NEUROTRANSMITTER TESTING
And
AMINO ACID THERAPY

By:
Marty Hinz, MD
of NeuroResearch
You cannot simply take amino acids and use them. Training is key in learning the proper application for full potential.

**INTELLECTUAL PROPERTY STATEMENT**

At the writing of this booklet, NeuroResearch has 8 patents pending or approved and is anticipating filing 2 more patents. Many things covered in this booklet are covered under the NeuroResearch patents. Permission is hereby given to use the information found in this booklet as long as NeuroResearch products are used. The only value of a patent is the ability to enforce it and it is the full intention of NeuroResearch to enforce patents as issued in cases where intellectual property is being used in treatment without NeuroResearch products.

The question is, “Why would you want to use anything else?”

NeuroResearch products cost less and work better.

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<table>
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<tr>
<th>TEST</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary Dopamine</td>
<td>50-250</td>
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<tr>
<td>Urinary Norepinephrine</td>
<td>30-65</td>
</tr>
<tr>
<td>Urinary Epinephrine</td>
<td>5.0-13.0</td>
</tr>
<tr>
<td>Urinary Serotonin</td>
<td>50-250</td>
</tr>
</tbody>
</table>

Therapeutic Ranges - Urinary Serotonin and dopamine Levels

<table>
<thead>
<tr>
<th>Urinary Serotonin</th>
<th>Therapeutic range</th>
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<tbody>
<tr>
<td>Diseases other than Weight</td>
<td>600-1200</td>
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<tr>
<td>Weight Management</td>
<td>1200-2400</td>
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<tr>
<td>Above Therapeutic Needs</td>
<td>&gt;2400</td>
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<tr>
<td>Dopamine levels therapeutic</td>
<td>400-600</td>
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</tbody>
</table>

5-HTP is not subject to regulation via a feedback loop or any other mechanism. 5-HTP is converted freely to serotonin, giving us the ability to establish systemic serotonin levels that are above the normal range.

Optimal Urinary Catecholamine Levels

<table>
<thead>
<tr>
<th>Urinary Catecholamine</th>
<th>Therapeutic range</th>
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<tbody>
<tr>
<td>Dopamine</td>
<td>100-225</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>35-65</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>8.0-12.0</td>
</tr>
<tr>
<td>Norepinephrine/Epinephrine ratio</td>
<td>3.0-6.0</td>
</tr>
</tbody>
</table>

The serotonin system and the catecholamine system must both be functioning properly in order for the system to be symptom free.

AMINO ACID DOSING

Amino acids are titrated on a weekly basis until the desired clinical responses are seen. Once a new dosing level is established, do not change the dose before 7 days has elapsed. In general, it takes 4 or 5 days to see the full effects of changing the dose. Adjusting the dose prior to 7 days will only lead to confusion.

The AM, Noon, and PM doses should be taken 1 hour before meals. If patients forget to take their pills, they may be taken with the meal. The evening doses should be taken 2 to 3 hours before bedtime.

START OF TREATMENT

(Step 1 → starting point)

<table>
<thead>
<tr>
<th>AM</th>
<th>Noon</th>
<th>PM</th>
<th>Evening</th>
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</thead>
<tbody>
<tr>
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<td>4 NeuroReplete</td>
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Step 2

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Step 3

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Step 4

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<th>PM</th>
<th>Evening</th>
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</thead>
<tbody>
<tr>
<td>4 NeuroReplete</td>
<td>4 NeuroReplete</td>
<td>6 RepleteExtra</td>
<td>6 RepleteExtra</td>
</tr>
</tbody>
</table>

USE OF CYSTEINE (pages 45-52)

All patients with low epinephrine levels (<5.0) should be started on “CysReplete” 2 pills 3 times a day (AM, Noon, and PM).

DO NOT FORGET TO EDUCATE!!! (pages 32-34)

Nausea during amino acid therapy is from 2 causes: depletion on start up and carbohydrate intolerance. See pages 13-15 for details on managing nausea during treatment.

NEUROTRANSMITTER TESTING (pages 25-32)

Initial urinary neurotransmitter testing should be obtained prior to the patient starting amino acid therapy. Tests should include: serotonin, dopamine, norepinephrine, and epinephrine levels.

Neurotransmitter testing during adjustment of amino acids should be performed prior to implementing each step above step 3.

Follow up amino acid testing should be performed at the 3rd and 6th month after the patient is stabilized, then every 6 months after stabilization has been achieved.
CONTACTING US FOR HELP

Mastery of amino acid therapy does not happen in a few weeks or months. It has been the experience of NeuroResearch that only after 1 to 2 years of direct patient care is the caregiver fully proficient in the use of amino acids.

If your patients are not getting the results you expected, or if you have questions or problems, please call the NeuroResearch toll free phone number at: 1-877-626-2220. You can e-mail NeuroResearch at info2@neuroreplete.com.

NeuroResearch sends out a 2 page monthly newsletter. If you would like to be on this mailing list, call or e-mail us. NeuroResearch maintains an “e-mail stream” where questions judged to be of better educational value are sent out each week to all clinics on the e-mail stream. If you would like to be placed on the e-mail stream, contact NeuroResearch. You can also visit the NeuroResearch web site: www.neuroreplete.com.

NeuroResearch does not take calls from or give advise directly to patients.

OUR HISTORY

NeuroResearch is a company formed from the research of the Morgan Park Clinic in Duluth, Minnesota. The following is a brief chronological overview of NeuroResearch.

**December 1995**, programming started on a computer program-database to assist caregivers in the treatment of obesity. At the heart of this program is the ability to answer the question, “Are patients positioned properly in weight loss to make goal weight?” Since 1999, the computer program has been served to clinics over the Internet and its database has documented weight loss in excess of 30 tons (60,000 pounds) involving the care of over 4,000 patients in almost 100 clinics around the United States.

**November 1997**, secondary to experiencing problems with weight loss drugs not working or drugs that quit working in almost 50% of patients, the Morgan Park Clinic began working with amino acids in an attempt to correct the problem. By early 1998, the problem was solved and the ability to keep virtually 100% of patients in appetite suppression was established.

**March 1999**, the first clinics outside of the Morgan Park Clinic using our program were established. These early programs were using prescription drugs with amino acids and computers to affect high performance weight loss in patients.

**December 1999**, after 6 months of intense work guided by the database, the first patients using amino acid therapy only and no prescription medications were started in weight loss. Database analysis at that time showed no compromise in group weight loss.

**Late 2001**, over 200 clinics around the United States are using the NeuroResearch amino acid formula for the treatment of weight loss and neurotransmitter diseases. NeuroResearch had its first patent approved in September of 2001 and has 7 additional patents pending.

At present, NeuroResearch has patents approved or pending on the treatment of over 60 diseases and illnesses that are caused by or associated with neurotransmitter dysfunction.

WHY WAS IT NOT DONE BEFORE?

From time to time, NeuroResearch is asked, “Why were you the first to perfect effective treatment of neurotransmitter diseases with amino acids and why hasn’t it been done before?”

In answering this question, there are several considerations. If amino acid therapy were simple and straightforward and only required picking up a bottle and giving it to your patients, everyone would know how to do it. The fact is, there are many pitfalls and things that must be learned in order to optimize results.

Other drawbacks in the lack of past success include:

1. Quality of the products used. Over 90% of 5-HTP on store shelves is very low quality and will not work.
2. Cost is another consideration. The average retail cost for patient under treatment with NeuroResearch formulas is about $275 a month. As we grew, our price lowered to an average wholesale cost to clinics of $45 per month.

In the past, people studying amino acids did not have access to large groups of patients in multiple clinics where data was collected at each visit. This has been the key to the success of NeuroResearch. Many times, what looks good in the examination room is not as good as we think when the computer database is reviewed.

WHAT ARE NEUROTRANSMITTERS

Neurotransmitters are naturally occurring chemicals in human beings and animals. They relay electrical messages between nerve cells known as “neurons”. This is not a simple process.

In the foods that we eat there are 4 basic components:

1) Vitamins
2) Minerals
3) Amino acids
4) Calories

Neurotransmitters are built in the body from amino acids with the assistance of vitamins and minerals known as “cofactors”. If the body does not take in enough of the amino acids, vitamins, or minerals to build neurotransmitters, a neurotransmitter deficiency state develops. Over time this leads to the development of diseases and illnesses caused by or associated with low levels of neurotransmitters.

Treating the illness that develops from low levels of neurotransmitters by giving the patient oral or IV neurotransmitters will not work since neurotransmitters will not cross the blood brain barrier and enter the brain. Drugs such as Zoloft, Prozac, and other drugs that work with neurotransmitters do nothing to increase the overall level of neurotransmitters in the brain. They work by a process known as “redistribution,” where neurotransmitters are simply moved from one place in the brain to another in order to trick the brain into thinking there are more neurotransmitters in the system. In fact, there are no more neurotransmitters in the already depleted brain. As discussed in this manual, drugs that work with neurotransmitters, over time, actually deplete the already low levels of neurotransmitters in many people, effectively making the real cause of the problem worse.

The only way to actually increase the level of neurotransmitters in patients suffering from neurotransmitter deficiency disease is by giving them amino acid precursors, vitamins, and minerals the body needs. Unlike neurotransmitters, precursors cross freely into the brain where the body converts them to neurotransmitters and actually increases the overall level of neurotransmitters in the deficient system as verified by laboratory testing.

So this begs the question, “Why don’t we simply train people to eat properly in order to get rid of their diseases?” As you will see by reading this booklet, simply designing the perfect diet is not practical or possible. We know from our database research as based on data from almost 100 clinics, that the perfect diet would involve eating the amount of protein found in 35 ounces of red meat or 18 eggs each day. 35 ounces of meat has 2,440 calories and would never keep a 140-pound female at 140 pounds, therefore we looked to nutritional supplements for help. Supplements are used within USDA guidelines and obtain results that cannot be achieved on a practical level from diet alone.

When neurotransmitters are excreted into the synapse, in response to an electrical stimulation traveling down the pre-synaptic neuron, the process is best thought of as one of modulation of the post synaptic neuron. Low levels of neurotransmitters in the synapse will cause ineffective firing of the post-synaptic neuron and high levels of neurotransmitters will cause an excited firing of the post synaptic neuron. The post-synaptic neuron has the potential to fire an electrical charge. It is the magnitude and the rate of firing that are controlled by the neurotransmitters as they come in contact with the receptors of the post-synaptic neuron.

