antibodies level changes was analysed. Western diet consists of 10–20 grams of gluten per day and as ‘safe’ is considered anything under 10 mg per day what is an equivalent to 1/350 of a piece of bread. Atypical gluten-free diet willconsists in any which gluten-poor diet, and gluten-free diet is rarely 100% without gluten i.e. proteins of plant origin from oats, rye, barley and wheat.

**Results** Mathematical simulations of the celiac disease immune response showed the differences in antibodies levels changes depending on the amount of gluten consumed by paediatric patients. The profile of the antibodies levels decrease after of changing diet form gluten containing to gluten free was also presented.

**Conclusions** Application of the nutritional systems biology approach in diet planning ensures detail insight in metabolic process and simple control of the metabolic reaction influenced by nutrient intake.

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**LIVER DISEASE IN PEDIATRIC PATIENTS TREATED AT THE CYSTIC FIBROSIS CENTRE OF THE UNIVERSITY HOSPITAL CENTRE ZAGREB**

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**Objective** To describe the characteristics of patients with cystic fibrosis-associated liver disease (CFLD), a complication of cystic fibrosis (CF) that is often asymptomatic until an advanced stage.

**Methods** Retrospective analysis included patients aged 0-20 years followed in 2018. at the Cystic Fibrosis Centre of the University Hospital Centre Zagreb. CFLD1 was diagnosed if ≥2 of the following were present: hepatomegaly and/or splenomegaly, elevated transaminases or gamma-glutamyl transferase (GGT) 3 times during 12 months, ultrasound signs of liver involvement or portal hypertension (PHTH), suggestive pathohistological findings. Severe CFLD was defined as a disease with signs of PTH.

**Results** 61 patients with a mean age of 10.9 years (9 months-19 years, male: female = 34:27) were included. 9/61 (14.8%) of them had CFLD, 6 girls and 3 boys, aged 2-19 years (average age 10.7 years). They all had at least one F508del mutation, and 7/9 were homozygous. Regarding the severity of the disease, 4 patients (3 boys and 1 girl, 6-19 years) had a severe form of CFLD with PTH and presumed cirrhosis, which was confirmed by liver biopsy in one patient. Two patients also had impaired synthetic liver function, two had hypersplenism with platelet count <80x109/L, and one had esophageal varices without bleeding. The remaining 5/9 patients had mild CFLD with ultrasound changes (hyperechoic or nodular liver parenchyma, periportal fibrosis) and/or elevated liver enzymes.

We observed a trend of poor nutritional status in patients with severe CFLD (mean BMI z-value -0.66, range -0.26 to 0.62) compared to those with mild form of CFLD (mean BMI z-value -0.41, range -2.76 to 1.49), but the difference wasn’t significant, and the most severely malnourished patient had mild CFLD.

We also assessed some noninvasive biomarkers of fibrosis: the APRI index was elevated (≥0.5) in all patients with severe CFLD and in one with mild CFLD, and Fibrosis-4 score was pathological in only one patient with PTH. Elastography was performed in 5 patients: it was normal in one patient with mild CFLD, whereas in four increased liver stiffness was found (significantly increased in two patients with severe CFLD, and mildly in two patients with mild CFLD).

4/9 patients with CFLD had meconium ileus, which is approximately twice the frequency compared to all included CF patients.

**Conclusion** The diversity of clinical expression and findings in our patients is consistent with the literature data on the spectrum of CFLD manifestations. We confirmed a higher incidence of meconium ileus and severe mutations, and male dominance in CFLD with PTH. In all CF patients, liver disease should be actively sought from an early age (clinical examination once a year + abdominal ultrasound + AST, ALT, GGT).

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**TRANSUCUTANEOUS NEUROMODULATION IN CHILDREN WITH CHRONIC INTRACTABLE CONSTIPATION**

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**Objective** Transcutaneous neuromodulation is a therapeutic method using electrical stimulation on nerve fibers. It may be optional therapy in children and adults with chronic constipation. The goal was to evaluate the effectiveness of this method in children with chronic refractory constipation who had been treated with conventional pharmacological and biofeedback therapy without complete improvement.

**Methods** 15 patients (8 boys and 7 girls), with median age of 9.03±2.98 years and diagnosis of intractable chronic functional constipation were assigned for neuromodulation. They had been previously treated conservatively following ESPGHAN guidelines, for the median period of 37 months (7-66 months) without achieving complete stool regulation. Biofeedback therapy had also been performed in 11 patients. Neuromodulation was added as an additional treatment, without removing previous therapy. Transcutaneous sacral (TSNS) or tibial (TTNS) nerve stimulation was performed at home, every day for 20 minutes, during the period of 2 to 3 months. Self-adhesive surface electrode was placed at sacral S2-S3 for TSNS and 4-5 cm cranial from medial malleolus for TTNS. The usefulness of this method was evaluated according to 3 parameters: the frequency of spontaneous defecation, the improvement of sensation for defecation, and reduction of rectal dimensions (followed by ultrasound before and after neuromodulation).

**Results** Data of 15 patients was analyzed. TSNS was performed in 13 (86.7%), and TTNS in 2 (13.3%) children. Positive effects were noticed in 9 (60%) children for all of 3 parameters.

Monitoring each parameter separately, a better dynamic of spontaneous defecation was achieved in 10 (66.7%) children, improving of sensation in 9 (60.0%) children, and decreasing of rectal diameter in 10 children, from the 11 that underwent an ultrasound (90.9%). Rectal diameter reduced from initially 4.98±1.24 cm to 3.80±1.15 cm, on average 1.18±0.91 cm, which was statistically significant (p=0.024). Every patient achieved improvement, on at least one of the parameters. 10...