sciendo

PROCEEDINGS OF THE LATVIAN ACADEMY OF SCIENCES. Section B,
Vol. 78 (2024), No. 4 (751), pp. 244–248.

DOI: 10.2478/prolas-2024-0034

Review

EXPLORING INTESTINAL PERMEABILITY: CONCEPT, DIAGNOSIS, CONNECTION TO BOWEL DISEASE, AND IRON DEFICIENCY

Olesja Basina[1,2,3,#], Aleksejs Derovs[1,2,3,4], Jeļena Derova[2,5], and Sandra Lejniece[1,2]

[1] Rīga East University Hospital, 2 Hipokrāta Str., Rīga, LV-1038, LATVIA

[2] Department of Internal Diseases, Rīga Stradiņš University, 16 Dzirciema Str., Rīga, LV-1007, LATVIA

[3] JSC Veselības centru apvienība, 16 Saharova Str., Rīga, LV-1021, LATVIA

[4] Department of Infectology, Rīga Stradiņš University, 16 Dzirciema Str., Rīga, LV-1007, LATVIA

[5] JSC Latvian Maritime Medicine Centre, 23 Patversmes Str., Rīga, LV-1005, LATVIA

[#] Corresponding author, drbasinao@gmail.com

Contributed by Sandra Lejniece

Over the recent years, intestinal permeability has become a major feature of gut health. The objective of this paper is to present a literature-based overview of the current understanding on intestinal permeability. The concept of intestinal permeability started its development from the discovery of tight junctions — protein complexes that are separated between the epithelial cells. Histopathology is the main option of microscopic diagnosis, which allows to determine changes that occur in the tight junction, inflammation, and damaged epithelial cells. Additionally, intestinal fatty acid-binding protein I-FABP and zonulin are suggested as biomarkers of epithelial barrier abruption. As for visual detection, literature proposes capsule endoscopy and confocal laser endomicroscopy. Using the latter it is possible to produce images of small intestinal morphology and visualise the small intestinal luminal elements, cells, villi as well as crypts. However, advancements in digital capsule endoscopy are more applicable and aid in research of intestinal permeability and enteropathy, also giving promising results in treatment. Although damage to intestinal permeability can be classified as a certain enteropathy and then the association of some enteropathies with iron deficiency already has been established, direct association of iron deficiency and intestinal permeability is yet to be explored.

Keywords: *intestine, endoscopy, enteropathy, bowel disease, iron deficiency anaemia.*

INTRODUCTION

Over recent years intestinal permeability has become a major feature of gut health. It determines the transfer of substances from the intestinal lumen to the bloodstream. The objective of this paper is to present an overview of the current state of intestinal permeability diagnosis, its connection to gastrointestinal disorders, and describe diagnostic methods and potential association of intestinal permeability with enteropathy and iron deficiency anaemia (IDA). This review examines relevant studies, including ones by Binienda *et al.* (2020), to explore the importance of intestinal permeability evaluation in clinical practice and to identify the gaps and future directions in this field.

CONCEPT OF INTESTINAL PERMEABILITY

Intestinal permeability refers to the ability of the intestinal barrier to transport some nutrients and digestion products as a normal function, while blocking the transmigration of bacteria and toxins that might result in inflammation. Maintain-

ing the intestinal barrier is one of the main factors to achieve well-being and gut health (Zhuge *et al*. 2022). The concept of intestinal permeability started its development from the discovery of tight junctions, which are protein complexes that are separated between epithelial cells. They form a steady barrier layer of cells, which regulates the passage of molecules through the paracellular pathway (Schoultz and Keita, 2020). These tracks have a significant influence on the health of the intestinal barrier (Ahnstedt *et al*., 2020). Another important part is epithelial lining of the intestine, the cell lining that constantly protects against external environmental invasion (Feng *et al*., 2020). The function of these cells is to engage in immune response and prevent infections and pathogens from ingested vegetables and other dietary items (Seethaler *et al*., 2021). The third part of the barrier is the mucus that is produced by irregularly shaped goblet cells that line the intestines and cover the epithelial border, also assisting in smooth movement of ingested food through the intestinal system (Iordache *et al*., 2022). Connected to the gut mucosal lymphoid and the lamina propria of the intestinal epithelial layer harbour various lymphocytes with short proximity to act quickly in case of pathogen infections, but it also maintains immune homeostasis (Al-Ayadhi *et al*., 2021). Microbial imbalance in the intestines involves different parts working in harmony to perfectly maintain mucosal barrier integrity, which is responsible for the effective recuperation of nutrients and exclusion of microbes and systemic inflammation (Binienda *et al*., 2020).

