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NEWSLETTER
Polskiego Towarzystwa Gastroenterologii, Hepatologii i Żywienia Dzieci

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Polskiego Towarzystwo Gastroenterologii, Hepatologii i Żywienia Dzieci

17-18.11.2023r. odbędzie się
IX Sympozjum „Standardy Gastroenterologiczne, Hepatologiczne i Żywieniowe w Praktyce Lekarza Rodzinnego i Pediatry"
organizowane przez Stowarzyszenie na Rzecz Wspierania i Rozwoju
Kliniki Gastroenterologii, Hepatologii, Zaburzeń Odżywiania i Pediatrii Instytutu Pomnik – Centrum Zdrowia Dziecka.

Profesor dr hab. n. med. Mieczysława Czerwionka-Szaflarska
ponownie powołana do pełnienia funkcji konsultanta krajowego w dziedzinie gastroenterologii dziecięcej.
Minister Zdrowia, z dniem 31 sierpnia 2023 roku, powołał Panią Prof. dr hab. n. med. Mieczysławę Czerwionkę-Szaflarską
do pełnienia funkcji konsultanta krajowego w dziedzinie gastroenterologii dziecięcej na okres 5 lat.
Pani Profesor – gratulujemy!

Webinar „Post ESPGHAN 23" – najistotniejsze informacje z 55-go zjazdu
Europejskiego Towarzystwa Gastroenterologii, Hepatologii i Żywienia Dzieci,
który odbył się w Wiedniu w dniach 17-20 maja 2023 roku

Wykaz wydarzeń naukowych i dydaktycznych

Konferencje i szkolenia w Polsce

Konferencje i szkolenia na świecie

Przegląd najważniejszych publikacji naukowych

Opublikowano wytyczne ESPGHAN prewencji, rozpoznawania i leczenia alergii na białko mleka krowiego.
An ESPGHAN position paper on the diagnosis, management and prevention of cow's milk allergy
Vandenplas Y, Broekaert I, Domellöf M, Indrio F, Lapillonne A, Pienar C, i in. An ESPGHAN position paper on the diagnosis, management and prevention of cow's milk allergy. Journal of Pediatric Gastroenterology and Nutrition.
DOI:10.1097/MPG.0000000000003897.
A previous guideline on cow's milk allergy (CMA) developed by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) was published in 2012. This position paper provides an update on the diagnosis, treatment, and prevention of CMA with focus on gastrointestinal manifestations. All systematic reviews and meta-analyses regarding prevalence, pathophysiology,

symptoms, and diagnosis of CMA published after the previous ESPGHAN document were considered. Medline was searched from inception until May 2022 for topics that were not covered in the previous document. After reaching consensus on the manuscript, statements were formulated and voted on each of them with a score between 1 and 9. A score of ≥6 was arbitrarily considered as agreement. Available evidence on the role of dietary practice in the prevention, diagnosis and management of CMA was updated and recommendations formulated. CMA in exclusively breastfed infants exists, but is uncommon and suffers from over-diagnosis. CMA is also over-diagnosed in formula and mixed fed infants. Changes in stool characteristics, feeding aversion or occasional spots of blood in stool are common and in general should not be considered as diagnostic of CMA, irrespective of preceding consumption of cow's milk. Over-diagnosis of CMA occurs much more frequently than under-diagnosis; both have potentially harmful consequences. Therefore, the necessity of a challenge test after a short diagnostic elimination diet of 2-4 weeks is recommended as the cornerstone of the diagnosis. This position paper contains sections on nutrition, growth, cost and quality of life.

Opublikowano wytyczne ESPGHAN/NASPGHAN diagnostyki i leczenia eozynofilowego zapalenia przewodu pokarmowego innego niż eozynofilowe zapalenie przełyku.

Joint ESPGHAN/NASPGHAN Guidelines on Childhood Eosinophilic Gastrointestinal Disorders beyond Eosinophilic Esophagitis

Papadopoulou A, Amil-Dias J, Auth MKH, Chehade M, Collins MH, Gupta SK, i in. Joint ESPGHAN/NASPGHAN Guidelines on Childhood Eosinophilic Gastrointestinal Disorders beyond Eosinophilic Esophagitis. Journal of Pediatric Gastroenterology and Nutrition.

