



Guide To Intestinal Health In Autism Spectrum Disorder

*A comprehensive review of intestinal health issues
in Autism Spectrum Disorders
and the options available for treating them.*

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THE KIRKMAN GUIDE TO INTESTINAL HEALTH IN AUTISM SPECTRUM DISORDER

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A Draft

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Preface

Kirkman is the only manufacturing company designing products specifically for the autism community. We are committed and focused to this medical arena and are fortunate to be able to work with the world's leading researchers, doctors and scientists in the field of autism in developing our products. We participate in and support clinical studies by these experts in the field.

Kirkman Laboratories began manufacturing supplements for autism in 1967 working with Dr. Bernard Rimland, the founder of the Autism Research Institute. With Dr. Rimland's guidance, a high B-6/Magnesium vitamin and mineral supplement was created called Super Nu-Thera. Since its inception, Super Nu-Thera has benefited more than 50,000 autistic children from around the world. Eighteen clinical studies using B-6 in autism are published showing improved eye contact, more speech and improved social skills. Kirkman now has nine versions of Nu-Thera products.

Working with the leaders in autism treatment and research, Kirkman now has over 100 products dedicated to nutritional supplementation in autism. Many of our products are formulated to "taste good" so that compliance is easy. Unique to Kirkman has been the development of HypoAllergenic forms of our supplements, because the research has indicated that many autistic individuals are prone to allergic reactions and ingredient sensitivities. With the flavored and the HypoAllergenic product lines, we have a comprehensive line which should suit the needs of everyone.

Autism is a multi-spectrum disorder which once baffled the medical community to the point where it was considered untreatable. Now nutritional intervention has been researched and has been shown to be clinically effective in reducing and even eliminating many symptoms in autism. There is a lot more work to be done however, in conquering the cause and cure of this complicated developmental disorder.

The rate of autism has exploded in the United States and in many Asian and European countries. It has devastated the families involved. It is our mission to offer and develop the most effective and up to date products known to improve the quality of life for the families affected by this disorder. At Kirkman, our company motto is, "Are we doing all we can?"

WHY IS KIRKMAN LABORATORIES WRITING THIS GUIDE?

For children with autism spectrum disorders, gastrointestinal health is a key issue and dysfunction of the intestinal tract has a significant impact on their health and well-being. Autistic children respond favorably when intestinal health is addressed and corrected. Improved digestive function and improved behavioral and developmental responses are just some of the noticeable positive effects. To understand the GI problems that the autistic child experiences, we must first explore what role the intestinal tract plays and look at what GI conditions tend to be commonly part of their medical problems.

Proper nutrition involves getting all of the essential nutrients (proteins, carbohydrates, fats, vitamins, minerals and water) supplied and utilized in adequate balance to maintain the proper equilibrium of body processes necessary for good health. The functioning of the GI tract is dependent on nutrients being properly digested, absorbed and then eliminated. Optimal nutrition is essential for reproduction, growth and for normal organ development and functioning. The gastrointestinal tract is an integral part of the immune system, thereby providing resistance to infection and disease as well as for the repair and healing of body tissues. When dysfunction, disease or impairment of the intestinal tract exists, a significant impact in the health and functioning of the individual results. Most autistic children suffer to some degree from intestinal dysbiosis, abnormal permeability of the intestine, malabsorption and nutritional deficiencies.

Kirkman is in a unique position. We talk to hundreds of parents of children with autism every day. We know

that in general, most of these kids are not being properly treated for gastrointestinal issues. It is crucial to restore the health and functioning of the intestinal system as it significantly impacts the overall health and medical progress of those with autism spectrum disorders.

Some procedures recommended for improving the condition of ASD patients require a healthy gut to be completely effective. The Defeat Autism Now (DAN!) protocol for heavy metal detoxification recommends intestinal repair prior to the chelation process. Correcting immune dysfunction involves the concurrent healing of gut abnormalities.

Parents need to be aware of the necessity to "heal the gut". Kirkman hopes that this guide provides information that will allow parents and health care professionals to openly discuss gastrointestinal treatment options for individuals with ASD.

This protocol is a work in progress type document. This is the first draft and we will continue to revise it as science emerges or as feedback from doctors and parents warrants changes. Kirkman will continue to work with clinicians in designing clinical studies related to the health of the intestinal tract. We welcome your comments on this preliminary version of the Kirkman Guide to Intestinal Health in Autism Spectrum Disorder.

WHAT IS THE SUPPORT BEHIND OUR RECOMMENDATIONS?

Kirkman has cited references throughout this guide. We have also used results of clinical trials where applicable. Most importantly, however, this protocol will have the endorsement and support of the noted scientists, physicians and health professionals considered to be the leaders in the field of autism. These endorsements are in progress and will be listed in the first printed edition. This protocol is meant to be a guide to parents in how to deal with gut abnormalities associated with autism.

There is no one product cure-all in autism. Each child is unique and will exhibit different symptoms. As a result each child will require utilization of different parts of this protocol. Parents working with their health professional will still have to determine the specific requirements and products necessary to restore intestinal health to the individual. There is no dispute that healing the "gut" is an essential step in improving autism spectrum disorders.

Disclaimer: This document does not represent a cure for autism spectrum disorders or the gastrointestinal problems found therein. It should not replace the proper diagnosis and treatment of any individual. Decisions about a particular individual's care must be made by that person's physician or health care professional. The endorsers of this document are in general agreement with the material presented herein, but may disagree individually when applying recommendations to particular situations or patients. This publication has not been evaluated by the Food and Drug Administration. It is not intended to diagnose, treat, prevent or cure any disease.

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Chapter 1

Understanding Digestive Function: The Properties of a Normal Gastrointestinal System

The Importance Of Digestive Health

Physicians have known for centuries that a well-functioning digestive system is one of the cornerstones of good health. When digestion is working optimally, other organs and systems in the body have a better chance of working optimally as well. This is because the digestive system is responsible for processing the nutrients in our food, which in turn are used as fuel for all of the other physiological processes in the body. Optimal nutrition is essential for growth, reproduction, development, tissue repair and healing, and for the normal functioning of every organ in the body. Therefore, the digestive system is very much responsible for supporting the health of the body as a whole.

In addition to providing fuel for the body through nutrition, the intestinal tract also plays an integral role in the functioning of the immune and nervous systems. In his book entitled *The Second Brain*¹, Michael Gershon explains the gut-brain connection and describes how two-thirds of all immune activity occurs in the intestinal tract. This is a remarkable discovery and helps us understand the inner connections between the gastrointestinal, immune, and central nervous systems.

In recent years, as popular interest in nutrition has grown, a great deal more attention has been placed on the treatment of illness and prevention of disease through diet. Many of the books written on the subject maintain that by eating a wholesome, well-balanced diet, it is possible to treat a variety of ailments and maintain good overall health. While proper nutrition is certainly one of the first places to start in the journey toward health, there are many people with excellent dietary habits who suffer from significant digestive problems. For these people, even the best diet in the world may be of little benefit if the body is not able to properly digest, absorb, and assimilate the nutrients from their food. This may in turn lead to nutritional deficiencies that can result in a whole host of systemic problems, from asthma and skin conditions to neurological and immune problems.

This discussion is especially pertinent when it comes to the autism spectrum disorders. The majority of children with ASD have some type of intestinal dysfunction, such as intestinal

hyperpermeability (“leaky gut syndrome”),² malabsorption,³ enterocolitis,^{4,5} liver detoxification problems,⁶ fungal and bacterial overgrowth,^{7,8} sulfation deficits,⁹ and others. One study of 36 children with autism revealed histological evidence of grade I or II reflux esophagitis in 25 subjects, (69.4%), chronic gastritis in 15 (41.7%), chronic duodenitis in 24 (66.7%), and low intestinal carbohydrate digestive enzyme activity in 21 (58.3%).¹⁰

All of the intestinal abnormalities found in autistic children can substantially compromise their digestive function, which in turn interferes with their ability to properly process foods and results in significant nutrient deficiencies. Some of the most common vitamin and mineral deficiencies seen in these individuals are zinc, magnesium, calcium, and vitamin B6. These deficiencies, along with other external insults such as food sensitivities, environmental chemical exposures, and heavy metal toxicities, may help explain the vast array of neurological, immunological, and other systemic complaints found in autistic children. For these individuals, then, gastrointestinal health is a key issue, and dysfunction of the intestinal tract has a significant impact on their health and well-being. The digestive system should therefore be the fundamental starting point in a comprehensive treatment approach for autism spectrum disorders.

Activities Of The Digestive System

The digestive tract can be thought of as a long tube, 25 to 35 feet in length, which runs from the mouth to the anus. The intestinal lining is one of the most important components of the digestive tract. In the most basic sense, it represents a living barrier between the “outside world” (food allergens, toxins, bacteria, fungi, and heavy metals) and the “inside world” (cells, enzymes, hormones, tissues, and organs). The intestinal lining has the daunting burden and responsibility of keeping harmful substances from passing through this barrier and entering the bloodstream, while at the same time allowing all the beneficial nutrients from foods to get through. Correcting the problems that adversely affect the intestinal membrane and beginning the process of healing and restora-

tion of these tissues is of paramount importance in the health of those with autism spectrum disorders.

The primary function of the digestive tract is to break down the large particles of food that we eat into small molecules that can cross over the intestinal lining, enter the bloodstream, and become fuel for the various metabolic processes in the body. In order to accomplish this function, the intestinal tract is involved in four primary activities: digestion, absorption, assimilation, and elimination. Each of these activities is described as follows:

Digestion: Digestion is defined as the process whereby food in the gastrointestinal tract is broken down chemically and mechanically into absorbable forms that can be utilized by the body. Digestion occurs primarily in the stomach and small intestine, and to a lesser extent in the mouth.

Absorption: Absorption is defined as the process whereby nutrients from digested foods cross the gut wall and pass from the intestinal tract into the bloodstream. Absorption occurs mainly from the small intestine, but also to a much lesser extent from the large intestine and stomach.

Assimilation: Assimilation is described as a series of steps in which the products of digestion are utilized for energy and are chemically converted by the body's metabolic processes into living tissue. Assimilation takes place on a cellular level.

Elimination: Elimination is defined as the excretion from the body of the waste products produced during the process of digestion, absorption, and assimilation. Wastes are eliminated through the intestines, kidneys, skin, and lymphatic system.

Properties Of The Digestive Tract

The intestinal tract is a complex and intricately configured organism. In order to help you better understand the properties of the intestinal tract and the problems that may occur when disease is present, here are a number of facts about its structure and function. The actual workings of the digestive organs will be discussed in greater detail in the next section.

- About 70% of the immune system in humans is located within the intestinal tract and digestive organs.
- The small intestine averages between 15 and 20 feet in length.
- The inner surface of the small intestine is composed of tiny folds and finger-like projections called villi and microvilli. The purpose of these is to provide the maximum possible surface area for absorption of the nutrients from foods. If the small intestine were to be unrolled, unwrinkled, and laid out flat, its total surface area would be about the size of a tennis court!
- The intestinal lining has the ability to repair and regenerate itself every 3 to 5 days.
- While the surface area of the small intestine is as large as a tennis court, its actual thickness is no greater than that of a human eyelid.
- Compared to the small intestine, the large intestine (colon) is much smaller: only 3 to 5 feet in length.
- When stretched out, the surface area of the colon is about half the size of a pool table.
- In adults, the colon absorbs about 2 gallons of water per day.
- It is estimated that at any given time, as many as 100 trillion (100,000,000,000,000) bacteria inhabit a healthy human intestinal tract.
- Some of these bacteria rank among the most toxic substances found in the environment.
- About 1/3 of stool is made up of these bacteria and their by-products.

A Journey Through The Digestive System

The purpose of this protocol is to identify what is damaged in the intestinal tracts of individuals with autism spectrum disorders and to discuss the best approaches to addressing and treating these problems. In order to understand what is malfunctioning, however, it is helpful to first understand how the digestive system functions normally. For this purpose, we will begin with a discussion of the different organs and tissues involved in the process of digestion, absorption, assimilation, and elimination. This information will provide the background for later chapters that address the specific intestinal problems most commonly seen in ASD.

1. The Mouth

The process of digestion begins in the mouth, where food is thoroughly chewed by the teeth in order to maximize its surface area and thereby make its nutrients more available for later absorption. Chewing also provides a signal to other components of the digestive system that the process of digestion has begun. For one, it stimulates the production of saliva by the salivary glands located under the tongue. Saliva mixes with the food, thereby liquefying it and softening it for greater ease of swallowing. Saliva also contains the enzyme salivary amylase, which has mild carbohydrate-digesting action and helps to break down some of the starches from food into simple sugars. Once the food has been chewed and swallowed, it passes through the esophagus and enters the stomach.

If a person does not chew their food thoroughly, such as when they eat too fast and swallow larger chunks of food, there is less of a surface area available for absorption and this in turn places a greater burden on the stomach. This person may suffer from resulting problems with indigestion, including heartburn, acid reflux, gas, and belching.

2. The Stomach

Once food enters the stomach, it continues to be broken down by both mechanical and chemical

processes. Mechanically, the stomach mixes the food and blends it with digestive secretions such as hydrochloric acid (stomach acid) and the enzyme pepsin. The end result is a product called chyme, which has a soupy consistency similar to liquid oatmeal.

Pepsin is the primary enzyme constituent of the gastric juices and is produced by the chief cells of the gastric glands. Its primary function is protein digestion, which it accomplishes by converting proteins into proteoses and peptones. It requires a highly acidic environment, with a pH of 1.5 to 2, in order to do its job.

Hydrochloric acid (HCl), which is secreted by the parietal cells lining the stomach, is essential for proper protein digestion and facilitates the absorption of vitamins and minerals. HCl is extremely acidic, but a thick layer of mucous coating the inside of the stomach helps prevent HCl from damaging the gastric lining. If this mucous layer becomes compromised for any reason, the HCl can irritate and burn the stomach lining, resulting in a gastric ulcer.

Stomach acid has a number of very important functions. It begins the process of protein digestion by breaking apart the protein chains in food. It acts as a sterilizing agent by killing the bacteria, yeasts, viruses, and parasites that we ingest by way of the foods we eat. It also helps break down our food and make the vitamins and minerals contained therein more available for absorption. Finally, HCl signals the pancreas to secrete the enzymes, bicarbonates, and hormones that are essential for the next stage of the digestive process, which takes place in the small intestine.

When insufficient amounts of hydrochloric acid are present, as some physicians believe to be true for many children with ASD, a number of problems can result. There may be a greater tendency to intestinal overgrowth with harmful microbes, such as bacteria, fungi, and parasites. Protein digestion may be inadequate, and improper processing of vitamins and minerals can lead to generalized deficiencies of these nutrients in the child. Another consequence of insufficient HCl may be abnormally low secretions of pancreatic enzymes, which results in food maldigestion and problems with food allergies, food sensitivities, and adverse reactions to gluten and casein peptides. Low levels of HCl may produce signs

and symptoms such as gas, bloating, belching after meals, vertical ridges on the fingernails, and a feeling like food is sitting in the stomach for a long time after eating.

Normally, food will remain in the stomach for a period of 1 to 4 hours, depending on the type of food consumed, the amount of gastric juices present, and the level of stress that the person is experiencing at the time. While the process of absorption occurs principally in the small and large intestines, there are a few things, such as water, alcohol, and aspirin, which are directly absorbed from the stomach into the bloodstream. Once the stomach has done its job and the food has been converted into chyme, it passes through the pyloric valve into the first portion of the small intestine known as the duodenum. This is where the secretions from the pancreas play an important role.

3. The Pancreas

The pancreas is situated behind the stomach, adjacent to the duodenum. Its primary function is the production of enzymes and other components that are necessary for the further digestion and absorption of food. Every day, the pancreas releases around 1.5 quarts of digestive secretions into the small intestine. The three most important of these secretions are insulin, bicarbonate, and digestive enzymes.

Insulin is a hormone that is responsible for the metabolism and proper regulation of glucose (blood sugar). When blood sugar levels are high, such as after a meal, the insulin secreted by the pancreas signals the cells to store glucose, thereby returning blood sugar levels to normal. Diabetes can result when these regulatory mechanisms fail.

Bicarbonate is secreted by the pancreas when food passes from the stomach into the duodenum, the first portion of the small intestine. Bicarbonate is an alkaline substance that neutralizes the chyme released by the stomach, thereby buffering it and protecting the delicate lining of the intestinal tract from becoming irritated by this digestive acid. Bicarbonate production by the pancreas is stimulated by the hormone secretin, which has become such a valuable therapeutic intervention for many individuals with autism.

Normally, secretin is released and activated when the acidic chyme from the stomach enters the duodenum. Once activated, secretin stimulates the pancreas to release large amounts of bicarbonate. Besides acting as a buffering agent to protect the small intestine from the acidity of the stomach juices, bicarbonate serves another important purpose: it provides an ideal environment for pancreatic enzymes to do their job. These enzymes, which require a slightly alkaline pH in order to function properly, are therefore highly dependent upon the availability of both secretin and bicarbonate.

Pancreatic enzymes are essential for continuing the process of digestion already begun in the stomach. Many children with autism are thought to have deficiencies in these enzymes and often respond extremely well to supplementation with digestive enzymes. The three most important groups of enzymes secreted by the pancreas are lipases, amylases, and proteases. The functions of these different enzymes are described as follows:

Lipases: Lipase enzymes work with bile to help in the digestion of fats. Lipase deficiency, which appears to be prevalent in many individuals with ASD, results in the malabsorption of fats and the fat-soluble vitamins A, D, E, and K. Clinically, fat malabsorption should be suspected whenever there are deficiencies in these nutrients, or when a child tends to have bowel movements where the stools are yellow, orange or pale in color.

Amylases: Amylase enzymes are important for carbohydrate digestion. Their primary function is to break down starches into smaller sugars. As discussed previously, a small amount of amylase is also present in saliva, but its primary action comes from the secretions of the pancreas.

Proteases: Protease enzymes assist in the digestion of protein by breaking down the proteins from food into single amino acids. This is another group of enzymes that appears to be deficient in autistic

children. A lack of protease activity can result in problems with food allergies, opioid reactions from gluten and casein peptides, and protein malabsorption. In addition to their role in digesting proteins, these enzymes serve a number of other important functions as well. They have antimicrobial activity and help to prevent colonization of the small intestine by bacteria, yeasts, and parasites. An individual with protease deficiency is therefore at greater risk of developing intestinal infections, including chronic problems with *Candida* overgrowth.

4. The Small Intestine

The small intestine is divided into three parts: the duodenum, which comprises the first 10 to 12 inches after the stomach; the jejunum, which is the middle portion and is about 8 feet in length; and the ileum, which makes up the final 12 feet before the large intestine. The primary function of the small intestine is the absorption of nutrients from foods. Once the digestion of fats, carbohydrates, and proteins has begun with the help of pancreatic enzymes, food travels through the small intestine and the absorption of nutrients occurs at various stages throughout its length. For example, the duodenum is the primary site for absorption of minerals; the jejunum is responsible for the absorption of protein, carbohydrates, and water-soluble vitamins; and the uptake of cholesterol, fat, and fat-soluble vitamins occurs in the ileum.

The inside membrane of the small intestine is specially structured to provide an optimal surface area for absorption to take place. It is composed of a series of microscopic folds called villi and microvilli, which resemble tiny finger-like projections along the length of the intestinal lining. When the intestinal lining is damaged by chronic irritation from infectious microbes, food allergens, or gluten and casein peptides, the villi and microvilli flatten out, reducing the surface area available for nutrient absorption. This is why people with chronic intestinal problems often suffer from malabsorption syndromes.

Besides its role in the absorption of nutrients from foods, the small intestinal lining also has the important function of acting as a barrier that

prevents unwanted substances, such as toxins and potentially harmful proteins, from crossing the gut wall and entering the bloodstream. Under normal circumstances, this barrier will remain intact. When there is chronic mucosal irritation, however, the intestinal lining will be compromised, allowing greater amounts of harmful substances to be taken up from the intestinal tract into the bloodstream. This results in a state of intestinal hyperpermeability, or leaky gut syndrome, a condition common to many children with autism spectrum disorders.

5. The Liver and Gallbladder

The liver is the primary organ of detoxification in the body. It cleanses the blood and helps to filter out the toxins that are absorbed from the gastrointestinal tract. It is also responsible for processing and neutralizing external toxins, such as heavy metals. Most of these toxins will later be excreted through the urine and feces. However, there are times when the liver is required to process more toxins than it can handle at one time. This may occur, for example, when a child is being treated for an intestinal *Candida* infection. As the yeasts are being killed off by antifungal agents, they release toxins that can enter the bloodstream and cause systemic problems such as headaches, fatigue, and behavioral aggravations. This phenomenon is known as the Herxheimer, or "die-off" reaction, and it is an experience well known to many parents who have taken their children through treatment for intestinal yeast infections. One approach to addressing the die-off reaction is to ensure that the liver's detoxification capabilities are functioning optimally. This is why many physicians who do heavy metal chelation recommend that their patients use liver-supportive supplements such as glutathione, NAC, and the herb milk thistle during the detoxification process.

In addition to detoxification, the liver has several other vital functions. It helps in the metabolism of a number of hormones, including thyroid hormone, estrogen, progesterone, and testosterone. It breaks down cholesterol and helps in the regulation of blood sugar, and it is also responsible for the production of bile.

Bile has a number of very important functions

in the digestive process. After being manufactured by the liver, it is either utilized by the small intestine (in the duodenum) or stored in the gallbladder for later use. In the intestinal tract, bile is necessary for the emulsification of fats, oils, fat-soluble vitamins, and cholesterol. With the help of the pancreatic lipase enzymes, it ensures that these fats are properly broken down so that they may be fully absorbed and utilized by the body. Bile also plays a similar role to the protease enzymes in keeping the intestines free of harmful microbes.

6. The Intestinal Immune System

Since the intestinal tract represents an important barrier between the external world and the internal environment, there are a number of immune mechanisms built in to the gut lining which help ensure that germs from the outside are neutralized before they can do potential damage inside the body. In fact, as previously stated, it is thought that up to 70% of the body's immune system is associated with the digestive tract. This intestinal immune system is known as Gut-Associated Lymphatic Tissue, or GALT.

When the specialized immune cells lining the digestive tract detect an unknown or possibly harmful substance (called an antigen), they signal the immune system to provide antibodies to help fight these antigens. Another immune defender that is present in the lining of the gut wall is known as Secretory Immunoglobulin A (SIgA). When antigens are present, SIgA can help to trap them in the mucous layer of the intestinal tract, thereby rendering them ineffective. Because the immune system has such an integral involvement with the digestive system, diseases or imbalances of the intestines can often result in significant immune dysfunction.

7. The Large Intestine

The final stage of our journey through the digestive system takes us to the large intestine, or colon. Once the process of absorption has been completed in the small intestine, food passes into the colon through the ileocecal valve, which is located in the lower right quadrant of the abdomen behind the hipbone. From the ileocecal valve, food passes up the ascending colon on the

right side of the abdomen, along a horizontal segment known as the transverse colon, and finally passes down the descending colon on the left side of the body to be eliminated through the rectum.

The large intestine has a number of functions, its most important ones being the formation of stool and the absorption of water, electrolytes, and remaining nutrients from the end products of digestion. Under normal circumstances, the transverse colon is where the process of stool formation begins, as water is absorbed from the waste products in the large intestine until they reach a consistency that allows them to be easily eliminated. If the stool remains in the colon for too long, however, too much water is absorbed and the stool becomes hard and dry, resulting in constipation. Conversely, if the waste products pass through the colon too quickly, not enough water is absorbed and this can lead to diarrhea.

In a healthy intestinal tract, stool is made up primarily of water, undigested fiber, and bacteria. There are trillions of bacteria that inhabit the large intestine. The bacteria that are beneficial and help support the health of the organism are referred to as probiotics. You may be familiar with some of these probiotics, such as *Lactobacillus acidophilus* (which is found in yogurt) and *Bifidobacterium bifidum*. These advantageous bacteria perform a myriad of functions, including:

- enhancing immune function
- eradicating harmful bacteria, yeasts, viruses, and parasites
- manufacturing vitamins A, K, and some of the B vitamins
- fermenting fiber in order to produce the short-chain fatty acid butyrate, which protects the cells of the intestinal membrane
- helping to prevent illnesses such as ulcerative colitis, inflammatory bowel disease, and colon cancer by ensuring a healthy intestinal environment

A number of drugs, including antibiotics, steroids, and hormone replacement products, can interfere with probiotics and disrupt the balance of these beneficial organisms in the colon. While antibiotics have the ability to eradicate harmful bacteria and have saved the lives of countless people with serious infections, one of their unfortunate

consequences is that they also kill off the beneficial bacteria (probiotics) in the large intestine. This in turn sets the stage for the development of a variety of digestive illnesses, including irritable bowel syndrome, chronic constipation or diarrhea, and intestinal overgrowth of *Candida* and other types of yeast. Many parents of autistic children feel that the majority of their child's problems started after the administration of multiple rounds of antibiotics. Besides disrupting the intestinal ecology, antibiotics can also compromise the health of the immune system, leading to more frequent colds and infections. In order to prevent these complications, it is always important to supplement with probiotics when antibiotics must be administered, both during the days the patient is on the antibiotics and also for several weeks after finishing the medication.

Summary

As the preceding discussion has shown, there are many complexities and intricacies involved in a properly functioning digestive system. From the processing of food to its link with the immune system, the intestinal tract plays a crucial role in supporting the health and wellness of the entire body. When digestive function is compromised, as is often the case in children with autism spectrum disorders, a number of problems can occur. In the following section, a list of signs and symptoms are provided that can serve as a guideline to help you determine whether your child might have an illness or imbalance of the digestive system.

Chapter 1: Understanding Digestive Function: The Properties Of A Normal Gastrointestinal System

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Chapter 1: Understanding Digestive Function: The Properties Of A Normal Gastrointestinal System

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Chapter 2

Symptoms of Intestinal Problems in Autism Spectrum Disorders

Introduction

How do you know if your child has an intestinal imbalance that needs to be corrected? For most parents, this is a question with very obvious answers. Problems with diarrhea, constipation, abdominal discomfort, and abnormal-appearing stools tend to plague the majority of children with autism spectrum disorders. Most physicians treating ASD report that the digestive system is one of the primary areas of dysfunction in these individuals, and that correcting their underlying intestinal imbalances can lead to significant clinical improvement, not only in regard to physical symptoms but also in such areas as behavior, attention, language, and development.

Even in the absence of obvious intestinal symptoms, however, there are many children with ASD who have significant gut issues that must be addressed as part of their overall treatment approach. A history of food allergies, gluten and casein intolerance, immune system problems, chronic fungal infections, and chemical sensitivities all point to an underlying imbalance within the digestive system. In addition, a number of external influences, such as vaccinations, heavy metals, and antibiotics, can compromise the health of the intestinal environment and lead to some of the syndromes frequently associated with ASD.

The signs and symptoms listed below are commonly seen in children with autism and are usually evidence of a deeper intestinal problem that needs to be addressed. These symptoms may occur alone or in combination, and can provide parents and physicians with an indication of whether it would be beneficial for their child to undergo further testing and treatment in order to evaluate the digestive system and ensure its proper functioning.

Indications Of Intestinal Problems In ASD

1. Overt signs and symptoms pertaining to the digestive tract

- Abdominal pain, cramping, or discomfort (this may manifest in behaviors such as crying or screaming, holding the abdomen, pointing to the abdomen, or wanting to lie in a fetal position)

- Problems with reflux or excessive burping
- Vomiting or spitting up food
- Abdominal bloating, especially after meals
- Excess gas
- Chronic constipation and/or history of fecal impaction; hard, dry stools
- Toe-walking (usually indicative of constipation)
- Chronic diarrhea or loose stools
- Foul-smelling stools
- Undigested food in stools
- Mucous in stools
- Abnormal consistency of stools (i.e. "oily" or "foamy" stools)
- Abnormal color of stools (i.e. yellow, orange, or pale stools)
- Rectal itching, burning, or apparent discomfort when passing stools
- Perianal rash

2. Problematic reactions to foods

- Gluten and/or casein sensitivity
- Food allergies and intolerances (may manifest with dark circles or puffiness under the eyes, redness of the cheeks or ears, chronic post-nasal drip, headaches, skin rashes, asthma, environmental allergies, attention deficit, and behavioral problems)
- Reactions to phenols and/or salicylates in foods

3. Past medical history

- Significant history of colic in infancy
- Poor immune function with history of frequent infections, including ear, throat, and respiratory infections
- May also have an overactive immune response, as in allergies or autoimmune conditions
- History of fungal infections, such as thrush, diaper rash, or skin rashes
- History of sensory defensiveness, including sensitivity to sounds, lights, tastes, textures, and other external stimuli

4. Family history

- Maternal history of fungal infections during pregnancy
- Family history of celiac disease, Crohn's disease, ulcerative colitis, or other inflammatory bowel conditions
- Family history of allergies and/or autoimmune disease

5. Prescription drugs and immunizations

- Frequent use of antibiotics in infancy and childhood
- History of adverse reactions to antibiotics, including diarrhea, thrush, diaper rash, or other abdominal problems
- Immunizations in the child, including adverse reaction(s) to immunizations and/or the onset of developmental delays shortly following immunization
- Maternal history of immunizations during pregnancy, including RhoGAM shots

Chapter 3

The Role of Laboratory Testing

Introduction

As the preceding sections have illustrated, there are many symptoms and signs of intestinal abnormalities that are commonly found in individuals with autism spectrum disorders. As every physician knows, much in the way of diagnosis can be done by taking a detailed history of a patient's symptoms and by performing a thorough physical examination. This information, along with the results obtained from certain well-selected laboratory tests, can help the physician identify the underlying problems and decide which treatment approach to take.

Many parents who are interested in the biological approaches to treating ASD have struggled to find a doctor who can provide them with the proper guidance on laboratory testing and treatment interventions for their child's intestinal problems. These parents are faced with the daunting and often overwhelming task of sorting through long lists of symptoms in order to determine what may be causing their child's problems and what they can do to treat them. This process is further complicated by the fact that different intestinal pathologies often present with very similar symptoms. For example, a child who has chronic abdominal discomfort, bloating, gas, and loose stools may be thought to have an overgrowth of the intestinal yeast *Candida albicans*. However, there are other intestinal microbes that may cause these same symptoms, including a number of bacteria and parasites. In addition, these symptoms may also be caused by food allergies, pancreatic enzyme insufficiencies, and/or sensitivities to gluten and casein. It would therefore be important to do appropriate laboratory testing in order to identify the underlying cause(s) of this child's symptoms so that the proper treatments may be implemented.

Many parents who have not had the opportunity to work with a physician familiar with biological interventions for ASD have treated their child's intestinal symptoms on their own, and many have done so with outstanding results. Even without laboratory testing, it is possible to make a significant impact on digestive health by taking certain measures to ensure a well-functioning intestinal environment. Many of these interventions are discussed later in this protocol. We strongly encourage you, however, to work with a physi-

cian who can guide your treatments, monitor your child's progress, and provide you with the appropriate diagnostic measures and therapeutic recommendations for your child.

Finding a physician who is familiar with the biological approaches to treating autism is much easier now than it was in the past. Thanks in large part to the pioneering work of Dr. Bernie Rimland¹ and the Autism Research Institute, there is a rapidly growing number of health care practitioners who recognize that ASD is not a psychological syndrome, as it was once thought to be, but rather a medical problem that can be treated. Since 1995, the Autism Research Institute has hosted the annual Defeat Autism Now! (DAN!) conference to provide information to parents and training to physicians on biological approaches to treating autism. A list of health care practitioners who have attended the DAN! conferences is available on the Autism Research Institute's website at www.autism.com/ari. As the awareness of autism is growing and the focus is shifting to include more of a biomedical approach, the diagnostic and treatment options available to children with ASD are continually expanding, thereby affording them an optimal chance for recovery through appropriate intervention.

Basic Laboratory Testing For Intestinal Disorders

The laboratory tests discussed below are offered as suggestions for possible routes of investigation into the intestinal disorders that are so frequently found in individuals with autism spectrum disorders. Based on your child's medical history, your physician may choose to order one or more of these tests for diagnostic purposes. This list is based on suggestions made by a number of physicians specializing in the treatment of ASD, but there may be additional tests that your physician will consider to be beneficial in order to determine an appropriate course of treatment for your child.

Keep in mind that the following recommendations for laboratory testing are intended to be specific for the evaluation of intestinal symptomatology. However, these recommendations presuppose that other basic, preliminary tests have already been performed by the child's

pediatrician. These routine tests will vary, but may include a complete blood count to check for anemia, a blood chemistry screen to assess liver and kidney function, a urinalysis, a thyroid function test, and others. In addition, there are other tests commonly recommended by physicians, such as screening for heavy metal toxicity, which can help shed some light on the origin and expression of gastrointestinal symptoms in children with ASD. Further information on these and other tests is available in the DAN! consensus report entitled "Biomedical Assessment Options for Children with Autism and Related Problems".²

Finally, it is important to note that many of the tests listed below are considered to be "functional" in nature; that is, they are intended to uncover biochemical imbalances in the body as opposed to overt manifestations of disease. As such, most of these tests are not ordinarily available through your local hospital or medical laboratory. In fact, many physicians may be unfamiliar with these tests unless they have received special training in nutritional medicine, or are familiar with the biological approaches to treating ASD. This should not discourage you from asking your physician to order the tests that you believe to be appropriate for evaluating your child's condition. There are many health care practitioners who are determined to do everything they can to provide optimal care for their autistic patients, and most of the laboratories listed below offer assistance to physicians by providing information on tests and interpretation of results.

1. Stool Analysis

The comprehensive digestive stool analysis (CDSA) refers to a group of diagnostic tests designed to evaluate the overall health and functioning of the intestinal tract. This analysis, which requires between one and three stool samples for evaluation, is considered by many physicians to be the most fundamental and important test for providing clinical insight into the workings of a patient's digestive system. For many physicians treating children with ASD, this test offers not only an avenue for the diagnosis of intestinal disorders, but also provides a way to monitor a patient's progress by evaluating the efficacy of certain therapies through repeat testing.

The CDSA provides physicians with a wealth of information about the workings of a patient's gastrointestinal system. It evaluates certain markers to measure digestive function by analyzing a patient's ability to break down the proteins, fats, and carbohydrates from their food. It determines how well the food is assimilated by the digestive system and assesses the level of pancreatic enzymes produced by the body. It also provides valuable information as to the balance of the bacteria, yeast (*Candida*), and parasites that make up the intestinal environment. It can reveal whether there are adequate levels of beneficial bacteria, such as *Lactobacillus acidophilus*, or whether there is a state of "dysbiosis" in which these advantageous bacteria have been crowded out by other less favorable, possibly disease-producing microbes. In addition, the CDSA provides information on how to treat these pathogenic microbes by culturing them and determining which medications are most effective at eliminating them.

The CDSA is available from the following laboratories:

(Please see the resources section at the end of this protocol for a complete list of addresses and other contact information for these laboratories.)

Doctor's Data:

(800) 323-2784

Great Plains Laboratory:

(913) 341-8949

Great Smokies Diagnostic Laboratory:

(800) 522-4762

MetaMetrix Clinical Laboratory:

(800) 221-4640

US BioTek Laboratories:

(877) 318-8728

2. Organic Acid Test

Organic acid testing has been used by physicians for many years in order to identify certain "inborn errors of metabolism" in young children. However, it was not until recently that the pioneering work of Dr. William Shaw³ demonstrated that many children with developmental disorders excrete large amounts of urinary organic acids that had not previously been studied by researchers. Upon further investigation, Dr. Shaw found these organic acids to be by-products of both normal and abnormal intestinal microbes, such as

the bacteria and yeasts that often inhabit the digestive tract. Furthermore, he discovered that the urinary levels of these compounds associated with abnormal intestinal microbes decreased when the children were treated with antibacterial or antifungal medications.⁴ The urine organic acid test developed by Dr. Shaw (available through Great Plains Laboratory) has the additional benefit of providing a metabolic marker for the detection and treatment of *Clostridium difficile*, an anaerobic bacterium found in the intestinal tracts of many children with autism that is otherwise difficult to diagnose. Based on these observations, many physicians who treat ASD have used the organic acid test, often in conjunction with the CDSA, as a way to monitor the efficacy of treatment with antifungal and antibacterial medications.

The following laboratories offer urine organic acid testing:

Great Plains Laboratory:
(913) 341-8949

Great Smokies Diagnostic Laboratory:
(800) 522-4762
("Cellular Energy Profile")

MetaMetrix Clinical Laboratory:
(800) 221-4640

3. Urinary Peptide Test

The term "peptides" is used to refer to small groups of amino acids that are the breakdown products of proteins. In a normally functioning digestive process, ingested dietary proteins are broken down by a group of enzymes into single amino acids that are then absorbed into the bloodstream to serve as building blocks for hormones, neurotransmitters, muscle tissue, and other proteins required by the body. In many children with ASD, this process of breaking down dietary proteins into single amino acids is incomplete, often as a result of pancreatic enzyme insufficiency or a "leaky" intestinal wall (see later chapters for further descriptions of these problems). As a result, peptides are absorbed into the bloodstream from the digestive tract, and once in the bloodstream these peptides can lead to a variety of behavioral problems through their opioid-like activity.

This observation was made years ago by F.C.

Dohan in regard to schizophrenia.^{5,6,7} More recently, researchers such as Dr. Karl Reichelt in Norway,^{8,9,10} Dr. William Shaw at Great Plains Laboratory,¹¹ Dr. Robert Cade at the University of Florida,^{12,13} and Dr. Paul Shattock in England^{14,15} have demonstrated a similar link between dietary peptides and autism. More specifically, it is the peptides from casein (a protein found in milk products) and gluten (a protein contained in wheat products and several other grains) that appear to cause the greatest opioid-like effects in individuals with autism. For this reason, removal of casein and gluten from the diet, as well as supplementation with peptidase enzymes in order to facilitate the breakdown of dietary proteins, have become two of the cornerstones of treatment for ASD.

Because the elimination of gluten and casein from the diet is such a difficult task, most parents prefer to first measure the gluten and casein peptides that are being excreted through their child's urine. If the report shows the levels of these peptides to be high, then elimination of these proteins from the diet for an extended period of time is warranted. In most cases, individuals who are sensitive to gluten and casein experience significant benefits from completely eliminating these proteins from their diet. These benefits may be seen almost immediately, but in some cases the improvements may not be evident for a number of months. In any case, it is essential that the diet be followed strictly, since even a small amount of gluten or casein can cause significant behavioral aggravations in sensitive children.

Urinary peptide testing is available through the following labs:

AAL Reference Laboratories:
(800) 522-2611

Great Plains Laboratory:
(913) 341-8949

Immunosciences Lab
(800) 950-4686

Karl Reichelt, M.D., Ph.D:
011-47-23-07-29-85 (Norway)

4. Food Allergy Testing

In addition to the opioid effects of gluten and

casein, many individuals with autism spectrum disorders have significant food allergies and can show dramatic clinical improvement upon elimination of the offending foods from their diet.¹⁶ While some of these food allergies are of the immediate-onset (IgE) variety, the majority are delayed hypersensitivity (IgG) reactions. These different types of reactions are discussed further in the section on food allergy.

Testing for food allergies has been a controversial issue for many years. A number of conventionally trained physicians believe that the only reliable ways to diagnose food allergies are through blood tests for IgE (immediate hypersensitivity) reactions and through skin prick testing, the latter of which is often exceedingly difficult to do in young children. A strict elimination/challenge diet, in which major offending foods are eliminated for a period of time and then reintroduced in order to determine whether an adverse reaction occurs, appears to be one of the most reliable means of diagnosing food allergies in adults. While the elimination/challenge diet can also provide useful information in ASD children, it may be of limited value since it is often difficult to gauge the full extent of the symptoms that may occur upon reintroduction of the offending foods.

Most physicians specializing in the treatment of ASD have found the ELISA blood test to be the most helpful tool in identifying potentially reactive foods. The advantage of this test is that it screens for both immediate (IgE) and delayed (IgG) hypersensitivity reactions to foods. This provides valuable information because the IgG food allergies are generally more problematic and usually the most difficult ones to identify, since reactions can take up to 24-48 hours to manifest.

The more complete ELISA food allergy panels test between 90 and 120 of the most commonly eaten foods, but shorter panels or individual food assays are also available. These tests also provide information on the severity of the food allergies, the overall susceptibility of the immune system to food allergens, and most labs will provide the patient with an individually designed food allergy elimination and rotation diet based on their specific test results. Many physicians will use the ELISA test in conjunction with a more traditional elimination/challenge

diet and, since food allergies are usually linked to a “leaky” gut wall, some physicians will also choose to run intestinal permeability studies (see below) along with the food allergy panel.

The following labs offer ELISA or IgG food allergy testing:

Great Plains Laboratory:
(913) 341-8949

Great Smokies Diagnostic Laboratory:
(800) 522-4762

Immuno Laboratories:
(800) 231-9197

Immunosciences Lab
(800) 950-4686

MetaMetrix Clinical Laboratory:
(800) 221-4640

US BioTek Laboratories:
(877) 318-8728

5. Intestinal Permeability Studies

Increased intestinal permeability, commonly referred to as “leaky gut syndrome”, is a condition that has been shown by researchers to be much more prevalent in children with autism than in non-autistic children.¹⁷ In addition, patients with celiac disease¹⁸ (an inflammatory condition of the intestines brought on by eating gluten) and other inflammatory bowel conditions¹⁹ also show significantly increased intestinal permeability on laboratory evaluation.

There are a variety of factors that can cause the intestinal wall to become more permeable. Any type of irritation to the intestinal wall, such as from harmful bacteria or yeasts, parasites, food allergens, poor diet, nutrient deficiencies, or vaccine injuries, can compromise the integrity of the intestinal barrier and lead to leaky gut syndrome. When the intestinal wall becomes more permeable due to these irritating agents, larger molecules (such as those from toxins, bacteria, food allergens, and dietary proteins) are able to “leak” out of the intestinal tract and pass into the bloodstream. Once in the bloodstream, they can lead to a variety of conditions, including behavioral problems, attention deficit disorders, food allergies, reactions to food peptides, chemical sensitivities, and autoimmune syndromes. Given the prevalence of these conditions in autism spectrum disorders, many physicians find that the

intestinal permeability studies provide them with valuable information as to the integrity of the gut wall.

The test itself is very simple and requires the patient to drink a solution containing two harmless molecules, mannitol and lactulose, both of which are water-soluble sugars that are not normally metabolized by the body. Since mannitol is a smaller molecule that is easily absorbed and lactulose has a larger size that is only slightly absorbed, a urine collection after ingestion of these two sugars can reveal how much of each of these substances is passing through the intestinal barrier into the bloodstream. Quantification of these results can shed light on the degree of permeability of the small intestine, provide the physician with guidelines for treatment, and give an indication of therapeutic response through repeated follow-up testing.

The following lab offers intestinal permeability studies:

Great Smokies Diagnostic Laboratory:
(800) 522-4762

Other Helpful Tests For Diagnosing Intestinal Abnormalities In ASD

There are a number of other tests that can assist in the diagnosis of intestinal problems in individuals with autism spectrum disorders. These tests are generally considered to be of secondary importance but may be extremely helpful in evaluating some children's symptoms. Your physician can help guide you in determining when these tests should be ordered, interpret the results in relation to other tests that have already been performed, and develop a course of treatment to address the underlying imbalances that the tests have revealed.

1. Gluten Antibody Studies

In patients with significant intestinal pathology that appears to be linked to gluten consumption, or where there is a high degree of suspicion for celiac disease (e.g. family history and/or other clinical signs and symptoms), serum antibody studies for gluten (including gliadin, endomesial, and reticulin antibodies) can be helpful for

confirming a diagnosis of celiac disease. In some cases, though, these results may be falsely negative, so the test is only clinically significant if it shows positive elevated antibody levels. Most gastroenterologists agree that while gluten antibody studies may be a useful screening tool, the only way to definitively diagnose celiac disease is through biopsy of the small intestine. However, since this procedure poses an obvious risk, many physicians evaluating infants and small children opt to begin with the gluten antibody studies.

Gluten antibody studies are performed by the following labs and may also be available through your physician:

AAL Reference Laboratories:
(800) 522-2611
Immunosciences Lab
(800) 950-4686

2. Secretory IgA Testing

Secretory IgA is an antibody that is found in the mucous secretions of the body, including in the mouth, digestive tract, respiratory system, and urinary tract. Secretory IgA plays an important role in the immune system of the digestive tract. While we do not usually envision the intestines to be in any way connected to the immune system, the secretory IgA antibodies that line the digestive tract help to provide our first line of defense against such outside "invaders" as viruses, bacteria, fungi, and parasites. Levels of secretory IgA, which can either be measured in saliva or stool, can therefore provide an indicator of the level of immune activity that is occurring within the intestinal tract.

Salivary secretory IgA testing is available through the following laboratories:

Diagnos-Techs Clinical Laboratory:
(800) 878-3787
Immunosciences Lab
(800) 950-4686

Fecal secretory IgA testing is available as part of the CDSA or as a separate test from the following laboratory:

Great Smokies Diagnostic Laboratory:
(800) 522-4762

3. Immunological Testing

Since many children with ASD have compromised immune function, some physicians find it useful to evaluate the status of the immune system through laboratory testing. Antibody Assay Laboratories (AAL) offers an "Immune Dysfunction Encephalopathy Panel" that measures such immune markers as quantitative immunoglobulins, activated T cell subsets, natural killer cells, lymphocytes, and others. More information on these individual tests is available in the DAN! Consensus Report mentioned in the references below. Your child's physician may also be able to order the appropriate testing through a local laboratory.

The Immune Dysfunction Encephalopathy Panel is available from:

AAL Reference Laboratories:
(800) 522-2611

4. Liver Detoxification Profile

A liver detoxification profile can provide valuable information on how well the body is able to process and eliminate toxic substances. Since the liver is the primary organ of detoxification in the body, measuring the liver's detoxification systems can provide an indication of its ability to transform potentially harmful substances into harmless compounds that are then easily excreted by the body. This can provide some valuable insights for the treatment of children with ASD, since many of these children have had significant exposures to toxins (i.e. from heavy metals, by-products of intestinal yeasts and bacteria, environmental chemicals, and others), and many also show weaknesses in their body's detoxification systems.

While this test may yield some very valuable information on liver function and provide further insight into treatment, it does require

that patients consume small, very safe amounts of caffeine, aspirin, and acetaminophen (Tylenol) in order to measure the liver's detoxification abilities. Although this does not pose a problem for most people, some children who have a significant sensitivity to salicylates may react adversely to the ingestion of the aspirin that is required for the test. However, such reactions are usually temporary and mild in nature.

