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Homo glutenicus

One Woman's Story

Melanie Turner was a healthy, dynamic young woman in 1992 at age 18 when she went away to college. She had been an active child, teenager, and co-captain of her high school lacrosse team until her first year of college when numerous medical problems surfaced. After only a few months of freshman dormitory living, she began to experience severe numbness in her hands and feet. At times, "the numbness was so intense I couldn't feel my legs and feet when I was walking." Soon, the numbness ascended her legs all the way up to her knees.

Melanie's family physician referred her to a rheumatologist who diagnosed her with Raynaud's disease, a disorder caused by spasm of the arteries in the arms and legs. Her doctor prescribed Procardia, a calcium channel blocker frequently used to treat angina, (chest pain caused by a lack of sufficient oxygen reaching the heart muscle). Procardia works by relaxing the smooth muscle contained in arterial walls and is often used to treat Raynaud's disease, but Melanie didn't respond well to the drug. "I didn't feel right," she said, "and my heart bothered me."

Additionally, Melanie suffered from extreme abdominal pain, which was diagnosed as an "intestinal infection." She became "sick all the time" and battled frequent yeast and bladder infections. A number of doctors prescribed various antibiotics, and over the course

of many months, Melanie was given penicillin, amoxicillin, Cipro, and others. Ultimately, blood tests showed that her liver enzymes were elevated and Melanie was diagnosed with autoimmune hepatitis. An endocrinologist prescribed prednisone for treatment of the autoimmune liver disease.

Melanie continued having "one problem after another." Severe and persistent joint pains soon made her situation worse. Joint pain is often associated with autoimmune hepatitis, therefore, another drug–sulindac–was added to the growing list of Melanie's daily medications, but she developed severe side effects from the drug, including fever and a widespread rash, so sulindac was withdrawn.

During the next few years, Melanie developed muscle weakness, persistent fatigue and was diagnosed with Hashimoto's thyroiditis, another autoimmune disorder. Accordingly, she was placed on a regimen of thyroid hormone replacement therapy (Synthroid).

In her early 20s, Melanie endured several bouts of pleurisy, an inflammation of the membranes surrounding the lungs. She also developed ulcers of the mucous membranes of her mouth and a skin disorder known as dermatitis herpetiformis.

Melanie continued taking prednisone for her liver condition and developed many food allergies throughout her 20s, saying "I got to the point where I was allergic to more foods than the ones I could eat." She also became allergic to the most commonly prescribed antibiotics and continued to suffer frequent yeast and urinary tract infections.

At 27 years old, a rheumatologist told Melanie she had lupus (systemic lupus erythematosusm SLE). Melanie had experienced all of the disturbing symptoms of lupus including fatigue, hair loss, pleurisy, joint pains, and mouth ulcers as well as periodic worsening of symptoms known as "flares." In 2001 she had a serious flare and developed pericarditis, a dangerous condition involving an accumulation of fluid around the heart.

In spite of everything, Melanie got married, and at age 32 became pregnant, but following successful delivery of her baby girl, Melanie's gastrointestinal pain and constipation worsened. Once again, she found herself sitting in a doctor's office, but this time an astute gastroenterologist finally identified the diagnosis that explained almost all of Melanie's problems: celiac disease. The doctor recommended a gluten-free diet. Celiac disease and its precursor,

gluten intolerance could account for the majority of Melanie's extensive list of health problems.

Gluten intolerance and celiac disease are terms that describe a continuum of signs and symptoms involving an immunologic response and inflammatory reaction to gluten. Gluten proteins are contained in wheat, barley, and rye, staple grains of the Western diet and is abundant in breads, flours, pastries, pizza, pasta, breakfast cereals, gravies, sauces, and soups. Almost 40% of Americans and Western Europeans are genetically susceptible to gluten intolerance. A proportion of these individuals, like Melanie, can develop immune reactions to gluten, which can result in a wide variety of diseases.