SYNAPTIC MODEL

Even though the NeuroResearch drawing on the next page depicts serotonin flow between the pre-synaptic and post-synaptic neurons, the same is basically true regarding the catecholamines (dopamine, norepinephrine, and epinephrine) as follows.
Simply substitute in the diagram above:

1. Tyrosine for tryptophan.
2. L-dopa for 5-HTTP.
3. The catecholamines for serotonin.

and the following basic observations remain the same.

1. Serotonin is produced from tryptophan, which is turned into 5-hydroxytryptophan (5-HTTP), which in turn is converted to serotonin inside the presynaptic neuron.
2. Serotonin is assimilated into the vesicles of the presynaptic neuron (also known as the “serotonin store”).
3. Serotonin is excreted into the synapse (the space between the presynaptic and postsynaptic neurons).
4. Serotonin then comes in contact with the receptors on the postsynaptic neuron and causes modulation of the postsynaptic neuron firing.
5. Serotonin does not stay in the synapse indefinitely, it is subject to one of three fates:
   A. Reuptake can happen and it is returned to the store.
   B. Serotonin is metabolized outside of the store by the Monoamine Oxidase system (MAO).
   C. It discharges from the synapse into the system and once again its ultimate fate is metabolism by the MAO system or reuptake by another synapse.

**DISEASES CAUSED BY NEUROTRANSMITTER DEFICIENCY**
BLOOD BRAIN BARRIER

A curtain of blood known as the “blood brain barrier” surrounds the brain. In general, water-soluble things cross the blood brain barrier and get into the brain, whereas fat-soluble things do not cross the blood brain barrier.

NEUROTRANSMITTERS

Neurotransmitters are the chemicals in the nervous system that relay and modulate electrical impulses between nerve cells known as “neurons.” Low levels of neurotransmitters cause diseases and illness. Neurotransmitters are fat soluble and do not cross the blood brain barrier, when given to a patient with low levels of neurotransmitters orally or IV, they will do nothing to increase neurotransmitter levels at the point of the problem, the brain.

AMINO ACIDS

The body builds neurotransmitters from amino acids. The building of neurotransmitters requires vitamins and minerals, which are known as cofactors, in order for the appropriate chemical reactions to occur in the brain. Only by giving the body what it needs to build neurotransmitters can the problem be properly addressed and the levels of neurotransmitters in the brain be increased. Through laboratory testing, we are now able to demonstrate this increase.
SIZE OF SEROTONIN NEURONS
The common conception is that serotonin neurons are extremely small. The fact is that the serotonin neurons in the adult human can be up to 12 inches long. The lines on the following brain represent one serotonin neuron arising from the base of the brain.

MIXED NEUROTRANSMITTER DYSFUNCTION THEORY
Based on clinical observations, NeuroResearch has formulated the following theory known as the “mixed neurotransmitter dysfunction theory”. 5% of patients with a given neurotransmitter dysfunction disease are purely a serotonin dysfunction, 5% of patients with a given neurotransmitter dysfunction disease are purely a catecholamine dysfunction and the remaining 90% are a mix of serotonin and catecholamine dysfunction lying somewhere along the spectrum between the two extremes.

BOTH SYSTEMS MUST FUNCTION PROPERLY
The serotonin system and the catecholamine system (dopamine, norepinephrine, epinephrine) must both be functioning properly for the entire system to be healthy and free of neurotransmitter disease. This appears to be reflected in neurotransmitter testing by the fact that patients with dysfunction of the catecholamine system tend to need higher serotonin levels to compensate and obtain a clinical response.

Prior to his retirement, the head of the clinical science department at the local medical school on many occasions said, “The serotonin and catecholamine systems must both be functioning properly for the system as a whole to function properly and be healthy.” Coming from the head of the clinical science department we took it as gospel truth. It was only after working with patients extensively in weight loss for several years did I fully appreciate what he meant.

There is one final truth to the equation and that is, “5% of patients with neurotransmitter disease relating to the serotonin and catecholamine system are purely a serotonin dysfunction, 5% are purely a catecholamine dysfunction, and the remaining 90% are a mix of serotonin and catecholamine dysfunction lying somewhere along the spectrum between the two ends.

If you understand the two concepts above and use them as reference points in working with patients who have neurotransmitter dysfunction, eventually you too will come to see the patients who are purely a catecholamine or serotonin dysfunction as well as the rest of the patients.

HOW DO YOU SEE THE PATIENTS?
In this discussion, I will turn to clinical experience in treating patients with depression and obesity, although the approach for other diseases are similar.

The head of the clinical science department at the medical school had a strong interest in the treatment of obesity and his assertion was that weight problems were caused by dysfunction of serotonin and/or norepinephrine. This assertion seems simple enough but the ramifications are profound. Since the head of the clinical science department at the medical school said it, I took it as true and in retrospect he hit the nail on the head. Along the way, I have come in contact with many physicians who did not have the benefit of a medical school department head as they started treating obesity and advocated numerous other things as being the cause, many of them not even related to neurotransmitters. Sure there are other things that affect weight loss, but from an appetite control and
suppression standpoint, it is ONLY serotonin and norepinephrine that have the ability to function.

So how do we know this? First, let’s answer this question from a clinical standpoint. The only prescription drugs that we have in medicine that induce appetite suppression are the drugs that work with serotonin and/or norepinephrine. There is no appetite suppression associated with any of the drugs that work with dopamine, epinephrine, or anything else for that matter.

The weight loss drug phentermine, for example, works in a very powerful way with norepinephrine and induces appetite suppression. Appetite suppression, in turn when used properly with proper patient positioning causes weight loss to occur.

Amphetamines have a very strong effect on serotonin. Fenfluramine was a very well known amphetamine that produced appetite suppression by increasing serotonin levels in the synapse. Tim Seaton, MD, the medical director for Meridia at Knoll pharmaceuticals personally told me of an animal experiment they had performed where micro-electrodes were wired into the synapses of rat brains and the rats were subsequently fed fenfluramine. The intersynaptic levels of serotonin went up 2,500 times.

Certain norepinephrine drugs and certain serotonin drugs can induce appetite suppression, but there is a third type of drug known as the serotonin norepinephrine reuptake inhibitors (SNRI), which works on both the serotonin and norepinephrine system. The prototype drug in weight loss is Meridia, which works on both systems and induces appetite suppression.

Over-the-counter preparations that work to induce appetite suppression include Ephedra and Phenylpropanolamine (which was recently pulled from the market). Both again exert their effects on the serotonin and norepinephrine systems.

So what did the first patient with norepinephrine dysfunction only look like? I was in the clinic seeing patients and we were having the patients fill out a form relating to serotonin diseases. The patient came into the clinic for weight loss, and by way of the survey she had filled out, indicated that she had no problems with serotonin disease. The real lynch pin was the history obtained. She previously had dieted on phentermine alone, lost 48 pounds and never was hungry. Anyone who has worked with phentermine only in weight loss knows what a feat that is. I had before me a pure norepinephrine dysfunction patient.

I have seen very few patients, who on 5-HTP alone lose all the weight they want. Obviously these people are a serotonin only dysfunction.

I hope I have planted the seeds here to, at least, get you thinking about neurotransmitter dysfunction in patients as lying along a spectrum, and who knows, maybe some day you too will see your first norepinephrine only dysfunction patient.

**TREATING ONLY ONE SYSTEM WILL NOT WORK IN ALL**

5-HTP has gained recognition as being helpful in and of itself in the treatment of neurotransmitter disease and we have studied its chemical properties and clinical applications extensively. Based on our experience and research from our large database, I would make the following observations on the use of only 5-HTP.

Only 35 to 40% of patients get some results using 5-HTP alone, the rest get no response. Sure there is the 10 to 15% of patients who get spectacular results from 5-HTP when used alone and are held up for all to see. The remaining 85 to 90% who get only a marginal response, or no response, are swept under the rug.

So, why do not all patients respond to 5-HTP only? Remember the assertions at the beginning of this section, “Both systems have to be functioning properly for the system to be healthy.” In using 5-HTP only to treat a group of patients, you are ignoring many things and many people do not get better. Hence the need for both 5-HTP and tyrosine with all the cofactors and supporting elements we have put in place. With the right combination (like we have put in the supplements) and proper training on how to treat with amino acids, 95%+ of patients will do as well as and arguably much better than any treatment available with prescription drugs.

**DEPRESSION THE SPECTRUM MODEL**

We have talked about the treatment of obesity as it relates to mixed neurotransmitter dysfunction, but the basic concepts just discussed are the same for virtually all neurotransmitter diseases relating to serotonin and catecholamines. To make the point, we will now explore the treatment of depression.
Focusing first on 5-HTP, if you treat patients with depression with 5-HTP only about 10 to 15% of patients will get good results with the rest getting marginal or no results. In medicine, there are prescription drugs that work almost exclusively with serotonin in the brain such as Celexa. Celexa is a highly selective serotonin drug that is effective in the treatment of depression, but again not in all cases. So what do doctors do in treating patients who do not respond to Celexa? Usually start a catecholamine drug such as Wellbutrin.

On the other side of the coin are patients with depression who are started on Wellbutrin only and do not respond. In these cases, doctors will add a serotonin drug such as Celexa. If you imagine the prescription drugs available for the treatment of depression as lying along a spectrum with Wellbutrin on the far catecholamine end of things and Celexa on the far serotonin end of things with other drugs such as Effexor, Prozac, Zoloft, Luvox (in that order from catecholamine to serotonin) lying on the spectrum in between the two extremes, you will have a clear picture. These drugs do not simply work on one system or the other. They all to some degree exert their effects on both systems.

Then there is Effexor, an SNRI drug that is in the middle of the spectrum that works on both the serotonin and norepinephrine system and is used extensively for depression in medicine.

There are older antidepressants such as tricyclic antidepressants, which work primarily on the norepinephrine system and the MAO drugs that work in depression on both the serotonin and catecholamine system.

The point is, medicine for a long time has known that depression is not caused by only the serotonin system or only the catecholamine system. It has to be viewed as a “mixed disease process” when treating a group of patients or not all patients will get relief.

