

# Interview with Dr. Arthur Krigsmann: evaluation and treatment of gastrointestinal pathology, common in children with autistic spectrum disorder

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## Abstract

The majority of children with autism spectrum disorders have gastrointestinal symptoms, the most common of which is diarrhea. Other symptoms include abdominal pain, constipation, growth failure, vomiting, and chronic gastroesophageal reflux. It is believed that the bowel disease present in children with autism contributes to many of the cognitive problems that these children experience, at the very least impeding their ability to maximally benefit from the many behavioral interventions available. When endoscopy is performed in ASD children with unexplained chronic gastrointestinal symptoms, a pattern of diffuse lymphonodular hyperplasia and multifocal non-specific acute and chronic enterocolitis emerges. These findings have been noted in the entire course of the gastrointestinal tract, from the esophagus to the anus. Potential consequences of this gastrointestinal pathology include brush border enzyme deficiency and malabsorption. Dietary components can exacerbate the inflammation. Treatments aimed at reducing the degree of inflammation in the GI tract is often successful in reducing the amount of abdominal pain experienced by the child which translates into more normal sleep patterns and improved in the educational environment and during therapies. Common treatments broadly include restrictive diets, anti-inflammatory medications, digestive enzyme supplementation, antibiotics, and probiotics. Individual patients may additionally benefit from anti-reflux therapy and conventional treatments to treat ongoing constipation.

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*It is my pleasure to welcome Dr. Arthur Krigsmann. Dr. Krigsmann holds dual board certification in general pediatrics and pediatric gastroenterology. He has extensive experience in the evaluation and treatment of gastrointestinal pathology, common in children with autistic spectrum disorder, and he has detailed the symptomatology and endoscopic histopathologic character of this disease. Dr. Krigsmann directed the Division of Pediatric Gastroenterology at New York's Beth Israel Medical Center, where he oversaw the pediatric GI clinic and consultation services.*

*He currently maintains an independent private practice in pediatric gastroenterology in New York, and Dr. Krigsmann is also a principal member of Thoughtful House of Austin, Texas, where he performs endoscopies and has a pediatric gastroenterology clinic.*

*Welcome, Dr. Krigsmann, and thank you for joining us.*

Thanks, Teri, and it's a pleasure to be here, and thank you for inviting me.

*Oh, you're quite welcome. Thank you for being with us. Dr. Krigsmann, how frequently do children with autism spectrum disorders have bowel symptoms?*

That's an excellent question. There have been primarily two studies that have looked into that question, and it seems to be that, clearly, the majority of children with autism spectrum disorders do have gastrointestinal symptoms of some type that are of concern to the parents and that impact the quality of life of the child.

*What bowel symptoms are seen in these children?*

The main gastrointestinal symptom that these children suffer from is diarrhea. These kids will often have frequent stools; one, two, three, four stools per day, and when we use the term diarrhea, it's important to emphasize that it's not the liquidy, watery stool that so many of us have had when we're sick with gastroenteritis, but it's more of a looser stool than usual, a soupy, pudding type of consistency, and that seems to be something that we deal with over and over again with these children.

So diarrhea is certainly the most frequent symptom. Abdominal pain is another very frequent symptom, and what becomes very challenging with these children is to determine how the child who is very often non-verbal, at the very least is non-communicative; how we know that they are having abdominal pain.

And we know that they have behaviors that they exhibit that seem to imply that they have pain. They put pressure on their abdomen; they'll posture a certain way so that pressure is placed on the lower abdomen; they'll lean up against – they'll lean over a sofa; they'll lean over edges of chairs; they'll lean over table ledges, all in an effort to apply pressure and something that gives comfort to the abdomen. But we know that that's, in effect, a true manifestation of symptoms because when we treat the underlying disease, those behaviors go away, even after having been there for a number of years. So bowel pain is a major symptom.

Constipation is another very frequent symptom and inability to have bowel movements or a great degree of straining and pushing to have the bowel movement. A lot of these kids have abdominal distention where the belly appears to be inflated, almost like the pictures you see of starving children in third

world countries. We'll often see growth failure in these children. A year goes by, a year and a half goes by, and these children haven't gained weight.

The parents say they haven't changed shoe sizes in a year. They haven't changed the size of their clothing in a year, year and a half, and, of course, those parents know that for a 3, 4, 5-year-old, you're always buying new clothes and bigger clothing, and that's the hallmark of pediatric health is the constant upward trend of the growth curve. So when you have that not present, that's a sign of gastrointestinal disease. Those are the major symptoms that we look at in these children.

*So you said diarrhea, abdominal pain, constipation and lack of growth appropriate for age.*

Correct, and I would add to that vomiting or chronic reflux symptoms are something we frequently see in these children.

*Vomiting and reflux; and you also mentioned that a bowel symptom could be leaning over things and applying pressure to the belly because of some sort of pain that they can't verbalize.*

That's correct.