Genetic susceptibility as well as various environmental triggers can cause certain individuals to develop signs and symptoms of gluten intolerance which can be considered early stages of an immunologic response to gluten. Celiac disease is as an autoimmune disease where eating gluten causes damage to the small intestine. It is a multisystem disorder which can involve the gastrointestinal, immune, endocrine, reproductive, muscle, and nerve systems.

Melanie attempted to follow a gluten free program, eliminating products containing wheat, rye, and barley. She had recently given birth and felt a need to add protein to her diet, so she began drinking a protein-rich, rice-based liquid thinking it would be safe, as rice contains no gluten, but after a few days Melanie's gastrointestinal symptoms, including persistent diarrhea and abdominal pain, increased, and she began to lose weight. At 5 feet 4 inches tall, she became markedly underweight, weighing only 90 pounds. She returned to the most recent physician who had diagnosed her with celiac disease, and he explained that the protein drink contained wheat-based fillers and was a significant source of "hidden" gluten. (Unfortunately, many manufactured foods that do not list wheat, barley, or rye among their ingredients still contain trace amounts of gluten, and such a concentration may be enough to provoke a serious reaction in a gluten-intolerant person.)

In the spring of 2006, Melanie began a new gluten free food plan with high hopes. The dramatic results were gratifying and immediate. Melanie regained 15 pounds within a few months, was living pain-free, and no longer experienced the debilitating diarrhea caused by hidden gluten in the rice drink.

Within two years, Melanie experienced even more remarkable

benefits of being gluten-free. Her allergies to a long list of foods receded and the spring and fall seasonal allergies she had endured for more than 10 years decreased in intensity, indicated by less itching, sneezing, and mucous membrane irritation. Additionally, her autoimmune hepatitis stabilized and her liver enzymes fell to lower levels allowing her to reduce her daily dosage of prednisone.

"I recovered a lot," Melanie said. Her gluten free food plan was working and many of her illnesses had largely resolved or, like the autoimmune hepatitis, had stabilized. Her joint pain subsided, but she continued to experience chronic fatigue, possibly related to lupus, as well as nerve pain in her hands and feet, related to Raynaud's disease. Her hair was also very thin, but even with these residual symptoms, her overall health was much improved.

In 2007 Melanie felt a pain in her right hip and fell down. An x-ray showed avascular necrosis in both hips. In avascular necrosis, the blood supply to a region of bone is interrupted and the affected bone begins to die. If avascular necrosis involves a joint such as the hip, both the surrounding bone and the joint cartilage may be affected. Melanie's ability to walk normally was in jeopardy.

She wanted to find a doctor who could "put all the pieces together," and treated her for one major condition rather than individual unrelated treatments for "ten different diagnoses." She made some calls and was recommended to our clinic, the Institute for Specialized Medicine, a center for integrative rheumatology in San Diego, California. After a physical examination and review of laboratory tests, we confirmed Melanie's earlier diagnosis of celiac disease, as well as immune reactions to dairy and egg proteins. We took her off prednisone and substituted prednisolone, another steroid that prevents the release of substances in the body that cause inflammation, enabling her body to do much less work. We also instructed her to eliminate dairy and eggs from her diet.

Melanie followed our advice and within two months her hair grew back, and she had "way more energy." She now walks regularly for exercise and began jogging "for the first time in two-and-a-half years". She is now 43 and the mother of a 10-year old daughter. She says, "I am so much better than I was 10 years ago." The key actions that made the difference were a completely gluten-free diet and eliminating dairy products and eggs, which were identified as additional immune system triggers.

Melanie describes herself as being very healthy when she was growing up. What happened to her? Now, Melanie is able to clearly identify the turning point. When she was a child her mother did all the cooking from scratch. The family ate fresh fruits and vegetables and rarely ate bread, pasta, or processed foods. When she left home for her first year at college, the only food available was cafeteria-style institutional food, heavily processed, nutrient-deficient, and white-flour-based. In Melanie's words, her diet consisted of "bread, waffles, and starch."