ASSESSING THE INTESTINAL PERMEABILITY

There is no golden standard for diagnosis of intestinal permeability. Typically, histopathology is the main option for microscopic examination of tissue samples, which allows to determine the shape of the microvillus, the length of the crypt between two adjacent epithelial cells, and other features (Di Vincenzo *et al*., 2024). Also, histological examination can indicate changes that occur in the tight junction, inflammation, and damaged epithelial cells, which are the main changes compromising the integrity of the gastrointestinal tract (Huang and Tanpowpong, 2023).

Some authors suggest that incorporation of clinical symptoms should be used to form an opinion on changes in gut permeability (Stadlbauer *et al*. 2020). Gastrointestinal symptoms such as diarrhea, abdominal pain, bloating, and faeces conditions are not really specific, but still remain an important part of the diagnosis (Sanchez-Alcoholado *et al*., 2020). Another diagnostic method is to incorporate system markers of inflammation like CRP, which is nonspecific, but still can be a marker of inflammation of the gut (Vanuytsel *et al*., 2021).

Several specific types of biomarker-based tests could be employed in order to assess intestinal permeability. These markers have been shown to be associated with integrity of gut epithelium (Hrncir *et al*., 2021). For example, intestinal fatty acid-binding protein I-FABP and zonulin are biomarkers of epithelial barrier abruption and structure of the tight junction, respectively (Cano-Ortiz *et al*. 2020; Martín-Mateos and Albillos, 2021).

Lastly, there is a holistic approach that employs histological, clinical, and laboratory techniques to ensure that both the diagnosis and interpretation of the intestinal permeability are accurate. Thus, in the future medical doctors will benefit from the creation of highly targeted and personalised medicines (Rodina and Derovs, 2022).

CONNECTION BETWEEN DIAGNOSES SIGNIFICANCE AND BOWEL DISEASES

The health of the intestinal wall is associated with disease conditions that affect its pathophysiology. The disruption of intestinal permeability has been linked with various gastrointestinal conditions, such as inflammatory bowel disease (IBD), celiac disease, irritable bowel disease, and others (Turpin *et al*., 2020). Experimental data prove that increases in intestinal barrier leakage result in the laceration of the gut opening and exposure to damaging particles, which, in turn, leads to undesirable inflammatory responses (Lucidi *et al*., 2021). For example, normal gastrointestinal barrier function is damaged by chronic inflammation and tissue injuries in the gut, signalising development of IBD (Gan *et al*., 2022). Similarly, celiac diseases or any other changes in epithelial permeability may lead to the integration of the immunogenic gluten peptides into the bloodstream that on the other hand can cause antigen-mediated reactions outside of the gastrointestinal tract (Ouyang *et al*., 2020). More importantly, high-fat or low fibre intake can aggravate intestinal permeability and stimulate diseases like Nonalcoholic Fatty Liver Disease (NAFLD), food intolerance, and autoimmune disorders (Isnard *et al*., 2021).

With an understanding of particular pathways of gut dysbiosis that lead to disorders of the digestive tract and intestinal permeability, a new therapeutic approach may be introduced, which targets the source of the gut damage directly (Ishida *et al*., 2022). In this respect, intestinal permeability may work as a key to understanding the interrelationship between various gastrointestinal conditions (Cayres *et al*., 2021).

EXPLORING INTESTINAL PERMEABILITY, ENDOSCOPIC DIAGNOSIS, AND ITS LINK TO ENTEROPATHY AND IRON DEFICIENCY ANAEMIA

The maintenance of intestinal permeability of the intestinal barrier is the main factor that ensures minimal leakage of substances across the intestine (Shen, 2020). The latest literature reviews suggest that best detection methods of intestine permeability include capsule endoscopy and confocal laser endomicroscopy (CLE), which have the possibility to produce images of small intestinal morphology and visualise small intestinal luminal elements, cells, villi as well as crypts (Varesi *et al*., 2022). The advancements in digital

capsule endoscopy confirm the idea that this method in research of intestinal permeability and enteropathy, and its application, is giving promising results in treatment (Fianchi *et al*., 2021; Vanuytsel *et al*., 2021).

