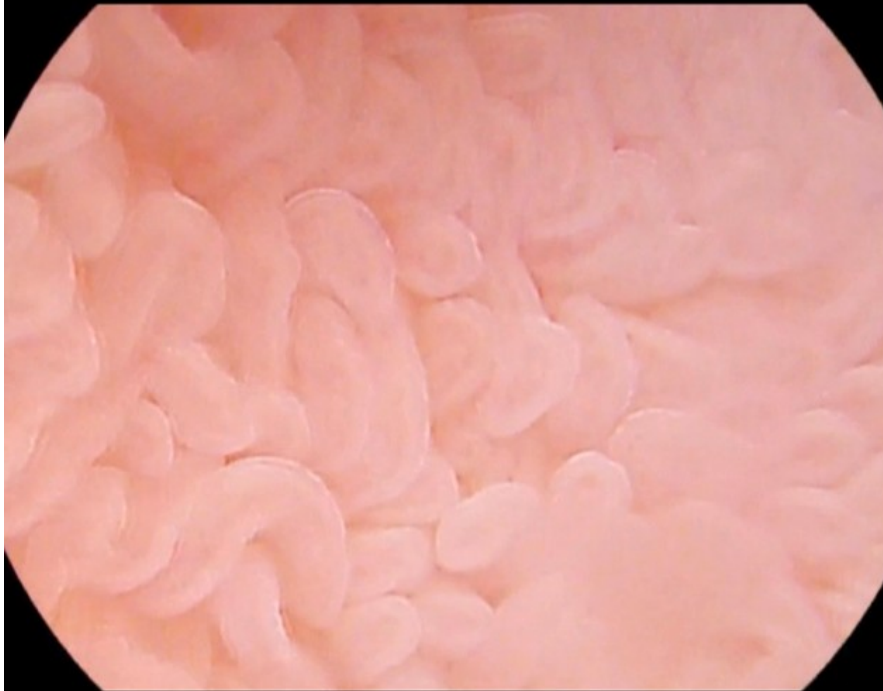


# Differential Diagnosis in Gluten Related Disorders

Professor David S Sanders

Royal Hallamshire Hospital & University of Sheffield, UK

**‘Doctor I have symptoms when I eat gluten!’:  
~10% chance of coeliac disease**



**Normal Villous  
Pattern**



**Total Villous  
Atrophy**

What is the estimated Prevalence of Non-Coeliac Gluten Sensitivity?

The screenshot shows a game show interface with a red background. At the top left, a circular timer displays '37'. At the top right, a circular counter displays 'QUESTIONS SURVIVED 0 WITH £0'. In the center, four brown rectangular boxes display percentages: 3%, 13%, 33%, and 100%. Below these boxes are four white rectangular buttons, each with a red minus sign and a red plus sign. In the center of the screen, there are five stacks of red and white rectangular blocks. At the bottom center, a large digital display shows '£1,000,000'. To the right of the display, there are links for 'FAQ' and 'Terms & Conditions'. At the bottom, there is a player list with three players: Nick, Luc, and Emma. Nick is listed as '3rd' with '0 questions with £0' and '3 restarts'. Luc is listed as '2nd' with '1 question with £1,000,000' and '3 restarts'. Emma is listed as '1st' with '0 questions with £0' and '1 restart'. On the far left, there is a Facebook icon and a button that says 'Tell friends you're playing'.