As a young child, Melanie's immune system never developed tolerance to gluten-containing foods. When her lifelong diet changed drastically during her freshman college year, her immune system responded to the presence of the new foreign protein—gluten. Her digestive system overloaded with gluten-containing grains and her immune system mounted a rapid and devastating defense against these foreign proteins.

Every one of her major health problems began after she encountered a gluten-centric diet. "If years ago I had been diagnosed with celiac disease instead of an intestinal infection, I would never have developed all those drug allergies, and many other problems could have been avoided." This is the great difficulty with gluten intolerance and celiac disease. These disorders can masquerade as autoimmune, rheumatologic, and metabolic diseases.

Melanie's medical history and experiences are both unusual and familiar. Unusual in terms of the variety and extent of her medical problems, and familiar to the many Americans and Europeans who live with gluten intolerance and celiac disease. The best news, is that there is a cure.

Living in a Wheat-Centric World

Wheat is everywhere. It's in your bread, your biscuits, your breakfast, and in your beer. We live in a wheat-centric world.

Wheat has provided great benefits for humankind. Entire civilizations have been built around this abundant and important crop. Primitive relatives of modern wheat have been found in excavations estimated to be 10,000 years old. Wheat was grown in Egypt, India, and China 5,000 years ago, is hardy, and adapts well to harsh conditions, which enabled humans to expand their range and

thrive in otherwise inhospitable regions. The wind-swept plains of Middle America's Oklahoma, Kansas, and Nebraska are natural planting grounds for wheat, as are regions as far-flung as the Mongolian steppes.

Wheat is a staple of the global economy. The United States Department of Agriculture's Foreign Agricultural Services states that 715 million metric tons of it was harvested worldwide in 2014. Wheat futures are an important commodity on the Chicago Board of Trade and a staple of the kitchen table. Americans consume more wheat than any other single food, and it accounts for 20% of the calories of the world's population, but there is a dark side to wheat.

For the many millions who are gluten intolerant, consumption of wheat can lead to serious health problems. Tens of millions, possibly 40-50 million Americans are gluten intolerant, and most do not realize it. Similar numbers of Europeans are also gluten intolerant.

What does it mean to be gluten intolerant? Remarkably, despite the long history of wheat in our global society, the human body cannot digest its primary proteins known in combination as gluten, which are what make wheat, wheat. Humans lack the necessary enzymes to break down gluten proteins into amino acids, the building blocks of protein and we don't have the genetic information necessary to build gluten-digesting enzymes. These undigested gluten proteins pass through the gastrointestinal system of some people without causing any harm, but for those who are gluten intolerant, gluten proteins can mean major health problems.

Gluten in History

Wheat cultivation began in approximately 10,000 years ago, in a region incorporating present day Israel, Iraq, western Iran, southeastern Turkey, and Syria, known as the Fertile Crescent. Wheat reached Great Britain, Ireland, and Spain approximately 5,000 years ago. Originally wheat species were genetically diverse, but grains that were genetically uniform produced more stable crops and higher yields. In addition, people selected the grains that worked best for bread making because they possessed a glue-like property that helped dough stick together. The structural proteins that produce yields of sticky dough are known as gluten.

As a result, gluten-containing wheat became the standard wheat

crop. Today, all wheat consumed around the world contains gluten. The protein in barley and rye is also predominantly gluten. If wheat is such a prevalent part of our diets, why are so many people gluten intolerant? Why aren't tens of millions of people intolerant to chicken or apples or spinach? These foods are all important parts of many families' regular meals. If exposure is the problem, why is gluten such a common culprit and why does it cause so many disorders? The answers to these important questions, although theoretical, are deeply complex.

Gluten Intolerance and a Competitive Advantage

In the United States today, life expectancy for men is approximately 76 years and for women, approximately 81 years. Only 100 years ago life expectancy in the U.S. was approximately 47 years for both sexes. In the middle ages in Europe, 30 years of age represented a good long life. The dramatic gains in life expectancy are the result of advances in the practice of medicine, specifically the development of antibiotics and vaccines, as well as widespread clean water and sanitation.