The Comprehensive Detoxification Profile is available from the following lab:

Great Smokies Diagnostic Laboratory:
(800) 522-4762

5. Sulfation Studies

Phenol sulfotransferase (PST) is an enzyme system that is normally involved in Phase II liver detoxification. Researchers have proposed that PST is compromised in autistic children.²⁰ A recent study performed by Rosemary Waring in England demonstrated that the PST enzyme system was functioning at sub-optimal levels in more than half of the autistic children tested.²¹ The result of a PST system that is not functioning normally is a deficiency of sulfur in the bloodstream, which was shown to be the case in the majority of autistic children evaluated in another study by Waring.²² Since the deficiency of sulfur in the bloodstream and impairment of the PST system interferes with the body's ability to process and eliminate phenols, this may explain why many children with autism are so sensitive to phenols ingested through certain foods. These phenol-containing foods include apples, bananas, grapes, chocolate, food colorings, and some herbs and spices.

When these types of sensitivities exist, sulfation studies may be helpful for determining the status of the child's PST enzyme system. Two studies are currently available for measuring sulfation. One is part of the liver detoxification profile described above and requires the use of acetaminophen (Tylenol) for measuring PST activity. The other test measures the ratio of two metabolites, MHPG Glucuronide and MHPG Sulfate, in the urine. Since adequate sulfation is necessary to maintain the health of the intestinal immune system, both types of sulfation studies can provide useful information on the origin of intestinal-related symptoms in autistic children.

The acetaminophen sulfation study is available from the following laboratory:

Great Smokies Diagnostic Laboratory:
(800) 522-4762

The test for MHPG Glucuronide and MHPG Sulfate can be done through the following laboratory:

Smith Kline Beecham Laboratories:
(888) 825-5249

6. Diagnostic Imaging Studies

In some instances, a physician may deem it necessary to perform further diagnostic imaging studies when there are significant intestinal problems present in a child with ASD. These may include an x-ray to rule out fecal impaction, or an endoscopy to evaluate the health of the GI mucosa and/or to obtain a biopsy of the intestinal lining.

What To Do When Laboratory Testing Is Not Available

While the laboratory tests described above represent a useful means to diagnose, evaluate, and determine the course of treatment for children with intestinal symptomatology, they are not always available as an option for those patients whose physicians are unfamiliar with the biological approaches to treating ASD. In these cases, there are still many things that parents can do to positively intervene in their child's health and to ensure an optimally functioning digestive system.

The following chapter, which briefly describes some of the intestinal abnormalities seen in children with autism spectrum disorders, may serve as a guide for narrowing the diagnostic focus. Further information on diagnosing and evaluating these conditions is given in a later section describing "Treatment Approaches For Specific Intestinal Problems In Autism".

In addition, there are some very basic therapeutic approaches that may be implemented without having done any kind of laboratory testing. These

interventions alone may yield very positive results and include the following:

- A trial elimination of gluten and casein from the diet.
- A trial elimination of the most common food allergens and implementation of a rotation diet (see chapter on food allergies for more information).
- A trial elimination of foods containing phenols, if there is thought to be a sulfation problem.
- A trial elimination of foods containing yeasts and molds, if there is thought to be a problem with intestinal Candida overgrowth.
- Implementation of a diet high in protein, fresh fruits and vegetables, and fiber; and low in sugars, refined carbohydrates, additives, preservatives, and food colorings.
- Supplementation with a multivitamin in order to repair any nutritional deficiencies that may exist as a result of malabsorption or improper diet.
- Supplementation with nutrients that promote proper digestion, such as enzymes and probiotics.
- Supplementation with nutrients that have healing properties for the gut wall, such as colostrum, certain amino acids, and lactoferrin.
- Supplementation with probiotics in order to maintain a healthy balance of beneficial intestinal microflora.

Additional discussions of these interventions may be found in the chapters entitled "General Approaches To Restoring Intestinal Health" and "Maintaining Long-Term Intestinal Health In Autism Spectrum Disorders".

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Chapter 4

Intestinal Problems In Children With Autism Spectrum Disorders

Introduction

What are some of the intestinal problems that are commonly seen in individuals with autism spectrum disorders? How did these problems develop, and why is the restoration of digestive health such an important part of these children's healing process? These are some of the questions that will be addressed in this section of the gut protocol.

As previously stated, the majority of children with ASD have some type of intestinal dysfunction. For many of these children, the problems are very mild and can easily be corrected. For others, however, there is significant gut pathology and addressing these imbalances is essential before overall healing can occur. The conditions most frequently encountered in these individuals are as follows:

- Intestinal dysbiosis (microbial overgrowth) – i.e. Candida, Clostridia
- Intestinal hyperpermeability (“leaky gut syndrome”)
- Gluten and casein sensitivity
- Food allergies and intolerances
- Maldigestion and malabsorption
- Constipation
- Diarrhea
- Inflammatory bowel disease (enterocolitis, gastritis, reflux esophagitis)
- Sulfation deficits
- Compromised intestinal immunity

Possible Causes Of Intestinal Abnormalities In ASD

There are many theories as to what contributes to the general onset of autistic symptoms in a previously healthy child, but what is thought to specifically cause the gastrointestinal abnormalities that are found in so many of these children? While there is still a great deal of research that needs to be done in order to fully answer this question, a few theories are worth mentioning here.

1. Genetics

It has been theorized that genetics may play a role in the pathophysiology of the gut problems

seen in autism, since it is not uncommon to see significant digestive disturbances in the parents and/or siblings of the affected child. However, while there have been a number of studies suggesting that there is a genetic component to the development of autism in general,^{1,2,3} there is only now starting to be more specific investigation into the connection between genetic susceptibility and autistic gastrointestinal disorders.

2. Gut Irritation And Inflammation

It is generally recognized that inflammation of the intestinal wall is caused by a variety of factors, including certain foods and medications, chemical toxins, incompletely digested food proteins, and infectious microorganisms in the intestinal tract. Gluten and casein can contribute to gut inflammation, as can those foods that the child is allergic to. Medications such as antibiotics, steroids, aspirin, and non-steroidal anti-inflammatory drugs can irritate the intestinal wall and cause the overgrowth of certain microbes such as yeasts, which in turn cause further irritation to the gut membrane. In fact, many parents of autistic children feel that their child's problems first began after the administration of multiple rounds of antibiotics. Chemicals ingested in foods, such as artificial additives and preservatives, food dyes, certain sweeteners, pesticides, and hormones, can contribute to the toxic burden on the digestive system and cause oxidative damage within the gut. Further problems can occur when there is an overgrowth of yeast, bacteria, parasites, or other organisms. The resulting inflammation of the intestinal wall usually leads to an overly permeable (“leaky”) gut membrane, which can be the origin of many of the systemic complaints seen in autism.

3. Viral Vaccine Damage

There is clearly documented evidence that some viral vaccines may play a significant role in the gastrointestinal abnormalities seen in many autistic children. Dr. Andrew Wakefield and his colleagues at the Royal Free Hospital in England have published several articles suggesting that the measles-mumps-rubella (MMR) vaccine has been linked to a damaged intestinal lining in

children with autism.^{4,5,6,7} Intestinal biopsies performed by Wakefield and his fellow researchers have revealed that autistic children show the presence of a particular strain of the measles virus in their gut membrane that is identical to that found in the MMR vaccine. As a result, there is a type of inflammatory bowel disease associated with this virus that has come to be known as “ileocolonic lymphoid nodular hyperplasia” (LNH), or “autistic enterocolitis”. While this connection between vaccines and intestinal damage in children with ASD has been vehemently debated in the medical community, there continues to be well-established documentation in favor of this conclusion.

4. Intestinal Damage From Heavy Metals

Another theory concerning the connection between vaccines and autism relates to damage from heavy metals, specifically the mercury-containing preservative thimerosal, that is present in many vaccines. In their excellent review article “Autism: A Novel Form Of Mercury Poisoning”, Sallie Bernard and colleagues summarize over 180 articles relating to the toxic effects of mercury and its relationship to autism.⁸ There is extensive research that documents how mercury can damage the kidneys⁹ and nervous system.⁸ Additionally, scientists and researchers are finding evidence that both injected and orally ingested mercury and other heavy metals can directly damage the epithelial lining of the gastrointestinal tract. One study found that application of mercury to the gut lining resulted in damage to jejunal (small intestine) epithelial cells, increased permeability of intestinal epithelial tissue, and direct genotoxic and cytotoxic effects on isolated intestinal epithelial cells in vitro.¹⁰ Another study of thimerosal, which consists of 49.6% ethyl mercury,¹¹ describes how it can cause direct damage to cells.¹²

Medical practitioners specializing in the treatment of autism spectrum disorders have recognized the significant impact that mercury and other heavy metals can have in affecting overall health. To address the consequences of these metals, a Consensus Report has been written and a protocol established for the removal of these toxic substances from the body.¹³ As

described in this report, one of the key prerequisites for starting a heavy metal detoxification program is the correction of nutritional deficiencies and the treatment of any underlying gastrointestinal disorders that may exist in the child with ASD. Therefore, it is important to clean up the gut, support the digestive processes, and heal the intestinal wall before beginning the process of removing (“chelating”) mercury and other heavy metals from the body.

Brief Definitions Of Gastrointestinal Abnormalities In ASD

Below are brief definitions of the most prevalent gastrointestinal disorders seen in children with autism spectrum disorders. Further elaboration of these conditions, along with supporting documentation, diagnostic guidelines, and treatment strategies, may be found in Chapter 7, “Specific Treatments For Intestinal Problems In ASD”.

1. Intestinal Dysbiosis

A condition characterized by an imbalance in the microflora (bacteria, yeast, viruses, parasites, and other organisms) in the intestinal tract. Dysbiosis occurs when there is an alteration in the normal balance of beneficial microflora and harmful organisms begin to overpopulate the digestive tract.

2. Intestinal Yeast / Candida Overgrowth

Overgrowth with intestinal yeast, including *Candida albicans*, is one of the most common forms of dysbiosis observed in autistic children.

3. Intestinal Overgrowth With Bacteria And Other Organisms

Besides Candida and other strains of yeast, it is also common to find pathogenic bacteria (including *Clostridium difficile*, *Citrobacter*, *Klebsiella*, and *Pseudomonas*), viruses, and parasites in the intestinal tracts of individuals with autism.

4. Intestinal Hyperpermeability / “Leaky Gut Syndrome”

Leaky gut syndrome is a term used to describe a phenomenon where there is increased intestinal permeability resulting from chronic irritation to the gut wall. A leaky gut wall can lead to a variety of systemic problems, including gluten and casein sensitivity and food allergies.

5. Gluten And Casein Sensitivity

Many children with ASD are unable to completely break down food proteins called gluten and casein, resulting in morphine-like reactions due to abnormal stimulation of opiate receptors in the brain.

6. Food Allergies And Intolerances

Children with autism tend to experience a wide range of food allergies, intolerances, and/or sensitivities that are usually caused by damage to the intestinal wall and dysfunction of the immune system.

7. Maldigestion And Malabsorption

Maldigestion is defined as the incomplete breakdown (digestion) of foods and can lead to malabsorption, a term that refers to the disordered or incomplete uptake of nutrients from the intestinal tract. Both of these are common problems in children with ASD.

8. Constipation And Diarrhea

Constipation is defined as difficult or infrequent bowel movements with the passage of abnormally dry or hard fecal matter. Diarrhea, on the other hand, is characterized by the frequent passage of watery, unformed stools. Both of these phenomena are symptoms of an underlying intestinal disorder.

9. Inflammatory Bowel Disease

Many children with autism suffer from a condition known as inflammatory bowel disease, which is characterized by inflammation of the digestive tract including the intestines (enterocolitis), stomach (gastritis), and esophagus (esophagitis).

10. Sulfation Deficits

Many children with ASD who appear to be sensitive to phenol-containing foods may have problems with a process known as sulfation and a deficit in an enzyme known as Phenol sulfotransferase (PST).

11. Compromised Intestinal Immunity

When there is marked gastrointestinal dysfunction, the immune tissue located in and around the digestive tract may also become compromised, resulting in significant immune problems.

Concluding Remarks

This chapter has provided a brief overview of some of the digestive problems, and their possible causes, that are commonly seen in children with autism spectrum disorders. Further information and research regarding these conditions, along with strategies for diagnosing and treating them, will be discussed in a later chapter. Before delving further into the details of these specific conditions, however, it is helpful to discuss some of the various therapeutic agents, including pharmaceutical drugs and natural supplements, which have been shown to be helpful in the treatment of gastrointestinal abnormalities in children with autism spectrum disorders.

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Chapter 5

Products Used for Treating Intestinal Problems in Autism

Introduction

This chapter will provide an overview of the therapeutic agents, including pharmaceutical drugs and nutritional supplements, that have been found to be helpful for treating the intestinal problems seen in children with autism spectrum disorders. We are including this discussion here so that when the products in question are mentioned in the chapters on treatment that follow, you will already have an understanding of the pharmaceuticals and nutritional supplements commonly used in ASD.

Nutritional Supplements

Many people, including both parents and physicians, are new to using nutritional supplements for biomedical intervention. While people may be unfamiliar with how to use them, the supplements themselves are not new. Physicians have been using many of them for hundreds of years to treat a variety of ailments. Dr. Bernie Rimland first popularized the use of nutritional supplements for ASD over 30 years ago, when he was searching for ways to help his own son. He uncovered research linking Vitamin B6 and Magnesium with positive improvements in many of the symptoms experienced by autistic children.¹ Much of this research came out of Europe, where the use of nutritional supplements by mainstream physicians was, and still is, an acceptable practice.

Many physicians in the United States are unfamiliar with how to use nutritional supplements simply because this was not a part of their medical school training. However, mainstream medicine is becoming increasingly accepting of these therapies, not only because they are yielding positive clinical results but also because there is a growing number of studies available to demonstrate their safety and efficacy. Some of these studies are listed below in the discussions of the individual products used for treating ASD. Since this is a growing field, however, there are a few products that only have limited scientific support at this time. These have a secondary role in our discussion, but they are nevertheless mentioned because many physicians and health care practitioners have reported excellent results when using these products with autistic children.

What is the advantage of using a biomedical approach to support intestinal health in children with ASD? For one, nutritional supplements are generally a good complementary therapy to pharmaceutical drugs, which can be hard on a young child's system. In fact, some pharmaceuticals have not been extensively studied for long-term safety in children, so many parents prefer to use safer, more natural therapies as much as possible. Secondly, laboratory testing has shown that nutrient deficiencies are very prevalent in autistic children, resulting in a variety of systemic problems. Medical science is learning more and more about the brain, and it is becoming increasingly evident that certain nutritional deficiencies can lead to dysfunction of the brain and nervous system. By repairing these deficiencies, clinical improvement is often seen.

Another advantage of the biomedical approach is that it does not simply mask or suppress symptoms. Rather, the goal of nutritional medicine is to get at the root of the problem and correct the underlying imbalance, so that the system as a whole can have a better chance of repairing itself. Take the example of leaky gut syndrome and food allergies: if the leaky gut wall is repaired, the food allergies may resolve as well. Food allergies are just the symptom of an underlying imbalance, which in this case is an overly permeable intestinal membrane.

Nutritional supplements are also beneficial for the repair process, especially in those children whose intestinal tracts have been damaged due to antibiotic use, vaccines, heavy metal toxicities, or other chemical insults. When using this approach, it is possible to support the body as a whole, including the digestive system, the nervous system, the immune system, and so on. Since all of these systems are so closely interconnected, strengthening one of them usually yields positive benefits in the others.

Pharmaceutical Drugs

A number of pharmaceutical drugs also play an important role in the treatment of intestinal disorders in autistic children. Sometimes it is

necessary to start with these drugs to get the best results, especially when there is significant intestinal overgrowth with bacteria, yeast, or other microbes. In these cases, the stronger pharmaceutical agents are necessary initially to eliminate these organisms, and nutritional supplements can be used concurrently as supportive measures and also later for follow-up care. Conversely, when the intestinal overgrowth is relatively mild, it may be possible to address this solely with probiotics, digestive enzymes, colostrum, herbal yeast control products, and other supportive supplements.

Ultimately, your child's physician should decide whether to start with nutritional supplements, pharmaceutical drugs, or both. This determination can be made through laboratory testing to diagnose the underlying problem and assess the severity of the disorder. With follow-up testing, the physician can also monitor the efficacy of the therapies that are being used.

The Role Of Kirkman's Products

Kirkman is a company that manufactures supplements specifically for the autism community. Therefore, many of the supplements discussed below are available through our company. Most of our products have been formulated under the guidance of physicians who specialize in the treatment of autism spectrum disorders, and we continually receive feedback on the efficacy of these products, both from the physicians who prescribe them and from the parents whose children are taking them. This information is then put to use for the modification of existing products and the development of new ones.

Besides Kirkman, there are many other excellent companies offering some of the nutritional supplements that will be discussed in the following sections. Before choosing a product from another manufacturer, however, it is important to determine whether that product meets the criteria for use in autism. Some of the characteristics of Kirkman products that can be used as a guideline to evaluate other supplements are:

1. Casein and gluten free, as determined by outside laboratory confirmation.

2. Easy-to-administer forms, such as small capsules, liquids, powders, and good tasting flavored versions.
3. Easy dosing information based on a child's weight.
4. Free of artificial flavors and colors, yeast, and soy.
5. Free of sugar, corn, starch, animal derivatives, and preservatives whenever possible.
6. Hypoallergenic versions of products for the extremely sensitive child who cannot tolerate additives.
7. Free of, or with the lowest possible levels of, pesticides, chemical impurities, and heavy metals, as determined by independent laboratory verification.
8. Shipping on ice and nitrogen packaging for products that are heat sensitive.

Section One

PRESCRIPTION DRUGS USED IN TREATING GUT ISSUES IN AUTISM

Yeast and microbial overgrowth in autism must be controlled. Other digestive and immune issues must also be treated proactively to aid in the road to recovery. Several prescription medications have shown promise in these areas. A brief description of the most widely used drugs follows:

- *Nystatin*
A very old and very safe antifungal drug which is not absorbed into the bloodstream, thereby producing few side effects. Usually very effective against *Candida* when first prescribed, but there are indications of the organisms building a resistance when used long term or when stopped and started repeatedly. This phenomenon could also be due to alteration of the microorganism or to the yeast genetically transforming human cells in the intestine.
- *Amphotericin B*
A safe antifungal when given orally. Similar action to Nystatin as it is not

absorbed significantly from the GI tract. Only available from compounding pharmacies in the U. S. as an oral suspension.

- *Diflucan (Fluconazole)*
An excellent antifungal that is very effective against yeast, especially *Candida albicans*. It is absorbed gastrointestinally and has central nervous system penetration as well. Certain strains of *Candida (krusei)* appear resistant to Diflucan. Liver and kidney function must be monitored when giving Diflucan as the function of those organs is affected by Diflucan.
- *Sporanox (Itraconazole)*
A very effective systemic antifungal against *Candida albicans* and other *Candida* strains often resistant to other antifungals. *Candida krusei* and *Candida parapsilosis* are eradicated by Sporanox. Sporanox has serious drug interactions and side effects so its use must be closely monitored by a physician knowledgeable about the drug.
- *Flagyl (Metronidazole)*
An antibiotic which is effective against many species of bacteria including *Clostridium*, *Eubacterium*, *Peptococcus*, and many others. It is also very effective against protozoa and other common parasites. Autistic patients very often exhibit high urinary concentrations of dihydroxyphenylpropionic acid (DHPPA) in the urine. *Clostridia* may be responsible for the production of DHPPA and related compounds and autistic patients exhibiting these high DHPPA like compounds have responded well to Flagyl. A compounded version of this preparation can be made using Metronidazole Benzoate which does not have the awful taste of pure Metronidazole. It takes 400 mg. of Metronidazole Benzoate to equal 250 mg. of the pure compound. Flagyl does have drug interactions and side effects that need to be monitored by a health professional. Flagyl will kill friendly flora so it is important to use appropriate probiotics immediately after drug therapy.

- *Vancomycin (as the hydrochloride)*
A powerful antibiotic used in autism to control *Clostridia* overgrowth or to treat infections resistant to other antibiotics. Children with high DHPPA and related compounds in the urine respond positively to Vancomycin. This antibiotic does kill friendly bacteria as well, so it is important to use probiotics after therapy with Vancomycin. Side effects are numerous, so a physician must monitor patients on this drug.
- *Nizoral (Ketoconazole)*
A synthetic broad spectrum anti-fungal agent available in 200 mg. scored tablets. Indicated in the treatment of systemic fungal infections including candidiasis, oral thrush, chronic mucocutaneous candidiasis, candidurea, and several mycoses conditions. Hepatotoxicity must be carefully monitored when using Nizoral.
- *IVIG (Intravenous Immunoglobulin)*
A component of human blood plasma which has been used intravenously to remove harmful pathogens. Many autistic patients have remarkable improvements when given IVIG, which is usually administered once per month because of a 28 day half-life of the compound. Though the exact reason IVIG causes improvement in ASD is not known, it is probably related to improving immunodeficiencies. Its use is acknowledged by the National Institute of Health.
- *Secretin*
Secretin is a gastrointestinal hormone present in the human body. It is being prescribed in autism in IV, oral and transdermal forms to significantly improve autistic symptoms in many children. It is usually given every 4 to 6 weeks with positive results appearing within two weeks. Success ratios vary depending on the clinician, with 35% to 70% of the children improving. The normal role of Secretin in the body is to "tell" the pancreas to release bicarbon-

ate to stop stomach acid. Many autistic children have a deficiency in this function and the gastrointestinal/brain association may be part of the reason for improvement. Secretin is also involved in the immune system. The exact reason that Secretin helps in autism is not known.

- *Bethanechol*
Bethanechol acts by stimulating the pathways of the parasympathetic nervous system. It stimulates gastric

mobility, increases gastric tone and often helps normalize impaired peristalsis. Dr. Mary Megson, a Virginia physician treating autism, reports remarkable improvements in autistic children when using Bethanechol following two months of natural vitamin A supplementation (Cod Liver Oil). Dr. Megson reports improvements in gut health, focusing, mood, concentration, sense of humor and speech often within thirty minutes of a single dose of Bethanechol.

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SECTION TWO

NUTRITIONAL SUPPLEMENTS FOR TREATING GUT ISSUES IN AUTISM

COLOSTRUM

A Broad Spectrum Supplement for a Healthy Gastrointestinal Tract

INTRODUCTION

Colostrum has been called "nature's first food" because it is secreted by the mammary glands of all female mammals in the first few days after they give birth. Colostrum supplies important immune factors (immunoglobulins), antimicrobial peptides (lactoferrin, lactoperoxidase, etc.) and growth factors (epidermal growth factor, IGF-I, etc.), along with a combination of vitamins and minerals to insure the health,

vitality, and growth of the newborn. This substance is highly beneficial in the unique manner in which it provides the body with numerous immune and biological factors that support and protect the intestinal tract. Of interest is that the immune and growth factors in colostrum are recognized to activate some fifty different processes in the newborn that are vital to growth and development.^{1,2}

Many nutritional, biochemical, immunological, and other biological properties of colostrums have been studied in relationship to gastrointestinal health. Recent studies suggest that peptide fractions from colostrum (individual peptides present in colostrums) might be useful for the treatment of a wide variety of gastrointestinal conditions, including inflammatory bowel disease, nonsteroidal anti-inflammatory drug-induced gut injury and chemotherapy-induced mucositis.³

Donald Henderson, M.D., MPH (Assistant Clinical

Professor of Medicine and Gastroenterology at UCLA School of Medicine) has shared his successful experience with Colostrum particularly in relationship to combating unspecified diarrhea. "Most importantly, I believe colostrum is effective in creating better overall health and well-being because of its beneficial remedy for the health of the entire gastrointestinal tract. The GI tract is really the body's major battleground against most invading diseases, toxins or any kind of pathogen. This is where the major assaults take place, and where we need to ward them off. Colostrum seems to help that battle in many significant ways. Not only does it either destroy pathogens and/or prevent them from attaching to the intestinal walls, but it also helps repair and regenerate the critical surface of the intestinal wall at a cellular level, partly because it contains many growth factors, notably epidermal growth factor. In addition to successfully combating harmful organisms in the intestines, colostrum also encourages the colonization of beneficial bacteria in the bowel." ⁴

HISTORY OF USE

Colostrum has had a long history of use, with some of the earliest documentation regarding its use as a medicinal, reported several thousand years ago in India and the Far East. Of interest is that in the United States, mainstream medical practitioners utilized colostrum in early years before the discovery of penicillin and sulfa drugs. Dr. Albert Sabin, the researcher who developed the first oral vaccine for poliomyelitis, found that colostrum contains antibodies against polio and he recommended colostrum as a dietary supplement for children who were vulnerable to polio. ⁵

CHARACTERISTICS/DESCRIPTION

Colostrum is a thick yellow fluid that is excreted for approximately 72 hours following birth, before the production of true milk begins. Colostrum provides potent immune defense against harmful bacteria, yeast, and parasites. It is rich in protein and contains a number of important growth factors. It is considered to be important in the nutrition, growth and development of newborn infants and is a vital part of the body's immune defense.

Humans produce relatively small amounts of colostrum, however cows produce approximately 9 gallons, which provides an excellent source for nutritional supplementation. Bovine colostrum is also unique in that it is recognized to be four times richer in immune factors than in human colostrum. Additionally colostrum has been found to be 21 times richer in Vitamin B-12 than milk, which is important because adequate levels of B-12 are recognized to significantly increase the immune system's ability to fight disease. ⁶

Along with essential nutrients, colostrum contains protease inhibitors that protect it from being destroyed by the process of digestion. In addition colostrum has been recognized to help build lean muscle, assist in burning fat, as well as stimulate the repair of the intestinal membrane by the action of its epithelial growth factors. Fortunately, the immune and growth factors in colostrum are known to be transferable from one species to another. This means that humans can use the immune-rich colostrum from cows to boost the immune system, accelerate healing, as well as perform other important functions.

FUNCTION OF COLOSTRUM IN THE BODY

Of interest to those with ASD are the recent studies that suggest that peptides present in colostrum might be useful for the treatment of a wide variety of gastrointestinal conditions, including inflammatory bowel disease. [Playford]. The research in this area provides compelling support for the use of colostrum in those diagnosed with the many gastrointestinal disorders (enterocolitis, duodenitis, esophagitis, etc.) seen in autistic children and that parallel the symptoms of inflammatory bowel disease.

Colostrum has been extensively researched and there is excellent documentation in the medical and scientific literature regarding its powerful action which is the results from: 1) Immune factors/Immunoglobulins 2) Antimicrobial peptides, and 3) Growth factors Each of these exert significant responses in the body ⁷ and are briefly described below.

IMMUNE FACTORS

Colostrum contains a unique combination of immune factors that are recognized to exert a positive influence in supporting and stimulating the body's immune response. Protection for the newborn is provided by a variety of immune factors from its mother's colostrum. Antibodies found in colostrum have been documented to protect against *E. coli*, *Salmonella*, *Shigella*, *V. cholera*, *Bacteriodes fragilis*, *Streptococcus pneumoniae*, *Clostridium*, *Streptococcus* and *Candida albicans*.⁸ Clinical trials have been conducted showing the effectiveness of the oral use of immune factors from colostrum against specific disease-causing organisms in the intestinal tract. The outcome of one study suggested that the "ingestion of bovine Colostrum immunoglobulins may be a new method of providing passive immunoprotection against a host of gut-associated antigens."⁹

IMMUNOGLOBULINS (IgA, IgD, IgE, IgG, and IgM). Immunoglobulins are proteins that function as antibodies, protecting the body from harmful invaders. Each of these immunoglobulins has specific functions in protecting the body from various foreign substances, including bacteria, viruses, yeast, inhalant and food allergens, and chemical toxins. For example, the immunoglobulin A (IgA), also known as secretory IgA (sIgA), is a crucial component of the mucosal membrane of the gastrointestinal tract where it helps protect against the entrance of foreign substances into the body. It has been recognized that sIgA is deficient in many autistic children, which sets up a cascade of consequences reflected in gastrointestinal and immune system dysfunction.¹⁰

Immunoglobulin G (IgG) functions by counteracting bacteria and toxins in the blood and lymph system. Of interest is a study that demonstrated that human colostrum contains only 2% of IgG while cow colostrum contains a phenomenal 20 times this amount.¹¹ Certainly this supports the use of colostrum supplements when there is a desire to support higher levels of IgG. Colostrum also contains immunoglobulin M (IgM) that is recognized to seek out and attach itself to viruses in the circulatory system where it helps inactivate them.

Immunoglobulins E and D (IgE and IgD) function by mediating allergic reactions and removing foreign substances from the bloodstream. Of interest are reports that certain immunomodulating factors in colostrum are able to regulate the IgE response (the classic allergic response). Additionally there is evidence that colostrum possesses some immune inhibitory functions. Crago and colleagues found a protein substance in colostrum which inhibits the overproduction of antigen-stimulated lymphocytes, and which may reduce symptoms associated with allergic (IgE) reactions.¹²

As you can see, each of these immunoglobulins present in colostrum provide important functions of neutralizing toxins and protecting the body against various viruses and bacteria that compromise the gastrointestinal system. Support regarding the immune stimulating properties of colostrum have been clearly documented in the literature. Research at State University of New York, Buffalo has shown that colostrum provides specific "antibody reactivity" to certain bacteria, viruses and yeasts responsible for conditions that affect the lungs, gastrointestinal tract, bones and blood.¹³

LACTALBUMINS: There is promising research indicating that lactalbumins may be highly effective in supporting the immune system.

CYTOKINES: Cytokines are immune protein molecules that have a broad range of cellular function and are in part responsible for regulating the duration and intensity of the immune response. Colostrum contains many cytokines, including interleukins (IL), tumor necrosis factor (TNF), lymphocyte activation factor (LAF), transforming growth factor, macrophage stimulating factors, etc. Cytokines are important because they serve as chemical communicators from one cell to another and have a significant impact on the immune response.

PROLINE-RICH POLYPEPTIDES (PRP): These compounds (considered to have hormone activities) are recognized to support and regulate the thymus gland. PRP has the ability to both stimulate an underactive or weak immune system and calm or balance an overactive immune response. Studies at McGill University in Montreal, Canada

showed that the PRP (Proline-rich polypeptide) is the first protein of mammalian origin that induces the growth and differentiation of reacting B lymphocytes.¹⁴ Additional studies have confirmed that this immunomodulating peptide in colostrum can stimulate an underactive immune system and tone down an overactive one.¹⁵ This is relevant in autism given the problem of autoimmunity seen in this disorder.

ANTIMICROBIAL FACTORS

LACTOFERRIN: Lactoferrin is an iron binding protein found in colostrum that exerts a number of important effects in body. Its primary function is to transport/carry iron to red blood cells. The iron binding quality of this protein is of importance because when iron binds with (is taken up by) the lactoferrin, it is then not available to be used by pathogenic organisms for their growth and development. Lactoferrin is documented to exert powerful antibacterial, anti-viral¹⁶ and anti-inflammatory activity and has also been shown to stimulate the growth of intestinal epithelial cells which, would have clear application for healing of intestinal membranes.¹⁷

ENZYMES: There are several enzymes including lactoperoxidase, thiocyanate and peroxidase that have function in helping to destroy bacteria by their ability to release hydrogen peroxide which burns up (hydrolyses) harmful bacteria.¹⁸ Along with anti-microbial function lactoperoxidase also has documented antiviral activity. The laboratory studies involving these components are supportive of their very promising use in functional foods inclusive of nutritional supplements.¹⁹

LYSOSOMES: These are proteins that have the capacity to breakdown or decompose a substance. Lysosomes in colostrum function to assist with the destruction of bacteria and viruses on contact. A Polish report in Veterinary Medicine showed that lysosomes in bovine (and human) colostrum are the enzymes present in saliva, tears and other body fluids that kills bacteria by dissolving their cell walls.²⁰ Of interest is that these lysosomes also have function in support of healthy bacteria/probiotics.

GLYCOPROTEINS: Glycoproteins are substances known as protease inhibitors and have been shown to help immune and growth factors

survive the passage through the highly acidic digestive system, which can be destructive to them.²¹ Of interest is that the glycoproteins in colostrum inhibit/ prevent the Helicobacter Pylori bacteria (this is the organism that has been shown to be the cause of peptic ulcers) from attaching onto the wall of the stomach and may play a role in the treatment of gastric ulcers.²²

OLIGOSACCHARIDES: These nondigestible carbohydrate fractions are recognized to attach and bind to pathogens such as E-coli, Clostridia, Salmonella, Streptococcus, Giardia, Shigella, and others preventing them from attaching to the intestinal mucosal membrane. Hansen and his colleagues found that immune factors from colostrum blocked the attachment of many types of bacteria including Streptococcus pneumococci (a major cause of ear infections) to the mucus membranes.²³ Oligosaccharides from colostrum are also recognized to blocked the attachment of many types of bacteria and prevented them from attaching to or entering the body through the mucus membrane. Additionally they function in allowing for proliferation of the healthy friendly bacteria (Bifidobacterium and Lactobacillus) that are crucial for a healthy intestinal tract.²⁴

GROWTH FACTORS

Colostrum contains many factors that influence cell growth, their differentiation and their function. These growth factors are crucial for the maintenance and integrity of the mucosal tissue as well as influence healing of the gastrointestinal lining.

NONPEPTIDE TROPHIC FACTORS are contained in colostrum and include glutamine, polyamines, and nucleotides. These factors play an important role in maintaining gastrointestinal mucosal mass and modulating the immune system by altering intestinal flora and influencing the actions of growth factors.

EPIDERMAL GROWTH FACTOR has been described as a "luminal surveillance peptide" which functions to stimulate the repair process in sites of injury in the intestinal membrane. There is some thought that EGF in colostrum may play a role in preventing bacterial translo-

cation 31. Additionally epidermal growth factor is noted to promote the growth of and protection of gastric mucosa against various gastric lesions.²⁵

INSULIN GROWTH FACTORS: Insulin-like growth factors (IGF-I and IGF-II) promote cell proliferation and they are expressed in high amounts in the small intestine. The growth factors in bovine colostrum are identical to human colostrum in their composition. Of interest however is that bovine colostrum contains significantly higher levels of IGF-I than does human colostrum. (500 compared with 18 ug/L).^{26,27} An important issue related to IGF-I is that these growth factors are stable in the acidic environment of the stomach and maintain their biological activity.

TRANSFORMING GROWTH FACTORS (TGF-1 and TGF-2) are produced within the mucosal membrane of the gastrointestinal tract (Cartilage) and have function in stimulating gastrointestinal growth, accelerating repair, stimulating mucosal restitution after injury, and increasing gastric mucin concentrations. As one can see these are crucial functions that significantly impact the healing of the intestinal mucosal membrane in those with ASD.

GROWTH HORMONE (GH) and its releasing factor GHRF is another constituent present in colostrum and is recognized to slow some of the signs of aging. GH also plays important modulating roles in gut growth and function, as GH receptors have been reported to be present throughout the gastrointestinal tract. [Delehay]

PLATELET-DERIVED GROWTH FACTOR (PDGF) is commonly recognized as a molecule originally identified from platelets, however it is also synthesized and secreted by macrophages. Of interest is that PDGF (found in colostrum) has been shown to facilitate ulcer healing when administered orally to animals.²⁸

VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) is another glycoprotein found in colostrum. The specific role of this growth factor is unclear however researchers suggest that VEGF may play an important role in the healing of conditions such as peptic ulceration.

APPLICATION/ROLE OF THIS SUPPLEMENT TO THOSE WITH AUTISM

Colostrum has been used to treat a full spectrum of diseases and disorders that range from skin and tissue repair to its successful application for diabetes, yeast infections, weight loss, heart disease, as well as numerous other conditions. Additionally, research has demonstrated that components in bovine colostrum showed inhibitory effect on some sarcoma (cancer) tumor cells in vitro²⁹ and may have application for chronic psychiatric disorders.³⁰

For our purposes we will discuss the relevance of colostrum in regard to conditions that specifically affect the gastrointestinal system in individuals with ASD.

GASTROINTESTINAL/INTESTINAL PERMEABILITY

Of interest to those with ASD are the recent studies that suggest that peptides present in colostrum might be useful for the treatment of a wide variety of gastrointestinal conditions, including inflammatory bowel disease, nonsteroidal anti-inflammatory drug induced gut injury, as well as chemotherapy induced mucositis. The research in this area provides compelling support for the use of colostrum in those diagnosed with the many gastrointestinal disorders (enterocolitis, esophagitis, etc.) that are seen in those with ASD.

Raymond Playford, M.D and colleagues from the Department of Gastroenterology, Imperial College of Medicine (London, England) wrote a comprehensive review article on some of the constituents of bovine colostrum⁷. They discuss the therapeutic possibilities of utilizing whole colostrum and individual peptides present in colostrum, for the treatment of various gastrointestinal conditions.

CLOSTRIDIUM DIFFICILE

A very interesting application for the use of colostrum is supported by studies undertaken at the Institute of Microbiology, University of Tartu, Estonia which have shown that colostrum inhibited the adhesion of *C. difficile* to CaCo-2 cells in

the laboratory. The researchers believe that inhibition of *C. difficile* to adhere to intestinal mucosa could be a promising new strategy for the prevention and treatment of antibiotic associated diarrhea. [Naaber] In another study involving a clinical trial and laboratory analysis, substances from colostrum neutralized the two main toxins of the infectious *Clostridium* bacteria.³¹ Other clinical trials point to the powerful impact that colostrum has in specifically neutralizing activity against *Clostridium difficile* toxins.³²

One of the consequences of repetitive use of antibiotics is the development of *Clostridia difficile* infections of the intestinal tract triggering pseudomembranous colitis. Of interest is that *Clostridia difficile* problems have been recognized as commonly occurring in those with autism and more recently when following a heavy metal/mercury detoxification program. *Clostridium* is known to proliferate and grow in the intestinal lining and feed off of the toxins and byproducts that are deposited into the bowel as waste products from detoxification. *Clostridium* then takes hold of the mucosal membrane and exerts a significant effect on the intestinal tract where it triggers acute diarrhea. These hearty and troublesome bacteria are generally eradicated with the use of powerful antibiotics but unfortunately there are frequent re-infections, despite repetitive use of these drugs.

Studies undertaken in the Gastroenterology Divisions of Beth Israel Medical Center and Harvard Medical School evaluated a bovine derived immunoglobulin concentrate (from colostrum of cows) immunized against *C. difficile* toxins and containing high concentrations of the neutralizing IgG antitoxin. Their results showed that the binding and neutralizing activity of this concentrate was maintained throughout the gastrointestinal tract and that its use may provide a non-antibiotic approach to the prevention and treatment of difficult antibiotic associated diarrhea and colitis.³³

These studies provide support for the use of colostrum as an adjunct in the treatment of *Clostridia difficile* infections. For a more comprehensive approach to deal with chronic *Clostridia* infections a combination of a colostrum supplement may be effectively used with high/therapeutic doses of probiotics (*L. acidophilus* (LA-5), *B. bifidum/lactis* (BB-12), *L. rhamnosus* (LGG) and

other strains of friendly flora) along with Beta 1,3/1,6 glucan. Clinicians utilizing this "cocktail" approach have reported encouraging response to this treatment approach.

VIRAL INFECTIONS

There are many double-blind, placebo controlled trials as well as in vitro (in the laboratory) studies undertaken confirming the biological activity of Colostrum and its important biological properties. Following is a brief review of some of the applications of Colostrum that have been investigated and documented in the medical literature.

A report in *The Lancet* described a controlled study where children were fed bovine colostrum and did not get rotavirus (human rotavirus is recognized as one of the leading cause of diarrhea in the world) while 13.8% of children who were fed an artificial infant formula acquired the virus.³⁴ Other studies have been undertaken with the use of immunoglobulins from colostrum (containing high titers of antibodies against a wide variety of bacterial, viral and protozoa pathogens and bacterial toxins) that show its effectiveness in the treatment of opportunistic infections associated with HIV and other immunosuppressed diseases. Studies involving the use of colostrum have not been specifically undertaken on autistic children. However, the safety and clinical effectiveness of colostrums use in those with significant immunosuppressive conditions (provides encouraging application for its use in ASD children, many of whom have immunocompromised systems.

ALLERGIES

Colostrum may also play a role in the treatment of allergies, as the PRP fraction has been demonstrated to reduce swelling and inflammation associated with allergies. There are studies to support the use of colostrum with autoimmune problems (rheumatoid arthritis, lupus, etc.) because of its ability to inhibit the overproduction of lymphocytes (white blood cells) and T-cells.

SAFETY ISSUES

QUALITIES TO EVALUATE - THE KIRKMAN LABORATORIES DIFFERENCE

The strictest manufacturing standards have been employed in making Kirkman's Colostrum Gold[®] formulation. The colostrum is specifically chosen from specially raised cattle and processed to yield a pure and potent product. Kirkman's colostrum is obtained from hormone, pesticide and antibiotic free cows only during the first 12 hours after they give birth. The colostrum goes through flash pasteurization, which has been shown not to denature the colostrum so that the biological activity is assured. This liquid colostrum concentrate is highly assimilable and bioavailable making it ideal for those with gastrointestinal problems.

Kirkman's Colostrum Gold[®] liquid is:

- Manufactured according to GMP (Good Manufacturing Practices)
- Sourced from USDA and FDA certified dairies
- Collected within 12 hours of production
- Free of synthetic hormones, pesticides and antibiotics
- Processed using minimal heat to ensure the bioavailability of its nutritional factors
- Unadulterated to maintain its natural wholeness and nutrition
- Formulated for autistic children and adults to be lactose, gluten and casein free
- Hypoallergenic formulation contains no flavors, sweeteners, preservatives or diluents. (Flavored product available for those who prefer one).

For optimal absorption and utilization colostrum is best taken on an empty stomach approximately 30 minutes before mealtime. Kirkman's Colostrum Gold[®] is casein-free and provides the safest product with the highest biological activity for use by children with autism. It is available in a liquid form to provide for optimal absorption and utilization by those autistic children with compromised gastrointestinal systems. Usual dosing is 1/2 to 1 teaspoon twice daily.

The safety of oral administration of colostrum has been clearly established in the medical literature with no known contraindications or overdoses.³⁵ However it is crucial to choose a colostrum product that is certified "casein free" because the absorption of opiate acting peptides from casein can trigger a number of adverse reactions in those with ASD.

Another important consideration is to choose a colostrum supplement that is guaranteed to be BSE free (Bovine Spongiform Encephalopathy) which is known as Mad Cow Disease. Although this problem primarily exists in England it is important to clear up any concerns regarding the purity and safety of this colostrum supplement. Kirkman's colostrum comes only from United States cattle.

SUMMARY

Colostrum has been shown to help significantly with intestinal permeability and irritable bowel symptoms. Colostrum contains a unique combination of anti-microbial factors to prevent the reproduction of pathogenic organisms as well as growth factors to provide some of the most important substances in stimulating the repair and healing the gut mucosal lining. The unique properties of this natural colostrum make it a key nutrient in the arsenal of supplements aimed at gastrointestinal healing. There is no other single nutrient that possesses the wide spectrum of biological activity, as does colostrum. Its use in combination with other nutritional supplements, adequate fiber and a healthy diet can provide important support for gastrointestinal healing.

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PROBIOTICS

Their Role In The Health And Functioning Of The Gastrointestinal Tract

Probiotics have been called “sustainers of life” and nature’s “internal healers” because of their crucial role in promoting the health and functioning of the gastrointestinal tract. These friendly bacteria are acknowledged to keep the intestinal environment in balance and exert other life-sustaining functions. Many of the gastrointestinal problems experienced by individuals with autism spectrum disorders (ASD) have responded positively to therapeutic supplementation with these friendly bacteria.

Achieving and maintaining gastrointestinal health is of paramount importance, since it has such a significant impact on the overall health and well being of children with ASD. With the guidance of a health care practitioner, a comprehensive treatment plan can be implemented that has the goal of restoring the health and functioning of the crucial digestive system. Probiotics should be a key component of any program aimed at healing and restoring the intestinal tract.

Dr. Eli Metchnikoff, a scientist from Eastern Europe, was awarded the Nobel Prize in 1908 for his research into the role of the friendly bacteria in gastrointestinal health. He was the first to theorize that the long, healthy lives of Bulgarian peasants were the result of a diet containing fermented milk products, specifically yogurt. He hypothesized that the bacteria in yogurt prevented or reversed gastrointestinal infections. In the decades that followed, he continued his research and was able to prove that the Lactobacillus strains of probiotic flora could combat pathogenic organisms and reduce the toxic by-products (endotoxins) that they produce.

There is a long history of use of natural probiotics (in the form of cultured dairy products such as fermented milk, yogurt, kefir, and others) to support intestinal health. The term “probiotic” means “for life” and is derived from the Latin “pro”, meaning “for”, and the Greek

“biotikos”, meaning “living”. Probiotics are friendly bacteria that are supportive of life. They have the remarkable ability to beneficially affect the delicate balance of the intestinal bacteria and the capacity to prevent or significantly reduce the effects of harmful pathogenic organisms.¹

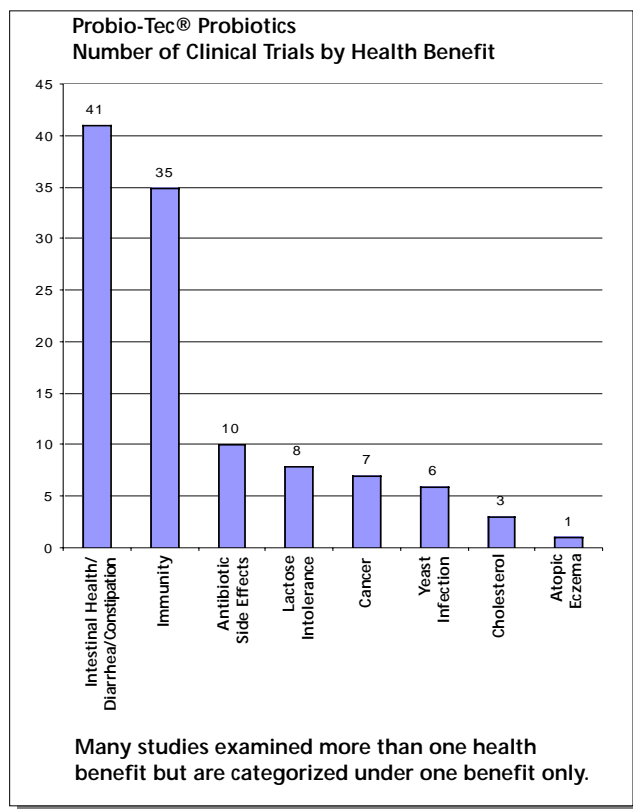
Gastrointestinal dysfunction is known to develop after the body has been assaulted by continuous, repetitive and cumulative exposures to a wide range of influences. These exposures may come from the ingestion of foods, from certain drugs (including antibiotics), chemical contaminants and additives in the diet, environmental exposures to toxins (heavy metals, pesticides, etc.), and pathogenic infections of the intestinal tract. Each of these factors contributes to the total load of physiological stress on the intestinal tract as well as on the immune system. The process of restoring gastrointestinal health begins with recognizing and addressing each of the factors that contributes to intestinal dysfunction.

