Two primary categories of nutritional deficiency exist. An absolute nutritional deficiency occurs when nutrient intake is not sufficient to meet the normal needs of the system. A relative nutritional deficiency exists when nutrient intake and systemic nutrient levels are normal while a change occurs in the system that induces a nutrient intake requirement that cannot be supplied from diet alone.

Reuptake inhibitors may facilitate conditions that deplete monoamines. Reuptake inhibitors will not function if monoamine depletion is significant. When significant monoamine depletion occurs, the placebo effect and/or drug effect may no longer be observed.

There are two basic types of nutritional deficiencies:
- Inadequate nutrient intake
- “Relative nutritional deficiency” occurs when changes in the system status induce nutritional needs beyond the abilities of dietary modification.

When reuptake inhibitors stop working, the primary cause is a therapeutically induced “relative nutritional deficiency.”

CHK Nutrition’s products have been formulated to properly address monoamine related relative nutritional deficiency.
Reuptake inhibitor induced relative nutritional deficiency

Illustrations courtesy of the National Institute of Drug Abuse

Figure 1: Inadequate levels of neurotransmitters in the synapse are associated with compromised electrical flow in the post-synaptic neurons leading to suboptimal regulation of function and/or development of symptoms.

Figure 2: The administration of reuptake inhibitors block monoamine transport back into the pre-synaptic neuron leading to a net redistribution of neurotransmitter molecules from the pre-synaptic neuron into the synapse. Increased levels of synaptic monoamines result in increased post-synaptic electrical flow.

Figure 3: When monoamines are in the pre-synaptic vesicles, they are not exposed to the enzymes that catalyze metabolism (MAO and COMT). When monoamines are relocated outside of the pre-synaptic vesicles into the synapse, they are exposed at a greater frequency to these destructive enzymes. Reuptake inhibitors force monoamines to remain in the synapse resulting in increased monoamine metabolic enzymatic activity. Relative nutritional deficiency occurs when monoamine enzymatic activity destroys enough monoamines that the system needs higher than normal monoamine levels in order to function properly.

SSRIs at therapeutic doses block this reuptake of serotonin by platelets leading to a depletion of serotonin after several weeks of treatment. 

Improperly balanced amino acid precursors deplete centrally acting monoamine neurotransmitters

Monoamine neurotransmitters and their amino acid precursors exist in two distinctly different physiological states:

- **THE ENDOGENOUS STATE** found when no amino acid precursors are being administered.
- **THE COMPETITIVE INHIBITION STATE** found when significant amounts of serotonin and dopamine amino acid precursors are being administered simultaneously.


How improperly balanced amino acids deplete monoamine neurotransmitters

**SYNTHESIS IN COMPETITIVE INHIBITION:** The same enzyme, L-aromatic amino acid decarboxylase (AAAD), is responsible for the synthesis of serotonin and dopamine. In the competitive inhibition state, if amino acid precursors of one system dominate the AAAD, an environment is created which decreases the synthesis of the non-dominant system resulting in its depletion.

**METABOLISM IN COMPETITIVE INHIBITION:** Serotonin and Dopamine are both metabolized by the monoamine oxidase (MAO) enzyme. Significantly higher levels of one system increases MAO activity which leads to increased metabolism and depletion of the non-dominate system.

**TRANSPORT IN COMPETITIVE INHIBITION:** Serotonin, dopamine, and their amino acid precursors compete for transport by the organic cation transporters. Significant increases in one will decrease monoamine and precursor transport of the non-dominant system. Transport of precursors into the cells is required for synthesis to take place.

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**Diagram:**

- **Aromatic amino acid decarboxylase**:
  - Tryptophan → 5-HTP
  - Tyrosine → L-dopa

- **MAO COMT**:
  - Dopamine norepinephrine epinephrine
  - Serotonin HVA 5-HIAA

- **Transport to the urine**:
  - Serotonin phase 1 or 3 at the transporter
  - Dopamine phase 2 or 3 at the transporter

- **OCT2 GATE-LUMEN REGULATION**

**THE PROTOCOL**

For the nutritional management of monoamine neurotransmitter relative nutritional deficiencies. When a patient presents with monoamine neurotransmitter depletion, CHK Nutrition’s products are designed to provide the proper balance of nutrients which may provide management of monoamine related relative nutritional deficiencies.

