# Allergie – maladie coeliaque – Gluten (NCGS*)- FODMAP’s

SSMG 10/12/2016

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*Non Coeliac Gluten sensitivity


Eh bien docteur, je ne sais plus quoi manger. Gluten, lait, lactose, céréales, œufs, arachide??? Allergie, intolérance? J'ai un leaky gut…
Je suis perdu!!!

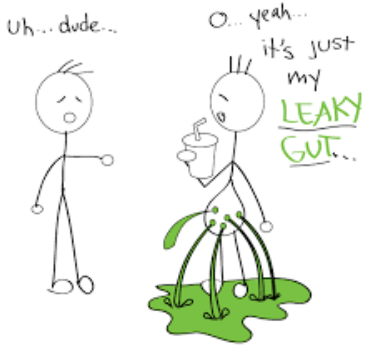
Bien l'aider à comprendre pour nuancer.

Eviter les messages simplistes

Complexe est différent de compliqué

Effectivement, je le comprends.

Comment faire pour qu'il ne sorte pas du cabinet en ayant plus peur qu'en entrant???!!!???

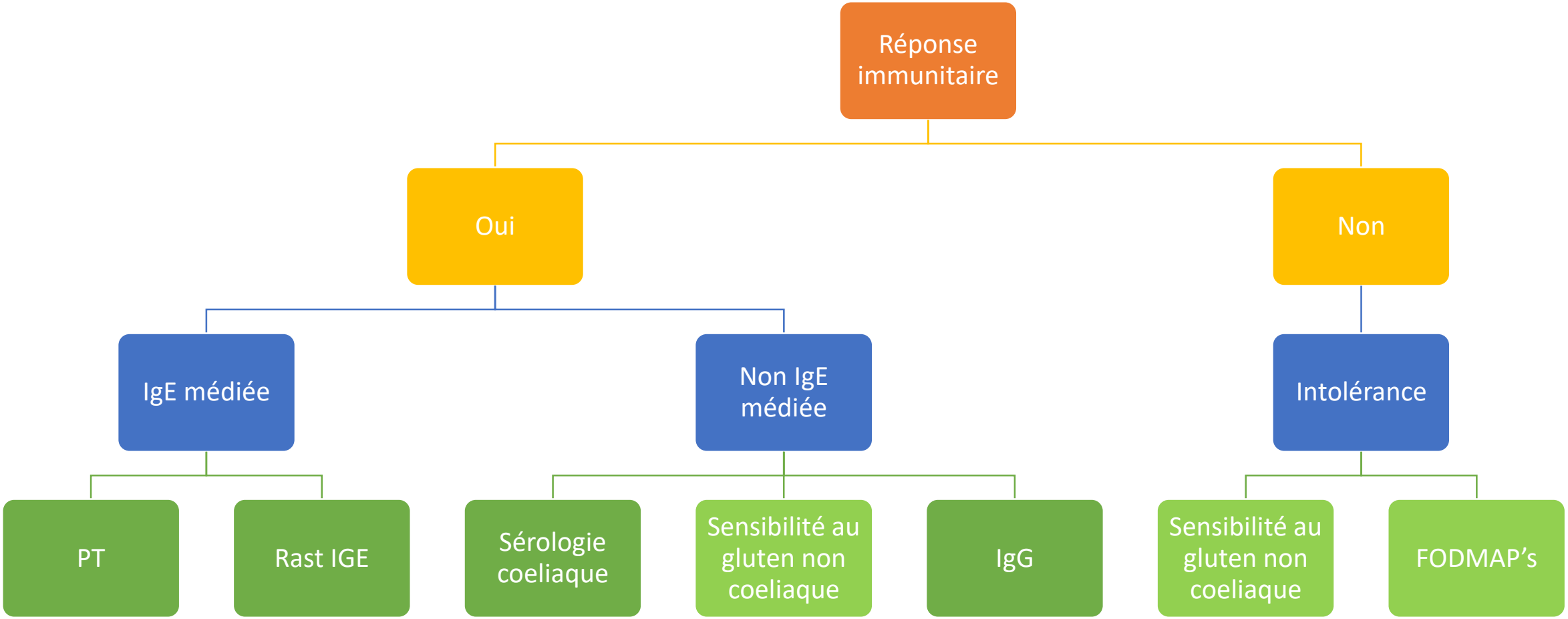



**C'est plus complexe que ça !**

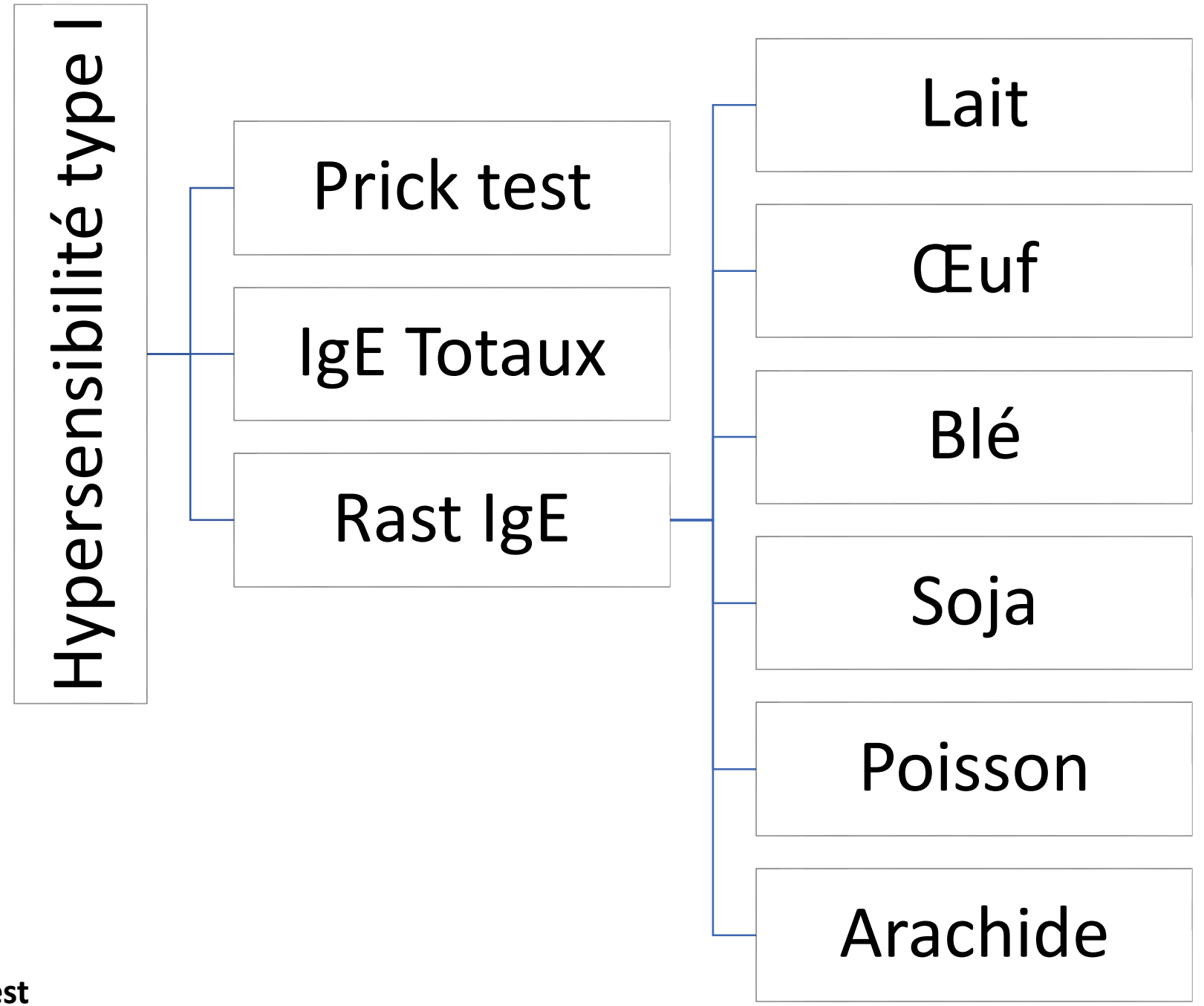
# Approche diagnostique et clinique

Du très connu au plus récent

# Troubles digestifs / extra digestifs



Réponse immunitaire




**Radioallergosorbant test**

Réponse immunitaire

# Hypersensibilité type IV


World Gastroenterology Organisation Global Guidelines

Maladie coeliaque

Avril 2012

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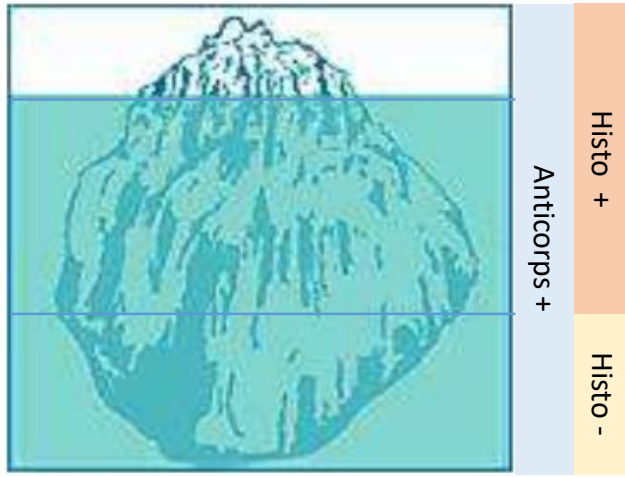


Suspicion clinique

Basse

Ig A / G

Anti transglutaminase

ou

Anti endomysium

et

Ig A / G

Anti peptides désaminés de la gliadine

Tous les tests -

Diagnostic exclu

Un test +

Biopsie duodénale

Haute

Biopsie duodénale

et

IgA anti Tg et endomysium

| Sérologie | Histologie | Maladie coeliaque | remarques |
|---|---|---|---|
| + | + | Confirmée | |
| + | - | Revoir biopsie<br>Répéter biopsie (1-2 ans) | Suivre |
| - | + | Autres causes d'entérite<br>Aucune ➔ R comme si + | HLA DQ2 DQ8 négatifs ➔ maladie coeliaque peu probable |
| - | - | Exclue | |

# The spectrum of noncoeliac gluten sensitivity

*Imran Aziz, Marios Hadjivassiliou and David S. Sanders*

World Gastroenterology Organisation Global Guidelines

## Maladie coeliaque

Avril 2012