DOI :10.1097/MPG.0000000000003877.

Introduction: Eosinophilic Gastrointestinal Disorders beyond Eosinophilic Esophagitis (non-EoE EGIDs) are rare chronic inflammatory disorders of the gastrointestinal (GI) tract. Diagnosis is based on clinical symptoms and histologic findings of eosinophilic inflammation after exclusion of a secondary cause or systemic disease. Currently, no guidelines exist for the evaluation of non-EoE EGIDs. Therefore, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) formed a task force group to provide consensus guidelines for childhood non-EoE EGIDs.

Methods: The working group was composed of pediatric gastroenterologists, adult gastroenterologists, allergists/immunologists, and pathologists. An extensive electronic literature search of the MEDLINE, EMBASE, and Cochrane databases was conducted up to February 2022. General methodology was used in the formulation of recommendations according to the Appraisal of Guidelines for Research and Evaluation (AGREE) II and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to meet current standards of evidence assessment.

Results: The guidelines provide information on the current concept of non-EoE EGIDs, disease pathogenesis, epidemiology, clinical manifestations, diagnostic and disease surveillance procedures, and current treatment options. Thirty-four statements based on available evidence and 41 recommendations based on expert opinion and best clinical practices were developed.

Conclusion: Non-EoE EGIDs literature is limited in scope and depth, making clear recommendations difficult. These consensus-based clinical practice guidelines are intended to assist clinicians caring for children affected by non-EoE EGIDs and to facilitate high-quality randomized controlled trials of various treatment modalities using standardized, uniform disease definitions.

(W wytycznych uwagę zwraca m.in. Tabela 6, gdzie zaproponowano progi odcięcia dla liczby eozynofilów/HPF potrzebnej do rozpoznania choroby zależnie od lokalizacji anatomicznej).

Terapia genowa skuteczna w zespole Crigler-Najjar.

Gene Therapy in Patients with the Crigler–Najjar Syndrome

D'Antiga L, Beuers U, Ronzitti G, Brunetti-Pierri N, Baumann U, Di Giorgio A, i in. Gene Therapy in Patients with the Crigler–Najjar Syndrome. New England Journal of Medicine. 17 sierpień 2023;389(7):620–31.

Background: Patients with the Crigler–Najjar syndrome lack the enzyme uridine diphosphoglucuronate glucuronosyltransferase 1A1 (UGT1A1), the absence of which leads to severe unconjugated hyperbilirubinemia that can cause irreversible neurologic injury and death. Prolonged, daily phototherapy partially controls the jaundice, but the only definitive cure is liver transplantation.

Methods: We report the results of the dose-escalation portion of a phase 1–2 study evaluating the safety and efficacy of a single intravenous infusion of an adeno-associated virus serotype 8 vector encoding UGT1A1 in patients with the Crigler–Najjar syndrome that was being treated with phototherapy. Five patients received a single infusion of the gene construct (GNT0003): two received 2×1012 vector genomes (vg) per kilogram of body weight, and three received 5×1012 vg per kilogram. The primary end points were measures of safety and efficacy; efficacy was defined as a serum bilirubin level of 300 µmol per liter or lower measured at 17 weeks, 1 week after discontinuation of phototherapy.

Results: No serious adverse events were reported. The most common adverse events were headache and alterations in liver-enzyme levels. Alanine aminotransferase increased to levels above the upper limit of the normal range in four patients, a finding potentially related to an immune response against the infused vector; these patients were treated with a course of glucocorticoids. By week 16, serum bilirubin levels in patients who received the lower dose of GNT0003 exceeded 300 µmol per liter. The patients who received the higher dose had bilirubin levels below 300 µmol per liter in the absence of phototherapy at the end of follow-up (mean [±SD]

baseline bilirubin level, 351±56 µmol per liter; mean level at the final follow-up visit [week 78 in two patients and week 80 in the other], 149±33 µmol per liter).
Conclusions: No serious adverse events were reported in patients treated with the gene-therapy vector GNT0003 in this small study. Patients who received the higher dose had a decrease in bilirubin levels and were not receiving phototherapy at least 78 weeks after vector administration. (Funded by Genethon and others; ClinicalTrials.gov number, NCT03466463. opens in new tab.)