In the UK ~ 3% of population on GFD (in the absence of coeliac disease) + 20% overlap with IBS symptoms

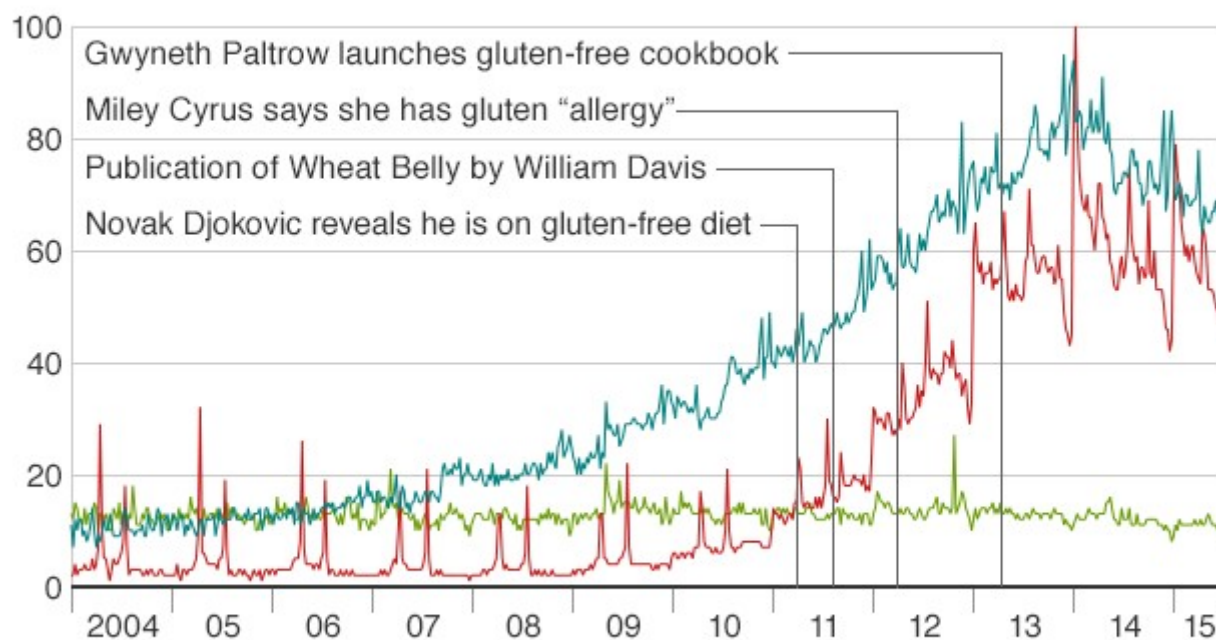


*Aziz I Am J Gastroenterol 2018 &  
Aziz I et al Eur J Gastroenterol &  
Hepatol 2013*

# Google Gluten Free Searches

## Gluten free references

Interest over time — “Gluten free” — “Paleo” — “Celiac”\*



\*US spelling of Coeliac

Source: Google Trends

BBC



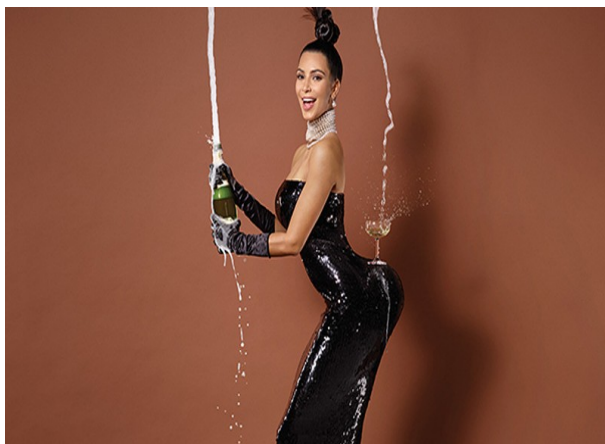
# Is Gluten the Devil!