*What about things like toe walking or you mentioned posturing. What about jumping up and down prior to a bowel movement?*

The toe walking and a lot of these stims that these children have; I'm not convinced that those are related to gastrointestinal symptoms, per se; in other words, I'm not convinced that that's a manifestation of pain or discomfort of the gastrointestinal tract. The jumping up and down hyperactivity before the bowel movement, I believe, is a manifestation of discomfort.

One of the major findings we see in these kids – we'll speak about that in a minute – is colitis, inflammation of the colon, and people who have colitis, who are able to say how intense the cramping is before they have their bowel movement, and it may be that these kids, of course, when they feel that, their response is to jump up and down and run around the room, and that we see a lot of.

The bowel movement that's passed and the jumping up and down hyperactivity seems to go away until the next time it happens.

*Why do so many children with autism spectrum disorders have bowel symptoms?*

Well that's the million-dollar question. The question really is – I'm going to rephrase that. What is the relationship – what is the nature of the association between the bowel movements or the bowel disease of these children and their autism, and the fact that the vast majority of these children have bowel symptoms cannot be a coincidence.

When you have the majority of children with ASD disorders, having bowel symptoms, intuitively, you know that this is part of the disease. We have come to believe that the bowel disease contributes to a lot of the cognitive problems that these children have, and how that works is still under investigation.

But we believe, primarily, that when you have bowel disease of the type that these kids have, there's a certain amount of absorption through the diseased gastrointestinal tract, absorption of foods, absorption of stool toxins or waste products that normally would not be absorbed in a healthy population, but the nature of the bowel inflammation in these children allow things to be absorbed through the gastrointestinal tract that would not otherwise be absorbed, and when that happens, those absorbed compounds seemingly have a toxic effect on the developing brain, probably during this critical stage of development at the age of 1-1/2, 2-1/2, 3, etc.

*That absolutely makes sense. So Dr. Krigsmann, what is the purpose of endoscopic procedures? When are they indicated? Are they very important to do, and does a parent need to feel nervous about this?*

Well, just to back up for a moment before I answer that question directly, we don't immediately do endoscopy on children with ASD and gastrointestinal disorders. They undergo the routine evaluation that any child, autistic or not, would undergo if they had chronic gastrointestinal symptoms. So there's a certain protocol that we, as gastroenterologists, follow when a patient presents to us with diarrhea, let's say, or chronic abdominal pain or constipation. A certain protocol and workup that will allow us to try and non-invasively figure out why this patient had these problems. Is it diet related? Are they on any other medications that's causing an alteration of the gastrointestinal tract function? Are there any other medications that these kids are on, supplements that might be affecting this? Do they have Celiac Disease? Do they have intestinal parasites? Do they have intestinal bacterial infections? Is there a hyperthyroid disorder? These are all things that can cause children to either have diarrhea, constipation or pain or any of those symptoms, and you can answer most of those questions non-invasively by doing a combination of blood tests or stool tests, abdominal X-rays; you can get a lot of information.

If we do our workup and we come up with no explainable cause for the gastrointestinal symptoms, then the next step, usually, is to get a piece of tissue in a biopsy of the gastrointestinal tract tissue, of the lining of the intestine; it's called mucosa. We get a biopsy of this mucosa, and we look under a microscope, and we see what's there, and typically, the patterns that we see under the microscope will allow us to determine whether inflammation is present or not.

So those patients whose blood test and stool test and other non-invasive tests are inconclusive and still lead us to a road that will allow us to treat the patient symptoms—those are the kids who will have to undergo an endoscopy and a biopsy simply to see what's there. It is a very safe procedure. It is done under general anesthesia, and there's no other choice, so we need to have these children sleeping; otherwise, they will never cooperate for this type of invasive test.

It is not painful. The prep is much easier than parents are worried about. It's actually a very easy process, very well tolerated by the vast majority of these children, and the idea of the prep for the colonoscopy is just to get the stool out of the colon so we can put the scope in and see where we're going from the biopsy. And the prep, typically, just lasts for one day, one day

prior to the endoscopy. And again, it's a very safe procedure when done, of course, with experienced anesthesiologists and experienced gastroenterologists.

*What tissue findings are there in the bowels of these children?*

Well, when we do an endoscopy on children with unexplained gastrointestinal symptoms who have ASD, we find, (1) just looking through the endoscope with the eye, without taking biopsies or getting a microscopic view of it, just a visual appearance of the lining of the intestine, we see a number of abnormal findings.

The most marked one, visually, is the lymphoid hyperplasia found in these children, and the term lymphoid hyperplasia refers to an enlarging of the lymphoid follicles of the lining of the intestine, although intestines are replete with immune cells, and these immune cells are in a series of little nests, and there are millions of these nests throughout the gastrointestinal tract.