The Role Of Probiotics In Gastrointestinal Health

Research on the use of probiotics has demonstrated that they have the ability to strengthen the intestinal tract’s immunological barrier. Specific probiotic strains (Probio®Tec® and LGG strains) are well documented to stimulate both specific and nonspecific immunity,² along with enhancing sIgA-producing cells in the mucosal membrane.³ Probiotics help control the overgrowth of harmful bacteria, viruses, and yeast (including *Candida albicans*)^{4,5,6} and have documented ability to colonize the intestinal membrane by adhering to human mucosal cells.^{7,8,9} They have a high tolerance for stomach acids (as low as a pH of 2 for BB-12 and a pH of 3 for LA-5 *Lactobacillus acidophilus*), as well as a tolerance to bile salts.^{10,11} These probiotic strains are recognized to produce anti-microbial substances that are active against pathogens, including *Salmonella* species, *E. coli*, *Clostridium*, and others.^{12,13} They are clinically effective at controlling diarrhea and constipation, gastroenteritis associated with rotavirus shedding, traveler’s diarrhea, antibiotic associated diarrhea, as well as infections of the genitourinary tract.^{14,15,16}

These probiotic strains have been shown to function in managing allergic inflammation,¹⁷ alleviating the symptoms of lactose intolerance,¹⁸ enhancing the nutritional content and bioavailability of nutrients, and in the production of natural antibacterial substances.¹⁹ They have also been shown to have an inhibitory effect on carcinogenic and mutagenic activity (specifically in the colon),²⁰ and have demonstrated the ability to reduce serum cholesterol.²¹ Just as important as the positive clinical effects of these probiotic strains is the documentation regarding their safety and tolerance.^{22,23} Please refer to the summary at the end of this section entitled "Clinically Proven and Tested Probiotic Strains", which provides supporting documentation pertaining to each of these probiotics.

Clinical Trials By Health Benefit



The Role Of Probiotic Supplementation In Treating Pathogenic Organisms In The Gut

1. Probiotics For Detoxification

Mark Brudnak, Ph.D., N.D. has recently published a landmark paper entitled "Probiotics as an Adjuvant to Detoxification Protocols",²⁴ in which he eloquently describes the pivotal role that probiotics play in detoxification. He suggests that the use of probiotics may be one of the missing components in detoxification treatment programs aimed at utilizing the body's own detoxification mechanisms. He describes how the enteric bacteria (found in the gastrointestinal tract) make up an enormous reservoir that can constantly and safely be replenished. The use of high-dose probiotic supplementation should be an important part of detoxification protocols, especially in individuals with autism.

Dr. Brudnak provides scientific support regarding the ability of probiotics to detoxify methyl mercury and outlines the process of how probiotics "can act directly on the organic mercury to reduce it to a less toxic form." He describes a process whereby high doses of probiotic bacteria can effectively sequester mercury and propel it along the gastrointestinal tract toward eventual elimination. This process of sequestering mercury reduces the opportunity for it to be reabsorbed into the body or to damage the intestinal membrane, where it normally exerts pathological effects on the enterocytes or gut associated lymphatic tissue (GALT). During detoxification, a potentially large amount of mercury is passed into the intestinal tract, where it is processed and ultimately eliminated from the body. High dose probiotic supplementation is key to this process. Dr. Brudnak's article provides a clearer understanding of the role of these friendly flora, not only in mercury detoxification but also in the health of the intestinal tract of those with ASD.

2. Candida Related Complex

Dr. William Crook, a recognized authority in the area of "Candida Related Complex", published

The Yeast Connection²⁵ and numerous other excellent books on the adverse health effects of chronic infections with the yeast *Candida albicans*. A large percentage of children with autism have persistent problems with *Candida* invading and setting up residence in the membrane of their intestinal tract. When the yeast take control and colonize the membrane of the bowel, they can change forms from a "budding yeast spore" to more invasive "hyphae" or "mycelium" forms. The hyphae yeast actually imbed themselves in the mucosal membrane, where they exert powerful control and have the ability to deeply penetrate the tissue. This attachment is made easier when the intestinal lining is damaged by yeast colonies that secrete enzymes (proteases, alkaline phosphatases, coagulase, phospholipase, and others). These enzymes further break down the intestinal lining, allowing for greater penetration of the mucosal tissue.²⁶ In addition, the acid proteases are thought to cleave secretory IgA from the mucosal membrane, thereby allowing the *Candida* to gain a stronger foothold without the normal protection afforded by sIgA. This destruction of the GI membrane can cause a cascade of symptoms, including inflammation of the intestinal tract that destroys the mucosal cells even further.

To compound the problem, when yeasts colonize the intestinal tract they produce toxins and other by-products that cross the mucosal membrane and are absorbed into circulation, where they can travel to different tissues and organs in the body, including the brain. This is referred to as "translocation" and can result in significant problems with the immune system and nervous system. These pathogenic organisms leave a trail of destruction throughout the intestinal tract. Among the toxins and toxic by-products they produce are substances like amines, ammonia, hydrogen sulfide, indoles, and phenols, all of which can accentuate the damage to the intestinal lining.²⁷

Of interest is the work by Guentzel, published in *Infection and Immunity*, which describes that infant mice were found to be far more susceptible to *Candida* overgrowth (infections) than older mice. If these mice were given antibiotics at an early age, they would develop more persistent *Candida* infections as compared to the older mice. In response to the antibiotics, the amount of *Candida* in the intestinal tract increased on an

average of 130 fold.²⁸ Human studies have demonstrated similar results.²⁹ This may explain some of the persistent *Candida* infections commonly seen in autistic children following repeated courses of antibiotics early on in their lives. Despite repeated treatment with different localized antifungals (Nystatin) and systemic antifungals (Nizoral, Sporonox, etc.), the *Candida albicans* is able to maintain its stronghold in the intestinal tract. Given this situation, there is a crucial role for the use of probiotic supplementation, which can help maintain a full spectrum of health-promoting bacteria in the gastrointestinal tract and displace any pathogenic organisms that may be present. Probiotics accomplish this by competing for attachment sites on the mucosal membrane and, if delivered in sufficient quantities, they can crowd out the pathogenic organisms, stimulate the intestinal immune response, and manufacture natural antibiotics and hydrogen peroxides that prove hostile to these unfriendly yeasts.

3. The Role Of Bacteria In Gastrointestinal Disease

A full spectrum of pathogenic bacteria, including *Clostridium difficile*, *Pseudomonas*, *Klebsiella*, *Bacteroides*, *Staphylococci*, *Helicobacter*, and others are recognized to cause many of the intestinal infections seen in children with ASD. However, the most problematic and frequently encountered of these organisms is *Clostridium difficile*.

Clostridia are generally present in small amounts in the intestinal tract. However, when the normal intestinal equilibrium is disturbed, *Clostridia* can flourish and cause major damage to the intestinal membrane. *Clostridia* are spore-forming bacterial organisms that are very resistant to treatment despite the use of high powered, broad-spectrum antibiotics including Vancomycin, which is usually the last line of defense against pathogenic bacteria. *Clostridia* are strict anaerobes, meaning that they cannot tolerate oxygen and therefore flourish in the intestinal environment that is devoid of oxygen. Unfortunately, even when powerful antibiotics are used, the *Clostridia* frequently resurface after the antibiotic therapy ends. Recently, there have been clinical studies demonstrating that probiotics can play a significant role in suppressing the growth of *Clostridia*. Dr. William Shaw made important observations

that eventually led to his discovery of a dihydroxyphenylpropionic acid-like (DHPPA-like) compound in the urine of autistic children.³⁰ This DHPPA-like compound was initially thought to be the by-product of an overgrowth of yeast (*Candida*). However, following collaborative studies with a German researcher, Dr. Shaw recognized that DHPPA was due to the *Clostridium difficile* bacteria and its relatives. Dr. Shaw and Dr. Walter Gattaz found that children and adults with *Clostridium difficile* infections of the intestinal tract had high levels of DHPPA in their urines. Specific testing of the urine of autistic children showed the values of DHPPA-like compounds to be extremely high, suggesting that this can be an important marker of *Clostridium difficile* infection of the gastrointestinal tract.

Key to the restoration and healing of the gastrointestinal tract is removing the pathogenic organism and re-establishing appropriate levels of the health-promoting bacteria. The use of *Lactobacillus acidophilus*, *Bifidobacterium bifidum* (*lactis*) and other friendly flora is of paramount importance in the treatment process, and there is extensive documentation and clinical research regarding the role of these probiotics in supporting and maintaining the integrity of the intestinal membrane.

Pulsing And Rotating Of Probiotics

An article entitled "Probiotic Applications: Pulse and Rotation" describes the current trends in probiotic supplementation that utilize high therapeutic doses for treating a number of gastrointestinal conditions. Specifically discussed are specialized probiotic supplements (containing 20 and 30 billion colony-forming units (CFUs) per capsule) that have been formulated to achieve clinically significant responses in those with autism-related gastrointestinal disorders.³¹

The focus of this article centers on the use of high therapeutic doses of probiotics such as *Lactobacillus acidophilus*, *Bifidobacterium bifidum*, and combinations of other well recognized strains. These formulations utilize a variety of probiotics, each with different functions that are complementary to one another. Recommendations are made for the use of high doses of probiotics, up to 100 billion CFUs per day, as indicated by the specific needs that are being addressed. Gener-

ally, this program has met with success, but Dr. Brudnak suggests that there may be some individuals who, after receiving initial benefit from high doses of probiotics, will note that improvement is not sustained. For example, initial supplementation may produce well-formed stools in a child, but then for some reason there is a reversion back to the previously noted problem with loose stools. In these circumstances, Dr. Brudnak recommends implementing a program where probiotics are pulsed when their clinical effects begin to change. He believes that taking a break from supplementation for a period of time, followed by repeat administration, may allow the body to "reset" itself by making it more hospitable to the probiotics.³²

The other option he suggests in place of withdrawing the probiotics for a period of time is to substitute another probiotic, or series of probiotic strains. This can be accomplished by rotating, or "pulsing", the different strains of probiotics. For example, a child might take *Lactobacillus rhamnosus* for a period of time, followed by a *Bifidobacterium* formulation and then by *Lactobacillus plantarum*, *Lactobacillus ruteri*, *Lactobacillus salivarius*, or any other single strains or combination of strains. There are numerous options that can be utilized in following a rotation protocol. Kirkman has developed a comprehensive line of probiotic supplements for this specific purpose.

Probiotic Supplementation

Hundreds of species of friendly bacteria flourish in the 25 to 28-foot long intestinal tract. Some are "resident" microorganisms, including *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus casei*, *Bifidobacterium bifidum* (*lactis*), and numerous others. These probiotics set up residence by attaching to the mucosal lining and colonizing the intestinal tract, where they crowd out the pathogenic (unfriendly) bacteria. Additionally, there are "transient" friendly flora, including *Streptococcus thermophilus* and *Lactobacillus bulgaricus*, which do not set up residence but instead travel through the intestinal tract and exert many positive benefits. Both the resident and transient strains of friendly bacteria may be among the most important nutritional influ-

ences on the health of the gastrointestinal tract. Their supplementation as part of a comprehensive treatment plan is of great importance in healing the intestinal disorders of children with ASD.

Kirkman Laboratories provides the "Gold Standard" in probiotic supplementation by utilizing the most extensively researched and clinically documented strains of health promoting microorganisms. Additionally, great care is taken in the manufacturing of these supplements in order to maintain the highest potency and stability of these live microorganisms. With the expertise of our scientific and technical consultant Jon Pangborn, Ph.D., along with the expertise of Mark Brudnak, Ph.D., N.D. (a recognized specialist in the areas of probiotics and enzymes), Kirkman Laboratories will continue to bring you products that meet the highest standards in the industry. Please refer to our website at www.kirkmanlabs.com for detailed information on all of our probiotic formulations.

Probiotic Strains Utilized In Kirkman Laboratories' Supplements

Lactobacillus acidophilus (LA-5)

Lactobacillus acidophilus is probably the most well recognized and prominent of all the different strains of probiotics. It sets up residence (implants itself) in the mucous membranes of the mouth and small intestine, as well as in the lining of the genitourinary tract. It performs many crucial functions, including inhibiting pathogenic organisms by preventing them from multiplying and colonizing. *L. acidophilus* aids in the digestion and absorption of nutrients, promotes regular bowel movements, and helps alleviate lactose intolerance caused by a deficiency of the enzyme lactase. Additionally, *L. acidophilus* has been shown to have a high tolerance for digestive acids and bile salts, which makes it a viable and hearty microorganism.

The LA-5 strain has been documented to produce a broad range of natural antimicrobial substances, including bacteriocin (named acidocin), lactocidin, acidophilin, and others.

These have activity against disease-producing microorganisms such as *Escherichia coli* (*E. coli*, which can cause "Montezuma's revenge" and chronic renal failure), *Staphylococcus aureus* (food poisoning and toxic shock syndrome), *Salmonella* (food poisoning), *Candida albicans* (yeast overgrowth and oral thrush), and *Shigella* (dysenteries). They have also recently been found to be effective against other undesirable pathogenic organisms, including strains of *Bacillus*, *Micrococcus* and *Cornebacteria*. Of interest is that *Lactobacillus acidophilus*, LA-1, has been shown to possess the ability to adhere to human enterocytes such as Caco-2 cells in culture, which is important for preventing the attachment and invasion of pathogenic bacteria.³³

Another study utilized a combination of Pro-Bio®Tec™ probiotic strains (LA-5, BB-12, *Streptococcus thermophilus* and *L. bulgaricus*), evaluating their effectiveness against *Clostridium difficile*. In a double-blind, placebo-controlled trial at Hudding University in Sweden, a group of subjects was given the antibiotic Clindamycin, 4 times daily for 7 days, plus a probiotic or a placebo capsule. The results showed that only 18% of the probiotic group was colonized with *Clostridium difficile*, compared to 47% of the placebo group. Recolonization of the friendly bacteria was faster in the supplemented group, which may be of importance in preventing *C. difficile* infections.³⁴

Based on these results, the use of Kirkman's Pro-Bio Gold™ formulation, which contains the strains utilized in the study, in combination with Culturelle, which contains LGG, may provide a comprehensive approach to dealing with *C. difficile* infections in children with ASD.

Lactobacillus rhamnosus

One of the crucial functions of *Lactobacillus rhamnosus* is its role as a primary "resident" in the small intestine. This important strain of *Lactobacilli* recently gained a great deal of attention for its ability to adhere to the intestinal mucosa and colonize the gastrointestinal tract, thereby exerting its important health-promoting functions. *Lactobacillus rhamnosus* has been shown to be effective in increasing the levels of secretory IgA in the mucus membrane of the intestines, which is crucial for autistic children who are generally recognized to have low sIgA

levels. This strain functions by competitive exclusion of pathogenic organisms, including *E. coli*, *Listeria*, *Clostridia*, *Shigella*, and *Salmonella*, thereby preventing gastrointestinal infections and diarrhea.

According to Canadian microbiologist Eduardo Brochu, Ph.D., *Lactobacillus rhamnosus* does not only colonize, acidify and protect the small intestine, but it can quickly establish itself in the large intestine, where it can inhibit the growth of *Streptococci* and *Clostridia*, create anaerobic conditions which favor the implantation of *Bifidobacterium*, and produce the biologically desirable L (+) lactic acid.³⁵

Lactobacillus GG

Culturelle™, with *Lactobacillus GG* (LGG), is one of the most researched strains of probiotics. The initial research on this particular *Lactobacillus rhamnosus* strain was undertaken by two Boston area scientists, Dr Sherwood Gorbach and Dr. Barry Golden. They isolated this strain, which they called *Lactobacillus GG*, and it received a patent in the US in 1987. This formulation is available only as a single strain offering 20 billion CFUs per capsule. It can be used alone or in combination with multi-strain formulations to provide comprehensive effects against *Clostridium difficile* infections.

Like other *Lactobacillus* strains, LGG possesses many crucial benefits for gastrointestinal health. It has been shown to control the overgrowth of harmful bacteria, adhere to and colonize the gastrointestinal wall, enhance the body's natural defenses, assist with lactose digestion, prevent milk-based allergic reactions, and treat acute diarrhea caused by antibiotics, rotavirus and bacteria. Its most impressive quality in regard to autism treatment is its reported effectiveness against severe intestinal infections, specifically *Clostridium difficile*. Studies undertaken on the LGG strain demonstrate its exceptional ability to control the infection and re-colonization of the *Clostridium difficile* organism in the gastrointestinal tract.³⁶

Bifidobacterium Bifidum / Lactis (BB-12)

Bifidobacterium bifidum, recently identified as *B.*

lactis, is the most prominent strain of probiotic residing in the large intestine, the last part of the small intestine, as well as in the vaginal tract. *Bifidobacterium bifidum* (*B. lactis*) performs several important functions, including preventing the colonization of invading pathogenic bacteria (*Clostridium*, *Salmonella*, and others) and yeast (*Candida albicans*). It accomplishes this by attaching itself to the intestinal membrane, crowding out the pathogens, and competing for nutrients.

B. bifidum is known for producing acetic and lactic acids, which lower the pH (increase the acidity) of the intestines, thereby creating an environment that is inhospitable to the undesirable bacteria. A double-blind, placebo-controlled study was undertaken with the BB-12 strain, which showed that symptoms of atopic dermatitis (eczema) were significantly reduced with its supplementation. Additionally, an in-vitro study showed that BB-12 increased the IgA production in the intestinal membrane, which the researchers felt might be helpful in reducing the risk of exposure to food antigens and preventing the onset of allergies in breast-fed infants.³⁷

The BB-12 strain is among the most investigated and tested *Bifidobacterium* strains available today. Numerous clinical trials undertaken on this strain have shown its versatile activity in protecting the intestinal flora and its potential application for treating allergic inflammation. A recent double-blind, placebo-controlled trial was undertaken with 27 infants diagnosed with atopic dermatitis (eczema). The infants were either given a formulation of BB-12, LGG, or a placebo that did not contain any type of probiotic. After two months, the probiotic-supplemented group showed significant improvements in their skin condition as compared with the non-supplemented group. According to the authors, "the results provide the first clinical demonstration of specific probiotic strains modifying the changes related to allergic inflammation. The data further indicate that probiotics may counteract inflammatory responses beyond the intestinal milieu."³⁸

Lactobacillus casei

Lactobacillus casei has some of the same im-

mune modulating effects that are seen with other members of the Lactobacilli family. It is commonly found in the mouth and within the membrane of the small intestine, where it inhibits pathogenic bacteria. The *L. casei* strain has been documented to secrete "peptidoglycan", which stimulates phagocytosis by macrophages. The cell wall of this strain contains "teichonic acid", which plays a role in the adherence of microorganisms to epithelial tissue.³⁹

Another important quality of this particular strain is that it is the most effective in enhancing the number of IgA-producing cells, which play an important role in the mucosal immune response. Additionally, when tested in malnourished mice, it increased IgA and IgM concentrations and improved the intestinal flora both qualitatively and quantitatively.⁴⁰

Lactobacillus bulgaricus

Lactobacillus bulgaricus is most notably known as the culture used in making yogurt. This microorganism does not set up residence in the intestinal tract, but transiently exerts a powerful influence primarily in the large intestine. In the bowel, it helps to decompose certain food components in fecal matter, assists in preventing putrefaction, and can play a beneficial role in helping to maintain regularity. *L. bulgaricus*, in combination with other friendly bacteria, has also shown an effect against *Candida albicans*.⁴¹

Streptococcus thermophilus

Streptococcus thermophilus is also considered to be a transient bacterium in the human intestine and exerts some positive influences on gastrointestinal health. One important function is its ability to enhance milk digestion through production of the enzyme lactase. Together with *Lactobacillus bulgaricus*, *S. thermophilus* produces a culture that is used in making yogurt. This strain produces lactic acid, which encourages a good environment for the resident flora (*Acidophilus* and *Bifidobacteria*) as well as inhibiting the less desirable and pathogenic bacteria.

A double-blind, placebo-controlled trial was

conducted with hospitalized infants at Johns Hopkins University. The results of this trial showed that *S. thermophilus* and BB-12 caused a significant reduction in the incidence of diarrhea and rotavirus shedding.⁴²

Lactobacillus plantarum

Lactobacillus plantarum has unique adhesive properties that keep *E. coli* from attaching to the mucosa of the intestinal tract, thereby preventing endotoxins from being delivered into circulation. Additionally, *L. plantarum* shows a strong ability to counteract sepsis of intestinal origin, specifically from *Clostridium difficile* infections.⁴³

Lactobacillus salivarius

This member of the *Lactobacillus* family has been shown to produce alpha-galactosidase, which can help reduce flatulence and has the additional property of being highly resistant to tetracycline and other antibiotics. *L. salivarius* is a hardy strain of probiotic and is able to maintain its potency at room temperature. Of interest are studies that demonstrated the ability of *Lactobacillus salivarius* to inhibit *Helicobacter pylori* colonization of human epithelial cells in vitro.⁴⁴

Lactobacillus helveticus

This unique *Lactobacillus* strain is fairly new as a nutritional supplement, but it appears, along with *Lactobacillus rhamnosus*, to contain analogs of the Dipeptidyl peptidase IV (DPP-IV) enzyme that is recognized for its ability to digest exorphins.^{45,46} Due to the presence of the DPP-IV analog produced by these friendly bacteria, the *L. rhamnosus* and *L. helveticus* strains may have an important role in treating gastrointestinal problems in children with autism spectrum disorders.

Lactobacillus ruteri

Lactobacillus ruteri is emerging as a probiotic strain with its own impressive qualifications, including a demonstrated ability to stabilize the intestinal flora, especially when used in combination with *L. acidophilus* and *B. bifidum*. *Lactobacillus ruteri* promotes additional benefits, such as

protection against pathogens and involvement in tissue morphogenesis.⁴⁷

Saccharomyces boulardii

Saccharomyces boulardii is considered to be a non-pathogenic, non-colonizing yeast species closely related to brewer's and baker's yeast. *Saccharomyces boulardii* gained a great deal of attention in the autism community when it was demonstrated that it could be used to prevent both infections and reinfections with *Clostridium difficile*.⁴⁸ There are recent studies to show the use of *Saccharomyces boulardii* as a potential adjunctive treatment for children with autism,⁴⁹ as well as demonstrating its application in the treatment of recurrent *Clostridium difficile* disease.⁵⁰

There are clinicians who report excellent results in utilizing *Saccharomyces boulardii* with their patients. Kirkman Laboratories has been asked to make this supplement available for use in the autism community. At this time, however, our scientific and technical advisers have decided not to distribute *Saccharomyces boulardii*. Instead, we will be offering an alternative probiotic formulation that does not use the live yeast extract. This formulation is described below.

Beta 1,3/1,6 Glucan With Lactobacillus Strains

Kirkman is finalizing the development of a probiotic formulation that contains the stellar immune-stimulating properties of Beta 1,3/1,6 glucan in combination with one or more well-researched probiotic strains. Beta 1,3/1,6 glucan is recognized to be a safe and very potent nutritional supplement that has a powerful impact on stimulating the immune response and helping the body defend itself against foreign substances. The Beta 1,3/1,6 glucan compound is plant based. It is derived from the cell wall of the *Sacchromyces cervesiae* organism, which is a relative of *Sacchromyces boulardii*. What makes it different, however, is that it is not the live yeast but a micro-particulate "ghost" cell of purified beta glucan that possesses the potent biological activity.⁵¹

The Beta 1,3/1,6 glucan supplement offered by Kirkman is completely safe, non-toxic, and the

purest form of the substance available. No known toxic or mutagenic properties have been demonstrated with this supplement. In fact, studies in patients with severely compromised immune systems, including patients with cancer, have shown both a high degree of tolerance to this supplement as well as a positive clinical response. Although Beta 1,3/1,6 glucan is derived from yeast, it is recognized to be a pure isolate and does not contain any yeast proteins that can trigger an allergic reaction. Extensive use of this nutrient has provided well-documented evidence pertaining to its safety, even in the sensitive individual.

The use of Beta 1,3/1,6 glucan in combination with specific strains of health promoting probiotics appears to offer one of the safest and most effective means of providing enhanced probiotic supplementation for *Clostridium difficile* infection. Kirkman Laboratories plans to have this special combination product available soon. This supplement is the first of its kind to offer all of the qualities attributed to both of these unique components.

Advancing The Standards Of Probiotics

Kirkman Laboratories offers a comprehensive approach to optimal probiotic supplementation. We are committed to maintaining the highest standards in manufacturing an exceptional line of probiotics. Following is an overview of the qualities found in this probiotic line:

Kirkman Laboratories' Quality Product Standards:

- In-house manufacturing facility
- Exclusive use of vegetable plant cellulose capsules in place of gelatin
- Use of pharmaceutical grade raw materials whenever possible
- Hypoallergenic supplement line available
- Highest degree of quality, purity and bioavailability
- Independent laboratory testing for stability where appropriate
- Elemental values of nutrients listed
- Certified gluten and casein free
- Custom formulating of products

- Commitment to Clinical Trials

Kirkman's Exceptional Probiotic Formulations:

- Certified strains using DNA fingerprinting
- Use of amber glass bottles
- Nitrogen flushing for stability
- Extensive clinical testing
- Available in capsules and powders
- Guaranteed potency through expiration date
- High-potency formulations
- Use of inulin in place of maltodextrin

Exceptional Quality Of Documented Probiotic Strains

Our probiotics are from MAK Wood, Inc., the definitive leader in the nutraceutical industry, supplying raw probiotic material from the world's premier manufacturers.⁵² All probiotic strains utilized in our formulations meet the highest standards of quality. They undergo innovative strain verification involving DNA fingerprinting, and special enumeration testing to ensure the highest potency and activity. All of these qualities provide a significant measure of assurance that exceptional probiotic formulations are available for use in an intestinal treatment protocol. Because of our partnering with MAK Wood, Inc., Kirkman Laboratories has access to extensive technical support and the ability to stay at the forefront of probiotic research and innovative product development.

Unique Probiotic Base

Kirkman utilizes a unique, all-natural base ingredient called Inulin in place of the standard maltodextrin (derived from wheat, corn or rice) that is commonly utilized in most probiotic formulations. Inulin is derived from the root of the chicory plant and belongs to a class of compounds known as oligosaccharides. Since this oligosaccharide is non-digestible, it is not broken down by the intestinal tract but passes into the colon intact. Once in the large intestine, inulin is selectively utilized by Bifidobacterium as a fuel source for the growth

and reproduction of these important, beneficial bacteria. These characteristics make inulin an ideal probiotic base.⁵³

Inulin also serves as a "prebiotic" that functions in nourishing and supporting the growth of healthy, friendly intestinal flora. In this role, it has a positive impact on increasing the levels of lactic acid bacteria that are so important in maintaining a healthy gastrointestinal tract. A unique quality of inulin is that it does not affect or alter blood sugar levels and is generally well tolerated by the diabetic. One of the compelling attributes of inulin is that it appears to be exceedingly well tolerated by sensitive individuals and, because it is derived from an exotic root vegetable, it is considered to be hypoallergenic. It has a pleasant taste and dissolves easily when the powder is mixed with foods and/or beverages.⁵⁴

Kirkman exclusively utilizes the naturally derived inulin oligosaccharide in place of the commercial fructo-oligosaccharides (FOS) commonly found in many probiotic formulations. It appears that inulin, unlike some types of FOS, is resistant to utilization by pathogenic bacteria, including *Klebsiella pneumoniae*.⁵⁵ This makes inulin a safe and well-tolerated probiotic base, supplying growth factors that are documented to support beneficial intestinal flora.

Safety Of Probiotic Supplementation

Lactic acid bacteria have a long history of safe use as nutritional supplements. A number of studies have been undertaken regarding the safety of the ProBio®Tec probiotic strains at doses ranging from 10 to 42 billion CFUs (colony forming units) per day, administered in capsule/powdered form. Additionally, there are clinical studies utilizing between 10 and 100 billion CFUs of these lactic acid bacteria (in fermented milk). In one study, 13 malnourished hospitalized infants with diarrhea due to post-gastroenteritis syndrome were administered the ProBio®Tec *L. acidophilus* and *L. casei* strains. The results of this supplementation eliminated the symptoms in four days, and in all cases it was possible for the children to return to normal feeding. Clearly, this speaks to the safety and efficacy of utilizing these certified strains at higher doses for more intensive care needs.⁵⁶

There are other compelling studies showing the

safety of the *L. acidophilus* and *B. bifidum* (lactis) strains in patients with compromised immune systems. A randomized, double-blind, placebo-controlled study was undertaken, evaluating the prophylactic effect of LA-5 and BB-12 on infections in patients undergoing chemotherapy for acute leukemia.⁵⁷ A dose of 24 billion CFUs per day was administered for 30 days, beginning at the start of chemotherapy. The results showed that no Lactobacilli were cultured from the blood, indicating no risk of septicemia from the probiotic. The LGG probiotic strain has also undergone extensive clinical evaluation, with the safe utilization of 20 to 40 billion CFUs. All of these results are encouraging and provide support for use of these specific strains in autistic children who have compromised immune systems.

Available Forms And Dosing Of Probiotics

Our entire line of probiotic supplements is available in both capsule and loose powder forms. Capsules deliver 7_ to 30 billion CFUs, and the powders deliver 15 billion CFUs per _ tsp. The capsules may be swallowed whole or opened and the contents mixed with food or beverages. The probiotic powders allow these friendly bacteria to be administered in the mouth and throughout the gastrointestinal tract. These extensively researched probiotic strains have a high tolerance for acids and bile salts, making them ideal for use in a powdered form. For this reason, Kirkman Laboratories offers probiotic supplements at 20 to 30 billion CFUs per capsule, as well as five powdered formulations delivering 15 billion CFUs per gram (_ tsp).

How And When To Take Probiotics

The question of when to take probiotics has been a subject of great debate among health practitioners. Some suggest that probiotics should be taken on an empty stomach (between meals), while others advise that they be taken with food and/or beverages.

For the answer, we have consulted with several microbiologists who are in agreement with the recommendation that optimal results are obtained when probiotics are taken with meals.^{58,59,60} It has been suggested that live microorganisms have three requirements, allowing them to grow

and set up residence in the gastrointestinal tract. They need: 1) shelter, 2) warmth, and 3) a food source. When taken with meals, these bacteria are afforded some protection and are buffered from the stomach acids as they make their way to the small intestine with the objective of adhering to and colonizing the GI mucosal membrane. In companionship with food, probiotics are also provided a warm environment as well as a source of nutrients, allowing them to proliferate. These conditions all favor the survival of these health-promoting bacteria so that they may colonize the gastrointestinal tract and exert a positive influence on intestinal health.

There may be some medical conditions or medications that prevent individuals from being able to take probiotics with meals. In these cases, experts suggest that the probiotics be taken between meals with an adequate amount of water to dilute and then move them through the stomach acids and into the intestinal tract.

Suggested Use And Dosage Recommendations

Most of Kirkman's probiotic formulations are designed to provide high therapeutic doses, so it is important start the probiotics at a lower dose and gradually increase. Follow the directions on the label or, preferably, follow the specific directions of your health care practitioner.

Take one (1) capsule or _ to 1 tsp daily, as directed by a medical practitioner. For more intensive use, take two (2) capsules daily (or the appropriate amount of powder), in divided doses, for a minimum of two weeks or as specifically recommended. This dose can then be decreased when the gastrointestinal functioning is more balanced.

For infants and children less than 30 pounds, use one half of the suggested dose and increase as recommended by a practitioner. The capsule may be opened, and the dose divided and taken at separate times during the day. Higher amounts may be safely utilized, but only under the care of a medical practitioner.

Directions For Use

For optimal results, it is recommended that the probiotics be taken with food (meals). This formulation may be taken in conjunction with digestive enzymes and other nutritional supplements without affecting their potency, stability or function. However, avoid the use of antibiotics, potent herbs, or anti-microbial foods/supplements such as garlic at the same time the probiotics are ingested.

Kirkman's Probiotics Do Not Contain:

All of Kirkman Laboratories' probiotic supplements have been formulated to be free of milk, casein, wheat, gluten, corn, soy, yeast, sugar, starch, MSG, maltodextrin, stearates, artificial sweeteners, colors or flavors, preservatives, salicylates, and other common allergens. This is to ensure that the purest and most non-reactive supplements are available for meeting the needs of the most sensitive individuals. Kirkman Laboratories has set the highest standards and initiated independent laboratory testing to assure the potency, as well as to certify that this supplement is free of gluten and casein.

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure or prevent any disease.

CLINICAL TRIALS UTILIZING PROBIO®TEC™ STRAINS

DIARRHEA/INTESTINAL HEALTH: JOHN HOPKINS UNIVERSITY HOSPITAL

A double-blind placebo-controlled trial was undertaken with hospitalized infants aged 5 to 24 months who received a formula with or without a ProBio®Tec™ Bifidobacterium (BB-12) strain. The subjects were evaluated for

diarrhea and rotavirus shedding for a total of 4447 inpatient days during 17 months.

REPORTS/CONCLUSIONS: Supplementation of infants with the probiotic significantly reduced the incidence of diarrhea ($P=0.035$) and rotavirus shedding ($P=0.025$). The probiotic-based formula was well tolerated by the children, many of whom were initially malnourished or immuno-compromised.

POST-GASTROENTERITIS: CHILDREN'S HOSPITAL OF TUCUMAN, ARGENTINA

Thirteen malnourished infants with post-gastroenteritis syndrome were fed milk fermented with a *L. acidophilus* (LA-5) and *L. casei* every 6 hours for 7 consecutive days. All children had not responded to conventional therapy, which included use of antibiotics, corticosteroids, soymilk, lactose free milk, and baby-fed milks with hydrolyzed lactose.

REPORTS/CONCLUSIONS: Treatment with milk fermented with the ProBio®Tec™ strains of probiotics eliminated the disease/symptoms in 4 days. It was possible to return to normal feeding according to the child's age.

IMMUNITY/SAFETY: MARSELISBORG HOSPITAL, DENMARK

A randomized, double-blind, placebo-controlled study was undertaken regarding the prophylactic effect on infections in 30 neutropenic patients undergoing cytoreductive chemotherapy for acute leukemia. Probiotics (*L. acidophilus* and *B. lactis/bifidum*) were given at a dose of 24 billion colony forming units (CFUs) daily for 30 days, beginning at the start of chemotherapy.

REPORTS/CONCLUSIONS: Fever was significantly postponed from 8 to 12 days with probiotics ($P=0.033$). No lactobacilli were cultured from the blood, indicating no risk of septicemia from these probiotics, utilized in these immune compromised patients.

**ANTIBIOTIC SIDE EFFECTS/CONTROL OF
PATHOGENIC BACTERIA:
HUDDING UNIVERSITY, SWEDEN**

In a double-blind, placebo-controlled study, 23 healthy subjects received 150 mg of the antibiotic Clindamycin 4 times daily for 7 days, plus a probiotic formulation or placebo capsules for 14 days. The effect on the intestinal microflora was evaluated.

REPORTS/CONCLUSIONS: The total number of microorganisms was significantly higher in the subjects receiving the probiotic ($P=0.02$). Only 18% of the probiotic group was colonized with *Clostridium defficile*, compared to 47% of the placebo group. Recolonization was faster in the supplemented group, which may be of importance in preventing colonization with *C. defficile*.

**LACTOSE INTOLERANCE:
UNIVERSITY OF MINNESOTA, ST. PAUL,
MINNESOTA**

10 lactose intolerant subjects consumed 9 test meals, which included 400 ml of low-fat milk, nonfermented yogurt milk or acidophilus milk containing various probiotic strains. One test meal was fed per day, with at least 1 day in between treatments. Lactose malabsorption was measured by the breath hydrogen test.

REPORTS/CONCLUSIONS: Only one probiotic strain, the Probio@Tec™ *L. acidophilus*, significantly decreased breath hydrogen values ($P=<0.05$) and this acidophilus strain also demonstrated low bile resistance and intermediate B-galactosidase activity.

**YEAST INFECTIONS:
ODENSE UNIVERSITY, DENMARK AND UNI-
VERSITY HOSPITAL, SWEDEN**

In a double-blind, placebo-controlled study, 69 women with *Candida albicans* vaginitis were given Miconazole (100 mg) or *Lactobacillus acidophilus* via vaginal application. The *Lactobacillus* preparation was effective in 73% of the patients after 14 days of treatment.

REPORT/CONCLUSION: According to the report the *L. acidophilus* gave a better effect than

Nystatin, which was only 54% effective in another investigation. In this study the Miconazole was 94% effective however the authors noted that with this medication there is always a risk of developing side effects, whereas treatment with a probiotic is not likely to give side effects.

CANCER/SAFETY

20 patients with superficial urinary bladder carcinoma were surgically treated, and then orally administered a combination of two *Lactobacillus* strains at 22 billion CFUs per day. Tumor recurrence was evaluated for 36 months.

REPORTS/CONCLUSIONS: Treatment with this combination of *Lactobacillus acidophilus* and *L. casei* minimized tumor recurrence after surgery and maintained or diminished the tumor recurrence after surgery. Only one relapse was detected. No adverse side effects, including hepatomegaly, splenomegaly or blood alterations were observed. According to the authors *Lactobacillus* fermented milk is recommended as potential immunopotentiators in tumor processes.

**CLINICALLY PROVEN AND TESTED
PROBIOTIC STRAINS**

Extensive research and documentation supports the numerous health benefits of the strains utilized in Kirkman Laboratories' line of probiotic formulations. All of the strains that we utilize have undergone extensive laboratory testing and clinical evaluation for safety, stability and activity. There are over 80 independent clinical studies and trials that have been undertaken demonstrating the intestinal and general health benefits of these strains. These include the following:

@Documented Ability To Adhere To Human Mucosal Cells And Colonize The GI Membrane

University of Turku, Finland, Kirjavainen P, et al., FEMS Microbiology Letters 1998; 167:185-189.

Children's Hospital, Rocourt, Langhendries JP, et al. Belgium Journal of Pediatric Gastroenterology and Nutrition 1995;21:177-181.

University Federal de Minas Gerais, Brazil, Silva AM, et al. Journal of Applied Microbiology 1999;86:331-336.

University of Turku, Finland, Salminen S, et al. Bioscience Microflora 15(2): 61-67.

University of Copenhagen, Denmark, Hove H, et al. American Journal of Clinical Nutrition 1994;59:74-79.

® Helps Control The Overgrowth Of Harmful Intestinal Bacteria, Viruses, And Yeast

Odense University, Denmark, Hansen BW, Prac Medical Professional Publication 1997:877-879.

Karolinska Institute/University, Sweden, Nord CE, et al. Clinical Microbiology and Infection 1997;3(1):124-32.

University of Western Ontario, Canada, Reid G. Applied and Environmental Microbiology 1999:3763-3766.

Long Island Jewish Medical Center, New York, Hiton E, et al. Annals of Internal Medicine 1992;116:353-357.

Marselisborg Hospital, Denmark, Black FT, et al. Internal Report of double-blind, placebo-controlled trial, 1995.

® High Tolerance For Stomach Acids And Bile Salts (pH of 2 for BB-12 and pH of 3 for LA-5/Lactobacillus acidophilus)

Chr. Hansen, Germany, Ghoier E. "Saeure und Gallentoleranz von Lactobacillus acidophilus und Bifidobakterien" 1992;26:769-772.

Victoria University of Technology, Australia, Dave R, Shah N. International Dairy Journal 1997;7:435-443.

National Public Health Institute, Helsinki, Finland, Miittinen M, et al. Microbiol Ecology in Health and Disease, 10:141-147.

North Carolina State University, Raleigh, N.C., Sanders, ME, et al. Journal of Dairy Science 1996;79: 943-955.

® Assists In Alleviating Lactose Intolerance Problems

University of Copenhagen, Denmark, Hove H, et al. Am Journal of Clinical Nutrition, 1994;59:74-79.

University of Minnesota, St. Paul, MN, Journal of Dairy Science 1991;74:87-95.

University of Minnesota, St. Paul, MN, Lin MY, et al. Journal of Dairy Science 1991;74:87-95.

® Strengthens The Intestinal Tract's Immunological Barrier

National Health Institute, Helsinki, Finland, Miittinen M, et al. Infection and Immunity 1996;64 (12):5403-5405.

Japan (Fecal IgA significantly increased), Fukushima Y, et al. Int Journal of Food Microbiology 1998;42:39-44.

® Production Of Anti-Microbial Substances With Activity Against Pathogens, Including Salmonella Species, E. Coli, Clostridium, and others

Institute of Chem Technology, Prague, Czech, Plockova M, et al. "Antifungal activity of L. acidophilus (CH5)." Protrav Vedy;15(1):39-48.

Children's Hospital, Argentina, Apella MC. Journal of Applied Bacteriology 1992;73:480-483.

Universidade Federal de Minas Gerais, Brazil, Silva AM. Journal of Applied Microbiology;86:331-336.

® Clinical Effectiveness In Controlling Diarrhea And Constipation, Gastroenteritis Associated With Rotavirus Shedding, Traveler's Diarrhea, Antibiotic-Associated Diarrhea, And Others

Children's Hospital of Tucuman, Argentina, Gonzalez S, et al. Biotherapy 1995;8:129-134.

Huddinge University, Stockholm, Sweden, Black FT, et al. Scandinavian Journal of Infectious Dis;23:247-254.

Children's Hospital, Rocourt, Belgium, Langhendries JP, et al. Journal of Pediatric Gastroenterology and Nutrition 1994;21:177-181.

® Assists In Regulating Intestinal Motility And Normalizing Bowel Function

John Hopkins Hospital, Baltimore, MD, Saavedra JM, et al. Lancet 1994;334:1046-1049.

® Production Of Natural Antibacterial Substances

University of Minnesota, St. Paul, MN, Gastroenterology (Supplement);108(4):A293.

Institute of Chemical Technology, Prague, Czech Republic, Chumchalova J, et al. Chem Mikrobiol Tech;17(5/6):145-150.

University Ghent, Belgium, Belgium Coordinated Collection of Microorganisms/Identification Certificate, LA-5, 1996.

® Stimulation Of Immune Function By Enhancement Of Both Cell-Mediated And Humoral Immunity

National Public Health Institute, Helsinki, Finland, Miettinen, M, et al. Infection and Immunity;64(12):5403-5404.

Marselisborg Hospital, Denmark, Ellegard J, et al. International Symposium on Infections in the Immunocompromised Host, 1992.

® Inhibitory Effect On Carcinogenic And Mutagenic Activity, Specifically In The Colon

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Hankuk Yakult Institute, Korea, Kim H, et al. Journal of Korean Cancer 1991;23:188-195.

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® Demonstrated Reduction Of Serum Cholesterol

University of Belgrade, Obradovic D, et al. Symposium on Lactic Acid Bacteria, Holland, 1996.

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® Documented Safety And Tolerance

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DIGESTIVE ENZYME SUPPLEMENTATION IN AUTISM

The use of digestive enzymes is a crucial part of a treatment protocol designed to address the complex gastrointestinal conditions experienced by children with autism. Enzyme deficiencies cannot be handled by any other means except through supplementation, utilizing specific enzymes that are deficient or recognized to be low in the autistic child. The goal for the use of digestive enzymes goes far beyond just breaking down foods so that they are properly absorbed and utilized for growth, development and repair.^{1,2} These digestive enzymes provide an arsenal of defense against the myriad of assaults that are aimed at the gastrointestinal tract. In this section, we will discuss the unique role that enzymes can play in addressing the complex gastrointestinal problems seen in children with autism.

Digestive Enzymes In Gastrointestinal Health

Enzymes play a key role in gastrointestinal health because of their multi-faceted functions. Digestive enzymes can exert a powerful influence in addressing a full range of commonly recognized gastrointestinal conditions including 1) Inflammation, 2) Maldigestion and Malabsorption, 3) Intestinal Hyperpermeability, 4) Intestinal Dybiosis, 5) Food Allergies and Sensitivities, and 6) Enzyme Deficiencies, including deficiency of the important enzyme Dipeptidyl peptidase IV (DPP-IV). Each one of these intestinal conditions can be supported by or helped with the use of broad-spectrum enzyme formulations, used alone or in combination with specialty enzymes such as Dipeptidyl peptidase IV (DPP-IV).³

The impact of digestive enzymes in gastrointestinal health has been recognized for decades. However, our understanding of their unique role in autism has only recently been unfolding. The following discussion pertains to the role that enzymes play in decreasing the burden on the digestive system, countering inflammatory reactions, supporting the healing of the intestinal membrane, and enhancing the amount of

nutrients available to the body.

First, it is important to discuss the gastrointestinal abnormalities and pathologies that have been recognized in individuals with autism spectrum disorders. This will be followed by a discussion of the scientific support and clinical documentation regarding the role of digestive enzymes in addressing each of these conditions. Intestinal abnormalities are frequently found in combination with one another and generally do not exist alone. The pathology of gastrointestinal dysfunction and the complexity of digestive disorders seen in autism provide a challenging landscape from which to work. A comprehensive treatment approach is warranted, with digestive enzymes playing one vital part of a protocol aimed at gastrointestinal healing.

1. Inflammation

Irritation and inflammation of the intestinal membrane are hallmark symptoms associated with autism spectrum disorders (ASD). They result from a number of factors, including exposure to drugs, the presence of food allergens and incompletely digested food proteins, chemical toxins from the diet, heavy metal toxicity, viral damage from vaccines, as well as the overgrowth of pathogenic organisms including yeasts, bacteria, parasites, and others. The consequences of these exposures result in significant inflammatory changes in the delicate mucosal membrane and manifest in a wide spectrum of inflammatory gastrointestinal conditions.

Dr. Andrew Wakefield, M.D., a noted gastroenterologist at the Royal Free Hospital in London, England and his colleagues have studied the intestinal abnormalities of children diagnosed with autism and published their finding in several prestigious, peer-reviewed medical journals. They performed colonoscopies and obtained biopsies from the intestinal tracts of these children. The results indicated that all had varying degrees of intestinal abnormalities and inflammatory processes, which Wakefield has described as "autistic enterocolitis".⁴

Independently, Dr. Karoly Horvath and colleagues at the University of Maryland School of Medicine demonstrated varying degrees of inflammation of the gastrointestinal mucosa in a group of autistic

children. Esophogastroduodenoscopies with biopsies were undertaken on each child and the results of this testing revealed reflux esophagitis in 69.4 %, chronic inflammation of the gastric mucosa in 41.7 %, and chronic duodenal inflammation (duodenitis) in 66.7 %.⁵

This inflammation of the gastrointestinal mucosal lining results in further damage to the membrane due to free radicals being produced as waste products. These free radicals accentuate the problem by causing additional damage, ultimately contributing to even greater inflammation and increased permeability of the gastrointestinal lining. One of the approaches to addressing intestinal inflammation involves the use of digestive enzymes, which take over a large part of the responsibility of digestion in the already compromised intestinal system. These enzymes support the appropriate breakdown of foods, ultimately lessening the overall irritation of the already inflamed intestinal tract.

2. Maldigestion And Malabsorption

The problem of maldigestion, often accompanied by malabsorption, is another condition that is frequently seen in those with autism. Maldigestion is the result of foods not being properly broken down into the elemental building blocks that are needed to nourish the tissues. When this occurs, the cells of the body do not receive sufficient quantities of the nutrients that are necessary to provide energy for the body, or to undertake the important tasks of repair and healing. This results in malabsorption, characterized by the incomplete uptake of nutrients, which leads to a lack of available fuel and oxygen for supporting the body's cellular function. Dr. Woody McGinnis has described this problem as "suboptimal nutrient status due to impaired digestion and assimilation."⁶

Digestive enzymes play an important role in addressing these malabsorption problems by thoroughly breaking down (digesting) foods, thereby allowing for more optimal absorption and utilization of the essential vitamins, minerals, fatty acids, amino acids, and other nutrients necessary for the proper functioning of vital tissues and organs.