## Hype?!

## Health?!



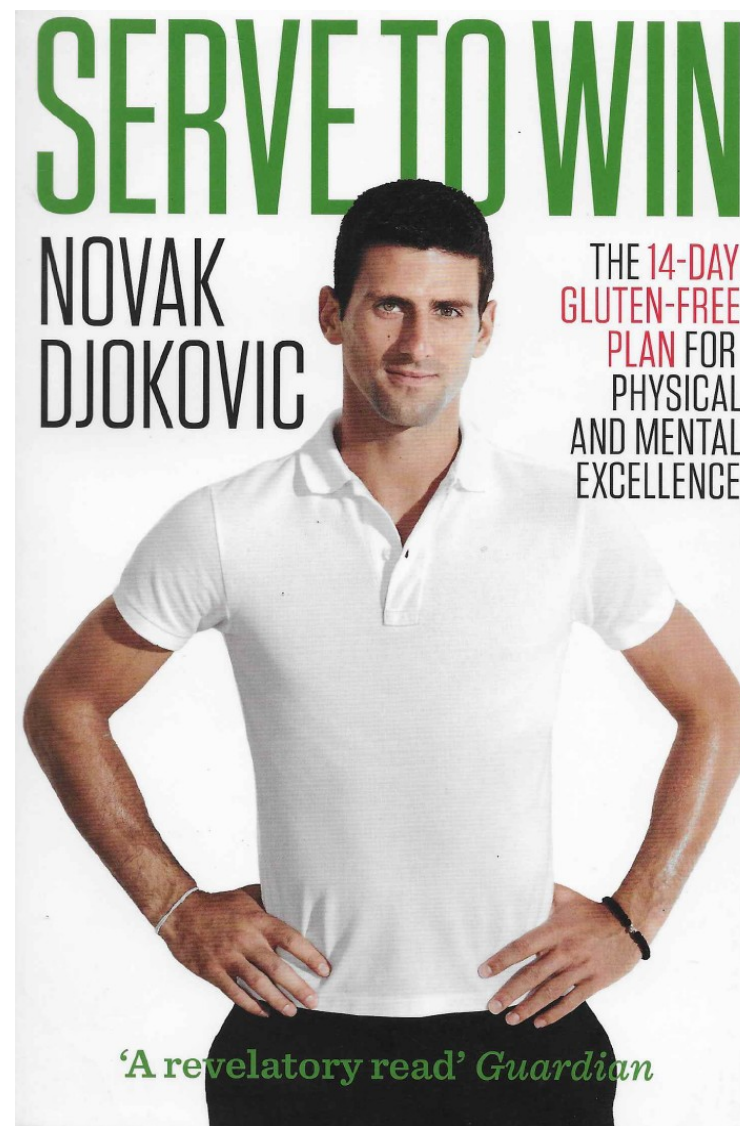
# What Do These Stars Have In Common?