Yes, you can treat with things that only work primarily with one system or the other, but you will not get optimal results in a group if that is the only approach you use. With all the work that we have done with amino acids in treatment of neurotransmitter disease, we know that treating everyone in the group with amino acids that cover both ends ends of the spectrum is the only way to achieve optimal results and have all patients in the group do well.

So, what about sorting out those patients who simply need 5-HTP or tyrosine with cofactors and not giving all the patients everything needed to cover both ends of the spectrum? We have simply found it too difficult to sort accurately the very few that can get by on treating only one end of the serotonin/catecholamine spectrum, although we have seen it. Besides, “Why would you need to do it?” The side effect profile of the amino acid formula that we have developed is similar to placebo.

CAUSES OF NEUROTRANSMITTER DYSFUNCTION

Patients with neurotransmitter diseases are suffering from low levels of serotonin and/or catecholamines. But how do these low levels of neurotransmitters develop? A number of years ago, I wrote papers for my patients on the genetic basis of neurotransmitter disease such as obesity. From a common sense standpoint it made sense. Certainly there are families where the grandparents, parents, and children are all suffering from obesity. As time passed and we began to work with amino acids, the results were astounding. Now I believe that the primary cause of neurotransmitter disease is from long-term dietary deficiency. I still come in contact with people who expound the genetic theory of neurotransmitter dysfunction as I once did, to them I answer, “Where did they learn to eat, from their parents.” This usually ends the conversation on genetics.

Over time we have begun to focus on three major causes of neurotransmitter dysfunction:

1. Nutritional deficiency.
2. Drugs and substances that deplete neurotransmitters.

NUTRITIONAL DEFICIENCY

The drug companies studying animal models have known for many years that feeding animals a diet that is void of a specific nutrient will induce a deficiency. For example, if the researchers want to deplete serotonin in animals, they will feed the animals a tryptophan free diet. The same is true with animals where depletion of the catecholamine system is desired and a tyrosine free diet is fed.
In weight loss successful people eat about 1/3 of the food they were prior to dieting and thus a nutritional deficiency can develop which in turn causes what we describe to the patients as, “bringing on the big appetite” and causes them to fail in weight loss.

Based on our experience in patient care over the last 4 years, we now firmly believe that the number one cause of neurotransmitter dysfunction in patients is long-term dietary deficiency.

**DRUG DEPLETION**

We will use the SSRI medications as the prototype for discussing neurotransmitter depletion induced by drugs. At the end of this booklet is a discussion of neurotransmitter testing results which specifically demonstrate depletion by drugs.

So why do drugs like Prozac, Zoloft, Paxil, Luvox, Celexa, Effexor, Welbutrin, and many others cause further depletion of neurotransmitters in many people?

We start with the assumption that the patient was depleted at the start of treatment as evident by the fact that they were suffering a depletion disease that was treated with one of the drugs listed on page 10. So the patient is put on Zoloft which acts by blocking serotonin reuptake and in the process of not letting the serotonin back into the pre-synaptic neuron, the synaptic levels of serotonin rise, tricking the brain into thinking there is more serotonin in the system and their brains starts functioning normally. But the real fact is that the drug has not created one additional molecule of serotonin in the system, it has merely worked by moving neurotransmitters from one place to another in the brain.

So now the serotonin molecules are subjected to being outside of the store in the pre-synaptic neuron on a much longer basis. The longer the molecules are outside the store, the more likely they are to come in contact with the Monoamine Oxidase System (MAO) which is the enzyme system that breaks down neurotransmitters (both catecholamines and serotonin).

For the patient who presented for treatment with a neurotransmitter deficiency disease, in many cases it was secondary to a dietary deficiency and by putting the patient on a drug that accelerates MAO metabolism without increasing nutrient intake gives the net effect of further depletion.

From a clinical standpoint, the most prominent thing seen is that the drugs quit working or a disease that gets worse (see page 21).

Now briefly back to the original weight patients that we were working with. 46% of patients under treatment with prescription medications found that the drugs quit working in weight loss on an average of 3.3 months into treatment. The problem here was two-fold. First, the patients became depleted on a lower intake diet. Second, the drugs used to treat the patients further depleted the patients and aggravated the picture. Both caused further depletion.

**NEUROTOXICITY**

Drugs with neurotoxic effects induce changes in the nervous system, “THAT ARE PERMANENT!” There are many things that are neurotoxic but they generally fall into one of three categories; heavy metals, chemicals and drugs. From a clinical standpoint, the effects of neurotoxicity look exactly the same as depletion and a neurotransmitter dysfunction is seen. Not all neurotransmitter dysfunction is a depletion issue; exposure to neurotoxins in the...
past may be the problem. The issue of neurotoxicity is an academic one. The symptoms, clinical presentations, and treatment with amino acid therapy are the same as depletion.

The prototype drug for inducing neurotoxicity is amphetamine. Damage with neurotoxins occurs at the receptors of post-synaptic neuron and the net effect is a dysfunction in the proper firing of the post-synaptic neuron. The same problem is seen with depletion.

Since 1975, articles have appeared in the literature regarding fenfluramine being neurotoxic in animals, but until now there has been no evidence of how it affects humans. Our data shows that people who took fenfluramine need 28% more amino acids in treatment to attain the proper clinical response. A fact that is even more significant considering it has been over 4 years since any of them have taken fenfluramine.

In the 1960’s and early 1970’s, doctors prescribed amphetamines to patients for diet. Today, many of these patients are suffering from neurotransmitter dysfunction disease. One patient in our practice, who is 43 years old, reported taking up to 100 white crosses (a form of street amphetamine) per day in her early and mid 20s. When she presented, she was suffering from extreme neurotransmitter disease. After only one week of treatment, her symptoms resolved.

**DRUG THAT WORK WITH NEUROTRANSMITTERS DO NOT WORK IF THERE IS NOT ENOUGH NEUROTRANSMITTERS TO WORK WITH!!!**

We started working with amino acids in an attempt to get prescription medications that were no longer working to work again. They indeed did start working again. Within 6 to 8 months we had fixed the initial process that we had set out to correct. For almost 3 years we have been saying, “Drugs that work with neurotransmitters do not work if there is not enough neurotransmitters to work with”. We had no basis in literature, only our research and experience. Then in the spring of 2000, the following was published by Dr. Delgado in the Journal of Clinical Psychiatry:

“NE-selective (norepinephrine-selective) antidepressant drugs appear to be primarily dependent on the availability of NE for their effects. Likewise, 5-HT-selective (serotonin-selective) antidepressants appear to be primarily dependent on the availability of 5-HT for their effects.”

In this paragraph, it would appear that the author is saying the same thing we have been saying for almost 3 years, “Drugs need neurotransmitters to work”. This whole thing seems simple now, but the fact is it has large implications. We did indeed get the drugs working in the weight patients again, but this can be applied to any situation where drugs that work with neurotransmitters quit working or do not work from the start of treatment. For the depressed patient who literally wakes up one day to find their Zoloft or other similar drugs are not working, amino acid therapy can restore the clinical picture.

We began using amino acids to get prescription drugs properly working. As time progressed we found we could get the same job done with amino acids alone, without using prescriptions drugs. The training and skill of the caregiver is critical to the outcome. If things are not turning out as you think they should, get in touch with NeuroResearch, we can help.

For now, we see only limited applications of prescription drugs; these are discussed in the section on disease management. In general, using depression as the prototype, we still recommend prescription drugs with patients who are suicidal, or in whom the depression is severe enough to interfere with day-to-day activities. In most of these cases, drugs are needed with amino acid therapy for only 4 to 8 weeks.

**THE HEALTHY AMERICAN DIET**

Many Americans believe that the following is a “healthy diet”:

1. Avoid red meat.
2. Lots of vegetables.
3. Lots of fruit.
4. Low fat foods.
5. Some white meat to include fish.

The fact is, this is a tryptophan and tyrosine deficient diet. It is little wonder so many people are suffering from diseases and illnesses caused by or associated with neurotransmitter deficiency.
DEPLETERS OF NEUROTRANSMITTERS

Luvox
Zoloft
Prozac
Celexa
Paxil
Trazodone (Deseryl)
Sinequan (Doxepin)
Serzone
Effexor
Meridia
Phendimetrazin (Bontril)
Phentermine (Adipex)
Phenylpropanolamine (Dexatrine)
Tenuate
Mazindol
Fenfluramine (racemic)
D-fenfluramine
Amphetamines (all to include Ritalin)
Ephedra
Caffeine
Alcohol (ETOH)
Nicotine
Imitrex
Zomig
Maxalt
Amerge
Amitriptyline (Elavil)
Nortriptyline (Norpramin)
Remeron
Wellbutin (Zyban)
Thioridazine (Mylan)

Cheeses
Chocolate
Citrus fruits
Tomatoes
Eggs
Onions
Mustard
Shell fish
Red wine
Monosodium Glutamate (MSG)
Anything strongly cultured or fermented
Nitrates & Nitrites
Meat tenderizers
Salad bars that spray with sulfites
Aspartame (nutasweet)
Saccharin
Smoked/cured meats
Cold cuts containing nitrates, etc.
Frankfurters containing nitrates, etc.
Food preservatives
Paint fumes & other chemical fumes
Excessive use of coffee or tea
Tempeh, Tomari, Tofu, Yogurt, Umbusi,
Soy sauce, (fermented)
Nuts and nut butters
Tobacco
Beer
Chemically processed decaffeinated coffee
Excessive exposure to fluorescent lighting

NEUROTRANSMITTER DYSFUNCTION

There are three principle causes of neurotransmitter dysfunction: 1) nutritional deficiency 2) depletion 3) neurotoxicity. The results of all three are the same: disease.
TESTING FOR DRUG INDUCED DEPLETION
Drugs that work with neurotransmitters have a very powerful ability to move neurotransmitters around through processes such as excretion and reuptake inhibition. Many patients on long-term prescription drugs that work with neurotransmitters may have normal neurotransmitter levels during the initial testing on the drug. To gain a true picture of the neurotransmitter status underlying the drug, it is important to obtain two sets of neurotransmitter tests. The first set should be obtained, if possible, when the patient is still taking the drug. The second set of tests should be taken once the patient has been off of the drug for a period long enough that the drug has been completely removed from the system. In medicine, it is recognized that after stopping a drug, it takes “4 half-lives” for the drug to be completely removed from the system. “One half-life” is the amount of time needed to remove 50% of the drug from the system. In some cases, the symptoms displayed by the patient, who is off of the medication, are severe. In these cases, it may be necessary to test and place the patient back on the drug before it is able to get fully out of the system. Symptoms always take priority over depletion testing.

