NANCY MULLAN, MD, is an author, lecturer, and sought-after clinician best known for her natural approach to treatment and recovery from ASD. She was educated at the University of Pennsylvania, Tufts University, and the University of Chicago. Dr. Mullan has been practicing for 30 years and is excited to be on the cutting edge of the newest innovations in non-pharmaceutical ASD therapies. Currently, Dr. Mullan is practicing nutritional medicine and psychiatry in Burbank, California, treating children on the autism spectrum and adults with hormonal, gastroenterologic, neurologic, and/or metabolic dysfunction.
The adult human intestine is home to an almost inconceivable number of microorganisms. The size of the population—up to 100 trillion—far exceeds that of all other microbial communities associated with the body’s surfaces and is ~10 times greater than the total number of our somatic and germ cells. Thus, it seems appropriate to view ourselves as a composite of many species and our genetic landscape as an amalgam of genes embedded in our Homo sapiens genome and in the genomes of our affiliated microbial partners (the microbiome).

Our gut microbiota can be pictured as a microbial organ placed within a host organ. It is composed of different cell lineages with a capacity to communicate with one another and the host; it mediates physiologically important chemical transformations; and it can manage and repair itself through self-replication. The gut microbiome, which may contain >100 times the number of genes in our genome, endows us with functional features that we have not had to evolve ourselves. (p.1915)

Colonization of the newborn’s GI tract starts immediately after birth. The earliest bacteria colonized can modulate the expression of genes in the host epithelial cells, thus creating a favorable environment for...

Studies have illuminated how the complex interaction of the immune system, the neuroendocrine system, and the microbial environment within the gut affects not only GI function but also the function of other organs and systems in the body, most notably the brain and nervous system.
AMY YASKO PHD, AMD, FAAIM, holds a doctorate in microbiology, immunology, and infectious diseases with an award for outstanding academic excellence from Albany Medical College.

She completed two research fellowships at Strong Memorial Hospital in Rochester NY; one as a member of the Dept. of Pediatrics and Infectious Diseases, the other as a member of the Wilmont Cancer Center. Dr. Yasko was also a fellow in the Department of Hematology at Yale Medical Center prior to joining a biotechnology company in Connecticut. She later co-founded a successful biotechnology company, where she was recognized as an expert in the field of DNA/RNA based diagnostics and therapeutics. Prior to shifting her focus to integrative healthcare she was consultant to the medical, pharmaceutical, and research communities for almost 20 years with an expertise in biochemistry, molecular biology, and biotechnology. Dr. Yasko continued her education in the area of integrative healthcare, receiving two additional degrees, a Doctor of Naturopathy and a Doctor of Natural Health.
Gut mucosal integrity can be compromised by a number of factors, including chronic microbial imbalance (dysbiosis), inflammation, and immune system dysregulation. Dysbiosis can produce mucosal damage, and the accompanying inflammatory processes may lead to a disruption in microvilli function and gut permeability. These, in turn, can manifest as gluten, casein, and/or lactose intolerance; food allergies or intolerance; abdominal pain and discomfort; or abnormal bowel function. Non-GI-related symptoms can also appear, such as headaches, skin irritations, chronic joint pain, anxiety, or depression.

Imbalances in the flora of the GI tract may begin as early as birth. Maternal streptococci, for example, can be transmitted from the mother to the neonate during delivery. Although researchers originally believed that transmission occurred solely via vaginal delivery, more recent data suggest that streptococcal infection can also occur in infants who have been delivered via cesarean section. The rate of mother-to-infant transmission of streptococci during vaginal delivery is between 20 and 30 percent.

Increased gut acidity also can predispose to microbial imbalance. Some of the factors that contribute to increased gut acidity and gut flora imbalances include vitamin B12 deficiency, decreased pancreatic or liver function, genetics/blood type, and antibiotic use.