When these immune nests in the gastrointestinal tract that are called Lymphoid follicles; when they come into contact with anything that they perceive as being foreign; that could be a foreign food, a food that they're allergic to, or a bacteria, or a virus – when they come in contact with this, any one of these stimuli, the function of these lymphoid follicles is to rapidly multiply the number of immune cells present in these follicles, and those immune cells then go out and kill and remove what it perceives as being foreign. And it will do this in a non-specific response of these – the lymphoid follicles will enlarge in response to any one of a variety of stimuli—again, viruses, bacteria, food allergies. The degree to which we see that in these children is quite remarkable, particularly in the terminal ileum—an area very rich in these immune cells.

That's an area that when you put the scope into the terminal ileum, you see an incredible degree of lymphoid hyperplasia, and in many of those cases, the lymphoid hyperplasia we see in the ileum really resembles that which we see in other known bowel diseases, such as Crohn's Disease, and that's one of the many similarities between the bowel disease in these children and Crohn's Disease.

It's very important to emphasize that the bowel disease these kids have is not Crohn's Disease. There are very, very important distinctions between the two, and the criteria that allow us to diagnose Crohn's Disease are absent in these children; however, even though it's not Crohn's Disease, it's a variant of a bowel inflammatory disease—we have inflammatory patterns that are there. So the one we have is marked lymphoid hyperplasia, and we see that not only in terms of ileum, but we see that in the colon as well, and we see that in the esophagus, and we see it in the small intestine, the duodenum.

The other finding we see, looking visually through the scope, is we'll see evidence of inflammation. We'll see ulcerations, aphthous ulcerations, in particular, are very common, and we see aphthous ulcerations classically in Inflammatory Bowel Disease, like Crohn's Disease and Ulcerative Colitis is another common finding, and we see that in the colons of these children. We see the aphthous ulcerations in the esophagus, the stomach and in the duodenum.

Aphthous ulcerations is a very common finding. We'll see clear-cut areas of inflammation and redness erythema, in the colon and also of the upper gastrointestinal tract. Those are the most common visual findings. When you look under a microscope at the biopsies, we see a whole range of inflammatory patterns. We'll see active inflammation, which is neutrophilic inflammation. We'll find chronic or lymphocytic inflammation; we see Cryptitis; we find crypt abscesses; we find eosinophilic inflammatory patterns—a whole range of inflammation.

Looking at it under the routine microscope, there seems to be a number of different types of inflammatory patterns, and no single pattern is classic for this disease, so it's more of a non-specific, diffuse, patchy inflammatory presence. Throughout the gastrointestinal tract, we see it from the esophagus all the way down to the anus and everywhere in between. Those are the most common microscopic findings.

There have been numerous publications that look at the inflammatory patterns on a molecular level. So when you go down even above the level of the microscope, you look at the molecular content of the bowels and the inflammatory cells, and there you find important distinctions between this and other inflammatory diseases like Celiac Disease or Crohn's Disease or Ulcerative Colitis.

You find a very unique molecular pattern that seems to be present throughout the gastrointestinal tract, and what we are working on at Thoughtful House is to further define the molecular nature of this inflammation so that we can categorize it and we can come to understand it better and perhaps figure out where this inflammation comes from and what's triggering it.

*I think that you may have, at least in part, answered my next question, which was based on analysis of many tissue cultures, has a pattern become apparent that suggests an etiology for any or all of the gut issues. And I think you said that you're working on that on a molecular level; you've found some diffuse, non-specific pathology throughout the gastrointestinal tract. Does this pathology suggest – first of all, am I correct in that? And second of all, does the gut pathology suggest an autoimmune condition?*

Well, you're absolutely correct, Teri. The key to understanding what the etiology of the inflammation is, is to do a series of very well designed studies that will help us narrow down the causes.

The most prominent suspects that we have as far as causes of this inflammation are (1) autoimmune disease, like you mentioned; that's one type of disease that can certainly make the bowel appear the way it does, and we're looking at the possibility of this being an autoimmune disease. We're also looking at the possibility of this being a food-mediated disease, where it's if you have a healthy bowel and certain foods that come down the gastrointestinal tract cause it to be diseased.

We know that Celiac Disease is a perfect example of that. You have a regular healthy bowel exposed to gluten-containing foods, and you get bowel disease. You take away the gluten, and then the bowel heals, so is this disease food-mediated, caused by food, or is the disease pre-existing, like an autoimmune disease, only it's exacerbated when food is introduced

that contains such things as gluten or caseine or perhaps other food components.

And the third possibility is: is this a viral infection of the intestine? Certainly the pattern of the inflammation present in these patients is suggestive of a possible viral infection. There are many similarities between the bowel disease that these children have and the bowel disease seen in patients with HIV. So these are all potential explanations of the bowel disease in these children, and, of course, the next question that begs to be asked is what is the nature of the association between the bowel disease and the cognitive symptoms that we call autism.

