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Studienauswahl zum Thema

Intermittierende leaky gut syndrom

Stand: 20.02.20221

Veröffentlichung 1[1]:

Leaky gut: mechanisms, measurement and clinical implications in humans - PubMed (nih.gov)

In: Gut. 2019 Aug;68(8):1516-1526.
doi: 10.1136/gutjnl-2019-318427. Epub 2019 May 10.

„Abstract

The objectives of this review on 'leaky gut' for clinicians are to discuss the components of the intestinal barrier, the diverse measurements of intestinal permeability, their perturbation in non-inflammatory 'stressed states' and the impact of treatment with dietary factors. Information on 'healthy' or 'leaky' gut in the public domain requires confirmation before endorsing dietary exclusions, replacement with non-irritating foods (such as fermented foods) or use of supplements to repair the damage. The intestinal barrier includes surface mucus, epithelial layer and immune defences. Epithelial permeability results from increased paracellular transport, apoptosis or transcellular permeability. Barrier function can be tested in vivo using orally administered probe molecules or in vitro using mucosal biopsies from humans, exposing the colonic mucosa from rats or mice or cell layers to extracts of colonic mucosa or stool from human patients. Assessment of intestinal barrier requires measurements beyond the epithelial layer. **'Stress' disorders such as endurance exercise, non-steroidal anti-inflammatory drugs administration, pregnancy and surfactants (such as bile acids and dietary factors such as emulsifiers) increase permeability.** Dietary factors can reverse intestinal leakiness and mucosal damage in the 'stress' disorders. Whereas inflammatory or ulcerating intestinal diseases result in leaky gut, no such disease can be cured by simply normalising intestinal barrier function. It is still unproven that restoring barrier function can ameliorate clinical manifestations in GI or systemic diseases. Clinicians should be aware of the potential of barrier dysfunction in GI diseases and of the barrier as a target for future therapy.“

1 Hinweis: Zu Vereinfachung sind die Abstracts – soweit vorhanden – mitabgedruckt und die Kernaussagen fett-dargestellt.

Veröffentlichung 2:

Leaky Gut, Leaky Brain? - PubMed (nih.gov)

In: Microorganisms. 2018 Oct 18;6(4):107.
doi: 10.3390/microorganisms6040107.

„Abstract

'Leaky gut' syndrome, long-associated with celiac disease, has attracted much attention in recent years and for decades, was widely known in complementary/alternative medicine circles. It is often described as an increase in the permeability of the intestinal mucosa, which could allow bacteria, toxic digestive metabolites, bacterial toxins, and small molecules to 'leak' into the bloodstream. Nervous system involvement with celiac disease is know to occur even at subclinical levels. Gluten and gluten sensitivity are considered to trigger this syndrome in individuals genetically predisposed to celiac disease. However, the incidence of celiac disease in the general population is quite low. Nevertheless, increased public interest in gluten sensitivity has contributed to expanded food labels stating 'gluten-free' and the proliferation of gluten-free products, which further drives gluten-free lifestyle changes by individuals without frank celiac disease. Moreover, systemic inflammation is associated with celiac disease, depression, and psychiatric comorbidities. This mini-review focuses on the possible neurophysiological basis of leaky gut; leaky brain disease; and the microbiota's contribution to inflammation, gastrointestinal, and blood-brain barrier integrity, in order to build a case for possible mechanisms that could foster further 'leaky' syndromes. We ask whether a gluten-free diet is important for anyone or only those with celiac disease.“

Veröffentlichung 3:

Leaky Gut As a Danger Signal for Autoimmune Diseases - PubMed (nih.gov)

In: Front Immunol. 2017 May 23;8:598.
doi: 10.3389/fimmu.2017.00598. eCollection 2017.

„Abstract

The intestinal epithelial lining, together with factors secreted from it, forms a barrier that separates the host from the environment. **In pathologic conditions, the permeability of the epithelial lining may be compromised allowing the passage of toxins, antigens, and bacteria in the lumen to enter the blood stream creating a "leaky gut." In individuals with a genetic predisposition, a leaky gut may allow environmental factors to enter the body and trigger the initiation and development of autoimmune disease.** Growing evidence shows that the gut microbiota is important in supporting the epithelial barrier and therefore plays a key role in the regulation of environmental factors that enter the body. Several recent reports have shown that probiotics can reverse the leaky gut by enhancing the production of tight junction proteins; however, additional and longer term studies are still required. Conversely, pathogenic bacteria that can facilitate a leaky gut and induce autoimmune symptoms can be ameliorated with the use of antibiotic treatment. Therefore, it is hypothesized that modulating the gut microbiota can serve as a potential method for regulating intestinal permeability and may help to alter the course of autoimmune diseases in susceptible individuals.“

Veröffentlichung 4:

Gut microbiota in autoimmunity: potential for clinical applications - PubMed (nih.gov)

In: Archives of Pharmacal Research. 2016 Nov;39(11):1565-1576.
doi: 10.1007/s12272-016-0796-7. Epub 2016 Jul 22.

