THE RE-INTRODUCTION OF GLUTEN AND CASEIN IN EXCLUSION DIETS FOR PEOPLE WITH AUTISM SPECTRUM AND RELATED CONDITIONS

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Pioneering parents, supported by a limited number of understanding professionals, have been introducing restrictive dietary interventions to ameliorate some of the difficulties of autism and related conditions for at least 30 years. The initial focus of their efforts was, as it still is today, to remove all traces of casein (the major protein in milk and dairy produce) and gluten (derived from wheat and some cereal produce) from the diet and to monitor developmental and other progress. It was soon realised that whilst a dietary change did not help everybody, the benefits could be substantial and the intervention was worthy of serious consideration. Such interventions were usually introduced in the teeth of opposition from the medical establishment. Sadly, this remains often the situation.

Probably the "best fit" explanation for observations of positive change following dietary intervention was, and still is, the opioid-excess theory for which there was a huge amount of (mainly) circumstantial evidence. These hypotheses depended upon the action of exorphin peptides, derived from incomplete digestion of large proteins (such as gluten and casein) passing from the intestines to the central nervous system (CNS) and interfering with transmission in all the major systems neural pathways. It was always understood that there must be other, possibly only tenuously related, mechanisms for activity probably involving modulations of the immune system. For a detailed consideration of possible mechanisms see Whiteley et al (2010).

For me (PS), the crucial element in accepting this occurred one evening in Rochester, NY in 1995. I met with a group of parents who were experimenting with a gluten- and casein- free (GF/CF) diet for their children with autism. We were discussing the consequences of infringements of diet. These parents were reporting the occurrences of serious adverse reactions within a very short period (an hour or even minutes in some instances) of such an infringement. I had not come across this phenomenon before but neither had I come across a room full of mothers who were using the diet so intensively. They referred to themselves as "Gluten Nazis" – politically incorrect of course, but those ladies were tough, gluten-free, cookies. Unquestioningly, I had already learned to accept the accuracy of the observations from such dedicated researchers.

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Clearly, responses so rapid and intense could not have resulted from the direct neurological mechanisms of the original model. The rapidity and seriousness of the effects indicated mediation through the immune system. Hard evidence was, however, largely lacking. By this time, we were already aware of some (but certainly not all) children who could tolerate milk as long as they were not eating gluten. In our "pictorial model," gluten was triggering permeability of the intestines (the so-called "leaky gut") and the peptides from casein were opportunistically transiting the intestinal wall to enter the blood stream and then progressing to the CNS. In the absence of gluten, cow milk had no obvious adverse effects that we could see in these children.

Although initially based upon empirical observations, Jyonouchi (2002) and Ashwood (2003) have published studies which strongly suggest an inflammatory response to gluten in the intestinal mucosa of children with autism.

Since these early days, we have considered this process more closely. My colleagues and I (PS) performed a long term study on the use of a gluten-free diet (Whiteley 1999). During the course of the study, some participants were required to return to their normal diet following some months on the GF diet. One had a seizure within a few days and was returned (by his mother) immediately to a GF diet. In the other two cases, there was no sign of an immediate regression but signs of abnormal behaviours began to creep in over several days' time with one of these children who then returned to the restricted diet. The third was able to remain on a normal diet. Clearly there were differences between individuals. There were also a number of veterans from the first Persian Gulf War who had experimented with a GF/CF diet and found it beneficial for some of their reported symptoms. Some found this to be helpful and some did not, but it was a long process compared to working with children. The benefits could easily take nine months to a year to become worthwhile. It also took a long period of dietary restriction (sometimes up to two years) before one could consider the re-introduction of offending foods.

THE PROCESS OF RE-INTRODUCTION OF GLUTEN AND CASEIN TO THE DIET OF PEOPLE WHO HAVE PREVIOUSLY BEEN ON A GF/CF DIET

MILK

As indicated previously, many children with autism can tolerate milk in moderation provided that they remain gluten free. The second point is that the effects of removing casein from the diet or of re-introducing it (and removing again later if necessary) are fairly rapid. Depending upon the age of the subject, it could be a few hours or a few days as a rule. For these reasons, we advocate that efforts are directed to re-introducing milk before progressing to gluten (and other offending foods).