Prior to the era of modern medicine, infections were the main causes of death. One part of a useful working theory for why gluten intolerance is on the rise suggests that in previous eras the vast majority of people died before they had time to manifest symptoms of intolerance. Many infants and children perished owing to a broad array of infectious diseases: influenza, pneumonia, whooping cough, diphtheria, measles, mumps, smallpox, and polio. Infants and children were also highly susceptible to death from gastrointestinal infections from contaminated water supplies and lack of sanitation.

In the case of ever-present gastrointestinal infections, those who survived attacks of colitis, jejunitis, gastroenteritis, cholera, dysentery, and chronic diarrhea were able to confer this important competitive advantage to their offspring, passing the genes responsible for this mysterious cloak of protection along to the next generation.

The children of those who survived were better able to recover from deadly gastrointestinal infections, and transmitted these survival characteristics to their children. What was the likely source of this competitive advantage that was now being selected by the formidable machinery of evolution? The probable source is the mechanism of

gluten intolerance itself.

As we've discussed, humans never developed the capacity to digest gluten. Wheat was not a food source when Homo sapiens became a distinct species in eastern Africa approximately 200,000 years ago. Wheat arrived relatively late on the scene, about 10,000 years ago. Our enzymatic system, based on our genetic code, has never caught up. What happens when we digest gluten-containing bread or wheat products? We can only partially digest gluten, breaking it down into large fragments.

In many people, these fragments provoke an immune reaction culminating in an inflammatory response. The focus of the inflammation is the lining of the gastrointestinal tract, specifically the lining of the small intestine. Many serious problems can develop if such an intestinal inflammation becomes widespread, but in most people the inflammatory changes are low-grade and do not cause symptoms, but in every person the intestinal inflammation has a side benefit. The inflammation provoked by gluten fragments confers a relative resistance to gastrointestinal infections which provided a competitive advantage. Those who developed inflammation were better able to survive, so the genes for gluten intolerance persisted and spread in the population. As a result, large numbers of people in the modern world are gluten intolerant. Serious problems are likely to develop in persons in whom gluten intolerance provokes more than a low-grade immune response.

Gluten Intolerance Is a Cause of Many Diseases and Disorders

As we shall see, people with clinically significant gluten intolerance experience a wide variety of symptoms and diseases. As the inflammation of the small intestine worsens, the person is less able to absorb nutrients, including proteins, vitamins, and minerals. This is known as malabsorption syndrome, and the long-term result is a lengthy list of digestive disorders and metabolic diseases stemming from a lack of proper nutrition.

Gluten-intolerance is also associated with a variety of autoimmune disorders, which may be linked to the immune reaction provoked by gluten. A person with an autoimmune disease makes antibodies that destroy their own tissues. These antibodies directed against the "self" are called autoantibodies. If they target joints, the person develops

rheumatoid arthritis. If they target the kidneys, the nervous system, the skin, and/or the heart, the diagnosis may be systemic lupus erythematosus (SLE), simply referred to as lupus. If they target the muscles, the person develops polymyositis or dermatomyositis. If they target the thyroid, the person develops Hashimoto's thyroiditis. Gluten-intolerance may also play a role in autism, attention deficit hyperactivity disorder (ADHD), and schizophrenia, although these links are not yet fully understood.

The bottom line is that the symptoms of gluten-intolerance are highly variable. Diseases that may be linked to gluten intolerance include:

- Attention deficit disorder
- Autism
- Diabetes
- Fibromyalgia
- Hashimoto's thyroiditis (an autoimmune endocrinopathy)
- Iron deficiency anemia
- Lupus (systemic lupus erythematosus)
- Mixed connective tissue disorder
- Neurologic disorders
- Osteoarthritis
- Osteopenia (loss of bone mass)
- Osteoporosis
- Pseudogout
- Rheumatoid arthritis
- Schizophrenia
- Sjögren's syndrome (a multisystem autoimmune disorder)

Gluten intolerance may be responsible for many unexplained symptoms including:

- Bloating and abdominal pain
- Chronic fatigue
- Diarrhea or constipation
- Failure to thrive
- Frequent colds and infections
- Frequent headaches
- Infertility
- Mood disorders including apathy and lethargy
- Recurrent fetal loss
- Short stature
- Vitamin deficiencies
- Weakness and fatigue

In many cases, persons with gluten intolerance do not have gastrointestinal-related symptoms. Instead, they have symptoms of the related diseases, such as attention deficit disorder or rheumatoid arthritis. It can be difficult for a physician to correctly identify the underlying cause of a person's ongoing symptoms and at present most affected individuals go undiagnosed.