„Abstract

Microbial habitation in the human body begins immediately after birth, and adults are colonized by microbes outnumbering human cells by a factor of ten. Especially, intestinal track is a living space for diverse microbial species that have coevolved symbiotically. A principal function of the gut microbiota is to protect the host from harmful bacteria and to provide benefits for the host through several mechanisms, including direct competition for limited nutrients, training of host immune systems to recognize specifically foreign materials and conversion of otherwise indigestible food into energy and absorbable nutrients. **Therefore, gut dysbiosis, a bacterial imbalance state, is related with the pathogenesis of various host diseases including autoimmune diseases. In the current review, we highlight the importance of gut microbiota in the normal health and autoimmune diseases. We also discuss regulation of gut dysbiosis and future direction for potential clinical applications, including treatment and diagnostics of autoimmune diseases.**"

Veröffentlichung 5:

Connecting the immune system, systemic chronic inflammation and the gut microbiome: The role of sex - PubMed (nih.gov)

In: Journal of Autoimmunity. 2018 Aug;92:12-34.
doi: 10.1016/j.jaut.2018.05.008. Epub 2018 Jun 1.

„Abstract

Unresolved low grade systemic inflammation represents the underlying pathological mechanism driving immune and metabolic pathways involved in autoimmune diseases (AID). Mechanistic studies in animal models of AID and observational studies in patients have found alterations in gut microbiota communities and their metabolites, suggesting a microbial contribution to the onset or progression of AID. The gut microbiota and its metabolites have been shown to influence immune functions and immune homeostasis both within the gut and systematically. Microbial derived-short chain fatty acid (SCFA) and bio-transformed bile acid (BA) have been shown to influence the immune system acting as ligands specific cell signaling receptors like GPRCs, TGR5 and FXR, or via epigenetic processes. **Similarly, intestinal permeability (leaky gut) and bacterial translocation are important contributors to chronic systemic inflammation and, without repair of the intestinal barrier, might represent a continuous inflammatory stimulus capable of triggering autoimmune processes.** Recent studies indicate gender-specific differences in immunity, with the gut microbiota shaping and being concomitantly shaped by the hormonal milieu governing differences between the sexes. A bi-directional cross-talk between microbiota and the endocrine system is emerging with bacteria being able to produce hormones (e.g. serotonin, dopamine and somatostatine), respond to host hormones (e.g. estrogens) and regulate host hormones' homeostasis (e.g by inhibiting gene prolactin transcription or converting glucocorticoids to androgens). We review herein how gut microbiota and its metabolites regulate immune function, intestinal permeability and possibly AID pathological

processes. Further, we describe the dysbiosis within the gut microbiota observed in different AID and speculate how restoring gut microbiota composition and its regulatory metabolites by dietary intervention including prebiotics and probiotics could help in preventing or ameliorating AID. Finally, we suggest that, given consistent observations of microbiota dysbiosis associated with AID and the ability of SCFA and BA to regulate intestinal permeability and inflammation, further mechanistic studies, examining how dietary microbiota modulation can protect against AID, hold considerable potential to tackle increased incidence of AID at the population level."

Veröffentlichung 6:

Relationships Between Vitamin D, Gut Microbiome, and Systemic Autoimmunity - PubMed (nih.gov)

In: Frontiers in Immunology. 2020 Jan 21;10:3141.
doi: 10.3389/fimmu.2019.03141. eCollection 2019.

„Abstract

There is increasing recognition of the role the microbiome plays in states of health and disease. Microbiome studies in systemic autoimmune diseases demonstrate unique microbial patterns in Inflammatory Bowel Disease, Rheumatoid Arthritis, and Systemic Lupus Erythematosus to a lesser extent, whereas there is no single bug or pattern that characterizes Multiple Sclerosis. **Autoimmune diseases tend to share a predisposition for vitamin D deficiency, which alters the microbiome and integrity of the gut epithelial barrier.** In this review, we summarize the influence of intestinal bacteria on the immune system, explore the microbial patterns that have emerged from studies on autoimmune diseases, and discuss how vitamin D deficiency may contribute to autoimmunity via its **effects on the intestinal barrier function**, microbiome composition, and/or direct effects on immune responses."

Veröffentlichung 7:

Leaky gut and autoimmune diseases - PubMed (nih.gov)

In: Clinical Review of Allergy and Immunology. 2012 Feb;42(1):71-8.
doi: 10.1007/s12016-011-8291-x.

„Abstract

Autoimmune diseases are characterized by tissue damage and loss of function due to an immune response that is directed against specific organs. **This review is focused on the role of impaired intestinal barrier function on autoimmune pathogenesis**. **Together with the gut-associated lymphoid tissue and the neuroendocrine network, the intestinal epithelial barrier, with its intercellular tight junctions, controls the equilibrium between tolerance and immunity to non-self antigens. Zonulin is the only physiologic modulator of intercellular tight junctions described so far that is involved in trafficking of macromolecules and, therefore, in tolerance/immune response balance. When the zonulin pathway is deregulated in genetically susceptible individuals, autoimmune disorders can occur. This new paradigm subverts traditional theories underlying the development of these diseases and suggests that these processes can be arrested if the interplay between genes and environmental triggers is prevented by re-establishing the zonulin-dependent intestinal barrier function. Both animal models and recent clinical evidence support this new**

paradigm and provide the rationale for innovative approaches to prevent and treat autoimmune diseases.“

Veröffentlichung 8:

All disease begins in the (leaky) gut: role of zonulin-mediated gut permeability in the pathogenesis of some chronic inflammatory diseases - PubMed (nih.gov)

In: Faculty oft he 1000Research. 2020 Jan 31;9:F1000 Faculty Rev-69. doi: 10.12688/f1000research.20510.1. eCollection 2020.