3. Intestinal Hyperpermeability

It is well documented in the medical literature that irritation and inflammation of the intestinal membrane can be caused by chronic exposure to incompletely digested foods, exposure to chemical contaminants in foods (preservatives, additives, artificial colorings and flavorings, and pesticide residues), the presence of food allergens (both IgE and IgG mediated reactions), and exposures to toxins (including heavy metals, pesticides, and solvents). These assaults on the mucosal membrane lead to further inflammation and significant damage to the intestinal lining, resulting in increased gastrointestinal permeability. This condition has been appropriately referred to as "Leaky Gut Syndrome". The consequences of this inflamed, overly porous mucosal membrane is that toxins, food allergens and undigested proteins pass into the lymph and circulatory systems, where they can trigger a cascade of neurological and systemic symptoms.⁷

Dr. D'Eufemia and colleagues at the Institute of Pediatrics, University of Rome, Italy were the first to document the presence of increased intestinal permeability in a large percentage of children with autism.⁸ He found that 43% of autistic children, none of whom had any clinical or laboratory findings consistent with known intestinal disorders, had gut mucosal damage. These findings may represent a possible mechanism for the increased passage of food-derived peptides, including gluten and casein, through the intestinal mucosal membrane. Prior to this study, there was little recognition of the potential role of intestinal permeability in children with ASD. Dr. D'Eufemia's work provides important confirmation that disruption of the intestinal membrane is a key issue in the intestinal health of children with autism. This has led scientists and medical practitioners to explore treatments aimed at addressing the healing of this important membrane.

Here again, digestive enzymes play a role in addressing intestinal hyperpermeability issues by allowing for the more optimal breakdown of foods, thereby preventing undigested food antigens and opiate peptides from passing through the leaky intestinal membrane and triggering a variety of systemic problems.

4. Intestinal Dysbiosis

Autistic children have a predisposition for "intestinal dysbiosis", a condition characterized by the overgrowth of pathogenic yeast, bacteria or other organisms in the digestive tract. These organisms set up residence and multiply along the lining of the intestinal tract, further accentuating the leaky gut problems. As the pathogens take control of the intestinal membrane, they crowd out the beneficial, health promoting bacteria such as *Lactobacillus*, *Bifidobacterium*, and others.

Contributing to the problem is that these yeasts and bacteria actually produce toxins and by-products that pass through the intestinal lining. Once absorbed into the circulation, these toxins are known to trigger a number of physical and neurological symptoms. William Crook, M.D., author of several books including *The Yeast Connection*, has eloquently described the wide spectrum of diverse symptoms that can result from the overgrowth of these yeasts.⁹

Digestive enzymes can help with the problem of intestinal dysbiosis in a unique way. Because these plant-based enzymes function even in the acidic environment of the stomach, they begin the work of breaking down foods early on in the digestive process. This in turn minimizes the amount of undigested food proteins available to potentially serve as a food source for the pathogenic organisms found throughout the gastrointestinal tract.

5. Food Allergies And Sensitivities

The term "food allergy" encompasses a wide range of reactions to the ingestion of foods. Children with autism tend to have a greater susceptibility to developing food allergies and sensitivities. It has been recognized that foods can trigger a number of physical as well as behavioral symptoms.¹⁰ The presence of these food allergies needs to be thoroughly evaluated and treated by a competent medical practitioner if optimal health of the gastrointestinal tract is to be accomplished.

Many food allergies are thought to be due to the "leaking" of partially digested food fragments across an overly permeable intestinal

membrane, provoking a series of immune responses that eventually cause the child to become allergic to one or more foods. Food sensitivities are also common among ASD children, with the most common reactions being to gluten and casein.

The problem of food allergies and sensitivities can, in part, be helped by the use of broad-spectrum digestive enzymes. In fact, this is one of the most important reasons for using enzyme formulations in autistic children. Digestive enzyme supplements assist in breaking down foods more completely so that only the essential elements are absorbed. When foods are thoroughly digested, the potential for developing hypersensitivity reactions to foods may be significantly lessened.

6. Enzyme Deficiencies

Among the gastrointestinal disorders seen in ASD is a complex range of enzyme deficiencies, including deficiencies of protease, amylase, lactase, maltase, lipase, and other digestive enzymes. As described previously, these deficiencies in specific enzymes have been recognized clinically in autistic children and documented in the medical literature.^{11,12} In addition to the enzymes produced by the pancreas, there are also deficiencies in enzymes secreted from the stomach lining as well as crucial enzymes produced by the brush border membrane of the small intestine.¹³ Studies suggest that these enzyme deficiencies may explain some of the significant intestinal problems, including chronic diarrhea and foul-smelling stools, described by so many parents of autistic children.

Dr. Karoly Horvath from the Department of Pediatrics and Pathology, University of Maryland School of Medicine wrote a landmark article entitled "Gastrointestinal Abnormalities in Children with Autistic Disorder."¹⁴ He and his colleagues conducted a clinical study of thirty-six children diagnosed with autism who presented with gastrointestinal symptoms including chronic diarrhea, abdominal pain, gas, abdominal bloating, sleep disturbances, and unexplained irritability. The aim of this study was to evaluate the structure and function of the gastrointestinal tract. The children underwent esophogastroduodenoscopy with biopsies, as well

as an evaluation of their small intestinal enzymes (lactase, maltase, sucrase, glucoamylase, and others) and an analysis of their pancreatic enzymes (lipase, amylase, trypsin, chymotrypsin and peptidase). Bacterial and fungal cultures were also obtained from the GI tract.

Horvath's study indicated that 58% of the children examined had disaccharide/glucoamylase enzyme levels below the normal range. The authors suggest that carbohydrate malabsorption may be the cause of many of the gastrointestinal symptoms seen in autistic children, including abdominal pain, gas and bloating, and chronic diarrhea or loose stools. According to the study, another frequent finding was low lactase activity, noted in 14 of 21 children, which also supports the disaccharidase insufficiencies. The authors believe that further gastrointestinal studies will help contribute to the understanding of a possible association between the brain and gastrointestinal dysfunction in children with autism. They suggest that gastrointestinal abnormalities may contribute to some of the behavioral problems frequently described in autistic children. This study provides compelling evidence in support of the use of broad-spectrum digestive enzymes, including the disaccharidase enzymes described in Dr. Horvath's paper.

Karl Reichelt, M.D., Ph.D. of the Pediatric Research Center in Oslo, Norway recognized the problem of the incomplete breakdown of protein peptides from casein and gluten and their role in autism. In his early work, he described the consequences of these opiate peptides passing through a permeable intestinal membrane and then stimulating the opiate receptor sites in the brain. This can in turn trigger a variety of CNS symptoms, including significant alterations in behavior, cognitive ability, and pain threshold.¹⁵ Paul Shattock, R.Ph. at the University of Sunderland in England and Robert Cade, M.D. of the University of Florida have found results similar to those of Reichelt.^{16,17}

There is excellent scientific support and clinical documentation to substantiate the deleterious effects of incompletely digested protein peptides from casein (caseomorphins) and gluten (gluteomorphins) in individuals with autism.^{18,19} Of interest are the observations made by Dr. Shattock, who monitored the urine of autistic children over time. He found that it could take up

to one year following the implementation of a casein-free and gluten-free diet before caseomorphin and gluteomorphin peptides were no longer being excreted in the urine.²⁰ Abnormalities in digestive enzyme activity may therefore have far-reaching implications for children with autism.

Dipeptidyl Peptidase IV (DPP-IV) Deficiency

Dipeptidyl peptidase IV (DPP-IV) is an enzyme that has gained a great deal of attention in the autism community. Some of the initial pioneering work and observations regarding DPP-IV's role in ASD were made by Jon Pangborn, Ph.D. and Alan Friedman, Ph.D., both of whom are scientists and fathers of autistic children. Dr. Pangborn, in conjunction with Bernard Rimland, Ph.D. (Founder of the Autism Research Institute) directed the DAN! research project on the very first digestive enzyme with high peptidase and DPP-IV activity. Dr. Pangborn subsequently wrote and spoke about the importance of DPP-IV in autism to the medical and autism communities. Dr. Friedman isolated and identified opioid peptides in the urine and serum of autistic children, with recognition that DPP-IV may be absent or deficient in some with autism.²¹

Following this earlier work, other researchers, including William Shaw, Ph.D. looked at the many environmental factors impacting DPP-IV and undertook a review of the literature confirming that these outside factors could have direct inhibitory effects on DPP-IV in the body. These include triggers such as Candida infections, antibiotics, environmental chemicals, pesticides, gelatin stabilizers in vaccines, and gluten and casein exposures. Each of these factors can be documented to suppress, inhibit or alter the function of DPP-IV.²²

What Is DPP-IV?

Dipeptidyl peptidase IV (DPP-IV) is a protein that has multiple functions in the body. It is known under different names depending on where in the body it is found. When DPP-IV is on the surface of the T-cell (lymphocyte), it is called CD26, and it travels in the circulation and helps support immune function. When this

enzyme is found on the mucosal membrane lining the intestinal tract, it is known as DPP-IV. This protein is also located in the surface tissues of the pancreatic duct, bile duct, colon, and kidney. Bile-duct cell surface molecule "GP110" is another name for DPP-IV.²³ In 1982, Dr. Gene Stubbs published his findings that a purine-regulating enzyme, called adenosine deaminase, was weak in autistic children.²⁴ A decade later, researchers recognized that DPP-IV is the binding protein, or anchor, that supports adenosine deaminase. It has been suggested that if DPP-IV levels are reduced or absent, this could explain the lower levels of amino acids seen in the profiles of many autistic children.

As observed by Dr. Karl Reichelt and Dr. Paul Shattock, a large percentage of autistic children have problems with the incomplete breakdown of gluten and casein, resulting in the development of opiate peptides. These peptides are recognized to function as false neurotransmitters, adversely affecting the central nervous system and triggering a number of adverse neurological and physiological consequences. Once absorbed into the bloodstream, these peptides also have the ability to stimulate undesirable immune and inflammatory responses in the body. Dipeptidyl peptidase IV (DPP-IV) stands out as potentially being one of the most important enzymes for addressing these problems.

This enzyme is unique in that it specifically breaks apart proline-containing peptides, including caseomorphin and gluteomorphin, which are generally resistant to being completely broken down by other enzymes. Of importance is that these opiate-like dietary peptides ("exorphins") have been shown to be excessively high in autism. DPP-IV is the enzyme that has specific activity for the digestion of these peptides, which are known to come from dairy products and cereal grains. Some researchers suggest that when there is an absence, deficiency or reduction of the crucial DPP-IV enzyme, this may explain the high levels of opiate peptides that are seen in autism.^{25,26}

Recently, a DPP-IV analog was developed in the nutritional supplement industry and is now available through Kirkman Laboratories. This product, called DPP-IV Forte™, is a plant-based enzyme that possesses DPP-IV activity. For

clarification, an analog is described as something that is similar to another compound. It is a replication of an original element that shares the same biochemical makeup as the original compound, but is derived from a different source. DPP-IV Forte™ is the plant-based analog of the human tissue DPP-IV enzyme and offers the same enzyme activity as human-derived DPP-IV.²⁷

DPP-IV Forte™ is one of the most exciting nutritional enzyme supplements available from Kirkman Laboratories. This state-of-the-art enzyme has significant application when used alone or in combination with other nutritional enzymes to optimally fortify digestive processes. The DPP-IV enzyme is indicated when there is hidden, accidental or intermittent exposure to casein and gluten in the diet. Those following a GF/CF diet, as well as those who have accidental or intermittent exposure to gluten and casein-containing foods, can safely use this supplement. Kirkman Laboratories supports the use of a gluten-free and casein-free (CF/CF) diet, as it has been scientifically and clinically documented to be effective in addressing the opiate peptide problems demonstrated in those with autism spectrum disorder.

Role Of Genomeceuticals In Autism

Mark Brudnak, Ph.D., N.D., a Molecular Biologist with a decade of expertise in the area of enzymes, has published research on the role of the genomeceutical Galactose, which is recognized to increase the expression as well as the amount of DPP-IV in the mucosal membrane of the intestinal tract. He has developed specialized enzyme formulations (inclusive of the enzyme DPP-IV) that have undergone clinical evaluation, and he continues to publish in the medical literature on the role of enzymes and probiotics in autism.²⁸

In his article entitled "Application of Genomeceuticals to the Molecular and Immunological Aspects of Autism",²⁹ Dr. Brudnak provides a remarkable framework for looking at autism spectrum disorders. He suggests that autism can be viewed as a combination of immune responses and genomic regulatory events. In the abstract for this paper, he provides the following summary of the position that he lays out in the article:

"Current theories indicate an important role of diet in the development of the

disease. It is thought that, as a result of maldigestion of casein and gluten, opiate-type peptides, or exorphins, are produced. Additionally, because of the time frame of development of the disease, there has been an association with childhood vaccination. Consequently, prevailing therapies attempt to address these causes in one, or a combination, of three ways: diet restriction (removing casein and gluten), supplementation with exogenous enzymes, and probiotic bacteria. Until recently, none of the therapies addressed the molecular mechanism that may be at work in the development and progression of autism. This paper presents potential molecular and cellular mechanisms related to autism as well as discusses their application to the treatment of the disease through the application of genomeceuticals."³⁰

This fascinating article presents some extraordinary concepts and guides the reader into a greater understanding of some of the potential molecular and cellular mechanisms at work in the development of autism. Just as important as the recognition of the possible causes for the development of autism are the possible biomedical treatment options that can be utilized, including enzymes and nutrition-based genomeceuticals.

You may be asking what a genomeceutical is. "Simply put, genomeceuticals are natural compounds which can cause a gene to either alter its expression pattern (i.e. make more or less of the product), affect the fidelity of the gene (i.e. how well that gene product works), or affect the integrity (i.e. whether or not a gene even functions at all) of the gene itself. They have the ability to act on the genome in a similar manner related to pharmaceuticals acting on biochemical pathways. That is to say, genomeceuticals can not just replace substances which may be missing (e.g., an enzyme diminished by mutation), but actually alter the expression and functionality of gene products in, and resulting from, genomic nutrient-sensing pathways."³¹

In the case of Kirkman's digestive enzyme formulation EnZymAid™, the genomeceutical that is present is galactose. "Galactose appears to be able to increase the expression of the Dipeptidyl peptidase IV (DPP-IV) gene, and this means that

adding galactose to the formulation can increase the amount of DPP-IV that is present. Now, if in autistics the situation is not that there is absolutely zero DPP-IV, but rather that the gene has been silenced or "turned down" (down-regulated), then the addition of galactose has the potential to reverse or circumvent that, the caveat being that the gene needs to at least be functional." Thus, the inclusion of galactose is by far the most potentially dynamic ingredient in the EnZymAid™.³²

EnZymAid™ Pilot Study Results

In January of 2001, a Multi-Center Pilot Study was completed that evaluated the response to a specialty enzyme formulation, Kirkman's EnZymAid™, in children diagnosed with autism spectrum disorders. This pilot study was sponsored by the Autism Research Institute and coordinated by six physicians working with ASD children. The study involved a 12-week clinical trial evaluating the response to this unique peptidase/protease enzyme specifically designed to break down casein and gluten as well as increase the levels of the Dipeptidyl peptidase IV (DPP-IV) enzyme. Parents evaluated their children utilizing 13 different parameters of function and behavior. The results of this pilot study were impressive and have attracted the attention of a major University and Medical Center, who now wish to undertake a double-blind, placebo-controlled study evaluating the effect of these enzymes in the gastrointestinal function of children with ASD.³³ A paper documenting the EnZymAid™ has been submitted for publication; however, a brief summary of the database is provided below.

Summary Of The Database

Following is a table summarizing the percentage of families that reported a moderate, significant and/or great improvement in their child's symptoms over a 12-week time period.

	<u>WEEKS 1-2</u>	<u>WEEKS 3-4</u>	<u>WEEKS 5-6</u>	<u>WEEKS 7-8</u>	<u>WEEKS 9-10</u>	<u>WEEKS 11-12</u>
<i>Eye Contact</i>	37%	47%	43%	56%	67%	67%
<i>Socialization</i>	42%	67%	71%	76%	81%	90%
<i>Attention</i>	40%	54%	63%	59%	73%	68%
<i>Mood</i>	36%	52%	57%	60%	55%	59%
<i>Hyperactivity</i>	31%	31%	50%	75%	75%	80%
<i>Anxiety/Compulsions</i>	20%	41%	46%	47%	41%	60%
<i>Stimming</i>	27%	38%	27%	38%	31%	50%
<i>Comprehension</i>	40%	45%	58%	55%	50%	63%
<i>Speech/Language</i>	27%	41%	53%	47%	38%	44%
<i>Sound Sensitivity</i>	17%	17%	18%	42%	25%	50%
<i>Digestion</i>	35%	50%	56%	50%	56%	50%
<i>Sleep</i>	23%	36%	43%	50%	64%	57%
<i>Perseveration</i>	33%	38%	44%	50%	39%	53%

The observations from this study suggest that EnZymAid™ can be effectively used to provide quite noticeable improvement in function and behavior of children who are on the autism spectrum. Further studies are planned with this formulation as well as with a separate DPP-IV analog supplement.

Plant-Based Enzyme Supplementation

The goal of supplementation with enzymes is to utilize sufficient quantities to adequately break down the foods being ingested so that there is optimal absorption of essential nutrients along with adequate breakdown of protein peptides. There are two sources from which digestive enzymes can be derived. The first are the "pancreatic" enzymes, which are derived from porcine (pork) pancreas and provide different enzymes including proteases, amylases and lipase. Of interest is that pancreatic enzymes are susceptible to being destroyed when exposed to gastric acid and pepsin, and thus need to be enterically coated so that they can survive the passage through the acidic stomach environment and arrive intact in the small intestine, where they begin their job of breaking down food. There is the potential, however, that these enterically coated capsules may fail to dissolve in the small intestine when there is a hyperacidity of the duodenum.

All of these issues point to the preferred use of plant-based enzyme supplementation in indi-

viduals with autism-related intestinal problems. Dr. Brad Rachman has described the unique features of non-animal based enzymes, or "plant-based" enzymes, which he suggests are associated with a number of important qualities. He describes the plant-based enzymes as offering "effective digestive support that works synergistically with, or as an alternative to, animal-derived enzymes and are free of some of the inherent limitations of conventional pancreatic enzymes."³⁴

The plant-based enzymes possess a number of important qualities that make them ideal for use with autistic children who have gastrointestinal abnormalities. They offer the broadest and most complete spectrum of enzyme activity, including protease, amylase, lactase, maltase, lipase, invertase/sucrase, and cellulase enzymes. This provides the most comprehensive approach to optimal digestion and relieves the pancreas of some of its burden of having to produce large quantities of enzymes for the thorough digestion of foods. Most importantly, these plant-based enzymes have been successfully and safely used in children with autism spectrum disorders. Following are some of the impressive qualities of the plant-derived enzymes.

Unlike the animal-based pancreatic enzymes, these highly concentrated and naturally derived plant-based enzyme formulations are effective in improving digestion in a full range of gastrointestinal pH conditions. They have the ability to digest a broad spectrum of foods throughout the length of the digestive tract because they are active in a pH range of 2 through 12. They start their digestive activities in the stomach, which has a very acidic pH of around 2. Pancreatic enzymes, on the other hand, are not able to survive the stomach acids without being degraded, so they are enterically coated and will only begin digesting foods once they reach the small intestine. Plant-based enzymes also have activity in the small intestine, with a pH of 4-8, and finally in the colon/large intestine, which has an alkaline pH range of 10-12. Therefore, given their great versatility, the plant-based enzymes make an excellent choice for use in autistic children.

The plant-based enzymes are derived from specially cultivated plant sources, specifically the *Aspergillus oryzae* species of plant molds, which have been used for decades in the manufacture of nutritional supplements. Although these enzymes are derived from plant molds, they undergo an extensive filtration process that separates the active enzyme from the original plant mold, leaving a pure product with a high degree of potency and biological activity. The end result is a safe and effective enzyme supplement that may be used even by highly sensitive individuals. In comparison, pancreatic enzyme supplements are derived from animal-based pancreatic tissue that is obtained from slaughterhouse bovine (cow) and porcine (pig) sources.

Alternatives To The Use Of Betaine HCl (Betaine Hydrochloride)

Some children diagnosed with autism spectrum disorders have the inability to secrete sufficient quantities of hydrochloric acid (HCl), or stomach acid. This condition, which is known as hypochlorhydria, can have a profound effect on the child's ability to thoroughly digest a broad range of foods, especially foods containing protein. If the stomach does not have sufficient amounts of hydrochloric acid, foods will be incompletely broken down and subsequently delivered into the small intestine as partially digested peptides,

including the opiate peptides gluten and casein. In addition, insufficient stomach acid has also been linked to gastrointestinal overgrowth with pathogenic organisms such as bacteria, yeast, and parasites, since stomach acid usually helps to keep these microbes under control.

Correcting hypochlorhydria through supplementation with Betaine Hydrochloride (Betaine HCl) is one way to address this problem, but this treatment approach carries some risks and should only be used under the close supervision of a medical practitioner. Supplementing with plant-based digestive enzymes may be a safe alternative to treating the problems caused by low stomach acid, since these enzymes will begin breaking down foods in the stomach and thereby lessen the stomach's burden of having to produce large amounts of HCl for the digestion of foods.³⁵

Digestive Enzymes For Gastrointestinal Support

Kirkman Laboratories offers a comprehensive approach to optimal digestion by providing four different enzyme formulations designed to address the unique needs of each individual with autism spectrum disorders. EnZymAid™ and EnZymAid Companion™ can be used in combination with one other for comprehensive digestive support that includes Galactose and DPP-IV-containing enzymes. The EnZym-Complete with DPP-IV™ supplement offers the ultimate high potency, broad-spectrum formulation, including 50,000 HUT of DPP-IV. Kirkman also offers DPP-IV Forte™, a Dipeptidyl peptidase IV analog that contains 60,000 HUT of this unique opiate peptide-degrading enzyme. All of these formulations can be used alone or in combination to optimally impact the proper digestion of a full range of foods. These enzyme supplements are state-of-the-art, scientifically formulated, and supported by clinical use and research.³⁶

Qualities To Evaluate In An Enzyme Formulation

Kirkman Laboratories' digestive enzyme formulations are designed for the sensitive individual who requires a hypoallergenic formulation free

of potentially reactive ingredients. All formulations are made without the use of rice bran or beetroot fiber as base ingredients. Only plant cellulose is used for encapsulation and, when needed, the essential amino acid L-leucine is used in place of other more commonly used lubricants (magnesium stearate, stearic acid). All of our enzyme formulations are designed to be free of milk, casein, wheat, gluten, gliadin, corn, rice bran, soy, egg, yeast, sugar, starch, MSG, stearates, palmitates, artificial sweeteners, colors, flavors, preservatives, salicylates, and other common allergens.

All of the papain utilized in Kirkman Laboratories' enzyme formulations is guaranteed to be sulfite free, offering one of the purest and highest quality papain enzymes for nutritional supplementation. By contrast, many other manufacturers will use a cheaper source of papain to get the high levels of enzyme activity they desire. The consequence is a high level of sulfites present in the enzyme formulation. When choosing digestive enzymes, be sure that the product is certified to be free of chemical sulfites.

EnZym-Complete™, EnZymAid%, EnZymAid Companion™, and DPP-IV Forte™ are all manufactured according to the highest pharmaceutical and nutraceutical standards. All of these formulations have been tested and are certified to be gluten and casein free.

All of Kirkman Laboratories' enzyme formulations are Kosher and have Rabbinical certification, making them an excellent choice for those who are maintaining Kosher households. In addition, these enzyme products can be used by those individuals who are following a Vegan or Vegetarian diet.

Available In Powder And Capsule Form

One of the things that separates Kirkman Laboratories from other nutritional supplement companies is that our enzyme formulations are available in both powdered and capsule forms to meet the unique needs of autistic children. The powdered enzyme supplements are specially packaged to include a measuring spoon for ease and accuracy of dosing. The powder may be mixed in with a small amount of food

or beverage and taken immediately prior to, or at the beginning of, a meal. The other enzyme formulations are encapsulated in the highest quality vegetable capsules, which may be swallowed whole.

Methods For Evaluating The Enzyme Activity Of Dietary Supplements

Kirkman Laboratories is working with an enzyme supplier who is recognized as the premier manufacturer and industry leader in the specialty area of plant-based enzymes. They utilize authorized compendial methods of measuring and expressing enzyme activity. These methods have been scientifically developed and have undergone validation procedures recognized by the Enzyme Technical Association. Some of these measurements are expressed in FCC units, while others are expressed according to newer technological standards that provide a more definitive characterization of activity and are recognized by the ETA as being equally acceptable units of activity. With Kirkman Laboratories' supplements, the potencies for these enzymes are expressed according to the industry's most current FDA-recognized standard for determining the activity of enzymes.

For example, when testing the enzymatic activity of bromelain, the FCC units may not represent the most accurate measurement of this enzyme's activity. On some product labels, bromelain is measured in Papain Units (FCCPU). However, the more appropriate and current standard for measuring bromelain is in Bromelain Tyrosine Units (BTU's), which Kirkman uses on the labels of our enzyme supplements. Because not all enzyme formulations follow this new standard, whenever possible we also provide the approximate equivalent activity units in parentheses. For example, bromelain will be accurately expressed as BTU's (Bromelain Tyrosine Units), but next to this will also be listed its equivalent value in FCCPU (Papain Units).³⁷

Kirkman Laboratories is committed to manufacturing enzyme formulations of the highest quality, potency and purity. We are working with MAK Wood, Inc., recognized in the industry as the definitive leader and premier supplier of nutritional enzymes, probiotics, and other specialty nutraceuticals.³⁸ They are known for the excellent quality of their research-based product line.

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AMINO ACIDS IN INTESTINAL HEALTH

During the last decade, medical researchers began to uncover a previously unsuspected feature of autism—a gut connection. Our intestinal tract is a tunnel through the body, in which food is digested and to which wastes are added by the liver. In the lower part of the intestinal tract, a vast population of microorganisms works to further process these wastes, sometimes into useful things like vitamins. Meanwhile, in the upper part of this tunnel, foods are being broken down into basic components. Only the basic components are allowed to pass through the tunnel wall into our bodies. The mucosal tissue that lines the intestinal tunnel controls this passage—as long as it remains healthy.

One of the digestive processes that begins in the stomach is digestion of food protein. In the stomach, proteins are broken into fragments called peptides—chains of amino acids from two to perhaps a hundred or more amino acids. These dietary peptides are then further digested in the small intestine to form individual amino acids. An amino acid is one of those basic food components that the intestinal mucosa welcomes into the body; proteins and most peptides are not supposed to be allowed in. The objective of protein digestion is to break down giant, complex chain of amino acids into individual, free-form amino acids. Inside the body, organs and tissues reassemble these amino acids into body proteins. Muscles, skin, hair, bone, the heart and other organs contain protein that is needed for structure and function. Besides being used for building materials, amino acids form components of the immune system, act as hormones (often when bound together as human peptides), operate tissue cleanup systems (detoxification), and they form enzymes, which are catalysts for operating the body's biochemistry.

In the early 1990s, Dr. Karl Reichelt (Oslo, Norway) and Paul Shattock (Sunderland University, UK) published their research showing dietary peptides in the urine of autistics. Subsequently others, both overseas and in the US, confirmed these findings. For this to happen,

the digestive process and the integrity of the gut mucosa must have failed in some respects. Dr. Andrew Wakefield (UK) has found one definite gut mucosal problem—“ileal hyperplasia” and measles virus in the wall of the lower small intestine. Many researchers and clinicians now believe that the gut-brain connection is part of autism. Biologically active peptides from the diet affect immune response, brain development and behavior.

But there is another aspect to maldigestion and leaky gut. While unwanted peptides get into the body, needed free-form amino acids from dietary protein may be in short supply. To investigate this, clinicians have performed amino acid analysis on blood and urine from autistics. Jon Pangborn (the author of this section of the Kirkman gut protocol) surveyed over 60 such analyses from various medical practices. In doing so, notable similarities were found in the laboratory-measured patterns of amino acids for autistic children, aged 3 years-9 years. About 55% showed overt signs of protein maldigestion, low levels of some nutritionally essential aminos and, concurrently, elevated levels of some small peptides that were measured in the same test. Sixty-two percent (39 of 63) showed need for taurine, a very biologically active amino acid. Fifty-four percent were frankly deficient in the essential amino acid lysine.

The Kirkman amino acid product “AMINO-SUPPORT” evolved from this study. Its contents are a weighted average of the needs as shown by statistics from the survey of autistic children and from human needs for amino acids as published by the US National Research Council (Recommended Dietary Allowances, 10th ed, National Academy Press, 1989).

Taurine: Helps form bile, spares magnesium in cells and in the body, normalizes glutamate/OABA neurotransmitter activity, and neutralizes the oxidant called “hypochlorite”. Taurine is present in human milk, but not in cows' milk.

Lysine: A nutritionally essential amino acid that is the anchor for vitamin B6 in enzymes that process the amino or nitrogen part of amino acids. Lysine is present in meat, fish and poultry protein.

Leucine, Isoleucine, and Valine: Essential “branched chain” amino acids that are important for formation of flexible, structural tissue such as skin. Leucine helps control pancreatic insulin release. All protein foods contain these amino acids.

Methionine: The essential precursor of cysteine, taurine and S-adenosylmethionine, “SAM”. This amino acid accounts for most of the body’s “methylation”. It provides sulfur that may eventually be used for sulfation (a type of detoxication or body cleanup process), but it needs vitamins B6, B12, and folate to be properly utilized. Organ meats, poultry, milk, and beef are rich in methionine.

Glutamine: Nonessential, but the major nitrogen carrying amino acid in the animal kingdom. Glutamine makes vitamin B3 work; it may reduce obsessive compulsive behaviors related to diet, and it nourishes gut mucosal cells. All animal protein is rich in glutamine.

Threonine: An essential amino acid that is the precursor of glycine and serine. It is the slowest amino acid to cross the intestinal mucosa and is typically low in malabsorption. Threonine is one of only a few amino acids that allow sugars to bond to proteins or peptides, examples of which are immunoglobulins, interferon, and cell-to-cell recognition molecules. Threonine is found in the same foods as lysine.

Phenylalanine: Another essential amino acid, and the precursor tyrosine which forms adrenal hormones called catecholamines.

Tyrosine: Nonessential (comes from phenylalanine and directly from dietary protein). Tyrosine becomes “dopa”, dopamine, noradrenalin, part of thyroglobulin (the part that attaches iodine), and it helps form melanin, a pigment or coloring substance in body tissues. Dairy products, fish and soy contain lots of phenylalanine and tyrosine.

Arginine: Sometimes essential in infants and young children, and “semiessential” throughout life. Our bodies make some but not enough, and diet provides the rest. It helps immune function (stimulates activity of natural killer cells), helps form creatine (for muscle metabolism), and forms urea (for nitrogen detoxification). Seeds, nuts, buckwheat, lamb, beef and soy are rich in arginine.

Asparagine: Nonessential, but the major nitrogen-carrying amino acid in the plant kingdom. Often a limiting amino acid for leukocyte and lymphocyte growth. Asparagine (like threonine), allows sugars to bond to proteins forming structures required for immune response and regulation.

Proline: Not essential, but very necessary for formation of connective tissues, such as ligaments, skin, and the intestinal mucosa. This is the amino acid that gets stuck in lots of peptides found in the urine of autistics. Wheat germ, barley, soy, dairy and fish are rich in proline.

Alpha-ketoglutaric acid: Not an amino acid but an organic acid, “A-KG” balances nitrogen levels in body tissues. AKG counteracts ammonia buildup, as can occur with gut bacterial overgrowth or infection, and it is necessary for cellular energy processes.

Most individuals tolerate amino acid supplements very well and they can derive remarkable benefits. Amino acids help immune function, build enzymes, support the body’s cleanup processes, and allow growth and repair of tissue. If your child does not tolerate amino acids, then this is an important clue that something is amiss and some testing, under a doctor’s supervision, is advisable. Amino acid intolerance can take many forms such as hyperactivity, increased perseveration, headaches, gastrointestinal distress, or onset of additional inappropriate behaviors. If any of these or other, not previously seen problems occur, then discontinue use of the amino acids and ask your doctor to investigate two possibilities: (1) intestinal dysbiosis (overgrowth of bad flora in the gut) by doing a stool analysis, and (2)

problems in metabolizing amino acids by doing a 24-hour urine or fasting blood plasma amino acid analysis. The DAN! Consensus Report, 2001 Edition, provides guidance on doing this testing. It is available from the Autism Research Institute in San Diego, (619) 281-7165. Also refer to the laboratory section of this protocol for testing information.

The amino acid L-Glutamine has been shown to have remarkable abilities to heal the intestinal lining when in an injured state. In fact it is the main nutrient necessary for intestinal repair. With the thin and often perforated intestines in autism, L-Glutamine is a very important healing supplement and is often given as a stand alone amino acid in larger doses than is present in multiple amino acid formulations. Kirkman does sell L-Glutamine capsules.

Normal dosing of the Amino Support is one to two teaspoons daily or as directed.

J. Pangborn, Ph.D.
Consultant to Kirkman Laboratories

MSM

MSM stands for methylsulfonylmethane, which is a natural substance present in food and in the human body. MSM is a source of sulfur, an element critical to the structure and functioning of body mechanisms. The following list highlights MSM's most significant actions when used as a dietary supplement:

1. Pain relief
2. Reduces inflammation
3. Increases blood flow
4. Helps restore normal bowel activity by inhibiting cholinesterase
5. Reduces muscle spasm
6. Has a normalizing effect on the immune system as seen in clinical studies involving autoimmune diseases such as lupus and arthritis

HOW CAN MSM HELP IN AUTISM?

Dr. Rosemary Waring reports that most autistic children show a deficiency of sulfates in their plasma. Of the autistic children she tested, 92% had sulfate levels that were only 12% of normal. Low sulfates can lead to a leaky gut, as well as a weakness in the phenolsulfotransferase (PST) system. A weakness in the PST system is often characterized by night sweats, red face and ears, runny nose, bloated stomach and extreme thirst. MSM adds sulfur to the diet and this sulfur may be oxidized to sulfates in the body thus aiding the PST pathway which is important in removing toxins.

Dr. Jeff Bradstreet, a widely respected Florida physician specializing in autism, reports good success using MSM when children sweat excessively or have abnormal odors. Dr. Bradstreet believes the MSM is in fact improving the PST pathway.

There are many reports that suggest MSM may reduce sensitivity to food allergies. It does not "cure" the allergy but rather improves tolerance. Some patients report that if they take MSM before eating, they have no problem with substances which previously were allergens. Trent Nichols M.D., medical director of the Center for Nutrition and Digestive Disorders (Hanover, Pennsylvania), reports MSM helpful against food allergies including his own.

KIRKMAN offers MSM in a good tasting flavored powder and in a pure hypoallergenic form. Usual dosing is 1-2 grams for smaller children and 3-4 grams for older children and adults.

MSM has been shown to be perfectly safe and free of side effects up to five grams per day. Kirkman's flavored MSM powder can be dissolved in water or various juices to produce a pleasant drink. The natural flavoring and sweetener make it much less bitter than pure MSM powder. Children's dosages are easily masked. Lemonade is one of the best vehicles for covering any bitterness. The hypoallergenic form can also be put in juices to cover the bitter flavor but obviously will not be as pleasant tasting as the flavored version.

Kirkman uses "Cardinal" brand MSM exclusively. This is the purest MSM available and has been thoroughly tested microbiologically for the absence of bacteria, yeast and mold. It has also been tested for the absence of heavy metals including mercury, lead, cadmium, aluminum and arsenic. There is no finer MSM available in the world. Usual dosing is 1-2 grams for smaller children and 3-4 grams for older children and adults.

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FIBER AND INTESTINAL HEALTH

Fiber is recognized to function in supporting a healthy intestinal wall, maintaining bowel regularity and in helping to bind to toxins and prevent the absorption of these substances from the gastrointestinal tract by escorting them out of the body.

FUNCTION AND ROLE OF FIBER

A review of the benefits of dietary fiber have been clearly outlined in the *Encyclopedia of Natural Medicine* and these include:

Beneficial Effects Of Dietary Fiber

- Decreased intestinal transit time
- Delayed gastric emptying, resulting in reduced after meals hypoglycemia
- Increased satiety
- Increased pancreatic secretion
- More advantageous intestinal microflora
- Increased production of short-chain fatty acids
- Decreased serum lipid levels
- More soluble fiber

ROLE OF FIBER IN AUTISM

The role of fiber in addressing gastrointestinal disorders in autistic children is of crucial importance. One of the most common gastrointestinal

complaints in a large portion of those with autism is the presence of chronic diarrhea/loose stools, which are exceedingly foul-smelling. A smaller percentage of autistic children will experience chronic constipation (associated with hard, dry stools that result in problems with impaction). Some will experience constipation with intermittent episodes of diarrhea. Whether the child is suffering from constipation, diarrhea, or both, the supplementation of fiber still plays a role in their gastrointestinal wellness.

Given the common problems with intestinal dysbiosis (overgrowth of yeast, bacteria, and other pathogens), malabsorption and/or maldigestion, along with intestinal permeability/leaky gut problems, it is understandable that fiber's role in addressing intestinal concerns in those with autism is not always understood. We do know however that fiber is an integral part of a treatment program aimed at restoring and supporting gastrointestinal health.

In the *Encyclopedia of Natural Medicine* the authors describe fiber's role in addressing chronic candidiasis problems. They recommend utilizing "3 to 5 grams of soluble fiber at bedtime - especially when anti-yeast therapies are employed to ensure that dead yeast cells are excreted and not absorbed" (Pizzorno, Textbook of Natural Medicine pages 421).

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CLINICAL DOCUMENTATION/SCIENTIFIC SUPPORT

Some of the most interesting and compelling research in regards to fibers role in autism is in regards to the use of marine derived alginates. Alginates are natural marine plants/seaweed, which have been demonstrated to inhibit heavy metal uptake in the gastrointestinal tract by binding and facilitating their removal from the body. There is more current research demonstrating that these alginates may specifically bind with aluminum, a heavy metal that is challenging to remove from the body.

Magnesium Sulfate (Baths and/or Cream)

Magnesium sulfate, otherwise known as Epsom Salts, has been valued by the medical community for many years because of its diverse therapeutic benefits. Rich in both magnesium and sulfur compounds, Epsom salt baths have been used to stimulate detoxification, reduce inflammation, promote healthy circulation, and normalize sleep patterns.

Recently, a number of studies, as well as close observation by parents, have indicated that there may be potential value in the use of magnesium sulfate for the management of autism. Parents of autistic children have reported improvements in areas such as language, behavior, mood, cooperation, sleep, and motor skills after starting their children on daily Epsom salt baths. Since Epsom salt baths may cause some children to develop dry, irritated skin, several physicians specializing in the treatment of autism are now prescribing magnesium sulfate cream to achieve these same therapeutic effects.

The benefits of magnesium sulfate appear to be linked to an enzyme system known as phenol sulfotransferase (PST), which was shown to be functioning at sub-optimal levels in more than half of the autistic children tested by Dr. Rosemary Waring in England¹. Normally, PST is involved in a process called sulfoconjugation, whereby a group of potentially harmful chemicals known as phenols are attached to sulfate and thereby eliminated from the body. When there is a deficiency of sulfate in the bloodstream, as was shown to be the case in the majority of autistic individuals evaluated in another study², phenolic compounds may build up in the brain and nervous system, and this in turn can interfere with neu-

rotransmitter function. Sulfate deficiency and the resulting impairment of PST activity may explain why many children with autism are sensitive to a variety of phenol-containing foods, such as apples, grapes, bananas, tomatoes, chocolate, food colorings, and some herbs and spices.

Besides its adverse effects on neurotransmitter function, impaired sulfation can have a variety of other harmful consequences, including decreased production of peptides, bile acids, CCK, and possibly secretin³. Since all of these are involved in digestive function, there may be a resulting decrease in the absorption of certain nutrients from the intestinal tract. It is well known that maldigestion and malabsorption are significant problems in many children with autism.

Perhaps the most damaging consequence of impaired sulfation is on the health of the intestinal lining. Normally, the intestinal tract is coated with a layer of mucoproteins that contain important immune cells (specifically IgA) and provide

protection for the integrity of the gut wall. Since these mucoproteins are actually sulfated glycoproteins, a deficit in the sulfation process can leave portions of the gut wall exposed, resulting in increased intestinal permeability (or “leaky gut” problems), inflammation, and other types of gut dysfunction.

While some individuals with documented sulfation problems have found some benefit from taking the sulfur-containing enzyme MSM, it appears that sulfate ions are not as well absorbed from the intestinal tract as they are through the skin. This may be why parents and physicians are seeing more significant benefits from transdermal administration through epsom salt baths or magnesium sulfate cream.

Kirkman’s Epsom Salt cream supplies 100 mg of Magnesium Sulfate USP and can be applied 1-3 times daily.

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ESSENTIAL FATTY ACIDS

ROLE OF ESSENTIAL FATTY ACIDS IN AUTISM

Essential fatty acid supplementation is critical in autism because they are a key ingredient of the membranes in all body tissues. Essential fatty acids also play a role in many crucial functions in the body including regulating nerve transmission, regulating pressure in the eye, joints and blood vessels, in the division of cells (growth and healing processes), response to pain, swelling and inflammation, regulating muscle reflexes, transporting of oxygen from cells to tissues and maintaining health of cell membranes. EFA’s

also are involved in mediating the immune response.

A deficiency of these essential fatty acids may be an important factor in the development of increased permeability of the mucosal membrane of the intestinal tract (described as “leaky gut”) in autistic children. The result of a “leaky gut” then allows incompletely digested foods, opiate peptides and other toxins to travel from the intestinal tract into the bloodstream where they form immune complexes and cause inflammatory reactions throughout the body. Kirkman offers a variety of essential fatty acid products designed to assist in the healing of these gastrointestinal conditions. These products are:

EFA-PLUS™ is a high quality, uniquely processed flaxseed product that is not only rich in essential fatty acids, but is rich in fiber and amino acids. This product is guaranteed to be stable and exceptionally pure assuring its nutritional integrity. EFA Plus contains 41% Fatty acids, 28% dietary fiber and 20% protein with a complete amino acid profile. Of the fatty acids present, 57% are poly-unsaturated Omega 3's and 16% are polyunsaturated Omega-6's.

COROMEGA™ is an omega-3 dietary supplement that provides all the excellent benefits of fish oil with no fishy taste or aftertaste. It is the result of ten years of research and development and is patented worldwide. Coromega™ is a tasty, natural orange flavored, pudding-like emulsion that comes in handy, individual dose and oxidation resistant, squeeze-pack foil pouches.

Coromega™ is an advanced essential fatty acid formula that delivers 650 mg. of Omega-3 (similar to a small serving of salmon), including 350 mg. of EPA and 230 mg. of DHA. Also present are small amounts of vitamins C, E and folic acid. It can be taken once or twice daily.

ProDHA™ is an omega-3 dietary supplement manufactured by Nordic Naturals™ is a revolutionary product in that it uses only the highest quality fish oil available in the world. This oil is produced using flash distillation and molecular distillation ensuring the highest quality Omega-3 oils while eliminating all PCB's and heavy metal contaminants. The oil is then deodorized which also improves the taste dramatically. ProDHA also contains a natural strawberry essence, which covers up the smell, and helps avoid the fishy burps. Pro-DHA™ is an advanced essential fatty acid formula that delivers 400 mg. total of Omega-3 fatty acids including DHA at 250 mg. and EPA at 100 mg.

PRO-EPA™ is another omega-3 dietary supplement manufactured by Nordic Naturals™. This formulation favors higher levels of EPA in conjunction with DHA. ProEPA is an advanced essential fatty acid formula that delivers 600 mg. of Omega-3's including EPA at 450 mg. and DHA at 100 mg. per soft gel capsule.

KIRKMAN'S COD LIVER OIL is also a source of EFA's. One-half teaspoon supplies 250 mg of EPA and 250 mg DHA.

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REDUCED L-GLUTATHIONE

Glutathione is considered a tri-peptide that is produced in the liver from three amino acids including cysteine, glutamic acid and glycine. It is found in cells of almost all living organisms and it plays a key role in the body's defense system. Glutathione functions intracellularly as well as extracellularly and is a very powerful antioxidant that prevents formation of free radicals and inhibits cellular damage. It protects the body against the damage caused by exposure to toxins and is a powerful detoxifier of heavy metals.

STRUCTURE OF GLUTATHIONE

Glutathione is present in two forms in the body; in a "reduced" or an "oxidized" form. The "L" reduced form of glutathione is the most active form and is found in healthy cells. Reduced L. glutathione is responsible for all of the vital biological activity /function of glutathione in the body. One of the interesting aspects is that in normal healthy cells the oxidized glutathione is quickly recycled back to its active reduced state. When it is in its reduced state glutathione is referred to as GSH.

APPLICATION/ROLE OF REDUCED GLUTATHIONE IN THOSE WITH AUTISM

Dr. Jon Pangborn describes the impact that glutathione has in the gastrointestinal functioning of those with autism. If dietary GSH is insufficient, oxidative stress, toxicity and cell damage

may occur to mucosal cells in the small intestine.

Many physicians implementing heavy metal detoxification protocols are utilizing reduced glutathione, in conjunction with DMSA and/or Lipoic acid. This is because glutathione appears to increase the detoxifying effects of the DMSA and Lipoic acid. The elimination of fat-soluble compounds, especially heavy metals like mercury and lead are dependant upon adequate levels of glutathione. (Pangborn reference) Prevention of free-radical damage, induced by gliotoxins, may be one of the reasons these supplements are effective.

SAFETY ISSUES

Generally GSH is well tolerated and the only contraindication is excessive doses in the insulin dependent diabetic.

QUALITIES TO EVALUATE AND DOSAGE

Only glutathione in the reduced (GSH) form is utilized in Kirkman Laboratories nutritional supplements, not the oxidized glutathione that does not possess active biological activity. Kirkman's Glutathione capsules are hypoallergenic and contain no casein, gluten, wheat, corn, soy, dairy products, sugar, artificial colors or artificial flavors. Consult your physician for dosage. Most suggest 100-200 mg. daily.

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LACTOFERRIN

INTRODUCTION

Lactoferrin is a versatile substance that has a number of important functions including contributing to the body's defense system against invading pathogenic organisms (specifically at the mucosal membrane), stimulating the immune system, helping in regulating the iron status in the body as well as serving as a natural antioxidant.