How is it that bowel disease of this nature, whatever the cause might be; how is it that you get disease of the intestine, and, as a result, have symptoms of autism? And the leading theory that we have to explain that seems to be that, as a result of the bowel being inflamed, it now has caused increased permeability and its ability to act as a barrier against absorption is diminished, and things—chemicals, compounds, substances that are located in the intestinal lumen that should remain there—are now allowed to be absorbed through this inflamed, permeable intestinal wall—this leaky gut that many of you have read about or heard about. We think that compounds, such as gluten and caseine are absorbed in a virtually intact state into the body, where they normally shouldn't be.

And once they get absorbed in their intact state, they undergo metabolism that none of us would usually see because we never absorb this compound, and the byproducts of the metabolism of compounds such as gluten and caseine are opium-like compounds. Opium-like compounds have a narcotic property to them that can, of course, affect the mental status and behaviors. If you have chronic exposure to those types of compounds at a very early developmental age, which we know, of course, is a critical time period, where if things go wrong during that time period, you often cause permanent damage—and if that would happened then, perhaps those can be the explanation for the symptoms of autism.

That's our leading theory right now, and again, these are all questions that can be answered with proper studies. Of course, proper studies require proper people to perform the studies, motivated investigators, and, of course, the appropriate funding.

*How is it that there are compounds that are absorbed that shouldn't be absorbed, yet there are nutrients that should be absorbed that are not absorbed?*

That's a very, very good question. On the one hand, when you have bowel inflammation, a very important component of the lining of the intestine, of the small intestine, is the enzymes, digestive enzymes. You have a number of digestive enzymes that are located in the lining of our intestine that serve the function of breaking down food within the lumen into much smaller molecules that then are absorbed into the body.

When you have a disease of the lining of the intestine, like Crohn's Disease and like Celiac Disease and like this disease in children with autism, the result is there's an enzyme deficiency, and a secondary malabsorption of a lot of the molecules that we need to live. So those molecules are now not being absorbed. On the other hand, the interesting dichotomy exists where

things that normally should not be absorbed are absorbed because you have increase permeability.

That has to do with the selectivity of the membranes; where on the one hand, things that shouldn't be absorbed are absorbed, and the things that should be absorbed are not absorbed, and this we see in other bowel inflammatory conditions as well. For example, Crohn's Disease, we know, the hallmark of Crohn's Disease, particularly pediatric Crohn's Disease, is now absorption and growth failure, and we see that excessively in pediatric Crohn's Disease.

On the other hand, we also know that there are levels of absorbed foods that are not normally present in the blood that are present in patients with Crohn's Disease, and as a result, there are antibodies, the RDG antibodies are present in Crohn's patients excessively compared to non-Crohn's control patients, and the meaning of that, we believe – a number of investigators believe the meaning of that is that food that normally would not be absorbed intact through the intestine of Crohn's patients is absorbed, which simulates an antibody IGG response, which you cannot measure in the blood.

So that dichotomy exists in a variety of bowel and inflammatory conditions, and it exists in these children as well.

*If bowel disease is present, how long will it need to be treated for?*

We don't know. We don't know the answer to that question. We'll only know that as the years go on, after we have acquired a long-term experience with these children to better be able to determine the optimal duration of treatment, and what we probably have to do is base it upon a symptom response, how good are we going to get at controlling the symptoms of diarrhea, constipation, abdominal pain, etc. And also, we have to keep in mind the issue of recurrence: how likely will it be that if we stop the medications after a year or two, after we've presumably suppressed the systems, that this child is GI symptom-free.

If we stop the medications, how likely are we to have a recurrence of the disease with possible cognitive consequences? So, all these things will be looked for over the course of the next few years.

*What percentage of children are seeing significant improvement via the current treatment plans in use?*

The vast majority of children. We haven't quantified our data yet. My experience with over 350 children—I estimate that between 70 and 80%, see significant improvement in their bowel symptoms. By significant, I mean complete resolution or virtually complete resolution to the extent that their quality of life is dramatically improved. It's important to realize that the objective is not to treat the autism. The objective is to take a child who is suffering from a chronic gastrointestinal symptom and take away that suffering, and that's what it's about.

That's our objective in treating the gastrointestinal tract, and, in that respect, we're very, very, very successful so that children who have pain are no longer in pain. Children who couldn't sleep through the night because they'd be screaming are now sleeping through the night. Children who couldn't con-

centrate on their ABA therapy, their physical therapy, their OT or their PT because they were distracted by how miserable they felt, are now able to spend an entire ABA session without distractions.

*You've just brought up a really important point, and that is that these children who cannot concentrate in their special education programs; maybe they don't just need a behavior plan. They need some real biomedical attention.*

That's very well put. The philosophy of *Thoughtful House* is that the disease that we're seeing with these children, the disease were calling autism and GI components in particular, is a biomedical disease and a behavioral disease. The two go hand in hand, and unless you address both of them in a formal treatment protocol, you will not get the success that you would otherwise get. You need to approach them both together—not separately, not sequentially, but concurrently—and that's when we believe we're going to have the best results, not just in their GI issues, but also in their autism issues. Because as you just said, Teri, when you have a child with GI illness, you're not going to get as far as you could otherwise get with just a behavioral approach because these children are sick—they're miserable, they're distracted, they're uncomfortable, they're not sleeping..