„Abstract

Improved hygiene leading to reduced exposure to microorganisms has been implicated as one possible cause for the recent "epidemic" of chronic inflammatory diseases (CIDs) in industrialized countries. That is the essence of the hygiene hypothesis that argues that rising incidence of CIDs may be, at least in part, the result of lifestyle and environmental changes that have made us too "clean" for our own good, so causing changes in our microbiota. **Apart from genetic makeup and exposure to environmental triggers, inappropriate increase in intestinal permeability (which may be influenced by the composition of the gut microbiota), a "hyper-belligerent" immune system responsible for the tolerance-immune response balance, and the composition of gut microbiome and its epigenetic influence on the host genomic expression have been identified as three additional elements in causing CIDs. During the past decade, a growing number of publications have focused on human genetics, the gut microbiome, and proteomics, suggesting that loss of mucosal barrier function, particularly in the gastrointestinal tract, may substantially affect antigen trafficking, ultimately influencing the close bidirectional interaction between gut microbiome and our immune system.** This cross-talk is highly influential in shaping the host gut immune system function and ultimately shifting genetic predisposition to clinical outcome. This observation led to a re-visitation of the possible causes of CIDs epidemics, suggesting a key pathogenic role of gut permeability. Pre-clinical and clinical studies have shown that the zonulin family, a group of proteins modulating gut permeability, is implicated in a variety of CIDs, including autoimmune, infective, metabolic, and tumoral diseases. These data offer novel therapeutic targets for a variety of CIDs in which the zonulin pathway is implicated in their pathogenesis.“

Veröffentlichung 9:

Exercise-induced stress behavior, gut-microbiota-brain axis and diet: a systematic review for athletes - PubMed (nih.gov)

In: Journal of the International Society of Sports Nutrition. 2016 Nov 24;13:43. doi: 10.1186/s12970-016-0155-6. eCollection 2016.

„Abstract

Fatigue, mood disturbances, under performance and gastrointestinal distress are common among athletes during training and competition. The psychosocial and physical demands during intense exercise can initiate a stress response activating the sympathetic-adrenomedullary and hypothalamus-pituitary-adrenal (HPA) axes, resulting in the release of stress and catabolic hormones, inflammatory cytokines and microbial molecules. The gut is home to trillions of microorganisms that

have fundamental roles in many aspects of human biology, including metabolism, endocrine, neuronal and immune function. **The gut microbiome and its influence on host behavior, intestinal barrier and immune function are believed to be a critical aspect of the brain-gut axis.** Recent evidence in murine models shows that there is a high correlation between physical and emotional stress during exercise and changes in gastrointestinal microbiota composition. For instance, induced exercise-stress decreased cecal levels of Turicibacter spp and increased Ruminococcus gnavus, which have well defined roles in intestinal mucus degradation and immune function. Diet is known to dramatically modulate the composition of the gut microbiota. Due to the considerable complexity of stress responses in elite athletes (from leaky gut to increased catabolism and depression), defining standard diet regimes is difficult. However, some preliminary experimental data obtained from studies using probiotics and prebiotics studies show some interesting results, indicating that the microbiota acts like an endocrine organ (e.g. secreting serotonin, dopamine or other neurotransmitters) and may control the HPA axis in athletes. What is troubling is that dietary recommendations for elite athletes are primarily based on a low consumption of plant polysaccharides, which is associated with reduced microbiota diversity and functionality (e.g. less synthesis of byproducts such as short chain fatty acids and neurotransmitters). As more elite athletes suffer from psychological and gastrointestinal conditions that can be linked to the gut, targeting the microbiota therapeutically may need to be incorporated in athletes' diets that take into consideration dietary fiber as well as microbial taxa not currently present in athlete's gut.“

Veröffentlichung 10:

Alzheimer's disease and gut microbiota - PubMed (nih.gov)

In: Science China Life Sciences. 2016 Oct;59(10):1006-1023.
doi: 10.1007/s11427-016-5083-9. Epub 2016 Aug 26.