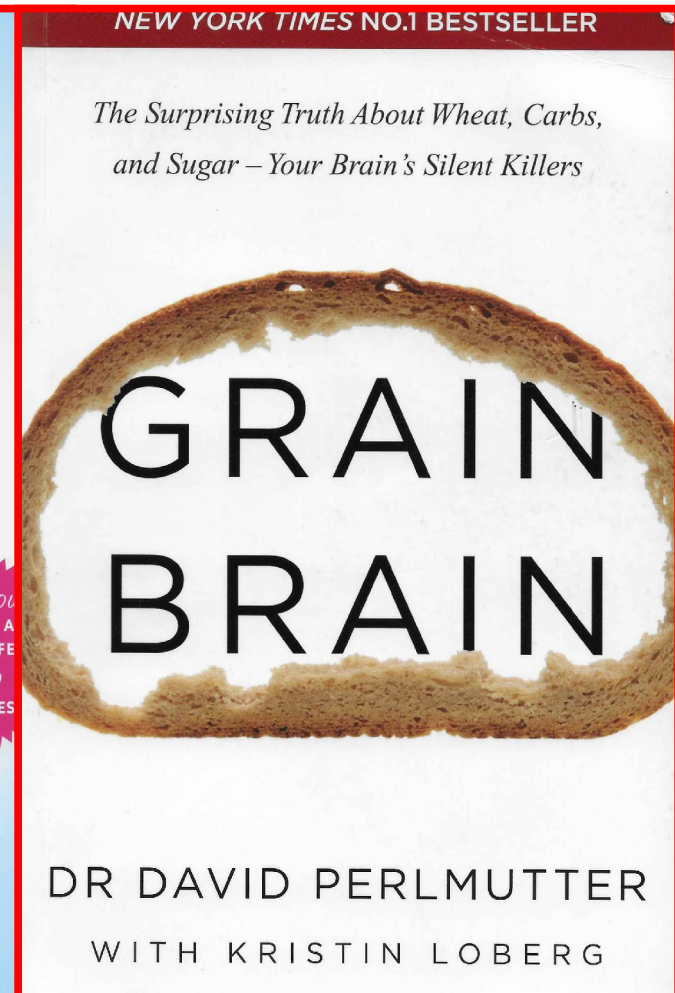
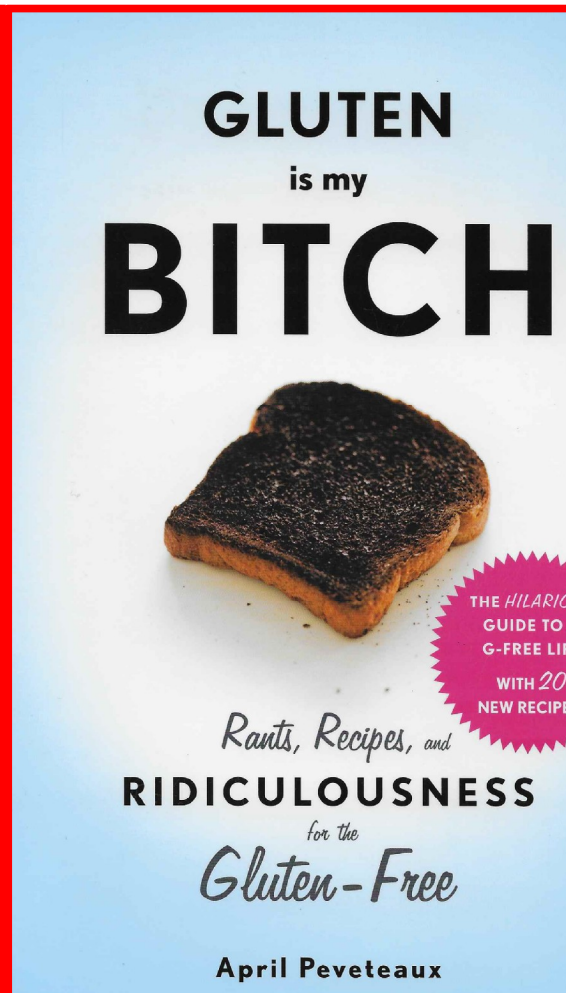
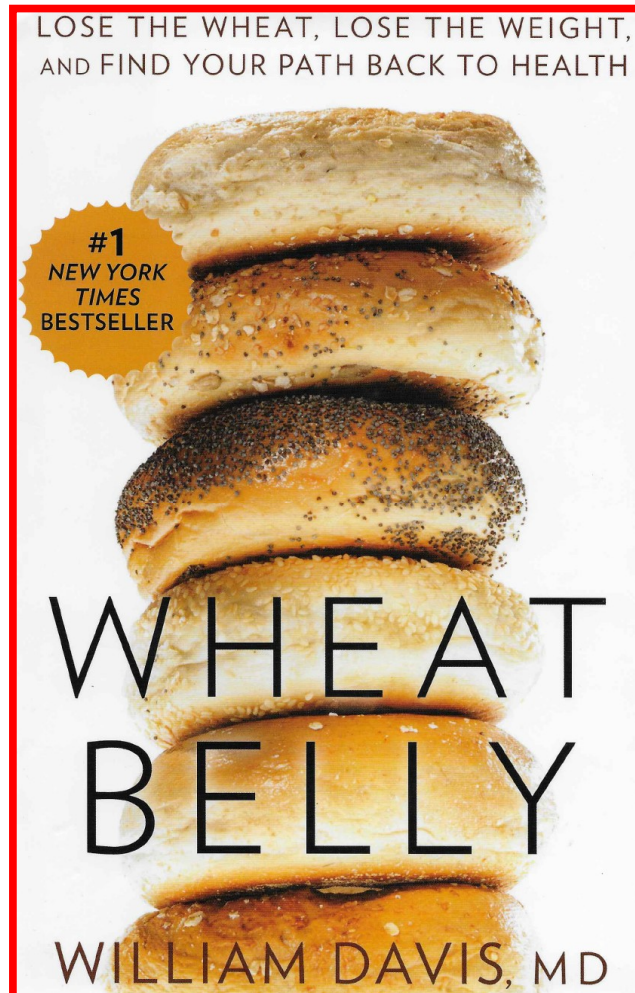




