

NOVEMBER 2011

IMD (Intestinal Mucosal Disorder)

Related to IBS, leaky gut, Crohn's disease, ulcerative colitis, immune diseases...

Intestinal mucosa: the forgotten factor in intestinal pathology  
Intestinal villi (leaky gut) is related to a malfunctioning  
Interventions such as glutamine and glutathione can help to  
Intestinal mucosa

The intestinal mucosa is involved in celiac disease, Crohn's disease, ulcerative colitis and many other intestinal pathologies.

Good intestinal permeability ensures a good intestinal barrier.

The quality of the "tight junctions" between the enterocytes and the paracellular space is a factor that determines the degree of disruption to the permeability of the intestinal mucosa.



Fig 1. Les micro-lésions ne sont détectables qu'avec des équipements spéciaux, tels que le microscope électronique

Fig 1. Micro-lesions can only be detected with special equipment such as an electron microscope

Nat Clin Pract Gastroenterol Hepatol. 2005 Sep;2(9):416-22.

**Mechanisms of disease: the role of intestinal barrier function in the pathogenesis of gastrointestinal autoimmune diseases.**

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"La compréhension du rôle de la barrière intestinale dans la pathogénie de maladies gastro-intestinales est un domaine de recherche pluridisciplinaire retenant actuellement beaucoup d'attention. Cette revue tombe à point pour souligner l'intérêt "du leaky gut" dans la pathogénie de maladies gastro-intestinales et l'apparition de nouvelles stratégies de traitement, comme l'utilisation de probiotiques."

"The understanding of the role of the intestinal barrier function in the pathogenesis of gastrointestinal diseases is a multidisciplinary research field that is currently getting a lot of attention.

This magazine comes in due time to underline the interest of the "leaky gut" in the pathogenesis of gastrointestinal diseases and the onset of new treatment strategies, such as the use of probiotics."

## Mechanisms of Disease: The role of intestinal barrier function in the pathogenesis of gastrointestinal autoimmune diseases

Alessio Fasano and Terez Shea-Donohue

The first function of the gastrointestinal tract is usually seen as it being the 'frontier' of the digestion and absorption of nutrients, electrolytes and water exchanges.

An analysis of the functioning and structure of the intestinal tract suggests that another extremely important function of this organ is its ability to regulate the transit of macromolecules between the environment and the host, through a barrier mechanism.

In association with lymphoid tissues and the neuro-endocrine meshing, the intestinal epithelial barrier, with its tight intercellular junctions, controls the balance between tolerance and immune response regarding antigens that are foreign to the body.

When this subtle transit of micro-molecule malfunctions, depending on individual genetic susceptibilities, autoimmune disorders in the intestine (and outside it) can occur.

This new paradigm overturns traditional theories on the development of autoimmune phenomena based on the so-called 'molecular mimicry', and suggests that autoimmune processes may be halted if the interaction between genes and the environment is prevented by re-establishing the functioning of the intestinal barrier.

The understanding of the role of the intestinal barrier function in the pathogenesis of gastrointestinal illnesses is a multidisciplinary field of research that is currently getting a lot of attention.

This is particularly timely in underlining the major role of the 'leaky gut syndrome' in the birth of gastrointestinal disorders and the onset of new treatment strategies such as the use of probiotics,

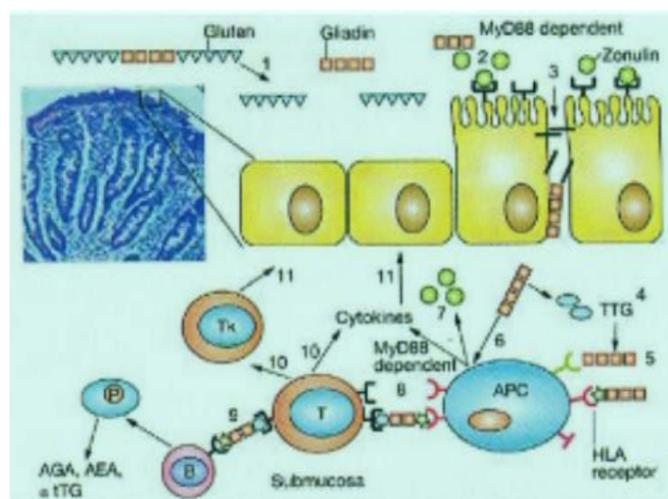


Figure 2: Schéma proposant un mécanisme de pathogénie de maladie coeliaque en cas d'une perméabilité intestinale anormale

Fig. 2 Diagram proposing a celiac disease pathogenesis mechanism in the event of abnormal Intestinal permeability

#### THE ROLE OF GLUTAMINE IN NUTRITION IN CLINICAL PRACTICE

*Campos FB, Waitzberg DL, Logulo AF, Mucerino DR, Habr-Gama A Departamento de Gastroenterologia, Faculdade de Medicina, Universidade de Sao Paulo. Arq Gastroenterol 1996 Apr-Jun; 33(2):86-92*

**Glutamine in the main fuel of enterocytes** and it plays a key role in maintaining the structure and the functioning of the intestine.