„Abstract

Alzheimer's disease (AD) is a most common neurodegenerative disorder, which associates with impaired cognition. Gut microbiota can modulate host brain function and behavior via microbiota-gut-brain axis, including cognitive behavior. Germ-free animals, antibiotics, probiotics intervention and diet can induce alterations of gut microbiota and gut physiology and also host cognitive behavior, increasing or decreasing risks of AD. **The increased permeability of intestine and blood-brain barrier induced by gut microbiota disturbance will increase the incidence of neurodegeneration disorders.** Gut microbial metabolites and their effects on host neurochemical changes may increase or decrease the risk of AD. Pathogenic microbes infection will also increase the risk of AD, and meanwhile, the onset of AD support the "hygiene hypothesis". All the results suggest that AD may begin in the gut, and is closely related to the imbalance of gut microbiota. Modulation of gut microbiota through personalized diet or beneficial microbiota intervention will probably become a new treatment for AD.“

Veröffentlichung 11:

Leaky gut biomarkers in depression and suicidal behavior - PubMed (nih.gov)

In: Acta Psychiatrica Scandinavica. 2019 Feb;139(2):185-193.
doi: 10.1111/acps.12978. Epub 2018 Nov 1.

„Abstract

Objective: Inflammation is associated with major depressive disorder (MDD) and suicidal behavior. According to the 'leaky gut hypothesis', increased intestinal permeability may contribute to this relationship via bacterial translocation across enterocytes. We measured plasma levels of gut permeability markers, in patients with a recent suicide attempt (rSA), MDD subjects with no history of a suicide attempt (nsMDD), and healthy controls (HC), and related these markers to symptom severity and inflammation.

Method: We enrolled rSA (n = 54), nsMDD (n = 13), and HC (n = 17). Zonulin, intestinal fatty acid binding protein (I-FABP), soluble CD14, and interleukin-6 (IL-6) were quantified in plasma. Montgomery-Åsberg Depression Rating Scale (MADRS) and Suicide Assessment Scale (SUAS) were used for symptom assessments.

Results: The rSA group displayed higher I-FABP and lower zonulin levels compared with both the nsMDD and the HC groups (all $P < 0.001$). IL-6 correlated positively with I-FABP ($r = 0.24$, $P < 0.05$) and negatively with zonulin ($r = -0.25$, $P < 0.05$). In all subjects, I-FABP levels correlated positively with MADRS ($r = 0.25$, $P < 0.05$) and SUAS scores ($r = 0.38$, $P < 0.001$), and the latter correlation was significant also in the nsMDD group ($r = 0.60$, $P < 0.05$).

Conclusion: The 'leaky gut hypothesis' may improve our understanding of the link between inflammation and suicidal behavior. These findings should be considered preliminary until replicated in larger cohorts.“

Veröffentlichung 12:

Intestinal Permeability in Inflammatory Bowel Disease: Pathogenesis, Clinical Evaluation, and Therapy of Leaky Gut - PubMed (nih.gov)

In: Mediators of Inflammation. 2015;2015:628157.
doi: 10.1155/2015/628157. Epub 2015 Oct 25.

„Abstract

The pathogenesis of inflammatory bowel disease (IBD) is multifactorial with data suggesting the role of a disturbed interaction between the gut and the intestinal microbiota. **A defective mucosal barrier may result in increased intestinal permeability which promotes the exposition to luminal content and triggers an immunological response that promotes intestinal inflammation.** IBD patients display several defects in the many specialized components of mucosal barrier, from the mucus layer composition to the adhesion molecules that regulate paracellular permeability. These alterations may represent a primary dysfunction in Crohn's disease, but they may also perpetuate chronic mucosal inflammation in ulcerative colitis. In clinical practice, several studies have documented that changes in intestinal permeability can predict IBD course. Functional tests, such as the sugar

absorption tests or the novel imaging technique using confocal laser endomicroscopy, allow an in vivo assessment of gut barrier integrity. Antitumor necrosis factor-α (TNF-α) therapy reduces mucosal inflammation and restores intestinal permeability in IBD patients. Butyrate, zinc, and some probiotics also ameliorate mucosal barrier dysfunction but their use is still limited and further studies are needed before considering permeability manipulation as a therapeutic target in IBD."

Veröffentlichung 13:

Metformin Reduces Aging-Related Leaky Gut and Improves Cognitive Function by Beneficially Modulating Gut Microbiome/Goblet Cell/Mucin Axis - PubMed (nih.gov)

In: Journal of Gerontology - Series A Biology Scienes and Medical Scienes. 2020 Jun 18;75(7):e9-e21. doi: 10.1093/gerona/glaa056.

„Abstract

Aging-related illnesses are increasing and effective strategies to prevent and/or treat them are lacking. This is because of a poor understanding of therapeutic targets. Low-grade inflammation is often higher in older adults and remains a key risk factor of aging-related morbidities and mortalities. **Emerging evidence indicates that abnormal (dysbiotic) gut microbiome and dysfunctional gut permeability (leaky gut) are linked with increased inflammation in older adults.** However, currently available drugs do not treat aging-related microbiome dysbiosis and leaky gut, and little is known about the cellular and molecular processes that can be targeted to reduce leaky gut in older adults. Here, we demonstrated that metformin, a safe Food and Drug Administration-approved antidiabetic drug, decreased leaky gut and inflammation in high-fat diet-fed older obese mice, by beneficially modulating the gut microbiota. In addition, metformin increased goblet cell mass and mucin production in the obese older gut, thereby decreasing leaky gut and inflammation. Mechanistically, metformin increased the goblet cell differentiation markers by suppressing Wnt signaling. Our results suggest that metformin can be used as a regimen to prevent and treat aging-related leaky gut and inflammation, especially in obese individuals and people with western-style high-fat dietary lifestyle, by beneficially modulating gut microbiome/goblet cell/mucin biology."