Występowanie alergii pokarmowej w wieku 1 roku jest powiązane z gorszą funkcją płuc w wieku 6 lat.

Infant food allergy phenotypes and association with lung function deficits and asthma at age 6 years: a population-based, prospective cohort study in Australia

Peters RL, Soriano VX, Lycett K, Flynn C, Idrose NS, Tang MLK, i in. Infant food allergy phenotypes and association with lung function deficits and asthma at age 6 years: a population-based, prospective cohort study in Australia. The Lancet Child & Adolescent Health. 1 wrzesień 2023;7(9):636–47.
Background: Food allergy is considered a precursor to asthma in the context of the atopic march, but the relationship between infant food allergy phenotypes and lung function and asthma in childhood is unclear. We aimed to examine the association between food sensitisation and challenge-confirmed food allergy in infancy, as well as persistent and resolved food allergy up to age 6 years, and the risk of lung function deficits and asthma at age 6 years.
Methods: The longitudinal, population-based HealthNuts cohort study in Melbourne, VIC, Australia, recruited 5276 infants children aged 1 year who attended council-run immunisation sessions between Sept 28, 2007, and Aug 5, 2011. At age 1 year, all children completed skin prick testing to four food allergens (egg, peanut, sesame, and either shrimp or cow's milk) and an oral food challenge (egg, peanut, and sesame) at the Royal Children's Hospital in Melbourne. Parents completed questionnaires about their infant's allergy history, demographic characteristics, and environmental exposures. At age 6 years, children were invited for a health assessment that included skin prick testing for ten foods (milk, egg, peanut, wheat, sesame, soy, shrimp, cashew, almond, and hazelnut) and eight aeroallergens (alternaria, cladasporum, house dust mite, cat hair, dog hair, bermuda grass, rye grass, and birch mix), oral food challenges, and lung function testing by spirometry. Questionnaires completed by parents (different to those completed at age 1 year) captured the child's allergy and respiratory history and demographics. We investigated associations between food allergy phenotypes (food-sensitised tolerance or food allergy; and ever, transient, persistent, or late-onset food allergy), lung function spirometry measures (forced expiratory volume in 1 sec [FEV1] and forced vital capacity [FVC] z-scores, FEV1/FVC ratio, forced expiratory flow at 25% and 75% of the pulmonary volume [FEF25–75%], and bronchodilator responsiveness), and asthma using regression methods. Only children with complete data on the exposure, outcome, and confounders were included in models. Infants without food sensitisation or food allergy at age 1 year and 6 years served as the reference group.
Findings: Of 5276 participants, 3233 completed the health assessment at age 6 years and were included in this analysis. Food allergy, but not food-sensitised tolerance, at age 1 year was associated with reduced FEV1 and FVC (aβ –0·19 [95% CI –0·32 to –0·06] and –0·17 [–0·31 to –0·04], respectively) at age 6 years. Transient egg allergy was associated with reduced FEV1 and FVC compared with never having egg allergy (–0·18 [95% CI –0·33 to –0·03] and –0·15 [–0·31 to 0·00], respectively), whereas persistent egg allergy was not (FEV1 –0·09 [–0·48 to 0·31]; FVC –0·20 [–0·62 to 0·21]). Transient peanut allergy was associated with reduced FEV1 and FVC (FEV1 aβ –0·37 [–0·79 to 0·04] and FVC aβ –0·55 [–0·98 to –0·12]), in addition to persistent peanut allergy (FEV1 aβ –0·30 [–0·54 to –0·06] and FVC aβ–0·30 [–0·55 to –0·05]), and late-onset peanut allergy (FEV1 aβ –0·62 [–1·06 to –0·18] and FVC aβ–0·49 [–0·96 to –0·03]). Estimates suggested that food-sensitised tolerance and food allergy were associated with reduced FEF25–75%, although some estimates were imprecise. Food allergy phenotypes were not associated with an FEV1/FVC ratio. Late-onset peanut allergy was the only allergy phenotype that was possibly associated with increased risk of bronchodilator responsiveness (2·95 [95% CI 0·77 to 11·38]). 430 (13·7%) of 3135 children were diagnosed with asthma before age 6 years (95% CI 12·5–15·0). Both food-sensitised tolerance and food allergy at age 1 year were associated with increased asthma risk at age 6 years (adjusted odds ratio 1·97 [95% CI 1·23 to 3·15] and 3·69 [2·81 to 4·85], respectively). Persistent and late-onset peanut allergy were associated with higher asthma risk (3·87 [2·39 to 6·26] and 5·06 [2·15 to 11·90], respectively).
Interpretation: Food allergy in infancy, whether it resolves or not, is associated with lung function deficits and asthma at age 6 years. Follow-up studies of interventions to prevent food allergy present an opportunity to examine whether preventing these food allergies improves respiratory health.

