Volume 2 Number 3
May 2010

The Physiological Medical Letter

International Centre for Study and Research in Aesthetic and Physiological Medicine

The Physiological Medical Letter

Vol. 2 May 2010 N° 3

INTEGRATIVE PROPOSAL FOR MALABSORPTION AND BAD DIGESTION PREVENTION

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Premise

The function of the digestive tract is to digest and absorb nutrients with removal of residual material. Foods are ingested macromolecules such as carbohydrates, proteins and fats and micronutrients such as vitamins and trace elements. The macromolecules, to be absorbed, must be broken up into molecules with more simple structure . The digestive process is played by pancreatic enzymes secreted into the intestinal lumen. The absorption occurs at the brush border of the intestinal cells. The alteration of the hydrolysis and the solubilization of foods not adequately prepared for absorption, are indicated as bad digestion, while the faulty transition of nutrients from the intestinal lumen is defined malabsorption.

The malabsorption may determine, in addition to malnutrition, steatorrhea, diarrhea and flatulence, even the appearance of food allergies.

Allergic hypersensitivity or food allergies is a term widely used for various responses associated with the recruitment of a particular food.

A historical overview tells us that:

- In 1978, Australian researchers published a 'exclusion diet' to remove chemicals present in foods used in the diet of patients with a possible role in the pathogenesis of chronic idiopathic urticaria (CIU).
- In 1995, the European Academy of Allergology and Clinical Immunology suggested classification of systemic reactions to food intake on the basis of pathogenesis in "food allergies" when they recognize immunological mechanisms and 'food intolerance' when there is no evidence immunological
- In 2003, the Committee on Nomenclature of the World Allergy published a report on nomenclature allergies and food intolerances, which has had general acceptance. Food intolerance is described as a 'non-allergic food hypersensitivity.

Today, food intolerance as a negative reaction, often delayed, for a food that produces symptoms in one or more organs in the body, without being a true food allergy. True food allergy requires the presence of IgE antibodies against food.

The food intolerances can be classified according to their mechanism:

- intolerance resulting from the absence or deficiency of specific enzymes necessary to digest a food substance.
- intolerance resulting from a deficiency in the body's ability to absorb nutrients.

- intolerance caused by chemicals in food.
- intolerance caused by drugs in food

The non-IgE-mediated food hypersensitivity (food intolerance) is usually a chronic disorder harder to diagnose that the food allergy. The symptoms of food intolerance vary widely and can be mistaken for symptoms of a 'food allergy. It can be difficult to determine the food that cause the food intolerance , because the answer is usually after a certain period of time. So the agent and the response are separated in time and can not be easily linked. Symptoms of food intolerance usually begin after a half hour from eating the food in question, but sometimes the symptoms may be delayed up to 48 h.

Food intolerance may experience symptoms affecting the skin, respiratory tract, gastrointestinal tract (GIT), individually or in combination. The more
common are abdominal cramps, nausea, bloating, diarrhea, constipation, irritable bowel syndrome, headaches and water retention.
A lack of digestive enzymes may also cause some types of food intolerances. In the most clinically obvious, such as lactose intolerance due to insufficient production of lactase and intolerance to gluten which causes damage also in the intestinal wall, is accompanied by milder forms resulting from the improper digestion of foods .

They can cause food intolerance, in addition to enzymatic defects in the digestive system, including the pharmacological effects of vasoactive amines in foods (histamine).
The exact immunopathological mechanism of food intolerance is not well known. It is thought to lymphocyte helper type 1 (Th 1), the formation of immune complexes, and complement activation. The diagnosis of food intolerance is normally made by ELISA for the detection of IgG against specific foods.

Scientific considerations

From the foregoing it appears that the optimization of the biological state, typical of Physiological Medicine, requires, in addition to a proper and balanced diet, the perfect functionality of the system, digestion and absorption of nutrients.
Based on a literature review we have highlighted:

- The administration of amino acids stimulates the synthesis of protease by promoting the translation system for these enzymes (*Naoto Hashimoto and Hiroshi Hara Dietary Amino Acids Promote Pancreatic Protease Synthesis at the Translation Stage in Rats J. Nutr. 133:3052-3057, October 2003*)
- Leucine, glutamine and tyrosine play a modulatory role in regulating protein synthesis liver and pancreatic (*O. Jameel Shah, David A. Antonetti, Scot R. Kimball and Leonard S. Jefferson, Leucine, Glutamine, and Tyrosine Reciprocally Modulate the Translation Initiation Factors eIF4F and eIF2B in Perfused rat Liver, December 17, 1999 The Journal of Biological Chemistry, 274, 36168-36175.*
- solubilized proteins can induce, with a possible paracrine mechanism, synthesis and secretion of proteinases. (*Lehane, MJ, Blakemore, D., Williams, S., Moffatt, M. R. Regulation of digestive enzyme levels in insects, Comparative Biochemistry and Physiology. B, Biochemistry & Molecular Biology*)
- diets containing egg protein stimulates the synthesis and secretion of trypsin, trypsin and amylase chyme (*Jean Twombly Snook and JH Meyer, Response of Digestive Enzymes to Dietary Protein, The Journal of Nutrition*)

That is, the recruitment of amino acids or protein induces an increase in the synthesis of enzymes necessary for their metabolism and absorption. Particularly through the phenomenon of cellular transcription or translation.