Systemic analysis (Kim *et al*. 2022) has proven the great variety for CLE application in differentiation of many gastrointestinal disorders, by giving an accurate view of microscopic intestinal mucosa structures on a cellular level, for example by measuring vascular integrity in celiac disease, determining mucosal permeability in inflammatory bowel disease, and visualising inflammation in irritable bowel syndrome. This makes it possible to determine epithelial integrity, tight junction integrity, and inflammation changes that have occurred in any location of gastrointestinal tract (Stiegeler *et al*., 2021). The reconnection of endoscopic services at a molecular level in the last few years made it possible to unveil the capabilities of the gastrointestinal barrier model and ultimately improve the diagnosis and therapeutics of digestive system diseases. Varesi *et al*. (2022) presented solid data indicating the link between enteropathy and alteration of epithelial and endothelial cell organoid-based barrier integrity. The small intestine, with its double-layered structure that constitutes a very tight barrier, can preserve its functional integrity and consists of cells arranged in tight junctions, which are placed between the epithelial and the mucin layer and microvilli (König *et al*., 2022).

However, if the damage to intestinal permeability can be classified as a certain enteropathy, then the association of some enteropathies with iron deficiency has already has been established (Tracy *et al*. 2020). The direct association of iron deficiency and intestinal permeability is yet to be explored, as to date there have been no studies that have attempted to explore this link. The association of inflammation of the intestine firstly, which is then followed by intestinal haemorrhage, is the direct cause for iron deficiency anaemia (Malesza *et al*., 2022). However, the loss of nutrients and minerals in theory should already start at the time of intestinal permeability diagnosis.

Moreover, the existing diagnosis of intestinal permeability improvement, which can be demonstrated by the development of some of the new diagnostic methods, has some vital drawbacks, especially in the standardisation, validation, and application of clinical characteristics (Muntieswertz *et al*., 2021). Besides that, no common diagnostic approach is being used in the different sectors. As a result, the findings are contradictory from different diagnostic approaches, and therefore there is a need for a unifying diagnostic rule in terms of the assessment of emergency services at any given time (Zhan *et al*., 2023). In addition, clinicians will utilise a wide range of patient groups for continuous monitoring of biomarkers and various imaging modality approaches to develop robust, reliable, and reproducible methods. Technology innovation would be a good thing, and the next step would entail the applicability of the technology in the clinical context and be as cheap as possible for the well-being of patients (Pohl *et al*., 2022). It can be concluded that the method of assessment that incorporates all three aspects, namely histology, findings from clinical studies as well as laboratory findings, is the most effective approach. This would enable us to determine intestinal permeability (Schwabe and Greten, 2020).

CONCLUSION

Although the technical breakthroughs of endoscopic approaches have aided in the diagnostics of intestinal permeability and knowledge about its association to enteropathy and IDA, there are still some aspects of the problem that are poorly investigated. Standardisation of criteria and protocols of the invasive methods for permeability assessment is vital to ensure the studies obtain the same results in various places and by different specialists. In conclusion, endoscopic methods like capsule endoscopy and CLE are worth mention, since they are valuable tools in the evaluation of intestinal permeability and their implications for gastrointestinal disorders such as enteropathy. Gaps in the diagnosis and the mechanisms of how these diseases proceed will be filled in time; thus, our ability to take care of them will be improved.

REFERENCES

Ahnstedt, H., Patrizz, A., Chauhan, A., Roy-O'Reilly, M., Furr, J. W., Spychala, M. S., D'Aigle, J., Blixt, F. W., Zhu, L., Alegria, J. B. (2020). Sex differences in T cell immune responses, gut permeability and outcome after ischemic stroke in aged mice. *Brain, Behav. Immun.*, **87**, 556–567. DOI: 10.1016/j.bbi.2020.02.001.