U dzieci i młodzieży odnotowano zwiększone ryzyko chorób psychicznych zarówno przed jak i po rozpoznaniu chorób autozapalnych, w tym autoimmunologicznych zapaleń wątroby i jelit.

Psychiatric disorders in paediatric-onset immune-mediated inflammatory diseases: a nationwide Danish study

Jansson S, Malham M, Carlsen K, Ingels H, Jørgensen MH, Virta LJ, i in. Psychiatric disorders in paediatric-onset immune-mediated inflammatory diseases: a nationwide Danish study. Archives of Disease in Childhood [Internet]. 28 sierpień 2023 [cytowane 29 sierpień 2023];
Objectives: To investigate the frequency of psychiatric disorders before and after onset of paediatric-onset immune-mediated inflammatory diseases (pIMID).
Study design: In a nationwide study from 1996 to 2018, we investigated psychiatric disorders in patients with paediatric-onset inflammatory bowel diseases, autoimmune liver diseases and rheumatic diseases, using Danish national

healthcare and population registers. Each case was matched with up to 10 controls from the background population. The cumulative incidence for psychiatric disorders prior to pIMID onset in patients was compared with controls. Cox proportional regression was used to estimate adjusted HRs (aHR) with a 95% CI between cases and controls after the index date.
Results: We included 11 208 cases (57% female) and 98 387 controls. The median age at disease onset was 12.5 years (IQR 8–15) and follow-up time 9.8 years (IQR 5–15). We found an association between psychiatric disorders before index date and a diagnosis of subsequent pIMID (OR 1.3, 95% CI 1.2 to 1.4). Notably, after index date, cases also had an increased risk (aHR 1.6, 95% CI 1.5 to 1.7) of psychiatric disorders compared with controls. This risk was increased for all groups of psychiatric disorders. Female patients had an increased risk of suicide attempt after index date (aHR 1.4, 95% CI 1.1 to 1.8).
Conclusion: Patients with pIMID are at increased risk for a broad spectrum of psychiatric disorders both before and after onset of pIMID. The results support the need for awareness of psychiatric morbidity in this young patient group and the need for coordinated healthcare for those with comorbid states.

Ultrasonograficzna ocena średnicy odbytnicy u niemowląt: górna granica normy w wieku 12 miesięcy to 2,64 cm.
Transabdominal ultrasound of rectal diameter in healthy infants: a prospective cohort study during the first year of life
Gatzinsky C, Sillén U, Borg H, Boström H, Abrahamsson K, Sjöström S. Transabdominal ultrasound of rectal diameter in healthy infants: a prospective cohort study during the first year of life. J Paediatr Child Health. 30 maj 2023.
Aim: Transabdominal rectal ultrasound (TRU) is used to measure transverse rectal diameter (TRD) in order to diagnose functional constipation (FC) and megarectum, and to evaluate treatment. The proposed cut-off value is 3.0 cm. Currently, no standardised values exist for children below the age of 4. We used repeated TRUs to establish reference TRD values in healthy infants and to describe rectal diameter in infants with FC.
Methods: This prospective observational cohort study enrolled healthy term babies from a maternity department. TRD measurements were taken at 2 and 12 months of age, and questionnaires completed in interviews helped diagnose FC according to Rome III criteria.
Results: Two hundred TRUs were performed on 110 infants (62 males). In infants without FC anytime, the mean TRD at 2 months was 1.56 (SD 0.32) cm and at 12 months 1.78 (0.47) cm, while the 95th percentiles were 2.26 and 2.64 cm, respectively. In 77 infants with two TRUs, the mean increase was 0.21 cm (95% confidence interval: 0.099–0.318). Thirteen infants were diagnosed with FC during the study period. At 2 and 12 months of age, there was no difference in TRD between infants with and without FC.
Conclusion: TRD increased from 2 to 12 months. We suggest 2.3 cm as an upper limit for normal TRD at 2 months and 2.6 cm at 12 months. Infants diagnosed with FC did not have a greater TRD than infants without, either before or after treatment. Further studies are needed to evaluate the usefulness of TRU in infants with FC or megarectum.