Veröffentlichung 14:

Gut permeability and mucosal inflammation: bad, good or context dependent - PubMed (nih.gov)

In: Mucosal Immunology. 2017 Mar;10(2):307-317.
doi: 10.1038/mi.2016.128. Epub 2017 Jan 25.

„Abstract

Inflammatory bowel disease (IBD) is a multifactorial disease. **A breach in the mucosal barrier, otherwise known as "leaky gut," is alleged to promote mucosal inflammation by intensifying immune activation**. However, interaction between the luminal antigen and mucosal immune system is necessary to maintain mucosal homeostasis. Furthermore, manipulations leading to deregulated gut permeability have resulted in susceptibility in mice to colitis as well as to creating adaptive immunity. These findings implicate a complex but dynamic association between mucosal permeability and immune homeostasis; however, they also emphasize that compromised gut permeability alone may not be sufficient to induce colitis. Emerging evidence further supports the

role(s) of proteins associated with the mucosal barrier in epithelial injury and repair: manipulations of associated proteins also modified epithelial differentiation, proliferation, and apoptosis. **Taken together, the role of gut permeability and proteins associated in regulating mucosal inflammatory diseases appears to be more complex than previously thought**. Herein, we review outcomes from recent mouse models where gut permeability was altered by direct and indirect effects of manipulating mucosal barrier-associated proteins, to highlight the significance of mucosal permeability and the non-barrier-related roles of these proteins in regulating chronic mucosal inflammatory conditions."

Veröffentlichung 15:

A human-origin probiotic cocktail ameliorates aging-related leaky gut and inflammation via modulating the microbiota/taurine/tight junction axis - PubMed (nih.gov)

In: JCI Insight. 2020 May 7;5(9):e132055.
doi: 10.1172/jci.insight.132055.

„Abstract

Inflammation is a major risk factor of morbidity and mortality in older adults. Although its precise etiology is unknown, low-grade inflammation in older adults is commonly associated **with increased intestinal epithelial permeability (leaky gut)** and abnormal (dysbiotic) gut microbiota. The increasing older population and lack of treatments to reduce aging-related microbiota dysbiosis, leaky gut, and inflammation culminates in a rise in aging-related comorbidities, constituting a significant public health concern. Here, we demonstrate that a human-origin probiotic cocktail containing 5 Lactobacillus and 5 Enterococcus strains isolated from healthy infant gut prevented high-fat diet-induced (HFD-induced) microbiota dysbiosis, leaky gut, inflammation, metabolic dysfunctions, and physical function decline in older mice. Probiotic-modulated gut microbiota primarily reduced leaky gut by increasing tight junctions, which in turn reduced inflammation. Mechanistically, probiotics modulated microbiota in a way to increase bile salt hydrolase activity, which in turn increased taurine abundance in the gut that stimulated tight junctions and suppressed gut leakiness. Furthermore, in Caenorhabditis elegans, taurine increased life span, reduced adiposity and leaky gut, and enhanced physical function. **The results suggest that such probiotic therapies could prevent or treat aging-related leaky gut and inflammation in the elderly.**"

Veröffentlichung 16:

Leaky Gut and Gut-Liver Axis in Liver Cirrhosis: Clinical Studies Update - PubMed (nih.gov)

In: Gut Liver. 2020 Oct 21.
doi: 10.5009/gnl20032. Online ahead of print.

„Abstract

Portal blood flows into the liver containing the gut microbiome and its products such as endotoxin and bacterial DNA. The cirrhotic liver acts and detoxifies as the initial site of microbial products. **In so-called "leaky gut," the increased intestinal permeability for bacteria and their products constitutes an important pathogenetic factor for major complications in patients with liver cirrhosis.** Prolonged gastric and small intestinal transit may induce intestinal bacterial overgrowth, a

condition in which colonic bacteria translocate into the small gut. Cirrhotic patients further show gut dysbiosis characterized by an overgrowth of potentially pathogenic bacteria and a decrease in autochthonous nonpathogenic bacteria. Pathological bacterial translocation (BT) is a contributing factor in the development of various severe complications. Bile acids (BAs) undergo extensive enterohepatic circulation and play important roles in the gut-liver axis. BT-induced inflammation prevents synthesis of BAs in the liver through inhibition of BA-synthesizing enzyme CYP7A1. A lower abundance of 7α-dehydroxylating gut bacteria leads to decreased conversion of primary to secondary BAs. Decreases in total and secondary BAs may play an important role in the gut dysbiosis characterized by a proinflammatory and toxic gut microbiome inducing BT and endotoxemia, as addressed in my previous reviews. Selective intestinal decontamination by the use of various antimicrobial drugs for management of complications has a long history. Lactobacillus GG decreasing endotoxemia is reported to improve the microbiome with beneficial changes in amino acid, vitamin and secondary BA metabolism. Current approaches for hepatic encephalopathy are the use of nonabsorbable antibiotics and disaccharides. Probiotics may become an additional therapeutic option for advanced liver cirrhosis.“

Veröffentlichung 17:

Leaky gut, dysbiosis, and enteric glia activation: the trilogy behind the intestinal origin of Parkinson's disease - PubMed (nih.gov)

In: Neural Regen Research. 2020 Jun;15(6):1037-1038.
doi: 10.4103/1673-5374.270308.

