mass, and physical performance, as shown in Figure 1 (adapted from the EWGSOP algorithm).



• Conclusion

A good nutritional health, physical activity and pharmacologic options are the most effective early interventions. The most promising nutritional interventions include high-quality, protein-enriched supplements, and multivitamin/multimineral supplements, especially vitamin D.

Brain energy rescue: an emerging therapeutic concept for neurodegenerative disorders of ageing

Cunnane SC, Trushina E, Morland C, Prigione A, Casadesus G, Andrews ZB, Beal MF, Bergersen LH, Brinton RD, Monte S, Eckert A, Harvey J, Jeggo R, Jhamandas JH, Kann O, Cour CM, Martin WF, Mithieux G, Moreira PI, Murphy MP, Nave KA, Nuriel T, Oliet S, Saudou F, Mattson M, Swerdlow RH, Millan MJ

Nat Rev Drug Discov. 2020 Sep;19(9):609-633

https://pubmed.ncbi.nlm.nih.gov/32709961/

• Background

The prevalence of neurodegenerative disorders of aging is growing due to increased longevity. These disorders, such as Alzheimer's and Parkinson's disease, represent a significant burden. Studies have shown that impaired brain energetics is involved in the cause and progression of these diseases. Brain energy metabolism declines in a progressive, region- and disease-specific manner. This is because the brain needs a continuous supply of energy in the form of ATP, most of which is produced from glucose. When glucose levels are reduced, ketone bodies prevenient from the liver can also become essential energy substrates. This review aims to evaluate the status and forecasts of different strategies to defy neurodegenerative disorders of aging by improving, preserving, or rescuing brain energetics. Strategies include restoring oxidative phosphorylation and glycolysis, enhancing insulin sensitivity, correcting mitochondrial dysfunction, ketone-based interventions, acting via hormones that modulate brain energy, RNA treatments, and positive lifestyle changes.

Similarly, as normal neurocognitive development during infancy depends on adequate brain energy supply, the maintenance of cognitive performance and cerebral function during aging depends on the brain continuing to meet its energy needs with success. This is a keystone for studies aiming to delay the onset and progression of aging neurodegenerative disorders.

The effect on preventing influenza infection with partially hydrolyzed guar gum

Takahashi C, Kozawa M

European Society for Clinical Nutrition and Metabolism (ESPEN) 2020

https://espencongress.com/wp-content/uploads/2020/09/ESPEN-2020-Programme-for-ON-DEMAND-eposters-and-LB-v3.pdf

• Background

Prevention from seasonal influenza infection is essential, especially in hospitalized elderly patients. This study aimed to assess the effect of prebiotic partially hydrolyzed guar gum (PHGG) on prevention of influenza infection.

• Methods

This was a single-center retrospective study that included 996 hospitalized patients. These patients received oral nutrition from April 2017 to March 2019 and were divided into two groups. One group, P-group (n=640), received PHGG continuously, and the other group, N-group (n=356), did not receive PHGG. The two groups were compared for the incidence rate of influenza, Bristol Stool Scale (BS), and fecal pH. Also, BS and fecal pH were compared in patients with and without influenza.

• Results

Both groups had similar baseline characteristics. Thirty-seven patients were diagnosed with influenza, all from N-group. P-group had a significantly lower incidence rate of influenza. Also, P-group had significantly better stool form conditions and significantly lower fecal pH. Patients with influenza had significantly higher BS and fecal pH.

	P-group	N-group	P value
Total	640	356	
Influenza +, n (%)	0/640 (0%)	37/356 (10.4%)	<0.001
BS, (n)	4.35 (271)	5.73 (45)	<0.001
Fecal pH, (n)	6.61 (110)	6.80 (63)	<0.001

	Influenza +	Influenza -	P value
Total	37	959	
BS, (n)	5.70 (33)	4.38 (270)	<0.001
Fecal pH, (n)	6.89 (28)	6.67 (145)	<0.001

• Conclusion

Prebiotic partially hydrolyzed guar gum may help prevent influenza infection. Moreover, Stool consistency was improved in participants who received prebiotics.

Supplementing glycine and N-acetylcysteine (GlyNAC) in aging HIV patients improves oxidative stress, mitochondrial dysfunction, inflammation, endothelial dysfunction, insulin resistance, genotoxicity, strength, and cognition: Results of an Open-Label clinical trial

S Kumar P, Liu C, Suliburk JW, Minard CG, Muthupillai R, Chacko S, Hsu JW, Jahoor F, Sekhar RV

Biomedicines. 2020 Sep 30;8(10):E390. doi: 10.3390/biomedicines8100390

https://pubmed.ncbi.nlm.nih.gov/33007928/

• Background

Premature aging in people with HIV (PWH) is becoming a public health challenge, with limited knowledge about its underlying mechanisms. This study aimed to assess if deficiency of the antioxidant protein glutathione (GSH) contributes to various defects that represent premature aging in these patients and whether these defects could be improved with supplementation of GSH precursors, glycine and N-acetylcysteine (GlyNAC).

• Methods

This open-label study assessed eight PWH and eight uninfected controls at baseline. Control participants were not supplemented. PWH were reassessed after twelve weeks of GlyNAC supplementation and again eight weeks after stopping GlyNAC. Outcome measures included GSH concentrations in red blood cells and muscle, mitochondrial function, genomic damage, cardiometabolic risk factors (e.g. oxidative stress, inflammation, endothelial function, insulin resistance, glucose production), muscle-protein breakdown rates, anthropometrics, and physical and cognitive function.

• Results

PWH exhibited defects in key metabolic and functional parameters and supplementation with GlyNAC significantly improved their outcome measures; however, these benefits diminished after stopping GlyNAC.

• Conclusion

This study highlights the impact of GlyNAC supplementation on several key defects associated with premature aging in PWH, including functional and cognitive decline. Dietary supplementation of GlyNAC could be developed as an effective nutritional strategy to improve cellular aging and health of PWH. More investigation should follow to assess the effects of longer durations of GlyNAC supplementation.