TIME OFF A DRUG FOR DEPLETION TESTING
Note: These are “mean half lives”, 50% of patients took longer 50% of patient took less to clear the drug.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Half life (T½)</th>
<th>4 half-lives</th>
<th>Time to test after stopping med</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celexa</td>
<td>35 hr</td>
<td>5.8 days</td>
<td>10 to 14 days</td>
</tr>
<tr>
<td>Depakote</td>
<td>16 hr</td>
<td>2.6 days</td>
<td>4-5 days</td>
</tr>
<tr>
<td>Effexor</td>
<td>11 hr</td>
<td>1.8 days</td>
<td>4-5 days</td>
</tr>
<tr>
<td>Luvox</td>
<td>15.6 hr</td>
<td>2.6 days</td>
<td>4-5 days</td>
</tr>
<tr>
<td>Meridia</td>
<td>16 hr</td>
<td>2.6 days</td>
<td>4-5 days</td>
</tr>
<tr>
<td>Paxil</td>
<td>21.0 hr</td>
<td>3.5 days</td>
<td>5-7 days</td>
</tr>
<tr>
<td>Phentermine</td>
<td>20 hr</td>
<td>3.3 days</td>
<td>5-7 days</td>
</tr>
<tr>
<td>Prozac</td>
<td>9.3 days</td>
<td>37.2 days</td>
<td>6 to 7 weeks</td>
</tr>
<tr>
<td>Remeron</td>
<td>40 hr</td>
<td>6.6 days</td>
<td>10-14 days</td>
</tr>
<tr>
<td>Wellbutrin</td>
<td>14 hr</td>
<td>2.3 days</td>
<td>4-5 days</td>
</tr>
<tr>
<td>Zoloft</td>
<td>27.2 hr</td>
<td>4.5 days</td>
<td>7-10 days</td>
</tr>
</tbody>
</table>

PHENTERMINE AND BONTRIL
The following neurotransmitter tests were collected from a patient who had been taking phentermine for approximately 18 months. The 9/14/01 test was collected while the patient was still on phentermine. 9/19/01 test was collected after the patient was off phentermine for 5 days.

<table>
<thead>
<tr>
<th>DATE COLLECTED</th>
<th>Dopamine AM</th>
<th>Norepinephrine AM</th>
<th>Epinephrine AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/14/01</td>
<td>112.50</td>
<td>35.00</td>
<td>4.50</td>
</tr>
<tr>
<td>09/19/01</td>
<td>201.80</td>
<td>60.30</td>
<td>2.80</td>
</tr>
</tbody>
</table>

The following tests were collected from a patient who had been on phentermine approximately 10 months. The 9/09/01 test was collected taking phentermine and the 9/19/01 test was collected after the patient was off phentermine for 5 days.

<table>
<thead>
<tr>
<th>DATE COLLECTED</th>
<th>Dopamine AM</th>
<th>Norepinephrine AM</th>
<th>Epinephrine AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/09/01</td>
<td>184.70</td>
<td>80.80</td>
<td>3.20</td>
</tr>
<tr>
<td>09/19/01</td>
<td>147.20</td>
<td>60.90</td>
<td>2.10</td>
</tr>
</tbody>
</table>

Effects of phentermine happen sooner than months into treatment. The labs below were collected 1 week prior to the start of treatment on 09/17/01. The second lab was collected on 10/06/01 after 7 days of treatment with phentermine, followed by 5 days off.

<table>
<thead>
<tr>
<th>DATE COLLECTED</th>
<th>Dopamine AM</th>
<th>Norepinephrine AM</th>
<th>Epinephrine AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/17/01</td>
<td>126.00</td>
<td>24.30</td>
<td>5.00</td>
</tr>
<tr>
<td>10/06/01</td>
<td>119.70</td>
<td>22.40</td>
<td>1.50</td>
</tr>
</tbody>
</table>

The following tests were collected from a patient who had been on Bontril for several months. The 9/25/01 test was collected taking phentermine. The 10/11/01 test was collected after the patient was off Bontril for 5 days.

<table>
<thead>
<tr>
<th>DATE COLLECTED</th>
<th>Dopamine AM</th>
<th>Norepinephrine AM</th>
<th>Epinephrine AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/25/01</td>
<td>202.30</td>
<td>42.50</td>
<td>6.20</td>
</tr>
<tr>
<td>10/11/01</td>
<td>117.00</td>
<td>68.40</td>
<td>4.30</td>
</tr>
</tbody>
</table>
DISCUSSION OF PHENTERMINE AND BONTRIL RESULTS
We feel the following is the best embodiment of thinking on the actions of phentermine and Bontril.

FROM U.S. Patent 4,885,312 (Wurtman)
Indirect-acting sympathomimetic amines (such as phentermine and Bontril) function by releasing stored norepinephrine from sympathetic nerve endings. The major problem with their use is that after a few doses, they often stop functioning, i.e., tachyphylaxis sets in. Tachyphylaxis is known to be associated with the partial depletion of norepinephrine in the nerve endings. This leads to the supposition that there are releasable and non-releasable pools of norepinephrine and when the drugs cease functioning, it is because the releasable pools have been severely depleted.

THE PHENTERMINE DEPLETION THEORY
As we started testing patients who had been treated with phentermine or Bontril and were off the drugs for 5 days, we expected to see low norepinephrine levels. This was not the case. In all cases, the norepinephrine level remained about the same or increased, while the epinephrine level uniformly decreased (see page 26). The next step was to explain why this happened. In doing so, the “Phentermine Depletion Theory” came into existence. The theory is as follows:

The ability of norepinephrine to be excreted into the synapse takes precedence over the ability of norepinephrine to act as a precursor. In the process, depletion of norepinephrine shows up through depletion of epinephrine.

We have seen similar results with dopamine drugs that are suspected of causing depletion of dopamine. Once the dopamine is stopped, the dopamine levels remain normal or elevated, but the norepinephrine and epinephrine levels fall. It was suggested along the way that phentermine may act as a reuptake inhibitor, but the fact is that the T1/2 of phentermine is 20 hours meaning it should be fully out of the system at testing 5 days (120 hours) later.

RESULTS OF TESTING → Prozac
The following lab results are from a female reportedly being on Prozac for 10 years. It was reported that she quit the Prozac because it was no longer working and she saw no point in taking it anymore. The neurotransmitter test was performed approximately 3 weeks after stopping the Prozac. Looking at the “half-life chart” on the preceding page, it is quite possible the patient still had Prozac in the system. These values may have been even lower 2 to 3 weeks after this test was performed. Most notable in the lab results reported is the fact that the Serotonin level of 15.5 is the lowest level seen in over 600 patients in the study so far.

As previously noted in this booklet, “drugs that work with neurotransmitters do not work if there is not enough neurotransmitters to work with”. In reviewing the testing, you can see the state that 10 years of Prozac therapy left this patient in and why her drugs were no longer working.

<table>
<thead>
<tr>
<th>DATE COLLECTED</th>
<th>Serotonin AM</th>
<th>Dopamine AM</th>
<th>Norepinephrine AM</th>
<th>Epinephrine AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/20/01</td>
<td>15.5</td>
<td>229.0</td>
<td>27.5</td>
<td>3.3</td>
</tr>
</tbody>
</table>

MORE THOUGHTS ON DRUG DEPLETION
The following is from the NeuroResearch patient orientation manual for high performance weight loss.

The appetite center of the brain is controlled by neurotransmitters. When neurotransmitter levels become low, diseases can occur. Prescription drugs work by moving neurotransmitters from one place to another in the brain. They do nothing to actually increase the overall number of neurotransmitter molecules in the brain. At the start of treatment there is still the same amount of neurotransmitter molecules. They have simply been redistributed from one place to another.

In the process of moving neurotransmitter molecules from one place to another in the brain, further depletion of neurotransmitters can take place effectively, making the cause of the problem worse. Drugs that work with neurotransmitters do not work if there are not enough neurotransmitters to work with. This is why
prescription drugs quit working in some people, do not work from the start of treatment in other patients or why some people feel worse when they stop the drugs.

Drugs like Phentermine, Phendimetrazin, Tenuate, Prozac, Zoloft, Paxil, Celexa, Effexor, Meridia, Trazodone, Serzone, Ephedra, and many more, can cause depletion of neurotransmitters in people.

If we had a drug that made the real cause of the problem worse, while making the symptoms better for a while, should we use it? This is exactly what happens in many people with these drugs.

**CENTRAL NERVOUS SYSTEM STIMULANTS**

The following test is from a patient taking the central nervous system stimulant Ritalin for hyperactivity on a long-term basis. Of importance here is the fact that the norepinephrine level is low with a normal epinephrine level. The use of central nervous system stimulants such as Ritalin and amphetamines are the only applications where we have seen a low norepinephrine level with normal epinephrine level. In all other cases, when the norepinephrine level is low, the epinephrine level is also low. It is noted that this patient was actively taking Ritalin. It is theorized that Ritalin acts as a sympathomimetic agonist, and in the process, it blocks excretion of norepinephrine. Testing patients on and off central nervous system stimulants shows a similar pattern that is distinctly different from phentermine testing on page 26.

<table>
<thead>
<tr>
<th>DATE COLLECTED</th>
<th>Serotonin AM</th>
<th>Dopamine AM</th>
<th>Norepinephrine AM</th>
<th>Epinephrine AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/10/01</td>
<td>93.40</td>
<td>94.30</td>
<td>3.90</td>
<td>6.30</td>
</tr>
</tbody>
</table>

**HYPERACTIVITY**

Hyperactivity in pediatric patients has shown results that are again unique. The following is from a 10-year-old male patient with a history of hyperactivity. As noted, the catecholamines are increased uniformly across the board. Dopamine, norepinephrine, and epinephrine are markedly elevated. The twist is as follows: the boy responded to amino acid therapy, the elevation in urinary catecholamines was due to an undetermined mechanism that enhances excretion of neurotransmitters from the kidney. This caused low systemic levels of neurotransmitters, which responded to treatment. Pediatric hyperactivity is the only circumstance so far identified where urinary neurotransmitter levels are not correlating with systemic levels.