Wysoka dokładność badania antybiotykooporności Helicobacter pylori przez sekwencjonowanie DNA izolowanego z kału pacjenta.
Helicobacter pylori Antimicrobial Resistance Using Next-Generation Sequencing in stool samples in a pediatric population
Bonilla S, Goldsmith J, Mitchell P, Bousvaros A. Helicobacter pylori Antimicrobial Resistance Using Next-Generation Sequencing in stool samples in a pediatric population. Journal of Pediatric Gastroenterology and Nutrition.
DOI:10.1097/MPG.0000000000003908.
Helicobacter pylori (H. pylori) eradication rates have declined globally, stressing the importance of antimicrobial susceptibility testing to inform treatment. Molecular tests such as next-generation sequencing provide susceptibility data for the antibiotics used in the treatment of H. pylori in a non-invasive, effective, and rapid manner. We obtained stool susceptibility testing using a novel -next-generation sequencing-based analysis and compared results with the current “gold standard” of gastric biopsy culture via agar dilution in 20 pediatric patients with evidence of H. pylori in gastric biopsies. Stool next-generation sequencing-based antimicrobial susceptibility analysis was highly concordant with agar dilution for no resistance (100% agreement), as well as clarithromycin, levofloxacin, and amoxicillin resistance (100%, 67%, and 100% agreement respectively) but not concordant for metronidazole in our cohort of patients. Future studies involving a larger number of patients and geographical regions are needed to further validate this analysis.

Niedostateczna jakość snu istotnie koreluje z ciężkością objawów zaburzeń interakcji mózg-jelito u dzieci i młodzieży.
Impact of sleep disturbance on fatigue, nausea, and pain: Mediating role of depressive symptoms among youth with DGBI
Bedree H, Tran ST, Koven ML, Wershil SJ, Fortunato JE, Essner BS. Impact of sleep disturbance on fatigue, nausea, and pain: Mediating role of depressive symptoms among youth with DGBI. Journal of Pediatric Gastroenterology and Nutrition. DOI:10.1097/MPG.0000000000003887.
Introduction: A high degree of sleep disturbance is reported among youth with disorders of gut-brain interaction (DGBIs). Given that sleep quality impacts a range of pediatric health outcomes including somatic sensations (e.g., pain) and depressive mood occurs relatively frequently among youth with DGBIs, there is a dire need to disentangle the unique contributions of sleep and depressive mood on the somatic sensations experienced by youth with DGBIs. We aimed to examine whether depressive mood mediates the relations among sleep disturbance and pain intensity, nausea, and fatigue among youth with DGBIs.

Methods: 118 patients aged 8-17 years (Mage= 14.05, SD= 2.88; 70.34% female), 83.05% White/non-Hispanic recruited at a pediatric neurogastroenterology clinic completed measures of sleep disturbance, nausea, fatigue, pain intensity, and depressive mood. Three mediation models examined the effect of sleep disturbance on nausea, fatigue, and pain, with depressive mood as a mediator.
Results: Participants reported moderate sleep disturbance. Depressive mood partially mediated the significant, respective relations between greater sleep disturbance and more severe nausea and fatigue. Sleep disturbance was significantly associated with higher pain intensity; however, depressive mood was not a significant mediator of this relation.
Conclusions: Sleep quality is a major concern among youth with DGBIs. Low sleep quality may worsen nausea and fatigue via co-occurring increases in depressive mood symptoms. In contrast, sleep disturbance may directly increase pain, regardless of youths' depressive mood symptoms. Future research should explore these relations through prospective studies leveraging a combination of subjective and objective assessment approaches.

