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Udderly New Insight About Milk and Autism: An Emerging New Hypothesis on A1 and A2 Beta-Casein

by Julie Matthews, Certified Nutrition Consultant

As an autism nutrition consultant, I've been supporting clients following the Gluten-Free Casein-Free (GFCF) diet for years. Some of my clients would report that their child could handle goat's milk or raw milk without allergic reactions. I began to wonder if all milk was created equally.

I conjured various theories: could the protein in goat's milk be different than cow milk, was it the pasteurization process (absent in raw milk) that made the difference, was it something else, or a combination of factors? Then, one of my clients introduced me to A1 and A2 beta-casein.

There are various types of casein. Goat's milk, as well as sheep and buffalo milk, contain A2 beta-casein. Raw milk, while often from cows, is typically produced from small herds of Jersey and Gernsey cows, both of which contain a high percentage of A2 beta-casein compared to most dairies that use mainly Holstein cow's that produce a majority of A1 beta-casein. Here's what I have learned through my research about casein and A1 versus A2 beta-casein.

Beta-casein is a protein that contains bioactive peptides and opioids. Bioactive peptides are important for protecting the undeveloped immune system of newborns, and stimulate the growth and development of organs like the gastrointestinal tract and gut. Bioactive peptides have also been shown to kill bacteria that normally cause immune system infections. Opioids have pain-killing effects, sedative properties, induce sleep, and play a role in the control of food intake. Opioids can be produced by the body in the form of endorphins, or be absorbed from digested food, such as milk and wheat, in the form of casomorphins and gluteomorphins (opioid proteins). Several forms of beta-casein exist and make up 25-30% of the proteins in cow's milk. There are approximately 13 beta-casein variants, with A1 and A2 variants being the most commonly occurring. A1 beta-casein contains the amino acid histidine at position 67 in the protein, while A2 beta-casein instead contains the amino acid proline at the same position. Studies have shown

that when digested, A1 beta-casein breaks down to a casomorphin protein called beta-casomorphin-7 (BCM7). This is a direct result of the histidine amino acid that A1 beta-casein contains, as A2 beta-casein does not form BCM7 (1).

Several enzymes in the digestive tract process beta-casein including DPPIV, (dipeptidyl peptidase IV) and cause the break down of bioactive peptides and opioids. Studies suggest that the digestion of cow's milk (containing A1 beta-casein), leads to the release of opioids, such as BCM7, and can cause harmful effects in children with autism (2) where DPPIV function may be impaired. As this amino acid structure is more difficult to breakdown, those with compromised or weak digestion may accumulate opioids more readily. Additionally, when the gut is "leaky" (referring to increased gut permeability), these opioids end up in the blood stream in much greater concentrations than in those people with a healthy gut wall that does not leak. BCM7 is not produced when A2 beta-casein is digested, so goat's, buffalo's, and sheep's milk that contain A2 beta-casein but not A1 beta-casein should not cause these harmful effects. There are other opioids that may also be formed; however, BCM7 appears to be the strongest.

As Jon Pangborn, Ph.D. describes, the enzyme DPPIV, which is also called CD26, has several other functions in the body, including involvement in signal transmission via lymphocyte receptors, and assisting the enzyme, ADA, in processing adenosine as an ADA binding protein. DPPIV is impaired by toxic heavy metals like mercury, lead and cadmium, a milk allergy, organophosphate insecticides, and yeast. Children with autism have greater toxic metal burdens, and one theory is that these heavy metals knock out this DPPIV enzyme, and the impaired DDPIV leads to improper processing of dairy and wheat. A supplemented plant analog version of DPPIV cannot substitute for the animal version completely, but it can certainly help.

While it is possible that A2 milk may also release opioids, Japanese and German scientists were unable to release BCM7 from A2 milk (1, 3). It appears that human breast milk may not release BCM7 either. Interestingly, this may explain why breastfeeding does not seem to cause a casein reaction to sensitive babies when dairy is avoided in a mother's diet. In addition to affecting autism, research suggests that BCM7 may lead to the onset of several diseases, such as heart disease, diabetes, and schizophrenia (4).

Studies have also shown that wheat products, which contain gluten, also cause health problems for children with autism (5) Gluten has long been established as a problematic protein for many individual, most well studied in celiac patients, causing inflammation in the gut, diarrhea, constipation, abdominal pain, digestive problems, and the improper absorption of nutrients. Similar responses are seen in many children with autism (that are not diagnosed with celiac). Gluten, along with an autistic person's already compromised digestive system, can exacerbate the ability of the body to break down beta-casein.

Scientists believe that opioids like gliadomorphin (a gluten opioid) and BCM7 (a casein opioid) are toxic for children with autism due to the fact that these children have an abnormal, leaky, gastrointestinal tract (6). Instead of completely digesting and excreting these opioid proteins, some of the partially digested gluten and casein proteins leak out of the gut and are transported to other parts of the body before they can be completely digested. These opioid proteins travel through the bloodstream, cross the blood brain barrier (the barrier between the brain and the rest

of the body), enter the brain, and stimulate morphine-like effects. Casein proteins (BCM7) negatively affect the brain by causing inattentiveness, unclear thinking, and irregular sleeping and eating patterns (7).

In children with autism, gliadomorphin and BCM7 can also cause the release of histamine, a chemical that regulates immune cell communication. Histamines are normally released in the body in response to an allergic reaction. This mis-regulation of immune cells weakens the immune system's ability to ward off harmful viruses and bacteria that cause diseases. This is consistent with the experience that many children with autism get frequent infections and illness.