CHARACTERISTICS/DESCRIPTION

Lactoferrin is a single peptide chain made up of 690 residues with carbohydrate side chains and two iron-binding sites. [Mannie] Lactoferrin is a protein, which is naturally found in milk but is also found in body secretions, specifically in the mucus, tears, saliva as well as the blood. Lactoferrin is found in the milk of all mammals however bovine colostrum contains highly concentrated (1250 mg/L) amounts of this unique substance. [Meisel] Of interest is that high lactoferrin concentrations are passed to the newborn, which supports the theory that lactoferrin serves as a protective protein complementing the immune system.

FUNCTION OF LACTOFERRIN AND SCIENTIFIC SUPPORT FOR ITS USE

Lactoferrins may play a role in addressing some of the gastrointestinal problems associated with ASD including overgrowth of pathogenic organisms on the intestinal mucosal membrane. This is because research indicates that lactoferrin may protect against pathogens in

the gastrointestinal tract as well as in the systemic circulation.

Lactoferrin is effective against threatening pathogenic bacteria like Enterobacteriaceae and Clostridia, yeasts like Candida, and viruses like rotavirus, Herpes, HIV and influenza. The mechanisms behind these protective effects are being studied in the laboratory. However it is recognized that lactoferrin functions by interfering with the integrity of the microbial cell wall, preventing the attachment of viral particles to host cells, stimulating cells of a specific immune response and inactivating inflammatory mediators. [Abstract at the World Food Summit] Clearly this summarizes the potential role that lactoferrin may play in addressing the significant gastrointestinal problems common in many children with autism.

IRON BINDING CAPACITY/FACILITATING IRON ABSORPTION

It is thought that lactoferrin functions in defending the body against invading pathogenic organism by depriving them of iron required for their growth. One of the unique aspects of many pathogenic organisms is their ability to utilize iron to grow and multiply. If they are deprived of iron, the death of these organisms results.

Lactoferrin has a dual role in regard to iron metabolism. Along with its ability to bind iron it is also able to enhance iron's absorption and thereby help protect against iron deficiency problems. What we can say is that lactoferrin has iron binding abilities where it is able to act as an iron carrier (facilitating iron transport in the body) but it is also an iron scavenger (minimizing the potential risk of free iron) and can exert positive influences with both of these roles.

ANTIFUNGAL

Of relevance to those with autism are the numerous studies suggesting that the active peptides of lactoferrin exert antifungal activity specifically against *Candida albicans* and *C. krusei*. Of interest was a study undertaken in Japan that found that *Candida albicans* was found to be highly susceptible to inhibition and inactivation by lactoferrin B a peptide in bovine colostrum. These findings suggest that active peptides from lactoferrin could potentially contribute to the body's defense against *C. albicans*.

ROLE OF LACTOFERRIN IN THOSE WITH AUTISM

Certainly some of the most compelling reasons for the use of lactoferrin supplementation in those with ASD stems from its ability to contribute to the body's immune defense system and in protecting against pathogens in the gut. This is most important when addressing the chronic *Candida* related gastrointestinal infections as well as ongoing problems with *Clostridia difficile* reinfections that are common in ASD.

SAFETY ISSUES

One of the concerns with the use of lactoferrin supplements in children with autism involves the presence of casein in most lactoferrin products. For those children with intestinal permeability problems the use of products containing casein proteins may trigger the development of opiate peptides (casomorphin) resulting in neurological and physical symptoms. Use lactoferrin supplements containing casein only under the care of a medical practitioner.

QUALITIES TO EVALUATE

Look for a Lactoferrin nutritional supplement that is hypoallergenic without the addition of excipients and stabilizers. Utilize a formulation that is certified to be "casein-free" by the manufacturer.

Kirkman's Super Colostrum Gold™ formulation contains 3% of natural lactoferrin, is certified to be casein free and can be safely and effectively used by those with ASD. Each teaspoon contains 150 mg. of lactoferrin.

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BETA 1, 3/1, 6 GLUCAN

There is a great deal of medical and scientific documentation regarding the immune system dysregulation seen in autism spectrum disorders. Sudhir Gupta, M.D., Ph.D., V. Singh, M.D., Gene Stubbs, Ph.D., Reed Warren, Ph.D., as well as numerous others have demonstrated significant immune abnormalities in children with autism.

An approach that can be utilized in addressing some of the immune abnormalities and resulting infections seen in the autism, may lay in part with the use of nutritional supplementation. Beta 1,3/1,6 glucan has been demonstrated to possess potent immune stimulating properties. Alone or in conjunction with other immune enhancing nutrients such as Colostrum or Lactoferrin, Beta 1,3/1,6 glucan may provide important support for both immune as well as gastrointestinal problems associated with autism. Of relevance to gastrointestinal healing is the work by Dr. S. Bengmark and colleagues which demonstrated that Beta glucan is able to protect and recondition the GI mucosal membrane.

WHAT IS BETA -1,3/1,6 GLUCAN

Beta-1,3/1,6 glucan is recognized as a safe and very potent nutritional supplement that has a powerful impact in stimulating the immune response to help the body defend itself against foreign substances. This unique compound triggers the immune system to help defend against bac-

terial, viral, fungal, parasitic and neoplastic (cancer causing) invaders. It is considered by experts as one of the most powerful immune-enhancing nutritional supplements known today.

MECHANISM OF ACTION:

Beta glucan works by activating the macrophage (important white blood cell), which traps and then engulfs foreign substances. Once these macrophage cells are activated they initiate a cascade of events that results in the immune system being alerted and then mobilized to respond to an insult or attack by a foreign invader. With this stimulation the immune system becomes amplified/heightened and a sequence of complex immune responses are initiated, aimed at defeating/inactivating these foreign invaders.

WHO CAN BENEFIT FROM USING BETA 1,3/1,6 GLUCAN?

Many individuals with autism spectrum disorders are recognized to have impaired/compromised immune systems resulting from a number of environmental factors that may include:

- Poor nutritional status and/or consuming of food additives, preservatives and other chemical contaminants.
- Chronic disease states resulting from viral (influenza, Lyme, herpes, CMV, etc.), fungal (Candidiasis, etc.), bacterial (bronchitis, otitis

media, strep throat, etc.) or parasitic infections.

- Allergy/sensitivity reactions/responses to foods, inhalants, chemicals, etc.
- Excessive exposure to radiation (x-ray) or other external exposures to UV light or electromagnetic fields.
- Physical or emotional stresses (including surgery, excessive exercise, etc.)
- States of reduced wound healing of the skin (dermal) and/or the mucosal membrane (epithelium) of the gastrointestinal tract. (Bengmark, S., et al., Gastrointestinal surface protection and mucosa reconditioning, Journal Parenter Enteral Nutrition, 1995, Sep-Oct).

WHY DOES BETA GLUCAN HAVE AN IMPACT ON THE IMMUNE SYSTEM?

One of the crucial activities of branched glucan is that it is recognized by phagocytes through specific receptors. Phagocytes (monocytes, macrophages, granulocytes) express a whole range of different surface receptors which can be likened to the "eyes and ears" of the cells. Depending on which receptor is engaged, the cells take adequate action of recognizing and binding foreign substances such as microbes, viruses, yeasts, and parasites.

CAN ALLERGIC REACTIONS OCCUR WITH THE USE OF BETA GLUCAN?

Questions have been asked regarding the potential for the yeast allergic individual to have a reaction to the Beta-glucan. Although Beta-1,3/1,6 glucan is derived from baker's yeast, it is recognized as a pure isolate and does not contain any yeast proteins that can trigger an allergic reaction. Extensive use of this nutrient has provided well-documented evidence pertaining to its safety, even in individuals who are sensitive to yeast.

ARE THERE ANY DRUGS OR OTHER SUBSTANCES THAT MAY HAVE AN ADVERSE INTERACTION WITH BETA GLUCANS?

There are no recognized adverse effects or known interactions (contraindications) with the use of Beta glucan with any pharmaceutical drugs, nutritional supplements or over the counter medications. It has however been recognized that Beta-1,3/1,6 glucan may enhance the effect of antibiotics and cholesterol lowering medications.

RECOMMENDATIONS AND SUGGESTED USE

It has been found that the absorption and bioavailability of this nutrient is enhanced when taken away from meals. As a nutritional supplement take one to two capsules daily and/or as recommended by a health care practitioner. For optimal absorption, take at least 1/2 to 1 hour (30 to 60 minutes) before meals or two to three hours following a meal.

Although there are no definitive studies regarding supplementation specifically for autism spectrum disorders, clinicians treating autistic children generally recommend a starting dose of 100-200 mg per day. For those with acute or chronic infections a dose of 500 to 1000 mg of Beta glucan can be safely taken, in divided doses, throughout the day. Ideally it is best to divide the doses, however, benefit can also be established with administration only once daily.

Availability: Kirkman Laboratories' Beta-1,3/1,6 glucan nutritional supplement is available in a size #3 capsule containing 100 mg of branched chain glucan. Capsules may be swallowed whole or may be opened and mixed with water or beverage (avoid hot beverages). There are no contraindications regarding having the powder in direct contact with the mucous membranes of the oral cavity.

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CRANBERRY EXTRACT

INTRODUCTION

Cranberry extract is emerging as an important nutraceutical (natural substance that exerts biological effect and function in the body) with growing application in those who are prone to genitourinary and gastrointestinal infections. The cranberry extract is recognized to function as a powerful antibacterial, anti-inflammatory and anti-infective supplement to support urinary and intestinal health.

STRUCTURE /FUNCTION OF THIS NUTRIENT

The chemical composition of cranberry extract is impressive and supported by scientific documentation of its biological activity in health. Following are some of the compounds that comprise the potent cranberry extract:

PROANTHOCYANIDINS: Initially it was thought that the acidity of cranberry made the bladder inhospitable to the bacteria causing urinary tract infections. Early researchers suggested that the acidifying of the urine and the antibacterial effects of hippuric acid (a component of cranberries) were responsible for its effectiveness in GI health. However more recent research has shown that the cranberries inhibit the bacteria in a totally different way than

was first suspected. They now recognize that the proanthocyanidin fraction of cranberries has the ability to inhibit or prevent the adherence of *E. coli* (the most common bacteria responsible for most urinary tract infections-UTIs) to the wall of the urinary tract and bladder. Because the bacteria are unable to attach themselves and set up residence they are thus unable to reproduce/multiply in great numbers and essentially the infection is prevented.^{5,6,7}

ORGANIC ACIDS: Cranberry is a rich source of natural organic acids including quinic, malic and citric acid, which are responsible for the sour taste and are recognized to acidify the urine as well as prevent kidney stones.¹

APPLICATION/ROLE OF CRANBERRY EXTRACT TO THOSE WITH AUTISM SPECTRUM DISORDER

The use of Cranberry extract can provide some positive response in supporting the bodies GU and GI tracts against pathogenic bacteria and yeast. Use of high doses of phenolic containing cranberry extract in autistic children with Phenosulfertransferase problems will need to be used only under the care of a medical practitioner. Although clinicians differ in their use of these supplements (some will use small amounts in those with PST problems when specifically indicated) it is of importance to discuss the pros and cons of using these supplements in those specifically di-

agnosed with this PST condition.

GASTROINTESTINAL DISORDERS: The role of cranberry concentrate has been suggested to serve as a digestive aid in part because of the high acidity. The active ingredients in cranberry can help in the digestion of fatty foods. There are reports that proanthocyanidins help to relieve diarrheal symptoms, although there is need for additional studies in this area. The proposed function is thought to result from the anti-bacterial activity in conjunction with its action as an astringent (any acidic substance that draws together and constricts tissue). It has been proposed that the proanthocyanidins cause the proteins to clump together to form rigid cakes, which prevents bacteria from using the proteins for food.¹

INFECTIONS/COLDS/FLU: Many children with ASD tend to have compromised immune function and since cranberry concentrate is recognized to be a good source of vitamin C and antioxidants, these nutrients can support the body's immune system in the prevention of or treatment of colds and other infections.

QUALITIES TO EVALUATE IN A CRANBERRY EXTRACT

Not all Cranberry extracts are of the same quality, purity, potency, and/or tolerance. Choose carefully the cranberry extract supplement that offers the purest extract available, with clearly documented activity and certification of their biological activity.

High Inhibition of Bacterial Growth: An important quality to look for in a cranberry extract is its ability to inhibit the growth of bacteria. A recent report in the *New England Journal of Medicine* confirms that cranberries anti-microbial activity is due in large part to a group of polyphenols (proanthocyanidins), which inhibit the adherence of *E. Coli*.¹⁶ In vitro (laboratory) studies show that 500 mg of Kirkman's Super Cranberry Extract is 64 times more effective as an inhibitor of bacterial growth than four other commercially available cranberry supplements. This means that the potency of Kirkman's Super Cranberry extract is high and that 1 capsule is equal to 4 to 8 capsules/tablets of other cranberry products. [Technical report from Shanstar Biotech, Incorporated, Microbiology and Analytical Laboratories]

Antibacterial Activity: The effectiveness of a cranberry extract should also include inhibitory activity against a full range of bacteria not just *E. coli*.¹⁷ Specific laboratory testing has been undertaken on the Super Cranberry Extract which Kirkman uses showing complete inhibition of the growth of the following bacteria:

- E. coli
- Staphylococcus aureus
- Bacillus subtilis
- Yersinia enterocolitica
- Serratia marcescens
- Salmonella typhimurium
- Pseudomonas aeruginosa
- Gardnerella vaginalis
- Pseudomonas fluorescens

Antioxidant Activities: The high polyphenol content of cranberry contributes to its antioxidant activity. Laboratory studies of Super Cranberry extract show it has very high levels of polyphenols. Testing was performed according to the AOAC Official Method 952.03 (Data and Methods available from Microbial and Analytical Labs of Cliffstar Corporation, Dunkirk, N.J.) Results specifically comparing Kirkman's cranberry extract with a leading brand showed that our formulation had 10 times more polyphenols.

Identifying and Quantifying Ingredients: Every batch of our Cranberry Extract is analyzed by HPLC (High Performance Liquid Chromatography) and quantified for anti-microbial and anti-oxidant activity. This standard for testing for activity far exceeds the standards employed by other manufacturers.

THE KIRKMAN DIFFERENCE

Kirkman's Super Cranberry Extract™ is a patented form of cranberry extract which is 64 times more potent than any other cranberry extract on the market. Each tablet is equal to about 10 gallons of cranberry juice. This supplement offers an active nutraceutical concentrate prepared from cranberries by a special proprietary resin-based process. This unique process yields a concentrated extract, which possesses far superior antibacterial properties, antioxidant properties and anthocyanin content than those usually associated with cranberry juice. By utilizing a unique patented purification process key bioactive constituents of this fruit have been concentrated.

Additionally it has also been tested in vitro on Candida yeast strains and has exhibited the ability to kill or deactivate the yeast cells yet it does not adversely affect lactic acid bacteria (L. acidophilus, B. bifidum/lactis, and other friendly flora).

RECOMMENDED DOSAGE:

Because each of Kirkman Super Cranberry Extract capsule and/or chewable tablet is equal to 10 gal-

lons of cranberry juice the recommended dose for this product is 1 (one) capsule or tablet 3 (three) times daily to provide optimal dosing of this supplement.

Super Cranberry Extract is available in a hypoallergenic capsule form as well as in a chewable tablet to meet the special needs of those with ASD. Additionally this formulation is naturally casein and gluten free.

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ALOE VERA CONCENTRATE *The Healing Herb*

INTRODUCTION

The use of Aloe vera can be an important part of a comprehensive protocol for reestablishing the health and functioning of the GI tract. This powerful botanical is recognized to function in a number of important ways that directly impact gastrointestinal health.

CHARACTERISTICS/STRUCTURE OF ALOE VERA

The Aloe vera leaf is comprised of three layers: 1) the fibrous outer part of the leaf serves a protective function, 2) the middle leaf layer (called the latex layer) where there is a bitter yellow sap that contains "anthraquinones" which exert a powerful laxative effect and 3) the inner portion of the leaf that contains a clear gel within the cells that is identified as Aloe vera.

Aloe vera contains biologically active substances that account for the health promoting properties attributed to it. The latest and perhaps most exciting compound discovered to be present in Aloe vera is a biologically active polysaccharide known as acetylated mannose. (Some have described this compound as mucilaginous-polysaccharides or MPS).

Acetylated mannose is only one of many saccharides that are contained in Aloe vera. The others include arabinose, cellulose, galactose, mannose and xylose. Another important component of aloe are the prostaglandins, which are thought to play a major role in wound healing. Additionally Aloe vera contains fatty acids, enzymes, amino acids, vitamins and minerals. Although the presence of these compounds exerts positive activity it is the acemannon that is clearly recognized as the primary active ingredient.

Of interest is that Aloe vera also contains a number of compounds known as "aloins", which are a group of chemicals referred to as anthraquinones. These compounds including aloin, barbaloin and aloe-emodium are known to exert a powerful laxative effect and therefore are extracted from most of the Aloe vera products that are available as nutritional supplements. [Corsi]

APPLICATION OF ALOE VERA TO AUTISTIC ENTEROCOLITIS

It is recognized that a large percentage of children with ASD suffer from what Andrew Wakefield, M.D. has described as autistic enterocolitis. Karoly Horvath, M.D. and his colleagues found that a large percentage of autistic children experienced duodenitis (54.2 %) and esophagitis (69.4%). Clearly each of these conditions reflects an inflammatory response throughout the gastrointestinal tract, which has been supported by other researchers and clinicians.

Acetylated mannose is documented to be effective in addressing a number of conditions, including many of the intestinal inflammatory responses associated with autism.

INTESTINAL INFLAMMATION

One of the common GI manifestations in autistic enterocolitis is a generalized inflammatory response throughout the intestinal membrane. When Wakefield and his colleagues took biopsies of the intestinal tract of ASD children, the biopsies showed significant abnormalities of the GI mucosal membrane, both in those children who had severe GI symptoms as well as in those with mild intestinal complaints.[Wakefield]

There is extensive documentation and clinical support for the use of Aloe vera mucopolysaccharides in individuals with advanced gastrointestinal disorders, including irritable bowel, ulcerative colitis, Crohn's disease, and others. The active fraction in Aloe vera has documented effect in stimulating the mucosal immune response and thus it has been investigated for its use in inflammatory bowel disease with encouraging results. [Robinson]

Many individuals with autistic enterocolitis seem to share similar symptoms as those that are seen in other intestinal disorders. Although the cause of these various gastrointestinal problems may be different, the symptom presentation and physical changes in the mucosal membrane share some similar characteristics. The anti-inflammatory function of Aloe vera and its ability to assist in the repair of damaged tissue by regenerating cells may be of crucial importance in healing the intestinal tract of children with ASD.

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KIRKMAN'S YEAST CONTROL™

INTRODUCTION

The presence of chronic yeast overgrowth in the intestinal tract, referred to as Candidiasis or Candida Related Complex, is a common gastrointestinal complaint among children with autism. Although Candida normally resides along with the friendly flora (*Lactobacillus acidophilus*, *Bifidobacterium bifidum* and others) in the digestive and urinary tracts, it can exert significant problems when this balance is upset. The use of repetitive courses of antibiotics, inflammatory reactions in the intestinal tract and overuse of certain medications will adversely affect this delicate balance. As a result Candida will take control, crowd out the friendly flora and begin to set up residence, invading the intestinal membrane and exerting its pathogenic influence.

The consequences of a Candida infection are not limited to the gastrointestinal and genitourinary tracts, but are far reaching involving many tissues and organs in the body. In fact the toxins and by-products produced by these yeasts will travel across a compromised intestinal membrane and

enter the circulatory system, causing physical as well as behavioral/psychological symptoms.

Chronic Candida related infections are best treated utilizing a comprehensive approach inclusive of 1) dietary avoidance of yeasty, moldy, fermented and sugary food aimed at starving the yeast, 2) use of anti-fungal medications ranging from use of localized antifungals like Nystatin to systemically acting drugs such as Nizoral, Sporonox, and others, 3) re-inoculation of the bowel with friendly flora through supplementation with health-promoting probiotics 4) use of well-selected nutrients and herbs for the control of intestinal yeast infections.

ROLE OF CANDIDA IN HEALTH PROBLEMS

Dr. Orian Truss first recognized and published an article on *Candida albicans* role in causing chronic health problems. William Crook, M.D., expanded on Truss's early observations and for the past 30 years Dr. Crook has brought to the attention of the medical community and lay public the significant role that Candida plays in triggering and potentiating a complex range of

physical and behavioral symptoms. The localized and generalized symptoms that occur as a consequence of this organism's influence are vast and have been clearly outlined in *The Yeast Connection*, Dr. Crook's most informative book.

FUNCTION/PURPOSE OF THE YEAST CONTROL™ FORMULATION

The well-established and traditional approach to treating Candida infections involves the use of prescription pharmaceuticals aimed at eradicating the overgrowth of this organism in the intestinal tract. Many families have utilized this approach in addressing chronic or persistent Candida infection in their autistic children. While the use of these well-recognized and clinically effective medications is often necessary to control these infections, many parents are concerned about the repetitive use of numerous (sometimes continuous) courses of prescription antifungals. There has been a great deal of interest in finding natural antifungal alternatives to be used alone or in a complementary role with these prescription medications.

Kirkman Laboratories was asked to formulate a natural antifungal preparation, containing well documented, clinically effective as well as safe natural non-prescription substances. The Yeast Control™ formulation was the answer to these requests, as it was specially designed for the special needs of autistic children. Dr. William Crook was instrumental in the development of this formulation, utilizing his extensive research and clinical experience in the area of Candida treatment options. His valuable input, in conjunction with the expertise of Kirkman's technical team, provided the basis for the Yeast Control™ formulation.

REGARDING USE OF YEAST CONTROL™

This unique formulation is designed to offer a natural approach aimed at combating chronic candida related infections. Yeast Control™ contains a combination of natural anti-yeast ingredients, including a medium chain fatty acid, phytochemicals and herbals that specifically function as antifungal and antimicrobial

agents, along with two vitamins recognized to support the immune system. This state-of-the-art formulation offers a full spectrum of natural antifungal activity that can be used in combination with prescription antifungal agents to support the control of Candida. It may also be used separately or cycled intermittently between courses of prescription antifungals, if approved by a medical practitioner.

YEAST CONTROL™ FORMULATION

Olive Leaf Extract has been used medicinally as a natural antibiotic since the early 1800's, but it has had widespread use since Biblical times. It was originally used to treat malaria infections as well as intestinal worms, flukes and yeasts. Research has shown that the leaves of olive trees contain a compound called "oleuropein". This compound has potent antimicrobial and specific anti-candida properties. The olive leaf also contains the bioflavonoids rutin, luteolin and hesperidin, which work synergistically with oleuropein to enhance its natural anti-microbial activity. [Walker and Tranter] The olive leaf used in Kirkman's Yeast Control formulation contains a standardized extract containing 6% Oleuropein for its powerful germ-killing activity.

Pau d'Arco (pronounced Paw-d-arco) is an herb obtained from the inner bark of a large tree that grows in tropical areas of South America. Native South Americans have used the inner bark medicinally for centuries. They would scrape the inner bark and brew a tea which was used to treat a number of conditions including malaria, infections, fever, cancer, and skin problems. [Jones]

Pau d' arco gained a great deal of attention when scientists performed studies on it and isolated the active compounds "lapachol" and "beta-lapachone" as the potent ingredients. Researchers have since isolated some 20 active chemicals in Pau d'arco, which have shown to have the ability to help destroy bacteria, fungi, parasites and viruses. It has also been demonstrated that this powerful herb is effective against yeast infections. [Dapler]

Goldenseal Extract is a member of the buttercup family of herbs and was used by the Native Americans for fighting infections. The under portion of the stem, called the rhizome, as well as the inner bark are the primary medicinal parts of

the plant. The goldenseal rhizome contains high concentrations of active alkaloids including berberine, hydrastine and candidine, which make it effective against a variety of organisms including *Candida*. [Balch] Kirkman uses a standardized extract of Goldenseal, guaranteeing the concentrations of the active alkaloids.

Of interest is that this herb is particularly effective in treating inflammation of the mucous membranes lining the upper respiratory as well as the gastrointestinal and genitourinary tracts. [Hanrahan] This makes the addition of goldenseal important because of the commonly recognized problems in the intestinal tracts of those with autism.

Caprylic Acid is recognized as a medium-chain fatty acid that possesses antifungal abilities, specifically effective against *Candida*. Fatty acids have different numbers of carbon atoms ranging from 2 in acetic acid to 24 or more in other fatty acids. Caprylic acid has 6 carbon atoms and is thus considered a medium chain length fatty acid. Research in the 1950's found that Caprylic acid possessed antifungal activity. [Shaw] Kirkman uses a stabilized form, calcium caprylate, to ensure gradual release throughout the intestinal tract.

Biotin is one of the essential B vitamins that normally is produced by the healthy bacteria in the intestinal tract. The use of antibiotics can eliminate the bacterial production of biotin leading to biotin deficiency. According to Dr. Shaw biotinidase deficiency is frequently associated with yeast and fungal infections.

Biotin supplementation appears to have a unique role of preventing the transformation of *Candida* to its mycelium form, which results in invasive penetration of the mucosal membrane. [#19 on page 93] This is very important because once yeast is in the mycelium form, it develops tendrils, which poke holes in the gut (causing leaky gut/ intestinal permeability), allowing yeast toxins and byproducts to enter the bloodstream.

Vitamin C is present in Yeast Control because it is an antioxidant and protects the body tissues from being damaged by the toxins released by *Candida*. Vitamin C is also a powerful immune booster, which is an important part of the overall yeast control program.

Cranberry Extract is a special concentrated,

patented form of cranberry prepared by a resin-based process, which yields a concentration of active constituents 64 times more potent than other cranberry products. In vitro studies show that *Candida* growth is inhibited in the presence of cranberry. It has been studied for its use as natural antibacterial/antifungal in the genitourinary and gastrointestinal tracts. Of interest is that it helps to relieve diarrhea and is recognized to possess anti-inflammatory activity. [Tran]

Oregano is an herb of the mint family, which has exhibited phenomenal anti-yeast properties. An article in the *Journal for Applied Nutrition* presented scientific studies showing its effectiveness. Dr. Jonathon Wright, M.D. the author of several health related books, has found that oregano is as clinically effective in some cases as the use of Nystatin.

Oregano has been demonstrated to inhibit the growth of *Candida albicans* in the laboratory when tested against several strains of *Candida*. It was found that "Carvacrol" a constituent of oregano oil effectively inhibits *Candida*.

GUIDELINES FOR USE

Although these natural antifungal agents do not require a prescription for their use it is still recommended that they be used under the supervision of a medical practitioner. As has been described elsewhere in this document, there exists the potential for "die-off" reactions when initially starting any *Candida* control program. For this reason it is advised you utilize the Yeast Control formulation under the guidance of a practitioner.

ADMINISTRATION AND DOSAGE

Kirkman's Yeast Control is offered in a hypoallergenic #1 plant cellulose capsule or as a flavored powder. The capsule should be swallowed whole, not emptied out as powder. The reason for this is that these anti-yeast ingredients have a very strong bitter taste and cannot be masked without using sweeteners and flavors, which are not acceptable for the hypoallergenic line.

Those individuals who can't swallow the capsules can use the Yeast Control flavored pow-

der. This powder contains a natural sweetener and natural flavorings that allow the powder to be mixed in various juices or beverages. The best vehicle for the powder is red grape juice because it covers up both the flavor and the particulate matter. Pink lemonade is also very good along with orange, grapefruit and apple juices or other tart beverages. (Please note that there will be a noticeable change in the color of the liquid with use of the powder).

DOSAGE RECOMMENDATIONS:

It is important to remember that a program to eradicate chronic yeast infections needs to be coordinated under the care of a health care or medical practitioner.

General Dosage Recommendations:

Under 25 pounds	Not Recommended
26 to 45 pounds	One or Two Capsules Daily
Over 45 pounds	Three Capsules Daily (AM, Midday and PM or two in AM/one PM)

SAFETY ISSUES

The safety of the herbal ingredients in Yeast Control have been well established, when specifically used as recommended. As with all herbal ingredients possible side effects of using larger doses may include nausea, diarrhea, stomach cramps, and other symptoms. When utilizing herbal based supplements always start with a low dose and gradually increase to the therapeutic dose.

The primary side effects that may be noted when initially starting a Candida Control program inclusive of natural or prescription antifungals is something described as a "die-off" also known as the Herxheimer Reaction. When yeast is being killed off, the dead candida cells and their toxic by-products are released. The body may not be able to clear these toxins as quickly as they are being produced. When this occurs, the child

may have flu-like symptoms or an increase in other symptoms for a few days. [Crook] To minimize the die-off reaction, the following procedures may be of help.

Eliminate sugar, yeasts, moldy and fermented foods.

Drink lots of spring or filtered/distilled water to help clean out the toxins.

Use Alka-Seltzer Gold to neutralize reactions produced by the yeast.

Start with small dosages of the antifungals and their natural alternatives, gradually building up to the recommended doses.

Utilize probiotic supplementation for gastrointestinal support.

During any yeast eradication program, be sure to discuss your child's progress, any side effects or complications with your health professional. With the immune and digestive issues present in individuals with autism, close monitoring is imperative.

QUALITIES TO LOOK FOR IN A YEAST CONTROL FORMULATION

Always make sure to choose the most reputable manufacturer when using products containing herbs. The purity and potency of these extracts is of importance and whenever possible choose only those that utilize standardized quantities of active ingredients. Kirkman Laboratories' Yeast Control™ formulation utilizes these high standards and quality control measures to assure a safe and effective product.

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Chapter 6

General Approaches To Restoring Intestinal Health

Introduction

Treating the gut and restoring proper digestive function in children with autism spectrum disorders is usually not a “quick fix” type of intervention. Many of these children have had significant intestinal problems for a number of years, and the resulting inflammation and gut irritation often takes a period of time to repair. The best approach to treating the intestinal tract is a multi-faceted one, involving the proper testing, diagnosis, and treatment in order to allow the greatest opportunity for the child to regain appropriate digestive function. Many different areas need to be addressed, such as gluten and casein sensitivity, possible food allergies, intestinal permeability issues, yeast and bacterial infections, malabsorption, and gut damage from heavy metals or vaccinations. Treatment for these conditions usually involves a broad spectrum of modalities, such as pharmaceutical drugs, nutritional supplements, dietary modification, and systemic support (i.e. heavy metal chelation and immune strengthening). When this multi-faceted approach is used, there is a greater likelihood that true healing will take place and that there will be a restoration of the intestinal tract into a more properly functioning organism.

While individual treatments for specific digestive problems will vary, most of these interventions can be applied to a general “treatment strategy” that encompasses the logical multi-faceted approach discussed above. Since treating the gut is usually a process, there are several different ways to approach this. One strategy that has been very effective, and has therefore been adopted by a number of physicians specializing in the treatment of gastrointestinal disorders, was outlined by Jeffrey Bland, Ph.D.¹ This strategy represents a “functional” approach to treating the gut, because it seeks not just to suppress a patient’s outward symptoms, but rather to restore the proper functioning of the digestive system as a whole. Because this approach to treating gastrointestinal problems is multi-faceted, most health care practitioners will utilize a biological approach inclusive of both prescription agents, when needed, and nutritional supplements that can aid in enhancing the digestive process, combating pathogens, and assisting with the healing of the all-important intestinal membrane.

In the outline below, we have adapted the strategy laid out by Dr. Bland to include a number of other important steps that are helpful in addressing the intestinal health of children with autism spectrum disorders. Keep in mind that these represent a general guideline for approaching the treatment of digestive problems, but that the individual treatments for specific conditions, which will be addressed in the next chapter, can actually be incorporated into this generalized approach as well. Here is a brief outline of the steps involved in healing the intestinal tract; each one will be discussed in more detail below.

1. Remove intestinal pathogens, chemical toxins, and other irritants
2. Restore proper digestive function
3. Re-establish normal intestinal flora
4. Repair the intestinal lining
5. Correct nutritional deficiencies
6. Strengthen the intestinal immune system
7. Reduce future damage to the gastrointestinal system

General Strategy For Healing The Intestinal Tract

1. Remove Intestinal Pathogens, Chemical Toxins, And Other Irritants

The first step in healing the gut involves addressing the problem of “dysbiosis”, or imbalanced intestinal flora, through the removal of infectious, pathogenic microbes from the digestive tract. Examples of such microbes include yeast/fungi (*Candida* and other species), bacteria (*Clostridia*, *Klebsiella*, *Helicobacter*, etc.), viruses, and parasites. A stool culture and/or Organic Acid Test will help to pinpoint which of these microbes may be causing the imbalance. The presence of these organisms in the intestinal tract can lead to a variety of problems, including inadequate digestion, malabsorption of nutrients, and constipation or diarrhea. Increased intestinal permeability, or “Leaky Gut Syndrome”, is another consequence of these pathogens and can result in further complications, such as food allergies, gluten and casein sensitivity, and other systemic conditions.

Essential to the restoration and healing of the gastrointestinal tract is specifically addressing and treating the cause of the dysbiosis. The process of removing these microbes can be accomplished using a variety of measures, including pharmaceutical agents such as Nystatin for Candida or Vancomycin for Clostridia. There are several nutritional supplements that have been found to be clinically effective in treating the overgrowth of specific fungi, bacteria and parasites. These include Colostrum, Lactoferrin, Beta-glucan, Probiotics, and Cranberry Extract. In addition, a number of botanical plant extracts have also proven to be safe and effective, as for example Caprylic acid, Goldenseal, Pau d'Arco, Olive leaf extract, and Oregano. For convenience, this combination of herbs can be found in Kirkman's formula, Yeast Control.

The second step in this part of the healing process is aimed at reducing exposure to toxic chemical substances that can damage the intestinal lining. These include antibiotics, steroids, aspirin, and nonsteroidal anti-inflammatory drugs (NSAIDs). These drugs are likely to damage the intestinal lining and upset the balance of beneficial bacteria in the digestive tract, leading to increased intestinal permeability and its resulting complications.

The final step consists of the avoidance of potential irritants to the intestinal wall, including food allergens, refined sugar, and gluten and casein. Chronic food allergy problems can result in irritation to and then inflammation of the gut wall, eventually leading to intestinal permeability problems. Incompletely digested proteins and dietary peptides can trigger the production of opioids, causing a number of adverse responses. Removing these substances from the diet can help diminish further irritation to an already compromised intestinal wall.

2. Restore Proper Digestive Function

Once the immediate insults to gut health have been removed, restoring proper intestinal function involves supporting those digestive processes that may be compromised. Among the most common of these problems seen in autistic children are deficiencies in digestive

enzymes and imbalances in the pH of the stomach and intestines.

Use of digestive enzymes can play a significant role in enhancing digestion and addressing some of the symptoms, such as gas and bloating, which can result from the incomplete breakdown of foods. The use of plant-based enzymes can also aid in breaking down the potentially allergenic components in foods that can cause adverse reactions. These highly concentrated and naturally derived enzyme formulations are effective at improving digestion in a full range of conditions, from a pH of 2 (very acidic) to a pH of 12 (very alkaline). For example, they are active in the stomach, an acidic environment with a pH of 1-2; in the small intestine, with a pH of 4-8; and finally in the large intestine, that has an alkaline pH of 10-12. This has important implications because it means that these digestive enzymes are effective at enhancing digestion and facilitating absorption in all parts of the intestinal tract.

In addition to supplementing with digestive enzymes, it is often necessary to address underlying gastrointestinal pH imbalances in autistic children. This can be accomplished through a variety of interventions, including Secretin therapy, treatment with the pharmaceutical drug Bethanechol, use of bicarbonate to enhance the action of the enzymes, and supplementation with Betaine hydrochloride.

3. Re-establish Normal Intestinal Flora

A vital step in the treatment of intestinal dysbiosis is the re-seeding of the intestinal tract with beneficial bacteria once the pathogenic microbes have been removed. The use of Lactobacillus acidophilus, Bifidobacterium bifidum (lactis), and other friendly flora are of paramount importance in re-establishing the health-promoting bacteria in the gastrointestinal tract. There is extensive research and clinical documentation regarding the role of probiotics in supporting and maintaining the integrity of the intestinal membrane. Additionally, clinical experience has shown that there are distinct advantages to the use of therapeutic doses of multiple-strain probiotics on a rotational basis in the autistic individual who suffers from intestinal dysbiosis.

It is recognized that all bacterial species, except for the lactic acid fermenting bacteria (*Lactobacillus acidophilus*, *Bifidobacterium bifidum*, and other beneficial species), require iron for their growth. Lactoferrin is an iron-binding protein that can have an effect in controlling the growth of pathogenic bacteria in the gastrointestinal tract. Lactoferrin is a specific peptide found in Colostrum that helps bind iron in the gastrointestinal tract, thus keeping it away from the harmful bacteria and thereby hindering their growth. It thus promotes a healthy intestinal environment by discouraging the presence of disease-causing bacteria.

4. Repair The Intestinal Lining

Repairing the intestinal lining is an important step in healing the gut and restoring the proper functioning of the digestive system. There are a number of nutritional supplements that can help facilitate this repair process and minimize the problems with food allergies and peptide reactions that result from a damaged intestinal barrier. Some of these supplements include Antioxidants, Colostrum, Glutamine, Reduced Glutathione (involved in mucosal healing), Essential Fatty Acids, the bioflavonoid Quercetin, and N-Acetyl Glucosamine (NAG). There are also a number of herbs that have been shown to be clinically useful in supporting the process of healing the gut wall, including Aloe vera, Slippery Elm, and Marshmallow root, and Deglycyrrhizinated Licorice (DGL).

Glutamine is a conditionally essential amino acid that helps maintain and restore the integrity of the intestinal wall. Its function is to increase mucosal healing and to strengthen the spaces in the intestinal membrane, thus decreasing the ability of foreign substances to pass through the gut wall and enter into circulation. Research has established that the use of gram quantities of Glutamine can have a significant impact in healing the mucosal membrane of the gastrointestinal tract.

Antioxidants provide an important defense against free radical induced tissue damage in the mucosal membrane of the intestinal tract. Exposure to environmental chemicals, use of nonsteroidal anti-inflammatory drugs or antibiotics, the presence of nutritional deficiencies, chronic

inflammatory or allergic conditions, as well as a number of other factors all result in oxidative stress and resulting damage to the intestinal tract. This depletion of antioxidants in the GI tract sets off a cascade of events that results in mucosal membrane inflammation and injury to the tissues. The use of potent natural antioxidants (Reduced Glutathione, Vitamins E and C, CoEnzyme Q10, Selenium, Zinc, and others) has been shown to help reduce oxidative damage and can assist in repairing the intestinal wall.

5. Correct Nutritional Deficiencies

It is crucial to correct nutritional deficiencies that may trigger, exacerbate, or be caused by gastrointestinal problems. Specialized laboratory testing can be undertaken by a health care professional to assess a child's status of vitamins and minerals, essential fatty acids, amino acids, and other important nutrients. This information can then be utilized to design a comprehensive program of nutritional supplementation that has the goal of repairing the intestinal tract and restoring the health of the body as a whole.

6. Strengthen The Intestinal Immune System

Since the intestinal tract plays such a vital role in the body's immune system, it is important to provide extra support for the immune system if the intestinal tract has been compromised in any way. In addition to taking all the necessary steps for healing of the digestive tract, the immune system can be supported through the use of supplemental Colostrum, Beta-glucan, Lactoferrin, Zinc, and Antioxidants. Some physicians may also choose to use Intravenous Immunoglobulin (IVIG) for their patients with severely compromised immune function.

7. Reduce Future Damage To The Gastrointestinal System

Once the necessary steps have been taken to repair the intestinal tract, create a healthy gut environment, and restore the digestive system to a proper level of functioning, it is important to ensure that the resulting improvement is sustained. There are many measures that can be

employed by parents and physicians in order to maintain the health of the gastrointestinal system and also to prevent future injury from occurring. Since this is such an important component of the journey toward intestinal healing, a separate chapter has been devoted exclusively to this topic (see Chapter 9, “Maintaining Long-Term Intestinal Health In Autism Spectrum Disorders”).

Summary

This chapter has outlined a general approach for treatment of intestinal problems in autism spectrum disorders. By following the above-mentioned strategy, parents and health care providers will ensure that an affected child will have an optimal chance of recovering healthy digestive function. The next chapter will outline some of the more common intestinal disorders seen in autism and provide specific recommendations for intervention and treatment.

Chapter 7

Specific Treatments for Intestinal Problems in Autism Spectrum Disorders

INTRODUCTION

In a previous chapter, we outlined some of the intestinal conditions that are commonly seen in individuals with autism spectrum disorders. This chapter is divided into eleven parts that will provide further details about these conditions and outline the steps that may be taken to treat them. Each part is divided into five sections:

1. Description of the condition. This will include a discussion of how the condition is thought to develop in the body, why it may be prevalent in autistic children, and the possible complications it can cause if left untreated.
2. Signs And Symptoms with which the condition most often presents. These will vary from person to person, but the lists of common signs and symptoms can guide parents and physicians in making a proper diagnosis.
3. Possible Causes of the condition. As with any medical problem, it is important to evaluate the possible underlying causes of these gastrointestinal imbalances and, if possible, remove them so that proper healing can take place.
4. Diagnosis of the condition through recommended laboratory testing and other diagnostic measures. Further information on most of these tests is given in Chapter 3. Please note that it is not necessary to run all of the tests that are listed, as some of them may or may not be indicated based on the child's individual history and presenting symptoms. A health care professional can provide guidance in selecting the appropriate sequence of laboratory testing.
5. Treatment Approach includes recommendations on pharmaceutical drugs (when appropriate), natural supplements, dietary interventions, and preventive measures that may be helpful in keeping the condition from recurring. Please note the following important points regarding this chapter on treatment:

- The guidelines given in the sections below are meant to be considered as treatment options instead of universal recommendations that must be followed by every affected child. This is because each child is an individual and will present with different combinations of symptoms in varying degrees of severity.
- You will notice that some of the basic steps of the individual treatment approaches overlap among the different conditions. In many cases, the steps follow those of the general treatment strategy outlined in chapter 6.
- In general, Kirkman has only provided dosing instructions for the supplements we manufacture and, in individual cases, for some of the other products listed below.
- Dosing instructions for Kirkman products are found in Chapter 5, which also includes more detailed discussions of each of these individual supplements.
- When using products from other manufacturers, please follow the dosing instructions on the product label or, if you have further questions, call the manufacturer directly.

Where To Start: The Basics

For some children who have severe gastrointestinal problems and a significant degree of gut wall irritation and inflammation, it may be necessary to start with some basic interventions before delving into the specific treatments for the individual conditions discussed below. For example, a child who has intestinal yeast overgrowth and a resulting leaky gut may develop even more unpleasant GI symptoms if a strong antifungal agent is given right away without first taking some measures to soothe an irritated gut wall.

Here are some basic, general steps that can be taken first, before implementing more specific treatments, in order to prevent these problems from occurring:

1. Always start with gluten and casein elimination.

Thousands of parents who have an autistic child with gut problems have found this to be the single most valuable intervention for normalizing intestinal function in their child.

2. Clean up the child's diet.

A great deal of irritation to the intestinal tract can be reduced by minimizing the child's intake of fast foods, refined carbohydrates, sweets, and food chemicals (artificial dyes, additives, preservatives, flavoring agents [MSG], synthetic sweeteners [aspartame], and the pesticides and hormones found in many foods).

3. Eliminate sugar from the diet.

Especially in cases where the child has intestinal dysbiosis with an overgrowth of yeast, bacteria, or parasites, this can be a helpful initial intervention before beginning treatment with antimicrobial medications.

4. Eliminate possible food allergens.

These include not only the most commonly allergenic foods (see Part 5 of this chapter), but also any other foods you suspect your child may be allergic to. A food allergy test can be a valuable diagnostic aid. Reducing the intake of allergenic foods will help minimize the amount of irritation to the intestinal tract.

5. Do a stool culture first to figure out what is wrong.

Of all the diagnostic tests available, this is one of the most important ones for determining the degree of intestinal pathology that is present.

6. Use digestive enzymes for immediate intervention.

By supporting and facilitating the digestive process through the use of enzymes, the GI tract has a chance to rest so that some healing can begin to take place.

7. Supplement with nutrients that are soothing and healing to the gut wall.

This can provide initial relief for some of the irritation and inflammation that may be present within the intestinal tract. These nutrients are discussed further in the section of this chapter entitled "Intestinal Hyperpermeability / Leaky Gut Syndrome".

8. Enhance the body's detoxification pathways by supporting liver function.

Since the liver is responsible for properly metabolizing and eliminating all of the toxins in the body, it often becomes overly burdened by the toxins generated from the microorganisms in the intestinal tract. When this happens, a number of supplements may be given that are known to support liver function and enhance the process of detoxification. These include the following:

- *Glutathione* – administered orally, in a transdermal cream, or intravenously in a physician's office. Glutathione acts as a potent antioxidant and supports the liver detoxification.
- The herb *Milk Thistle* helps protect liver tissue and promotes the excretion of toxins from the body.
- N-Acetyl Cysteine supports detoxification by acting as an antioxidant and as a precursor to Glutathione synthesis.
- *MSM (Methylsulfonylmethane)* supports liver function through its high sulfur content.
- *Vitamin C* is an important antioxidant and helps support liver function.
- *Magnesium Sulfate (Epsom salts)* – administered in a transdermal cream or by giving the child regular baths with Epsom salts. (The general amount of Epsom salts used is 2 cups per bath full of water.) This product supports Phase II liver detoxification and provides sulfate ions for the Phenol sulfotransferase (PST) enzyme.

Part 1

INTESTINAL DYSBIOSIS

Description

Dysbiosis is a concept that was first introduced in the early 20th Century by Dr. Elie Metchnikoff, who popularized the theory that an imbalance of bacteria in the intestinal tract is the cause of most systemic disease. The term dysbiosis alludes to symbiosis, which describes a state where two organisms of different species live together in a harmonious relationship. However, when this balance is upset, a state of dysbiosis (“dys” meaning “disordered”) results.

Dr. Metchnikoff spent a good part of his life studying the peasants of Bulgaria, who were known for their long life spans. He theorized that the bacteria found in the yogurt that these peasants consumed had the ability to prevent and reverse infections with other, more harmful bacteria. Today, we refer to the beneficial bacteria found in yogurt as probiotics, a word meaning “beneficial for life”. Some examples of probiotics include *Lactobacillus acidophilus*, *Lactobacillus bulgaricus* (named by Dr. Metchnikoff in honor of the Bulgarian peasants), *Bifidobacterium bifidum*, and *Streptococcus thermophilus*.

“Intestinal dysbiosis”, then, is a term used to describe a state in which the microorganisms living in the intestinal tract are in a state of imbalance and disorder. In contrast to the beneficial probiotics, some of the harmful organisms that may be present in large numbers in the intestinal tract include yeast, viruses, bacteria, and parasites. *Candida albicans* is the most common type of yeast to exist in a state of dysbiosis, and it has been widely discussed in the medical community because of the systemic problems it can cause. Some of the bacteria most commonly seen in intestinal dysbiosis include *Clostridia*, *Citrobacter*, *E. coli*, *Klebsiella*, *Pseudomonas*, *Salmonella*, and *Staphylococcus aureus*.