Sensitivity: Internal









## Gluten Does Not Induce Gastrointestinal Symptoms in Healthy Volunteers: A Double-Blind Randomized Placebo Trial



Iain David Croall,<sup>1</sup> Imran Aziz,<sup>2</sup> Nick Trott,<sup>2</sup> Paola Tosi,<sup>3</sup> Nigel Hoggard,<sup>1</sup> and David S. Sanders<sup>2</sup>

Gastroenterology 2019;157:881–883

### Will Science Sway Beliefs About Gluten?



See “Gluten does not induce gastrointestinal symptoms in healthy volunteers: A double-blind randomized placebo trial,” by Croall ID, Aziz I, Trott N, et al, on page 881.

controls, so such a study was needed to fill this gap. This study showed that, among healthy subjects started on a background GFD, ingesting 14 g/d of gluten did not induce gastrointestinal symptoms or fatigue,<sup>1</sup> compared with a gluten-free placebo.



## NON-CÆLIAC GLUTEN SENSITIVITY?

SIR,—Further to the letter on food allergy by Professor Dickerson and colleagues (April 8, p. 773) we would like to report the case of a 43-year-old woman who presented in January, 1974, with a 4-month history of loose motions, three times a day with no blood or mucus. The diarrhoea was accompanied initially by periumbilical colic, which recurred intermittently, and abdominal distension, but she had not lost weight and had retained her appetite. She had been taking tetracycline for 6 years for acne conglobata; she smoked 15 cigarettes a day but drank very little. She had no pets and had not been abroad.

Examination was unremarkable apart from the acne. Investigations, which included examination of faeces for ova, cysts, parasites, and occult blood, X-rays (barium meal, small-bowel meal, barium enema), sigmoidoscopy, and jejunal biopsy, were all normal except for a hiatus hernia. She did not improve when tetracycline was withdrawn or when antidiarrhoeal agents or tranquillisers were tried. Her symptoms continued for 2 years. However, when a gluten-free diet was tried the diarrhoea stopped within 4 days and the patient felt very much better. Jejunal biopsy was repeated after 6-week gluten challenge (accompanied by recurrence of diarrhoea) but was normal in every way including normal intraepithelial lymphocyte-counts. Resumption of the gluten-free diet was followed by a rapid disappearance of all her symptoms.

We consider it very likely that this woman's symptoms were due to gluten sensitivity. Her recovery is unlikely to be a placebo response because other treatments had failed; moreover,