Targeting mitochondrial calcium uptake with the natural flavonol Kaempferol, to promote metabolism/secretion coupling in pancreatic β-cells

Bermont F, Hermant A, Benninga R, Chabert C, Jacot G, Santo-Domingo J, Kraus MR, Feige JN, De Marchi U

Nutrients. 2020 Feb 19;12(2):538

https://pubmed.ncbi.nlm.nih.gov/32093050/

• Background

Preservation of β-cells function is essential to prevent type 2 diabetes, as they secrete insulin, which lowers blood glucose after a meal. Insulin secretion in pancreatic β-cells is activated by mitochondrial matrix calcium. The transporter's molecular identity, the mitochondrial calcium uniporter (MCU), was recently discovered and clarified its role in mediating mitochondrial calcium update and pancreatic β-cell signal transduction modulation. This study aimed to explore the effects of a mitochondrial Ca2+ targeted nutritional intervention strategy on metabolism/secretion coupling in a model of pancreatic insulin-secreting cells (INS-1E).

• Methods

The effect of the paradigmatic natural plant flavonoid supposed MCU activator kaempferol on mitochondrial Ca2+ rise, insulin secretion, and cell death, during glucose stimulation, in pancreatic INS-1E β-cells was measured. The MCU inhibitor mitoxantrone effect on mitochondrial Ca2+ rise and granule exocytosis in both glucose-stimulated and kaempferol on pancreatic INS-1E cell function was also quantified. Finally, the impact of kaempferol on insulin secretion in a model of human pseudo-islets was validated.

• Results

Mitochondrial calcium rise during glucose stimulation was enhanced by acute treatment of INS-1E cells with kaempferol, at a low micromolar range, without affecting the expression level of the MCU and with no cytotoxicity. Enhanced mitochondrial calcium rises potentiated Glucose-induced insulin secretion. On the other hand, mitoxantrone inhibited mitochondrial Ca2+ uptake and prevented the effects of glucose-induced insulin secretion and kaempferol. This kaempferol-dependent potentiation of insulin secretion was finally validated in a model of a standardized pancreatic human islet.

• Conclusion

Kaempferol activates the metabolism/coupling in insulin-secreting cells by modulating mitochondrial calcium uptake.

Mitochondrial oxidative capacity and NAD+ biosynthesis are reduced in human sarcopenia across ethnicities

Migliavacca E, Tay SKH, Patel HP, Sonntag T, Civiletto G, McFarlane C, Forrester T, Barton SJ, Leow MK, Antoun E, Charpagne A, Seng Chong Y, Descombes P, Feng L, Francis-Emmanuel P, Garratt ES, Giner MP, Green CO, Karaz S, Kothandaraman N, Marquis J, Metairon S, Moco S, Nelson G, Ngo S, Pleasants T, Raymond F, Sayer AA, Ming Sim C, Slater-Jefferies J, Syddall HE, Fang Tan P, Titcombe P, Vaz C, Westbury LD, Wong G, Yonghui W, Cooper C, Sheppard A, Godfrey KM, Lillycrop KA, Karnani N, Feige JN

Nat Commun. 2019 Dec 20;10(1):5808

https://pubmed.ncbi.nlm.nih.gov/31862890/

• Background

Declines in skeletal muscle mass and strength during normal aging are well characterized. However, the molecular features underlying pathological age-related muscle wasting and weakness, known as sarcopenia, are less known. This study aimed to characterize genome-wide transcriptional changes in sarcopenia.

• Methods

This study compared the genome-wide transcriptomic profiles of skeletal muscle biopsies from older men diagnosed with sarcopenia with those of age-matched controls using high coverage RNA sequencing. A total of 119 men from Singapore, Hertfordshire, and Jamaica were included.

• Results

Participants with sarcopenia demonstrated a transcriptional signature of mitochondrial bioenergetic dysfunction in skeletal muscle, as evidenced by low PGC-1α/ERRα signaling, and downregulation of genes related to oxidative phosphorylation and mitochondrial proteostasis. These changes were reflected on a functional level by fewer mitochondria, reduced mitochondrial respiratory complex expression and activity, and reduced NAD+ levels through impaired NAD+ biosynthesis and salvage in sarcopenic muscle.

• Conclusion

This study offered an integrated molecular profile of human sarcopenia across different ethnicities, showing that altered mitochondrial metabolism has a significant role in the pathological loss of skeletal muscle mass and function in older adults.

Boosting NAD level suppresses inflammatory activation of PBMCs in heart failure

Zhou B, Ding-Hwa Wang D, Qiu Y, Airhart S, Liu Y, Stempien-Otero A, O'Brien KD, Tian R

J Clin Invest. 2020 Nov 2;130(11):6054-6063

https://pubmed.ncbi.nlm.nih.gov/32790648/

• Background

Innate immunity is affected by mitochondrial function; however, the relationship between mitochondrial dysfunction and inflammation in heart failure (HF) is not clearly understood. This study's objective was to assess the mechanistic connection between mitochondrial dysfunction and inflammatory activation in peripheral blood mononuclear cells (PBMCs) and the effect of boosting NAD in counteracting inflammation.

• Methods

This study included 19 hospitalized stage D HF patients and 19 healthy participants. Their PBMC mitochondrial respiration was compared. An in vitro model of sterile inflammation was built by giving MitoDAMP (Mitochondrial Damage-Associated Molecular Patterns) to healthy PBMC isolated from human heart tissue. Afterward, stage D HF patients took 5-9 days of oral nicotinamide riboside (NR), and their blood was sampled.

• Results

A reduced respiratory capacity and an elevated proinflammatory cytokine gene expression are associated with HF. This model showed that PBMCs treated with MitoDAMP secreted IL-6, decreasing mitochondrial respiration by reducing Complex I activity. Administration of oral NR increased PBMC respiration, and decreased proinflammatory cytokine gene expression in 4 patients with HF.

• Conclusion

Systemic inflammation in HF is causally connected to the mitochondrial function of the PBMC. Mitochondrial respiration may be enhanced by increasing NAD levels, which may also attenuate proinflammatory activation of PBMC in HF.