„No abstract available“

Veröffentlichung 18:

A Viewpoint on the Leaky Gut Syndrome to Treat Allergic Asthma: A Novel Opinion - PubMed (nih.gov)

In: Evidence-based Complementary and Alternative Medicine. 2017 Jul;22(3):378-380.
doi: 10.1177/2156587216682169. Epub 2016 Dec 22.

„Abstract

Asthma is a common respiratory disease characterized by airway inflammation, airway hyperreactivity, and reversible airflow obstruction. Despite current treatments, the prevalence of asthma has increased markedly over decades. **According to the theories proposed to explain the pathophysiology of autoimmune diseases in integrative medicine, leaky gut syndrome is a phenomenon of increased intestinal permeability due to the disruption of tight junctions and is thought to be related to many chronic diseases, such as food intolerance, inflammatory bowel disease, rheumatoid arthritis, asthma, and other autoimmune disease.** One of the classical approaches used by integrative physicians to treat l**eaky gut syndrome is to repair intestinal permeability to prevent allergic cascade**. Due to several mechanisms that have been mentioned in the protective effects of plant gums and plantain family seeds on the intestinal epithelium, we can propose an effective management for leaky gut syndrome to treat asthma.“

Veröffentlichung 19:

Leaky Gut - PubMed (nih.gov)

In: Nursing Standard. 2011 Aug 24;25(51):30.
doi: 10.7748/ns2011.08.25.51.30.p6185.

„Abstract

Leaky gut syndrome is an increase in permeability of the intestinal mucosa to luminal macromolecules, antigens and toxins."

Veröffentlichung 20:

Lubiprostone improves intestinal permeability in humans, a novel therapy for the leaky gut: A prospective randomized pilot study in healthy volunteers - PubMed (nih.gov)

In: PLoS One. 2017 Apr 14;12(4):e0175626.
doi: 10.1371/journal.pone.0175626. eCollection 2017.

„Abstract

Background and aims: The barrier function of the small intestinal mucosa prevents the introduction of undesired pathogens into the body. **Breakdown of this barrier function increases intestinal permeability. This has been proposed to induce not only gastrointestinal diseases, including inflammatory bowel disease and irritable bowel syndrome, but also various other diseases, including allergies, diabetes mellitus, liver diseases, and collagen diseases, which are associated with this so called "leaky gut syndrome."** As such, a method to prevent leaky gut syndrome would have substantial clinical value. However, no drugs have been demonstrated to improve disturbed intestinal permeability in humans to date. Therefore, we investigated whether a drug used to treat chronic constipation, lubiprostone, was effective for this purpose.

Methods: Healthy male volunteers were treated with lubiprostone (24 μg/day) for 28 days. Intestinal permeability was evaluated by measuring the lactulose-mannitol ratio (LMR) after administration of diclofenac and compared with an untreated group. The examination was conducted three times in total, i.e., at baseline before diclofenac administration and after 14 and 28 days of lubiprostone treatment. Blood endotoxin activity was also evaluated at the same time points.

Results: The final analysis was conducted on 28 subjects (14 in the lubiprostone group and 14 in the untreated group). The LMR after 28 days of treatment was significantly lower in the lubiprostone group than that in the untreated group (0.017 vs. 0.028, respectively; 95% confidence interval, -0.022--0.0001; p = 0.049). Blood endotoxin activity exhibited almost no change over time in the lubiprostone and untreated groups and displayed no significant differences at any time point of examination.

Conclusions: **This study is the first to report an improvement in leaky gut using an available drug in humans. The result suggests that lubiprostone may prevent and ameliorate "leaky gut syndrome"**. However, a pivotal trial is needed to confirm our finding."

Veröffentlichung 21:

Leaky Gut and Autoimmunity: An Intricate Balance in Individuals Health and the Diseased State - PubMed (nih.gov)

In: International Journal of Molecular Scienes. 2020 Dez 21;21(24):9770.
doi: 10.3390/ijms21249770.

„Abstract

Damage to the tissue and the ruining of functions characterize autoimmune syndromes. This review centers around leaky gut syndromes and how they stimulate autoimmune pathogenesis. Lymphoid tissue commonly associated with the gut, together with the neuroendocrine network, collaborates with the intestinal epithelial wall, with its paracellular tight junctions, to maintain the balance, tolerance, and resistance to foreign/neo-antigens. **The physiological regulator of paracellular tight junctions plays a vital role in transferring macromolecules across the intestinal barrier and thereby maintains immune response equilibrium. A new paradigm has explained the intricacies of disease development and proposed that the processes can be prevented if the interaction between the genetic factor and environmental causes is barred by re-instituting the intestinal wall function**. The latest clinical evidence and animal models reinforce this current thought and offer the basis for innovative methodologies to thwart and treat autoimmune syndromes."