VITAMIN B12 DEFICIENCY: Intrinsic factor, a substrate produced by the gastric lining, is necessary for the uptake of vitamin B12 by the small intestine. Sufficient stomach acid is necessary for intrinsic factor activation. The secretion of stomach acid and the secretion of intrinsic factor parallel one another, and loss of gastric secreting cells decreases both intrinsic factor and stomach acid. Proton pump inhibitors, a group of drugs widely used for peptic ulcer disease and other hyperacrid conditions, antagonize stomach acid levels and lead to decreases in intrinsic factor and decreased uptake of B12. A significant lack of B12 has been found in autism, irrespective of age. Efforts by the body to increase B12 levels lead to increased intrinsic factor and would be expected to increase stomach acid. While the growth of many bacteria is inhibited in an acidic (low pH) environment, streptococci are among those bacteria that can survive and flourish at a lower pH. Increased stomach acid secondary to B12 deficiency, therefore, leads to a gut environment that predisposes to the growth of streptococci and other pathogenic bacteria that can survive in an acid milieu, such as Escherichia coli.

DECREASED PANCREATIC OR LIVER FUNCTION: One of the roles of bile is to neutralize stomach acid. Lack of bile due to decreased pancreatic or liver function contributes to an acidic gut environment. Impairments in liver or pancreatic function due to toxin overload or infectious diseases such as rubella (which is known to infect the pancreas), therefore, decrease the body’s ability to neutralize excess acid.

GENETICS AND BLOOD TYPE: Genetics and blood type can predispose to colonization with streptococci. For example, single nucleotide polymorphisms (SNPs) that decrease the level of B12 in the body can contribute to an environment that is conducive to the growth of streptococci. Blood type also appears to play a role, which may be related in part to the increased acidity seen in those with blood type O. Effects of different carbohydrate groupings on the surface of blood cells of varying blood types may also have an impact on the ability of streptococci to aggregate in the system.

ANTIBIOTICS: Normal flora help to protect the gut from the growth of pathogenic organisms. Antibiotic use is well known to cause imbalances in normal gut flora. The use of antibiotics without concurrent addition of probiotics, therefore, can predispose to the growth of streptococci as well as other pathogenic organisms such as clostridia. Fecal flora studies of children with ASD have found that the number of clostridial species are greater and the clostridial counts higher in ASD children when compared with controls.

CLOSTRIDIAL AND OTHER SPECIES

Clostridia are spore-forming, Gram-positive anaerobes. The growth of anaerobes is inhibited or significantly slowed in the presence of oxygen. The dearth of oxygen in the lumen of the small and large intestines predisposes this environment to the growth of anaerobic organisms. There are more than 50 species of clostridia, a number of which cause significant illness. To name only a few examples, Clostridium botulinum causes botulism, C. perfringens causes gas gangrene and food poisoning, C. tetani causes tetanus, and C. difficile causes pseudomembranous colitis. Table 1 provides a more comprehensive list of the many conditions associated with clostridial infection.

**WHAT CAUSES CHRONIC MICROBIAL IMBALANCE**

Gut mucosal integrity can be compromised by a number of factors, including chronic microbial imbalance (dysbiosis), inflammation, and immune system dysregulation.
**C. difficile** is most often found in the gut and is part of the normal GI flora in 2-10 percent of humans. However, the suppression of normal GI flora that accompanies oral antibiotic use allows **C. difficile** to proliferate and produce cytopathic toxins and enterotoxins that are disruptive to cells and the intestine. The range of symptoms that **C. difficile** infection can cause is significant. Symptoms vary from diarrhea alone to marked diarrhea and necrosis of the GI mucosa with accumulation of inflammatory cells and fibrin. The **C. difficile** organism is resistant to most commonly used antibiotics. This is because many antibiotics work by interrupting an aspect of the target organism’s growth cycle, and this kind of antibiotic is less effective with slow-growing organisms such as **C. difficile**. Although laboratories are required to label some growth of the **C. difficile** organism as “normal,” if it is growing in an individual who does not have sufficient methionine and folate cycle activity to produce T and B cells for adaptive immune function, then any growth of **C. difficile** can be pathogenic. This also includes individuals who are immunocompromised, have heavy metal toxicity, or who have viruses, bacteria, and fungi in their systems. Similar patterns hold true for organisms other than clostridia. Many organisms normally found in the gut can become pathogenic in the face of poor methionine and folate cycle function, insufficient immune function, and high total toxic burden. For example, some streptococci are normally present in the gut, but because of the host’s physiologic status, the organism’s presence may become pathogenic.