Tableau **1** Classification de Marsh modifée des lésions de l'intestin grêle induites par le gluten [33,34]

| | |
|---|---|
| Stade 0 | Muqueuse pré-infiltrée; jusqu'à 30% des patients avec une dermatite herpétiforme (DH) ou avec une ataxie liée au gluten ont des biopsies de l'intestin grêle apparemment normales |
| Stade 1 | Augmentation du nombre des lymphocytes intra-épithéliaux (LIE) à plus de 30 pour 100 entérocytes |
| Stade 2 | Hyperplasie des cryptes. En plus de l'augmentation des LIE, la profondeur des cryptes est augmentée sans diminution de la hauteur des villosités. Ces modifications peuvent être induites par un challenge au gluten, mais peuvent également être présentes chez 20% des patients non traités avec une dermatite herpétiforme et une maladie coeliaque |
| Stade 3 | Atrophie villositaire: A, partielle; B, subtotale; C, totale. Ce stade correspond à l'aspect dit classique de la maladie coeliaque et s'observe chez 40% des patients avec une DH. En dépit de changements prononcés de la muqueuse, de nombreux individus sont asymptomatiques et donc classés comme cas subcliniques ou silencieux. Cette lésion, bien que caractéristique, ne suffit pas pour le diagnostic de la maladie coeliaque car elle se rencontre aussi dans le cas de lambliase sévère, d'allergie alimentaire chez l'enfant, de réaction du greffon contre l'hôte, d'ischémie chronique de l'intestin grêle, de sprue tropicale, de déficits en immunoglobulines et autres maladies immunes et de rejet de greffons |


# Gluten et épithélium intestinal

Mécanismes

American Physiological Society Physiological Reviews

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# Zonulin and Its Regulation of Intestinal Barrier Function: The Biological Door to Inflammation, Autoimmunity, and Cancer

Alessio Fasano

Physiological Reviews Published 1 January 2011 Vol. 91 no. 1, 151-175 DOI: 10.1152/physrev.00003.2008