This appears to be a very important finding out of the neurotransmitter testing work being done by Pharmasan Labs and NeuroResearch. Obviously the next step is to explain why the increased excretion of neurotransmitters is occurring.

<table>
<thead>
<tr>
<th>DATE COLLECTED</th>
<th>Serotonin AM</th>
<th>Dopamine AM</th>
<th>Norepinephrine AM</th>
<th>Epinephrine AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/10/01</td>
<td>200.5</td>
<td>438.2</td>
<td>172.9</td>
<td>13.2</td>
</tr>
</tbody>
</table>

**RESULTS IN OBESITY INITIAL TESTING**

The obese patient is considered to have a neurotransmitter deficiency disease, but at the start of treatment many of these patients have normal serotonin and dopamine levels. 20% have low norepinephrine levels. 79% have low epinephrine levels. If obesity is a combination of serotonin and norepinephrine deficiency in 90% of patients, “Why doesn’t it show up in more patients at the start of treatment?”

About 5 years ago we formulated “The strainer theory”. The main cause of neurotransmitter deficiency is from nutritional deficiency. The theory is: “In order for the 300-pound female to function on a nutritionally poor diet found on intake to the weight programs, the patient needs to eat enough calories to keep her at 300 pounds in order to get the nutrients needed.

**Typical lab results on starting weight loss**

<table>
<thead>
<tr>
<th>DATE COLLECTED</th>
<th>Serotonin AM</th>
<th>Dopamine AM</th>
<th>Norepinephrine AM</th>
<th>Epinephrine AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/18/01</td>
<td>123.5</td>
<td>130.5</td>
<td>30.1</td>
<td>3.5</td>
</tr>
</tbody>
</table>

**TESTING FOR APPETITE SUPPRESSION**

In the last 4 years, as we have worked to induce appetite suppression with amino acids, we knew all along that 5-HTP was not subject to a chemical regulatory feedback loop meaning that higher than normal serotonin levels could be obtained in the system. Suppose you take a group of 100 people and treat them with only 5-HTP. We know for a fact that only 30% or so will get some response. The rest will no have a clinical response. Both the
catecholamine system and the serotonin system have to be functioning properly for the entire system to obtain a clinical response. In the catecholamine system, tyrosine and cofactors are loaded; in the process the body has ample supplies of nutrients. It builds catecholamines whenever it needs them.

Appetite suppression can be induced by either norepinephrine drugs, such as phentermine, or by serotonin drugs, which increase the synaptic levels of neurotransmitters above normal levels. In the case of our amino acid formula, it is the 5-HTP supported by tyrosine which induces the appetite suppression. The following are the results of actual lab testing at the start of treatment and 4 weeks into treatment of obesity.

<table>
<thead>
<tr>
<th>DATE COLLECTED</th>
<th>Serotonin AM</th>
<th>Dopamine AM</th>
<th>Norepinephrine AM</th>
<th>Epinephrine AM</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/17/01</td>
<td>200.5</td>
<td>168.7</td>
<td>43.6</td>
<td>6.1</td>
</tr>
<tr>
<td>10/15/01</td>
<td>2365.4</td>
<td>170.5</td>
<td>41.8</td>
<td>5.8</td>
</tr>
</tbody>
</table>

In treatment of disease and illness other than weight, we have defined the “therapeutic range for serotonin” as being 600 to 1,200. For the treatment of obesity, we have defined the therapeutic range as being 1,200 to 2,400, although, we have seen patients with optimized catecholamine levels doing well in weight loss with serotonin levels as low as 600. In weight loss, levels above 2,400 appear to be of no benefit. In fact, it may distract from the patient’s ability to be successful in weight loss. Serotonin has a very powerful effect. It induces a “laid back feeling of well being,” and it appears that the patient’s motivation to monitor calorie intake may be affected by serotonin levels that are too high.

Neurotransmitter testing really comes into its own in the patient who is on high dose amino acid therapy and is not responding clinically. In almost all cases, neurotransmitter testing can verify if the patient needs more amino acids and establish a need to increase amino acids even further without overloading the system. Prior to amino acid therapy, we set the highest dosing of 5-HTP needed in patients at 900 mg per day. Since we have started using neurotransmitter testing, we have found a few patients who need as high as 1,400 mg per day in order to get into the desired therapeutic range.

At present, I have one patient under active treatment for fibromyalgia who is on 1,400 mg. of 5-HTP with 6,000 mg. of tyrosine a day, lab testing showed a serotonin level of 925.

Some people simply have the ability to metabolize and excrete neurotransmitters and precursors more than others.

Amino acid therapy is highly effective in weight loss, but only if proper patient guidance is put in place. The NeuroResearch database has an excess of 111,000 patient days of treatment with phen-fen, which was pulled from the market in September of 1997. Results obtained with amino acid therapy in weight loss are much greater than the weight loss results obtained with phen-fen.

So how could this be? We know from the NeuroResearch database that 46% of patients taking phen-fen plateaued and quit losing weight an average of 3.3 months into treatment. This appears to have occurred secondary to the depletion of neurotransmitters by the phen-fen and by nutritional deficiency due to fewer nutrients being taken in.

Amino acid therapy in weight loss is not the cure in and of itself. Proper positioning of patients is the key once appetite suppression is achieved..

Calorie counting is controversial in weight loss programs, but we have no doubt in asserting, “If you want to maximize the number of patients making goal weight, you need to have your patients count calories.” In appetite suppression on amino acids, patients can eat comfortably at 900 calories per day or 3,000 calories per day. It is up to the patient to monitor food intake for maximum results. For a complete set of orientation materials in weight loss see, www.USAweightloss.com and click the “literature hyperlink”.

GI UPSET

GI upset is divided into two groups, “start up” and “carbohydrate intolerance”. It would appear, in the past, that problem has not been fully understood. Once the causes of these problems are understood, they are easily managed, allowing patients the full ability to use natural amino acid therapy in place of prescription drugs in the treatment of disease. GI upset is easy to manage if you explain it to the patient at the start of treatment. If you do not tell your patients about this, you may not have a patient once treatment is underway.
GI UPSET ON STARTUP = DEPLETION
About one out of every 150 patients experience GI upset on starting treatment. This GI upset builds with every dose until about 3 days out when patients can no longer tolerate it and they stop taking their supplements. Our database has shown that patients who experience this problem are the most serotonin-depleted patients, as evident by the large number of other neurotransmitter illnesses present. It is ironic that these rare patients are the ones that need NeuroReplete the most for neurotransmitter deficiency disease.

All patients need to be warned about this problem at initiation of therapy. The problem is best managed by restarting the patient on only one capsule at bedtime (when ready to go to sleep). Increase the dosing by one pill after 3 to 4 days of no symptoms, with subsequent increases in dosing in a similar manner until the normal starting dose is achieved in 3 to 4 weeks.

GI UPSET WEEKS INTO TREATMENT = CARBOHYDRATE INTOLERANCE
This problem of GI upset was very difficult to pin down. However, once understood, it was easy to deal with by both the caregiver and the patient. As we treated patients over the last 3 years with the amino acid dosing schedule in “NeuorReplete”, up to 70% of patients reported periodic GI upset. They tended to blame their GI upset on the supplements. In the end, it was not “the supplements,” but a carbohydrate intolerance that had developed with treatment.

Carbohydrates are high calorie foods with very little nutritional value. Common examples include bread, noodles, candy, cereals, chips, popcorn, pies, cakes, pop, pancakes, waffles, and syrup. Typically, intolerance symptoms come on 2 or 3 hours after eating, and lasts 30 minutes to an hour. **CHANGING ONE FOOD USUALLY CURES IT.** For example, we have seen patients who change from white bread to whole wheat bread and no longer experience further symptoms.

If a patient is **one or more weeks into treatment** and begins to experience GI upset 2 to 3 hours after eating, they should:
1. Read a NeuroResearch patient brochure.
2. Be instructed to remember what they just ate.
3. Usually it is easy to identify the carbohydrate that just caused the problem.
4. In most cases, it is only one specific carbohydrate causing the problem.
5. In many cases it is a favorite food.
6. Patients should also be instructed on this problem at the start of treatment.

CASE STUDY #1
CARBOHYDRATE INTOLERANCE
A 48-year-old male under treatment with NeuroReplete came into the clinic at 10AM complaining of GI upset and nausea. Even though he had been orientated on carbohydrate intolerance, he did not make the connection. On questioning, he had eaten 2 eggs and 2 slices of bread for breakfast. **IT WAS THE BREAD.** He changed from white bread to whole wheat bread and had no further problems. One month into treatment, his migraine headaches were gone, he was sleeping better at night and he was having no further problems with depression.

CASE STUDY #2
CARBOHYDRATE INTOLERANCE
A 37-year-old female under treatment with NeuroReplete for fibromyalgia reported 2 weeks into treatment that she was experiencing nausea every morning about 3 hours after eating. The only thing she ate consistently every morning was her favorite cereal, Shredded Wheat. She quit eating Shredded Wheat and subsequently reported that she could eat any other cereal including Wheaties with no problems. The patient reported feeling great, with her fibromyalgia 80% better 4 weeks into treatment.

CASE STUDY #3
CARBOHYDRATE INTOLERANCE
34-year-old female with severe depression began having GI upset mid-afternoon. She reported that she had been on 14 different antidepressant drugs in the past, without relief. She was dieting and eating only a salad for lunch. The salad dressing turned out to be a high calorie dressing that was carbohydrate based. She switched salad dressings and had no further problems. The patient reported that her depression began to lift 3 to 4 weeks into treatment with NeuroReplete.
The following is the incidence of side effects reported at clinic visits considered:

1. Dry mouth ---- 34 (2.1%)
2. Insomnia ------ 14 (0.9%)
3. Headache ----- 12 (0.7%)
4. Nausea-------- 10 (0.6%)
5. Dizziness------- 6 (0.4%)
6. Constipation--- 6 (0.4%)

The following side effects were reported at the rate of 0.2% or less (4 per 1,604 visits or less):

- Moodiness (2), cold extremities (1), cravings (4), diarrhea (4), drowsiness (2), irritability (2), fingers tingle (1), sweats (2), Jittery (2), fatigue (4), flatulence (2), palpitations (4), flush face (1), hypoglycemia (1), light headed (2), sore tongue (glossitis) (4), depression (1), thirst (2), abdominal pain (1), abdominal burning (1), spots before eyes (1), non-specific dermatitis (2).