Nicotinamide riboside supplementation alters body composition and skeletal muscle acetylcarnitine concentrations in healthy obese humans

Remie CME, Roumans KHM, Moonen MPB, Connell NJ, Havekes B, Mevenkamp J, Lindeboom L, de Wit VHW, van de Weijer T, Aarts SABM, Lutgens E, Schomakers BV, Elfrink HL, Zapata-Pérez R, Houtkooper RH, Auwerx J, Hoeks J, Schrauwen-Hinderling VB, Phielix E, Schrauwen P

Am J Clin Nutr. 2020 Aug 1;112(2):413-426

https://pubmed.ncbi.nlm.nih.gov/32320006/

• Background

Nicotinamide Riboside (NR) is a precursor for NAD+, with supplementation shown to increase cellular NAD+ concentrations. Evidence from preclinical studies suggests NR can have profound effects on metabolic health. The objective of this study was to explore the effects of supplementation with NR for six weeks on insulin sensitivity, mitochondrial function, and other metabolic health parameters in obese and overweight volunteers.

• Methods

This was a randomized, double-blind, placebo-controlled, crossover intervention study that included 13 healthy overweight or obese participants who received supplementation with NR (1000 mg/d) or placebo for six weeks. The impact on markers of metabolic health was assessed via hyperinsulinemic-euglycemic clamps, magnetic resonance spectroscopy, muscle biopsies, and assessment of ex vivo mitochondrial function and in vivo energy metabolism.

• Results

Compared with placebo, markers of increased NAD+ metabolism were higher in skeletal muscle following NR supplementation. NR also led to modest improvements in body composition and increased sleeping metabolic rate without impacting total body weight. Skeletal muscle acetylcarnitine concentrations and capacity to form acetylcarnitine with exercise were both significantly increased with NR vs. placebo.

In contrast, NR had no effects on insulin sensitivity, mitochondrial function, hepatic and intramyocellular lipid accumulation, cardiac energy status, cardiac ejection fraction, ambulatory blood pressure, plasma markers of inflammation, or energy metabolism.

• Conclusion

In healthy, overweight or obese adults, supplementation with NR for six weeks increased skeletal muscle NAD+ metabolites, altered skeletal muscle acetylcarnitine metabolism, and led to minor changes in body composition and sleeping metabolic rate, with no impact on other metabolic health markers.

Acute nicotinamide riboside supplementation improves redox homeostasis and exercise performance in old individuals: a double-blind cross-over study

Dolopikou CF, Kourtzidis IA, Margaritelis NV, Vrabas IS, Koidou I, Kyparos A, Theodorou AA, Paschalis V, Nikolaidis MG

Eur J Nutr. 2020 Mar;59(2):505-515

https://pubmed.ncbi.nlm.nih.gov/30725213/

• Background

Older people have low levels of NADH. Previous research found that supplementing young rats with an NAD(P)(H) precursor, nicotinamide riboside (NR), impaired exercise performance. This suggests that supplementation with redox agents may only have an ergogenic effect in individuals who are deficient. This study aimed to evaluate the impact of acute NR supplementation on redox homeostasis and physical performance in young and older adults.

• Methods

This double-blind study included 12 young and 12 older male participants who received NR or placebo in a crossover design. Blood and urine samples were collected before and 2 hours after supplementation. Physical performance, as assessed via VO_2max, muscle strength, and fatigue, was measured after the second blood sample.

• Results

Older participants had lower erythrocyte NAD(P)H levels, higher urine F2-isoprostanes, and lower erythrocyte glutathione levels at rest, compared to younger participants. NR supplementation increased NADH and NADPH in both groups, and decreased F2-isoprostanes in older adults only. NR tended to increase glutathione in older men only, but this was not significant. NR had no effect on VO_2max or concentric peak torque, but significantly improved isometric peak torque and fatigue index in the older cohort. On the other hand, NR supplementation did not have any redox or physiological effect in young males.

• Conclusion

Improvements in NAD(P)H levels, oxidative stress, and physical performance following NR supplementation were observed in older subjects only, supporting the hypothesis that benefits of redox supplementation may limited to those with antioxidant deficiencies.

Combined metabolic cofactor supplementation accelerates recovery in mild-to-moderate COVID-19

Altay O, Yang H, Aydin M, Alkurt G, Altunal N, Kim W, Akyol D, Arif M, Zhang C, Dinler-Doganay G, Turkez H, Shoaie S, Nielsen J, Boren J, Doganay L, Uhlen M, Mardinoglu A

https://www.medrxiv.org/content/10.1101/2020.10.02.20202614v1

• Background

There are strong interactions between the viral pathobiology of SARS-CoV-2 and components of metabolic syndrome and metabolic abnormalities. This study aimed to evaluate combined metabolic cofactors supplementation (CMCS) (L-serine, N-acetyl-L-cysteine (NAC), nicotinamide riboside (NR), and L-carnitine tartrate) for the treatment of patients with COVID-19.

• Methods

This was a placebo-controlled, phase 2 study that included 100 ambulatory COVID-19 patients. They were randomly assigned on a 3:1 basis to hydroxychloroquine plus CMCS or hydroxychloroquine plus placebo. Hydroxychloroquine was given five days and CMCS or placebo 14 days. Daily evaluations of the patients' clinical status were made by phone, using a binomial scale for subject-reported presence or absence for multiple COVID-19 related symptoms. Plasma samples were collected on days 0 and 14.

• Results

93 participants completed the trial. The CMCS/hydroxychloroquine combination significantly reduced the average complete recovery time (6.6 days vs. 9.3 days with placebo). A significant reduction in ALT, AST, and LDH levels on day 14 was also noted in the CMCS/hydroxychloroquine group. Reported adverse events were uncommon and these were also self-limited.

• Conclusion

CMCS supplementation significantly reduced COVID-19 recovery time and liver enzymes associated with hepatic function. Incidence of adverse events associated with CMSC was low.