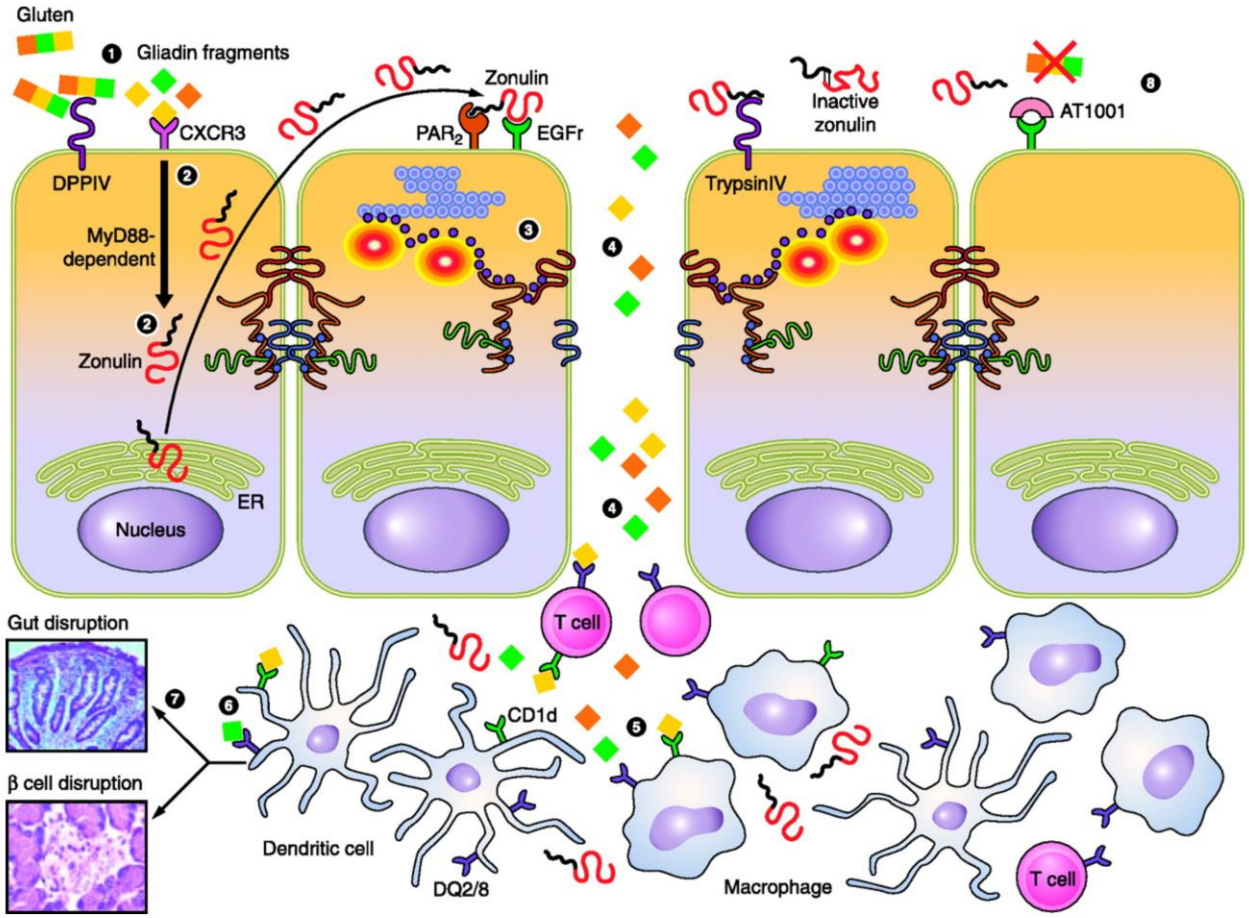


FIG. 14. Mechanisms of gliadin-induced zonulin release, increased intestinal permeability, and onset of autoimmunity. The production of specific gliadin-derived peptides by digestive enzymes causes CXCR3-mediated, MyD88-dependent zonulin release (*2*) and subsequent transactivation of EGFR by $PAR_2$ leading to small intestine TJ disassembly (*3*). The increased intestinal permeability allows non-self antigens (including gliadin) to enter the lamina propria (*4*), where they are presented by HLA-DQ, -DR molecules (*5*). The presentation of one or more gliadin peptides leads to abrogation of oral tolerance (switch to Th1/Th17 response) and a marked increase in peripheral immune responses to gliadin. Furthermore, gliadin-loaded dendritic cells migrate from the small intestine to mesenteric and/or pancreatic lymph nodes (*6*) where they present gliadin-derived antigens. This presentation leads to migration of $CD4^-CD8^-$ $\gamma\delta$ and $CD4^-CD8^+$ $\alpha\beta$ T cells to the target organ (gut and/or pancreas) where they cause inflammation (*7*). Implementation of a gluten-free diet or treatment with the zonulin inhibitor AT1001 (*8*) prevents the activation of the zonulin pathway and, therefore, of the autoimmune process targeting the gut or pancreatic $\beta$-cells.

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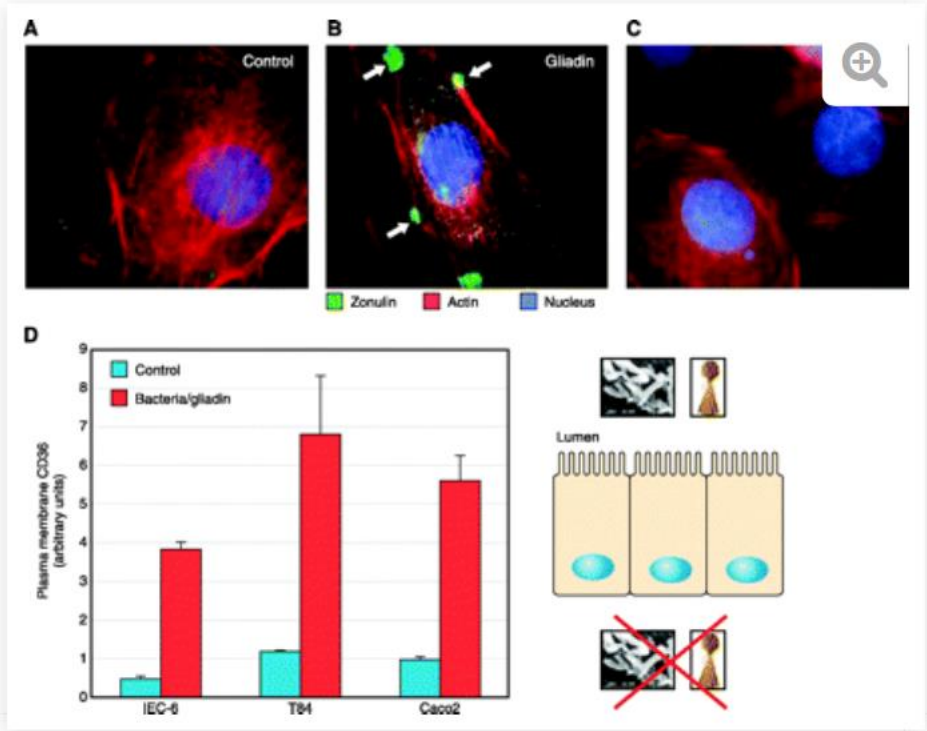


**Fig. 7.**

**Download figure** | **Open in new tab** | **Download powerpoint**

Stimuli causing polarized zonulin release from intestinal epithelial cells. *A–C*: anti-zonulin immunoflourescence staining of human intestinal Caco2 cells. Cells exposed to gliadin/PT-gliadin (*B*) react by packaging preformed zonulin in vesicles (arrows) that gradually approached the cell membrane and then released their zonulin content in the cell medium within a few minutes of the exposure to gliadin. No packaging was detected in nonstimulated cells (control, *A*) or cells incubated with PT-casein (*C*). The nucleus is in blue (DAPI), cytoskeleton in red (RITC), and zonulin in green (FITC). Magnification ×100. *D*: polarized zonulin secretion of intestinal cells exposed to either bacteria or PT-gliadin. Both rat (IEC6) and human (Caco2 and T84) intestinal epithelial cells exposed to either nonpathogenic bacteria or gliadin secrete large amounts of zonulin in the bath medium compared with the amount of zonulin measured in media of cells exposed to control. This secretion was detected only when the triggers were added to the luminal (apical) aspect of the cell monolayers.

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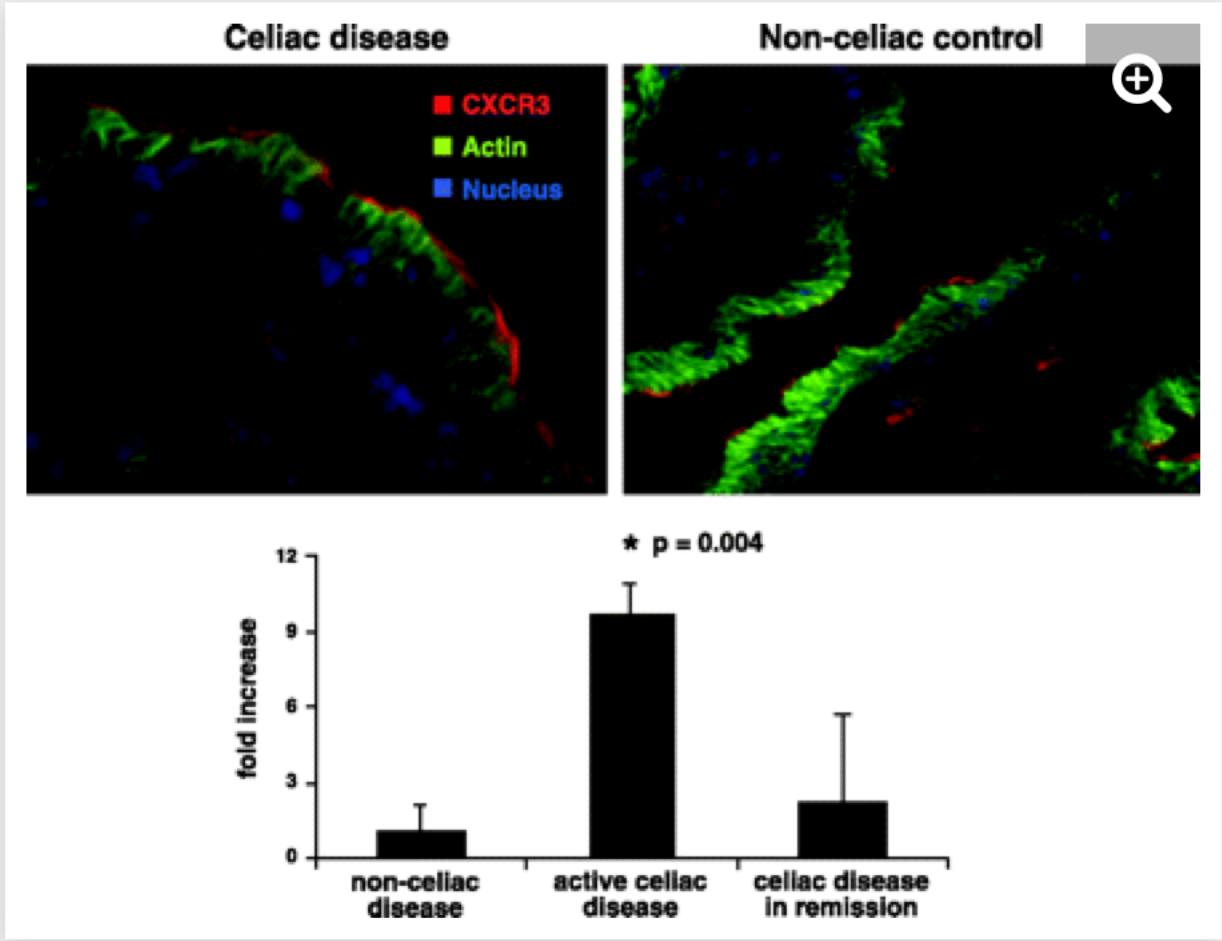