Intestinal dysbiosis is commonly seen in children with autism spectrum disorders, as discussed by Dr. William Shaw in his book *Biological Treatments for Autism and PDD*.¹ Physicians who

specialize in the treatment of ASD report that the majority of their patients who present with gastrointestinal symptoms have some form of dysbiosis. There may be an overgrowth of harmful bacteria, a deficiency of beneficial bacteria, or both. Whatever the case may be, correcting this underlying imbalance is essential before complete healing of the digestive system can occur.

Intestinal dysbiosis is problematic for a variety of reasons. First, many of the abnormal microbes are considered to be pathogenic, meaning they are capable of causing disease in the body. These microbes produce toxins that are then released into circulation, leading to a variety of systemic complaints. There are published studies that identify a number of conditions as being caused by dysbiosis, including autoimmune disease, inflammatory bowel disease, food allergies, eczema, psoriasis, arthritis, and chronic fatigue syndrome.

Secondly, an imbalance in the normal bacterial flora of the intestinal tract can lead to inflammation of the gut wall. This in turn can cause the “Leaky Gut Syndrome” that is also a common problem among children with ASD. In addition, the toxins from the pathogenic bacteria can overload and eventually weaken the immune system, decreasing our resistance against invading viruses and bacteria from the environment.

Finally, perhaps one of the most serious consequences of dysbiosis is that the harmful bacteria in the intestinal tract can overcrowd and possibly even kill off the beneficial probiotics, preventing them from doing their job. Probiotics are responsible for a number of important functions in the body, including keeping harmful microbes at bay, enhancing digestion, producing certain vitamins, preventing intestinal illness, and supporting the workings of the immune system. When these beneficial activities are compromised, the stage is set for the development of disease.

Signs And Symptoms

The signs and symptoms associated with intestinal dysbiosis are usually due to both a lack of

beneficial probiotics and also to the specific types of pathogenic organisms that are present in the GI tract. Possible consequences of intestinal dysbiosis include:

- Abdominal pain, cramps, or discomfort
- Gas
- Abdominal bloating
- Constipation, diarrhea, or alternating constipation and diarrhea
- Foul-smelling stools
- Bad breath
- Indigestion
- May have loss of appetite, food aversions, or food cravings
- Food allergies
- Leaky gut syndrome
- Inflammatory gastrointestinal conditions (gastritis, colitis)
- Systemic problems such as headaches, fatigue, and skin problems

Possible Causes

The causes of intestinal dysbiosis are diverse and vary from individual to individual. The main factors behind the development of this condition include:

1. *Pharmaceutical drugs*
A significant history of antibiotic use is by far the most common cause of intestinal dysbiosis in children with autism. Antibiotics can eradicate both the harmful and beneficial bacteria in the intestinal tract, setting the stage for overgrowth with yeast, viruses, parasites, and other bacteria that were resistant to the antibiotic that was used. The *Lactobacillus* and *Bifidobacterium* bacteria are particularly vulnerable to eradication from antibiotics. A number of other pharmaceuticals, such as corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs), can also upset the microbial balance of the intestinal tract and lead to dysbiosis.
2. *Poor diet*
The amount of harmful and beneficial flora present in the GI tract is directly related to diet. For example, a diet that is high in fiber favors the proliferation

of the beneficial bacteria. On the other hand, a diet high in fat, sugar, starchy food, meat, dairy proteins, and processed foods can disrupt this balance and cause the overgrowth of harmful organisms, damage to the gut wall, and a decrease in beneficial probiotics.

3. *Improper digestion*
When there are insufficient amounts of stomach acid (HCl) or digestive enzymes present in the GI tract, this can lead to incomplete breakdown of foods and a tendency to have an overgrowth of harmful parasites, bacteria, and yeast. Slow transit time of food through the intestinal tract can also result in increased proliferation of unfavorable microbes.
4. *Toxic exposure*
The intestinal tract is exposed to ever increasing amounts of toxins by way the food that we eat and the water we drink. These toxins can cause direct damage to the cells of the intestinal tract, produce inflammation of the gut lining, compromise the beneficial microflora, and weaken the immune system.
5. *Stress*
Chronic stress can interfere with the body's normal digestive processes by slowing down the rate at which food moves through the intestinal tract. When food moves too slowly through the intestines (constipation), potentially harmful microbes have a greater chance of proliferating and crowding out the beneficial ones. Stress can also weaken the immune system and lead to compromised defenses.
6. *Lowered Immune Function*
A weakened intestinal immune system may explain why some children with ASD have a tendency toward chronic intestinal overgrowth states with pathogenic yeast and bacteria.

Diagnosis

1. *Comprehensive Digestive Stool Analysis (CDSA)*
The best way to identify the presence of intestinal dysbiosis is by performing a stool culture. Not only will this test assess the presence and numbers of the beneficial probiotics in the digestive tract, but it will also determine whether any abnormal organisms are present. In addition, some labs do sensitivity testing in order to determine which therapeutic agents will be most effective at eliminating the harmful bacteria and yeast.
2. *Organic Acid Test*
This urine test can also be diagnostic for intestinal dysbiosis by identifying the presence of certain metabolic markers. One of these markers, called dihydroxyphenylpropionic acid (DHPPA), appears to be associated with the pathogenic bacterium *Clostridium difficile*, an organism that is otherwise difficult to detect.

Treatment Approach

The information given here on intestinal dysbiosis represents a very general treatment strategy. More information on the specifics of this approach is found later on in this chapter and elsewhere in the treatment guide.

1. *Identify and Remove The Underlying Cause*
Since dysbiosis rarely occurs in the absence of a precipitating cause, it is crucial to identify what the underlying problem is so that appropriate treatment measures may be taken. This involves testing for the balance between the beneficial probiotics and unfavorable organisms that inhabit the GI tract.
2. *Treat Intestinal Overgrowth Conditions*
Use appropriate nutritional supplements and pharmaceutical drugs to eradicate any harmful organisms that may be present in the GI tract.
3. *Restore Intestinal Balance by Supplementing with Probiotics.*
Once the abnormal microbes have been removed, it is crucial to supplement with probiotics in order to replace the levels of beneficial bacteria and prevent future overgrowth with harmful organisms.
4. *Heal and Repair the Intestinal Lining*
Since "Leaky Gut Syndrome" is a frequent complication of intestinal dysbiosis, it is necessary to take the appropriate measures to heal and repair the intestinal lining. This is discussed in further detail in Part 3 of this chapter.
5. *Strengthen and Support The Immune System*
Using appropriate measures to strengthen the intestinal immune system, and the immune system in general, will help to prevent and minimize the intestinal overgrowth that leads to dysbiosis.
6. *Use Pharmaceutical Drugs Cautiously*
While it is often necessary to prescribe antibiotics or use NSAIDs for acute conditions, they should be used carefully and as infrequently as possible. In addition, the appropriate measures should be taken to minimize adverse reactions from these substances.
7. *Dietary Interventions*
While many children with autism are notorious for consuming a very limited diet, there are some general guidelines that may be followed to support the gut as much as possible through dietary means. Limiting the intake of sugar, starchy foods, and refined carbohydrates will decrease the amount of fuel available to feed the unfavorable yeast and bacteria. Ensuring an adequate intake of fiber can also support the health of the intestinal lining and the proliferation of probiotics in the intestinal tract.
8. *Replace Deficient Digestive Secretions*
Supplementing with digestive enzymes can help support the proper breakdown

of food, minimizing irritation to the gut wall by incompletely digested dietary proteins. Supporting digestive function with enzymes may also be helpful in the eradication of bacteria, yeast, and other unfavorable intestinal microbes.

9. *Minimize Exposure To Toxins And Other Irritants*

Exposure to toxins and chemicals through food and water can exacerbate a state of

dysbiosis by diminishing the quantity and potency of beneficial bacteria in the gut. In addition, toxins and other irritants can delay the healing process because they produce intestinal inflammation and cause direct damage to the gut membrane.

REFERENCES - Intestinal Dysbiosis

¹ Shaw, William, Ph.D. Biological Treatments for Autism and PDD. Overland Park, KS: ©William Shaw Ph.D., 1998.

Part 2

INTESTINAL YEAST / CANDIDA OVERGROWTH

Description

Overgrowth with intestinal yeast is one of the most common forms of dysbiosis observed in autistic children. Stool cultures performed on these children will most often reveal an intestinal overgrowth with the yeast *Candida albicans*, but other strains of yeast may be present as well. Since this is such a prevalent problem, and since so many autistic children have benefited greatly from the use of medications for the treatment of this condition, it is warranted to devote an entire section to the discussion of intestinal yeast overgrowth.

Candida is considered to be a “conditionally pathogenic” fungus. It is a prevalent type of yeast that is part of the natural microbial flora of the mouth, intestinal tract, vagina, and other mucous membranes. Ordinarily, *Candida* is present only in small amounts, being prevented from growing too quickly by a strong immune response and by the beneficial bacteria (probiotics) that keep it in check. When present in normal amounts, *Candida* is generally harmless and does not cause symptoms. However, there may be an overgrowth of yeast when the balance of probiotics is upset, as after treatment with antibiotics, or when there is

a problem with the immune system. This most commonly results in yeast infections of the mouth (known as thrush), vagina, intestinal tract, or infants may develop diaper rash. All of these infections are considered to be superficial in that they are limited to the surface mucous membranes of the body. They should not be confused with the disseminated, or systemic, yeast infections that are only seen in severely immunocompromised patients.

Awareness of the problems caused by intestinal *Candida* infection was greatly increased after the publication of two important books on the subject, Dr. Orian Truss’s *The Missing Diagnosis* and Dr. William Crook’s *The Yeast Connection*.^{1,2} There has been some speculation that an overgrowth of yeast in the gut can cause neurological disorders, including autism. Dr. William Shaw has identified the presence of a number of yeast metabolites in the urine of many autistic children.³ While cause and effect has not yet been proven, it is clear that some children with autism experience remarkable improvements when treated for yeast. In an informative paper entitled “*Candida-Caused Autism?*”, Dr. Bernie Rimland of the Autism Research Institute summarizes the issue clearly:

“It is much too early to reach a firm conclusion, but, based on the weight of the information gathered to date, it seems to me highly probable that a small, but significant, proportion of children diag-

nosed as autistic are in fact victims of a severe candida infection. I further believe that if the candida infection were successfully treated in these few cases – much easier said than done – the symptoms of autism would show dramatic improvement.”⁴

Like other forms of dysbiosis, intestinal yeast infections can cause damage to the lining of the digestive tract and result in a variety of systemic problems. Damage to the gut wall begins when the yeast take control and colonize the intestinal tract, thereby crowding out and further depleting the amount of beneficial bacteria in the system. The yeast then transform from a budding spore to a more invasive “hyphae” or “mycelium” form. The hyphae yeast have the ability to imbed themselves into the tissue of the gut wall, where they secrete enzymes that slowly break down this tissue and thereby allow them to penetrate even deeper. This destructive chain of events can cause inflammation and increased permeability of the intestinal membrane, leading to a condition known as “Leaky Gut Syndrome”.

To compound matters even further, the yeast produce dozens of toxins^{5,6} and other by-products that can leak across an overly permeable gut wall and adversely affect the immune system⁷ and nervous system. Of interest is a study that identifies infant mice as being much more susceptible to intestinal Candida overgrowth than older mice.⁸ When antibiotics were administered to these mice at an early age, the amount of Candida in their intestinal tract increased approximately 130-fold and they developed persistent yeast infections of long duration. This may explain why Candida infections are so prevalent in autistic children despite repeated treatment with antifungal medications such as Nystatin and Sporanox. There are a number of studies demonstrating the effects of antibiotics on intestinal yeast overgrowth in humans.^{9,10}

Besides antibiotics, a diet high in sugar has also been linked to intestinal candidiasis. In one study, the growth of *Candida albicans* in the digestive tracts of mice receiving sugar water was 200 times greater than that of mice receiving only plain water.¹¹ Many physicians have noted a similar correlation between sugar intake and yeast overgrowth in autistic children. In addition, researchers have also found an association be-

tween sugar consumption and yeast infections of the mouth¹² and vagina.^{13,14}

Signs And Symptoms

When the toxic metabolites of *Candida* enter into circulation, they can interfere with neurotransmitter function and cause a variety of neurological problems. There have even been cases where patients have experienced symptoms similar to alcohol intoxication, including loss of coordination and slurred speech, due to the fermentation of simple sugars by yeast in the gut. Systemically, intestinal yeast infections have been linked to conditions such as allergies, skin problems (eczema, psoriasis, hives), chronic fatigue, and chronic recurrent infections. Other signs and symptoms associated with intestinal yeast overgrowth include:

1. Digestive Symptoms

- Abdominal pain or discomfort
- Gas
- Abdominal bloating
- Constipation and/or diarrhea
- Mucous in stools
- Bad breath
- Belching
- Indigestion or feeling of fullness, especially after eating starches
- Food cravings for sweets, bread, pasta, and other simple starches
- Persistent rectal itching or irritation

2. Neurological Symptoms

- Hyperactivity
- Uncontrolled laughter, especially after meals
- Emotional disturbances such as depression, mood swings, agitation, irritability, and aggression
- Inattention, “spaciness”, decreased ability to focus
- Poor memory
- Distorted thinking
- Lack of coordination
- Dizziness or loss of balance

3. Immune Problems

- Increased tendency toward food

- and environmental allergies, especially allergies to molds
- Chronic vaginal yeast infections or persistent vaginal itching
- Chronic tinea (fungal) infections elsewhere on the body, including athlete's foot, toenail fungus, "jock itch", and fungal infections of the skin (ring-worm)

4. *Other Systemic Symptoms*

- Fatigue or lethargy
- Drowsiness
- Sleep disturbances
- Muscle aches or weakness
- Headaches
- Increased sensitivity to strong odors (perfumes, soaps, tobacco), household chemicals (cleaning agents, insect repellants), and environmental chemicals (gasoline, pesticides)
- Symptoms may be worse in moldy homes or in damp, humid weather

Possible Causes

- Chronic, recurrent use of broad-spectrum antibiotics, both recently and in the past
- Certain other drugs such as corticosteroids and immunosuppressive drugs
- Diet high in sugar and simple carbohydrates
- Altered intestinal microflora, with a decrease in the beneficial intestinal bacteria known as probiotics
- Low-fiber diet
- Multiple nutrient deficiencies that may be due to poor diet, malabsorption, maldigestion, or other intestinal problems
- Impaired immune function
- Decreased digestive secretions, including pancreatic enzymes and stomach acid
- Maternal history of yeast infections during pregnancy
- Constipation may aggravate intestinal yeast overgrowth

Diagnosis

The diagnosis of chronic candidiasis is best made by evaluating a patient's clinical picture and past medical history. The presence of many of the signs and symptoms listed above, as well as a history of some of the factors known to cause intestinal yeast overgrowth, suggest a strong likelihood that the child is suffering from a yeast infection of the digestive tract. There are also a number of laboratory tests that are helpful in confirming the presence of intestinal yeast, but they should not be relied on as the sole diagnostic measure. In his book *The Yeast Connection Handbook*, Dr. William Crook states that the best way for a physician to make the diagnosis of yeast-related illness is by taking a complete history, performing a thorough physical examination, and doing the appropriate laboratory testing.¹⁵ To facilitate the process of taking a history, Dr. Crook has developed a series of excellent Yeast Questionnaires that are found throughout his works. One questionnaire in particular is very helpful for diagnosing intestinal yeast problems in children. This, along with a brief list of the laboratory tests that may be helpful in making a diagnosis, is provided below.

1. Yeast Questionnaire For Children¹⁶

This questionnaire was developed by Dr. William Crook as a useful tool for evaluating the possibility of intestinal yeast overgrowth in a child. Parents can circle the appropriate point scores in the questions below and compare their child's total score to the analysis at the end of the questionnaire.

	Point Score
1. During the two years before your child was born, were you bothered by recurrent vaginitis, menstrual irregularities, premenstrual tension, fatigue, headache, depression, digestive disorders, or "feeling bad all over"?	30
2. Was your child bothered by thrush? (Score 10 if mild, score 20 if severe.)	10 20

3. Was your child bothered by frequent diaper rashes in infancy?
(Score 10 if mild, 20 if severe or persistent.)

10 20

4. During infancy, was your child bothered by colic and irritability lasting over 3 months?
(Score 10 if mild, 20 if moderate to severe.)

10 20

5. Are his symptoms worse on damp days or in damp or moldy places?

20

6. Has your child been bothered by recurrent or persistent "athlete's foot" or chronic fungal infections of his skin or nails?

30

7. Has your child been bothered by recurrent hives, eczema or other skin problems?

10

8. Has your child received:

a. 4 or more courses of antibiotic drugs during the past year? Or has he received continuous "prophylactic" courses of antibiotic drugs?

60

b. 8 or more courses of "broad-spectrum" antibiotics (such as amoxicillin, Keflex, Septra, Bactrim, or Ceclor) during the past three years?

40

9. Has your child experienced recurrent ear problems?

20

10. Has your child had tubes inserted in his ears?

10

11. Has your child been labeled "hyperactive"? (Score 10 if mild, 20 if moderate to severe.)

10 20

12. Is your child bothered by learning problems (even though his early development history was normal)?

10

13. Does your child have a short attention span?

10

14. Is your child persistently irritable, unhappy, and and hard to please?

10

15. Has your child been bothered by persistent or Recurrent digestive problems, including constipation, diarrhea, bloating, or excessive gas?
(Score 10 if mild; 20 if moderate; 30 if severe.)

10 20 30

16. Has he been bothered by persistent nasal congestion, cough and/or wheezing?

10

17. Is your child unusually tired or unhappy or depressed?
(Score 10 if mild, 20 if severe.)

10 20

18. Has he been bothered by recurrent headaches, abdominal pain, or muscle aches?
(Score 10 if mild, 20 if severe.)

10 20

19. Does your child crave sweets?
10

20. Does exposure to perfume, insecticides, gas, or other chemicals provoke moderate to severe symptoms?
30

21. Does tobacco smoke really bother him?
20

22. Do you feel that your child isn't well, yet diagnostic tests and studies haven't revealed the cause?
10

TOTAL SCORE

Analysis:

- Yeasts possibly play a role in causing health problems in children with scores of 60 or more.
- Yeasts probably play a role in causing health problems in children with scores of 100 or more.
- Yeasts almost certainly play a role in causing health problems in children with scores of 140 or more.

2. Laboratory Testing

a) Comprehensive Digestive Stool Analysis (CDSA)

A CDSA is a valuable tool for establishing the presence of intestinal yeast. Because it can identify the abnormal organisms that are causing a child's symptoms, the CDSA is especially useful since there are some bacteria and parasites that mimic many of the signs and symptoms of intestinal yeast. Through sensitivity testing, the results of the CDSA can suggest which antifungal medications will be effective at eradicating the organism in question.

b) Organic Acid Test (OAT)

The organic acid test is a helpful test

that complements the CDSA and identifies the presence of certain yeast metabolites in the urine.

c) Intestinal Permeability Studies

Performing intestinal permeability studies to assess the presence of leaky gut syndrome can be a helpful way to assess the degree of damage that the yeast may have caused to the intestinal wall.

Treatment Approach

Treating intestinal yeast overgrowth can be a challenging process. Usually, there is no single therapy that provides a complete cure. Rather, the best results are obtained by incorporating a comprehensive treatment program that addresses all of the interventions discussed below.

1. Remove Intestinal Yeast By Using Medicines That Eradicate Them

a) Pharmaceutical Drugs

Intestinal yeast infections can be very difficult to eradicate and keep under control. It is often necessary to start the treatment process by using prescription antifungal drugs, which are generally much stronger and more effective at getting rid of yeast than some of the natural supplements. A stool culture can help identify which of these drugs will be most effective against the strain of yeast that is present. Working with a physician who can prescribe these medications, dose them appropriately, and supervise their use is important. Some of the pharmaceuticals that are commonly used for treating yeast are further discussed in Chapter 6 and include:

- Nystatin
- Amphotericin B
- Diflucan
- Nizoral
- Sporanox

b) Nonprescription Antifungal Compounds

There are a number of herbs and naturally occurring compounds that have been used to inhibit the growth of *Candida albicans* and other types of intestinal

yeast. While many individuals have experienced significant benefits from using these natural agents, they are generally less effective than prescription antifungals and are best used as an adjunct to conventional therapy. A good approach is to begin treatment with one of the pharmaceutical drugs and then follow this with natural supplements to keep the yeast under control.

Examples of some of the herbs and other compounds that are often used alone or in combination include:

- Oregano oil has been shown to inhibit the growth of *Candida albicans* in vitro¹⁷ and is one of the strongest and most effective antifungal herbs.
- Caprylic acid is a fatty acid found in a wide variety of foods that has a long history of use in the treatment of intestinal yeast.^{18,19}
- Goldenseal is most widely known for its immune enhancing properties, but it also has strong antimicrobial properties due to its berberine content. Berberine is an alkaloid that has been shown to be effective against bacteria, protozoa, and fungi, especially *Candida albicans*.^{20,21,22}
- Pau d'arco is an herb that contains the active constituents lapachol and beta-lapachone, which have anti-yeast properties.
- Olive leaf extract contains a compound called oleuropein, which is reported to have antimicrobial and antifungal properties.
- Cranberry extract has been tested on *Candida* yeast strains in vitro and has exhibited the ability to kill or deactivate these yeast cells. Please see Chapter 5 for more information.
- Garlic extract has been shown to have potent antifungal activity in both animal and laboratory studies.^{23,24,25} When selecting a commercial garlic preparation at the health food store, make sure that the active component of the garlic, known as allicin, is present.

In general, experience has shown that

using high quality supplements containing a combination of several different antifungal agents tends to produce better results than treating with single herbs alone. Dosage instructions will vary depending on the age of the child and the type of herbal preparation used, so if you have questions it is best to consult a qualified professional who can guide you in the proper use of these supplements.

It is important to remember that any medications that kill yeast, whether they be pharmaceutical drugs or natural supplements, can cause what is known as a Herxheimer, or "die-off" reaction. This will be discussed in more detail below. Finally, keep in mind that all herbs are relatively high in naturally occurring compounds called salicylates. A number of children with ASD are very sensitive to salicylates and may therefore not respond as well to herbal supplementation.

2. Minimize Herxheimer ("Die-Off") Reactions

A number of patients undergoing treatment for intestinal yeast overgrowth will experience an initial worsening of symptoms. This temporary aggravation is known as the Herxheimer reaction, or "yeast die-off reaction". The die-off reaction happens when antifungal medications are given and there is a rapid eradication of yeast in the intestines. As they are killed, these organisms generate toxins that are subsequently absorbed from the digestive tract into the bloodstream. When the body is unable to get rid of these toxins as quickly as they are being generated, the patient may feel worse for a period of time during the initial phase of therapy.

The die-off reaction usually lasts for a few days to a week, but in some cases may be more prolonged. Symptoms associated with yeast die-off include:

- Gas, bloating, and abdominal discomfort
- Worsening of constipation or diarrhea
- Headache
- Nausea, sometimes with vomiting
- Skin rashes
- Fatigue and drowsiness

- Worsening of behaviors, including hyperactivity, repetitive behaviors, and “stimming”
- Emotional disturbances, such as mood swings, aggression, or sadness

While parents understandably become concerned when their child exhibits any of these reactions, yeast die-off is fairly common and self-limited. However, given the significant digestive and immune-related problems present in so many individuals with autism, it is imperative that the child be closely monitored for any side effects or complications from the antifungal products.

Here are some suggestions for preventing or minimizing the symptoms of the die-off reaction:

- Start any antifungal medications or supplements at a low dose and gradually increase over a period of 1-2 weeks until the full therapeutic level has been achieved.
- Eliminate sugar from the diet before beginning treatment. This simple intervention has been reported by many parents to have been of benefit for their child.
- Encourage the intake of large amounts of filtered water to assist the body in eliminating the toxins generated by the yeast.
- Take measures to ensure that the child is having regular bowel movements, at least one per day.
- Support the liver and the body's detoxification pathways by supplementing with nutrients such as Glutathione, N-Acetyl Cysteine, and MSM. Giving the child regular baths with Epsom salts, or using a transdermal Magnesium Sulfate (Epsom salt) cream, is also helpful for liver support and detoxification.
- Buffered Vitamin C is extremely helpful for neutralizing the yeast toxins and supporting the body's detoxification pathways. For this purpose, Vitamin C is generally given between meals and dosed at 500-1,000 mg, 3 times per day.
- Alka-Seltzer Gold has been helpful for reducing acute symptoms in many children experiencing a die-

off reaction. It works by neutralizing some of the acids produced by the yeast toxins. Other forms of Alka-Seltzer do not have the same benefits. A typical dosage is 1 tablet dissolved in water, administered 2-4 times per day on an empty stomach.

- Some practitioners recommend giving activated charcoal tablets to absorb yeast-generated toxins from the intestinal tract and minimize long lasting die-off reactions. However, Bentonite Clay is generally safer than charcoal and works by the same mechanism. It is available from health food stores and is usually dosed at 1 teaspoon 2-4 times per day, between meals. Follow instructions on the label. Do not give bentonite clay at the same time you are also administering supplements, since the clay can bind to these nutrients and prevent their absorption from the GI tract.

3. Replace Deficient Digestive Secretions

Promoting proper digestive function is another essential component in the treatment of intestinal yeast infections. In a normally functioning gastrointestinal system, secretions such as Digestive Enzymes, bile, bicarbonate, and hydrochloric acid (stomach acid) all function to prevent the overgrowth of yeast in the intestines. The pancreatic enzymes called proteases, for example, are normally responsible not only for breaking down food proteins, but also for preventing the colonization of the small intestine by yeast, bacteria, and parasites.^{26,27} When these pancreatic proteases or other digestive secretions are present in decreased quantities, as is often the case in individuals with autism, there is a greater susceptibility to Candida overgrowth. Therefore, restoring proper levels of these components is an important part of the overall treatment approach.

4. Restore Intestinal Balance By Supplementing With Probiotics.

Restoring healthy intestinal bacterial balance with

Probiotics is one of the most crucial interventions in the treatment of intestinal yeast overgrowth. Probiotics have the important function of keeping the pathogenic (harmful) intestinal microorganisms in check, including yeast, bacteria, and parasites. The Lactobacilli in particular have been shown to inhibit the overgrowth of unfriendly bacterial and yeast by competing with them for food, by altering the pH of the gut to make it less favorable for their survival, and by preventing these pathogenic organisms from adhering to and damaging the intestinal wall. Probiotics are therefore helpful not only in the treatment of intestinal yeast infections, but also for preventing future overgrowth with these and other organisms.

5. Heal And Repair The Intestinal Lining

As described in the introduction above, there are several mechanisms by which the yeast and their by-products can irritate and inflame the intestinal wall. The common result is an abnormal increase in the permeability of the intestinal membrane, known as Leaky Gut Syndrome. Part of the process of restoring the intestinal tract to a place of health is to take appropriate measures for repairing the gut wall. The steps involved in doing this are discussed further in Part 3 of this chapter. However, some of the nutrients that may be helpful include:

- Colostrum
- Zinc
- L-Glutamine
- Essential Fatty Acids
- Antioxidants
- MSM (Methylsulfonylmethane)
- A number of herbs that have healing and anti-inflammatory properties

6. Strengthen And Support The Immune system

In most cases, patients who have chronic yeast overgrowth of the intestinal tract also suffer from weakened immune function. As referenced above, yeast have been shown to release a large number of toxins into the bloodstream. The immune system responds by working overtime to reduce the toxic load being placed on the body. This chronic drain on the immune system leaves the individual vulnerable to infection with other organisms, such as viruses and bacteria, resulting

in an even further strain on the immune system. The person is then caught in a vicious cycle in which the intestinal tract becomes even more susceptible to yeast overgrowth, leading to increased colonization by yeast and an even greater drain on the immune system. Therefore, a vital part of the treatment approach for chronic candidiasis is supplementing with nutrients that are known to enhance and support the function of the immune system. These are discussed in Part 11 of this chapter and include:

- Zinc
- Colostrum
- Vitamin C
- Antioxidants
- Beta-glucan
- Lactoferrin

7. Take Measures To Discourage The Future Overgrowth Of Yeast

a) Give Nonprescription Antifungal Compounds

After the initial phase of treatment with pharmaceutical drugs, it is often helpful to control future yeast overgrowth by supplementing with some of the non-prescription antifungal compounds described above.

b) Continue Supplementing With Probiotics

Regular supplementation with probiotics is important to keep the yeast in check and control future overgrowth.

c) Dietary Interventions

Much has been written about controlling intestinal yeast infections through dietary interventions. Many of the books by Dr. William Crook give helpful guidelines and provide delicious recipes for fighting Candida and other intestinal yeast. By way of a brief summary, the basic guidelines of the anti-yeast diet are:

- Avoid dietary sugars, including white (table) sugar, brown sugar, honey, molasses, maple syrup, and large amounts of fruit juice. These sugars provide fuel for the yeast and make them proliferate.
- Limit the intake of fruits, refined carbohydrates, and starches

(breads, pastas, potatoes, etc.). These break down into simple sugars in the digestive tract and can also feed the yeast.

- Minimize the intake of fast foods, which are low in nutrients and high in sugar, refined carbohydrates, and often contain excitotoxins such as MSG and other additives and preservatives.
- Eat a diet high in protein, fiber, and complex carbohydrates. These generally do not feed yeast in the way that the above-

mentioned foods do.

- Eliminate foods from the diet that contain yeast and molds, since these may also stimulate the growth of *Candida*. Yeast and mold are found in foods such as breads, baked goods, dried fruits, cheeses, peanuts, and many fermented foods.
- Eliminating gluten and casein is important for autistic children, not only because of their opioid effects, but also because these foods can also provide fuel for the yeast.

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Part 3

INTESTINAL HYPERPERMEABILITY/ LEAKY GUT SYNDROME

Description

Intestinal Hyperpermeability, or "Leaky Gut Syndrome", are terms used to describe a phenomenon where there is increased intestinal permeability resulting from chronic irritation to the gut wall. The intestinal membrane has the paradoxical function of being both a barrier that separates the contents of the digestive tract from rest of the body, while at the same time allowing beneficial nutrients from foods to be absorbed into the bloodstream. Normally, tiny openings in this membrane, called tight junctions, allow very small molecules, such as vitamins and minerals from the foods we consume, to enter the bloodstream and be systemically utilized in order to maintain the body's proper nutritional balance. When there is excess inflammation of the gut wall, these tight junctions enlarge, thereby allowing larger molecules such as food proteins to enter into circulation. This condition is described as hyperpermeability because the intestinal membrane has become overly permeable, or porous. It is also referred to as leaky gut syndrome because the enlarged tight junctions allow food proteins and toxins to "leak" across the intestinal membrane into the bloodstream.

Leaky gut syndrome is not a disease in and of itself, but rather an abnormal expression of a natural physiological process. The presence of this disorder is usually a reflection of a deeper underlying problem that is occurring within the intestinal tract. In most cases, it is the result of irritation to and inflammation of the gut wall. Researchers have known for years that inflammatory bowel conditions such as celiac disease¹ (an inherited intolerance to gluten), Crohn's disease,² and acute gastroenteritis are almost always accompanied by intestinal hyperpermeability. In addition, an overgrowth of yeast, bacteria, or other microbes in within the GI tract can irritate the gut wall and cause it to become more porous. Leaky gut syndrome may also be caused by other factors, such as poor diet, improper digestion, or the use of certain pharmaceutical drugs. Almost any individual with intestinal dysbiosis will have some degree of Leaky Gut Syndrome due the irritating effect of the pathogenic microorganisms on the gut wall.

Leaky Gut Syndrome can trigger a cascade of events that may result in a variety of systemic problems. When the intestinal wall is overly permeable, substances such as toxins and large food proteins are inappropriately "leaked" from the digestive tract into the bloodstream. Once inside the bloodstream, the immune system recognizes these molecules as antigens, or foreign invaders, and develops antibodies to try

and eradicate them. This can cause the immune system to become over-stimulated, and there is evidence that leaky gut syndrome can lead to chronic problems such as food allergies and autoimmune disease. In addition to causing this abnormal immune response, the toxins that are transferred from the intestinal tract to the bloodstream can place a great deal of stress on the liver. Since the liver is the primary organ of detoxification in the body, its ability to appropriately metabolize other toxins becomes compromised when its reserves are overwhelmed due to the increased antigenic load from a leaky gut wall.

Len Saputo, M.D., has identified a number of conditions that may be caused by intestinal hyperpermeability.³ These are:

- Attention deficit disorders
- Symptoms resembling autism
- Chronic and rheumatoid arthritis
- Chronic fatigue syndrome
- Eczema
- Food allergies
- Inflammatory bowel disease
- Irritable bowel syndrome
- Joint and collagen problems (autoimmune diseases)
- Compromised liver function
- Malnutrition
- Multiple chemical sensitivities
- Psoriasis
- Symptoms resembling schizophrenia
- Skin disorders ranging from urticaria (hives) to acne and psoriasis

There is documented evidence that individuals with autism often suffer from leaky gut syndrome. One study found that increased intestinal permeability was present in 43% of autistic children, whereas none of the children in the control group showed any evidence of this problem.⁴ Leaky gut syndrome also appears to be associated with other neurological problems ranging from poor memory and “spaciness” to ADHD and schizophrenia.⁵ It is thought that some of the symptoms seen in autism are due to the leaking of gluten and casein peptides across an overly permeable intestinal membrane.⁶⁻¹³ These peptides apparently stimulate the opioid receptors in the brain, compromising neurotransmitter function and leading to some of the neurological and behavioral problems

observed in individuals with autism. One of the goals of treatment should therefore be to heal and repair the intestinal membrane in order to minimize the adverse effects of leaky gut syndrome.

Signs And Symptoms

There are dozens of clinical signs and symptoms that have been associated with leaky gut syndrome. Some of the more important ones for our discussion of the autism spectrum disorders are:

- Constipation and or diarrhea
- Abdominal pain and discomfort, indigestion
- Abdominal bloating
- Excessive gas
- Mucous in the stools or otherwise abnormal appearing stools
- Food allergies and sensitivities, including to gluten and casein
- Poor immune function with recurrent infections (ear, throat, respiratory)
- Asthma, hayfever, and other environmental allergies
- Confusion, poor memory, and difficulty concentrating
- Mood swings, anxiety, hyperactivity, and aggressive behavior
- Fatigue, low energy, and chronic tiredness
- Bed wetting
- Skin conditions such as eczema, hives, rashes, and psoriasis

Possible Causes

As stated previously, any condition that causes irritation to and inflammation of the gut wall can eventually lead to Leaky Gut Syndrome. Some of these conditions are:

- Intestinal overgrowth or infection with harmful microbes such as yeast, bacteria, viruses, and parasites (dysbiosis)
- Decreased amounts of beneficial intestinal bacteria (probiotics)
- Food allergies
- Gluten and casein sensitivity
- Certain medications, including antibiotics, corticosteroids, aspirin, and other non-steroidal anti-inflammatory drugs (NSAIDs)

- Chemicals and toxins from the environment or ingested through food and water
- Intestinal damage from vaccines¹⁴
- Intestinal damage from heavy metals¹⁵
- Digestive enzyme deficiency that results in insufficient breakdown of food proteins which can irritate the intestinal wall
- Inflammatory bowel diseases such as celiac disease, Crohn's disease, and ulcerative colitis
- Malnutrition or poor diet, resulting in lack of available antioxidants and nutrients to facilitate intestinal healing
- Acute gastrointestinal infection, as in viral gastroenteritis
- In some cases, there appears to be a genetic component¹⁶

Diagnosis

1. *Intestinal Permeability Studies*
The most accurate test for diagnosing and determining the degree of leaky gut syndrome is through intestinal permeability studies. Periodic follow-up tests are helpful to assess the progress of treatment.
2. *Comprehensive Digestive Stool Analysis (CDSA)*
Since intestinal dysbiosis is a common cause of leaky gut syndrome, the CDSA is an important test for determining the balance of beneficial versus harmful organisms in the gut. It can also provide an indication of the body's ability to properly digest and absorb foods.
3. *Organic Acid Test (OAT)*
The OAT is a complementary test to the CDSA for diagnosing intestinal dysbiosis as an underlying cause of leaky gut syndrome.
4. *Food Allergy Testing*
The presence of food allergies should be investigated as a possible cause of intestinal hyperpermeability.
5. *Gluten Antibody Studies / Lactose Breath Test*
If a child is not following a gluten and casein free diet, it is important to rule out

celiac disease and lactose intolerance, since these conditions can cause significant inflammation of the intestinal wall.

6. *Liver Detoxification Profile*
A vital component of the healing process involves supporting liver function if the body's detoxification pathways become compromised as a result of intestinal hyperpermeability. In some cases, it is helpful to monitor this process by doing a liver detoxification profile.
7. *Heavy Metal Testing*
Since one of the causes of leaky gut syndrome may be damage from heavy metals, it is important to assess this as a potential causative factor. Tests such as a DMSA Urine Challenge or a Packed Red Blood Cell Study can provide clues to the amount of heavy metals in a child's system. For more information on testing for and treating heavy metal toxicity, please consult the DAN! Consensus Report on mercury chelation.¹⁷
8. *Immune Assays*
As discussed above, an overly permeable gut wall can in some cases cause significant immune dysfunction. Evaluating the status of the immune system by performing Immunological Studies or testing for Secretory IgA can provide an indication of whether this system needs to be supported as part of the overall healing process.
9. *Nutritional Profile Testing*
Tests to diagnose nutritional deficiencies can indicate which vitamins, minerals, amino acids, essential fatty acids, and other nutrients need to be supplemented in order to support the healing of the intestinal membrane.
10. *Diagnostic Imaging*
In cases where the leaky gut syndrome is related to significant inflammatory dysfunction, it may be necessary to evaluate and possibly biopsy the gastrointestinal mucosa through imaging procedures such as colonoscopy and endoscopy.

Treatment Approach

1. Identify And Remove The Underlying Cause

- Remove gluten and casein from the diet, as these are common causes of intestinal irritation and inflammation. A long-term gluten-free diet was actually able to normalize the intestinal permeability tests of patients with celiac disease,¹⁸ which is a promising finding for ASD children who are on a GF/CF diet.
- Remove foods from the diet that the child is allergic to, also because of their pro-inflammatory characteristics.
- Decrease the amount of sugar in the child's diet and increase the amount of dietary fiber, since fiber supports a healthy intestinal tract.
- Try to increase the child's intake of nutrient-rich foods (fruits, vegetables, whole grains, protein sources, beans, legumes, and essential fatty acids), since the body requires a good supply of nutrients in order for healing to take place.
- If the diet is deficient in nutrients, supplement with a good high-quality multi-vitamin and mineral formula.
- Be cautious with pharmaceutical drugs that can damage the GI membrane, including antibiotics, corticosteroids, aspirin, and other non-steroidal anti-inflammatory drugs. Speak with your child's physician about the use of these drugs.
- Try to limit the amount of chemicals ingested in foods, such as artificial additives and preservatives, food dyes, certain sweeteners and flavoring agents, pesticides, and hormones.

2. Replace Deficient Digestive Secretions

- Digestive Enzymes: In many

cases, leaky gut syndrome responds positively to supplementation with digestive enzymes. This is because the enzymes help to make sure that the food is properly broken down, minimizing the amount of undigested proteins that can potentially irritate and inflame the intestinal wall.

- Other Digestive Secretions: Supporting the digestive process through treatment with Secretin, Bicarbonate, or Bethanechol may also be helpful for some children.

3. Correct Intestinal Dysbiosis

- Eradicate harmful intestinal microbes and treat underlying dysbiosis with the appropriate supplements and pharmaceutical drugs.
- Replace the beneficial intestinal microflora by supplementing with probiotics.

4. Heal And Repair The Intestinal Tract

A number of natural supplements have been found to be very helpful for healing the gut wall and repairing the "holes" in the intestinal membrane. These supplements tend to exert their positive benefits through their soothing and anti-inflammatory properties. Supporting the therapeutic process with some of these supplements gives the intestinal membrane a chance to "rest" and thereby allows the process of healing and repair to begin. Some of these supplements are listed below:

- *Colostrum* is an important nutrient because it not only has direct healing effects on the intestinal mucosa, but also helps to strengthen and support the immune system.
- *Zinc* is essential for tissue repair, growth, and wound healing. It is an important mineral for the cells in the body that have rapid turnover, including those cells lining the intestinal tract.
- *L-Glutamine* is an amino acid whose use is supported by studies that document its gut-healing

- properties. It promotes new protein synthesis, is important for wound healing, and provides fuel for the cells lining the digestive tract.
- *Reduced Glutathione* is involved in mucosal healing.
 - *Essential Fatty Acids* (e.g. flaxseed oil, fish oils, evening primrose oil) are thought to be helpful for intestinal healing because of their anti-inflammatory properties.
 - *Antioxidants such as Vitamins E, C, Selenium, and Coenzyme Q10* can help prevent and repair damage to the intestinal tract caused by free radicals (chemicals, toxins, etc.).
 - *MSM (Methylsulfonylmethane)* has been found by some physicians to be helpful in the treatment of Leaky Gut Syndrome because it tends to be soothing and healing to the intestinal mucosa.
 - A number of *herbs, such as Aloe Vera gel, Slippery Elm, and Marsh-mallow Root*, have been used in the treatment of Leaky Gut Syndrome because of their soothing and healing properties.
 - *Deglycyrrhizinated Licorice (DGL)*, another gut-healing herb, is supported by a number of research studies to have significant benefit in treating inflammatory conditions of the stomach.^{19,20}
 - *Quercetin*, a bioflavonoid, has anti-inflammatory properties.
 - *N-Acetyl Glucosamine* may also be helpful in the gut-healing process.

5. *Strengthen And Support The Immune System*

Since the presence of Leaky Gut Syndrome can place a strain on the immune system, part of the healing process may involve supplementing with nutrients that are

known to strengthen immunity in general. Some of the nutrients discussed above that help to heal the intestinal membrane are also useful for boosting immune function. These are Colostrum, Zinc, and the Antioxidants. In addition, a few others are also known to strengthen and support the immune system, including:

- Beta-glucan
- Lactoferrin

6. *Support Liver Function*

Leaky gut syndrome can place a strain on the liver and weaken the body's detoxification pathways through the mechanisms discussed in the introduction to this section. When detoxification is significantly impaired, a number of liver-supportive nutrients may help to enhance this process. These include:

- The herb Milk Thistle
- Reduced Glutathione
- N-Acetyl Cysteine (NAC)
- Transdermal Magnesium Sulfate Cream
- MSM (Methylsulfonylmethane)
- Vitamin C

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Part 4

GLUTEN AND CASEIN SENSITIVITY

Description

A significant number of studies by doctors and researchers specializing in autism spectrum disorders have established elevated urinary excretion of peptides in children with autism. This observation was originally made years ago in relation to schizophrenia.^{1,2,3} More recently, researchers such as Dr. Karl Reichelt in Norway,^{4,5,6} Dr. William Shaw at Great Plains Laboratory,⁷ Dr. Robert Cade at the University of Florida,^{8,9} and Dr. Paul Shattock in England^{10,11} have demonstrated a similar relationship between dietary peptides and autism. These elevated peptides are thought to derive from incompletely digested gluten (found in wheat and some other grains) and casein (found in all dairy products), and are referred to as gluteomorphin and caseomorphin.

Deficiencies of digestive enzymes in children with autism contribute to this incomplete breakdown of gluten and casein, producing peptides that can enter the bloodstream by leaking through an overly permeable (“leaky”) gut wall. Once in the bloodstream, they circulate throughout the body and react at specific sites in the brain called opiate receptors. When these gluten and casein peptides stimulate the opiate receptors in the brain, they can significantly affect behavior, emotions, cognitive ability, speech, learning, pain threshold, and some of the other areas commonly recognized as being affected in individuals with autism.

Signs And Symptoms

Gluten and casein sensitivity can manifest itself in a variety of ways. For some children, the peptides from these foods can significantly irritate the gut wall, causing direct gastrointestinal symptoms. These children may present with diarrhea or loose stools, constipation, foul-smelling stools, chronic abdominal pain, gas, bloating, and other signs and symptoms of abdominal dysfunction. In addition, children who crave certain foods or self-limit their diets sometimes have complete resolution of these problems when gluten and casein

are removed from their diets.

For other children, however, the brain opiate issues are more significant, and the effects of gluten and casein predominantly manifest themselves in behavioral issues. Parents and physicians have reported that removal of these offending proteins from the diet can cause marked improvements in language, eye contact, “stimming”, sleep patterns, attention span, ability to focus, and many other behavioral and developmental issues.

Possible Causes

The obvious cause of this syndrome is ingestion of gluten and casein. However, there are usually some underlying reasons why these foods cause problems in the first place, such as insufficient breakdown of these peptides by digestive enzymes, or an overly permeable gut wall that allows the peptides to leak out into circulation. There is also growing evidence that a deficiency in the DPP-IV enzyme within the gut lining of autistic children may explain why there is an incomplete breakdown of gluten and casein peptides. Therefore, addressing these other areas should also be a part of the treatment plan.

Diagnosis

1. Urinary Peptide Test

Laboratory diagnosis is usually made by way of a Urinary Peptide Test that measures the levels of gluteomorphin and caseomorphin being excreted through the urine. This provides parents with a good diagnostic indicator of whether it would be helpful to remove these foods from the diet. However, most physician treating children with autism stress that even when one or both of these urine peptide levels are not elevated, the child may still respond in a very positive way to a gluten-free/casein-free (GF/CF) diet. In most cases, this diet is an important place to start in the treatment of any child with autism spectrum disorders.

One thing to keep in mind is that food allergy testing is not diagnostic of the opioid problems caused by gluten and casein. This is a common point of confusion among parents. Many children are allergic to dairy products and/or to gluten-containing grains. The presence of these food allergies, however, does not necessarily indicate that the same child also has opioid problems from these foods. It is therefore necessary to do the urinary peptide test instead of, or in addition to, a standard food allergy panel.

2. *Gluten Antibody Studies/Lactose Breath Test*

Although not diagnostic of the presence of gluten and casein opioids, these tests may be complementary for determining the possible presence of celiac disease (inherited gluten intolerance) and lactose intolerance.

3. *Other Considerations*

When laboratory testing is not an option, it is still possible to “diagnose” gluten and casein sensitivity through a strict elimination diet. In fact, this is the first intervention that some parents use with their child, and many claim that starting a GF/CF diet was the most important therapeutic intervention they ever used because it allowed their child to make the greatest gains.

Treatment Approach

1. *Dietary Interventions*

Children with autism and other developmental disorders commonly improve when gluten and casein are removed from the diet. Because gluteomorphin and caseomorphin often trigger opiate or morphine-like reactions in the body, withdrawal symptoms sometimes occur when these proteins are removed from the diet. Hyperactivity, insomnia, aggressiveness, and refusal to eat can be possible symptoms, and often these reactions are more dramatic in younger

children (ages 2-4). A more gradual removal of the casein and gluten may be necessary in these cases. Eventually, the symptoms do disappear.