Most physicians are not trained to recognize the signs and symptoms of gluten intolerance. If a person is experiencing chronic joint pain, a physician would have to be very well informed to include gluten intolerance in her list of diagnostic possibilities. Likewise, if a child demonstrates early signs of autism, the large majority of pediatricians and pediatric psychologists would not consider gluten intolerance as a possible primary cause.

This lack of awareness among physicians and the public too often leads to misdiagnosis, inappropriate and ineffective treatment, significant decreases in quality of life, and persistent and aggravated symptoms. For example, if a person complains of fatigue, weakness, muscle aches, and joint pain, their family physician might order blood tests for rheumatoid arthritis and lupus. If these tests are negative the patient could be referred to a rheumatologist. If the rheumatologist is not familiar with gluten intolerance and celiac disease, he might offer a diagnosis of mixed connective tissue disorder and prescribe a

course of steroid medication. If the real cause isn't corrected, symptoms will continue and may worsen, and the side effects of inappropriate medication may create additional problems.

Quality of life is a day-to-day concern for those affected by gluten intolerance. Some people suffer from debilitating diarrhea while others have bloating and abdominal pain. The fatigue, weakness, muscle aches, and joint pains associated with gluten intolerance may be profound. Such persons may dread getting up in the morning because they know the day will bring prolonged periods of discomfort, pain, and stress.

Quality of life can deteriorate further following an ineffective interaction with a physician. If the physician does not have gluten intolerance or celiac disease in mind, they may choose to go down a diagnostic pathway that appears to fit the patient's symptoms, but misses the underlying cause. Much time is then wasted in specialist referrals, unnecessary diagnostic tests, and prescription of ineffective and potentially harmful medications. Patients naturally get their hopes up when they begin receiving some kind of treatment, but the ultimate persistence of very uncomfortable symptoms can be devastating.

Heightened awareness of gluten intolerance and celiac disease is the key to effective diagnosis. Family physicians as well as specialists in all fields see what they look for and recognize what they know. Habits of thought are useful, but they restrict the ability to create new associations and identify situations that don't fit into previously established patterns. Correctly identifying gluten intolerance and/or celiac disease as the cause of rheumatic, immunologic, and endocrine diseases will have wide-ranging benefits for millions of people. To achieve this goal, The National Institutes of Health Consensus Statement on Celiac Disease calls for education of physicians, nurses, dietitians, and the public. This book is intended to meet that goal and raise awareness and understanding of gluten intolerance and celiac disease with the public and those entrusted with the health of patients seeking treatment.

When to Suspect Gluten Intolerance and Celiac Disease

Gluten intolerance and celiac disease may show classical symptoms, but these disorders are also great mimickers. Physicians need to have a clear working knowledge of gluten intolerance and celiac disease. Also critical is an understanding of the association and relationship of gluten intolerance and celiac disease with many important disease categories including autoimmune disorders, endocrine diseases, neuropsychiatric conditions, infertility, and malignancy.

Diagnosing gluten intolerance and celiac disease in infants and young children is relatively straightforward. Affected children in these age groups generally have diarrhea and abdominal bloating. Their physical development will lag behind expected standards regarding height and weight. Such delayed development is known as failure to thrive. Vomiting, constipation, and irritability may also be observed. In infants and young children, such an array of signs and symptoms should place gluten intolerance and celiac disease at the top of the list of suspected causes.