Skuteczność leków zwiększających apetyt w zwiększeniu masy pacjentów z mukowiscydozą.

Evaluation of the Use of Appetite Stimulants in Pediatric Patients with Cystic Fibrosis

Kennedy K, Lee M, Sathe M, Ueng CS, Sharma P. Evaluation of the Use of Appetite Stimulants in Pediatric Patients with Cystic Fibrosis. Journal of Pediatric Gastroenterology and Nutrition. DOI:10.1097/MPG.0000000000003886.
Objective: Poor nutrition in patients with cystic fibrosis (CF) has been associated with lower lung function and increased morbidity and mortality. Conversely, better nutritional status has been associated with improved pulmonary function and fewer CF-associated complications. There is no consensus regarding appetite stimulant therapy in patients with CF (pwCF). The primary objective of this study was to determine if the use of appetite stimulants was associated with weight changes in pediatric pwCF in the ambulatory care setting.
Methods: This was a retrospective study that evaluated 62 pediatric pwCF who received cyproheptadine or mirtazapine for appetite stimulation for at least 6 consecutive months. Weight z-scores were collected for each patient at baseline, 3, 6, and 12 months of therapy, if available.
Results: Increase in weight z-score after 3 months of therapy was statistically significant based on both univariable and multivariable models when evaluating the entire cohort. The adjusted mean difference for change in weight z-score was 0.33 ($p< 0.001$) from baseline to month 3. There was a statistically significant improvement in pulmonary function after 3 and 6 months of therapy.
Conclusions: Appetite stimulant therapy is associated with improvement in weight z-score in the first 3 months of treatment. Appetite stimulant therapy was associated with improvement in pulmonary function in the first 3 months of therapy, which supports the relationship between weight gain and improved pulmonary function in pwCF. These findings suggest that appetite stimulants contribute to weight gain in pediatric pwCF, particularly within the first 3 months of therapy.

Amerykańskie Towarzystwo Gastroenterologiczne wydało zalecenia wykorzystania biomarkerów w diagnostyce i leczenia u (dorosłych) pacjentów z niealkoholowym stłuszczeniem wątroby.

AGA Clinical Practice Update on the Role of Noninvasive Biomarkers in the Evaluation and Management of Nonalcoholic Fatty Liver Disease: Expert Review

Wattacheril JJ, Abdelmalek MF, Lim JK, Sanyal AJ. AGA Clinical Practice Update on the Role of Noninvasive Biomarkers in the Evaluation and Management of Nonalcoholic Fatty Liver Disease: Expert Review. Gastroenterology [Internet]. 4 sierpień 2023 [cytowane 29 sierpień 2023].
Best Practice Advice Statements
Best Practice Advice 1: NITs can be used for risk stratification in the diagnostic evaluation of patients with NAFLD.
Best Practice Advice 2: A Fibrosis 4 Index score <1.3 is associated with strong negative predictive value for advanced hepatic fibrosis and may be useful for exclusion of advanced hepatic fibrosis in patients with NAFLD.
Best Practice Advice 3: A combination of 2 or more NITs combining serum biomarkers and/or imaging-based biomarkers is preferred for staging and risk stratification of patients with NAFLD whose Fibrosis 4 Index score is >1.3.
Best Practice Advice 4: Use of NITs in accordance with manufacturer's specifications (eg, not in patients with ascites or pacemakers) can minimize risk of discordant results and adverse events.
Best Practice Advice 5: NITs should be interpreted with context and consideration of pertinent clinical data (eg, physical examination, biochemical, radiographic, and endoscopic) to optimize positive predictive value in the identification of patients with advanced fibrosis.
Best Practice Advice 6: Liver biopsy should be considered for patients with NIT results that are indeterminate or discordant; conflict with other clinical, laboratory, or radiologic findings; or when alternative etiologies for liver disease are suspected.
Best Practice Advice 7: Serial longitudinal monitoring using NITs for assessment of disease progression or regression may inform clinical management (ie, response to lifestyle modification or therapeutic intervention).
Best Practice Advice 8: Patients with NAFLD and NITs results suggestive of advanced fibrosis (F3) or cirrhosis (F4) should be considered for surveillance of liver complications (eg, hepatocellular carcinoma screening and variceal screening per Baveno criteria). Patients with NAFLD and NITs suggestive of advanced hepatic fibrosis (F3) or (F4), should be monitored with serial liver stiffness measurement; vibration controlled transient elastography; or magnetic resonance elastography, given its correlation with clinically significant portal hypertension and clinical decompensation.