Targeting NAD+ in translational research to relieve diseases and conditions of metabolic stress and ageing

Gilmour BC, Gudmundsrud R, Frank J, Hov A, Lautrup S, Aman Y, Røsjø H, Brenner C, Ziegler M, Tysnes OB, Tzoulis C, Omland T, Søraas A, Holmøy T, Bergersen LH, Storm-Mathisen J, Nilsen H, Fang EF

Mech Ageing Dev. 2020 Mar;186:111208

https://pubmed.ncbi.nlm.nih.gov/31953124/

• Background

Ageing is a natural process being studied for mechanisms that delay or limit the rapid functional decline seen in old age. Basic researchers and clinicians have investigated the molecular mechanisms and translation potential of NAD+ to target ageing and age-predisposed diseases. The importance of NAD+ in this process has been shown, but there are still significant gaps in applying laboratory science to design the most valuable trials.

• Methods

The Norwegian Centre on Healthy Ageing (NO-Age) pursues the definition of a multi-disciplinary research network to focus on the challenges of ageing and to encourage healthy ageing and lifestyles in old age. This mini-review was centered on the program and discussions of the 3rd NO-Age Symposium held in Norway on the 28th October 2019 and hosted at the Akershus University Hospital. This meeting got together leading basic investigators and clinicians involved in NAD+ augmentation-related clinical studies and covered NAD+ in-depth: from biochemistry to current clinical. Talks about NAD+ synthetic pathways, subcellular homeostasis, and the benefits of its augmentation.

• Results

While most laboratory and clinical data suggest a substantial translational potential for NAD+ -boosting compounds, some studies have described little-to-no effect, introducing new questions. Children and patients with different diseases may have different responses; thus, separate data should be established for each specific condition and age group. The speakers also recommend including 'exercise' since it may play a synergistic role with NAD+.

• Conclusion

Growing evidence, from laboratory animals to humans, suggest NAD+ augmentation improves healthspan and extends lifespan, as well as alleviates the symptoms of a broad range of age-related diseases. NAD+ plays this fundamental role by regulating energy biogenesis, redox homeostasis, cell metabolism, and the arbitration of cell survival via linkages to apoptosis and autophagic pathways. Despite the optimism, there are still outstanding questions in the field. A consensus is rising concerning the design of clinical trials to measure significant parameters and confirm safety.

Age-related NAD+ decline

McReynolds MR, Chellappa K, Baur JA

Exp Gerontol. 2020 Feb 22;134:110888

https://pubmed.ncbi.nlm.nih.gov/32097708/

• Background

Nicotinamide adenine dinucleotide (NAD+) is an essential metabolite that is fundamental to life. There is evidence from preclinical and human research that the concentration of NAD+ decreases with age in multiple tissues. However, there is significant variability across studies in the degree of decline and which tissues are affected.

• Methods

This review examines the evidence supporting an age-related decline in NAD+, and looks at the different mechanisms with the potential to contribute to this deterioration.

• Results

Existing literature supports health benefits associated with NAD+ supplementation in rodents. Nevertheless, the NAD+ metabolism must be better understood and human clinical data on NAD+ restoration is needed. Human clinical trials will show how increasing NAD+ availability will affect human physiology.

• Conclusion

More studies will help target strategies to maintain NAD+ availability, such as direct delivery of precursors to sites where NAD+ is low and inhibition of NAD+ consumers in specific tissues.It is a thrilling time for NAD+ investigation, but much remains to be understood about the causes and consequences of age-related NAD+ decline and potential therapeutic applications.

NAD+ homeostasis in health and disease

Katsyuba E, Romani M, Hofer D, Auwerx J

Nat Metab. 2020 Jan;2(1):9-31

https://pubmed.ncbi.nlm.nih.gov/32694684/

• Background

Within the past decade, the nicotinamide adenine dinucleotide (NAD+) field has experienced a genuine scientific renaissance with new data on the beneficial effects of different strategies to restore cellular NAD+ levels accumulating rapidly. Although the therapeutic potential of boosting NAD+ levels is undeniable, several issues must be resolved to determine the research's actual translational value on NAD+.

NAD+ levels decline during aging, and alterations in NAD+ homeostasis can be found in virtually all age-related diseases, including neurodegeneration, diabetes, and cancer, affecting different organs in either humans or rodent models.

This review has analyzed the basics of NAD+ biochemistry and metabolism and its roles in health and disease and discussed current challenges and the future translational potential of NAD+ research. Several studies have been completed, and more than 30 human clinical trials are currently ongoing or recruiting participants. These studies' promising outcomes have triggered a series of clinical trials, which are now testing the efficacy of NAD+ therapeutics in human disease.

The available data indicate that the translation from the rodent models to humans might not be as straightforward as expected. Although the studies show that different doses and durations of nicotinamide riboside (NR) administration all lead to an increase in NAD+ levels in humans and do not appear to be associated with severe adverse effects, NR has not resulted in striking improvements in any disease setting to date. Despite the disappointing outcomes, some points require consideration: the doses of NAD+ precursors used were far lower than those used in preclinical animal models. The duration of the human study might have been too short for NR to show full therapeutic benefit.

• Conclusion

Carefully planned clinical studies of longer duration with higher doses, involving large numbers of patients should be performed to offer convincing evidence of benefits in the context of human diseases. The knowledge of basic NAD+ biology remains incomplete. Methods for accurate and reproducible NAD+ quantification should be applied more carefully. Only with systematic progress in the basic and clinical understanding of NAD+ biology can the preventive and therapeutic potential associated with maintaining healthy NAD+ homeostasis be exploited.

Nutritional status as a mediator of fatigue and its underlying mechanisms in older people

Azzolino D, Arosio B, Marzetti E, Calvani R, Cesari M

Nutrients. 2020 Feb 10;12(2):444

https://pubmed.ncbi.nlm.nih.gov/32050677/

• Background

Aging is accompanied by substantial body composition changes, like reducing lean body mass and increasing adiposity. These modifications contribute to the onset of frailty in older persons. Frailty is associated with several adverse outcomes, including falls, hospitalization, functional decline, and mortality. Fatigue is commonly considered a typical manifestation of aging, making it a prevalent but often-neglected symptom in older adults. It is usually associated with the weakening and/or depletion of the individual's physical and/or mental resources and is observed in many diseases. Given the lack of a gold standard for fatigue assessment, it does not yet receive adequate attention in clinical settings.