**Fig. 8.**



*Top:* in situ immunofluorescence microscopy of CXCR3 in human small intestinal biopsies obtained from either celiac patients or nonceliac controls. CXCR3 staining in red (RITC) is homogeneously visible on the apical side of intestinal epithelial cells of biopsies from celiac disease patients, while the CXCR3 staining is patchy in nonceliac controls. *Bottom:* quantitative real-time PCR of the CXCR3 gene confirmed an increased expression of the receptor compared with nonceliac controls that decreased after treatment with a gluten-free diet. Note the increased infiltrate of CXCR3-expressing immune cells in celiac disease biopsies compared with nonceliac controls. The nucleus is in blue (DAPI) and the cytoskeleton in green (FITC). Magnification ×60.

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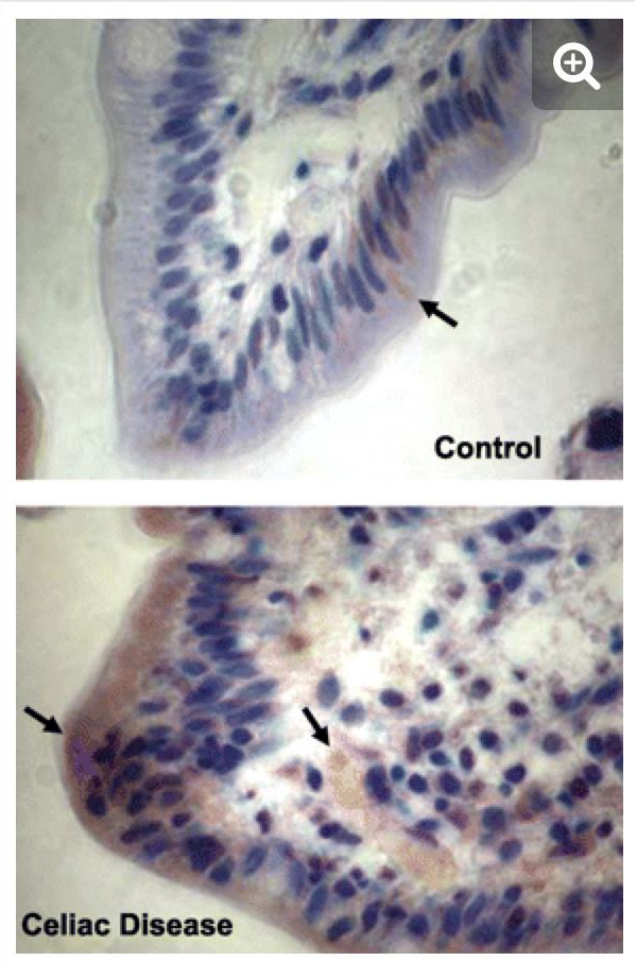


**Fig. 10.**

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Photomicrographs of immunohistochemistry on small intestinal tissues from a healthy control and an active CD patient stained with zonulin cross-reacting anti-Zot antibodies. Zonulin is visualized both in enterocytes and in cells of the lamina propria (arrows) and is overexpressed in active CD patients compared with controls.

# Sensibilité au gluten non coeliaque

**Review criteria**

A literature search was conducted using PubMed and the search term "non-coeliac gluten sensitivity", with the final search performed in March 2015. Systematic reviews, case series, case–control studies and randomized controlled clinical trials were analysed for the creation of this Review, with particular focus on manuscripts published in the past 5 years.

# The spectrum of noncoeliac gluten sensitivity

*Imran Aziz, Marios Hadjivassiliou and David S. Sanders*

**Abstract** | The past 5 years have seen an increase in the use of a gluten-free diet outside a diagnosis of coeliac disease or IgE-mediated wheat allergy. This trend has led to the identification of a new clinical entity termed noncoeliac gluten sensitivity (NCGS). In this Review, we discuss the evidence for NCGS as demonstrated by the results of double-blind, placebo-controlled dietary rechallenge studies. Furthermore, the characteristic phenotype of individuals with NCGS is described as well as the symptom manifestations commonly reported after gluten exposure, which include intestinal symptoms consistent with IBS, and extraintestinal symptoms such as neurological dysfunction, psychological disturbances, fibromyalgia and skin rash. Moreover, emerging evidence suggests that NCGS can be associated with organic gastrointestinal pathologies, such as IBD, in which its presence might be a reflection of severe or stricturing disease. However, NCGS is not without its controversies and uncertainties, in particular pertaining to whether it is gluten or nongluten components of the grain evoking symptoms; evidence suggests that fermentable carbohydrates, amylase trypsin inhibitors and wheat-germ agglutinin can also be responsible culprits. Finally, we discuss the novel techniques that might help diagnose NCGS in the future.

Aziz, I. *et al. Nat. Rev. Gastroenterol. Hepatol.* **12**, 516–526 (2015); published online 30 June 2015; doi:10.1038/nrgastro.2015.107

- No diagnostic biomarkers to differentiate between gluten and nongluten components currently exist; positive antigliadin antibodies support the diagnosis of NCGS but have limited sensitivity and specificity


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# Non-Celiac Gluten Sensitivity: Literature Review

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[b] Internal Medicine , Sciacca Hospital (Agrigento ASP) and University of Palermo , Palermo , ITALY

Published online: 17 Feb 2014.



**Table 1.** Gluten Sensitivity Diagnosis Criteria

| Diagnotics Tools | Celiac Disease | Gluten Sensitivity |
|---|---|---|
| Celiac disease serology: | | |
| Antitissue transglutaminase | Positive | Negative |
| Antigliadins antibodies | Positive | Positive (50% of the cases) |
| Anti-endomysial antibodies | Positive | Negative |
| Deaminated gliadin peptide antibodies | Positive | Negative |
| Duodenal histology (Marsh-Oberhüber classification) | Positive (Marsh 1–3) | Negative (Marsh 0–1) |
| HLA haplotypes (DQ2-DQ8) | Present | Absent/present |
| IgE-based assays (prick tests or serum-specific IgE dosage) | Negative | Negative |
| Clinical features | Troubles caused by wheat ingestion and their disappearance on gluten-free diet | Troubles caused by wheat ingestion and their disappearance on gluten-free/wheat-free diet |

HLA = human leukocyte antigen, Ig = immunoglobulins.