It should be noted that when the director of the local family practice residency program was shown the side effect profile, he immediately stated, “That is the same incidence as a placebo”. We believe he is right.

THE CRITICAL BALANCE

There are prescription drugs, when used in combination the undesirable effects of one drug are cancelled out by the other drug. This appears to be true with the use of tyrosine and 5-HTP in combination. If you treat a group of patients with a higher dose 5-HTP alone, complaints of tiredness develop. If you treat a group of patients with higher dose tyrosine alone, complaints of headaches, anxiety and anxiousness develop. When the two are used in proper balance, these complaints seem to vanish.

5-HTP THAT DOES NOT WORK

In 1997, as we started working with amino acids and prescription drugs that did not work, we sent our patients out with shopping lists so they could buy the things they needed at local health food stores and pharmacies. The initial 6 patients we worked with went to the same health food store and bought the same brand of products. This was a lucky stroke for us, results were good and by the end of 1997, we were sending all patients out with shopping lists. But the luck was not to continue. Of the first 40 or so patients started on the list of nutritional supplements, most were not doing well. We soon identified a small sub-group of patients who were doing well. We found that all were going to the same health food store and buying the same products. As we looked further, we found that 90%+ of the 5-HTP sold in retail stores did not work. Since then, we have found the problem is the lack of uniform set standard for the manufacturing of 5-HTP in the
United States. Many of the products in retail stores contained 10% or less 5-HTP. The 5-HTP in our products is processed in Switzerland and is manufactured under the European guidelines, which have stringent pharmaceutical standards (99.5%+ pure).

PEAK-X

In August of 1998, Mayo clinic released a report indicating that most of the 5-HTP tested contained a substance known as “Peak-X”. Tryptophan was pulled from the U.S. and Canadian markets in 1989, secondary to the contaminant that formed during the fermentation process, causing an outbreak of a disease known as “Eosinophilia Myalgia Syndrome”. It was speculated by Mayo clinic that “Peak-X” could have the potential to cause symptoms similar to Eosinophilia Myalgia Syndrome, although none had been reported. The 5-HTP used in our products has been assayed by the University of Minnesota, and is certified as “Peak-X free”. If you have patients who raise concerns about “Peak-X,” contact us and we can fax you a copy of the assay. In the past, this has effectively dealt with the concerns.

MOST SENSITIVE TO B6

As we sent the initial patients out with shopping lists to pick up the nutritional supplements, not all patients bought everything on the list. We immediately began keeping data on which supplements the patients were taking. In analyzing this data, it became apparent the whole system was most sensitive to Vitamin B6. In some patients, this need was so great that you could give them all the tyrosine and 5-HTP you wanted, but if there was not enough B6 the system would not work.

SWITCH THEORY FORMULATED

I was originally trained as an Industrial Chemist and thoroughly indoctrinated with the ability to understand and formulate chemical models. I wrestled for a long time with the concepts of Serotonin and Norepinephrine regulating the appetite center.

What was the basic chemical model that held the two together in appetite regulation? The following theory is the best explanation I can offer for the interrelationship between Serotonin and Norepinephrine in the appetite center of the brain. This theory is used as a working model and serves as a reference point until something better comes along.

SWITCH THEORY

If the regulation of appetite by the neurotransmitters Serotonin and Norepinephrine are like a light bulb with two switches, then the light bulb needs to shine brightly in order for the appetite to be gone.

SWITCH THEORY DISCUSSION

Serotonin, by virtue of properties observed in weight loss, has an absolute threshold property that acts like an “on-off” switch. Patients with low levels of Serotonin experience more time where the switch of light bulb is off, than those with normal levels of Serotonin, leading to increased hunger and weight problems.

Norepinephrine acts like a dimmer switch hooked to the light bulb. While the Serotonin switch may be fully on, lower levels of Norepinephrine contribute to the dimming of the light bulb. This is why Serotonin takes the spotlight so much in weight loss. Its dramatic “on-off” effect is more readily observed and appreciated than the subtle effects of the Norepinephrine dimmer switch.

It is our experience that some patients (5%) only have a problem with the dimmer switch (Norepinephrine) causing eating and weight problems. While other patients (5%) only have problems with the “on-off” switch (Serotonin) causing eating and weight problems. Most patients appear to have a combination problem with both neurotransmitters.

DOsing NEEDs

Average dosing needs for the group can be calculated from the database, but individual needs vary widely. At the extreme low end of things, we have seen a few patients lose large amounts of weight on 75 mg of 5-HTP per day with 750 mg of tyrosine per day. On the extreme high end of things, we have seen patients
who needed 1,400 mg of 5-HTP per day with 6,000 mg of tyrosine in order to have their appetite under control. (It is noted at this higher level that neurotransmitter testing verified that the patient’s system was not over loaded and the need was actually there.)

In general, group dosing needs can be divided into 2 categories:

1) Treatment of obesity  
2) Treatment of diseases other than obesity.

In studying the NeuroResearch database in the treatment of obesity, the average group dosing was 425 mg of 5-HTP per day and 4,250 mg of tyrosine per day. For diseases other than obesity, the average dosing was 300 mg of 5-HTP per day and 3,000 mg of tyrosine per day. In treating diseases other than obesity, in general less amino acids are required but not always on an individual basis.

**SO, HOW MUCH SHOULD YOU USE?**

First, follow the dosing schedule on page 2. If after one week the desired clinical response is not seen, increase the patient to the next step on the dosing schedule. How much do you use in the end?

**ENOUGH!!!**

Using too much amino acids is not needed and may even be detrimental in some treatments. The ability to measure neurotransmitter levels is very helpful in establishing where the patient is at and what is needed next. Do not be afraid to push your patients to a higher dosing level, they probably need it. As we started to evaluate neurotransmitter testing, we were amazed to see patients on 900 mg of 5-HTP per day with low serotonin levels.

**AGGRESSIVE ADJUSTING OF AMINO ACIDS**

In assisting clinics over the last 2½ years, one of the largest and most consistent problems we have seen is, “Not adjusting the supplements aggressively enough.” If the clinical response you are looking for is not present after 7 days, increase the dose. The ingredients are not toxic. Aggressive adjusting of the dose, until the clinical response is seen, is very beneficial in the end. On the extreme end of things, we have seen clinics that simply started a patient on the starting dose and the patient was kept there for 3 months even though a clinical response was not seen.

**TIME BETWEEN DOSE CHANGES**

Once you start to change a dosing, it takes 4 to 5 days to observe the full effects of the new dosing. Working with amino acids is not like taking an aspirin, where you take a pill and see the effects 30 to 45 minutes later. Be patient and do not increase the dosing more than once every 7 days. We have seen clinics and patients “chasing their tail.” by increasing doses every 2 or 3 days.

**EXTRA IN THE PM**

Referring now to the dosing schedule on page 4, at visit number two the RepleteExtra is added in the PM (before the evening meal). From an amino acid stand point:

1 pill of “RepleteExtra” = 2 pills of “NeuroReplete”

We made this recommendation due to the fact that neurotransmitter levels drop off as the day progresses. Feeling worse in the evening or feeling hungrier in the evening is seen as neurotransmitter levels drop off later in the day. Higher dosing of amino acids later in the day has proven to be very beneficial.

**NEVER ADJUST BY “ONE PILL”**

So you have a patient who seems to be much better at times, but is not quite there all the time, “What do you do next?” Remember the “switch theory,” the patient is probably sitting on the threshold, “clicking in and out.” Your next step should be to continue to adjust the patient’s amino acid dosing. If you are going to adjust the patient in the future, add at least 2 pills per day to the patient’s dosing regime. As a rule thumb:

If you only want to add one pill to the patient’s daily dosing, you do not need to do any adjustments.

**FIND THE LOWEST DOSE**

After the patient has been stable for 6 to 8 weeks, with no symptoms, you may try and find the lowest dose of amino acids to maintain the patient on. To do this, have the patient cut back at the rate of 1 pill every two weeks until symptoms
return, then increase to the dose needed to keep symptoms under control.

SUPPLEMENTS QUIT WORKING
From time to time, we encounter patients who have been under treatment for several months who claim that the supplements have quit working. In virtually all cases, the problem was the patient was not taking the supplements properly. Remember the “switch theory?” If a patient misses 1 or 2 doses and is sitting just above the threshold needed for symptoms to resolve, the patient can find the symptoms return for a few days. If the patient repeatedly misses supplements throughout the week, from the patient’s perspective the supplements have quit working. To manage a patient who believes the supplements have quit working, we have the patient carry a notebook and journal all times and doses of supplements taken. It is amazing how many patients return in a week or two with the supplements once again working.

Another thing you should do for the patient in whom the supplements have quit working is, “Evaluate the importance of the supplements in the patient’s mind.” Some patients think the supplements are not important and subsequently, do not take them properly.

THE TIRED PATIENT
You may encounter the rare patient who, at the start of treatment, reports that he or she is, “Too tired to function”. Out of all the clinics, NeuroResearch has 6 to 8 reports of this happening each year. To manage this problem, it is recommended you cut back on the NeuroReplete dosing to the maximum level where symptoms resolve, and simply titrate the patient up using plain tyrosine and do follow-up neurotransmitter testing as outlined on page 4.

THE ANXIOUS PATIENT
Should you encounter the rare patient that complains of feeling anxious or jittery at the start of treatment, cut back the NeuroReplete to the maximum dose that keeps symptoms under control and titrate up from there using plain 5-HTP.

LONG HOURS
In general, the response to amino acid therapy in the system starts to taper off after 4 to 5 hours. This is important in patients who work long hours, such as nurses doing double 8 hours shifts and long haul truck drivers. If you have such a patient and they complain of the effects of the amino acids wearing off late in the day, simply give them one or two additional doses later at night.

For people like nurses who work odd hours and ask, “When should I take my supplements?” The answer is, “When you get up is the AM dose. Ten hours before bed is the Noon dose. Six hours before bed is the PM dose.”

ALCOHOL USE
We tell our patients that one or two drinks are OKAY but four or more drinks are not. Alcohol can reverse the effects of the amino acids. This observation has been most pronounced in the use of amino acid therapy in weight loss. We have seen patients who were doing well for several months that “partied hearty” one night, only to find their hunger had returned for 4 or 5 days. If the patient is not doing well, evaluate their alcohol intake.