*Right, and none of us would want to go to a job at the office under those conditions.*

Absolutely.

*Now, I asked about the percentage of children seeing significant improvement via the current treatment plans in use, and you said about 70 to 80% emphasizing that what you're doing is trying to improve their gastrointestinal condition, and as a, let's say "coincidence," what percentage of the children see an improvement in their cognitive functioning?*

That's very difficult to answer. To answer that question requires a very well designed, very rigid study with an excellent developmental pediatrician and behaviorist. The only way to really gauge if there is cognitive improvement is to do a very well designed study. That's doable, and that will be done at *Thoughtful House* as well, but I will say, without any reservation, that these kids clearly learn better and respond better in their behavioral therapy when they're not miserable.

And that's a universal observation of the parents. So clearly; there's no doubt, from our experience that we help them cognitively. The question is: are we simply helping them cognitively because they feel better, as any of us would if we were taken out of our gastrointestinal misery, or is there some direct impact on brain healing that treating the gut might offer?

And that's the million-dollar question.

*That's a very important question. Are there additional approaches that can augment the gastrointestinal treatment plan, such as special diet?*

Absolutely. The nature of this bowel inflammation is such that dietary components will exacerbate the inflammation. A common finding is that you have a child who has a dietary infraction; gets a hold of a piece of pizza, and for the next few days will have horrendous diarrhea and pain and gas, and whenever the remnants of that pizza go away, then those symptoms subside. There's no question that food content will exacerbate the inflammation, and therefore, dietary restriction plays a huge role in treating the bowel disease and bowel symptoms.

The other treatment approaches that we employ for the bowel disease include enzymes; again, because the feeling is that the simpler the food substance is that's being introduced to the gastrointestinal tract, the more broken down it is, or the simpler molecule it is, the less likely it is to exacerbate and irritate an already irritated lining of the intestine. So enzymes play a role in that respect. And we also know from unpublished studies that there is an enzyme deficiency of the lining of the intestines; that there are much broader enzymes normally present than the lining of the bowel, in the small bowel, are diminished in these children, which is exactly what you'd expect in any bowel inflammatory condition that involves the mucosa.

So, getting supplemental enzymes seems to make a huge difference in many of these children.

*And that's in addition to special diet?*

That's in addition to the diets, right. And what we do, in addition to both of those; we also like to give probiotics for the very simple reason that we know that Crohn's Disease altering the bowel flora, seems to have a positive impact on the level of inflammation in Crohn's Disease. And we extrapolate that information, and apply it to these children as well and often with improvement as far as from a GI symptom standpoint.

Those patients who have food allergies; we'll give them medications like Cromolyn Sodium or Gastrochrome in an effort to diminish the allergic nature of the process that we see in some of the children. So it's a multi-model approach, all with the goal of decreasing the inflammation, allergic or autoimmune in nature—whatever the nature of the inflammation is, we're going to be decreasing it in our treatments.

*Now, was that Gastrochrome?*

Gastrochrome.

*Gastrochrome, and is that prescription or over-the-counter?*

That's prescription. It's a oral version of a frequently inhaled drug. It's an inhaled drug that we use with asthma, and asthma, of course, is an allergic, an autoimmune condition, and we use that same principle for allergies of the gastrointestinal tract by giving this drug orally and that lessens the inflammation.

*Okay, so you mentioned special diet, probiotics, Gastrochrome, which is by prescription, and enzymes. Are there any other pharmacological treatments that you use once you've been able to make a diagnosis?*

Yes, we also frequently use anti-reflux treatments in these children. The vast majority have evidence of esophagitis or inflammation of the esophagus. It's not clear to us if the esophagitis is simply reflux in nature or if it's a combination of autoimmune disease, allergy and reflux. Sometimes, the findings overlap on the microscope, and it is difficult to tease them apart. Clearly, whatever the etiology of the esophageal disease is, the presence of acid would only make things worse, so we frequently give an acid-blocking therapy to those patients with evidence of esophagitis. That's one more thing that we frequently use.

And beyond that—beyond those treatments that we just mentioned—if there are specific symptoms that are particularly troubling to individual patients, we'll tailor a treatment protocol for that patient. For example, if constipation is a huge issue for some patients, and in many patients, it is a huge issue, we'll have to devise a laxative regimen that's going to be safe for that patient in light of other medications they may or may not be taking.

That's just an example, but there are other GI conditions that some of these children have that are chronic in nature that are unique for those particular patients, and we need to design treatments for them on an individual basis.