# The spectrum of noncoeliac gluten sensitivity

*Imran Aziz, Marios Hadjivassiliou and David S. Sanders*

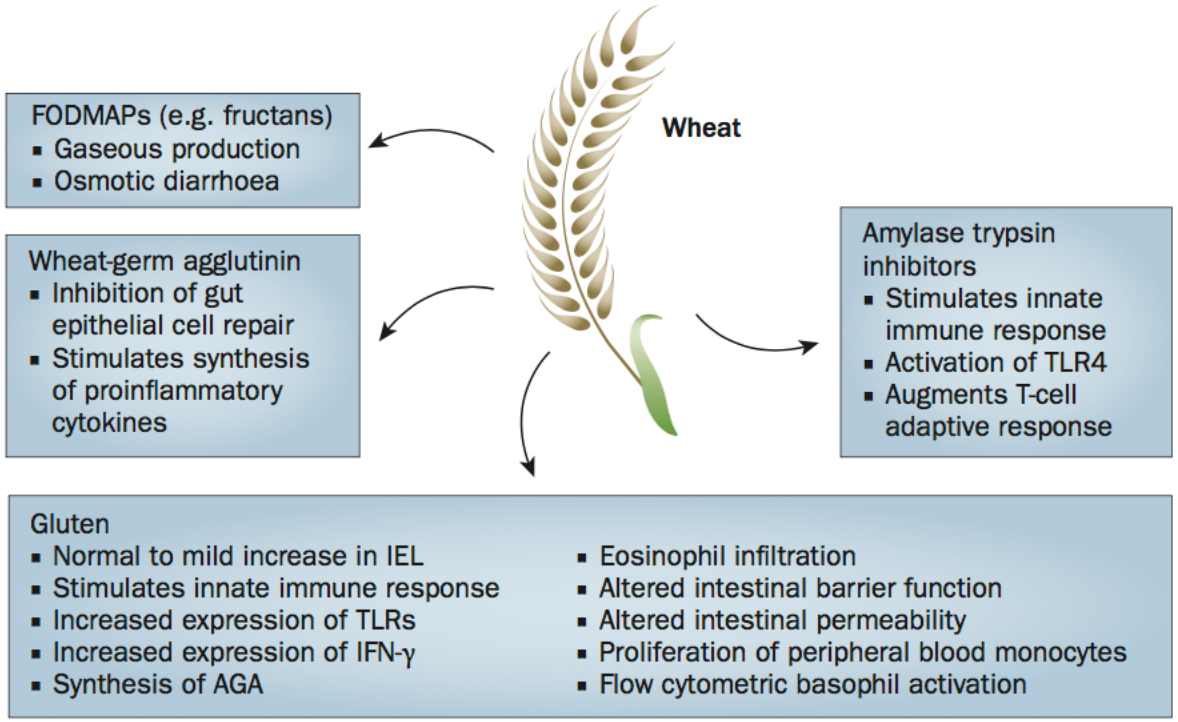


**Figure 3** | Proposed effects of wheat-based constituents that trigger clinical symptoms in NCGS. Gluten, FODMAPs, amylase trypsin inhibitors and wheat-germ agglutinin have been identified as causing symptoms in patients with NCGS. Some of the effects attributed to gluten might be caused by nongluten components. Abbreviations: AGA, antigliadin antibody; FODMAP, fermentable oligosaccharide, disaccharide, monosaccharide and polyol; IEL, intraepithelial lymphocyte; NCGS, noncoeliac gluten sensitivity; TLR, Toll-like receptor.

Wheat-germ agglutini = Lectine

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Published online: 17 Feb 2014.

*Non-Celiac Gluten Sensitivity*

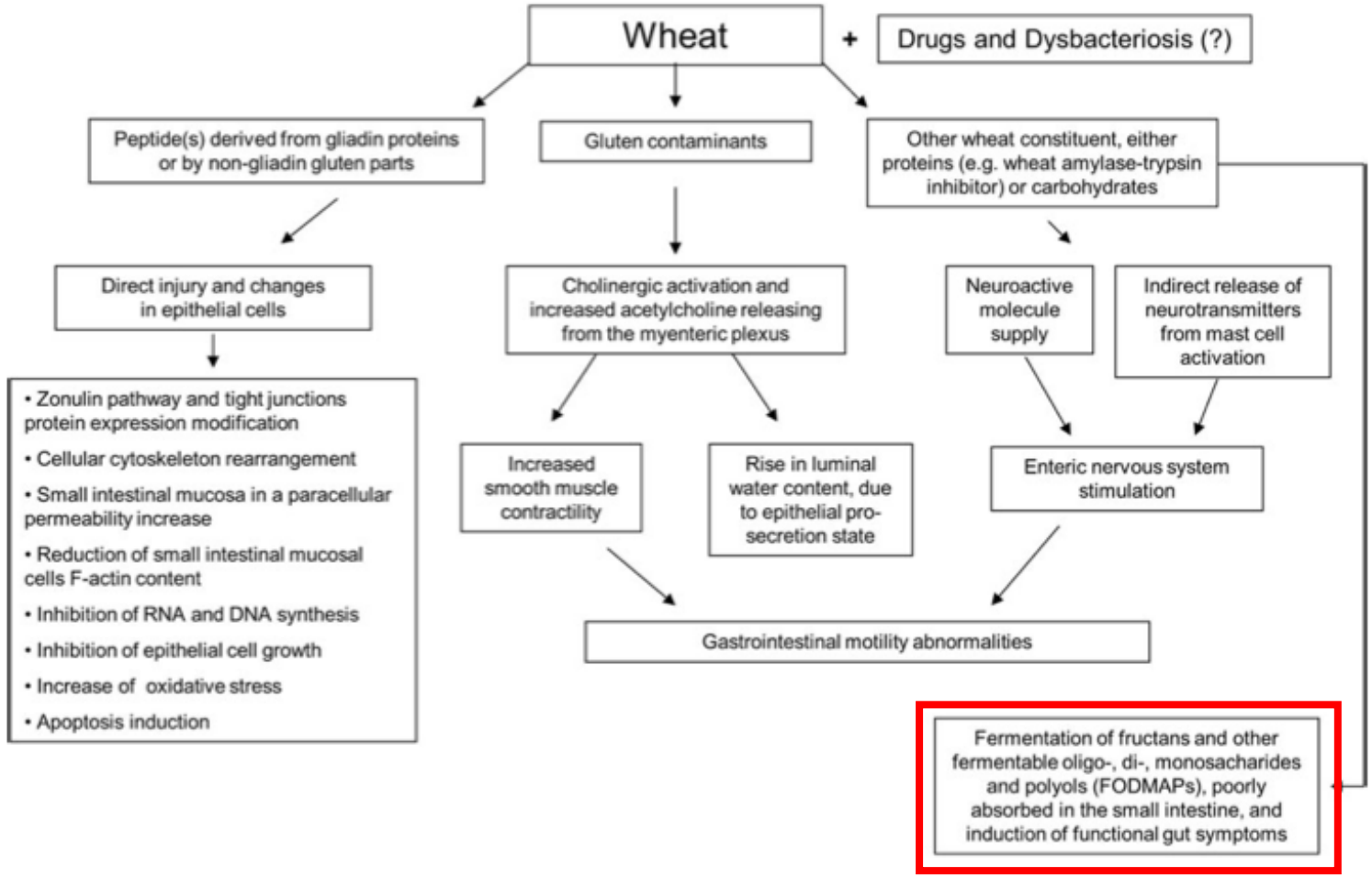



**Fig. 1.** Damage and abnormalities in epithelial cells induced by wheat through nonimmunomediated mechanisms.

# The spectrum of noncoeliac gluten sensitivity

*Imran Aziz, Marios Hadjivassiliou and David S. Sanders*

**Box 1** | Characteristic phenotypes of self-reported NCGS*

Female prevalence: 72–84%
Mean age: 38 years

**Lower gastrointestinal symptoms**

- Diarrhoea: 16–54%
- Constipation: 18–24%
- Altered bowel habit: 27%
- Abdominal pain/discomfort: 67–83%
- Bloating: 72–87%
- Weight loss: 25%