This review provides a summary of the patterns that affect tiredness in older people and identifies approaches to recognize the pathophysiological processes related to frailty, with a special focus on nutrition. Other parameters used to understand fatigue are sleep quality, autonomic nervous system functioning, and biological patterns.

Modifications in food intake and changes in body composition, alone or in combination with sleep disorders, seem to influence fatigue perception, probably through the mechanisms of inflammation and mitochondrial dysfunction. Some dietary components seem to be promising against the symptom of fatigue. Nutritional interventions should be individually adjusted considering some elements: nutritional status, physical activity level, disease status.

• Conclusion

Despite being a symptom frequently described by older adults, fatigue's core mechanisms are still inadequately understood, and these complaints are often underestimated by the medical community. A dedicated research and a clear identification of its mechanisms will allow the pursuing of specific pharmacological and non-pharmacological approaches and an increased awareness on this condition.

Glutathione serum levels and rate of multimorbidity development in older adults

Pérez LM, Hooshmand B, Mangialasche F, Mecocci P, Smith AD, Refsum H, Inzitari M, Fratiglioni L, Rizzuto D, Calderón-Larrañaga A

J Gerontol A Biol Sci Med Sci. 2020 May 22;75(6):1089-1094

https://pubmed.ncbi.nlm.nih.gov/31086967/

• Background

This study aimed to explore the relationship between baseline levels of total serum glutathione (tGSH) and chronic disease accumulation rate over time.

• Methods

This was a population-based longitudinal study that included data from 2,596 participants aged 60 years and older. Participants were clinically evaluated at baseline and had follow-ups of 3- and 6-years. Multimorbidity was assessed as the number of chronic conditions using a previously determined list of 60 diseases. Linear mixed models were employed to analyze the association between baseline tGSH levels and the rate of multimorbidity progression over six years of follow-up.

• Results

At baseline, participants with at least four diseases had lower tGSH levels than participants without any chronic conditions (3.3 vs. 3.6 μmol/L; $p < 0.001$). At follow-up, lower levels of baseline tGSH were associated with a higher rate of multimorbidity development (β * time: -0.044, $p < 0.001$), after adjusting for major confounders: age, sex, education, levels of serum creatinine, C-reactive protein, albumin, body mass index, smoking, and time of dropout or death.

• Conclusion

Serum tGSH levels are inversely related to multimorbidity development, and this relationship extends beyond the link between tGSH and specific chronic conditions. The results support tGSH's importance as a biomarker of multisystem dysregulation. More studies are required to better understand its relationship with biological changes and aging.

Mitochondria in health and disease

Annesley SJ, Fisher PR

Cells. 2019 Jul 5;8(7):680

https://pubmed.ncbi.nlm.nih.gov/31284394/

• Background

Mitochondria are generally believed to be essential for eukaryotic life, as they produce most of the energy or ATP required by the cell. The mitochondria have their genome (mtDNA), which is replicated independently of the host genome, but most mitochondrial proteins are encoded by the nuclear genome and are imported into the mitochondria. Mitochondria play essential roles in numerous processes, and defects in these processes can lead to disease. This special issue with 12 publications, nine review articles, and three original research articles aimed at understanding the mechanisms of mitochondrial biology, including its morphology and dynamics, like fission/fusion and mitophagy. They covered diverse areas of mitochondrial function and biology in health and disease and analyzed how models have contributed to understanding these processes.

The reviews and research articles illustrate the intimate roles that mitochondria play in almost all cellular function aspects. They cover diverse areas of mitochondrial biology and function and how defects in these areas can lead to disease. Model organisms have contributed significantly to the understanding of mitochondrial biology in health and disease. Many articles highlight the contributions of organisms like yeast, plants, and rodents and how they could model complex diseases with a mitochondrial involvement.

• Conclusion

The close interaction between mitochondria and the rest of the cell is why mitochondria and their dysregulation participate in the cytopathological processes underlying such diverse diseases as cancer, neurological diseases, and metabolic diseases.

Role of age-related mitochondrial dysfunction in sarcopenia

Ferri E, Marzetti E, Calvani R, Picca A, Cesari M, Arosio B

Int J Mol Sci. 2020 Jul 23;21(15):5236

https://pubmed.ncbi.nlm.nih.gov/32718064/

• Background

Declines in skeletal muscle mass and function are among the most notable corollary of aging. It can rapidly progress in physically inactive persons and set acute or chronic conditions. The term sarcopenia describes the loss of muscle mass, strength and power with aging (i.e., dynapenia) and it's associated with reduced quality of life. It affects nearly one-third of the older population and is one of the main factors leading to negative health outcomes in older patients. Although the exact mechanisms responsible for sarcopenia's development and progression are not fully understood, mitochondrial dysfunction has emerged as a central pathogenetic factor. Indeed, mitochondria serves several vital functions within the cell, including energy production, regulation of intracellular calcium homeostasis, modulation of cell proliferation, and integration of apoptotic signaling.

This review aimed to summarize available evidence supporting mitochondrial dysfunction as a mechanism contributing to musculoskeletal aging and sarcopenia, and to illustrate the involvement of mitochondria in cellular senescence to highlight the relationship between musculoskeletal cellular senescence induced by mitochondrial dysfunction and the onset of sarcopenia.

Several systemic and muscle-specific processes have been shown to play a role in the pathogenesis of sarcopenia. Mitochondrial dysfunction in skeletal myocytes is recognized as a significant driver of sarcopenia.

• Conclusion

Sarcopenia is a complex geriatric condition associated with various negative health-related outcomes, and full comprehension of its etiology is far from being reached. Noticeably, age-related muscle wasting is potentially preventable and treatable. Further research is necessary to understand whether mitochondrial dysfunction in muscle arises from primary organelle defects or defective quality control. The contribution of systemic processes to mitochondrial muscle dysfunction remains to be fully elucidated. Answers to these open research questions will enable the development of targeted, person-tailored interventions against one of the most burdensome conditions of old age.

Mitochondria as central hub of the immune system

Breda CNS, Davanzo GG, Basso PJ, Saraiva Câmara NO, Moraes-Vieira PMM

Redox Biol. 2019 Sep;26:101255

https://pubmed.ncbi.nlm.nih.gov/31247505/

• Background

In the last years, cellular metabolism has been widely studied to understand how cells use their energy to perform their functions, especially concerning metabolic-related diseases like obesity, diabetes, and cancer. Immunometabolism explores the metabolic alterations that affect immune cells. Recent findings suggest that immune cell subtypes use distinctive metabolic procedures to execute their functions.