**Table 1.**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Condition</th>
<th>Toxin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C. perfringens</strong></td>
<td>Soft-tissue infection: crepitant cellulitis, myositis, clostridial myonecrosis</td>
<td>α-toxin (others)</td>
</tr>
<tr>
<td><strong>C. perfringens</strong> type A</td>
<td>Food poisoning</td>
<td>Enterotoxin</td>
</tr>
<tr>
<td><strong>C. perfringens</strong> type C</td>
<td>Enteritis necroticans</td>
<td>β-toxin</td>
</tr>
<tr>
<td><strong>C. difficile</strong></td>
<td>Antibiotic-associated colitis</td>
<td>Toxin A</td>
</tr>
<tr>
<td><strong>C. septicum</strong> (others)</td>
<td>Neutropenic enterocolitis</td>
<td>Unknown, possibly β-toxin</td>
</tr>
<tr>
<td><strong>C. septicum</strong></td>
<td>Colorectal malignancy</td>
<td>δ-toxin</td>
</tr>
<tr>
<td></td>
<td>Hemolysis by septicolysine</td>
<td>α-toxin</td>
</tr>
<tr>
<td></td>
<td>Tissue necrosis</td>
<td>α-toxin</td>
</tr>
<tr>
<td></td>
<td>DNA lysis by DNase</td>
<td>β-toxin</td>
</tr>
<tr>
<td></td>
<td>Hyaluronan lysis by hyaluronidase</td>
<td>γ-toxin</td>
</tr>
<tr>
<td><strong>C. tetani</strong></td>
<td>Tetanus</td>
<td>Tetanospsamin</td>
</tr>
<tr>
<td><strong>C. botulinum</strong></td>
<td>Botulism</td>
<td>Botulinal toxins A-G</td>
</tr>
<tr>
<td><strong>C. perfringens, C. ramosum (many others)</strong></td>
<td>Abdominal infections: Cholecystitis, peritonitis, ruptured appendix, bowel perforation, neutropenic enterocolitis</td>
<td>β-toxin</td>
</tr>
</tbody>
</table>

**Figure 1.**

The impact of infection on neurotransmitter formation

The effect of infection overall is to increase oxidative stress, which in itself impairs the production of BH4 and hence neurotransmitters. Beyond this, the consequence of the T cell activation, cytokine production, and macrophage activation that accompany infection is to shift the conversion of H2NTP from BH4 to neopterin, which increases the immune response.

cell activation, cytokine formation, and macrophage activation, increasing oxidative stress, which impairs neurotransmitter formation (Figure 1).

Dihydroxyphenylpropionic acid (DHPPA) is a marker for bacterial infection with clostridial species, \(^{21}\) *Pseudomonas* species, \(^{22}\) and *E. coli*. \(^{23}\) The production of DHPPA that results from infection with these bacteria may reduce formation of the neurotransmitter dopamine through its depletion of the enzyme tyrosinase. \(^{24}\) There are two pathways for dopamine synthesis in the body. In the primary pathway, phenylalanine is hydroxylated to tyrosine in a reaction catalyzed by phenylalanine hydroxylase. This reaction is dependent on tetrahydrobiopterin (BH4) (see Figure 2). The resulting tyrosine is hydroxylated to L-DOPA [3,4-dihydroxyphenylalanine] by the enzyme tyrosine hydroxylase in a second BH4-dependent reaction. L-DOPA is then decarboxylated in a reaction catalyzed by aromatic acid decarboxylase to synthesize dopamine. Dopamine is the substrate for the subsequent synthesis of the catecholamines norepinephrine and epinephrine.

This primary pathway for dopamine synthesis can be compromised by a number of factors. For example, microbes can increase the serum phenylalanine-tyrosine ratio, which inhibits the first step in the pathway. Besides inhibiting this pathway, high levels of phenylalanine may also cause a drop in serotonin and/or GABA (gamma-aminobutyric acid), which may result in obsessive-compulsive disorder (OCD) behaviors. \(^{25}\) The exigencies of tyrosine hydroxylase activity also have an impact on this dopamine synthesis pathway. \(^{26-28}\) If levels of norepinephrine and epinephrine increase as the result of stressors (including infections), feedback inhibition on tyrosine hydroxylase will result. Increased glutamate also decreases tyrosine hydroxylase activity. Glutamate (via NMDA receptors) and dopamine (via D2 receptors) decrease tyrosine hydroxylase phosphorylation by decreasing cAMP, a messenger derived from adenosine triphosphate (ATP) that is important in many biological processes. Because tyrosine hydroxylase activity is stimulated by phosphorylation, a situation of decreased tyrosine hydroxylase phosphorylation leads to decreased enzyme activity and lower levels of dopamine. \(^{29}\)