**Upper gastrointestinal symptoms**

- Epigastric pain: 52%
- Nausea: 9–44%
- Aerophagia: 36%
- Gastro-oesophageal reflux: 32%
- Aphthous stomatitis: 31%

**Extraintestinal symptoms**

- Skin rash (eczema or dermatitis): 6–40%
- Brain: depression 15–22%; foggy mind 34–42%; anxiety 39%; confusion 5%; headaches 22–54%
- Limb numbness: 6–32%
- Joint or muscle pains (fibromyalgia-like symptoms): 8–31%
- Fatigue: 23–64%
- Lack of well-being: 68%

Data taken from several reports.[16,35,39,40] *In adults. Abbreviation: NCGS, noncoeliac gluten sensitivity.

# The spectrum of noncoeliac gluten sensitivity

*Imran Aziz, Marios Hadjivassiliou and David S. Sanders*

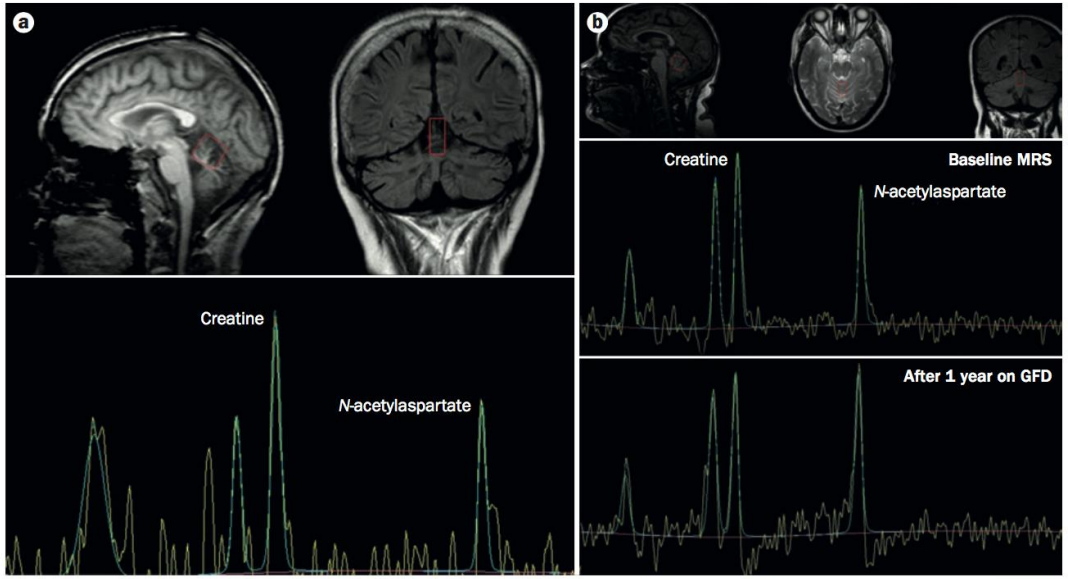



**Figure 1** | MRS of the cerebellum in patients with gluten ataxia. These patients had cerebellar ataxia with positive AGA, but no evidence of enteropathy. The voxel was placed in the cerebellar vermis, which is primarily affected in gluten ataxia. In healthy individuals, the ratio of *N*-acetylaspartate:creatine should be >1. **a** | In the first patient, the ratio of *N*-acetylaspartate:creatine was 0.56, which was markedly reduced. **b** | In the second patient the *N*-acetylaspartate:creatine ratio improved from 0.65 to 1.01 after 1 year on a GFD. This increase was associated with clinical improvement of the ataxia. Abbreviations: AGA, antigliadin antibody; GFD, gluten-free diet; MRS, magnetic resonance spectroscopy.

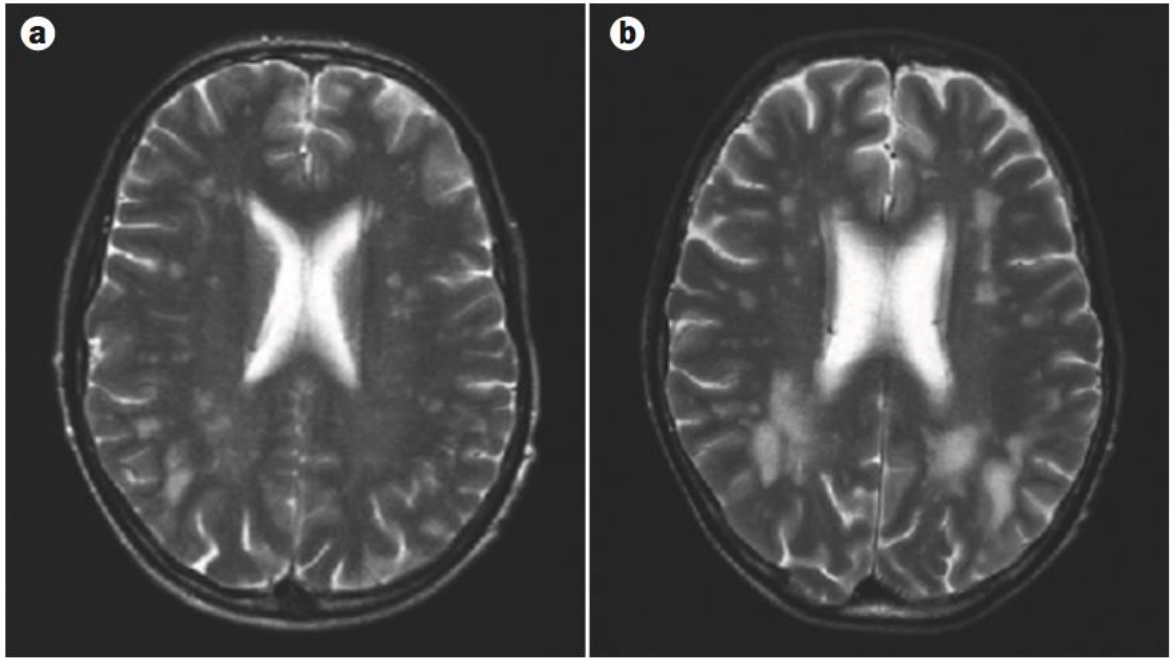
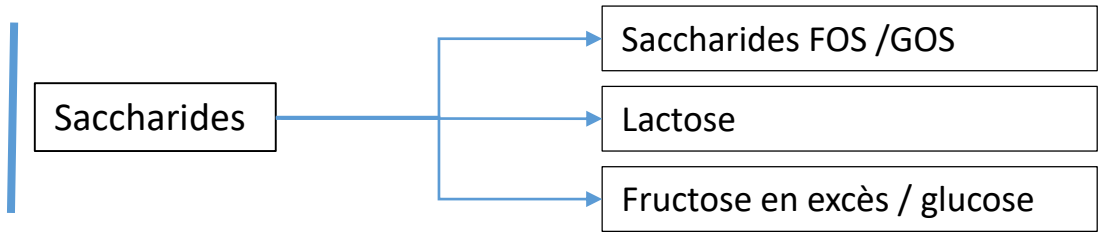



**Figure 2** | A head MRI of a 55-year-old patient with intractable headaches and positive AGA (gluten encephalopathy), but no evidence of enteropathy. Initial adherence to a GFD was associated with improvement of the headaches but the patient was unable to adhere to the diet after 3 months. The left scan at baseline shows white matter abnormalities often seen in the context of gluten sensitivity. The right scan 2 years later shows considerable progression of the white matter changes. Strict adherence to a GFD is usually associated with no progression of the white matter changes as well as resolution of the headaches. Abbreviations: AGA, antigliadin antibody; GFD, gluten-free diet.