**NeuroReplete**
Take four NeuroReplete pills in the morning and four NeuroReplete pills approximately 5 to 6 hours before bedtime (usually around 4 PM for most individuals).

**CysReplete**
Take two pills of CysReplete, three times a day with the first dose at noon. CysReplete is required since ingestion of L-tyrosine and/or L-dopa is associated with depletion of sulfur amino acids.

**ADDRESSING THE RELATIVE NUTRITIONAL DEFICIENCY**

**APPLICATIONS**
When addressing relative nutritional deficiency:
- It takes 3 to 5 days to achieve amino acid equilibrium and observe the full effects

**ADMINISTERING ONLY:**
- L-tryptophan may deplete dopamine
- 5-HP may deplete dopamine
- L-tyrosine may deplete serotonin
- L-dopa may deplete serotonin

Serotonin and dopamine amino acid precursors need to be administered in proper balance.

(See the bottom of page 2 for the mechanism.)

**SIDE EFFECT MANAGEMENT**

**GI UPSET → ON START UP**

**THE PROBLEM:** Approximately 1 to 2% of patients experience GI upset or nausea when starting amino acids. Typically this starts with the first dose and builds with every dose until the third day, at which point the patient can no longer tolerate the symptoms.

**THE CAUSE:** Patients who have the greatest neurotransmitter depletion often experience GI upset or nausea when starting the amino acids. These patients may benefit the most from amino acid supplementation to address their relative nutritional deficiency.

**MANAGEMENT:** Restart NeuroReplete taking only one pill at bedtime. It is important that the pill is taken when the patient is ready to sleep, not when getting in to bed to watch television or read a book. If the patient is able to fall asleep within 20 minutes of taking the NeuroReplete pill, there should be no problems with GI upset. After 3 or 4 nights without GI upset, increase to two pills of NeuroReplete at bedtime. Once the patient is able to take two pills at bedtime without GI upset, start one NeuroReplete pill in the morning. After 3 to 4 days without problems, increase the patient to two NeuroReplete pills. Once the patient is taking two NeuroReplete in the morning and two NeuroReplete at night, it is recommended that the health care provider obtain a urinary transporter evaluation.

**SIDE EFFECTS**

**THE PROBLEM:** The recommendation is to leave all drugs in place when starting the amino acids. In 3 to 5% of patients, side effects not associated with the amino acids may occur when starting or changing the amino acid dose.

**THE CAUSE:** In patients taking a reuptake inhibitor, as amino acids are administered, drug side effects may display as well.

**WHEN MANAGED PROPERLY, SIDE EFFECTS CAN BE EFFECTIVELY ADDRESSED. THESE AMINO ACID FORMULATIONS DO NOT NEED TO BE STOPPED ON A LONG-TERM BASIS.**

<table>
<thead>
<tr>
<th>Possible Amino Acid Only Side Effect Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth ................................ 34 (2.1%)</td>
</tr>
<tr>
<td>Insomnia .................................. 14 (0.9%)</td>
</tr>
<tr>
<td>Headache .................................. 12 (0.7%)</td>
</tr>
<tr>
<td>Nausea ................................... 10 (0.6%)</td>
</tr>
<tr>
<td>Dizziness .................................. 6 (0.4%)</td>
</tr>
<tr>
<td>Constipation .............................. 6 (0.4%)</td>
</tr>
<tr>
<td>All other side effects occur at a rate less than 1 in 500 visits</td>
</tr>
</tbody>
</table>

Kohlstadt I. editor. Food and Nutrients in Disease Management CRC Press; 2009, 465-481
Other causes of neurotransmitter depletion

Administration of improperly balanced monoamine amino acid precursors and sulfur amino acids may deplete neurotransmitters.


“A possible mechanism for the depletion of dopamine by 5-HTP might be attributable to displacement of the dopamine stores by the serotonin formed from 5-HTP.” Arch Pharmacol, 303 pp. 63-72. Elsevier Publishing, 1978 February.