Antibodies are also released to help target and remove unwanted opioid proteins. IgA is an antibody that can be found in blood, saliva, tears, and mucous membranes of the respiratory system and gastrointestinal tract. IgG antibodies are the most common antibodies in the body, and can be located in all bodily fluids. IgG antibodies are the only form of antibody that can cross the placenta in pregnant woman to protect a fetus (unborn baby). IgG antibodies also play a major role in fighting viral and bacterial infections. When the immune system detects foreign particles such as viruses, bacteria, fungi, or cancer cells it stimulates the production and release of antibodies. These antibodies attach to the foreign particles, labeling them as hazardous so that they can be destroyed and removed from the body (8). So while the peptides from casein or gluten trigger an IgG immune response, the opioids trigger an IgA immune response. So it is not just opioids that trigger an immune response, casein and gluten protein can do so also, just using different types of antibodies.

Studies have shown that in autistic and schizophrenic patients, large amounts of gliadomorphin and BCM7 can be detected outside the gut (8). This further indicates that their bodies are not able to properly break down and utilize these opioid proteins. These studies also showed that in 86% of schizophrenic patients, IgA antibodies that were targeting gluten were released into the body, and 67% had IgA antibodies that were targeting casein. In patients with autism, approximately 30% of the patients had IgA antibodies targeting gluten and casein present in the body. The release of IgG antibodies targeting gluten and casein were also detected in these patients. More than 80% of the autistic and schizophrenic patients had elevated levels of IgG antibodies in their blood.

In recent years, the adverse effects of gluten and casein led researchers and to believe that autistic and schizophrenic patients should be placed on a gluten-free/casein-free diet, and this has become a widespread treatment for both diseases (9). Case studies that involved putting patients with schizophrenia and autism on a gluten-free/casein-free diet normally lead to some improvement of symptoms, but more clinical trials need to be performed to get a better picture of why this is the case. There is not enough data yet to understand all of the complexity behind gluten and casein and the challenges with them, but the experience of thousands of patients support the science we know so far: that a gluten-free/casein-free diet helps. And of course implementing the diet always depends on the patient's needs, the caregiver's willingness to try it, and professional supervision (10).

Schizophrenic patients who were put on a gluten-free/casein-free diet or treated with dialysis, a process that cleans the blood in order to rid the body of gliadomorphin and BCM7, were relieved

of their symptoms, and low levels of the opioid proteins were detected. Approximately 81% of patients with autism who were put on a gluten-free/casein-free diet for at least 3 months were also relieved of their symptoms. A few parents, who stated that their child with autism had seizures before going on the diet, noticed that the frequency of the seizures either decreased or ceased all together. As previously stated, opioid proteins can cause an allergic response in the body, which leads to the release of histamines. Histamines have a direct effect on immune cell regulation. The disturbed immune response leads to a higher production of antibodies, such as IgA and IgG, as a means of further breaking down and excreting harmful gliadomorphin and BCM7 particles. In other words, the high levels of antibodies that are detected in patients with autism are a direct result of complications that occur when gluten and A1 beta-casein are consumed (8).

A vast majority of children that consume dairy consume cow milk products so removal of dairy on the GFCF diet would be the removal of A1 beta-casein in most instances. This may be the reason the GFCF diet is so successful for children on the autism spectrum. I'd like to pose a new hypothesis, maybe it is not ALL casein but the A1 beta-casein that is actually the primary problem with milk for children with autism.

With that said, there are most likely are other reactions and problems with dairy for some (if not many) individuals, so I do not think this preliminary information justifies abandoning the GFCF diet. (In fact, I hesitated writing and talking about this topic for a long time, as I did not want to confuse parents new to diet.) I have seen many wonderful results from GFCF and know many clients that cannot seem to tolerate goat or raw dairy. I don't want children to miss out of the full benefit from diet by not trying a GFCF diet.

Through my clinical experience, I have found that it is very important to give the GFCF diet a complete trial, free of any infractions. Once a child has been on this diet for 3-6 months and you see what progress can be made with it, then and only then, do I feel that a parent may experiment with diet and try adding goat's milk or some other A2 milk back. It seems that for some children, their casein sensitivity is mild and A2 milk works well. For others, once the gut is healed, they are able to consume small amounts of A2 milk. I often hear that as a child's digestive systems improve, they are able to handle goat's milk yogurt or raw milk. It is possible that the BCM7 issue is a primary factor for some people, and that A2 milk may provide an option for some individuals.

While milk is not "necessary" in the diet, dairy has health benefits when the individual is not intolerant to it. (Note that when people are intolerant, it can be very harmful regardless of the "benefits.") If there is a way to include some dairy in some children's diets, there can be a positive benefit to having this flexibility and nutrition in the diet. Dairy makes wonderful probiotic-rich fermented foods such as yogurt and kefir to support a healthy intestinal tract—and often nuts, nut milk and coconut-based fermentations are not tolerated. Dairy contains essential fatty acids, fat-soluble vitamins A, D, and K, and calcium. Additionally, as I describe in *Nourishing Hope for Autism*, butyrate, (also butyric acid), found in dairy, "has been shown to clear ammonia and nitrogen, modulate local electrolyte flux, supports the reduction of diarrhea and improves very large, hard stools. Butyric acid also supports and fuels the intestinal walls to

support a healthy gut and is used as an anti-candida substance." Raw dairy contains phosphatase (an enzyme important for calcium absorption), probiotics, unadulterated protein, and higher nutritional content (because of what is normally destroyed during pasteurization and because they are pasture-grazed). This new A1 and A2 information may allow some children with autism to receive the benefits of milk without the problems it can cause.

Please share your experience with A2 milk.

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