Metabolic energy is provided mainly by mitochondria, but these dynamic organelles can also regulate cell development and have an impact on immunity.

This review focuses on how mitochondria lead immune cells' development and function, emphasizing their main metabolic characteristics and directing other metabolism-independent roles that sustain cell function.

Mitochondria modulates metabolic and physiologic states in different types of immune cells. Recent research has demonstrated that mitochondrial metabolites and mtROS are vital mechanisms of signaling pathways and cell fate in innate and adaptive immune cells.

• Conclusion

Different functions of mitochondria have been revealed, but other aspects must be understood, regarding their orchestration on immune cells. The knowledge of cell metabolism in vivo remains a challenge in immunometabolism. The modulation of mitochondria in immune cells may be a path to treat a wide range of illnesses, like cancer and several inflammatory diseases.

Mitochondria: the indispensable players in innate immunity and guardians of the inflammatory response

Mohanty A, Tiwari-Pandey R, Pandey NR

J Cell Commun Signal. 2019 Sep;13(3):303-318

https://pubmed.ncbi.nlm.nih.gov/30719617/

• Background

Mitochondria, the cellular powerhouses in all the eukaryotic organelles, serve as energy storehouses to supply energy when energy needs must be met. Recent studies have shown that mitochondria are involved in regulating innate immunity and inflammatory responses. This review aimed at exploring the current understanding of the relationship between mitochondria and other cellular processes, like autophagy in controlling mitochondrial homeostasis and regulation of innate immunity and inflammatory responses.

Alterations in the dynamic of mitochondria namely fusion/fission, electron transport chain (ETC) architecture and cristae organization have been correlated to modulating metabolic activity and immune function of innate and adaptive immune cells. Mitochondria have also been identified as key signaling platforms in antiviral immunity in vertebrates. They have a function in activating adaptive immune cells: by mitochondrial antiviral signaling protein (MAVS) present in the outer membrane; by mitochondrial DNA acting as danger-associated molecular pattern (DAMP); and by mitochondrial reactive oxygen species.

The understanding of mitochondria's role in toll-like receptor-mediated innate immune responses and NLRP3 inflammasome complex activation, has highlighted its role in innate immunity.

The signals stemming from the endoplasmic reticulum operate together with the mitochondria to activate the NLRP3 inflammasome to reply to associated organelle stress responses with inflammatory consequences.

• Conclusion

These findings lead to research of new mitochondrial targets as novel therapeutics to treat infections, inflammatory and autoimmune conditions.

Mitophagy, mitochondrial dynamics, and homeostasis in cardiovascular aging

Wu NN, Zhang Y, Ren J

Oxid Med Cell Longev. 2019 Nov 4;2019:9825061

https://pubmed.ncbi.nlm.nih.gov/31781358/

• Background

Biological aging is associated with a gradual decline in the organismal reproductive and regenerative capacity. Maneuvers targeting the biological aging process are expected to improve aging-related complications and well-being in the elderly. The cardiovascular system becomes more vulnerable with ageing, which results in more cardiovascular diseases with a disproportionate prevalence. Several theories have been postulated for the pathogenesis of aging-related cardiovascular dysfunction, among which mitochondrial injury has received close attention over the past decades.

There is an overall decline of mitochondrial function with aging: the mitochondrial quality control system fails to repair mitochondrial defects, progressively compromising its network due to loss of balanced mitochondrial fission and fusion. Inefficient mitophagy finally leads to a buildup of dysfunctional mitochondria.

Aging is potentially malleable via metabolic and genetic interventions, such as caloric restriction and exercise. Antioxidants are of limited benefit. In various model organisms, physiological and pharmacological inducers of mitophagy and modulators of mitochondrial dynamics improve mitochondrial function and health span.

• Conclusion

Mitochondria are part of a dynamic network and interact with other cellular components as an answer to different physiological processes and stress. Aging-related diseases, namely cardiovascular diseases are a result of alterations in mitochondria. More studies are needed to understand how to preserve and attenuate aging-induced diseases, from targeting the mechanisms of mitochondrial homeostasis to counteracting early mitochondrial damage.

Physical exercise and selective autophagy: benefit and risk on cardiovascular health

Wu NN, Tian H, Chen P, Wang D, Ren J, Zhang Y

Cells. 2019 Nov 14;8(11):1436

https://pubmed.ncbi.nlm.nih.gov/31739509/

• Background

A healthy lifestyle should include regular physical exercise, as it advances cardiorespiratory fitness, and together with lifestyle modifications are an important piece of the non-pharmacological of cardiovascular diseases. A number of theories at the cellular and molecular levels have been postulated towards cardiovascular benefits related to exercise, including mitophagy, which is the selective autophagy of mitochondria. The objective of this review was to understand the role of mitophagy in the risk-benefit of physical exercise on cardiovascular function.

Regular exercise of moderate intensity is indicated for cardiovascular health, because of its potential benefits on body weight, blood pressure, insulin sensitivity, lipid and glucose metabolism, heart function, endothelial function and body fat composition. Exercise improves dynamics of the cardiovascular system, reduces prevalence of coronary heart diseases and cardiomyopathies, enhances cardiac reserve capacity and autonomic regulation. Regular exercise may represent an exceptional way of inducing physiological stress capable of triggering adaptation, while selective autophagy may be permissive to cardiovascular adaptation.

Mitophagy from conventional ways is slightly different from exercise-induced mitophagy. The ligase Parkin is crucial for exercise-induced mitophagy. Exercise stimulates mitophagy flux through increased recruitment of Parkin to mitochondria, while Parkin knockout doesn't impact basal mitophagy.

• Conclusion

Mitochondria have a crucial function in the maintenance of cardiac homeostasis. Endurance exercise training may help protect cardiovascular system from acute stress through maintaining homeostatic mitophagy. There is a lack of studies describing how exercise impacts cardiovascular function through the regulation of mitophagy, namely examining different types of exercise on autophagy and selective autophagy levels.