Al-Ayadhi, L., Zayed, N., Bhat, R. S., Moubayed, N. M. S., Al-Muammar, M. N., El-Ansary, A. (2021). The use of biomarkers associated with leaky gut as a diagnostic tool for early intervention in autism spectrum disorder: A systematic review. *Gut Pathogens*, **13** (1), 54. https://doi.org/10.1186/s13099-021-00448-y.

Binienda, A., Twardowska, A., Makaro, A., Salaga, M. (2020). Dietary carbohydrates and lipids in the pathogenesis of leaky gut syndrome: An overview. *Int. J. Mol. Sci.,* **21** (21), 8368. DOI: 10.3390/ijms21218368.

Cano-Ortiz, A., Laborda-Illanes, A., Plaza-Andrades, I., Membrillo del Pozo, A., Villarrubia Cuadrado, A., Rodríguez Calvo de Mora, M., Leiva-Gea, I., Sanchez-Alcoholado, L., Queipo-Ortuño, M. I. (2020). The connection between the gut microbiome, systemic inflammation, gut permeability, and FOXP3 expression in patients with primary Sjögren's syndrome. *Int. J. Mol. Sci.,* **21** (22), 8733. DOI: 10.3390/ijms21228733.

Cayres, L. C. de F., de Salis, L. V. V., Rodrigues, G. S. P., Lengert, A. van H., Biondi, A. P. C., Sargentini, L. D. B., Brisotti, J. L., Gomes, E., de Oliveira, G. L. V. (2021). Detection of alterations in the gut microbiota and intestinal permeability in patients with Hashimoto thyroiditis. *Frontiers Immunol.*, **12**, 579140. DOI: 10.3389/fimmu.2021.579140.

Di Vincenzo, F., Del Gaudio, A., Petito, V., Lopetuso, L. R., Scaldaferri, F. (2024). Gut microbiota, intestinal permeability, and systemic inflammation: A narrative review. *Intern. Emerg. Med.*, **19** (2), 275–293. https://doi.org/10.1007/s11739-023-03374-w.

Fang, J., Yu, C.-H., Li, X.-J., Yao, J.-M., Fang, Z.-Y., Yoon, S.-H., Yu, W.-Y. (2022). Gut dysbiosis in nonalcoholic fatty liver disease: Pathogenesis, diagnosis, and therapeutic implications. *Frontiers Cell. Infect. Microbiol.,* **12**, 997018. DOI: 10.3389/fcimb.2022.997018.

Feng, Y.-K., Wu, Q.-L., Peng, Y.-W., Liang, F.-Y., You, H.-J., Feng, Y.-W., Li, G., Li, X.-J., Liu, S.-H., Li, Y.-C., Zhang, Y., Pei, Z. (2020). Oral *P. gingivalis* impairs gut permeability and mediates immune responses asso-

ciated with neurodegeneration in LRRK2 R1441G mice. *J. Neuroinflamm.*, **17** (1), 347. https://doi.org/10.1186/s12974-020-02027-5.

Fianchi, F., Liguori, A., Gasbarrini, A., Grieco, A., Miele, L. (2021). Nonalcoholic fatty liver disease (NAFLD) as a model of the gut–liver axis interaction: From pathophysiology to potential target of treatment for personalized therapy. *Int. J. Mol. Sci.*, **22** (12), 6485. DOI: 10.3390/ijms22126485.

Gan, J., Nazarian, S., Teare, J., Darzi, A., Ashrafian, H., Thompson, A. J. (2022). A case for improved assessment of gut permeability: A meta-analysis quantifying the lactulose: mannitol ratio in coeliac and Crohn's disease. *BMC Gastroenterol.*, **22** (1), 16. https://doi.org/10.1186/s12876-021-02082-z.

Giron, L. B., Dweep, H., Yin, X., Wang, H., Damra, M., Goldman, A. R., Gorman, N., Palmer, C. S., Tang, H.-Y., Shaikh, M. W. (2021). Plasma markers of disrupted gut permeability in severe COVID-19 patients. *Frontiers Immunol.*, **12**, 686240. DOI: 10.3389/fimmu.2021.686240. Erratum in: Front Immunol. 2021 Oct 04;12:779064. DOI: 10.3389/fimmu.2021.779064.