Managing a GF/CF diet is not as easy as it sounds. For one, the diet must be adhered to 100%, because sensitive children who eat even a little bit of gluten or casein will not improve as much as they could if their diet were completely free of these proteins. In addition, parents must learn what products contain gluten and casein, and must get used to carefully reading product labels. This is important because gluten and casein can sometimes be “hidden” from the consumer’s view on a label. Once the parameters are understood, what seemed like an impossible diet to comply with becomes much more tolerable and manageable.

a) Casein elimination

Casein is present in dairy products. For most parents, it is easiest to begin with casein restriction because there are fewer foods containing dairy products. Eliminating casein sounds simple – just remove all dairy products from the diet, including:

- Milk in all forms (including skim, powdered and goat’s milk)
- Butter
- Cheese
- Yogurt
- Lactose
- Whey
- Caseinates

Unfortunately, it is not that simple. Most prepared foods contain dairy products such as powdered milk, cheese or whey. Soup mixes usually do as well. You must read the labels carefully to be sure that dairy products are not present in frozen, prepared, dried, or canned foods. You must also check bakery goods and snacks for the presence of these casein sources. Reading the labels is a critical issue. Eggs and most types of mayonnaise do not

contain casein. There are dairy-free margarines available, but read the labels carefully. Some of these products contain whey.

There are acceptable casein-free substitutes available. Milk alternatives made with rice, potato or soy are commercially available in specialty sections of grocery stores or in health food stores. Some sensitive individuals also react to soy, so be careful on this issue. There are also dairy free yogurts and "mock" cheese products on the market. Using your imagination along with these specialty products will allow you to create your own versions of recipes that traditionally contain dairy products. A 1998 book by Lisa Lewis, Ph.D. entitled *Special Diets For Special Kids*¹² gives hundreds of creative ideas for casein and gluten free diets. Another valuable guide in how to execute the diet is Karyn Seroussi's excellent book, *Unraveling The Mystery of Autism And Pervasive Developmental Disorder*.¹³

b) Gluten elimination

Gluten elimination is more difficult and requires more effort than a casein-free diet. It is also easier to have "accidents" because gluten can be hidden in a lot more products. The following grains contain gluten and must be avoided:

- Wheat
- Oats
- Barley
- Rye
- Semolina
- Spelt
- Triticale
- Kamut

These grains are present in most commercial cereals, breads, flours, baked goods, instant mixes, and prepared foods. Reading the label carefully is mandatory to ensure that they are not present. Often this becomes difficult, however, because natural or artificial flavorings along with spices, gravies and dressings can also contain gluten. If in doubt, you will have

to check with the manufacturer of the product.

Fortunately, there are safe alternative grains and flours for gluten-free diets. Acceptable grain substitutes are:

- White rice
- Brown rice
- Sweet rice
- Tapioca
- Potato starch
- Bean flours (Garbanzo and Garfava)
- Lentil
- Corn
- Soy

Another factor that makes the gluten-free diet difficult is the "contamination factor." For example, wheat flour makes a very good anti-caking or anti-stick compound for some manufactured or packaged products and is not listed on the label because it is not a component of the actual product. Rather, it is used to "dust" the equipment in order to prevent tackiness. Also, a factory that packages a gluten-free product may use the same equipment as it does for foods that do contain gluten, without cleaning the equipment in between. Know your supplier and, if in doubt, call and ask about potential contaminations and demand to receive a copy of their standard operating procedures that outline how equipment is cleaned. If the supplier or manufacturer will not share this information with you, chances are they are hiding something.

If everyone in the family is not gluten free, be careful of in-home contamination from pot, pans, cutting boards, utensils, countertops and dishes. Most individuals sensitive to gluten are sensitive at minute levels (a few parts per million). What might seem insignificant, such as wheat residue on a breadboard, could have serious repercussions to the gluten sensitive person. This is why, when both gluten and casein are eliminated from the diet, it is absolutely essential to follow the diet 100%, because eating even the slightest

amount of these proteins can cause significant problems.

In addition to the excellent books by Lisa Lewis and Karyn Seroussi mentioned above, there are many other valuable publications that explain the importance of the GF/CF diet and provide guidelines on its implementation. Please see our "Resources" section for further information and support on the GF/CF diet.

2. Other Interventions For Gluten And Casein Sensitivity

a) Supplement with digestive enzymes

Supplementing with a digestive enzyme that has high peptidase activity and DPP-IV activity may be helpful for some children with gluten and casein sensitivity. These enzymes can be given as an adjunct to the GF/CF diet, and may help to minimize adverse reactions when gluten and casein are accidentally ingested.

It should be emphasized, however, that supplementing with digestive enzymes can by no means take the place of eliminating gluten and casein from the diet. There is a popular misconception that children who have been following, and have benefited from, a GF/CF diet are able to start eating these foods again as long as they are being supplemented with a peptidase enzyme. This is a dangerous assumption to make, since many parents who have tried this approach report that their child has severely regressed after going off the diet. Unless there is sufficient evidence to demonstrate that digestive function has been restored and the intestinal wall completely healed, it is unwise to reintroduce gluten and casein into the diet if the child has improved from the elimination of these foods.

b) Heal and repair the intestinal lining

Since a large part of the reason why children with ASD tend to be sensitive to gluten and casein is that these peptides leak into circulation through an overly permeable gut wall, healing and restoring the integrity of the intestinal membrane may help some children overcome this sensitivity. A number of physicians have reported cases where children have been able to eat gluten and casein on a limited basis after undergoing intensive therapy to heal the intestinal tract, detoxify the system, repair nutritional deficiencies, support the nervous and immune systems, and remove heavy metals from the body. While this process can take several years and may not help all children who are sensitive to these peptides, it is nevertheless an important goal of all therapy aimed at healing these children's intestinal tracts.

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Part 5

FOOD ALLERGIES AND INTOLERANCES

Description

Children with autism tend to be sensitive to a large number of factors in their environment, including many foods. The relationship between food allergies and behavior has been extensively documented in regard to Attention Deficit Disorder (ADD) and Hyperactivity (ADHD), with the evidence showing a positive correlation between the consumption of allergenic foods and resulting behavioral aggravations in the children who were studied.^{1,2} In addition to simple allergies, food sensitivities to dyes and colorings has also been linked to impaired learning and poor academic performance in children suffering from hyperactivity.³ Similar

behavioral aggravations and neurological disturbances resulting from food allergies have also been observed in children with autism.^{4,5}

There are several different categories into which food reactions can be classified. Type 1 food allergies are also known as immediate hypersensitivity reactions because they generate symptoms immediately or very shortly after ingesting the allergenic food. These allergies are mediated by an antibody (immune cell) called Immunoglobulin E (IgE) and are often hereditary. They cause clear symptoms and strong reactions which, in some cases, may be life threatening because they can result in anaphylactic shock. People who have these types of immediate hypersensitivity reactions often have to carry an Epi-pen (Epinephrine) in case of accidental ingestion of the offending food. This is a relatively uncommon type of reaction and only makes up about 10% of all

food allergies. The foods most commonly associated with Type 1 food allergies are nuts and shellfish.

Type 2 food allergies are referred to as delayed hypersensitivity reactions because they can cause symptoms as much as 48 hours after eating the allergenic food. These allergies are often associated with the antibody known as Immunoglobulin G (IgG), but there may also be other factors, including non-antibody mechanisms, that are involved. Type 2 food allergies can be extremely difficult to diagnose because of the delay in onset of symptoms. The symptoms associated with these allergies are usually milder than those caused by Type 1 reactions, and they are not as frequently caused by hereditary factors. About 90% of food allergies can be classified as delayed hypersensitivity reactions.

While the body may develop an allergy to any food, there are a number of foods that are considered to be much more common allergens. These high-risk foods include, but are not limited to, the following:

- Wheat
- Dairy products
- Eggs
- Peanuts
- Soy
- Corn
- Citrus fruits
- Chocolate
- Tomatoes
- Sugar
- Yeast

Some food reactions are not true allergies but instead are referred to as food sensitivities or intolerances. These include not only reactions to dietary proteins but also to the additives, colorings, flavoring agents, chemicals, pesticides, and other contaminants found in foods. Food sensitivities can be either immediate or delayed, and symptoms may range from mild to severe. These sensitivities can also be difficult to diagnose because they may not trigger a measurable antibody response. Instead, they appear to cause their adverse effects by binding to certain receptor sites in the brain, mimicking neurotransmitters, and causing direct toxicity to nerve cells. Some of the substances that cause

these sensitivities, such as monosodium glutamate (MSG), are referred to as excitotoxins because they have a directly stimulating effect on the nervous system. Dr. Russell Blaylock offers a summary of how these chemicals can damage the nervous system in his outstanding book, *Excitotoxins: The Taste That Kills*.⁶

Signs And Symptoms

Food allergies can present with a variety of signs and symptoms. It is important to note that these allergies do not always manifest in overt symptoms such as hives or intestinal problems, but rather may show themselves in more chronic conditions such as eczema, headaches, behavioral problems, and immune problems. In children, one or more of the following may be present:

Digestive symptoms:

- Chronic diarrhea (often the most common symptom of food allergies)
- Alternating constipation and diarrhea
- Stomach aches or abdominal pain
- Foul-smelling stools
- Abdominal bloating and gas
- Food cravings or addictions
- Food aversions; being a "picky" eater

Other signs and symptoms:

- Allergic "shiners" (dark circles under the eyes)
- Puffiness under the eyes
- Chronic sinus drainage (post-nasal drip)
- Red rashes on the cheeks or ears, especially after eating
- Erratic behavior, such as unexplained giddiness, silliness, or laughter
- Hyperactivity
- Moodiness or irritability
- Trouble concentrating or focusing on tasks
- Sleep problems, including bed-wetting and teeth-grinding
- Foul-smelling breath, perspiration, or feet
- Inflammatory skin conditions, such as eczema, psoriasis, or hives
- Systemic reactions, including headaches, asthma, or allergies
- Recurrent infections, especially ear and throat infections
- Inappropriate weight gain

Possible Causes

There does not appear to be one specific cause for the development of food allergies and sensitivities. Instead, a variety of factors may play a role, including the following:

1. *Genetic factors* appear to play an important role in the development of allergies. It has been found that when both parents are affected with allergies, their children have a 67% chance of also having allergies. By contrast, if only one parent has allergies, the chance that their offspring will be affected is 33%.⁷
2. *Food allergies are frequently the result of an overly permeable intestinal membrane* (see discussion on Leaky Gut Syndrome above), leading to the absorption of food proteins into circulation and a resulting immune response. This is why children often end up developing allergies to those foods that they were repeatedly exposed to as an infant, or even in utero.
3. *Poor digestive processes* are often associated with the development of food allergies. Specifically, a deficiency of stomach acid and/or pancreatic enzymes can prevent the proper breakdown of foods, making a person much more susceptible to developing an allergy to these foods. Studies performed in the 1930s showed that supplementing with digestive enzymes was beneficial in the treatment of food allergies.⁸ Although these studies might be questionable because they are outdated, many physicians still use digestive enzymes for the treatments of food allergies and get very positive results.
4. *Exposure to environmental chemicals, toxins, and allergens* may also predispose a person to food allergies and sensitivities. There is increasing evidence that mercury from vaccines and heavy metals from the environment can damage the intestinal lining, increasing its permeability and ultimately resulting in the development of food allergies. One study found that application of mercury to the gut lining resulted in damage to the

epithelial cells of the jejunum (small intestine), leading to an increase in the permeability of the intestinal epithelial tissue.⁹

5. *Finally, a compromised intestinal immune system* may also set the stage for food allergies. A common factor appears to be a decrease in the amount of Secretory IgA produced by the mucosal cells lining the gastrointestinal tract.

Diagnosis

1. *Blood Testing For Food Allergies*
The subject of testing for food allergies and sensitivities is a controversial one. While blood tests often serve as a useful screening tool for uncovering some of the hidden food allergies caused by delayed hypersensitivity reactions, many scientists question their accuracy. Still, ELISA testing is preferred by many physicians who treat autistic children because, as a blood test, it is relatively easy to perform and provides parents with valuable guidelines for eliminating allergenic foods from their child's diet. ELISA food allergy testing is available from the labs discussed in Chapter 3.
2. *Skin Testing For Food Allergies*
There are several types of skin tests available for the diagnosis of food allergies. These include the skin prick test, the skin scratch test, and intradermal testing. The latter approach necessitates the injection of allergens under the skin and tends to be more accurate than tests in which the skin is merely pricked or scratched. While some allergists believe that skin tests are generally more reliable than blood tests, they can be very uncomfortable for a child and may in fact be impossible to perform in a non-compliant child.
3. *Allergy Elimination Diet*
This diet is an often intensive process that involves the complete elimination

of suspected allergenic foods for a period of time, followed by a “challenge” phase during which these foods are reintroduced in order to assess potential allergic reactions. The elimination phase usually lasts for 3 to 4 weeks, after which foods are reintroduced one by one, with the patient waiting about 4 days before the reintroduction of each new food. This 4-day wait is important because of the delayed hypersensitivity reactions, which may take up to 48 hours to cause potential symptoms. If there is an allergy to the food in question, a variety of symptoms may occur, so when working with children it is necessary for parents to closely monitor their child for any adverse reactions. While allergy elimination diets can be very accurate and do not require the financial expense of traditional allergy testing, they are only able to diagnose allergies to those foods that are removed from the diet. If all of the highly allergenic foods are removed from the diet but the child continues to eat a food they are mildly allergic to, they may still experience some of the adverse symptoms associated with food allergies. Numerous books are available on how to successfully implement an allergy elimination diet, including *Tracking Down Hidden Food Allergy* by Dr. William Crook.¹⁰

4. *Other Helpful Tests For Evaluating Food Allergies*

A number of other tests for digestive markers may also be helpful for evaluating and treating the possible cause(s) of the food allergy. These tests include:

- **Intestinal Permeability Studies:** To evaluate the presence and extent of “leaky gut syndrome” as a reason for the food allergy.
- **Comprehensive Digestive Stool Analysis (CDSA) and Organic Acid Test (OAT):** To assess the presence of intestinal dysbiosis that may be leading to the intestinal hyperpermeability. Results from the CDSA can also indicate whether there may be

a deficiency of digestive enzymes or stomach acid.

- **Secretory IgA Testing:** To determine whether there is a deficiency in this immunoglobulin that may make the intestinal tract more susceptible to the potentially allergenic properties of certain foods.

Treatment Approach

1. *Dietary Interventions*

- a) Eliminate known or suspected allergens from the diet.
- b) Avoid sugars and refined carbohydrates, which can feed yeast and other unfavorable intestinal microbes.
- c) Eat a “clean” diet, with plenty of fiber to ensure regular eliminations and support a healthy intestinal wall.
- d) If food allergy testing is not available, try an elimination diet followed by a challenge diet.
- e) A rotation diet may also be helpful for preventing future food allergies and for decreasing irritation to the gut wall by current food allergens.¹¹

2. *Heal And Repair The Intestinal Lining (See “Leaky Gut Syndrome” section)*

- a) Treat underlying dysbiosis (imbalanced microflora of the intestinal tract) with appropriate medications, including pharmaceutical drugs and nutritional supplements.
- b) Replenish the beneficial bacteria of the intestinal tract by supplementing with probiotics.
- c) Restore gut wall integrity by supplementing with nutrients that heal and decrease inflammation to the gut intestinal lining.

3. *Replace Deficient Digestive Secretions*

- a) Supplement with digestive enzymes, which have been shown to be beneficial in the treatment of food allergies

- b) Prescription agents such as Secretin, Bethanechol, and IVIG may be beneficial for supporting the body's digestive processes. Supplement with Betaine HCl (hydrochloric acid, or stomach acid), only where appropriate and under the guidance of a physician. Please refer to Chapter 6 for more information on this product.
- c) Supplement with Betaine HCl (hydrochloric acid, or stomach acid), only where appropriate and under the guidance of a physician. Please refer to Chapter 5 for more information on this product.

4. *Reduce Allergic Reactivity*

- a) A number of supplements, including Vitamin C, bioflavonoids such as Quercetin, and proanthocyanidins such as Grape Seed Extract, tend to reduce allergic reactivity by stabilizing mast cells, which are the cells involved in the histamine response.
- b) MSM may also be helpful because it can decrease histamine release, which is the main cause of most of the symptoms associated with allergies.

5. *Consider Using Complementary Allergy Elimination Treatments*

Some practitioners use techniques for treating allergies that are not generally accepted by the mainstream medical community. In spite of the "complementary" nature of these therapies, many parents of ASD children have reported remarkable improvements in the severity of their child's food allergies, and in some cases the adverse food reactions have been eliminated altogether. Two of the most common methods of allergy elimination treatment are:

- a) Enzyme Potentiated Desensitization (EPD) Allergy Therapy:
This may be a promising approach for eliminating food allergies in some patients. EPD requires strict control of food and dietary exposures to allergens, as well as a

series of injections to neutralize the allergies in question, so it may be a difficult therapy for very young children. More information is available from the American EPD Society in New Mexico at (505) 983-8890, or from their website at www.food-allergy.org/epd.

- b) Nambudripad's Allergy Elimination Technique (NAET):

Like EPD, this is another potentially useful allergy elimination technique that, though not widely accepted by the mainstream medical community, has been reported by some parents to be beneficial in eliminating their child's food allergies. NAET is generally noninvasive and utilizes applied kinesiology and specific pressure points on the body. More information on this technique is available at www.naet.com.

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- ¹¹ For more information on implementing a rotation diet, see the books and educational materials by nutritionist Sally Rockwell, Ph.D. A good place to start is with the book: Rotated Allergy Recipes – Delicious, Allergy-Free, Quick and Easy Meals! Available at many bookstores and from the Alternative Medicine Connection website (www.arxc.com)

Part 6

MALDIGESTION AND MALABSORPTION

Description

Maldigestion and malabsorption¹ are two very common intestinal problems seen in children with autism spectrum disorders. Maldigestion is defined as the incomplete breakdown (digestion) of foods. It often leads to malabsorption, a term that refers to the disordered or incomplete uptake of nutrients from the intestinal tract.

Since various nutrients (vitamins, minerals, proteins, carbohydrates, fats) are absorbed in different portions of the intestinal tract, malabsorption problems can potentially lead to nutrient deficiencies. Even if a person is eating the best diet in the world, they will invariably have nutritional deficiencies if the food they are consuming is not being properly digested. Maldigestion is usually due to a lack of digestive "juices", such as stomach acid, pancreatic

enzymes, and other secretions. In a similar light, even if the digestive process is functioning well and food is being properly broken down, there may still be nutrient deficiencies if the food is not being adequately absorbed from the intestinal tract into the bloodstream. Malabsorption may be caused by conditions where there is damage to or inflammation of the intestinal wall.

Deficiencies in digestive secretions, including stomach acid and pancreatic enzymes, can lead to many of the problems that are commonly encountered in children with ASD. Pancreatic fluid, for example, has significant antibacterial activity against intestinal organisms such as *E. coli*, *Shigella* species, *Salmonella* species, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. In addition, the pancreatic secretions also have fungistatic activity against *Candida albicans*.² When there is a deficiency of these pancreatic secretions, the intestinal tract is more prone to overgrowth and infection with these pathogenic microbes.

In a similar fashion, hydrochloric acid (HCl, or

stomach acid) also helps to keep these infectious organisms at bay. A deficiency of HCl, also referred to as hypochlorhydria, leads to increased sensitivity to intestinal infections³ and a higher rate of Candida overgrowth in the stomach.⁴

The consequences of malabsorption can be profound. Besides causing overt gastrointestinal symptoms such as diarrhea, gas, and abdominal pain, this condition can also lead to a variety of systemic problems. Because the body is an intricate system that requires all available nutrients in order to function, a deficiency in even one nutrient can have serious implications and eventually lead to disease.

In order to illustrate this point further, let us take the example of just one nutrient: the mineral zinc. Zinc deficiency, as measured by plasma (blood) zinc concentration, is a common consequence of intestinal inflammation.^{5,6} When zinc deficiency is present, there is a resulting decrease in normal cellular immunity, making the intestinal tract more prone to infection with pathogenic bacteria and viruses.⁷ These types of intestinal infection can produce diarrhea, further diminishing nutrient absorption and leading to even greater malabsorption and nutritional deficiencies.⁸

The zinc deficiency that results from this vicious cycle can show its effects in a variety of ways. Since zinc appears to play an important role in inducing the synthesis of metallothionein, an enzyme that acts as a scavenger of metals and free radicals, zinc deficiency can make the system more vulnerable to damage from heavy metals and other toxins.^{9,10} Zinc is an important nutrient for the immune system, and supplementation with this mineral has been shown to reduce the duration of the common cold^{11,12} and suppress the inflammation in the respiratory tract caused by the human rhinovirus, the virus responsible for the common cold.¹³ Of particular interest to the discussion of autism is that zinc deficiency during development can adversely affect learning, memory, and attention,¹⁴ as well as being associated with reduced activity, reduced participation, and slower response times.¹⁵

Zinc is only one of the many nutrients in the body that can become deficient if there is significant maldigestion and/or malabsorption. Because these problems are so prevalent in autistic chil-

dren, it is important not only to address nutrient deficiencies by supplementing with a complete multi-vitamin and mineral formula, but also to correct the underlying digestive imbalances so as to ensure that the nutrients in foods can be appropriately utilized in the future.

Signs And Symptoms

Some of the common signs and symptoms of these conditions are:

- Abdominal cramps and pain
- Indigestion (belching, bloating, reflux, or discomfort after meals)
- Excessive gas; foul-smelling gas
- Diarrhea, constipation, or alternating constipation and diarrhea
- Abnormal color of stools (yellow, orange, or pale stools)
- Abnormal texture of stools (unformed, runny, or "foamy" stools)
- Undigested food in the stools
- Mucous in the stools
- Foul-smelling stools
- Rectal burning or itching
- Dry skin, brittle hair, or vertical ridges on the fingernails
- Mental difficulties such as depression or inability to focus
- Tendency to bruise easily
- Weight loss, or difficulty gaining weight

Possible Causes

1. *Maldigestion may be caused by:*
 - Insufficient mechanical breakdown (chewing) of food in the mouth
 - Deficiency of hydrochloric acid (stomach acid)
 - Insufficient pancreatic secretion of digestive enzymes
 - Insufficiencies in other secretions necessary for proper digestion, such as bicarbonate, Secretin, cholecystokinin (CCK), and bile
 - Excessive use of antacids or drugs that block stomach acid
 - Diseases involving the pancreas, such as cystic fibrosis or cancer

2. *Malabsorption may be caused by:*
 - Intestinal infections or overgrowth with yeast, bacteria, parasites, and other harmful organisms (“intestinal dysbiosis”)
 - Food allergies and sensitivities (including gluten and casein)
 - Celiac disease (a genetic disease of gluten intolerance)
 - Inflammatory bowel diseases
 - Chronic diarrhea resulting in overly rapid bowel transit time
 - Poor diet, especially a diet high in sugar and low in fiber
 - Certain drugs
 - Weakened intestinal immune system and impaired ability to repair the tissue of the intestinal wall

Diagnosis

1. *Comprehensive Digestive Stool Analysis (CDSA)*
The CDSA tests for markers that indicate the body's ability to digest and absorb the nutrients in foods. It also reflects pancreatic enzyme status and identifies the presence of abnormal microorganisms in the intestinal tract.
2. *Organic Acid Test*
This can be a good complementary test, along with the CDSA, to diagnose underlying states of intestinal dysbiosis.
3. *Gluten Antibody Studies / Lactose Breath Test*
In cases of malabsorption, it is important to rule out celiac disease and lactose intolerance if the child is not completely gluten and casein free.
4. *Food Allergy Testing*
Eating allergenic foods can cause irritation to and inflammation of the gut wall, potentially leading to diarrhea and malabsorption. It is essential to explore the possibility of food allergies as being the underlying cause of the malabsorption problems.

5. *Intestinal Permeability Studies*
Intestinal Permeability Studies are helpful to evaluate the efficiency of absorption and also to check for the presence of “Leaky Gut Syndrome”, which may also adversely affect the processes of digestion and absorption.
6. *Nutritional Profile Testing*
Tests to diagnose deficiencies in vitamins, minerals, amino acids, essential fatty acids, and other nutrients can provide an indication of whether there are problems with the absorption of these nutrients from the intestinal tract.
7. *Diagnostic Imaging*
Looking at the gastrointestinal mucosa through endoscopy or colonoscopy may be necessary in some cases to evaluate the state of intestinal inflammation and dysfunction. An accompanying biopsy of the GI tissue may also be indicated.
8. *Stomach Acid Analysis*
Some nutritionally oriented physicians find it valuable to perform certain tests, such as the Heidelberg Test, that evaluates gastric acidity and provides an indication of whether there is sufficient stomach acid available for the proper digestion of food. While this may be a valuable approach, the test traditionally has been somewhat invasive and difficult to perform in a child. New technology may be making this test more feasible, and it may be worthwhile discussing this with your physician.

Treatment Approach

1. *Identify And Remove The Underlying Cause*
 - Use antacids conservatively and speak with your child's physician if s/he is taking drugs that block stomach acid or any other drugs that may result in malabsorption.
 - Remove gluten and casein from the diet, as these are common causes of intestinal irritation and inflammation.

- Remove foods from the diet that the child is allergic to, also because of their pro-inflammatory characteristics.
- Decrease the amount of sugar in the diet and increase the child's consumption of fiber and nutrient-rich foods (fruits, vegetables, whole grains, protein sources, beans and legumes, and essential fatty acids).

2. *Replace Deficient Digestive Secretions*

- Digestive Enzymes: Most cases of maldigestion respond very well to supplementation with digestive enzymes.
- Secretin: Many children with autism have received significant results from Secretin therapy, not only in improving digestion, but also in behavioral and cognitive function.
- Bethanechol: Dr. Mary Megson pioneered the use of the pharmaceutical drug Bethanechol stimulate the digestive process.
- Betaine HCl: In clear cases of hypochlorhydria (low stomach acid), it may be necessary to supplement with Betaine HCl (hydrochloric acid) in order to improve digestive processes. However, Betaine HCl should be used only when appropriate and under the guidance of a physician. Please refer to Chapter 5 for more information on this product.

3. *Heal And Repair The Intestinal Tract*

- Treat underlying intestinal dysbiosis with the appropriate supplements and pharmaceutical drugs.
- Replace the beneficial intestinal microflora by supplementing with probiotics.
- Take measures to repair the intestinal wall by supplementing with gut-healing nutrients and preventing future irritation by chemicals, toxins, and offending foods.
- Support the intestinal immune

system so that the body has adequate resources for gut healing to take place.

4. *Supportive Measures*

- Correct nutritional deficiencies by supplementing with a complete multi-vitamin and mineral formula, and with any other nutrients that may be deficient due to prolonged malabsorption.

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Part 7

DIARRHEA

Description

Diarrhea is defined as the frequent passage of watery, unformed stools. It occurs when there is an overly rapid bowel transit time, which means that the fecal matter does not stay in the colon long enough for fluid to be reabsorbed into the body, resulting in watery stools. In cases of chronic diarrhea, or when there is

acute diarrhea that is severe, this insufficient reuptake of water from the stool may result in dehydration. In addition, prolonged diarrhea can lead to multiple nutrient deficiencies because food is not staying in the digestive system long enough for vitamins, minerals, proteins, and other nutrients to be absorbed.

Diarrhea is a common affliction of children with autism spectrum disorders. Diarrhea is not a disease in and of itself, but rather reflects the varying degrees of intestinal pathology that are present in the child. Some individuals with ASD

experience mild, transient episodes of diarrhea, while for others the problem is serious and persistent. There can be many different causes for this disorder, so appropriate testing and diagnosis are essential. It is important to work with a physician in cases where the symptoms are severe, since there may be serious consequences such as dehydration or nutritional deficiency.

Signs And Symptoms

- Loose, watery, unformed stools
- Excessively frequent bowel movements
- Evidence of undigested food in the stool
- Abnormally colored stools
- Foul-smelling stools
- May be accompanied by abdominal cramping, bloating, and gas

Possible Causes

Chronic diarrhea may be due to a number of factors, including:

- Food allergies (chronic diarrhea is one of the most common manifestations of food allergies)
- Lactose intolerance and gluten enteropathy in individuals who are not gluten and casein free
- Malabsorption syndromes, especially inadequate bile secretion leading to fat malabsorption
- Intestinal dysbiosis (infection with yeast, bacteria, viruses, or parasites)
- Probiotic deficiency
- Insufficient pancreatic production of digestive enzymes
- Deficiency of the hormone Secretin
- Inflammatory bowel disease
- Irritable bowel syndrome
- Fecal obstruction that can result in overflow diarrhea

Acute episodes of diarrhea, or recent development of diarrhea, may be due to:

- Antibiotic therapy
- Recent introduction of high doses of Vitamin C or magnesium
- Use of drugs such as laxatives or magne-

- sium-containing antacids
- Contaminated water supply leading to parasite infection
- Acute viral or bacterial intestinal infection (usually accompanied by fever)
- Consumption of large amounts of certain low-calorie sweeteners, such as mannitol, xylitol, sorbitol, and fructose

Diagnosis

The underlying factors causing the diarrhea should be thoroughly investigated by a physician through history, physical exam, and appropriate laboratory testing. It is important to correct this problem, since it can lead to some potentially serious consequences. Some of the laboratory tests that may be helpful include:

1. *Comprehensive Digestive Stool Analysis (CDSA)*
The purpose of this test is to assess the status of probiotics and to identify whether there are any abnormal organisms present in the digestive tract.
2. *Parasitology Testing*
Usually performed along with the CDSA, parasitology testing detects the presence of harmful parasites in the stool.
3. *Organic Acid Test*
This may be helpful, along with the CDSA, to diagnose underlying states of dysbiosis and determine whether there may be a problem with the bacterium *Clostridium difficile*.
4. *Food Allergy Testing*
Since chronic diarrhea is one of the most common symptoms of food allergies, doing a test for the presence of these allergies can provide guidelines for the elimination of offending foods from the diet.
5. *Gluten Antibody Studies / Lactose Breath Test*
If the child is not completely gluten and casein free, it may be necessary to perform gluten antibody testing to rule out celiac disease, a common cause of diarrhea. A lactose breath test can also

be diagnostic for lactose intolerance, which is frequently responsible for diarrhea in children.

6. *Diagnostic Imaging*

If fecal impaction is suspected as producing an overflow diarrhea, your child's pediatrician may choose to do an abdominal x-ray to rule this out. In addition, chronic bowel problems may warrant further diagnostic studies, including endoscopy, colonoscopy, and possibly accompanying tissue biopsies.

Treatment Approach

Ideally, a physician should always be consulted when working with a patient who has chronic diarrhea. In the following cases, the patient should be evaluated by a physician as soon as possible:

- Acute, sudden-onset diarrhea
- Bloody diarrhea
- Severe diarrhea in an infant or child less than 6 years old
- Diarrhea with significant signs of dehydration, such as sunken eyes, decreased skin turgor, or strong body odor

Treatment approaches for diarrhea are as follows:

1. *Identify And Remove The Underlying Cause*

- Taper doses of Vitamin C and magnesium until diarrhea stabilizes, then gradually increase until maintenance doses are reached.
- Eliminate or decrease potentially problematic sweeteners, such as mannitol, xylitol, sorbitol, and fructose.
- Eliminate irritating foods from the diet, such as food allergens, gluten, and casein.
- Stop or decrease the use of laxatives, if these appear to be causing the diarrhea.
- Replace beneficial intestinal probiotics if the child develops diarrhea from antibiotic therapy.

2. *Correct Intestinal Dysbiosis*

- Give appropriate treatments to eradicate pathogenic yeast, bacteria, viruses, and parasites. (See the following sections for more information.)
- Re-establish a healthy bacterial balance by supplementing with probiotics.

3. *Replace Deficient Digestive Secretions*

- Digestive enzymes can be helpful for treating diarrhea because they enhance digestion and correct malabsorption.
- Secretin therapy has been extremely helpful for many autistic children with chronic diarrhea and other intestinal problems.

4. *Restore Intestinal Balance By supplementing With Probiotics*

Supplementing with probiotics is essential when treating any type of diarrhea, but especially diarrhea that has resulted from the use of antibiotics. *Lactobacillus acidophilus* has been shown to be effective in treating both viral and antibiotic-produced diarrheas.¹ Another strain of probiotic, *Lactobacillus GG*, appears to produce positive benefits when used in the treatment of diarrhea related to *Clostridium difficile*.^{2,3}

5. *Pharmaceutical Drugs To Treat Diarrhea*

These drugs may be necessary in cases of diarrhea that do not respond to dietary intervention or natural supplementation.

- In cases of persistent diarrhea that is due to pathogenic bacteria, it may be necessary to give antibiotics in order to eradicate these bacteria and give the intestinal tract a chance to heal. However, since antibiotics also tend to cause diarrhea, aggressive supplementation with probiotics is warranted.
- There are several drugs that can slow gastrointestinal motility and thereby decrease the rate at which food is passing through the intestinal tract. Examples of these

drugs are Imodium and Lomotil. While these drugs may be helpful for eliminating symptoms, it is crucial that they only be used in the treatment of chronic diarrhea after obtaining a stool culture. If there is an intestinal infection or overgrowth with a pathogenic organism, slowing down intestinal motility can actually end up prolonging the infection.

- The use of Secretin has also been helpful for many children with autism who suffer from chronic diarrhea.

6. *Nutritional Supplements For The Treatment Of Diarrhea*

- Digestive Enzymes
- Probiotics
- Calcium: Calcium may be helpful in the symptomatic treatment of diarrhea because it is mildly constipating in nature and can help to firm up stools.
- Pectin and Kaolin: Pectin is a type of fiber found in some fruits and vegetables. While too much fiber can actually cause diarrhea, small amounts of pectin fiber can bind up the water in the stool, making it firmer and minimizing diarrhea. Pectin may be used alone or in combination with Kaolin, a type of clay that acts as a bulking agent and can improve the consistency of the stool. Pectin can be taken alone (available from health food stores) or in combination with Kaolin (commercially available in the non-prescription product Kaopectate).
- Carob Powder: Carob has long been considered a safe and effective agent for the symptomatic treatment of diarrhea. It appears to have especially good benefits for treating diarrhea in young children. In one study of 41 infants conducted in a hospital setting,⁴ the duration of diarrhea in the group given carob powder was 2 days, whereas the children who were given a placebo had

diarrhea for an average of 3.75 days. Carob was also effective at reducing vomiting and other side effects, and no adverse effects from this supplement were reported. Carob powder is available from most health food stores and can be mixed into applesauce and other foods. It is generally dosed at 1 teaspoon 2-3 times per day, until symptoms resolve.

- Zinc: A recent study demonstrated that zinc deficiency can result in a weakened intestinal immune system, making the digestive tract more prone to infection with certain parasites.⁵

7. *Supportive Measures*

- Dietary Support: In cases of acute diarrhea, many nutritionists recommend following a bland diet, called a BRAT diet, until symptoms have resolved. BRAT stands for "Bananas, Rice, Applesauce, and Toast" (gluten-free, in this case). All of these foods are soothing to the intestinal tract and contain some gentle forms of fiber that can help to bulk up the stools.
- Replace Fluids: When diarrhea is significant, it is important to replace lost fluids and electrolytes. Make sure your child is drinking plenty of water. Electrolyte drinks, such as Pedialyte and Gatorade, are also indicated for replenishing electrolytes.
- Prevent Nutrient Deficiencies: If the diarrhea has been chronic and prolonged, testing for and correction of nutritional deficiencies is a good idea. This is because diarrhea usually results in nutrient deficiencies when the food does not stay in the intestinal tract long enough for it to be properly broken down and absorbed.

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Part 8

CONSTIPATION

Description

Constipation is defined as difficult or infrequent bowel movements with the passage of abnormally dry or hard fecal matter. Constipation is not a disease in and of itself, but instead a symptom of an underlying disturbance, usually of the intestinal system. It is important to find the underlying cause of the constipation in order to be able to treat it effectively. While there are no specific criteria for the ideal number of daily or weekly bowel movements, researchers generally consider two or fewer bowel movements per week to be constipation. Most nutritionally oriented health care providers try to regulate their patients' digestive function so that they are having 1-2 well-formed bowel movements per day. This supports the body's detoxification mechanisms and also helps prevent the potentially detrimental consequences of abnormal gut fermentation that can result from constipation.

Constipation is another common problem among children with autism¹ and ASD. One should always suspect underlying problems with constipation when there is toe-walking in the child. It is important to address this problem, since untreated constipation may result in more serious consequences such as fecal impaction.

Signs And Symptoms

- Infrequent bowel movements
- Abnormally dry or hard stools that are difficult to pass
- Bowel movements may be painful
- Abdominal discomfort and/or bloating is often present
- Chronic constipation can result in the development of hemorrhoids
- Toe-walking in an autistic child may indicate constipation problems

Possible Causes

1. *Dietary Factors*
 - A diet that is low in fiber and high in refined, processed foods
 - Insufficient intake of fluids
 - Hyperglycemia (high blood sugar) has been shown in a number of studies^{2,3,4} to cause constipation by decreasing gastrointestinal motility. While most of these tests were performed on subjects who were diabetics, there is much evidence to suggest that a diet high in sugar and carbohydrates can have similar effects in the causation of constipation.
 - Food allergies and sensitivities
2. *Intestinal Disorders*
 - Leaky gut syndrome
 - Intestinal overgrowth with pathogenic yeast and bacteria

- Structural abnormalities of the bowel
- Decreased smooth muscle tone of the intestines
- Nerve disorders of the bowel

3. *Pharmaceutical Drugs and Nutritional Supplements*

- A number of pharmaceutical drugs may cause constipation, including some drugs in the following categories:
 - Anti-seizure medications
 - Antidepressants
 - Pain relievers
 - Aluminum containing antacids
- There are also some nutritional supplements that tend to be constipating:
 - Calcium
 - Iron

4. *Other Potential Causes*

- Stress
- Low thyroid function
- Magnesium deficiency
- Lack of exercise and physical activity
- Some autistic individuals may be unaware of the urge to defecate, which can lead to chronic constipation

Diagnosis

1. *Comprehensive Digestive Stool Analysis (CDSA)*

The CDSA is a valuable test for diagnosing intestinal dysbiosis and determining whether there are any potentially harmful microbes that might be causing the constipation.

2. *Organic Acid Test*

This test may also be helpful, along with the CDSA, to diagnose underlying states of intestinal dysbiosis.

3. *Food Allergy Testing*

While food allergies more commonly result in chronic diarrhea, they can also cause constipation and this should be investigated as a possible causative factor.

4. *Metabolic Screening And Thyroid Panel* Hypothyroidism (low thyroid function) is a

common cause of constipation and is being diagnosed increasingly more often in children with developmental disorders. Metabolic screening can pick up magnesium deficiency and calcium excess, both of which can also contribute to constipation.

5. *Diagnostic Imaging*

A special type of x-ray study known as a KUB can reveal the presence of fecal impaction as the cause of constipation. Other diagnostic imaging studies are useful for determining whether there are structural abnormalities of the bowel or acute bowel strictures.

Treatment Approach

1. *Identify And Remove The Underlying Cause*

- Modify doses of calcium and iron, if these are suspected to have led to constipation.
- Speak with your child's physician if the constipation started shortly after introducing a new pharmaceutical drug.
- Supplement with magnesium if there is shown to be a deficiency.
- Treat any underlying thyroid or other metabolic disorders.
- Ensure that your child is getting adequate exercise and physical activity.

2. *Dietary Interventions*

- Reduce dietary intake of sugars, simple carbohydrates, and refined and processed foods.
- Increase the intake of dietary fiber, which is found in fruits, vegetables, whole grains, beans, legumes, nuts, and seeds. Make these changes gradually, since a rapid increase in the consumption of dietary fiber can lead to gas.
- Increase water and other fluids. For many children who suffer from chronic constipation, this

simple intervention is often enough to help them have more regular bowel movements.

- Eliminate foods from the diet that the child is allergic or sensitive to.

3. *Correct Underlying Digestive Dysfunction*

- Remove intestinal pathogens such as yeast and bacteria.
- Treat leaky gut syndrome by repairing the intestinal wall.
- In rare cases, surgery may be necessary to correct structural abnormalities of the bowel.

4. *Restore Intestinal Balance By Supplementing With Probiotics*

- Probiotics: These beneficial bacteria are extremely important in the treatment of constipation. Improving intestinal microflora through probiotic supplementation can increase bowel motility.

5. *Replace Deficient Digestive Secretions*

- Digestive Enzymes: Supplementing with digestive enzymes can also be helpful in the treatment of constipation.

6. *Pharmaceutical Drugs To Treat Constipation*

These drugs may be necessary in cases of constipation that do not respond to dietary intervention or natural supplementation.

- X-Prep (Senokot): A laxative containing Senna that can be helpful in stimulating intestinal motility.
- Miralax: A synthetic polyglycol that causes water to be retained in the stool, thus making the stool softer and easier to eliminate.
- Fleet® Enema For Children: In some cases of severe constipation that is not responding to oral treatment, the topical stool-softening effects of an enema become necessary for bowel

evacuation.

- Docusate Sodium: A stool softener that can facilitate the elimination of stool.

7. *Nutritional Supplements For The Treatment Of Constipation*

- Probiotics
- Digestive Enzymes
- Fiber: Supplementing with fiber is a helpful intervention for children who are unable to get sufficient amounts of fiber through their diet. Pectin is a type of fiber that occurs in some fruits and vegetables and is very gentle on the system. Psyllium fiber comes from the husk of the psyllium seed and has been shown in studies to be more effective in treating chronic constipation than the pharmaceutical stool softener docusate sodium.⁵ These fiber products are available from most health food stores. Ground flaxseed meal, available from Kirkman Laboratories, is also an excellent source of fiber and has the added benefit of containing beneficial Omega-3 fatty acids.
- Magnesium: This mineral has been helpful for many autistic children who suffer from constipation. Magnesium is a smooth muscle relaxant, and it helps to eliminate stool by promoting intestinal peristalsis (rhythmic contractions of the intestinal smooth muscle). One of the side effects of high amounts of magnesium supplementation is diarrhea, so the child's dose should be increased gradually until the desired effects are achieved.
- Vitamin C: Vitamin C is a stool softener and can help promote elimination by making the stool easier to pass.
- Aloe vera: The resin (not the gel) from the inside of the leaf of the Aloe vera plant has shown great benefits as a laxative. It is best taken in capsule form (available from health food stores), and the

- manufacturer's dosage recommendations should be followed.
- Omega-3 Fatty Acids: Supplementing with essential fatty acids, such as flaxseed oil, can help lubricate the bowel and promote more regular eliminations.
 - Methylsulfonylmethane (MSM): This supplement has been found to be beneficial in many cases of mild constipation. It appears to have its effects through its high sulfur content.
 - Senna: This herb is part of many laxative teas and herbal formulas that are sold in health food stores. It should be used with caution, since many people with chronic constipation have become depen-

dent upon its laxative effects. For children with autism, it can be a good "rescue" measure when other therapies have not helped and there is an acute state of significant constipation.

- Mineral Oil: This is a remedy for constipation that has been used for many years. The mineral oil is taken orally, and it has a lubricating effect on the intestines and usually produces a bowel movement within 24 hours. It should also be used with caution, however, because it may interfere with the absorption of essential fatty acids and the fat-soluble vitamins A, D, E, and K.

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Part 9

INFLAMMATORY GASTROINTESTINAL DISEASE

Description

Studies have revealed that many children with autism spectrum disorders suffer from a number of inflammatory gastrointestinal conditions. One study of 36 children with autism revealed histological evidence of grade I or II reflux esophagitis in 25 subjects, (69.4%), chronic gastritis in 15 (41.7%), chronic duodenitis in 24 (66.7%), and low intestinal carbohydrate digestive enzyme activity

in 21 (58.3%).¹ Reflux esophagitis is an inflammation of the esophagus produced when the gastric contents reflux (flow backward) from the stomach into the esophagus. It can cause pain, discomfort, and may ultimately result in ulceration of the esophageal tissue due to the acidity of the gastric juices. Gastritis is characterized by inflammation of the stomach lining that may result from infection, dietary factors, or a deficiency of hydrochloric acid (stomach acid). Duodenitis is an inflammatory condition of the duodenum, the first part of the small intestine.

Another inflammatory condition of the intestinal tract, referred to as "autistic enterocolitis",

has recently been identified as a form of bowel inflammation unique to children with autism.² Enterocolitis is defined as an inflammation of the intestines and colon and may be caused by a number of factors, including food sensitivities, improper digestion, heavy metal toxicity, and injuries from vaccines. Inflammation of the intestines can lead to the development of “leaky gut syndrome”, characterized by an overly permeable gut wall that is the primary cause of other problems such as food allergies. All of these inflammatory bowel disorders are conditions that can lead to potentially serious problems such as malabsorption, leaky gut syndrome, diarrhea, and even ulceration of the intestinal membrane.

Signs And Symptoms

There are so many possible signs and symptoms associated with the inflammatory gastrointestinal diseases that it would be difficult to list them all. However, some of the more common manifestations are listed below.

1. *Reflux esophagitis may present with the following symptoms:*
 - Heartburn; burning sensation in the throat, stomach, or behind the breastbone
 - Frequent belching
 - Sour taste in the mouth
 - Chest discomfort or pain over the breastbone
 - Frequent coughing or asthma at night
 - Hiccups
 - Hoarse voice
 - Difficulty swallowing food or drink
2. *Gastritis may present with the following symptoms:*
 - Stomach pain or discomfort, especially after meals
 - Indigestion
 - Feeling of fullness after meals
 - Bad breath
 - Loss of appetite
3. *Enterocolitis and duodenitis may be associated with the following:*
 - Abdominal pain, cramps, or discomfort

- Diarrhea or loose stools
- Abnormal stools (color, texture, odor)
- Mucous in the stools; possibly blood in the stools
- Abdominal bloating
- Gas
- Malabsorption with resulting nutrient deficiencies
- Damage to the intestinal membrane, including leaky gut syndrome
- May have loss of appetite, weight loss, or difficulty gaining weight

Possible Causes

1. *Dietary Irritants*
 - Food allergies
 - Gluten and casein
 - A high-sugar, low-fiber diet
 - Chemicals ingested in foods, such as artificial additives and preservatives, food dyes, certain sweeteners, pesticides, and hormones (these can cause oxidative damage to the gut lining, making the tissue more prone to inflammation)
2. *Digestive Imbalances*
 - Intestinal overgrowth or infection with pathogenic bacteria, yeast, viruses, or parasites (intestinal dysbiosis)
 - Lack of beneficial intestinal bacteria (probiotics)
 - Insufficient digestive secretions, leading to incompletely digested food proteins that can irritate the gut wall
3. *Medications*
 - Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) are widely recognized to cause damage to the gastrointestinal mucosa.
 - Antibiotics can cause inflammatory bowel disorders such as Crohn's disease.³ Many parents who have an autistic child believe that their child's symptoms first began shortly after receiving multiple rounds of antibiotics.
 - Corticosteroids have also been linked to intestinal damage and inflammation.