The translation in eukaryotic cells is a process that allows the formation of protein messenger RNA.

Molecular biology of translation

The so-called **central dogma of molecular biology** is the principle that the flow of genetic information is unidirectional from the nucleic acids to arrive to proteins . In this process are three identifiable points: the genetic information is stored in the DNA that is **transcribed** in the form of RNA, which is then translated to proteins, form the "operational" information contained in the genome.

In molecular biology, **transcription** is the process by which the information contained in DNA is transcribed enzymatically in a complementary RNA molecule. Conceptually, this is the transfer of genetic information from DNA to RNA. Transcription is through specific enzymes generically called **RNA polymerase**. These proteins are often referred to as DNA-dependent RNA polymerase, since they produce an RNA molecule from a DNA.

The transcript consists essentially of three phases: initiation, elongation and termination.

The RNA polymerase binds to DNA only at specific sequences, called promoters, which are not transcribed. From the promoter starts, entering nucleoside triphosphate, to form a sequence of nucleotides that is complementary to the DNA strand being transcribed. After the discovery of the promoter, RNA polymerase makes DNA suitable for transcription.

The **control of gene expression** is an essential process in every organism. This assertion is obvious in multicellular organisms, where the various cell types perform highly specialized functions and are programmed to express only some of their genes and not others. The cell has developed mechanisms for repress all genes that are not necessary, activate only when needed. The control of gene expression patterns most popular are those related to **operon** function.

The operon is a complex of genes that encode proteins needed to carry out a coordinate function, eg the synthesis of enzymes required for utilization of substrate. For better understanding we give an example:

The metabolism of lactose requires two enzymes: the β-galattossidasi that splits the disaccharide lactose into glucose and galactose, and the permeases that involved the transport of lactose into the cell. These enzymes are encoded by two contiguous structural genes. The structural genes are transcribed in a single molecule of mRNA. Upstream of the structural genes is the regulatory gene that encodes a protein called **repressor** that blocks the expression of structural genes. The block is determined by the binding of repressor to a portion of DNA that works in conjunction with the **promoter** which, normally, attaches the 'RNA polymerase to initiate transcription. Preventing the attack of 'RNA polymerase prevents the reading of the structural genes.

The repressor protein has two different binding sites: a site is able to specifically recognize the sequence of operator, while the other site is the recognition of lactose or other similar molecules. The repressor protein when it binds to lactose undergoes changes conformational (allosteric transition) that lowers the affinity of repressor to operator sequences with detaching from the operator sequences. It follows the transcription of enzymes and the production of these.

Scientific considerations

This mechanism of prokaryotic cell is, more complicated but similar in function, even in eukaryotic cells (Man.)

The important concept that we highlight in our discussion is that gene expression is regulated by external substances. In particular, the synthesis of enzymes required for digestive process is activated by the same substances that we digest.

Furthermore, studies in rodents have shown that some nutrients and supplements in the diet may alter gene expression in animals, activating or deactivating certain genes. It is unclear whether the foods have the same effect in humans, but an article published in the Journal New Scientist states that there are good reasons to believe so. In the future, the researchers believe it may be possible to cure

certain diseases through diet. A study by Moshe Szyf and colleagues at McGill University in Montreal at a conference on environment epigenome in Durham United States, showed that L-methionine acting by altering response to stress on a glucocorticoid gene, adding methyl groups to the gene through a process called methylation (methylation occurs on histones -histone H3 lysine 9- by the methyltransferase and is associated with transcription inactivity). Researchers are now investigating to see if you can cause a positive behavioral change, rather than negative, using a natural chemical called trichostatin A (TSA) has an opposite effect on the genes compared to L-methionine, depriving them of methyl groups. The study demonstrates the importance of supplements and nutrients: the research has also shown that the alimentation of a mother can influence the level of DNA methylation and thus gene expression in the offspring.

Conclusions

The saying "we are what we eat" is becoming increasingly true. Pending developments in science lead to a real highlight pharmacological role of individual nutrients, we would like to make a proposal for treatment of the malabsorption and bad digestion.

Given the direct action of individual foods on stimulating production of digestive enzymes and in particular the specific effect that Leucine, Glutamine, and Tyrosine have dell'eIF4F training complex, essential for initiation of translation in eukaryotic cells, we propose that before the main meals will be made a useful supplement to enable the formation of digestive enzymes. The integrator should consist of two phases:

1. The first, containing amino acids, simple sugars and fatty acids would function by intestinal absorption, stimulate transcription activating the genetic locus of the operator and facilitating the reading of the structural genes for digestive enzymes.
2. The second, containing Leucine, Glutamine, and Tyrosine to induce the formation dell'eIF4F complex, essential for initiation of translation in eukaryotic cells.

This would provide a more concentrated enzyme at mealtime facilitating the hydrolysis and absorption of macronutrients of completely digested products.

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