Mitophagy and DNA damage signaling in human aging

Babbar M, Basu S, Yang B, Croteau DL, Bohr VA

Mech Ageing Dev. 2020 Mar;186:111207

https://pubmed.ncbi.nlm.nih.gov/31923475/

• Background

Data indicate that by 2050, one in six people will be over 65 years old, and 426 million people will be over 80 - triple the number from 2019. Aging is related to multiple different pathologies. Studies have linked mitochondrial homeostasis to age-related disorders and longevity. The aim of this review was to examine molecular signaling pathways involved in the regulation of damage and repair of DNA and of mitophagy, highlighting potential clinical approaches targeting these mechanisms to improve quality of life while aging.

Mitochondrial homeostasis comprises generation, biogenesis and elimination of dysfunctional mitochondria through mitophagy. Mitophagy is regulated by different factors, either mitochondrial or extra-mitochondrial, that include morphology, oxidative stress and DNA damage. Historically, DNA damage and inefficient DNA repair were considered main causes for disorders related to aging. Although defects in DNA damage recognition and repair and mitophagy are well known, the relationship between these pathways is unknown. The efficiency of mitophagy decreases with age, which results in the accumulation of dysfunctional mitochondria and therefore an increase in the severity of age-related disorders, such as neurodegenerative conditions, cancer, diabetes and other inflammatory diseases. Supplementation with NAD+ is one of the interventions being explored for both defective DNA repair and mitophagy.

• Conclusion

Understanding the molecular biology underlying regulation of mitochondrial activity and mitophagy as it relates to DNA damage will reveal both mechanistic links and therapeutic targets. Understanding the function of mitophagy in nuclear DNA repair could be a main crossroads of investigation for a combined therapy towards longevity. Therapeutic interventions targeting mitophagy could have a significant impact on human health. Future studies are needed to develop specific gene therapies and drugs that can induce mitophagy.

Measuring biological aging in humans: A quest

Ferrucci L, Gonzalez-Freire M, Fabbri E, Simonsick E, Tanaka T, Moore Z, Salimi S, Sierra F, de Cabo R.

Aging Cell. 2020 Feb;19(2):e13080
https://pubmed.ncbi.nlm.nih.gov/31833194/

• Background

By the year 2050, the population over 65 years old will have reached 1.6 billion. Elderly may present with chronic diseases, which leads to complex pharmacotherapy and greater risk of physical and cognitive disability. There are no well-established clinical guidelines to improve or preserve the health and quality of life of older people. The objective of this review was to summarize what measures of aging biology are available, limited to those that can be obtained in humans.

Currently, physicians treat the elderly with focus on symptom treatment rather than approaching the root cause. Geroscience is challenging this approach, by proposing that the underlying biological mechanisms of aging are the center of the global increase in disease and disability susceptibility. There are strong correlations between health dimensions and phenotypes that present as typical of ageing, especially with autophagy, mitochondrial function, cellular senescence and DNA methylation.

Current investigation is centered in measuring the pace of aging to identify those who are "ageing faster" in order to test and develop interventions to prevent or delay the progression of morbidities and disabilities. Once the mechanisms of aging are understood, there is a possibility to categorize resilience mechanisms, and impact on stress responses.

• Conclusion

The authors were inspired by articles that outline the hallmarks and the pillars of aging. In what concerns biomarkers, it is unknown if they represent damage, compensation or a combination of both. To find a reference metric for the rate of biological aging is fundamental to understand the molecular nature of the aging process. The definition and validation of this metric in humans will bring a new medicine, approaching health in a global perspective.

Correcting glutathione deficiency in aging: Impact on mitochondrial and metabolic health

Sekhar RV

Congress abstract: 2020 International Conference on Frailty & Sarcopenia Research (ICFSR), Toulouse, France

J Frailty Aging. 2020;9(1):Symposium 8; Communication 2

https://frailty-sarcopenia.com/docs/oral2020.pdf

• Background

Some factors that are believed to have an important impact on aging processes are oxidative stress and mitochondrial dysfunction. There is limited capability to intercede and reverse them in humans. Other conditions associated with aging, including insulin resistance, inflammation, declining muscle strength, and higher body fat, are also incompletely understood and have limited interventions.

• Methods

Complementary translational studies in aged rodents and older people were performed.

• Results

Evidence was found that the lack of adequate endogenous glutathione might be a critical factor in age-related declines. Reduced availability of glycine and cysteine amino acids (but not glutamic acid) was related to glutathione deficiency. This insufficiency can be rectified via supplementation with GlyNAC (mixture of glycine plus cysteine in the form of N-acetylcysteine). Correcting glutathione deficiency led to the recovery of impaired mitochondrial fuel oxidation while lowering oxidative stress. It also positively impacted insulin resistance, body fat, mitochondrial dysfunction, and conditions related to the aging process.

• Conclusion

Glutathione deficiency seems to accelerate the aging process, as observed by impaired mitochondrial function, muscle weakness, and inflammation in patients with HIV. Supplementing GlyNAC can help improve the effects of glutathione deficiency. These findings can significantly improve aging adults' wellbeing and may represent a profound change in the approach to care of older individuals.

The impact of age associated cellular decline on bioenergetics and functional impairment

Goodpaster BH

Congress abstract: 2020 International Conference on Frailty & Sarcopenia Research (ICFSR), Toulouse, France

J Frailty Aging. 2020;9(1):Symposium 8; Communication 1

https://frailty-sarcopenia.com/docs/oral2020.pdf

There is a need for better understanding of the biological mechanisms driving aging processes and age-related diseases, including the declines in physical and cognitive function which lead to frailty.

Factors related to aging phenotypes such as body composition, changes in energy balance and metabolism, declines in physical function, and neurodegeneration have all been studied. Particular attention has been paid to understanding how loss of muscle mass and strength lead to mobility limitations with age. Older adults experience declines in muscle mass and strength, and the loss of strength tends to be three times greater, which means a loss of muscle quality with age.