“1 or 2 drinks is OKAY, 4 or more is not”

TAPERING OFF MEDICATIONS
If the patient is on a serotonin or catecholamine medication for the treatment of neurotransmitter dysfunction disease, the recommendation for tapering medications is as follows: in general, wait until the patient has been on the amino acid therapy for 6 to 8 weeks and is doing well prior to tapering. The goal of tapering is to have the least impact on the patient while working for a positive outcome. In tapering most medications such as Zoloft, Prozac, etc., step down one dose every 2 weeks. In general, drugs that work on the catecholamine end of things such as Effexor and Wellbutrin are harder to stop and require vigorous use of cysteine and patience. We have cared for patients on Wellbutrin that required 4 months of slow taper. Paxil is another drug that is difficult to taper. In extreme cases, custom formulation of Paxil by a pharmacist may be needed in order to decreased dosing at the
rate of only 1 or 2 mg every two weeks. If you have problems with tapering meds, call NeuroResearch.

AMINO ACID / DRUG INTERACTIONS
From time to time, we get questions about the use of amino acids with various prescription drugs. We know of no amino acid / drug interactions that would preclude the use of amino acids. All drugs appear to be safe and have no interactions or contraindications that we know of when used with amino acids.

USE IN PREGNANCY
Should you have a female patient who becomes pregnant, you may advise her that the use of amino acids in pregnancy appears to be safe. But, due to the lack of studies, it is recommended the amino acid formulation not be used during the first trimester of pregnancy (first 13 weeks). The fact is, they are already getting these thing to some degree from their food.

Amino acids are water soluble and not excreted in high doses into breast milk which concentrates fat soluble things. We know of no studies indicating that there have been any problems with their use in the nursing mothers.

5-HTP SUPPORTS TRYPTOPHAN

Tryptophan → 5-HTP → serotonin

\[ \uparrow \quad \downarrow \]

Tryptophan hydroxylase

Regulation of the conversion of tryptophan to serotonin is via the 5-HTP regulatory feedback loop. As more 5-HTP is available in the system, further deactivation of tryptophan hydroxylase takes place and less 5-HTP and serotonin is made. 5-HTP is turned freely into serotonin without being subject to regulation. This is why we can achieve serotonin levels above normal by taking 5-HTP. In the process, 5-HTP shuts down tryptophan hydroxylase making more tryptophan available for other needs in the body.

A STORY OF TRYPTOPHAN AND PROZAC
Tryptophan is classified as an essential amino acid. Meaning, it needs to be supplied in adequate amounts in the diet and cannot be synthesized within the body.

In the 1980’s, tryptophan was available over-the-counter. People used it for depression and other neurotransmitter diseases.

In 1989, a batch of tryptophan from Japan was brought into the United States and Canada. The batch contained a contaminant that caused an outbreak of a disease known as, “Eosinophilia Myalgia Syndrome.” The source of the contaminant was a by-product of the fermentation process used to produce tryptophan. Tryptophan was not the problem; it was a contaminant in the tryptophan.

A few months later, after tryptophan was pulled from the market, Prozac, the first serotonin drug, came on the market. The rest is history.

At present, tryptophan is only available for human use in infant preparations. It is the only essential amino acid that we cannot buy off the shelves. I have always marveled at the coincidence of tryptophan being pulled from the market within months of the first serotonin drug becoming available in the U.S. At present, the SSRI industry in the U.S. is a $10 billion a year industry.

NEUROCHEMISTRY OF SEROTONIN
On page 11 is the serotonin synthesis pathway. The whole process is very simple in comparison to the catecholamine pathway. The precursor tryptophan is used for the synthesis of serotonin. It is subject to the “5-HTP → tryptophan hydroxylase feedback loop”. The implications of the feedback loop are that the body will only produce a certain amount of serotonin (usually in the normal range). With the use of 5-HTP, two important things happen:

1. 5-HTP is not subject to a feedback loop of any other regulation and in the process higher than normal levels of serotonin can be achieved.

2. With an abundance of 5-HTP in the system, the tryptophan hydroxylase is virtually 100% inhibited meaning that none of the tryptophan in the system will
be converted to 5-HTP making it exclusively available for other bodily needs such as protein synthesis.

**NEUROCHEMISTRY OF CATECHOLAMINES**
Both the catecholamine system and the serotonin system have to function properly for the system as a whole to be disease free.

In our study of neurotransmitters, through Pharmasan Labs, we have found that 79% of patients have low epinephrine levels and 20% of patients have low norepinephrine levels. No patients had low dopamine levels. This does not mean low dopamine levels do not exist, they are just fairly rare on testing.

A key point to interpreting what is going on with the neurotransmitters is the “Phentermine depletion theory” as discussed on page 27. We believe this phenomenon occurs not only with the norepinephrine – epinephrine system, but with the dopamine – norepinephrine – epinephrine system as well. **The ability of the system to excrete neurotransmitters into the synapse takes precedence over the ability for the neurotransmitter to act as a precursor.** So, when you see a low epinephrine level there is a high probability there is also a problem with norepinephrine. Taking this one step further, when you see low norepinephrine and epinephrine levels there is a high probability there is also a problem with dopamine.

Other factors come into play regarding catecholamine levels; most notable is a system involving cysteine, homocysteine, methionine, S-adenosylmethionine (SAMe), folate, vitamin B6 and vitamin C. The key player in this system is SAMe.

In September of 2000, secondary to experiencing problems in patients who were stopping phentermine and after being placed on amino acid therapy, we began working with cysteine. Initial results were very good and this led us into a whole new world of amino acid therapy. Of the first 9 patients placed on cysteine for the problem of amino acids not working after stopping phentermine, 7 obtained dramatic results. We initially explained the phenomenon as a dysfunction of the “tyrosine hydroxylase enzyme”. We focused on tyrosine hydroxylase as a rate-limiting step in the formation of catecholamines. We researched the enzyme extensively, from the DNA to the feedback loop. The decision to start cysteine was based on the fact that at the heart of the tyrosine hydroxylase enzyme is a “heme-thiolate protein” made up of a cytochrome P-450 iron complex and a cysteine molecule.

**HEMETHIOLATE PROTEIN**
The rate-limiting step in the formation of catecholamines is the enzyme tyrosine hydroxylase. At the heart of the tyrosine hydroxylase enzyme is the “heme-thiolate protein,” depicted below. This protein is made up of a cytochrome P-450 iron complex (Fe) and a cysteine amino acid. The “S” sulfur group is from the cysteine (Cys). Depletion of cysteine can lead to decreased production of the tyrosine hydroxylase enzyme, which in turn leads to decreased production of catecholamines.

**TYROSINE HYDROXYLASE REGULATION**
The rate-limiting step in the formation of catecholamines is tyrosine hydroxylase. Tyrosine hydroxylase activity is controlled by the norepinephrine feedback loop. Norepinephrine via phosphorylation inactivates tyrosine hydroxylase. The higher the concentration of norepinephrine the more inactivation occurs.
Cysteine, Methionine, Homocysteine, SAMe cycle
Note, “S-adenosylmethionine (SAMe) in the upper right corner.
Folate, B12, and B6 are needed to turn homocysteine into methionine.

SAMe
The fact that cysteine was at the heart of the rate-limiting enzyme in the formation of catecholamines led to the use of cysteine.
Results were so good that we filed our eighth patent application based on this fact. As time progressed, it became apparent there was a much larger cysteine system in the picture.
S-adenosylmethionine (also known as SAMe “sam ie”) is a methyl donor in the formation of epinephrine from norepinephrine.
There is an abundance of literature on SAMe, methionine, homocysteine and cysteine. Low levels of SAMe can cause low levels of epinephrine and the synthesis is compromised.
Homocysteine has taken a spotlight in medicine in recent years as a risk marker for cardiac disease. It is still somewhat controversial.
I know a cardiologist who does not recognize it and family practitioners who do. Folate, B6 and B12 are all needed for proper conversion of homocysteine to methionine. If there is a deficiency of any of the three, elevated homocysteine levels will occur. In speaking with physicians who routinely screen for and treat elevated homocysteine levels on patients over 40 years old, it was the consensus that a full 50% of patients tested have elevated homocysteine levels. Treatment is the use of folate and B6. B12 is made naturally in the body and unless there is a deficiency with the intrinsic factor, B12 problems do not enter the picture. The physicians report, in general, it takes 4 to 6 months for homocysteine levels to return to normal with this treatment.
So how does this relate to neurotransmitters? Again the literature is clear that elevated homocysteine levels are associated with lower levels of SAMe in the peripheral circulation and the CNS. (J Neurol Neurosurg Psychiatry 2000 Aug;69(2):228-32 Bottiglieri et al.).
Plugging up the cycle on the preceding page lowers levels of SAMe. SAMe has far reaching implications. It is actively involved in over 40 major pathways in the body as a methyl donor.
We believe this is another piece to the puzzle and why we now have folic acid (folate) in the NeuroResearch products.
There are patients with normal homocysteine levels that respond to cysteine therapy, “What is going on here?” Cysteine is involved in many chemical pathways also. Until recently methionine was considered to be an “essential amino acid.”
Cysteine to Methionine
Methionine was originally classified as an essential amino acid meaning it could not be synthesized in the body and needed to be supplied in the diet. With the discovery of the pathway below it has been reclassified as semi-essential in some scientific circles. The pathway shows methionine synthesis from cysteine.

When the pathway on the shown above was defined which shows that methionine can be synthesized from cysteine. It also shows that cysteine, methionine, homocysteine, and SAMe are in balance and when a deficiency exists in the system, giving any one of the 4 can get the whole system functioning optimally again. In the patients who had normal homocysteine level and responded to cysteine treatment, it is postulated that the system overall was in fact low and the addition of cysteine to the system put it back in balance.

Why not use SAMe instead of cysteine? We find full clinical response in treating a group of patients with cysteine in dosing at the 4,500 mg per day. SAMe is expensive, costing $40 at our local health food store for 60-200 mg pills. We do not believe the clinical response is different enough to warrant using many pills of SAMe every day in place of cheap cysteine.