*Okay, so if you try one treatment, and your child doesn't well tolerate it, there are alternatives?*

Yes, that's a very important point. The medications that we use; the anti-inflammatories, in particular, are sometimes not well tolerated by some of these kids, the same way that foods, routine foods, are not well tolerated by these children because of their unique Inflammatory Bowel Disease; then medications are the same way. Medication is just one more substance you put down into the GI tract, like the food, that the body may or may not be sensitive to, and if you're sensitive to a variety of foods, very likely, you will be sensitive to a variety of medications.

And that's what we see with many of the things that we do use. If that were to happen, if there were to be a sensitivity to a medication, whether it's allergy or whether it's behavioral or tolerances or major sleep disturbances or the appearance of aggressive behavior—these are all things that we've seen from time to time with these medications—we try an alternative, and it's very, very rare that I've had a child who did not tolerate anything, a child that was so intolerant that everything we gave them resulted in bad behavioral responses. So definitely, we keep trying until we find the right one.

*Do you see a difference in age groups insofar as which age group has diarrhea and which age group has constipation?*

You know, I've never thought about it quite that way. Off the top of my head, what I would say is that the 2 and 3-year-olds are the ones who are most intensely affected with diarrhea. They will have that for a year or two, a period of horrendous diarrhea two, three, four times a day, a lot of irritability, up all night, never comfortable. That's the age where we see that most intensely. When you get to the kids who are like 7, 8 or 9, you'll get typically a decrease in the frequency of diarrhea, and

the kids with chronic constipation happen to be the kids who are 7, 8 and 9. We don't really find the kids who are 2 and 3 complaining or suffering of constipation.

*Is it possible for a child to be passing the soupy stools, but still have some sort of impaction?*

That's possible, and that clearly is called overflow diarrhea, and that's not been our experience though, despite what other people have observed with their patients. It is a widespread impression that overflow diarrhea is present in these kids, and we just haven't see that. We haven't gotten that—we don't get the impaction. We get colons full of stool; colons that are full of the soupy, gunky mush, but not the classic impaction with liquidy stool flowing around.

*I would imagine that it's really not healthy to be retaining so much stool in the bowels.*

No, it's not. It's very, very unhealthy, and what's interesting about this disease is that when you have bowel inflammation, you have Crohn's Disease or Ulcerative Colitis; diarrhea is a hallmark of those diseases. When you have bowel inflammation, you tend to get increased motility of the GI tract; increase frequency of stool, looseness of stool. What these kids have, very frequently, is a hypomotility state secondary to their inflammation, so the bowel actually functions slower than it usually should.

Motility of the bowel is decreased, and again, kids whose primary symptom becomes that of constipation and severe straining, and when we say constipation and straining; what is the interesting thing about these kids is that they can go four, five, six days without a bowel movement; they push and strain to pass the stool, and then what comes out is this soupy mush, not the brick you'd expect it to be based upon the length of time the stool's been in the bowel plus the straining the bowel to get it out.

What that speaks to is this dysmotility, this hypomotility state, where the bowel, because of the inflammation, cannot move things forward, and we know that exists in Bowel Inflammatory Disease. It's well documented in literature.

*Does constipation also exacerbate reflux?*

Well, constipation can, but I would actually rephrase that and say that dysmotility causes the constipation, which also results in reflux. What dysmotility is, is the inability of the intestines to move things from mouth to anus in a sequential fashion. When that sequential contraction of the intestinal muscle is interrupted by dysmotility, then you get reflux. If it's not moving downwards, it's going to move upwards.

*Do the treatments that you propose help the stool, help the motility, help the formation of the stool, etc.?*

Yes, they do all of that. That's the goal of our treatment.

*Two more questions. Do children exhibit behaviors that are assumingly unrelated to GI symptoms, but that go away once*

*the GI symptoms and pathology are addressed? I know I heard about a girl, who was putting her arm over her head, and nobody could figure out why, and it went away once her GI symptoms were addressed.*

That can clearly happen. It would depend on the individual's response to their pain. What we've seen over and over again, as mentioned before in this interview, is there are certain classic behaviors or position that these kids assume that we know is a result of their abdominal distress, so this posturing is leaning over the edges of tables, sofas and some children will put pillows underneath their abdomen laying on the couch. Other children will put their parent's hand on their abdomen. They will want to be stroked over there. Those are all things that we've come to know are behavioral manifestations of pain and discomfort.

On an individual basis, it's certainly possible that the individual child will put their hand over their head or lift up a leg or do whatever it is that that child feels is helping them.

*I was thinking about if they have say severe erosion of their esophagus; what things they might do, and what can parents look out for as indicators?*

The frequent behavior that we see with esophageal disease are kids who will bang against their chest.

*Oh, my!*

They will bang their hand against their chest. That's something that's a behavior that intuitively makes sense. Once you know that you have this disease there, you see this child doing it, and you put two and two together, and the answer is obvious, but that, we see over and over again. That's the only sign that comes to mind.