Hrncir, T., Hrncirova, L., Kverka, M., Hromadka, R., Machova, V., Trckova, E., Kostovcikova, K., Kralickova, P., Krejsek, J., Tlaskalova-Hogenova, H. (2021). Gut microbiota and NAFLD: Pathogenetic mechanisms, microbiota signatures, and therapeutic interventions. *Microorganisms*, **9** (5), 957. DOI: 10.3390/microorganisms9050957.

Huang, J. G., Tanpowpong, P. (2023). Pediatric gastrointestinal endoscopy in the Asian-Pacific region: Recent advances in diagnostic and therapeutic techniques. *World J. Gastroenterol.*, **29** (18), 2717. DOI: 10.3748/wjg.v29.i18.2717.

Iordache, M. M., Tocia, C., Aschie, M., Dumitru, A., Manea, M., Cozaru, G. C., Petcu, L., Vlad, S. E., Dumitru, E., Chisoi, A. (2022). Intestinal permeability and depression in patients with inflammatory bowel disease. *J. Clin. Med.*, **11** (17), 5121. DOI: 10.3390/jcm11175121.

Ishida, I., Ogura, J., Aizawa, E., Ota, M., Hidese, S., Yomogida, Y., Matsuo, J., Yoshida, S., Kunugi, H. (2022). Gut permeability and its clinical relevance in schizophrenia. *Neuropsychopharmacol. Rep.*, **42** (1), 70–76. https://doi.org/10.1002/npr2.12227.

Isnard, S., Lin, J., Bu, S., Fombuena, B., Royston, L., Routy, J.-P. (2021). Gut leakage of fungal?related products: Turning up the heat for HIV infection. *Frontiers Immunol.*, **12**, 656414. https://doi.org/10.3389/fimmu.2021.656414.

Khoshbin, K., Khanna, L., Maselli, D., Atieh, J., Breen-Lyles, M., Arndt, K., Rhoten, D., Dyer, R. B., Singh, R. J., Nayar, S. (2021). Development and validation of test for "leaky gut" small intestinal and colonic permeability using sugars in healthy adults. *Gastroenterology*, **161** (2), 463–475. DOI: 10.1053/j.gastro.2021.04.020.

Kim, D. H., Krishna, S. G., Coronel, E., Kröner, P. T., Wolfsen, H. C., Wallace, M. B., Corral, J. E. (2022). Confocal laser endomicroscopy in the diagnosis of biliary and pancreatic disorders: A systematic analysis. *Clin. Endosc.*, **55** (2), 197–207. DOI: 10.5946/ce.2021.079.

König, R. S., Albrich, W. C., Kahlert, C. R., Bahr, L. S., Löber, U., Vernazza, P., Scheibenbogen, C., Forslund, S. K. (2022). The gut microbiome in myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS). *Frontiers Immunol.*, **12**, 628741. DOI: 10.3389/fimmu.2022.878196.

Lucidi, L., Pettorruso, M., Vellante, F., Di Carlo, F., Ceci, F., Santovito, M. C., Di Muzio, I., Fornaro, M., Ventriglio, A., Tomasetti, C. (2021). Gut microbiota and bipolar disorder: An overview on a novel biomarker for diagnosis and treatment. *Int. J. Mol. Sci.,* **22** (7), 3723. DOI: 10.3390/ijms22073723.

Malesza, I. J., Bartkowiak-Wieczorek, J., Winkler-Galicki, J., Nowicka, A., Dzięciołowska, D., Błaszczyk, M., Gajniak, P., Słowińska, K., Niepolski, L., Walkowiak, J., Mądry, E. (2022). The dark side of iron: The relationship between iron, inflammation and gut microbiota in selected diseases associated with iron deficiency anaemia: A narrative review. *Nutrients*, **14** (17), 3478. DOI: 10.3390/nu14173478.

Martín-Mateos, R., Albillos, A. (2021). The role of the gut-liver axis in metabolic dysfunction-associated fatty liver disease. *Frontiers Immunol.*, **12**, 660179. DOI: 10.3389/fimmu.2021.660179.