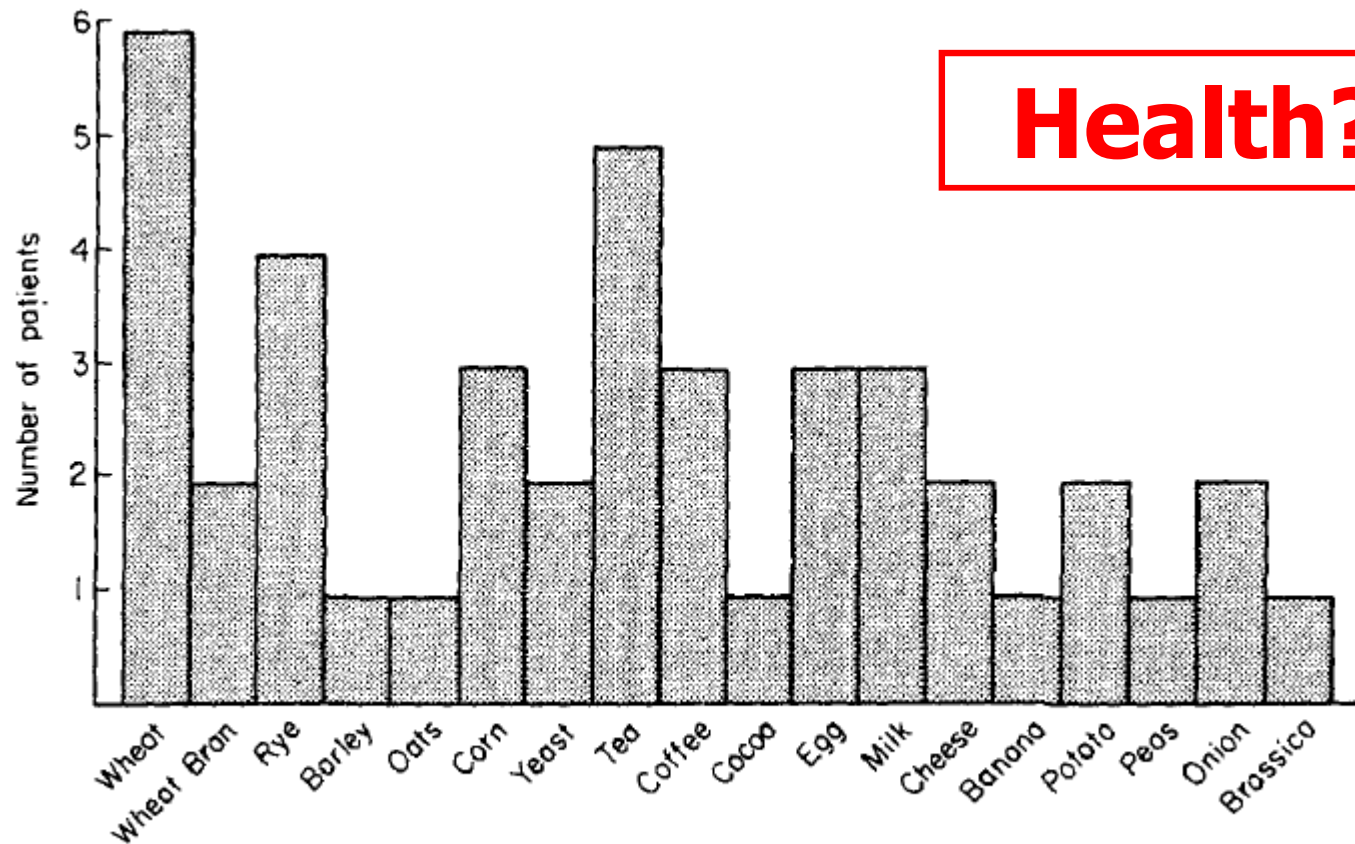
A. ELLIS

B. D. LINAKER

THE LANCET, JUNE 24, 1978



# Food intolerances and IBS



**Health?!**

The number of patients with IBS intolerant to each of the 18 foods identified.

