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WHEAT, BREAD, GLUTEN AND HEALTH:

Where do we
stand in 2024?

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During the past decade an increasing number of consumers have reduced their consumption of wheat products, due to concerns about adverse effects of wheat, bread and gluten on health. This has been driven by social media posts, articles in the press and popular books claiming that consumption of wheat causes gastrointestinal complaints, obesity, diabetes, cardiovascular and immune diseases. As a result, the number of people reporting health complaints after consumption of bread and other foods that contain wheat and gluten has increased sharply in a relatively short period of time.

Interestingly, many consumers who report adverse reactions after eating modern factory-produced bread but not after eating pasta or after eating bread made using traditional processes or from modern spelt bread, although all these products contain gluten. An important point here is that the symptoms perceived are real but that there is in most cases no clear organic explanation.

The lack of plausible explanations (and mechanisms) for these reactions led to the establishment of the international research consortium ‘Well on Wheat?’ in 2016. The aim of the research program was to determine whether differences in types of wheat and bread-making processes, and the naturally occurring compounds present in the grains and breads, could play a causal role in the gastrointestinal complaints experienced.

All steps in the grain processing chain that influence the composition of the bread, and thereby may impact on health and / or the perception of gastrointestinal complaints, were evaluated, namely: grain cultivation, milling, mixing, baking and consuming bread.

In the “WellonWheat?” research program Maastricht University, Wageningen University Research, Rothamsted Research (UK) and the Dutch Bakery Center, worked together with other Universities and crop research centres. “Well on Wheat?” was financed by a grant of the Dutch Government “TKI- Top Knowledge Institute” and by a wide range of additional partners* from the Agri-Food chain who donated unrestricted research grants. *These

partners are: AB-Mauri bakery Ingredients, , Made, Netherlands; Borgesius Holding BV-Albert Heijn, Stadskanaal Netherlands; CSM innovation Bakery Center, Bingen, Germany; CYMMIT, Texcoco, Mexico; DSM Food Specialties, Delft, Netherlands; Fazer Bakeries Oy, Helsinki, Finland; Health Grain Forum, Vienna, Austria; ICC- Intl. Vienna, Austria; IWGA, Kansas 66210, USA; Lantmännen EK , Stockholm, Sweden; Mondelez , Saclay, France; Nederlands Bakkerij Centrum, Wageningen, Netherlands; Baking Industry Research Trust, Wellington, New Zealand; Nutrition et Sante, Revel, France; Puratos BV, Groot Bijgaarden, Belgium; Rademaker BV-Bakery equipments, Culemborg, Netherlands; Sonneveld Group BV, Papendrecht, Netherlands; Zeelandia- HJ Doeleman BV, Zierikzee, Netherlands.

Causes and prevention of health problems related to grain consumption

Gastrointestinal complaints due to eating grains that contain gluten can be divided into three types: celiac disease, gluten sensitivity in the absence of celiac disease and wheat allergy.

What is gluten?

Gluten is a protein fraction that is present in all types of wheat: bread wheat, spelt, emmer, durum, einkorn, triticale (a man-made cross between wheat and rye) and tritordeum (cross between durum and wild barley). These include types of wheat are marketed under trade names, such as Kamut™ and Khorasan™ wheat. Semolina, farro, farina, bulgur and couscous are all products made from wheat and all contain gluten.

Gluten is a mixture of related proteins that are stored in the grain to support germination. They constitute 70 to 75 percent of the total proteins in wheat grain and are classified into two types, gliadins and glutenin's. The amount and composition of the glutenin fraction is an important factor determining dough strength, and hence breadmaking quality, with the gliadins contributing to dough viscosity and extensibility.

Barley and rye grains contain related proteins, called hordeins and secalins, and are also considered as ‘gluten sources’ in ‘gluten-free recommendations’.

In addition to gluten, wheat also contains other components

that may lead to intestinal complaints in some people, including amylase-trypsin inhibitors (ATIs) and rapidly fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs), the most important being fructo-oligosaccharides (fructans). The fermentation of FODMAPs may result in rapid gas formation causing sensations of bloating in the large intestine and an urge to defecate (figure 1).

Gluten and Celiac Disease (CD)

Celiac disease is caused by exposure of the intestinal epithelium to peptides released by the partial digestion of gluten.

Gluten, like most other plant proteins, is easily digestible (>94 percent). However, this digestion may release fragments (peptides containing the amino acids proline and glutamine) that cannot be further broken down into individual amino acids by our digestive enzymes. In certain circumstances, these peptides can pass through the intestinal wall, after which in a series of steps, they are detected by our immune system as a foreign, unwanted protein. This can then lead to inflammatory reactions and cause damage to the intestinal wall, which reduces the absorption surface of the intestine and can lead to nutritional deficiencies.