The levels of BH4 in the body are critical to both dopamine and serotonin synthesis. However, BH4 is a vulnerable molecule and can be deficient for a number of reasons, some of which involve gut bacteria. As a substrate for various reactions, BH4 is especially subject to depletion. Biopertin deficiency will reduce available BH4, as will oxidative stress. In addition, the presence of aluminum or lead inhibits the activity of dihydrobiopterin reductase, which catalyzes BH4 synthesis from dihydrobiopterin (BH2). BH4 levels also are profoundly decreased by infection because the body’s immune response produces neopterin, which reduces the production of BH4 (see Figure 1). Finally, individuals with MTHFR A1298C mutations may have a reduced ability to synthesize BH4. \(^{30}\) The product of the MTHFR enzyme reaction, 5-methyltetrahydrofolate, has been shown to be directly related to BH4 levels \(^{31-33}\) and to be reversible, with BH4 production being the outcome of the reverse reaction. \(^{34-36}\)

Although the primary sequence for dopamine production is through the pathway shown in Figure 2, this pathway may not always function. Alternatively, the enzyme tyrosinase can act on tyrosine to produce L-DOPA in a one-step process, \(^{37}\) following which aromatic acid decarboxylase can act on L-DOPA to produce dopamine. This alternative pathway is able to circumvent the blockages that can result from problems with phenylalanine levels, tyrosine hydroxylase activity,
In ASD patients, in particular, the GI tract is a natural place for biofilms to form; the lack of cell-mediated immunity in these patients predisposes them to biofilm growth.

lack of BH4, or oxidative stress. With the depletion of tyrosinase that results from bacterial infection-induced production of DHPPA, however, both the primary and the secondary pathways for the production of dopamine can be compromised. In addition, the production of norepinephrine and epinephrine are likely to be decreased because dopamine subsequently converts to norepinephrine and epinephrine.

BIOFILMS AND STREPTOCOCCI
A biofilm is a community of one or several diverse species of organisms that firmly fix to a surface and grow within a self-produced polymer matrix. Ultimately, the group of organisms begins to function as a unit. The community aspect of biofilm formations offers a number of advantages, including protection from hostile environmental conditions and the opportunity to sequester nutritional resources. In addition, a microbial community offers the possibility for a variety of different organisms (bacteria, fungi, viruses, and single-celled parasites) to live together, exchange genetic information, communicate through chemical signaling, act cooperatively, and, in so doing, enhance their own survival and the survival of the collective. It has come to be recognized that the formation of biofilms is the preferred form of growth for organisms, whereas growth of planktonic (single-celled or free-floating) organisms is an artifact of in vitro culture. Certain organisms have evolved genetically to be viable only in a biofilm. The take-home message here is that organisms don’t really live on their own in nature – they live in communities.

Biofilms can form quickly. In a human body that is experiencing nutrient depletion or high oxidative stress, E. coli bacteria can activate genes that form biofilms in a variety of environments within 24 hours. In ASD patients, in particular, the GI tract is a natural place for biofilms to form; the lack of cell-mediated immunity in these patients predisposes them to biofilm growth. Moreover, the range of GI symptoms caused by biofilms is clearly identifiable in the ASD population.

Among many other organisms, streptococci have been identified in biofilms. This form of organization gives streptococci an adaptational advantage and the capacity to thrive in a wide range of pH conditions and environments in which they otherwise would not survive. Generally, bacteria elicit a B-cell-mediated immune response and viruses a T-cell-mediated immune response. Streptococci, however, prompt the elaboration of a large number of extracellular toxins, all of which have the ability to nonspecifically stimulate T cells. Once an immune response is mounted against streptococcal species, therefore, the response involves both B cells and T cells, resulting in a major inflammatory reaction. In addition, streptococcal infection increases the production of hydrogen peroxide (H2O2), thereby increasing oxidative stress in the body, and depletes the peroxidase enzyme necessary for the production of thyroid hormone, possibly reducing levels of thyroxine (T4) and triiodothyronine (T3). This and other consequences of streptococcal infection are summarized in Figure 3.