Intolérance

# FODMAP's

- **F** ➔ **F**ermentescibles (sucres non/partiellement digérés et fermentés par les bactéries du côlon)
- **O** ➔ **O**ligo
- **D** ➔ **D**i (lactose)
- **M** ➔ **M**ono
- **A** ➔ **A**nd
- **P** ➔ **P**olyols (sorbitol, mannitol, xylitol et maltitol)



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PMCID: PMC4918736

# Efficacy of the low FODMAP diet for treating irritable bowel syndrome: the evidence to date

Wathsala S Nanayakkara,[1] Paula ML Skidmore,[1] Leigh O'Brien,[2] Tim J Wilkinson,[3] and Richard B Gearry[3]

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## Table 2

Examples of food high in FODMAPs and suitable low FODMAP alternatives

| Types of sugars | High FODMAPs food | Low FODMAP alternatives |
|---|---|---|
| Oligosaccharides | FOS<br>Grains: wheat-, rye-, and barley-based products<br>Vegetables: onion, garlic, artichokes, leeks, beetroot, and savoy cabbage<br>Fruits: watermelon, peaches, persimmon, prunes, nectarines and most dried fruit<br>GOS<br>Legumes: red kidney beans, baked beans, and soya beans<br>Vegetables: beetroot and peas | Fruit: banana, most berries (except boysenberries and blackberries), grapes, lemon, lime, mandarin, orange, kiwi fruit, pineapple, passion fruit, and rhubarb<br>Vegetables: capsicum, bok choy, green beans, parsnip, silverbeet, cucumber, carrots, celery, eggplant, lettuce, potatoes, yams, tomatoes, and zucchini<br>Grains: wheat-free grains/flour, gluten-free bread or cereal products, and quinoa |
| Disaccharides | Lactose<br>Dairy products: cows/goat milk, and yoghurt | Dairy products: lactose-free, almond or rice-based milk, yoghurt and ice cream, hard cheese, feta and cottage cheese |
| Monosaccharides | Fructose (in excess of glucose)<br>Fruits: apples, pears, watermelon, mango, cherries, boysenberries and fruit juice from high-fructose foods<br>Honey<br>Sweeteners: high-fructose corn syrup<br>Vegetable: asparagus and snap peas | Fruit: banana, grapes, honeydew, melon, kiwifruit, lemon, lime, mandarin, orange, passionfruit, paw paw, and most berries (except boysenberries and blackberries)<br>Sweeteners: maple syrup and golden syrup |
| Polyols | Sorbitol<br>Fruit: apples, pears, avocado, apricots, blackberries, nectarines, peaches, plums, prunes, and watermelon<br>Mannitol<br>Vegetables: sweet potato, mushrooms, cauliflower, and snow peas | Sweeteners: Maple syrup, and sugar (sucrose)<br>Fruits: banana, grape, honeydew, melon, kiwifruit, lemon, mandarin, orange, passionfruit, and paw paw |

**Notes:** Data from Monash University. Low FODMAP Diet Application. Available at: http://www.med.monash.edu/cecs/gastro/fodmap/. Android version accessed August 26, 2015.72

**Abbreviations:** FODMAP, fermentable oligosaccharide, disaccharide, monosaccharide, and polyols; FOS, fructo-oligosaccharides; GOS, galacto-oligosaccharides.

**FOS**

**Légumes**
Artichaut, asperges, betterave, brocoli, chou de Bruxelles, choux, aubergine, fenouil, ail, poireau, oignon (toutes les variétés), échalote.
**Céréales :**
Blé, orge, seigle, en grande quantité
ex. : pain, craquelins, biscuits, couscous, pâtes alimentaires.
**Autres**
Chicorée, pissenlit, inuline, pistaches.

**GOS**

**Légumineuses**
pois chiches, haricots rouges, lima, mungo, lentilles, fèves de soya.

**Lactose**

Lait
Yaourt
Fromage blanc .

**Fructose**

**Fruits**
Pomme, poires, mangue, melon, cerises, jus de fruits
**Édulcorants**
Fructose, sirop de maïs à haute teneur en fructose.
**Dose totale de fructose élevée**
Figues, dattes, raisins secs.
**Autres**
Sirop de maïs

**Polyols**

**Fruits**
Pomme, abricot, avocat, mûres, cerise, longane, litchi, nectarine, pêche, poire, prune, pruneau, melon d'eau.
**Légumes :**
Chou-fleur, poivron vert, champignon, maïs sucré, pois mange-tout
**Édulcorant**
Sorbitol (420), mannitol (421), isomalt (953), maltitol (965), xylitol (967).

# Outil facile

## ALIMENTATION PAUVRE EN FODMAPs


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Halmos E. et al, 'A diet low in fodmaps reduces symptoms of irritable bowel syndrome', Gastroenterology 2014; 146:67-75