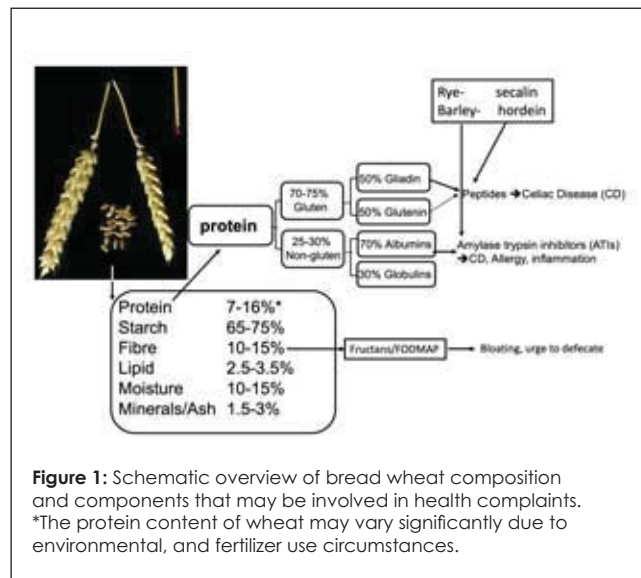
Many celiac-active peptides (often called epitopes) have been identified which are particularly abundant in (but not restricted to) gliadins. Research has shown that CD can only develop in individuals who have a specific hereditary predisposition to it. Depending on the region of the world, this genetic predisposition is present in approximately 25-40 percent of the total population. However, only approximately 4 percent of these individuals develop the disease, which results in an overall CD-prevalence of about 1 percent of the global population.

Complexity of the complaint pattern

The abdominal and health complaints frequently reported to be associated with wheat and gluten consumption overlap with the patterns of symptoms of other diseases, such as intestinal inflammatory diseases and irritable bowel syndrome (IBS). As a result, CD may fail to be diagnosed and the CD may be higher than the commonly quoted 1 percent of the population. CD is more common in women than in men (ratio 60-40 percent), the reason for this is unclear. CD-related intestinal damage and other symptoms are greatly reduced or almost completely disappear after following a strict (lifelong) gluten-free diet.

Wheat allergy

Food allergy usually results from reactions to specific proteins in consumed foods (e.g. nuts, fish, crustaceans and shellfish, milk protein, soy) and occurs in approximately six percent of children



and three percent of adults. Figures for wheat allergy in children vary depending on age and country between <0.1% and 1 percent but then 80 percent of these children ‘outgrow’ the allergy before reaching the age of eight and 96 percent before the age of 16. The percentage of adults suffering from wheat allergy is therefore low, approximately 0.25 percent.

Based on protein analysis wheat grains contains over 1000 different proteins, several of which are classified as potential allergenic. Wheat allergy occurs as respiratory allergy (bakers’ asthma), contact urticaria (hives), and as food allergy.

The incidence of asthma (1-10 percent) and hay fever (18-29 percent) is high in professional bakers due to exposure to flour dust, which can enter the lungs during breathing. The allergic symptoms are usually reduced or disappear completely after avoiding exposure to wheat and other grains that contain gluten.

Gluten or wheat sensitivity?

There have been numerous suggestions in the media and popular press, including the popular books ‘Wheat Belly’ and ‘The Food Hourglass’, that gluten/bread consumption leads to health problems in many people due to ‘being sensitive to gluten’. This has greatly stimulated consumer demand for ‘gluten-free’. However, important questions remain, on the true nature of the condition, how it can be diagnosed, the true prevalence in the population and how (and by what) the reaction is triggered.

Originally, the term ‘non-celiac gluten sensitivity’ (NCGS) was used because gluten was considered to be the causative agent. However, because other components from wheat may also play a role, the term



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‘non-celiac wheat sensitivity’ (NCWS) is increasingly used. Table 1 provides a brief overview of the main characteristics of the wheat-related diseases.

Do non-gluten components trigger adverse reactions?

Amylase-trypsin inhibitors (ATIs) are natural plant proteins that inhibit the digestion of the starch (by amylase) and protein (by trypsin) in the wheat grain by harmful insects and thereby contribute to protection of the plant. In this respect they may be considered as ‘natural plant pesticides’. However, ATIs, particularly in bakers’ asthma, may play a role in the development of CD.

Gluten and ATIs occur together in the grain and flour and are therefore both present in wheat products. They are also difficult to separate which makes it difficult to separate their effects in gluten-related disorders.

In many studies, vital gluten (which is prepared by industrial separation from starch) has been added to a gluten-free meal (which itself serves as a control), assuming that it is 100 percent pure. However, this gluten-isolate also contains a significant quantity of ATIs, as well as other proteins. Consequently, differences in responses to consumption of ‘gluten-free’ and ‘with gluten’ foods could be caused by gluten, ATIs or both components. In addition, ATIs exist in multiple forms (at least 19 ATI isoforms in wheat) which may differ in their biological activity. Because ATIs are very difficult to purify, the effects of individual isoforms have not been determined. As a result, it is not known which isoforms and in what amounts may cause adverse health reactions in humans.