Opublikowano międzynarodowe wytyczne przeszczepiania mikrobioty jelitowej w nieswoistych zapaleniach jelit (pacjenci dorośli).

The first international Rome consensus conference on gut microbiota and faecal microbiota transplantation in inflammatory bowel disease

Lopetuso LR, Deleu S, Godny L, Petito V, Puca P, Facciotti F, i in. The first international Rome consensus conference on gut microbiota and faecal microbiota transplantation in inflammatory bowel disease. Gut. 1 wrzesień 2023;72(9):1642–50.

Background: Several randomised clinical trials (RCTs) performing faecal microbiota transplantation (FMT) for the management of inflammatory bowel disease (IBD), particularly for ulcerative colitis, have recently been published, but with major variations in study design. These include differences in administered dose, route and frequency of delivery, type of placebo and evaluated endpoints. Although the overall outcomes appear to be promising, they are highly dependent on both donor and recipient factors.

Objective: To develop concensus-based statements and recommendations for the evaluation, management and potential treatment of IBD using FMT in order to move towards standardised practices.

Design: An international panel of experts convened several times to generate evidence-based guidelines by performing a deep evaluation of currently available and/or published data. Twenty-five experts in IBD, immunology and microbiology collaborated in different working groups to provide statements on the following key issues related to FMT in IBD: (A) pathogenesis and rationale, (B) donor selection and biobanking, (C) FMT practices and (D) consideration of future studies and perspectives. Statements were evaluated and voted on by all members using an electronic Delphi process, culminating in a plenary consensus conference and generation of proposed guidelines.

Results and conclusions: Our group has provided specific statements and recommendations, based on best available evidence, with the end goal of providing guidance and general criteria required to promote FMT as a recognised strategy for the treatment of IBD.

Wykazano związek między mikrobiotą jelitową i dietą a odpowiedzią na szczepienie przeciwko SARS-CoV-2.

Gut microbiome and dietary fibre intake strongly associate with IgG function and maturation following SARS-CoV-2 mRNA vaccination

Lunken GR, Golding L, Schick A, Majdoubi A, Lavoie PM, Vallance BA. Gut microbiome and dietary fibre intake strongly associate with IgG function and maturation following SARS-CoV-2 mRNA vaccination. Gut [Internet]. 22 grudzień 2022 [cytowane 29 sierpień 2023].

(Brak abstraktu – short report) Autorzy w niezależnie przeprowadzonym badaniu potwierdzili pierwsze doniesienia o zależności między stanem jelita a odpowiedzią na szczepienie przeciwko SARS-CoV-2 (Ng i wsp. Gut 2022, DOI:10.1136/gutjnl-2021-326563). Szczególną rolę zwrócono na zmniejszenie odpowiedzi przy większych stężeniach rozgałęzionych kwasów tłuszczowych, a także przy większej obfitości bakterii Megasphaera, które je produkują. Zidentyfikowano także bakterie powiązane z lepszą odpowiedzią. Wyniki badania sugerują na istotne znacznie przewodu pokarmowego dla prawidłowej odpowiedzi na szczepienia, co mogłoby mieć istotne znaczenie także dla dzieci.

Określone zaburzenia składu mikrobioty jelitowej są związane z dwukrotnym zwiększeniem ryzyka choroby Leśniowskiego-Crohna u krewnych pierwszego stopnia pacjentów.