Veröffentlichung 22:

Increased expression of activation antigens on CD8+ T lymphocytes in Myalgic Encephalomyelitis/chronic fatigue syndrome: inverse associations with lowered CD19+ expression and CD4+/CD8+ ratio, but no associations with (auto)immune, leaky gut, oxidative and nitrosative stress biomarkers - PubMed (nih.gov)

In: Neuroendocrinology Letters. 2015;36(5):439-46.

„Abstract

Background: There is now evidence that specific subgroups of patients with Myalgic Encephalomyelitis / chronic fatigue syndrome (ME/CFS) suffer from a neuro-psychiatric-immune disorder. This study was carried out to delineate the expression of the activation markers CD38 and human leukocyte antigen (HLA) DR on CD4+ and CD8+ peripheral blood lymphocytes in ME/CFS.

Methods: Proportions and absolute numbers of peripheral lymphocytes expressing CD3+, CD19+, CD4+, CD8+, CD38+ and HLA-DR+ were measured in ME/CFS (n=139), chronic fatigue (CF, n=65) and normal controls (n=40).

Results: The proportions of CD3+, CD8+, CD8+CD38+ and CD8+HLA-DR+ were significantly higher in ME/CFS patients than controls, while CD38+, CD8+CD38+, CD8+HLA-DR+ and CD38+HLA-DR+ were significantly higher in ME/CFS than CF. The percentage of CD19+ cells and the CD4+/CD8+ ratio were significantly lower in ME/CFS and CF than in controls. There were highly significant inverse correlations between the increased expression of CD38+, especially that of CD8+CD38+, and the lowered CD4+/CD8+ ratio and CD19+ expression. There were no significant associations between the flow cytometric results and severity or duration of illness and peripheral blood biomarkers of oxidative and nitrosative stress (O&NS, i.e. IgM responses to O&N modified epitopes), leaky gut (IgM

or IgA responses to LPS of gut commensal bacteria), cytokines (interleukin-1, tumor necrosis factor-α), neopterin, lysozyme and autoimmune responses to serotonin.

Conclusions: The results support that a) increased CD38 and HLA-DR expression on CD8+ T cells are biomarkers of ME/CFS; b) increased CD38 antigen expression may contribute to suppression of the CD4+/CD8+ ratio and CD19+ expression; c) there are different immune subgroups of ME/CFS patients, e.g. increased CD8+ activation marker expression versus inflammation or O&NS processes; and d) viral infections or reactivation may play a role in a some ME/CFS patients."

<u>Anmerkungen:</u> Diese Studie soll die Notwendigkeit zur laborchemischen Untersuchung von immunologischen Parametern bei CFS demonstrieren, welche beim Patienten auch auffälligen waren (IL17 positiv = Nachweis eines autoimmunen Prozesses).

Veröffentlichung 23:

Chronic fatigue syndrome: oxidative stress and dietary modifications - PubMed (nih.gov)

In: Alternative Medicine Review, 2001 Oct;6(5):450-9.

„Abstract

Chronic fatigue syndrome (CFS) is an illness characterized by persistent and relapsing fatigue, often accompanied by numerous symptoms involving various body systems. The etiology of CFS remains unclear; however, a number of recent studies have shown oxidative stress may be involved in its pathogenesis. **The role of oxidative stress in CFS is an important area for current and future research as it suggests the use of antioxidants in the management of CFS. Specifically, the dietary supplements glutathione, N-acetylcysteine, alpha-lipoic acid, oligomeric proanthocyanidins, Ginkgo biloba, and Vaccinium myrtillus (bilberry) may be beneficial. In addition, research on food intolerance is discussed, since food intolerance may be involved in CFS symptom presentation and in oxidation via cytokine induction.** Finally, recent evidence suggests celiac disease can present with neurological symptoms in the absence of gastrointestinal symptoms; therefore, celiac disease should be included in the differential diagnosis of CFS."

Veröffentlichungen 24.

Reduced diversity and altered composition of the gut microbiome in individuals with myalgic encephalomyelitis/chronic fatigue syndrome - PubMed (nih.gov)

In: Microbiome. 2016 Jun 23;4(1):30.
doi: 10.1186/s40168-016-0171-4.

„Abstract

Background: Gastrointestinal disturbances are among symptoms commonly reported by individuals diagnosed with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). However, whether ME/CFS is associated with an altered microbiome has remained uncertain. Here, we profiled gut microbial diversity by sequencing 16S ribosomal ribonucleic acid (rRNA) genes from stool as well as inflammatory markers from serum for cases (n = 48) and controls (n = 39). We also examined a set of inflammatory markers in blood: C-reactive protein (CRP), intestinal fatty acid-binding protein (I-FABP), lipopolysaccharide (LPS), LPS-binding protein (LBP), and soluble CD14 (sCD14).