Furthermore, wheat products also contain indigestible dietary fibres, which pass into the colon, where they are subject to fermentation by the microbiota. Some of the non-digested/non-

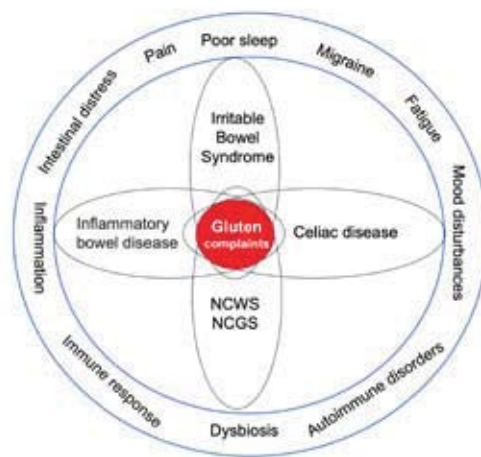


Figure 2: The strong similarities between symptoms that patients report when self-diagnosing and symptoms of other gastrointestinal disorders makes it difficult to make a rapid and correct diagnosis. Dysbiosis = abnormal intestinal flora (microbiota). NCWS: Sensitivity to wheat in the absence of CD, NCGS: Sensitivity to gluten in the absence of CD

absorbed carbohydrates are called FODMAPs (Fermentable Oligo-, Di- and Monosaccharides and Polyols). These can lead to osmosis-induced water retention in the intestine while fermentation may result in gas formation, which may result in unpleasant bloating, flatulence, abdominal pain and loose stools/diarrhoea. There is increasing evidence that FODMAP (not gluten) are the cause of many of the complaints reported as gluten sensitivity.

When does non-celiac wheat/gluten sensitivity occur?

There is uncertainty about the occurrence of NCWS/NCGS. The available figures are self-reported and differ worldwide, with a



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range reported for European countries of 6.2 percent to 13 percent.

It is striking that the reported gastrointestinal complaints are usually present within a very short time after consumption (minutes to hours). The precise cause of the complaints is often unknown and this makes it difficult to provide specific advice to patients. Because the experience of symptoms can be strongly influenced by 'expectations created by hearsay', the possible role of psychological effects is very relevant. A reliable diagnosis of NCWS is at present problematic because no reliable biomarkers are available and many of the symptoms reported during 'self-diagnosis' overlap with other conditions such as IBS and chronic intestinal inflammation (IBD).

To better understand NCWS/NCGS, a study was carried out in Italy on patients who were referred to a university gastrointestinal clinic for a period of two years because of their complaints. 292 patients who reported that they were certain that their symptoms occurred immediately after eating gluten, were selected for further study. These individuals were required to follow a gluten-free diet

for six months and the occurrence of symptoms was recorded. After this gluten-free period, gluten was added to the diet for 1 month and symptoms were recorded.

This showed that that 86 percent of people with self-reported wheat/gluten sensitivity did not experience any effects when gluten was reintroduced into the diet. In addition, 6 percent of those selected were shown to suffer from celiac disease. It is therefore important to rule out celiac disease in case of persistent gastrointestinal complaints (which can be done by a blood test).

A small group of patients (6.88 percent) experienced symptoms after ingesting gluten (which would also contain ATIs) without celiac disease. The observation of immune reactions, changes in intestinal permeability (which allows unwanted substances and bacteria to enter the body) and increased numbers of white blood cells in the intestines in some of these patients shows that further research into the possible causes is urgently needed.

(References available upon request)

Table 1: overview of the most important characteristics of the wheat-related disorders. CD=celiac disease, WA=wheat allergy, NCWS/NCGS=self-reported wheat/gluten sensitivity in the absence of celiac disease. In a Dutch study this figure was 6.2 percent. *Based on testing after a period of gluten-free eating followed by a gluten challenge test, the true figure is estimated to be lower (5-7 percent).

	Celiac disease (CD)	Wheat allergy (WA)	NCWS/NCGS
Prevalence	0.6-2%, mean 1%, more in women than in men (ratio 2:1 - 3:1).	Ca. 0.25%	6.2% to 13%*.
Time to complaints	Weeks to years	Minutes to hours	Hours to 2 days
Gut surface damage	Almost always	Not observed	Not observed
Symptoms	Complaints pattern not different between CD, WA en NCWS. Intestinal bloating, pain, diarrhea, nausea, irregular defecation/ consistency, gut microflora disturbances, inflammation. Other complaints: general malaise, tiredness, headache, anxiety, foggy mind, impaired quality of life.		

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