4. *Vaccinations*

New evidence has been emerging in recent years that some of the viral vaccines may play a role in the inflammatory bowel conditions seen in many autistic children. Dr. Andrew Wakefield and his colleagues at the Royal Free Hospital in England have published several articles suggesting that the measles-mumps-rubella (MMR) vaccine has been linked to a damaged and inflamed intestinal lining in children with autism.^{4,5,6,7} Intestinal biopsies performed by Wakefield and his fellow researchers have revealed that autistic children show the presence of a particular strain of the measles virus in their gut membrane that is identical to that found in the MMR vaccine. This appears to be associated with a particular form of intestinal inflammation known as "ileocolonic lymphoid nodular hyperplasia" (LNH). While this connection between vaccines and intestinal damage in children with ASD has been vehemently debated in the medical community, there continues to be well-established documentation in favor of this conclusion.

5. *Heavy Metals*

Any outside factor that irritates or damages the gut wall can cause the intestinal tract to become inflamed. Recently, a great deal of focus has been placed on a mercury-containing preservative called thimerosal that is present in many vaccines. In their excellent review article "Autism: A Novel Form Of Mercury Poisoning", Sallie Bernard and colleagues summarize over 180 articles relating to the toxic effects of mercury and its relationship to autism.⁸ In specific regard to the intestinal tract, scientists and researchers are finding evidence that both injected and orally ingested mercury and other heavy metals can directly damage the epithelial lining of the gastrointestinal tract. One study found that application of mercury to the gut lining resulted in damage to jejunal (small intestine) epithelial cells, increased permeability of intestinal epithelial tissue, and direct genotoxic and cytotoxic effects on isolated intestinal epithelial cells in vitro.⁹ Another study of thimerosal, which

consists of 49.6% ethyl mercury,¹⁰ describes how it can cause direct damage to cells.¹¹ It is clear that the damage resulting from these heavy metals can in part explain the significant inflammatory processes that are seen in the intestinal tracts of many children with autism.

6. *Compromised Intestinal Immunity*

Inflammatory bowel diseases can both be the cause of and also the result of a weakened intestinal immune system. Generally, if the intestinal immune system is compromised, it is unable to respond adequately to the inflammatory processes that are occurring in the gut. This can delay the healing process and prolong the inflammatory dysfunction.

Diagnosis

Other than relying on overt signs and symptoms, the only way to accurately diagnose inflammatory bowel disease is through an endoscopy or colonoscopy with biopsy of the gastrointestinal tissue. In order to understand the underlying cause of the inflammation, however, some of the following adjunct tests may be run as a way to narrow the focus of therapeutic intervention. If you suspect that your child is experiencing colitis, gastritis, or reflux esophagitis, it is important to consult a physician as soon as possible for the appropriate evaluation, since these conditions can lead to serious consequences if left untreated.

1. *Comprehensive Digestive Stool Analysis (CDSA)*

This test can help determine whether the underlying cause of the intestinal inflammation might be dysbiosis, digestive enzyme insufficiency, deficiency of other digestive secretions, or lack of beneficial intestinal bacteria (probiotics).

2. *Organic Acid Test*

This test can also be helpful, along with the CDSA, to diagnose underlying states of intestinal dysbiosis.

3. *Food Allergy Testing*
Since consuming allergenic foods can irritate and cause inflammation of the gut wall, food allergy testing is a valuable part of the therapeutic approach.
4. *Gluten Antibody Studies / Lactose Breath Test*
In cases of malabsorption, it is important to rule out celiac disease and lactose intolerance if the child is not completely gluten and casein free, as these proteins can cause profound inflammation of the intestinal wall.
5. *Intestinal Permeability Studies*
Performing intestinal permeability studies to assess the presence of leaky gut syndrome can be a helpful way to assess the degree of damage that the inflammatory bowel changes may have caused to the intestinal wall.
6. *Heavy Metal Testing*
Since one of the causes of inflammatory bowel conditions may be damage from heavy metals, it is important to assess this as a potential causative factor. Tests such as a DMSA Urine Challenge or a Packed Red Blood Cell Study can provide clues to the amount of heavy metals in a child's system. For more information on testing for and treating heavy metal toxicity, please consult the DAN! Consensus Report on mercury chelation.¹²
7. *Immune Assays*
In some cases of significant inflammatory bowel disease, the immune system may become severely compromised, and assessing its status through laboratory testing can further refine the treatment approach. Performing Immunological Studies or testing for Secretory IgA can help shed light on the health of the intestinal immune system.

Treatment Approach

The best way to treat the inflammatory gastrointestinal diseases is to by using a "go-slow"

approach. In cases of severe GI inflammation, it may be necessary to start with nutrients that are healing and soothing to the gut wall before delving into some of the more specifically directed treatments. For example, a stool culture may reveal an insufficient balance of probiotics in the intestinal tract. If probiotics are supplemented right away and there is a great deal of intestinal inflammation present, the child may experience significant gas and abdominal discomfort that can make it appear that their condition is getting worse instead of better. In this case, a gentler approach would be to begin treatment with anti-inflammatory and gut-healing nutrients such as Colostrum, Essential Fatty Acids, L-Glutamine, Zinc, and a number of soothing herbs that are discussed in Chapter 5 and also in the section on treating Leaky Gut Syndrome. It is often necessary to give these supplements for a month or two until the GI inflammation has improved, and then begin further treatment with the appropriate nutrients that address the underlying cause of the inflammation. The general treatment approach for gastrointestinal inflammation is as follows:

1. Identify and Remove The Underlying Cause

- Remove gluten and casein from the diet, as these are common causes of intestinal irritation and inflammation.
- Remove foods from the diet that the child is allergic to, also because of their pro-inflammatory characteristics.
- Decrease the amount of sugar in the diet and increase the child's consumption of fiber and nutrient-rich foods (fruits, vegetables, whole grains, protein sources, beans and legumes, and essential fatty acids).
- Be cautious with pharmaceutical drugs that can damage the GI membrane, including antibiotics, corticosteroids, aspirin, and other non-steroidal anti-inflammatory drugs. Speak with your child's physician about the use of these drugs.
- Try to limit the amount of chemicals ingested in foods, such as artificial additives and preserva-

tives, food dyes, certain sweeteners, flavoring agents, pesticides, and hormones.

2. *Replace Deficient Digestive Secretions*

- **Digestive Enzymes:** Many cases of inflammatory bowel disease respond positively to supplementation with digestive enzymes, especially when the inflammation is caused by food allergies, casein and gluten sensitivity, and insufficient breakdown of dietary proteins. However, in cases where there are severe inflammatory changes with ulceration of the gastrointestinal membrane, digestive enzymes may further irritate the already compromised gut membrane. In these cases, it is important to use digestive enzymes under the guidance of a physician.
- **Other Digestive Secretions:** Treatment with Secretin, Bicarbonate, or Bethanechol may also be helpful for some children.

3. *Heal And Repair The Intestinal Tract*

- Treat underlying intestinal dysbiosis with the appropriate supplements and pharmaceutical drugs.
- Replace the beneficial intestinal microflora by supplementing with probiotics.
- Take measures to repair the intestinal wall by supplementing with gut-healing nutrients and preventing future irritation by chemicals, toxins, and offending foods.
- Support the intestinal immune system so that the body has adequate resources for gut healing to take place.

4. *Supplement With Anti-Inflammatory Nutrients*

A number of natural supplements can have anti-inflammatory effects on the intestinal membrane because of their soothing and healing properties. As mentioned previously, it may be necessary

to begin therapy by giving these first in cases where there is a significant amount of inflammation and irritation. This gives the intestinal membrane a chance to “rest” and thereby allows healing and repair to begin. Some of these nutrients that have direct or indirect anti-inflammatory effects include:

- Colostrum
- Essential Fatty Acids (e.g. flaxseed oil, fish oils, evening primrose oil)
- L-Glutamine
- Zinc
- Vitamin E
- A number of healing and soothing herbs, such as Aloe Vera gel, Slippery Elm, and Marshmallow Root
- Deglycyrrhizinated Licorice (DGL), another gut-healing herb, is supported by a number of research studies to have significant benefit in treating inflammatory conditions of the stomach.^{13,14}
- Quercetin and other bioflavonoids

5. *Strengthen And Support The Intestinal Immune System*

Since the inflammatory gastrointestinal diseases often result in compromised intestinal immune function, it may be helpful to supplement with certain nutrients that are known to strengthen general immunity. These supplements include the following:

- Zinc
- Colostrum
- Vitamin C
- Other antioxidants, such as Selenium, Vitamin E, and Coenzyme Q10
- Beta-glucan
- Lactoferrin

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Part 10

SULFATION DEFICITS

Description

Many children with autism spectrum disorders appear to be sensitive to compounds known as phenols that are present in certain foods. The foods that contain the greatest concentration of phenols are:

- Apples
- Oranges and other citrus fruits
- Bananas

- Grapes
- Chocolate
- Food colorings
- Some herbs and spices

This sensitivity to phenols appears to be linked to the Phenol sulfotransferase (PST) enzyme system, which plays an important role in Phase II liver detoxification. Normally, PST is involved in a process called sulfoconjugation, whereby the potentially harmful phenols are attached to sulfate ions and thereby eliminated from the body.

Researchers have found that the action of PST is compromised in many children with autism.¹ Rosemary Waring, a researcher in England, conducted a study in which it was found that the PST enzyme system was functioning at sub-optimal levels in more than half of the autistic children tested.² This does not so much appear to be due to an actual deficiency in the PST enzyme itself, but rather to a deficiency of sulfur in the bloodstream.³ When there is a shortage of available sulfate in the body, there are not enough sulfate ions available to ensure the adequate functioning of the PST enzyme system. Consequently, phenolic compounds are not being adequately excreted and may build up in the brain and nervous system, which can in turn interfere with the action of neurotransmitters. This is why the consumption of phenol containing foods can have such adverse effects on areas like behavior, mood, and neurological function.

In addition to its detrimental effects on neurotransmitter function, impaired sulfation may also play a role in some of the gastrointestinal problems seen in children with autism. This is because sulfation is normally necessary for the production of peptides, bile acids, CCK, Secretory IgA, and possibly secretin.⁴ Since all of these are involved in supporting the health and proper functioning of the digestive system, a sulfation deficit may be one explanation for the maldigestion and malabsorption that are common problems for children with autism. Addressing this sulfation deficit is essential not only as a means of correcting food sensitivity and gastrointestinal dysfunction, but also for ensuring that the liver's Phase II detoxification pathways are functioning as optimally as possible.

Signs And Symptoms

A number of clues may be present to suggest the presence of a sulfation deficit and PST enzyme weakness in a child with ASD.⁵ These include the following:

- Sensitivity to phenol containing foods, including behavioral, neurological, and gastrointestinal symptoms
- Migraine headache, or history of migraines in a family member
- Red face
- Red ears

- Dark circles under the eyes
- Abdominal bloating
- History of colic in infancy
- Chronic runny nose or post-nasal drip
- Eczema
- Asthma
- Excessive thirst
- Perspiration during sleep (night sweats)
- Unexplained high fevers with or without vomiting
- Bad odor with perspiration

Possible Causes

As discussed above, compromised sulfation is usually the result of a deficiency of sulfate ions in the body, leading to a weakness in the Phenol sulfotransferase enzyme system.

Diagnosis

Many parents suspect the presence of sulfation problems based on a sensitivity to phenolic foods and the presence of one or more of the signs and symptoms listed above. A more accurate assessment of a child's sulfation status may be made through the following laboratory tests:

1. *Liver Detoxification Profile With PST Assessment*
This assessment for Phenol sulfotransferase is part of the general Liver Detoxification Profile and requires the use of acetaminophen (Tylenol) to measure the activity of PST via urine markers.
2. *MHPG Glucuronide / MHPG Sulfate*
This urine test measures the ratio of two metabolites, MHPG Glucuronide and MHPG Sulfate, to provide an indication of sulfation status.

Treatment Approach

1. *Dietary Interventions*
An elimination diet that restricts the child's intake of phenol-containing foods (see list of foods above) can be both diagnostic and therapeutic in

nature. Eliminating these foods for a period of time while undergoing the therapies mentioned below is helpful, followed eventually by a careful and gradual reintroduction of the foods in question. With the proper therapy, some children will once again be able to consume dietary phenols, while other children do better with continued avoidance of these compounds in their diet.

2. *Oral Supplementation*

Since PST weakness is usually due to a deficiency sulfate ions in the body, the most logical and clinically useful approach to correcting this enzyme insufficiency is to supplement with nutrients that provide the system with available sulfur. Many parents and physicians have attempted to correct this sulfur deficiency through oral supplementation with sulfur-containing nutrients. This can provide some improvement in symptoms but may not correct the problem completely because free sulfate is poorly absorbed from the gastrointestinal tract. Nonetheless, some positive clinical benefits have been reported from supplementation with the following sulfur containing compounds:

- Methylsulfonylmethane (MSM)
- The amino acid Cysteine (L-cysteine or N-acetyl cysteine)
- The amino acid Taurine

3. *Transdermal Supplementation*

Because of the apparent inadequacy of oral sulfur supplementation, the focus has recently shifted to the possibility of transdermal (through the skin) adminis-

tration. In general, parents are reporting much more positive benefits from this transdermal administration than from oral supplementation, although the two may also complement one another. The two most common ways to boost sulfur levels transdermally are:

- **Epsom Salt Baths:** This is an easy and inexpensive way to provide sulfur that can be absorbed through the skin. Epsom salts are actually magnesium sulfate, and appear to have their positive benefits through both the magnesium and the sulfate components. Parents have reported improvements in their child's language, behavior, mood, cooperation, sleep patterns, and motor skills when administering these baths on a daily basis. A general dose is 2 cups of Epsom salts per bathtub full of water. One drawback appears to be the development of dry, irritated skin in some children, which may be offset by adding 1/2 cup of Baking Soda to the bath.
- **Magnesium Sulfate Cream:** Recently, some laboratories and compounding pharmacists have developed magnesium sulfate cream to reproduce the effects of Epsom salt baths in a form that is easier to administer. While the use of this therapy is relatively new, both physicians and parents have found very positive results with using the transdermal form of magnesium sulfate. More information on dosage is available in the section of Chapter 5 on Supplements.

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Part 11

COMPROMISED INTESTINAL IMMUNITY

Description

Since as much as 70% of the body's immune system is located within and around the digestive tract, it is not surprising that diseases or imbalances of the intestines can often result in significant immune dysfunction. This intestinal immune system is referred to as Gut-Associated Lymphatic Tissue, or GALT. It plays a vital role in ensuring that the germs from within the intestinal tract are neutralized before they have a chance to enter the bloodstream and potentially harm the body as a whole.

The intestinal immune system works through a variety of mechanisms, including antigen-antibody reactions and protection from Secretory IgA. A more detailed explanation of these mechanisms can be found in Chapter 2. When the intestinal immune system becomes compromised, the body is no longer as capable of neutralizing the germs within the gut and they are thus more likely to produce illness and infection throughout the body. Indeed, many children with ASD present with significant immune problems that are evident both clinically and also on laboratory testing. Therefore, an important part of healing the intestinal tract in these children is to support the strength of the immune system as a whole.

Signs And Symptoms

A weakness in the functioning of the intestinal immune system can manifest in a variety of ways, including:

- Tendency toward overgrowth states with pathogenic intestinal microbes such as yeast, bacteria, and parasites
- Frequent gastrointestinal infections
- Recurrent systemic infections, including ear infections, respiratory infections, and throat infections

Possible Causes

- Chronic intestinal overgrowth with Candida and other yeast
- Chronic intestinal overgrowth with harmful bacteria
- Parasite infections
- Food allergies and sensitivities, including gluten and casein
- Inflammatory bowel changes, with chronic irritation to the gut wall
- Generalized immune dysfunction

Diagnosis

Diagnostic measures that can help to define the specific nature of the immune dysfunction include:

1. *Immunological Studies*
This refers to a panel of blood tests that can provide an indication of the overall status of the systemic immune system, including immunoglobulin levels and other important immune cells.
2. *Secretory IgA testing*
This test, that can be performed using stool or saliva samples, can indicate whether there is a deficiency of this important immunoglobulin that normally lines the GI tract and plays a vital role in intestinal immunity.
3. *Diagnostic Imaging*
Gastrointestinal imaging studies, such as those performed by Dr. Andrew Wakefield in England and Dr. Tim Buie in Boston, can provide physicians with a visual picture of the state of the gut membrane and possible inflammation of the intestinal lymphatic tissue. Intestinal biopsies accompanying these imaging studies can also show evidence of any histological changes within the intestinal tissue.

Other tests may also be necessary to assess the underlying state of the intestinal tract and to

determine whether there are any organisms or imbalances present that could be compromising the health of the intestinal membrane. Some of the tests that may be helpful for this purpose include:

1. Comprehensive Digestive Stool Analysis (CDSA)
2. Urine Organic Acid Test
3. Urinary Peptide Test (for gluten and casein sensitivity)
4. Food Allergy Testing
5. Intestinal Permeability Studies

Treatment Approach

1. *Identify And Remove The Underlying Cause*

Since underlying intestinal dysfunction is often the cause of a compromised intestinal immune system, it is necessary to correct these problems in order to strengthen the immune tissue. This involves addressing conditions such as intestinal dysbiosis, food allergies, gluten and casein sensitivity, Leaky Gut Syndrome, and digestive insufficiencies. Taking appropriate measures to heal the gut wall is also a necessary part of this therapeutic approach.

2. *Minimize Systemic Insults To The Immune System*

When one component of the immune

system is affected, the rest of the body may suffer as well. Conversely, when insults to the immune system in general are kept to a minimum, this takes the burden off the intestinal immune tissue and gives it a chance to heal. Minimizing these insults involves strengthening the immune system as a whole (see below) and making sure that appropriate measures are taken to prevent and treat food allergies, environmental allergies, asthma, and chronic or recurrent infections.

3. *Strengthen The Immune System As A Whole*

There are many nutritional supplements that have been found to be clinically useful in strengthening and supporting the immune system in general. There is a great deal of research to support the use of these supplements for this particular purpose. They include:

- Zinc: A recent study demonstrated that zinc deficiency can compromise the intestinal immune system and make the digestive tract more prone to infection with certain parasites.¹
- Colostrum
- Vitamin C
- Other antioxidants, such as Selenium, Vitamin E, and Coenzyme Q10
- Beta-glucan
- Lactoferrin
- Intravenous Immunoglobulin (IVIG)

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Chapter 8

EVALUATING TREATMENT RESULTS

Introduction

Once treatment has been implemented for the specific intestinal disorder(s) that a child with autism is facing, how do we determine whether that child is improving? The obvious answer would be that this improvement is reflected in a recovery of digestive function and in a resolution of the clinical symptoms the child was initially experiencing. Other signs may also be present to suggest that gastrointestinal healing is occurring. For example, there may be improved markers seen on laboratory testing, teachers and therapists may report positive behavioral changes in the child, and some of the secondary manifestations of digestive imbalances, such as food allergies and sensitivities, may become much less severe.

Keep in mind that there are several long-term goals for healing the intestinal tract. These include:

- Decreasing irritation to and inflammation of the intestinal wall
- Removing harmful microbes from the digestive tract
- Improving digestion and absorption to allow for optimal nutrient assimilation
- Ensuring regular, normal eliminations
- Replenishing pancreatic enzymes and other digestive secretions
- Repairing a “leaky” gut wall
- Creating and maintaining a healthy intestinal environment with plenty of beneficial probiotics
- Diminishing food allergies and sensitivities
- In some cases, reduced reactivity to gluten and casein
- Correcting imbalances in intestinal pH
- Enhancing the body’s detoxification pathways
- Supporting and strengthening the intestinal immune system

Evaluating a child’s treatment regimen and assessing whether these long-term goals are being met can best be determined using two markers: (1) clinical improvement [observations by parents, health care providers, teachers, and therapists], and (2) follow-up testing [improvements in laboratory test results].

1. Clinical Markers Of Improved Gastrointestinal Health

Evidence of a child’s response to therapeutic intervention is usually first reflected in improved outward (clinical) signs and symptoms. While each child has their own unique physiological makeup and will respond differently to the various forms of treatment, there are certain clinical markers that usually suggest a positive therapeutic response. These include, but are not limited to, the following:

- Decrease in the number and severity of gastrointestinal symptoms (abdominal discomfort, gas, bloating, belching, vomiting, etc.)
- Resolution of constipation or diarrhea
- More normal-appearing stools (soft, brown, well-formed, easy to pass, without the presence of mucous or undigested food)
- Resolution of rectal itching and/or perianal rash
- Gradual decline in severity of food allergies and sensitivities (including phenols, salicylates, and possibly gluten/casein)
- Ability to eat a greater variety of foods (no longer a “picky” eater)
- Improved appetite and decrease in food cravings
- Healthy-appearing skin, hair, and nails (evidence of proper mineral absorption)
- Stronger immune function (fewer colds, flus, and other infections)
- Improvements in behavior, language, eye contact, motor skills, and other developmental markers
- Less sensitivity to external and environmental stimuli

2. Laboratory Evidence Of Improved Gastrointestinal Health

In addition to assessing therapeutic efficacy through the observation of improved clinical symptomatology, it is helpful to do periodic laboratory testing as an additional way to monitor how well the child is responding to treatment. Since each child has different degrees of intestinal dysfunction, there are no

standard guidelines regarding the frequency with which these follow-up tests should be performed. In addition, depending on the nature of the underlying imbalance, it is not necessary to order every one of these tests for each patient. Your child's physician will help you to determine which tests should be ordered, and when.

Some of the routine follow-up tests that physicians have found helpful in monitoring their patients' progress include the following:

- Stool Culture (to assess the efficacy of antimicrobial therapies)
- Organic Acid Test (for the same reason as the stool culture; also to evaluate improvements in certain metabolic functions)
- Urinary Peptide Test (to monitor gluten and casein sensitivity)
- Intestinal Permeability Studies (to determine the status of a "leaky" gut)
- Food Allergy Testing (to assess improved tolerance to foods and ensure that no further food allergies have developed)

Chapter 9

Maintaining Long-Term Intestinal Health In Autism Spectrum Disorders

Introduction

For most children with autism spectrum disorders, digestive dysfunction is a significant issue, and restoring intestinal health is a key component of their overall treatment and general improvement. But the repair process does not simply end once the intestinal tract has been treated, a healthy gut environment has been created, and the digestive system has been restored to a proper level of functioning. Rather, sustaining these improvements is actually the most important part of the treatment strategy for attaining the highest degree of gastrointestinal health possible for each particular child.

There are some practical steps that parents and health care providers can take in order to support the continued health and appropriate functioning of the digestive system. These steps are not only relevant for children with ASD, but they can apply to a number of other situations as well.

For example, some children with ASD do not appear to have symptoms of any significant intestinal problems, and a laboratory workup will also reveal that their digestive processes are functioning normally. However, if these children are ever in a situation where their digestive health is temporarily compromised, such as during a viral intestinal illness or during antibiotic therapy for an ear infection, it would also be beneficial to follow these steps in order to ensure that their intestinal health is not compromised in the long run.

Many parents with an autistic child are concerned about preventing intestinal illness in their other children, especially in the younger siblings of the affected child. They may have noticed a tendency toward digestive problems in their own personal history and be concerned about the possible development of similar problems in their other children. For those parents who desire a strategy aimed at preventing these problems from occurring, the following recommendations can also be of benefit to them.

Intestinal Healing In ASD: Strategy For Maintenance And Prevention

1. Support a healthy intestinal environment

Maintaining intestinal health begins with taking steps for the ongoing support of a healthy gastrointestinal environment. After undergoing the necessary treatments to remove pathogenic microbes from the digestive tract and supplementing with probiotics in order to replenish the levels of beneficial bacteria, it is often helpful to continue giving these probiotics on an ongoing basis in order to avoid the occurrence of future overgrowth with harmful organisms. As discussed previously in the chapter on supplementation, optimal results are obtained when probiotics are used on a rotational basis, alternating between a number of different strains and potencies. It is useful to monitor results by doing occasional stool culture testing in order to make sure that the GI tract is being adequately re-colonized with the beneficial bacteria, and also to ensure that there is no further overgrowth with harmful microbes.

2. Ensure gut wall integrity by minimizing irritants

The process of repairing a “leaky” gut wall can often be a long one. Even after a child has shown marked clinical improvement and significant reduction in the severity of their intestinal symptoms, the intestinal membrane continues to require special protection and support in order for optimal healing to occur. This is accomplished in several ways, including supplementation with gut-healing nutrients and the avoidance of irritants that can cause renewed damage to the intestinal wall. Some of the nutrients that may be beneficial include Colostrum, Antioxidants, Reduced Glutathione, the amino acid Glutamine, the bioflavonoid Quercetin, and N-acetyl glucosamine (NAG). Other supplements can aid in reducing inflammation of the intestinal tract, such as Essential Fatty Acids, Zinc, MSM, and the bioflavinoid Quercetin.

Minimizing irritation to the gut wall must also be accomplished by avoiding certain substances that are known to be problematic. These include foods that can cause inflammation, including

casein, gluten, and allergenic foods. Eating foods high in fiber can be very helpful during the “maintenance phase” because fiber helps to nourish and fuel the mucosal cells lining the intestines. Finally, it is also important to minimize the use of pharmaceuticals that can compromise the integrity of the intestinal membrane, including antibiotics, steroids, aspirin, and nonsteroidal anti-inflammatory drugs. If any of these are used, especially antibiotics, the appropriate measures should be taken right away to prevent against damage from these agents (see below).

3. Take appropriate preventive measures when using antibiotics

If a child does have to use antibiotics (i.e. for an ear or respiratory infection, or in order to treat an intestinal bacterial infection such as Clostridia), what can be done in order to prevent adverse consequences to the process of intestinal healing? For one, it is always necessary to supplement with a high-potency, multi-strain probiotic that includes Lactobacillus acidophilus and Bifidobacterium bifidum. Since antibiotics destroy not only the disease-causing bacteria but also the beneficial bacteria in the intestinal tract, it is essential to replenish any of these good bacteria that have been lost during antibiotic therapy. In addition, if there appears to be significant intestinal irritation resulting from the antibiotics (i.e. diarrhea, abdominal pain, and other adverse symptoms), it is wise to supplement with some gut-healing nutrients for a month or so after finishing the antibiotic, until these symptoms have resolved.

There are a few guidelines for the use of probiotics in conjunction with antibiotic therapy. First, probiotics may be given as soon as a child begins taking their prescription of antibiotics. This often prevents the diarrhea and other complications that frequently accompany antibiotic therapy. However, it is important to never administer the probiotic at the same time as you give the antibiotic, since the latter can negate the action of the former. It is best to wait at least two hours after giving the antibiotic in order to administer the probiotic, and then to wait at least two hours again before the next dose of the antibiotic.

In addition, supplementation with probiotics should continue for at least 1-2 months after the child finishes their course of antibiotics, and in some cases even longer. This will ensure maximum re-colonization of the intestinal tract with beneficial bacteria, and will help support the normalization of other digestive processes.

4. Maintain a healthy intestinal immune system

One of the ways to avoid or minimize the use of antibiotics is to ensure that the intestinal immune system and the immune system as a whole continue to be supported and strengthened during the recovery process. Decreasing the intake of refined sugar, avoiding food allergens, and eating a well balanced diet are just a few of the dietary measures that can be taken in order to support the immune system. Supplementing with immune-strengthening nutrients can also be helpful. These include Colostrum, Lactoferrin, Beta-Glucan, Zinc, and other Antioxidants.

5. Ensure optimal nutrient intake, absorption, and assimilation

In children with a significant history of intestinal problems, it is essential to support their nutritional status because often the intestinal dysfunction has prevented their bodies from adequately digesting, absorbing, and assimilating the nutrients from their foods. Supplementing with digestive enzymes will help to ensure that food is properly broken down so that it can be better absorbed and used by the body as fuel. Since most kids with ASD have dietary restrictions and/or tend to be picky eaters, it is usually necessary to supplement with a high-potency multi-vitamin and mineral formula in order to replenish lost nutrients and make up for inadequate dietary intake of these nutrients. Supplementation will also help to support the immune system, which in turn can decrease the frequency of illness and minimize the need for antibiotics.

6. Ensure normal eliminations

Ensuring that your child has regular, normal bowel movements is another important step in maintaining the health of their digestive tract. Many parents will check their child’s stools regu-

larly for color, consistency, and the presence of undigested food or other abnormalities. If any of these problems are noted and continue to persist, they should be corrected as soon as possible. Following some of the measures outlined in previous sections on constipation and diarrhea may be helpful for stools that are excessively loose or hard. Supplementing with digestive enzymes can often resolve the problem of undigested food in the stools. Sometimes it is necessary to do a stool culture in order to test for the presence of yeast, bacteria, or other organisms that might cause abnormal eliminations. In any case, ensuring that your child is eliminating well is essential for preventing irritation to the gut wall and minimizing exposure to toxins from the fecal waste products.

7. Minimize the toxic burden on the body

Besides ensuring regular eliminations, it is also helpful to decrease the burden on the liver by minimizing chemical exposure and detoxifying the body if this is indicated. Many children with ASD have very toxic systems and would benefit greatly from measures aimed at supporting the body's pathways of elimination. The reason for the toxic burden in these children varies, but it is often related to heavy metals (mercury, lead, arsenic, and others), exposure to environmental toxins, and ingestion of chemicals in foods (additives, preservatives, dyes, pesticides, hormones, and genetically modified organisms [GMO's]). If there is a history of leaky gut syndrome and intestinal overgrowth with harmful yeast, bacteria, or parasites, the by-products generated in killing off these organisms can further increase the amount of toxins released into circulation.

For these reasons, it is important to avoid exposing the child to chemicals and toxins as much as possible, and also to undergo appropriate detoxification, such as heavy metal chelation. (See the DAN! Mercury Protocol¹ for further information and instructions on heavy metal chelation.) Supporting the liver, the primary organ of detoxification in the body, is also a helpful and necessary step for many children. This can be accomplished by ensuring a well balanced diet and also by supplementing with certain liver-supportive nutrients, such as Glutathione, N-acetyl cysteine (NAC), Methylsulfonylmethane (MSM), the herb Milk Thistle, Antioxidants, and Essential Fatty

Acids. In addition, Epsom salt baths and/or using transdermal Magnesium sulfate (Epsom salt) creams can help encourage proper liver detoxification.

8. Work on improving diet and nutrition

In general, children with autism spectrum disorders are notorious for being very self-limiting in their dietary intake. They often crave fried foods and carbohydrates, eat insufficient amounts of protein and fiber, and refuse to eat any fruits or vegetables. They may avoid specific foods because of texture, color, or taste. Many times, cravings for and fixations on certain types of food are actually the result of allergies to those very same foods. Most nutritionally oriented physicians have observed that their patients tend to crave the very foods that they are allergic to.

While it can be a daily struggle for parents to get their children to eat a healthier, more well balanced diet, the majority of children will gradually begin to lose their food cravings and dietary fixations as their intestinal tract is healed. Many parents have reported that after a period of focused treatment for leaky gut syndrome, their children have been both willing and able to eat a much greater variety of foods than before. In fact, there are some children who, after several years of therapy to heal the intestinal tract, detoxify the body of heavy metals, and support the overall health of the immune and nervous systems, have been able, at least on a limited basis, to resume eating casein, gluten, and some of the foods that they were previously allergic to. This should provide hope to parents of autistic children who struggle with enforcing the numerous dietary restrictions, however helpful they may be. Reintroducing these "forbidden" foods, however, should be done very carefully, under the close supervision of a physician, and only after a sufficient period (often several years) of intensive intervention to heal the intestinal tract and support the health of the body as a whole.

There are a few general dietary guidelines that parents can follow in order to help their child maintain a healthy intestinal environment and support the integrity and continued healing of the gut wall. These are summarized as follows:

foods.²

- Avoid giving your child any foods that are irritating to the gut wall, such as casein, gluten, and foods that they are allergic to.
- Be a food detective! If you suspect that any food is causing problems (i.e. tummy aches, constipation, diarrhea, behavioral changes, or other symptoms), your child is probably allergic to that food, even if it did not show up on food allergy testing. Avoid giving your child that food for a period of time to see whether that makes a difference in their symptoms.
- Eliminate refined sugar from your child's diet and minimize their intake of natural sugars (fruits, fruit juices, honey, molasses, etc.) and simple carbohydrates (white rice, white potatoes, sweets, etc.). These can feed yeast and harmful bacteria in the digestive tract, causing them to proliferate, which eventually leads to intestinal dysbiosis. These foods can also have directly irritating effects on the gut wall.
- Ensure an adequate intake of complex carbohydrates. These include fiber-containing whole grains (including gluten-free grains such as brown rice, quinoa, and millet), fruits, vegetables, nuts, and seeds. The fiber in these foods helps to support a healthy intestinal wall and can aid in preventing the absorption of toxins from the intestinal tract.
- Encourage a "clean diet". This means avoiding or minimizing the intake of chemicals in foods, including artificial additives and preservatives, dyes, artificial sweeteners and flavoring agents, pesticides, hormones, and genetically modified organisms (GMO's).
- If your child has a tendency toward food allergies and problems with leaky gut syndrome, consider implementing a rotation diet in order to prevent the development of future food allergies. This type of a diet involves limiting the frequency with which certain foods are eaten (usually rotating between different foods every 4 days), thereby giving the digestive system a rest by minimizing irritation from potentially allergenic

Finally, it is important to optimize your child's overall healing by supporting the health of their body as a whole. This includes not just the intestines, but also the nervous system, immune system, brain, and other organs. Take the necessary measures to ensure that your child is getting good sleep (to support healing), adequate nutrition (to support growth and repair), and plenty of fresh air and exercise (to support the body's natural detoxification pathways). Obtain the guidance of a physician who can address any other underlying health problems that your child may have. Screening tests for nutritional deficiencies, heavy metal toxicity, autoimmune processes, blood coagulation abnormalities, thyroid problems, seizure disorders, and other imbalances can be an essential part of the healing process. Behavioral interventions, such as Applied Behavioral Analysis (ABA), can help your child make significant gains in language, focus, and social interaction. Using therapeutic interventions to target specific areas, such as Auditory Integration Therapy (AIT), Sensory Integration, or Vision Therapy, has also been beneficial for a large number of children with autism spectrum disorders.

We encourage you to consult the "Resources" section at the end of this protocol for further information about these different therapeutic options. Most parents with a child who has recovered from autism report that they used an integrated approach, with a variety of different modalities, in order to facilitate their child's journey toward healing. Since autism is primarily a medical condition, working to correct whatever nutritional and biochemical imbalances are present produces the greatest strides in most children and gives hope that full recovery is eventually possible. And, from the medical side of things, healing and supporting the intestinal tract in a child with autism is usually the place to begin, because a well-functioning digestive system provides the foundation upon which other medical treatments may be based. These treatments, along with endless amounts of love, encouragement, and prayer, can give your child the greatest chance for profound healing and lasting recovery.

REFERENCES: Maintaining Long-Term Intestinal Health In Autism Spectrum Disorders

- ¹ *Defeat Autism Now! (DAN!) Mercury Detoxification Consensus Group Position Paper*. May 2001. Available from the Autism Research Institute (www.autism.com/ari/).
- ² For more information on implementing a rotation diet, see the books and educational materials by nutritionist Sally Rockwell, Ph.D. A good place to start is with the book: [Rotated Allergy Recipes – Delicious, Allergy-Free, Quick and Easy Meals!](#) Available at many bookstores and from the Alternative Medicine Connection website (www.arxc.com)

Chapter 10

Summary Of Treatment Strategies: Restoring Intestinal Health In Autism Spec- trum Disorders

- I. Do laboratory testing to identify underlying intestinal dysfunction.**
 - A. Basic laboratory testing:
 1. Stool analysis
 2. Organic acid test
 3. Urinary peptide test
 4. Food allergy testing
 5. Intestinal permeability studies
 - B. Additional laboratory testing that may be helpful:
 1. Gluten antibody studies
 2. Secretory IgA testing
 3. Liver detoxification profile
 4. Sulfation studies
 5. Diagnostic imaging studies
 6. Immunological testing

 - II. Take general measures that can provide rapid relief of symptoms.**
 - A. Eliminate gluten and casein from the diet.
 - B. Supplement with a broad-spectrum digestive enzyme product.
 - C. Do a trial elimination of foods containing phenols and/or salicylates.
 - D. Do a trial elimination of the most common allergenic foods.
 - E. Supplement with a multi-vitamin and mineral formula specifically targeted to children with autism spectrum disorders.
 - F. Supplement with probiotics to replenish any deficiencies in beneficial intestinal bacteria.
 - G. Supplement with nutrients known to have properties for healing and decreasing inflammation in the gut wall.

 - III. Remove intestinal pathogens, chemical toxins, and other irritants.**
 - A. Correct dysbiosis by treating for underlying intestinal overgrowth of yeast, bacteria, viruses, and parasites. Use pharmaceutical agents and natural supplements as appropriate.
 - B. Support the liver and detoxification pathways to minimize "die-off" (Herxheimer) reactions.
 - C. Reduce exposure to pharmaceuticals known to damage the intestinal lining (antibiotics, steroids, aspirin, NSAIDs).
 - D. Avoid other potential irritants to the gut wall, such as food allergens, refined sugar, gluten, and casein.

 - IV. Restore proper digestive function.**
 - A. Use digestive enzymes to encourage the proper breakdown and absorption of foods.
 - B. Use appropriate measures to correct imbalances in intestinal pH.

 - V. Re-establish normal intestinal flora.**
 - A. Use therapeutic doses of multiple strains of probiotics to restore normal levels of beneficial intestinal bacteria.
 - B. Supplement with Lactoferrin to control the growth of harmful bacteria.

 - VI. Repair the intestinal lining.**
 - A. Use nutritional supplements that are known to support the process of healing the gut wall, such as Antioxidants, Colostrum, L-Glutathione, and Essential Fatty Acids.
 - B. Avoid further damage to the gut wall by reducing exposure to irritants (food allergens, casein, gluten, certain pharmaceuticals and chemicals in food and water).

 - VII. Treat specific intestinal conditions with carefully selected therapeutic agents.**
 - A. Work with a physician to obtain the proper diagnosis in order to focus the direction of therapeutic intervention.
 - B. Use pharmaceutical drugs when indicated to treat significant intestinal dysfunction.
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- C. Use nutritional supplements to augment the healing process, correct underlying metabolic and biochemical imbalances, and restore the digestive tract to a proper level of functioning.

VIII. Correct nutritional deficiencies.

- A. Do laboratory testing to assess nutritional status.
- B. Supplement with the appropriate nutrients to correct underlying nutritional deficiencies. Nutrients that may be found to be deficient include vitamins, minerals, amino acids, essential fatty acids, and others.

IX. Strengthen the intestinal immune system.

- A. Support the healing of the intestinal tract.
- B. Supplement with nutrients known to increase overall immune function, such as Colostrum, Beta-glucan, Lactoferrin, Zinc, and Antioxidants.

X. Evaluate treatment results on a periodic basis.

- A. Assess clinical response by monitoring whether there is improvement in the child's outward signs and symptoms.
- B. Do follow-up laboratory testing for objective measures of treatment results.
- C. Work with a physician or other knowledgeable health care provider to adjust or fine-tune treatments if the clinical and laboratory markers are not improving as anticipated.

XI. Reduce future damage to the intestinal tract through maintenance and prevention.

- A. Support a healthy intestinal environment.
 - 1. Supplement with probiotics on an ongoing basis.
 - 2. Do periodic stool testing to monitor the intestinal environment.
- B. Ensure gut wall integrity by minimizing irritants.
 - 1. Supplement with gut-healing nutrients after there has been an insult to the intestinal tract (i.e. after antibiotic use or intestinal infection).
 - 2. Continue to avoid exposure to substances (foods, drugs) that are known to irritate the gut wall.
- C. Take appropriate preventive measures when using antibiotics.
 - 1. Replenish with probiotics during and after antibiotic therapy. Follow the guidelines given in Chapter 9 for proper administration.
 - 2. Supplement with gut-healing nutrients if there has been significant intestinal irritation from the antibiotics.
- D. Maintain a healthy intestinal immune system.
- E. Ensure optimal nutrient intake, absorption, and assimilation.
 - 1. Supplement with digestive enzymes to ensure that the nutrients in foods are being optimally utilized.
 - 2. Supplement with a high-potency multi-vitamin and mineral formula to replenish lost and insufficient nutrients.
- F. Ensure normal eliminations.
 - 1. Monitor your child's bowel habits to determine the presence of abnormal stools.
 - 2. Take appropriate measures to treat for constipation, diarrhea, and other abnormalities.
 - 3. Supplement with digestive enzymes if there is undigested food in the stools.
 - 4. Do a stool culture to determine what is out of balance if the problem is not resolved with treatment.
- G. Minimize the toxic burden on the body.
 - 1. Support the liver and other detoxification pathways through a well balanced diet and the use of appropriate supplements, including Glutathione, NAC, MSM, Milk Thistle, Antioxidants, and Essential Fatty Acids.
 - 2. Minimize exposure to environmental toxins.

3. Minimize exposure to heavy metals, including those found in vaccines, certain types of fish, and some dental fillings.
 4. Minimize exposure to chemicals in foods, such as artificial additives and preservatives, dyes, artificial sweeteners or flavoring agents, pesticides, hormones, and GMO's.
 5. Do detoxification when indicated, such as chelation for heavy metals and liver support when treating intestinal microbial overgrowth.
- H. Work on improving diet and nutrition.
1. Keep in mind that food cravings and fixations will often resolve as the child's intestinal tract heals.
 2. Follow specific dietary guidelines to maintain a healthy intestinal environment and support the integrity and continued healing of the gut wall:
 - a) Avoid foods that are irritating to the gut wall.
 - b) Eliminate allergenic foods, gluten, and casein.
 - c) Eliminate or minimize the intake of refined sugar, natural sugars, and simple carbohydrates.
 - d) Ensure an adequate intake of fiber and complex carbohydrates.
 - e) Encourage a clean diet free of chemicals.
 - f) Implement a rotation diet if there is a history of food allergies and sensitivities.

XII. Use a multi-faceted approach to achieve optimal healing and recovery.

- A. Support other systems and organs in the body, including the brain, nervous system, and immune system.
- B. Support your child's overall health by ensuring good sleeping habits, adequate nutrition, and plenty of fresh air and exercise.
- C. Work with a physician who can order the necessary screening tests to uncover other biological imbalances in the body, and address these areas as needed.
- D. Complement the biomedical approach with other appropriate interventions, such as Applied Behavioral Analysis (ABA), Auditory Integration Therapy (AIT), Sensory Integration, and Vision Therapy.
- E. Correcting the biomedical imbalances in autism usually begins with healing the gut!

Chapter 11

Resources For The Treatment Of Autism Spectrum Disorders

General Autism Resources

Autism Resources

www.autism-resources.com

Autism Research Institute

www.autism.com/ari/

Autism Society of America

www.autism-society.org

Developmental Delay Resources

www.devdelay.org

Families for Early Autism Treatment (FEAT)

www.feat.org

Future Horizons

www.futurehorizons-autism.com

Gluten-Free / Casein-Free Diet Resources

Autism Network for Dietary Intervention (ANDI)

www.autismndi.com

GFCF Diet Website

www.gfcfdiet.com

Information On Vaccines And Vaccine Safety

Institute for Vaccine Safety

www.vaccinesafety.edu

National Vaccine Information Center

www.909shot.com

Safe Minds

www.safeminds.com

Therapeutic Interventions

Applied Behavioral Analysis (ABA)

- Institute for Applied Behavioral Analysis

www.iaba.com

Auditory Integration Training (AIT)

- AIT Services
- Georgiana Institute

www.auditoryintegration.net
www.georgianainstitute.org

Sensory Integration

- Sensory Integration Network

www.sinetwork.org

Vision Therapy

- Association for Comprehensive NeuroTherapy
- College of Optometrists in Vision Development (COVD)
- Optometrists' Network

www.latitudes.org

www.covd.org

www.children-special-needs.org

Laboratories (See Chapter 4)

AAL Reference Laboratories, Inc.

1715 E. Wilshire #715

Santa Ana, CA 92705

www.aalrl.com

Tel (800) 522-2611

(714) 972-9979

Fax (714) 543-2034

Laboratories (See Chapter 4) continued

Doctor's Data, Inc. P.O. Box 111 West Chicago, IL 60186 www.doctorsdata.com	Tel (800) 323-2784 Fax (630) 377-8139 (630) 587-7860
Great Plains Laboratory 11813 West 77 th Lenexa, KS 66214 www.greatplainslaboratory.com	Tel (913) 341-8949 Fax (913) 341-6207
Great Smokies Diagnostic Laboratory 63 Zillicoa Street Asheville, NC 28801 www.gsdl.com	Tel (800) 522-4762 Fax (828) 253-0621 (828) 252-9303
Immuno Laboratories 1620 West Oakland Park Boulevard Fort Lauderdale, FL 33311 www.immunolabs.com	Tel (800) 231-9197 Fax (954) 486-4500 (954) 739-6563
Immunosciences Lab, Inc. 8693 Wilshire Boulevard Beverly Hills, CA 90211 www.immuno-sci-lab.com	Tel (800) 950-4686 Fax (310) 657-1077 (310) 657-1053
MetaMetrix Clinical Laboratory 4855 Peachtree Industrial Boulevard Norcross, GA 30092 www.metametrix.com	Tel (800) 221-4640 Fax (770) 446-5483 (770) 441-2237
Karl Reichelt, MD, PhD Director, Clinical Chemistry Department of Pediatric Research Rikshospitalet – The National Hospital N 0027 Oslo, Norway	Tel 011-47-23-07-29-85
Smith Kline Beecham Laboratories P.O. Box 13398 Research Triangle Park, NC 27709 www.us.gsk.com	Tel (888) 825-5249 Fax (919) 483-2100
US BioTek Laboratories 13758 Lake City Way NE Seattle, WA 98125 www.usbiotek.com	Tel (206) 365-1256 Fax (206) 363-8790

Online Articles About Autism

Articles by Dr. Paul Shattock
<http://osiris.sunderland.ac.uk/autism>

Articles by Dr. Karl Reichelt
www.panix.com/~donwiss/reichelt.html

Chapter 12

CONCLUSIONS

General Conclusions

Restoring intestinal health is a significant component of the treatment of autism spectrum disorders. Gastrointestinal function is intimately involved in the immune system, the nervous system, enzymatic and metabolic processes, and the absorption of nutrients from food. Dysfunction of the digestive system and healing of the gastrointestinal tract are complex issues with many variables. This complexity is accentuated by the fact that every child with ASD is an individual with unique symptoms and requirements for healing.

We at Kirkman Laboratories hope that this document will serve as a guide to parents, family members, and health care professionals for understanding the intestinal problems that are commonly seen in ASD and the options available for treating them.

Disclaimer: This document does not represent a cure for autism spectrum disorders or the gastrointestinal problems found therein. It should not replace the proper diagnosis and treatment of any individual. Decisions about a particular individual's care must be made by that person's physician or health care professional. The endorsers of this document are in general agreement with the material presented herein, but may disagree individually when applying recommendations to particular situations or patients. This publication has not been evaluated by the Food and Drug Administration. It is not intended to diagnose, treat, prevent or cure any disease.