Furthermore, a glutamine supplement has turned out to be beneficial to the immune system, it improves the nitrogen balance and nutritional parameters in the post-operative period and reduces protein loss in severe catabolic conditions.

#### GLUTAMINE: EFFECTS ON THE IMMUNE SYSTEM, THE METABOLISM OF PROTEIN AND THE INTESTINAL FUNCTION

*Roth E, Spittler A, Oehler R Chirurgisches Forschungslaboratorium, Universitätsklinik für Chirurgie, Allgemeines Krankenhaus, Wien. Wien Klin Wochenschr 1996; 108(21):669-71*

In conclusion, **glutamine is an important metabolic substrate** for rapid cell proliferation. It has an influence on cell hydration and has several effects on the immune system, the intestinal function and protein metabolism. In many pathological conditions glutamine can therefore become an essential nutrient that can be contributed exogenously during artificial nutrition.

The table below clearly shows the relationship between disrupted intestinal permeability and the disruption to the TNFalpha function.

Given that high intestinal permeability is often an underlying cause of many intestinal disorders, it is possible to re-establish the integrity of the mucosa with natural substances, basically glutamine.

**Table 1** Relationship between barrier dysfunction and TNF $\alpha$  in selected diseases

<i>Disease/model</i>	<i>Species</i>	<i>Intestinal permeability</i>	<i>Antigen</i>	<i>TNF<math>\alpha</math> level</i>	<i>Effect of TNF<math>\alpha</math> antagonism</i>
Crohn's disease	Human	Increased <sup>90</sup>	Gut flora ?	Increased <sup>91</sup>	Restores barrier function <sup>84</sup>
Ulcerative colitis	Human	Increased <sup>92</sup>	?	Increased <sup>89,91</sup>	Variable results <sup>93,94</sup>
IL-10 knockout	Mouse	Increased <sup>78</sup>	Gut flora ?	Increased <sup>78</sup>	Slows progression <sup>95</sup>
Dominant negative cadherin transgene	Mouse	?	?	?	?
Systematic T-cell activation	Mouse	Increased <sup>96,97</sup>	None	Increased <sup>96,97</sup>	Decreases diarrhea <sup>96</sup>
Graft vs host disease	Human	Increased <sup>98</sup>	Host	Increased <sup>99</sup>	Variable results <sup>100-102</sup>
Graft vs host disease	Mouse	Increased <sup>75</sup>	Host	Increased	Decreases severity, corrects barrier defect <sup>75,85</sup>
Celiac sprue	Human	Increased <sup>27,22</sup>	Gluten	Increased <sup>103</sup>	Clinical-histological regression (case report) <sup>104</sup>
Enteropathogenic <i>E. coli</i> infection	Human	Increased <sup>30,31</sup>	?	?	?
<i>C. difficile</i> infection	Human	Increased <sup>105-107</sup>	?	?	?

## L-glutamine

Glutamine is a common amino acid found in many food proteins. It is important for several bodily functions, for example the detoxification of ammonia. It is one of the most important nutrients for treating the 'leaky gut syndrome' because it is the preferred fuel of the enterocytes. These cells are able to directly absorb glutamine without waiting to be supplied by the blood stream. Glutamine is also necessary for the production of intestinal mucosa and the secretion of Type A immunoglobins (IgAs). As a result, a good supplementation of glutamine can help to repair the small intestine and keep it healthy. These functions, such as the ability of glutamine to prevent the translocation of bacteria through the intestine into the blood stream, have been established in a large number of clinical studies - both on animals and human beings - in pathological conditions that involve intestinal permeability.

- In disorders of the intestinal mucosa, irritable bowel syndrome, Crohn's disease, ulcerative colitis, immune diseases and related pathologies... disrupted permeability of the intestinal mucosa - i.e. 'leaky gut'- is often detected.
- This disruption can only be detected with an electron microscope.
- Glutamine, one of the 20 natural amino acids, is an important fuel in the structure of the intestinal mucosa.
- Glutamine is present in large quantities in cottage cheese, yoghurt, milk and eggs. Furthermore, the amino acid is also found in soy, wheat, spinach, cabbage, beans and tofu.
- Enterocytes directly absorb glutamine without waiting for the return via the blood stream.

This is why a good dietary supplement should also contain glutamine to re-establish the intestinal mucosa.

Gabriël Devriendt R&D

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