**DOPAMINE AND SAMe AND FOLATE**
While SAMe is not directly involved in the conversion of L-dopa to dopamine the system does appear to affect SAMe levels according to the literature. There are several studies, which indicate placing additional L-dopa in the system will lead to decreased SAMe and epinephrine levels. This appears to be primarily due to the fact that the main inactive metabolite of L-dopa requires SAMe for conversion. There is other literature that suggests the L-dopa may inhibit the conversion of norepinephrine to epinephrine through these decreases in SAMe.

Another hint of the problems involved are from an article which demonstrated that a decrease in SAMe levels caused an increase in catecholamine metabolites in the system.

The bottom line of this discussion is the addition of folate to the NeuroReplete formula. This is the first change in the original formula in 2 years. The daily recommendation is 1,600 mcg to 2,400 mcg of folate per day.

**SELENIUM**
This discussion would not be complete without talking about the selenium in CysReplete. As we began to work with cysteine, a doctor made us aware of scientific world literature from the
late 1980s that talked about the ability of cysteine to concentrate mercury in the body and into the brain. We found the literature. Once mercury gets into the body, it is methylated. It is this methylated mercury that cysteine has the ability to concentrate into the brain. By giving 200 mcg per day of selenium, the mercury is bound into an inactive biological form by the selenium and the problem is solved.

**GLUTATHIONE**

Next to the importance of cysteine in the system is the Glutathione system. There is much talk about anti-oxidants and detoxification. The fact remains that the Glutathione system is the most powerful system in the body for neutralizing toxins. The synthesis of Glutathione is dependent on the availability of cysteine. The sulfur group on the cysteine is the powerhouse of the detoxification on the Glutathione molecule.

Overloading the system with toxins can deplete cysteine and the Glutathione system, which in turn can lower catecholamine levels. Extreme stress can deplete the catecholamine system affecting the ability of the body to handle toxins.

As a practicing MD of 20 years, who was trained in the straight and narrow of allopathic medicine, a few years ago I would not have believed that fat-soluble toxins could cause such problems. I have seen it with my own eyes in our weight patients. I’ve seen patients, like firemen, who have 30 years on the job and who have been repeatedly exposed to toxins in the work place. They developed skin lesions in weight loss on the upper torso, proximal arms, and face. When this first happened, a fire captain pointed out that these were from fat-soluble toxins leaching out as the fat store diminished and became supersaturated with toxins. Detoxification took the lesions away. Later, as we started working with cysteine, we found that cysteine was also effective in dealing with the lesions. The whole experience leaves us asking the question; If firemen and other people with toxic exposure are the extreme cases, how many people have toxins but never develop skin lesions in weight loss?

**GLUTATHIONE SYNTHESIS**

The Glutathione system is the primary system in all life for handling toxins in the cells. Depletion of cysteine can lead to depletion of Glutathione and increased toxin load in the body, which in turn causes increased cell damage. Increased toxin load can cause depletion of cysteine, which in turn affects the production of SAMe and neurotransmitters.
PERIPHERAL AND CENTRAL SEROTONIN

The fact is, serotonin does not cross the blood brain barrier and it has been speculated that peripheral testing of serotonin levels may not correlate with central levels. As we approached neurotransmitter testing, I did not know what the truth was other than what we were doing worked.

Dr. Kellerman at Pharmasan Labs had literature showing that there was indeed a correlation between peripheral and central serotonin levels. Beyond that, the following facts are true.

- 5-HTP crosses the blood brain barrier freely and once a steady state is achieved, the central and peripheral levels of 5-HTP are indeed the same. From the perspective of 5-HTP, there is no blood brain barrier, only one body. It distributes equally throughout. 5-HTP is not subject to regulation or a feedback loop, whenever it comes in contact with a carboxylase enzyme it is converted to serotonin. Over time, the system equilibrates and the peripheral and central serotonin levels are indeed in equilibrium.

- Reflecting on the nature of amino acid therapy, recommendations for testing exists. Full effects of starting or changing the dose of amino acids are not seen for 4 to 5 days. Next, do not perform testing until 7 days have passed since the dosing of the amino acids was started or changed. Time is the critical factor, allowing the system to equilibrate. We also make the assumption that patients, at the start of testing, are in steady state. If given time to equilibrate, the central and peripheral serotonin levels do indeed correlate. It is under conditions where there has been a recent change that they might not.

WAS MAN DOOMED TO SUFFER?

There appears to be two distinct groupings of patients in the treatment of neurotransmitter deficiency disease:

1. Obesity
2. Diseases other than obesity

In focusing on “diseases other than obesity,” it would appear that in most patients, the symptoms of diseases could be brought under control at the 300 mg of 5-HTP / 3,000 mg of tyrosine per day dosing level. With this information in hand, in early 2000, we set out to design a diet that might have the same effects. Such a diet must contain protein as the source of amino acids. Nutritional books were reviewed and the final conclusion was that such a diet does not exist.

The two foods that were identified as leading contenders in the diet were meat and eggs. To get the dosing equivalent of 300 mg of 5-HTP and 3,000 mg of tyrosine per day from red meat, the patient would have to eat 35 ounces of red meat per day, which equals 2,440 calories per day. This would not keep a 140-pound female at weight. To get the same dosing equivalent from eggs, the patient would have to eat 18 eggs per day, which equals 1,440 calories per day. You could keep the 140-pound female at 140 pounds, but there would be nothing else she could eat other than eggs.

“Was man doomed to suffer?” became the question. As we stared deeply at the question, we became aware of “The thing that is broken.” There is something else in the system not working that prevents us from controlling neurotransmitter diseases with food. We could probably write an entire booklet on, “The thing that is broken,” but for now will simply leave it here for you to ponder.

DEPRESSION

Treatment of mild to moderate depression with amino acid therapy is excellent, but where it really excels is in the treatment of severe and refractory depression.

For the most part, initiation of treatment of depression can be done with amino acid therapy without the use of prescription medications. In cases where suicidal thoughts exist or where there is severe compromise in day-to-day function, it is recommended that the patient be started concomitantly on prescription medications and amino acid therapy. In general, with these more severe cases medications can be tapered after two months of therapy.

Our experience with the treatment of depression has shown the ability to differentiate a small sub-group of patients, who in the past were easily overlooked. If after 6 to 8 weeks of amino acid therapy in treating the patient for depression, the clinical symptoms
have not improved markedly, consider the possibility that the patient is suffering from the depressive form of bipolar disorder. Other than the standard DSM IV criteria, other things that might point you in that direction are a long standing (many years) history of depression, where the patient has seen many physicians and has been on many medications without success. Starting the patient on Lithium or Depakote, in addition to any antidepressants or amino acids the patient may be on, has shown dramatic results. Based on personal practice experience in working with depressive bipolar patients, there is reluctance on the part of the patient to taper the antidepressant medication or amino acids once relief is gained.

MIGRAINE HEADACHES
Migraine headaches are mediated by the 5HT1BD serotonin receptors in the temporal region of the head. Based on clinical experience with amino acid therapy, it is our opinion that approximately 15% of patients who present with a working diagnosis of “migraine headaches” from other practices have been misdiagnosed. With true uncomplicated migraine headaches (where there is not a second source of pain present such as temporal mandibular joint syndrome or herniated cervical disk) most headaches resolve after the first day of amino acid therapy.

FIBROMYALGIA
Treatment results with fibromyalgia have been excellent and tend to take 2 to 4 weeks for the full effects to be seen. In general, 80% of patients with fibromyalgia are pain-free and the remaining 20% are so much better that they no longer care about their pain. If you find a fibromyalgia patient who seems to be refractory to treatment, make sure you look for other causes of pain.

INCIDENCE OF NEUROTRANSMITTER DISEASE
We started using the “1A survey” in 1997. At first we viewed this as a simple survey of 24 neurotransmitter diseases and illnesses caused by or associated with low levels of neurotransmitters. Formal diagnostic criteria was not established. This is a survey of diseases present for the perspective of the patient. In 70% of patients starting a weight program, there are other diseases present. In many cases, there are 5 to 7 of these diseases present. The record at this time, is 18 of 24 diseases present. The following are the incidence of some of the diseases surveyed in patients starting medical weight management:

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>31.5%</td>
</tr>
<tr>
<td>Migraine</td>
<td>20.1%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>20.5%</td>
</tr>
<tr>
<td>PMS</td>
<td>27.2%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>24.8%</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>7.1%</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>7.9%</td>
</tr>
<tr>
<td>Compulsivity</td>
<td>36.6%</td>
</tr>
<tr>
<td>Irritable bowel</td>
<td>10.2%</td>
</tr>
<tr>
<td>Myoclonus</td>
<td>11.2%</td>
</tr>
<tr>
<td>PMS</td>
<td>27.2%</td>
</tr>
<tr>
<td>Compulsivity</td>
<td>36.6%</td>
</tr>
<tr>
<td>Aggression</td>
<td>4.7%</td>
</tr>
</tbody>
</table>

THE “1A SURVEY”
The NeuroResearch Survey can be viewed by going to the website:
http://www.usaweightloss.com/107%201A%20SURVEY.pdf

FOR OVER TWO YEARS NOW WE HAVE SAID:
******************************************************************
If we had a drug for treating renal hypertension that made the high blood pressure better but made the kidney disease worse, “Could we use it?”
If we had a drug for treating angina from coronary artery stenosis that made the chest pain better but made the stenosis worse “Could we use it?”
Why are we using neurotransmitter drugs, which make the symptoms better while making the real problem “neurotransmitter depletion” worse?
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It was pointed out recently that clinics who have attended a NeuroResearch training seminar are using 20 to 30 times the product, meaning they have 20 to 30 times the revenue and patients over those clinics that think they can merely pick up a bottle and
ADDEDUM

Since the writing of this booklet 9 months ago there has been much research done that has brought us much new insight. In the near future this booklet will be updated completely. But with this press run we simply added the following addendum.

TWO SYSTEM FUNCTION AS ONE

In working with L-dopa whose over the counter source is mucuna, based on lab testing it is apparent that the serotonin system and the catecholamine system function essentially as one system. The following illustrates what happens to urinary serotonin and dopamine levels when L-dopa (only) is added to the picture.

Treating only one system with 5-HTP alone for example will not effect optimal group outcomes. You need to treat the whole picture. From time to time we hear, “How can you have a patent on that stuff, I have used it in the past”. The patents cover optimizing group outcomes with the amino acids when used in combination. Something that has not been done before.