Several species of streptococci are well characterized as causing neuropsychiatric symptoms and disorders such as autism and anorexia nervosa. Autoantibodies to group A streptococcal sugar moieties are implicated in OCD, Tourette syndrome, chronic tic disorders, ADHD, and Sydenham chorea, a neuropsychiatric complication of rheumatic fever. Sydenham chorea is one of the best examples of postinfectious autoimmunity produced by molecular
Bacterial infection promotes accumulation and retention of heavy metals in the body, which contributes to oxidative stress and impairs neurotransmitter formation.

The association between chronic bacterial infection and neurologic and psychiatric disorders can additionally be explained by the fact that streptococcal and other bacterial infections cause the breakdown of tryptophan, a direct precursor of serotonin. States of persistent immune activation diminish the availability of free serum tryptophan and compromise serotonin production. As immune activation accelerates tryptophan degradation, tryptophan depletion, in turn, may downregulate the immune response. In addition, a breakdown product of tryptophan degradation, quinolinic acid, begins to accumulate. Quinolinic acid is another excitotoxin and may contribute to the development of the neuropsychiatric disorders seen in the presence of chronic infection and serotonin depletion.

**GUT IMBALANCES AND HEAVY METALS**

Bacterial infection promotes accumulation and retention of heavy metals in the body, which contributes to oxidative stress and impairs neurotransmitter formation. Metals may be retained in the body through several mechanisms. We have documented the sequestration of aluminum and lead in the organisms of the microbiome and the impacts of retention of these metals at length elsewhere. The elimination of abnormal gastrointestinal flora and excretion of the metals they retain, therefore, may be essential for proper function of the biochemical pathways in the body, along with maintenance of proper balance among the organisms that should be present in the gastrointestinal tract.

Streptococcal infections act in a number of ways to retain heavy metals in the body, including sequestering metals within the cell walls of the bacteria. Another mechanism related to metal retention involves sulfhydryl groups, which ordinarily bind and eliminate toxic and heavy metals. Streptococcus produces an extracellular enzyme called sulfhydryl protease that is capable of cleaving these sulfhydryl groups, leading to a deficiency of sulfur-containing moieties in the body. Streptococci proliferate in the presence of iron and reduce the capacity of the body to excrete this heavy metal. Iron, in turn, increases the virulence of many bacteria, including streptococci. In addition, iron is necessary for biofilm formation. Excess iron can increase microbial imbalances in the body, including but not limited to streptococcal infections.

Aluminum is a well-documented and undisputed neurotoxin that is associated with cognitive, psychological, and motor abnormalities. Both clinical observation and animal experiments have documented neurotoxicity from excess brain exposure to aluminum, which has been found in elevated levels in the brains of patients with Parkinsonism, amyotrophic lateral sclerosis (ALS), and Alzheimer-type dementia. Aluminum induces encephalopathy and causes neuroanatomical and neurochemical changes in the brain, including neurofilament disturbances followed by nerve cell loss. Primate studies have provided evidence of aluminum’s ability to induce seizures.

While staphylococci are especially prone to retaining aluminum, it is likely that other bacteria also can do so. Moreover, aluminum may increase the propensity for bacteria to form a biofilm, in part because of its pro-oxidant activity. It has been characterized as having direct effects on biofilm activity in other systems.
HELCOBACTER PYLORI IN AUTISM SPECTRUM DISORDERS

*Helicobacter pylori* (H. pylori) is a Gram-negative, spiral-shaped bacterium that lives in the stomach and duodenum. This ulcer-causing gastric pathogen is able to colonize the harsh acidic environment of the human stomach. Although the stomach is protected from its own gastric juice by a thick layer of mucus that covers the stomach lining, *H. pylori* takes advantage of this protection by living in the mucus lining itself. It does so by using long, whip-like flagella that facilitate locomotion through the mucus layer (see Figure 4). Although the organism is best known for its etiologic role in ulcers and impaired digestion, it also can induce vasovagal symptoms after eating, including weakness, skin pallor, profuse sweating, and sensations of loss of consciousness that resolve after eradication of the infection.  