Gut Microbiome Composition Is Associated With Future Onset of Crohn's Disease in Healthy First-Degree Relatives

Background & Aims: The cause of Crohn's disease (CD) is unknown, but the current hypothesis is that microbial or environmental factors induce gut inflammation in genetically susceptible individuals, leading to chronic intestinal inflammation. Case-control studies of patients with CD have cataloged alterations in the gut microbiome composition; however, these studies fail to distinguish whether the altered gut microbiome composition is associated with initiation of CD or is the result of inflammation or drug treatment.

Methods: In this prospective cohort study, 3483 healthy first-degree relatives (FDRs) of patients with CD were recruited to identify the gut microbiome composition that precedes the onset of CD and to what extent this composition predicts the risk of developing CD. We applied a machine learning approach to the analysis of the gut microbiome composition (based on 16S ribosomal RNA sequencing) to define a microbial signature that associates with future development of CD. The performance of the model was assessed in an independent validation cohort.

Results: In the validation cohort, the microbiome risk score (MRS) model yielded a hazard ratio of 2.24 (95% confidence interval, 1.03-4.84; P = .04), using the median of the MRS from the discovery cohort as the threshold. The MRS demonstrated a temporal validity by capturing individuals that developed CD up to 5 years before disease onset (area under the curve > 0.65). The 5 most important taxa contributing to the MRS included Ruminococcus torques, Blautia, Colidextribacter, an uncultured genus-level group from Oscillospiraceae, and Roseburia.

Conclusion: This study is the first to demonstrate that gut microbiome composition is associated with future onset of CD and suggests that gut microbiome is a contributor in the pathogenesis of CD.

Badania w modelach zwierzęcych wykazały, że inhibitor karboksypeptydazy kwasu glutaminowego II jest obiecującym kandydatem na lek przeciwko nieswoistym zapaleniom jelit.

A gut-restricted glutamate carboxypeptidase II inhibitor reduces monocytic inflammation and improves preclinical colitis

Peters DE, Norris LD, Tenora L, Šnajdr I, Ponti AK, Zhu X, i in. A gut-restricted glutamate carboxypeptidase II inhibitor reduces monocytic inflammation and improves preclinical colitis. Sci Transl Med. 9 sierpień 2023;15(708):eabn7491.

There is an urgent need to develop therapeutics for inflammatory bowel disease (IBD) because up to 40% of patients with moderate-to-severe IBD are not adequately controlled with existing drugs. Glutamate carboxypeptidase II (GCPII) has emerged as a promising therapeutic target. This enzyme is minimally expressed in normal ileum and colon, but it is markedly up-regulated in biopsies from patients with IBD and preclinical colitis models. Here, we generated a class of GCPII inhibitors designed to be gut-restricted for oral administration, and we interrogated efficacy and mechanism using in vitro and in vivo models. The lead inhibitor, (S)-IBD3540, was potent (half maximal inhibitory concentration = 4 nanomolar), selective, gut-restricted (AUCcolon/plasma > 50 in mice with colitis), and efficacious in acute and chronic rodent colitis models. In dextran sulfate sodium–induced colitis, oral (S)-IBD3540 inhibited >75% of colon GCPII activity, dose-dependently improved gross and histologic disease, and markedly attenuated monocytic inflammation. In spontaneous colitis in interleukin-10 (IL-10) knockout mice, once-daily oral (S)-IBD3540 initiated after disease onset improved disease, normalized colon histology, and attenuated inflammation as evidenced by reduced fecal lipocalin 2 and colon pro-inflammatory cytokines/ chemokines, including tumor necrosis factor–α and IL-17. Using primary human colon epithelial air-liquid interface monolayers to interrogate the mechanism, we further found that (S)-IBD3540 protected against submersion-induced oxidative stress injury by decreasing barrier permeability, normalizing tight junction protein expression, and reducing procaspase-3 activation. Together, this work demonstrated that local inhibition of dysregulated gastrointestinal GCPII using the gut-restricted, orally active, small-molecule (S)-IBD3540 is a promising approach for IBD treatment.

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