*Journal of Human Nutrition and Dietetics (1991), 3, 19-23*



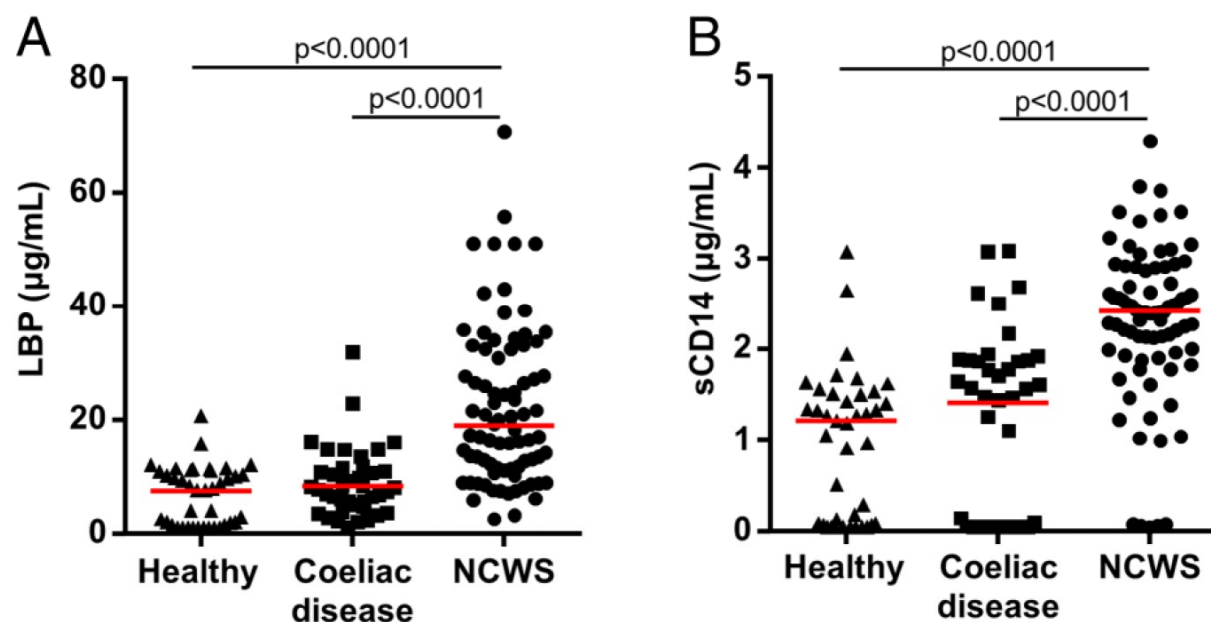
ORIGINAL ARTICLE

# Intestinal cell damage and systemic immune activation in individuals reporting sensitivity to wheat in the absence of coeliac disease

Melanie Uhde,<sup>1</sup> Mary Ajamian,<sup>1</sup> Giacomo Caio,<sup>2</sup> Roberto De Giorgio,<sup>2</sup> Alyssa Indart,<sup>1</sup> Peter H Green,<sup>1,3</sup> Elizabeth C Verna,<sup>1</sup> Umberto Volta,<sup>2</sup> Armin Alaedini<sup>1,3,4</sup>

## What are the new findings?

- ▶ Reported sensitivity to wheat in the absence of coeliac disease is associated with significantly increased levels of soluble CD14 and lipopolysaccharide-binding protein, as well as antibody reactivity to microbial antigens, indicating systemic immune activation.
- ▶ Affected individuals have significantly elevated levels of fatty acid-binding protein 2 that correlates with the markers of systemic immune activation, suggesting compromised intestinal epithelial barrier integrity.



**Wheat accounts for the largest quantity of fructans in our diet because bread (containing fructans) is the most eaten food stuff**

## What is the Causal Agent?

**Wheat-germ Agglutinin**

**Gluten**

**FODMAP's**

**Amylase Trypsin Inhibitors**

**Nocebo**



Aziz I, Hadjivassiliou M, Sanders DS. *Nature Reviews Gastroenterology & Hepatology* 2015

Whelan K et al *Intern J Food Sci & Nutr* 2011  
Dunn S et al *European J Clin Nutr* 2011





## REVIEW

DOI: <http://dx.doi.org/10.15403/jgld.2014.1121.273.avy>

## Clinical Application of Dietary Therapies in Irritable Bowel Syndrome

Anupam Rej<sup>1</sup>, Amanda Avery<sup>2</sup>, Alexander Charles Ford<sup>3</sup>, Anne Holdoway<sup>4</sup>, Matthew Kurien<sup>1,5</sup>, Yvonne McKenzie<sup>6</sup>, Julie Thompson<sup>7</sup>, Nick Trott<sup>1</sup>, Kevin Whelan<sup>8</sup>, Marianne Williams<sup>9</sup>, David Surendran Sanders<sup>1,5</sup>