In the mucus lining, *H. pylori* survives the stomach’s acidic conditions by producing urease, an enzyme that catalyzes hydrolysis of urea into ammonia and bicarbonate. As strong bases, ammonia and bicarbonate produce a cloud of alkalinity around the bacterium, making it impossible for the body’s normal defenses (such as T cells, natural killer cells, and other white blood cells) to get to it in the gastric mucus layer. Polymorphs, white blood cells containing a segmented nucleus and that are first responders to infection sites, release superoxide radicals on stomach lining cells in an increasing inflammatory response. Other factors that contribute to *H. pylori* colonization of the gastric mucosa include adhesins, molecules that make the bacteria adhere to the mucosa, and genes encoding proteins with chemotaxis into the mucus.  

Incidentally—but importantly—*H. pylori* infection increases TNF-alpha levels. The organism binds to the mucin and uses it to burrow into the cells lining the mucosal layer to create an infection. It very deeply infects those cells and is distributed evenly throughout (see Figure 5).


*H. pylori* infection increases TNF-alpha levels.
**H. pylori** is positive in a high percentage of ASD and other chronically ill patients. *H. pylori* is, in fact, a critical piece of the ASD puzzle. Many factors that we have been dealing with in autism for a long time are related to *H. pylori*, including problems with gluten and casein, breakdown of glutathione, excess stomach acid, and the high norepinephrine seen in ADD and ADHD. All of these factors can be accounted for by the presence of *H. pylori* and, additionally, can act to increase *H. pylori* in the GI tract.

**NEUROTRANSMITTERS:** *H. pylori* affects neurotransmitters and brain neurochemistry, creating neurological symptoms that include psychotic disorders related to imbalances in serotonin and tryptamine levels (see Tryptamine below). It also affects acetylcholine release and levels of epinephrine and norepinephrine.

**INTESTINAL PERMEABILITY:** The GI epithelium is protected by a mucosal barrier that separates it from the contents of the GI lumen (Figure 8). This mucosal barrier is formed by the interactions of various mucosal secretions. *H. pylori* activates claudins (intercellular adhesion molecules) that insert themselves in between the epithelial cells,
The mucosal barrier separates the internal milieu from the luminal environment. The function of the barrier depends on the integrity of the mucosa—from the endothelium through to the epithelial cell lining—and the reactivity of dynamic defensive factors such as mucosal blood flow, epithelial secretions, and immunocompetent cells. The mucus layer is formed by the interaction of various mucosal secretions, including mucin glycoproteins, trefoil peptides, and surfactant phospholipids. However, resident bacteria are the crucial line of resistance by exogenous microbes.

Abnormalities in the production of ketone bodies have been studied in individuals with mental disease for over 60 years. Observations record abnormally high ketone body formation in schizophrenia and other mental disorders. When \textit{H. pylori} is present, a ketogenic diet may exacerbate mental symptoms, and even without \textit{H. pylori} infection, a shift to using fat for energy may create psychosis. Excess ketones secondary to \textit{H. pylori} infection, a shift to using fat for energy may create psychosis. Excess ketones secondary to \textit{H. pylori} infection, inefficient ACAT enzyme activity, or starvation, can create neurological and emotional disorders. The state of ketosis induced by \textit{H. pylori} may also be involved with language delay and apraxia. However, some practitioners find the ketogenic diet helpful for seizures. Physiological situations are highly individual, so it is always advisable to check with the patient’s overseeing physician.

TRYPTAMINE: Tryptamine is a trace amine found in very low concentrations in the mammalian central nervous system, localized in neurons with a very high turnover and short half-life. Tryptamine has been postulated to be a neuromodulator, perhaps opposing the actions of serotonin, otherwise known as 5-hydroxytryptamine (5-HT). As shown in Figure 10, the serotonin and tryptamine molecules are very closely chemically related. Given this close relationship, tryptamine may be involved in the regulation of mood, emotion, sleep, and appetite, which are the cardinal functions of serotonin.

Ketosis increases tryptamine levels in animal models. Elevated tryptamine urinary excretion has been observed in schizophrenic patients, suggesting that tryptamine may be involved in the pathophysiology of schizophrenia. Due to the delicate balance in the body between serotonin metabolites, melatonin, 5-hydroxyindoleacetic acid (5-HIAA), and tryptamine, factors such as \textit{H. pylori} infection can disturb the balance of these metabolites. This may cause neurologically-based symptoms affecting mood, appetite, emotions, sleep, OCD behaviors, and psychosis. In fact, the psychotic impact of tryptamine has been compared to LSD and mescaline. Tryptamine-induced symptoms include vegetative states, athetoid movements, delusions, hallucinations, autistic-like behavior, language disturbances, spatial and temporal perception disturbances, euphoria, and anxiety.