Muntjewerff, E. M., Tang, K., Lutter, L., Christoffersson, G., Nicolasen, M. J. T., Gao, H., Katkar, G. D., Das, S., Ter Beest, M., Ying, W., Ghosh, P., El Aidy, S., Oldenburg, B., Van Den Bogaart, G., Mahata, S. K. (2021). Chromogranin A regulates gut permeability *via* the antagonistic actions of its proteolytic peptides. *Acta Physiologica*, **232** (2), e13655. https://doi.org/10.1111/apha.13655.

Ouyang, J., Lin, J., Isnard, S., Fombuena, B., Peng, X., Marette, A., Routy, B., Messaoudene, M., Chen, Y., Routy, J.-P. (2020). The bacterium *Akkermansia muciniphila*: A sentinel for gut permeability and its relevance to HIV-related inflammation. *Frontiers Immunol.*, **11**, 645. DOI: 10.3389/fimmu.2020.00645.

Pohl, K., Moodley, P., Dhanda, A. (2022). The effect of increasing intestinal short-chain fatty acid concentration on gut permeability and liver injury in the context of liver disease: A systematic review. *J. Gastroenterol. Hepatol.*, **37** (8), 1498–1506. https://doi.org/10.1111/jgh.15899.

Rodina, J., Derovs, A. (2022). Establishing the cut-offs of leaky gut syndrome diagnostic: Where are we now? *Proc. Latvian Acad. Sci., Section B,* **76** (5–6), 569–577. DOI: https://doi.org/10.2478/prolas-2022-0089.

Safadi, J. M., Quinton, A. M., Lennox, B. R., Burnet, P. W., Minichino, A. (2022). Gut dysbiosis in severe mental illness and chronic fatigue: A novel trans-diagnostic construct? A systematic review and meta-analysis. *Mol. Psych.,* **27** (1), 141–153. DOI: 10.1038/s41380-021-01032-1.

Sánchez-Alcoholado, L., Ordóñez, R., Otero, A., Plaza-Andrade, I., Laborda-Illanes, A., Medina, J. A., Ramos-Molina, B., Gómez-Millán, J., Queipo-Ortuño, M. I. (2020). Gut microbiota-mediated inflammation and gut permeability in patients with obesity and colorectal cancer. *Int. J. Mol. Sci.,* **21** (18), 6782. DOI: 3390/ijms21186782.

Schoultz, I., Keita, Å. V. (2020). The intestinal barrier and current techniques for the assessment of gut permeability. *Cells*, **9** (8), 1909. DOI: 10.3390/cells9081909.

Schwabe, R. F., Greten, T. F. (2020). Gut microbiome in HCC: Mechanisms, diagnosis, and therapy. *J. Hepatol.*, **72** (2), 230–238. DOI: 10.1016/j.jhep.2019.08.016.

Seethaler, B., Basrai, M., Neyrinck, A. M., Nazare, J.-A., Walter, J., Delzenne, N. M., Bischoff, S. C. (2021). Biomarkers for assessment of intestinal permeability in clinical practice. *Amer. J. Physiol.-Gastrointest. Liver Physiol.*, **321** (1), G11–G17. https://doi.org/10.1152/ajpgi.00113.2021.

Shen, L. (2020). Gut, oral, and nasal microbiota and Parkinson's disease. *Microbial Cell Factories*, **19** (1), 50. https://doi.org/10.1186/s12934-020-01313-4.

Solitano, V., D'Amico, F., Allocca, M., Fiorino, G., Zilli, A., Loy, L., Gilardi, D., Radice, S., Correale, C., Danese, S. (2021). Rediscovering histology: What is new in endoscopy for inflammatory bowel disease? *Ther. Adv. Gastroenterol.,* **14**, 17562848211005692. DOI: 10.1177/17562848211005692.

Stadlbauer, V., Engertsberger, L., Komarova, I., Feldbacher, N., Leber, B., Pichler, G., Fink, N., Scarpatetti, M., Schippinger, W., Schmidt, R., Horvath, A. (2020). Dysbiosis, gut barrier dysfunction and inflammation in dementia: A pilot study. *BMC Geriatrics*, **20** (1), 248. https://doi.org/10.1186/s12877-020-01644-2.