*So how major a role to you feel rectifying gastrointestinal issues are to a positive prognosis for most children diagnosed with autism?*

We think it's crucial. We think it's crucial for the most simple of reasons, like we said before; if you want to have a good behavioral outcome, a good developmental outcome, which, of course, is the main goal; then you cannot achieve that if you are physically sick.

And it's crucial to address the general medical concerns, not just GI concerns. If a patient had autism and hyperthyroidism, you can imagine how difficult it would be to behaviorally approach their cognitive problems if they're hyperthyroid.

*Good point.*

Or if they have a broken leg.

*Good point. Dr. Krigsmann, please tell our listeners about Thoughtful House and the April 3 Thoughtful House Spring Conference, Austin in Action, the Evolving Medical Model in Childhood Developmental Disorders, Implications for Clinical and Educational Care.*

Well, *Thoughtful House Center for Children* is a new clinical and research initiative that is based in Austin, Texas, directed by Dr. Andrew Wakefield. My role is that of medical director, and I will be personally involved in the medical management of children with ASD and gastrointestinal disease. The goal of *Thoughtful House* is to provide a dual approach to treatment, both a behavioral approach—Dr. Doreen Granpeesheh will be directing the behavioral interventions at *Thoughtful House*. The medical interventions initially, in Phase I, will consist of gastrointestinal interventions. We have already brought on board a well known physician who will treat the generalized medical and biochemical aberrations in these children and we will be formally introducing him at the Sunday conference. By generalized medical care, I mean a full biomedical interventional approach with the ultimate goal of research, so this is not a place that is going to be there just to be one more location to get enzymes or probiotics but rather a complete clinical and research center for these children.

This is going to be a center where every intervention that we do; every bowel, medical, and behavioral intervention that we do, will be tracked and will be monitored and will be studied and that will help us determine which of these treatments are, indeed, helpful; which aren't helpful. Is it helpful to chelate your child? Is it a waste of time and money because it's dangerous? Is chelation only going to be effective if you combine it with something else? Is there a subgroup of children that are most likely to respond to behavioral therapies or to GI interventions?

Those are all questions that, as parents, you're dying for these answers because you're faced with a slew of choices, very few of which have been explored in a scientific fashion. The feeling that we have at *Thoughtful House* is we're going to subject the most common treatment interventions to scientific scrutiny and see what holds up, and we'll be able to make recommendations based upon our findings, and we'll be able to hopefully tailor those recommendations to specific patient groups. The autistic world has been clamoring for exactly this type of institute, and now we have it.

The inaugural conference will be this coming Sunday in Austin, Texas at the Omni Hotel, and all of you are invited to visit our web site at [www.thoughtfulhouse.org](http://www.thoughtfulhouse.org) for a full listing of the speakers, the presenters, and the main thrust of the presentations this coming Sunday will be to demonstrate the immunologic basis for this disease.

*Please keep in mind that no doctor can answer questions on air in such a manner as applies to a specific child without actually being very familiar with the specific child's complete medical history or examining the patient. Dr. Krigsmann, we have a question here. What has been found to be the best way to improve motility? This is in reference to children with no constipation, but chronically full colons seen in KUB's and very slow motility times seen in Sitzmark testing. Laxatives and enemas have no effect.*

That's an interesting question. It seems to me that this is a patient who would, despite getting laxatives, has the KUB finding of a colon filled with stool and without constipation. A KUB finding of stool in the colon without clinically evident

constipation or a decrease in the number of stools per every couple of days or the frequency of the stools; then that would not be constipation. Constipation cannot be diagnosed, based upon a KUB finding, unless there's a clinical symptom that goes accompanies it.

*Okay. This one gets a little bit specific about the patient, so we'll just do what we can. Our listener in Mobile, Alabama asks, "I have a 32-month-old son diagnosed with ASD at 20 months, and then PDD at 22 months after introduction of a gluten-free/casine-free diet. After many different types of behavioral intervention and gluten-free/casine-free diet, he is doing really well, and I suspect that he would not meet the criteria for PDD diagnosis. He is testing at age for language and is pretty sociable; nonetheless, we have made no headway on his bowel problems, despite anti-fungals, antibiotics, digestive enzymes, restricting carbohydrates, etc. His diapers are always smelly, mushy, sometimes watery with undigested foods, despite digestive enzymes. What is the next step? Endoscopy? How do you determine when endoscopy is necessary for correct diagnosis? How are treatments for autistic enterocolitis different from treatment for other gastrointestinal diseases or problems?"*

Wow! That's a pretty comprehensive question, but I think that question covers the bulk of what we've been speaking about over the last hour and certainly capsulates it very well. The approach for this child would be the same as in any child, neurotypical, autistic or PDD or whatever. If you've got chronic loose stools; then that needs to be evaluated, and there's a protocol for that evaluation, and any pediatric gastroenterologist is qualified to do that evaluation, and if, despite the evaluation, a non-invasive evaluation, the explanation for diarrhea, chronic diarrhea, eludes us, then the next step is to get a biopsy. It's really as simple as that. As far as what treatments are out there, for those patients demonstrating inflammation on biopsy, the same anti-inflammatory drugs that we use in classic inflammatory bowel diseases are the ones that are used in ASD related bowel disease as well, with the addition, as mentioned before, of an enzyme approach, a probiotic approach, and a dietary approach.