J Gastrointestin Liver Dis, September 2018 Vol. 27 No 3: 307-316

Type of diet	N=number	Response
FODMAP	501	50-76%
GFD	255	34-71%
Wheat Free	276	30%



Review

## Gluten-Free Diet and Its 'Cousins' in Irritable Bowel Syndrome

Anupam Rej<sup>1</sup> and David Surendran Sanders<sup>1,2,\*</sup>

<sup>1</sup> Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield S10 2JF, UK; anupam.rej@sth.nhs.uk

<sup>2</sup> Academic Unit of Gastroenterology, Department of Infection, Immunity and Cardiovascular Disease, University of Sheffield, Sheffield, S10 2RX, UK

\* Correspondence: david.sanders@sth.nhs.uk; Tel.: +0114-226-1179

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Journal of **Gastroenterology**  
and **Hepatology**



doi:10.1111/jgh.13701

REVIEW ARTICLE

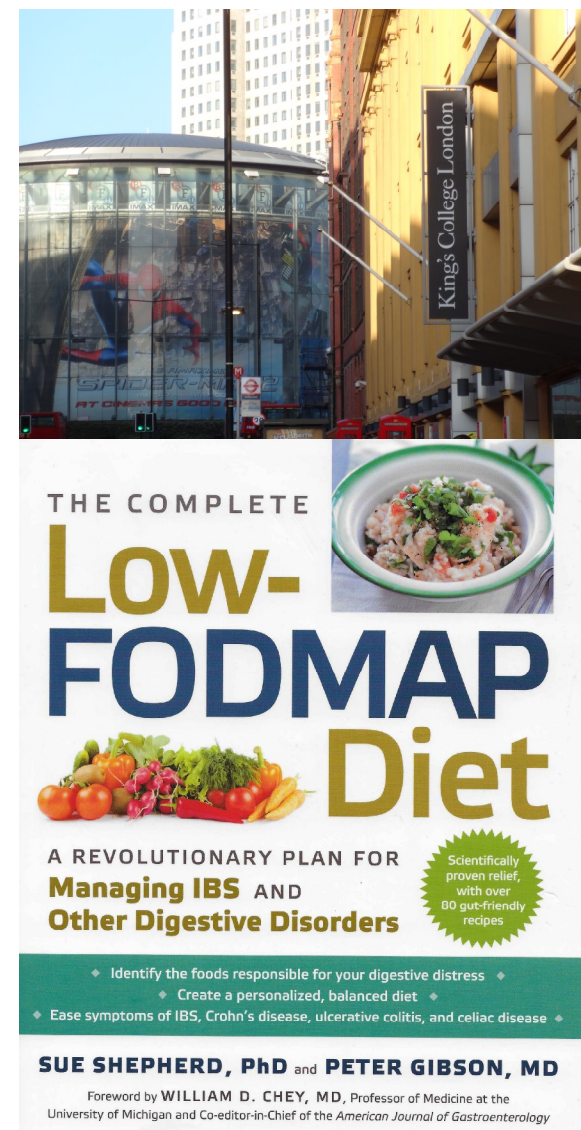
## When the low FODMAP diet does not work

Emma P Halmos

Department of Gastroenterology, Central Clinical School, Monash University, Melbourne, Victoria, Australia

- Top Down approach = Low FODMAP (elimination)
- Bottom Up approach = GFD or wheat free (exclusion)

Sensitivity: Internal



# The role of gluten in GI disease including IBS is all about how the patient presents to the doctor

## SPECTRUM

DEFINE YOUR PATIENT

Rej A& Sanders DS *Nutrients* 2018