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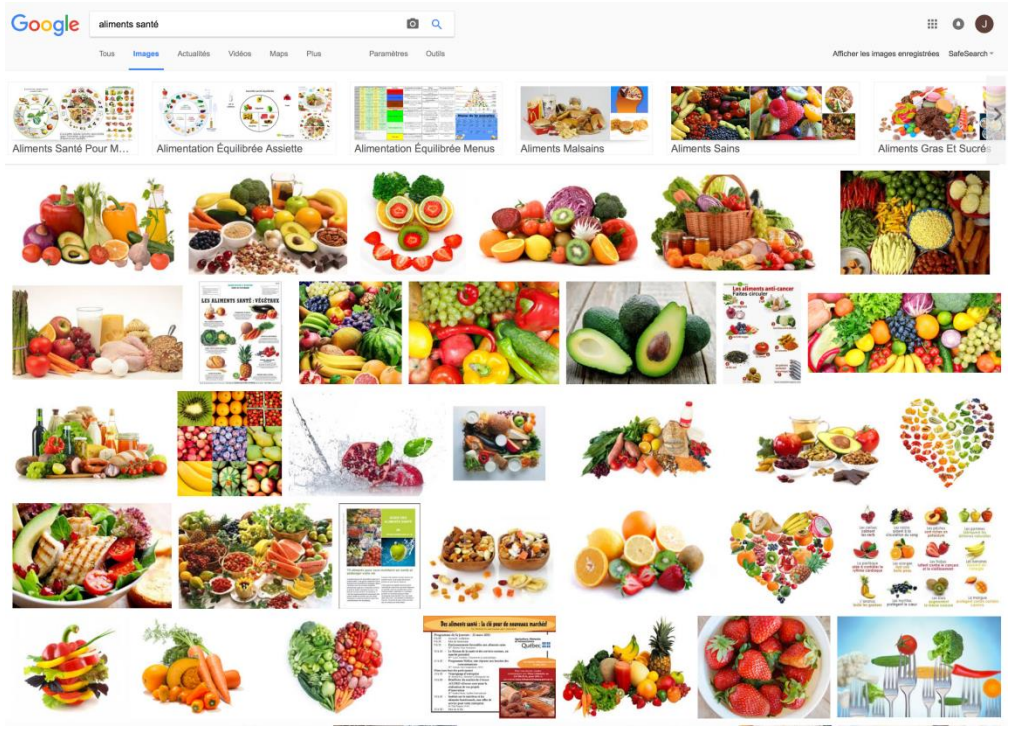
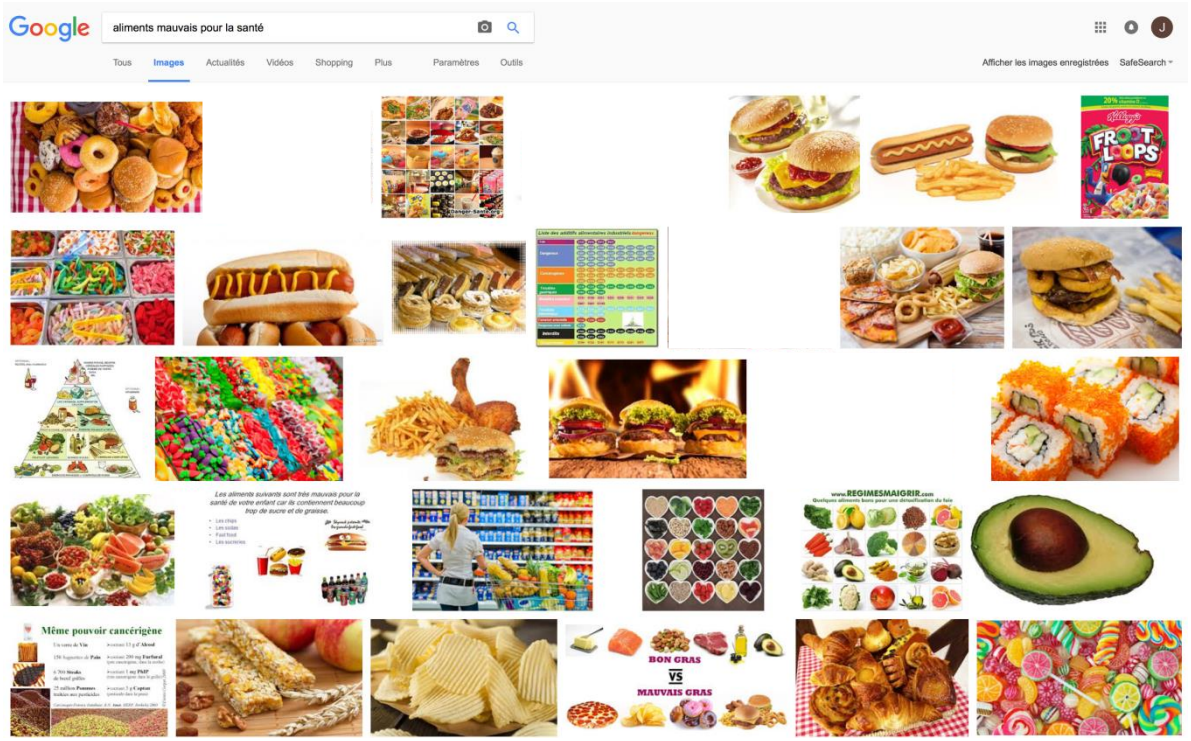
# Blanc / noir – Bon/ mauvais –
# Ou quand le bon devient l'ennemi du bien



# Vigilance

Aliments bons pour la santé

Plus de bon n’est pas mieux

FODMAP’s

Peu de bon est mauvais pour intestin et microbiote

Voir projet FOOD4gut

Professeur N Delzenne

# Traduction clinique en  proverbe Tibétain

Quand le mieux devient l’ennemi du bien

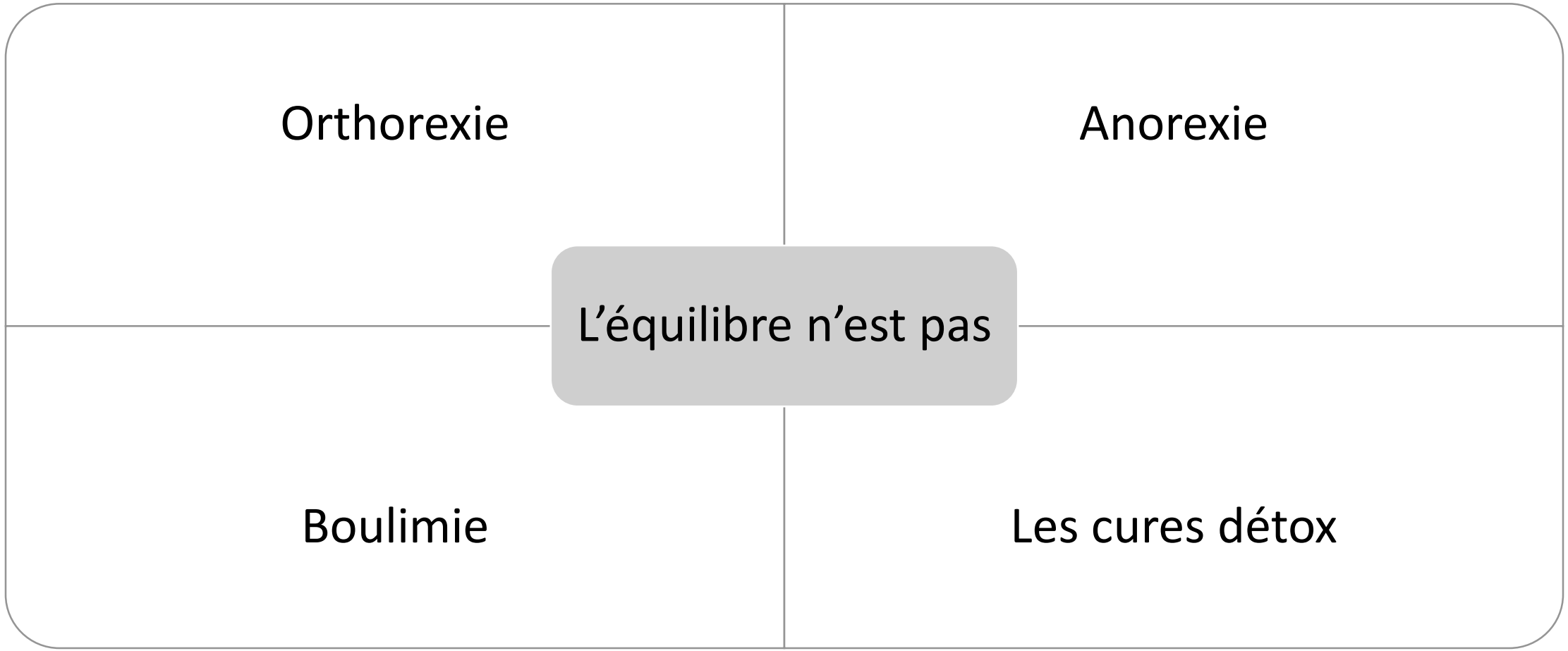
Be open-minded

but not so open-minded

that your brains fall out.

# Parce que qui mange comme une vache…

…comme une vache!!!


Orthorexie
Anorexie
L’équilibre n’est pas
Boulimie
Les cures détox

# Conclusions

Be open-minded

but not so open-minded

that your brains fall out.

Se former et comprendre

Entendre le patient

Expliquer - Informer

Nuancer

Libérer le patient