Results: We observed elevated levels of some blood markers for microbial translocation in ME/CFS patients; levels of LPS, LBP, and sCD14 were elevated in ME/CFS subjects. Levels of LBP correlated with LPS and sCD14 and LPS levels correlated with sCD14. Through deep sequencing of bacterial rRNA markers, we identified differences between the gut microbiomes of healthy individuals and patients with ME/CFS. We observed that bacterial diversity was decreased in the ME/CFS specimens compared to controls, in particular, a reduction in the relative abundance and diversity of members belonging to the Firmicutes phylum. In the patient cohort, we find less diversity as well as increases in specific species often reported to be pro-inflammatory species and reduction in species frequently described as anti-inflammatory. Using a machine learning approach trained on the data obtained from 16S rRNA and inflammatory markers, individuals were classified correctly as ME/CFS with a cross-validation accuracy of 82.93 %.

Conclusions: **Our results indicate dysbiosis of the gut microbiota in this disease and further suggest an increased incidence of microbial translocation, which may play a role in inflammatory symptoms in ME/CFS.**"

Veröffentlichung 25:

Gut dysbiosis, leaky gut, and intestinal epithelial proliferation in neurological disorders: towards the development of a new therapeutic using amino acids, prebiotics, probiotics, and postbiotics - PubMed (nih.gov)

In: Nature Reviews in Neuroscienes. 28.01.2019;30(2):179-201.
doi: 10.1515/revneuro-2018-0024.

„Abstract

Here we offer a review of the evidence for a hypothesis that a combination of ingestible probiotics, prebiotics, postbiotics, and amino acids will help ameliorate dysbiosis and degeneration of the gut, and **therefore promote restoration of nervous system function in a number of neurological indications**."

Veröffentlichung 26:

The Possible Role of the Microbiota-Gut-Brain-Axis in Autism Spectrum Disorder - PubMed (nih.gov)

In: Internation Journal of Molecular Science. 2019 Apr 29;20(9):2115.
doi: 10.3390/ijms20092115.

„Abstract

New research points to a possible link between autism spectrum disorder (ASD) and the gut microbiota as many autistic children have co-occurring gastrointestinal problems. This review focuses on specific alterations of gut microbiota mostly observed in autistic patients. **Particularly, the mechanisms through which such alterations may trigger the production of the bacterial metabolites, or leaky gut in autistic people are described**. Various altered metabolite levels were observed in the blood and urine of autistic children, many of which were of bacterial origin such as short chain fatty acids (SCFAs), indoles and lipopolysaccharides (LPS). A less integrative gut-blood-barrier is abundant in autistic individuals. This explains the leakage of bacterial metabolites into the patients, triggering new body responses or an altered metabolism. Some other co-occurring

symptoms such as mitochondrial dysfunction, oxidative stress in cells, altered tight junctions in the blood-brain barrier and structural changes in the cortex, hippocampus, amygdala and cerebellum were also detected. Moreover, this paper suggests that ASD is associated with an unbalanced gut microbiota (dysbiosis). Although the cause-effect relationship between ASD and gut microbiota is not yet well established, the consumption of specific probiotics may represent a side-effect free tool to re-establish gut homeostasis and promote gut health. The diagnostic and therapeutic value of bacterial-derived compounds as new possible biomarkers, associated with perturbation in the phenylalanine metabolism, as well as potential therapeutic strategies will be discussed."

Veröffentlichungen 27:

The Gut-Brain Axis, Including the Microbiome, Leaky Gut and Bacterial Translocation: Mechanisms and Pathophysiological Role in Alzheimer's Disease - PubMed (nih.gov)

In: Current Pharmaceutical Design. 2016;22(40):6152-6166.
doi: 10.2174/1381612822666160907093807.

„Abstract

Alzheimer's disease (AD), the most common form of dementia, is a progressive disorder manifested by gradual memory loss and subsequent impairment in mental and behavioral functions. Though the primary risk factor for AD is advancing age, other factors such as diabetes mellitus, hyperlipidemia, obesity, vascular factors and depression play a role in its pathogenesis. The human gastrointestinal tract has a diverse commensal microbial population, which has bidirectional interactions with the human host that are symbiotic in health, and in addition to nutrition, digestion, plays major roles in inflammation and immunity. The most prevalent hypothesis for AD is the amyloid hypothesis, which states that changes in the proteolytic processing of the amyloid precursor protein leads to the accumulation of the amyloid beta (Aβ) peptide. Aβ then triggers an immune response that drives neuroinflammation and neurodegeneration in AD. **The specific role of gut microbiota in modulating neuro-immune functions well beyond the gastrointestinal tract may constitute an important influence on the process of neurodegeneration. We first review the main mechanisms involved in AD physiopathology. Then, we review the alterations in gut microbiota and gut-brain axis that might be relevant to mediate or otherwise affect AD pathogenesis, especially those associated with aging. We finally summarize possible mechanisms that could mediate the involvement of gut-brain axis in AD physiopathology, and propose an integrative model.**"