PHOSPHOLIPIDS AND MEMBRANE FLUIDITY: When \textit{H. pylori} infection is present, it changes the way functionally important phospholipids are positioned in the neuronal cell membrane. Direct contact of \textit{H. pylori} with epithelial cells induces externalization of the inner leaflet enriched host phospholipid, phosphatidylserine (PS), to the outer leaflet of the host plasma membrane. When cells begin to undergo apoptosis, a collapse of lipid asymmetry occurs with concomitant exposure of PS at the outer leaflet of the plasma membrane, which serves as an "eat me" signal for phagocytes, thus inciting neuronal cell death.

OTHER EFFECTS: \textit{H. pylori} also decreases levels of B12 in the body; decreases iron levels; increases ammonia and taurine; and can produce glaucoma in young individuals that resolves when the \textit{H. pylori} is treated. \textit{H. pylori} infection is not just an immediate acute infection. Rather, it is a long-term chronic problem that may take months or years to eradicate. Chronic \textit{H. pylori} gastritis alters feeding behaviors, delays gastric emptying, alters gastric neuromuscular function, impairs acetylcholine release, produces greater antral muscle relaxation upon electrical field stimulation, and increases the density of SP- and CGRP-containing nerves in a mouse model. These effects can persist for months after the infection has been eradicated. Multiple mechanisms, including persistent immune
Many organisms normally found in the gut can become pathogenic in the face of poor methionine and folate cycle function, insufficient immune function, and a high toxic burden. Therefore, it is essential to treat imbalanced gut flora whenever these conditions are present.

Vitamin D plays a critical role in mucosal barrier homeostasis by preserving the integrity of tight junction complexes and the healing capacity of the colonic epithelium. Vitamin D deficiency, therefore, may compromise the mucosal barrier. An extended period may be necessary before gastric physiology can return to normal after successful *H. pylori* treatment.

**TREATMENT CONSIDERATIONS**

Many organisms normally found in the gut can become pathogenic in the face of poor methionine and folate cycle function, insufficient immune function, and a high toxic burden. Therefore, it is essential to treat imbalanced gut flora whenever these conditions are present. Although organisms such as *E. coli* and streptococci often are reported on stool analyses as normal flora, any such organisms appearing on the stool culture of an immunocompromised individual should be considered possible pathogens. These organisms’ potential pathogenic impacts in significantly immunocompromised individuals are amply documented, even if mainstream opinion continues to consider them nonpathogenic.

Our treatment approach emphasizes specialty nutritional products developed for the purpose of rebalancing. The use of prescription antibiotics often leads to further depletion of normal flora and additional imbalances, whereas herbal agents and specialty nutritional products can be utilized more safely.

Where iron is concerned, we do not give iron for documented or imagined iron deficiency, such as a low red blood cell count. We regard laboratory findings of iron deficiency or iron excretion from the body as an indication for lactoferrin and/or other specialty nutritional products designed to place iron appropriately in the body.

Vitamin D is an excellent tool for treating a number of conditions. The presence of vitamin D receptors on intestinal cells is a key factor in maintaining optimal function of the gut. For example, achieving sufficient levels of B12 will preclude the use of prescription antibiotics and help to promote the growth of beneficial flora rather than favor dysbiosis. Appropriate support with probiotic flora can lay the groundwork for an internal GI environment more conducive to normal bacterial growth. Additional steps to optimize the GI environment include focusing on pH levels, reducing hyperacidity, using digestive enzymes, reaching ideal B12 levels, and implementing other GI supports appropriate to the individual. All of these measures can help to promote the growth of beneficial flora rather than favor dysbiosis.

It is important to directly address dysbiotic and imbalanced flora in immunocompromised individuals. Treatment of streptococci and *H. pylori*, along with clostridia, *Pseudomonas* species, *E. coli*, and Klebsiella, among others, should be strongly emphasized no matter whether they are reported as normal or imbalanced. Getting the gut environment in balance, populating it with appropriate normal flora, and eradicating symptom-producing dysbiotic and imbalanced flora are key steps to achieving gastrointestinal health, gut epithelial wall integrity, neurotransmitter balance, and symptom resolution.

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REFERENCES


