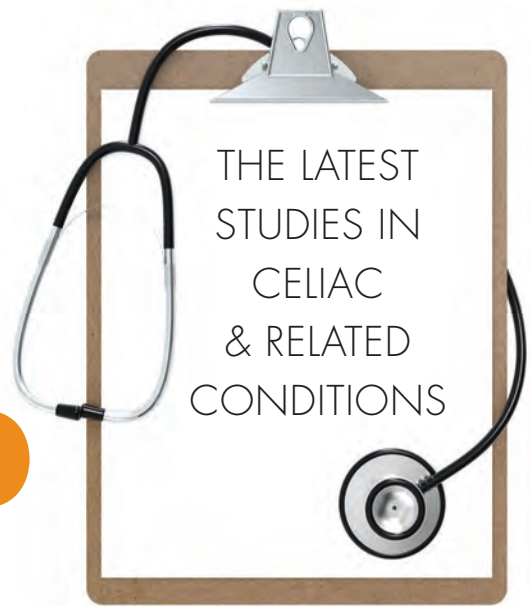


Research Roundup



In this issue's Research Roundup, we're focusing on the question: are people with celiac disease more susceptible to infection? The recent studies presented here specifically address respiratory infection, *Streptococcus pneumoniae*, and rotavirus.

An evaluation of nasal mucociliary clearance time in children with celiac disease.

The function of the nasal mucociliary clearance system is to protect the respiratory system from damage by inhaled substances, including bacteria and viruses. Impairment of nasal mucociliary clearance can result in diseases of the upper airways. Nasal mucociliary clearance also has implications for nasal drug absorption. After intranasal administration, drugs are cleared rapidly from the nasal cavity, resulting in fast systemic drug absorption.

The study included children with celiac disease and without. Nasal mucociliary clearance time was measured using the saccharin test. The children's saccharin taste time was recorded in seconds.

Sixty-five children were included: 43 patients with celiac (66.2 percent) and 22 healthy children (33.8 percent). Of all the children, 42 (64.6 percent) were female, and the average age was 11.8 ± 4 years. Nasal mucociliary clearance time of patients with celiac (531 ± 155 s) was significantly prolonged in comparison to that of healthy children (448 ± 80 s) ($p = 0.006$). No relationships were found between the diagnosis age, celiac type, and histopathological phase and compliance with the gluten-free diet and nasal mucociliary clearance time of patients with celiac.

This study showed that nasal mucociliary clearance was prolonged in patients with celiac. A defect in nasal mucociliary clearance increases the risk of infection and inflammation in small airways. Studies reported a high prevalence of respiratory tract infections in patients with celiac, which was associated with malnutrition, vitamin deficiency, and hyposplenism (reduced spleen function). The findings of the present study indicate that impairment of nasal mucociliary clearance could play a role in the development of frequent lung infections in patients with celiac.

Reference:

Evaluation of nasal mucociliary clearance time in children with celiac disease. *International Journal of Pediatric Otorhinolaryngology*. Feb 8, 2020. 133:109936. Comba, A., Atan, D.

A significant portion of patients with celiac disease and other autoimmune diseases have a fear of vaccination due to a potential risk of vaccine-triggered disease exacerbation. Recently, a group of Italian experts addressed an issue regarding the necessity of pneumococcal vaccination in individuals affected by celiac.

Lung infection with *Streptococcus pneumoniae* (pneumococcus) is a particularly dangerous morbid

condition in both the general population and celiac patients. Pneumococcal vaccination is the most effective means for its prevention. The panel of experts was trying to ascertain which subsets of celiac patients may benefit the most from pneumococcal vaccination. Presumably, patients with celiac disease and hyposplenism (more specifically, with functional hyposplenism) are among those who benefit from the vaccination the most.

The integrity and proper function of the spleen are considered important for the protection against infectious diseases. The reduction of splenic function encountered in various pathological conditions is called functional hyposplenism (FH). FH is a term first used a few decades ago (1969) when some children suffering from sickle cell disease presented with the same clinical symptoms as splenectomised patients, despite the fact that their spleen had not yet been removed (their spleen was in fact enlarged due to their illness).

FH is a condition accompanying many diseases such as sickle cell disease, celiac, alcoholic liver disease, hepatic cirrhosis, lymphomas, and autoimmune disorders. It is characterized mostly by defective immune responses against infectious agents, especially encapsulated organisms, including *Streptococcus pneumoniae*.

The conclusions of the article state:

- Hyposplenism, a well-known risk factor for pneumococcal infection, is not routinely investigated and evaluated in celiac patients.
- Every physician should investigate blood and/or ultrasound signs of hyposplenism and splenic atrophy in celiac patients.
- A systematic evaluation of spleen function should permit the selection of celiac patients who may benefit from vaccination, in order to reduce the risk of invasive pneumococcal disease.
- Celiac patients with impaired immunologic function and functional hyposplenism need to undergo a complete vaccination protocol with pneumococcal vaccine.

Reference:

Pneumococcal vaccination in celiac disease. *Expert Review of Gastroenterology & Hepatology.* June 2019. 13(6):541-546. Casella, G., Ingravalle, F., Abbate, G., et al.