One standard protocol would be:

1. Introduce small quantities of milk (or dairy product) from a non-bovine (cow) source. Try goat, sheep, camel or buffalo dairy products as appropriate or available. If no problems occur within the predetermined time – move on.

2. If the product is available one can introduce variants of bovine milk which, theoretically at least, may be safer. The so-called A2 milks are available in some parts of the world (Australasia in particular). Differing structurally from the more widely used A1 dairy sources, A2 dairy proteins have long been suggested as an alternative milk source for combating a variety of health issues. If problems occur at this stage, it would seem likely that factors other than opioid peptides could be implicated given the difference in proteins between A1 and A2 milks. For example, allergies to cow milk may exist or lactose intolerance could be involved. It is known that certain intestinal viral infections will selectively infect those cells producing enzymes such as lactase. Thus, an acquired lactose intolerance could result from such an infection. A lingering intestinal measles infection would be a possibility and, certainly, such problems are frequently encountered in those children whose parents allege the involvement of the combined measles-mumps-rubella (MMR) vaccination in triggering autistic symptoms.

3. If successful, one can move on to small amounts of dairy produce such as yoghurts or cheese from typical (A1) dairy cattle. It is likely that some--but not all-- of the opioid peptides will have been destroyed during the fermentation processes used in their preparation.

4. If there are still no problems, move on to a diet containing moderate amounts of normal milk produce.

If at the end of, say, one further month, there have been no regressions it would probably be safe to move on to the gluten element. However, it must be born in mind that the re-introduction of gluten could result in the milk becoming problematic once again. If such proves to be the case, it would be logical to remove all gluten products immediately and await a return of the previous benefits.

Many parents have found that supplementary enzyme-based products may be useful during this and the following stages of the protocol. Thirty years ago, we were employing products containing bromelain, derived from pineapples and possessing considerable peptidase activities (degrading peptides to

their constituent amino acids). Nowadays, products which are safer and offer greater stability have been manufactured specifically for people with autism and related disorders. There exists considerable anecdotal evidence for efficacy, and some published support as well (Brudnak et al, 2002). Absolute evidence of effectiveness is still, however, awaited.

It is difficult or perhaps impossible to gauge the precise dose of enzyme supplements that will be needed as the requirement will vary with the choice of product, the severity of the symptoms, the individual's diet at the time, the "nature" of the autism and the size and age of the subject.

We generally advise consultation with an experienced practitioner (e.g. physician, dietician, nutritionist) alongside input from other parents who have used similar preparations at this stage as it is very much a case of tailoring the dosage regime to the individual. We often advocate taking some enzymes, in accordance with the manufacturers' recommendations, and then gradually increasing the amount of potentially risky food. Manufacturers and suppliers are extremely helpful and supportive in addressing consumer questions and concerns (SerenAid™, Klaire Laboratories; Peptizyde™, Houston Nutraceutical; EnZymAid™, Kirkman are amongst the better known products).

Once the desired level of gluten-containing foods is reached, one can gradually reduce the levels of enzyme products employed. More enzymes can be introduced on a short-term basis for particular occasions (Christmas, birthday parties, etc.) if required.

Each manufacturer has devised products which differ somewhat in the choice and relative amounts of the actual enzymes included. Subjects tend to vary in their responses to each product. It is quite common for a subject to respond or fail to respond to a particular brand, but to respond much more to one or more of the others. If a particular brand is not working, we would suggest switching to an alternative before (temporarily perhaps) abandoning the approach.

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WHEN DO WE START THE RE-INTRODUCTION?

Accidental infringements of the restrictive diet are difficult to avoid. Parents learn to recognise the signs that their child has taken a slice of cake or that the tuna fish has been injected with milk proteins. After a period of time (say six months for a toddler or two years for a Gulf War Veteran), these accidental (or deliberate) infringements do not have the serious consequences that they perhaps once did. This is the time to consider the process described previously. It is as if the gut has healed up (at least partially). However, it has not been permanently cured and over a prolonged period, intestinal damage may, once again, be a consideration.

CONCLUSIONS

1. We should always endeavour to make the life process, including diet, as unrestricted as possible.
2. Many people can, by using a rational approach and common-sense, return to something approaching a normal diet.
3. Some people have multiple or complex problems with certain foods and, for the time being at least, restrictive diets may be necessary for the foreseeable future.
4. We also recognise that for a considerable subset of individuals, dietary interventions are clinically valueless.

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