Stiegeler, S., Mercurio, K., Iancu, M. A., Corr, S. C. (2021). The impact of microRNAs during inflammatory bowel disease: Effects on the mucus layer and intercellular junctions for gut permeability. *Cells*, **10** (12), 3358. DOI: 10.3390/cells10123358.

Tracy, M. S., Yasuda, J. L., Rufo, P. A. (2020). Protein-losing enteropathy in the setting of iron deficiency anemia: A case series. *JPGN Rep*., **1** (2):e009. DOI: 10.1097/PG9.0000000000000009.

Turpin, W., Lee, S.-H., Garay, J. A. R., Madsen, K. L., Meddings, J. B., Bedrani, L., Power, N., Espin-Garcia, O., Xu, W., Smith, M. I. (2020). Increased intestinal permeability is associated with later development of Crohn's disease. *Gastroenterology*, **159** (6), 2092–2100. DOI: 10.1053/j.gastro.2020.08.005.

Vanuytsel, T., Tack, J., Farre, R. (2021). The role of intestinal permeability in gastrointestinal disorders and current methods of evaluation. *Frontiers Nutr.,* **8**, 717925. DOI: 10.3389/fnut.2021.717925.

Varesi, A., Campagnoli, L. I. M., Fahmideh, F., Pierella, E., Romeo, M., Ricevuti, G., Nicoletta, M., Chirumbolo, S., Pascale, A. (2022). The interplay between gut microbiota and Parkinson's disease: Implications on diagnosis and treatment. *Int. J. Mol. Sci.,* **23** (20), 12289. DOI: 10.3390/ijms232012289.

Zhan, Y., Al-Nusaif, M., Ding, C., Zhao, L., Dong, C. (2023). The potential of the gut microbiome for identifying Alzheimer's disease diagnostic biomarkers and future therapies. *Frontiers Neurosci.,* **17**, 1130730. DOI: 10.3389/fnins.2023.1130730.

Zhuge, A., Li, S., Lou, P., Wu, W., Wang, K., Yuan, Y., Xia, J., Li, B., Li, L. (2022). Longitudinal 16S rRNA sequencing reveals relationships among alterations of gut microbiota and nonalcoholic fatty liver disease progression in mice. *Microbiol. Spectrum*, **10** (3), e00047-22. https://doi.org/10.1128/spectrum.00047-22.

Received 18 June 2024
Accepted in the final form 24 July 2024

ZARNU CAURLAIDĪBAS PĒTĪŠANA: KONCEPTS, DIAGNOZE, SAISTĪBA AR ZARNU SLIMĪBĀM UN DZELZS DEFICĪTA ANĒMIJA

Pēdējos gados zarnu caurlaidības koncepts ir kļuvis par galveno zarnu veselības stūrakmeni. Šī raksta mērķis ir veikt literatūras pārskatu, izklāstot pašreizējo izpratni par zarnu caurlaidību. Zarnu caurlaidības jēdziens sāka attīstīties, atklājot ciešus savienojumus — proteīnu kompleksus, kas atdala epitēlija šūnas. Histopatoloģija vēsturiski ir galvenā mikroskopiskās diagnostikas iespēja, kas ļauj noteikt iekaisumu, bojātās epitēlija šūnas un kas notiek ciešā savienojumā. Turklāt zarnu taukskābes saistošais proteīns I-FABP un zonulīns tiek ieteikti kā epitēlija barjeras caurlaidības bojājuma biomarķieri. Attiecībā uz vizuālo diagnostiku literatūrā tiek piedāvāta kapsulas endoskopija un konfokālā lāzera endomikroskopija. Pēdējai ir iespēja attēlot tievo zarnu morfoloģiju un vizualizēt tievās zarnas luminālos elementus, šūnas, bārkstiņas, kā arī kriptas. Tomēr, pateicoties digitālās kapsulas endoskopijas attīstībai, šī metode kļūst daudz piemērotāka zarnu caurlaidības un enteropātijas pētījumos, sniedzot daudzsološus rezultātus ārstēšanā. Lai gan zarnu caurlaidības bojājumus varētu klasificēt kā noteiktu enteropātiju un dažu enteropātiju saistība ar dzelzs deficītu ir noteikta, saikne starp dzelzs deficītu un zarnu caurlaidību vēl jāizpēta.