In adults the diagnosis is much less clear. Adults with gluten intolerance and celiac disease classically have diarrhea, abdominal bloating, and abdominal pain, but in the last 10 years diarrhea has been the main complaint in less than 50% of patients. The real difficulty in diagnosis occurs when abdominal symptoms are entirely absent. In such circumstances, a high index of suspicion is needed. In adults, gluten intolerance and celiac disease may also be suspected in cases of autoimmune disease, endocrine disorders, iron deficiency anemia, neurologic disorders, osteoporosis, and/or problems with fertility. The list of diseases associated with any of these disorders is extensive, however gluten intolerance and celiac disease should always be considered, even when other causes have been identified. Many people with celiac disease are seeking treatment for a wide variety of common symptoms, none of which is particularly suggestive of celiac disease. It is important for physicians to question their assumptions, continue to question the evidence, and seek answers beyond those that are obvious. Persistence of symptoms even with treatment is the single most important clue that the diagnosis is incomplete, inaccurate, or both.

Despite its unfamiliarity to many physicians, celiac disease is a common disorder, affecting approximately one in every 100 adults. In

the majority of these individuals, gluten intolerance and celiac disease remain undiagnosed, emphasizing the need for knowledge and awareness.

Accurate information empowers people to take positive action on their own behalf. The modern improving medical environment focuses on a doctor–patient partnership. Doctors do not "know everything" and patients can bring a lot to the relationship, provided they are well informed. With respect to gluten intolerance and celiac disease, knowledge and awareness are the key elements in identifying a correct diagnosis.

It is important for patients to seek help from a doctor who is well versed on celiac disease and the correlation to other autoimmune diseases. An important question for any patient to ask a doctor is "What conditions are on your differential list?" In today's harried medical environment, time is at a premium, but time constraints cannot be used as justification for failing to thoroughly analyze a patient's particular circumstances. Physicians need to be reminded to stop and think. Asking, "What conditions are on your differential list" will do just that.

Skilled physicians are trained to arrive at a diagnostic conclusion by considering all the evidence. The process involves eliminating suspected disorders that might be responsible for a given set of symptoms. The doctor develops a short list of conditions, usually five or six, and rank-orders them. The top three diseases on the list will probably account for more than 95% of cases and the remaining two or three are uncommon conditions that must be considered until they're eliminated.

For example, unexplained persistent fever, joint pain and joint swelling, weakness, and fatigue could be caused by rheumatoid arthritis, lupus, reactive arthritis, infectious disease, and malignancy. The complete list is much longer, and more than one of these conditions can be present, complicating the analysis. The important point is to consider a group of suspected conditions rather than jumping to an easy conclusion and focusing on the top one or two. Experienced clinicians can do all this in their heads. They've gone through these parameters hundreds of times, but it's easy to forget to be rigorous. Asking "What conditions are on your differential list" reminds your doctor to slow down and consider unlikely alternatives. You can even be more direct and say, "Please be sure to consider

gluten intolerance and celiac disease in your list of differential diagnoses."

Homo glutenicus

The birth of *Homo glutenicus*, or gluten cautious individuals has been in the making for over 10 years. *Homo glutenicus* is the mass of people creating a community that is influencing the food industry for more gluten free options, the medical community for more education and awareness, and society for more acceptance and support for individuals who are embarking on a gluten free lifestyle

The good news is that awareness of gluten intolerance and its close association with a wide variety of serious conditions is developing critical mass. There are dozens of well written web sites focusing on gluten intolerance and many more offering lifestyle tips and gluten free recipes. A number of good books on gluten intolerance have been published recently, and articles on gluten intolerance and a gluten-free lifestyle appear regularly in blogs, newspapers, and healthy living magazines. The gluten free revolution is happening now.

In this book, we will explore the hidden roles that gluten and gluten intolerance play in millions of lives and discuss the science behind gluten intolerance and the evidence showing how gluten intolerance may be linked to a variety of major health problems, from arthritis to autism. Most importantly, we will present and describe a surprisingly simple, safe, and inexpensive cure: a gluten free diet. Along the way, we will share stories of real people who, like Melanie, have transformed their lives by eliminating gluten.