*Okay, next question: "I have heard that if autistic enterocolitis is an autoimmune disease that we shouldn't give the kids immune-boosting supplements. Do you agree? The supplements I'm concerned about are Methyl B-12 injections, Transfer Factor and/or colostrum and Lauricidin. My kids are the ones that have not gotten sick since their GI issues started."*

I think the question is that there's the concern that perhaps we should not be giving substances that would increase the ability of the body's immune system in the face of an autoimmune disease, and that's one of the interesting paradoxes here. On the one hand, when you have Autoimmune Disease, you may have an immune deficiency going on. The reason why the body's immunity is hyperimmune can be the result of, on some levels, of an immune deficiency, so those two are not mutually exclusive, and one doesn't necessarily rule out the other.

I'm not particularly familiar with the details of Methyl B-12 and the other immune-boosting regimens so I'm probably not

qualified to speak about them, but on a conceptual level, having Autoimmune Disease does not necessarily exclude the conceptual approach to giving immune-boosting "agents."

*Personally, I've asked a similar kind of question and was reassured that what I wanted to give to help the immune system be stronger was okay, and I will forward that question further to someone who can address another component of it.*

As an addition to that last question, because what most commonly gets asked is: if you have a disease with a relative immune deficiency, so for some reason, the immune system is not working or cannot remove certain antigenic stimulants such as viruses or foods, and you have this exuberant immune reaction in the intestine as a result of that, why would you want to give an immunosuppressant? Why would you want to give an anti-inflammatory drug if the body's immune system is having difficulty mounting an immune response? And that's what many parents will ask me. That's an interesting question, but the bottom line is still that when you have an inflammatory disease of the lining of the intestine that's causing symptoms, the most effective way of getting rid of those symptoms is by suppressing the inflammatory response, despite the other side of the equation, where there may be some specific immune deficits that are in place – despite that, the only way to really effectively get rid of these GI symptoms is to give a drug that will suppress a good part of the immune response.

*Next question: "My son was recently diagnosed with Asperger's Syndrome. He has always had difficulty having regular bowel movements. Sometimes, he goes for a week. He's currently taking some probiotic complete medicine and a homeopathic called Tipatica. He is taking this under the direction of a doctor and holistic medicine professional. Is there anything else we should do to help our son in this area?" Any general advice, non-specific to the unique patient?*

Again, were there gastrointestinal symptoms in this patient?

*Yes, Asperger's. He's always had difficulty having regular bowel movements, sometimes going for a week. He's taking probiotics and homeopathic remedy.*

Again, my advice would be to pursue that constipation issue and treat this child as you would any child who's constipated and see what it turns up. That's all we're doing. We're doing nothing unique with these children from a GI approach. We are just taking their symptoms seriously and exploring those symptoms as we would a child who did not have ASD, and we're surprised at the results.

*We can only address one more. Is there any scientific proof that children with Celiac Disease can have autistic-like symptoms?*

I'm not aware of that. That's sort of a double question. This is a patient who's neurotypical, who has Celiac Disease, but can have like perhaps hand-slapping or toe-walking as an isolated symptom, but not be autistic. Is that the meaning of the ques-



tion? If that's the question, then I've never heard of that. We do know that patients with Celiac Disease can have a variety of neurological symptoms, but I'm not aware of seeing Celiac or a case report of Celiac patients having isolated autistic-like behaviors without being autistic.

Conversely, if we ask the question the other way—do any of the ASD patients that we've seen at endoscopy have Celiac disease? And the answer is that in the almost 400 children that I've endoscoped, I've only seen one (Asperger's) with clear cut Celiac Disease. So it seems to be quite rare and that the gluten intolerance that these children show does not seem to be Celiac Disease. However, it is important to realize that most ASD children undergoing endoscopy have already been gluten free for a considerable period of time so that diagnosing celiac dis-

ease at that time is impossible. The gluten sensitivity of ASD seems to be something other than celiac disease, a different form of intolerance. It doesn't involve the characteristic damage to the duodenum and small bowel that we see in Celiac Disease.

*Okay, Dr. Krigsman, on behalf of Autism on Radio and Autism Help, Hope and Healing, I'd like to thank you for being with us today and for your continuing to search for and provide answers to a big piece of the healing puzzle for these children.*

Teri, thank you so much for having me, and Teri, thank you for all the work that you do on behalf of all these children. You're not only a mother working for your child, but you're also a mother working for everyone's children, so thank you.