A systematic evaluation of spleen function should permit the selection of celiac patients who may benefit from vaccination, in order to reduce the risk of invasive pneumococcal disease.



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Rotavirus historically has been linked to various gastrointestinal ailments, including acute diarrhea and gastroenteritis; this study evaluates the capability of the rotavirus to cause the transition of nonceliac gluten sensitivity into full-blown celiac disease.

Nonceliac gluten sensitivity (NCGS) can be defined as a nonallergic condition in which the consumption of gluten can lead to symptoms similar to those observed in celiac disease. NCGS is characterized by the absence of celiac-specific antibodies and an absence of classical enteropathy.

Patients with NCGS may have variable HLA status, and positivity for HLA-DQ2 and/or DQ8 has been found in roughly 50 percent of patients with NCGS. Serological analyses of NCGS patients revealed a high prevalence (40-50 percent) of first-generation anti-gliadin IgG antibodies.

NCGS is characterized by symptoms that usually occur soon after gluten ingestion and disappear or improve with gluten withdrawal but relapse following gluten ingestion. The clinical presentation of NCGS may be a combination of gastrointestinal symptoms, including abdominal pain, bloating, bowel habit abnormalities (diarrhea or constipation), and systemic manifestations like “brain fog,” fatigue, muscle/joint pain, leg/arm numbness, eczema and skin rashes, depression, and anemia.

Rotavirus is a double-stranded RNA virus belonging to the family of Reoviridae. The virus is transmitted by the fecal-oral route and infects intestinal cells causing gastroenteritis. Rotaviruses are the main cause of severe acute diarrhea in children less than 5 years of age worldwide. They were responsible for 528,000 child deaths worldwide in 2000, though that number dropped to an average of 215,000 child deaths worldwide in 2013 and 128,500 in 2016. Most cases of death (85 percent) occur in developing countries.

There is a previously established link between rotavirus infection and celiac disease, demonstrating that in active celiac disease, a subset of anti-transglutaminase IgA antibodies recognize the rotaviral protein (VP-7) and are able to increase intestinal permeability and induce monocyte (type of white blood cell) activation. Also, it was shown that anti-rotavirus VP7 antibodies may be detected before celiac onset and the detection of anti-tissue transglutaminase and anti-endomysium antibodies, showing their predictive role in the development of celiac disease. Furthermore, these antibodies were able to induce biological processes that represent many typical features of celiac disease.

The aim of the reviewed work is to clarify some aspects of NCGS pathogenesis. The results suggest NCGS may have an autoimmune origin. This is based both on gene expression data and on serological markers of autoimmunity in NCGS. The generated data also indicate a possible involvement of rotavirus infection in the pathogenesis of NCGS similarly to what was previously shown in celiac disease.

Reference:

Immune Response to Rotavirus and Gluten Sensitivity. *Journal of Immunology Research*. March 15, 2018. 2018:9419204. Puccetti, A., Saverino, D., Opri, R., et al.

A study from Finland showed that rotavirus vaccination can reduce the risk of celiac disease in children.

In the Rotavirus Efficacy and Safety Trial, conducted between 2001 and 2003, the participant children received either the RotaTeq vaccine or placebo in 1:1 ratio.


In 2015, as a follow up to the trial, a questionnaire was sent to the parents of 19,133 Finnish participants of which 5,764 (30 percent) returned the questionnaire. Researchers wanted to know the prevalence of a diagnosis of type 1 diabetes, biopsy-proven celiac disease, and other autoimmune disease over the following 11-14 year period.

At the time of the questionnaire, the prevalence of type 1 diabetes was similar in both groups, 0.97 percent (25 of 2,580 children) in the placebo group and 1.04 percent (33 of 3,184 children) in the vaccine group (P = 0.810).

The prevalence of celiac was significantly higher in placebo recipients (1.11 percent; confidence interval: 0.78 to 1.6 percent) than in vaccine recipients (0.60 percent; confidence interval: 0.38 to 0.93 percent) (P = 0.027).

It was concluded that a rotavirus vaccination using RotaTeq did not alter the occurrence of type 1 diabetes but decreased the prevalence of celiac in childhood and adolescence. It was proposed that wild-type rotavirus may trigger celiac disease, but the trigger can be prevented or reduced by a rotavirus vaccination.

Reference:

Rotavirus Vaccination Does Not Increase Type 1 Diabetes and May Decrease Celiac Disease in Children and Adolescents. *The Pediatric Infectious Disease Journal.* May 2019. 38(5):539-541. Hemming-Harlow, M., Lähdeaho, ML., et al. 

It was proposed that wild-type rotavirus may trigger celiac disease, but the trigger can be prevented or reduced by a rotavirus vaccination.

As always, consult a medical professional before beginning any new protocol.



ABOUT THE AUTHOR:

Dr. Alexander Shikhman, founder of the Institute for Specialized Medicine, is board certified in internal medicine and rheumatology. Dr. Shikhman also launched Gluten-Free Remedies™, a line of all natural supplements which help treat the complications that can arise from celiac disease. Find Dr. Shikhman at ifsmcd.com and glutenfreeremedies.com.



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