Mitochondrial dysfunction and impaired mitochondrial energetics appear to have a role in several aging phenotypes, including loss of cardiorespiratory fitness and muscle strength. Exercise and weight loss both improve insulin sensitivity, while exercise has more significant effects than weight loss on the mitochondrial ability for fatty acid oxidation. However, substantial uncertainties persist regarding the effects of exercise and weight loss on molecular mechanisms of insulin resistance.

Better insights into the cellular mechanisms associated with aging changes are needed to optimize strategies for intervention.

A report on the accelerated aging and cellular decline expert consensus and framework

Cherubini A

Congress abstract: VIRTUAL CONGRESS of the European Union Geriatric Medicine Society; online satellite symposium October 7-9, 2020

European Geriatric Medicine. 2020. Online satellite Symposium.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7750635/

Aging is an extremely complex biological process and a significant risk factor for numerous diseases, eventually increasing death susceptibility. Aging results from the interaction of genetic and environmental factors and involve several biological mechanisms. There is much heterogeneity in the aging process, and individuals experience different rates of decline.

A virtual expert panel was created to discuss the occurrence of accelerated age-related deterioration from a theoretical and practical perspective. The initiative had the participation of an interdisciplinary group of specialists with expertise in clinical practice and scientific research. New terminology was proposed to define the biological background predisposing to the progression of age-related conditions: AACD (accelerated aging and cellular decline). There was a consensus regarding potential risk factors, early signs, and clinical manifestations of AACD. 13 factors affecting AACD, like chronic diseases, obesity, and unfavorable genetic precedents were identified.

The clinical detection of AACD might often be challenging, as the development is gradual and nonspecific. The clinical signs and symptoms might have several causes and sources. Some clinical factors were considered significant as early indications (e.g., tiredness, low quality of sleep, and low mood) and were included on a preliminary checklist. A combination of biomarkers was recommended as a potential approach to help distinguish AACD from other conditions.

Further academic work and scientific study are essential to establish a more definitive structure to the concept of AACD. This construct should be considered as preliminary and not yet prepared for routine use in clinical practice. Its confirmation may potentially allow the early recognition of accelerated aging and pave the way to preventative interventions meant to promote healthy aging.

Reversing age-associated mitochondrial dysfunction and oxidative stress: impact of a novel nutritional approach

Sekhar RV

Congress abstract: VIRTUAL CONGRESS of the European Union Geriatric Medicine Society; online satellite symposium October 7-9, 2020

European Geriatric Medicine. 2020. Online satellite Symposium.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7750635/

Interventions to reverse the oxidative stress and mitochondrial dysfunction which contribute to age-associated cellular decline and the aging process are limited or lacking in older adults.

Mechanisms that contribute to elevated oxidative stress and impaired mitochondrial fuel oxidation have been investigated via complementary translational studies in aged rodents and older humans. A novel nutritional intervention has been developed to correct these defects. Subsequent human clinical trials were conducted, and an association with significant improvements in human health was found.

The results from these studies could help improve cellular nutrition and have an important impact on aging humans' health.

Targeting muscle mitochondrial bioenergetics in sarcopenia

Feige J

Congress abstract: The GSA 2020 Annual Scientific Meeting Online. November 4-7, 2020

Innovation in Aging 2020

https://www.geron.org/meetings-events/future-gsa-annual-scientific-meetings

• Background

Aging is characterized by a physiological deterioration of tissues and cellular processes. Managing these symptoms is central to preserving health span and quality of life in older people. Directly contributing to physical disability, loss of independence, and mortality in the older population, sarcopenia is the age-related loss of muscle mass and function.

• Methods

The Multi-Ethnic Molecular determinants of Sarcopenia (MEMOSA) study explored the mechanisms that differentiate sarcopenia from healthy aging across different ethnicities.

• Results

A prominent transcriptional and functional signature of mitochondrial bioenergetic dysfunction in skeletal muscle, which parallels a decline in NAD+ levels, was reproducibly demonstrated in people with sarcopenia.

• Conclusion

Mitochondrial homeostasis appears to be a key influencer of pathological muscle decline during aging. Specific nutritional interventions targeting mitochondria to support recovery of the functional capacity of sarcopenic muscle are a current focus of nutrition research.

Early detection of age associated cellular decline: Report of an expert consensus

Guralnik JM, Cesari M, Cherubini A, Beresniak A, Rodriguez-Mañas L

Congress abstract: The GSA 2020 Annual Scientific Meeting Online. November 4-7, 2020

Innovation in Aging.2020

https://www.geron.org/meetings-events/future-gsa-annual-scientific-meetings

• Background

Age is associated with a decline in cellular processes. As these processes decline, cells lose their ability to function optimally, which can lead to organ-specific dysfunction and ultimately the development of systemic age-related diseases. Age-Associated Cellular Decline describes the relationship between the cellular hallmarks of aging and clinical signs and symptoms observed with aging.

• Methods

An expert consensus study group was organized to develop an initial framework for creating a tool for adults over 50 years old to help identify self-reported indicators and observable signs thought to be early and/or surrogate markers of age-associated cellular decline.

• Results

The panel identified 16 potential early signs and symptoms of age-associated cellular decline.

• Conclusion

These results should be validated in further research.

Emerging nutritional interventions for age associated cellular decline

Singh A

Congress abstract: The GSA 2020 Annual Scientific Meeting Online. November 4-7, 2020

Innovation in Aging.2020

https://www.geron.org/meetings-events/future-gsa-annual-scientific-meetings

A gradual deterioration in cellular health, leading to dysfunction in organs with a high metabolic requirement, is commonly observed during aging. Impairment of mitochondrial quality control pathways like mitophagy is a key feature of age-associated cellular decline. These deficits lead to a compromise in cellular bioenergetics which contributes to the development of mitochondrial dysfunction over time. The objective of this work was to present and review recent literature on the evidence for nutritional interventions to support mitochondrial health.

Nicotinamide riboside (vitamin B3 precursor) and Urolithin A (a gut metabolite of compounds found in pomegranates) are nutritional interventions that have been shown to promote mitochondrial health via distinct mechanisms of action. Results of recent research suggest that dietary interventions such as these are encouraging approaches that can be used to help manage age-associated cellular decline.

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