Reflux / GERD Application Guide

Clinical Context

Many patients in functional medicine practice have reflux or the further progression into gastroesophageal reflux disease (GERD). Reflux occurs when stomach contents move back up into the esophagus. The most pressing issue is that long-standing irritation of the esophagus can drive Barrett's esophagus, where persistent reflux of acid creates changes to the lining of the lower esophagus that are associated with an increased risk of esophageal cancer. Esophageal cancer has a 15% survival rate. So, it's crucial to address reflux decisively.

Mechanical Considerations

Reflux can be driven by mechanical pressure that pushes the uppermost portion of the stomach up through the diaphragm, including the possibility of hiatal hernia. This can occur with pregnancy or weight gain, or with bloating that accompanies SIBO.

Delayed Stomach Emptying (Gastroparesis)

Reflux is also associated with gastroparesis. Stomach emptying is a neurologically mediated process. In other words, motor signals are required for the stomach to empty. Anything that interferes with those motor signals can contribute to gastroparesis. Key factors include:

1. Diminished vagal motor outflow.
2. Glycemic dysregulation – 90% of diabetics have gastroparesis.
3. Consumption of fatty foods.
4. SIBO – 60% of gastroparesis patients have SIBO. (Reddymasu, SC, et al. Small Intestinal Bacterial Overgrowth in Gastroparesis. J Clin Gastroenterology. 2010. 44 (1): e8–e13.).
5. Dysbiosis – this can include h. pylori or other forms of dysbiosis in addition to SIBO.

Lower Esophageal Sphincter Relaxation

Some foods mechanically relax the lower esophageal sphincter (LES), located at the bottom of the esophagus. When LES relaxation occurs, acidic stomach contents can move up into the lower esophagus, yielding irritation of the esophageal lining. These foods include mint, chocolate, citrus, tomato, garlic, onion, and fatty foods. Different foods seem to affect people differently, even to the extent that a person who has trouble with tomato sauce might have no problem with ketchup.

Treatment Considerations

Address vagal motor outflow.

Refer to materials in Cogence for full details of this. In summary, consider the following:

1. Transcutaneous vagal motor stimulation, using a TENS device. There are Clinical Pearls on this. Take a look.
2. Chew each mouthful 40x. This creates substantial sensory input via the trigeminal nerve, which stimulates vagus nerve motor activity. In short, chewing turns on intestinal activity, including down-going motility.
3. Attend to inflammation. Remember that vagal motor outflow inhibits TNFα production in the small intestine and spleen, and inhibits IL-6 production in Kupfer cells in the liver. Loss of adequate vagal motor outflow yields inflammation. If that turns into CNS inflammation, it will reinforce the loss of vagal motor outflow.
4. Other vagus-activating activities like meditation, singing at high volume, etc.
5. Cholinergic support. This may be especially important in patients with PEMT or MTHFD1 gene snp's, as their choline status is more likely to be impaired.

Phosphatidylcholine (Pure Encapsulations) – 1 QD or BID, to support acetyl choline production. Acetyl choline is the neurotransmitter in the synapses through which vagus nerve motor signals are conveyed.

Alpha-GPC – 100 to 200mg BID, to promote acetyl choline production.

Huperzine A – 50-100mg BID, to promote acetyl choline production.
As with any cholinergic support, neuromuscular junctions involve acetyl choline, so increasing cholinergic activity can yield cramps. This can be reduced with magnesium.

Address SIBO as needed

Typical approaches involve the following or similar, based on your clinical judgement:

Microdefense (Pure Encapsulations) – 2 or 3 BID, per clinical judgement, away from food, for 3-4 weeks, to remove dysbiotic organisms.

AC Formula II (Pure Encapsulations) – 2 or 3 BID , per clinical judgement, away from food, for 3-4 weeks, to remove dysbiotic organisms.

SunButyrate (Pure Encapsulations) – 1 tsp BID, to promote favorable microbiome changes.

Saccharomyces Boulardii (Pure Encapsulations) – 4 to 7 capsules at a time, **twice per week**. See the Application Guide on Probiotics and Clinical Pearls on probiotics for more info on this dosing pattern.

Attention to Foods, Consumption Patterns, and mechanics.

a. No food near bedtime. Lying down removes the advantage of gravity, so it's much easier for food to exert pressure "upward" on the underside of the LES.
b. No LES relaxer foods in second half of the day. Some people need complete avoidance. Some just need to avoid these foods close to when they'll be lying down.
c. Raise the head of the bed two inches, typically using bricks.

Address Dysglycemia.

In addition to standard approaches to dysglycemia, consider looking at the "Insulin Resistance Application Guide."

Perspective, Deeper Dive, Treatment Points

It's important to recognize multiple connections between SIBO, vagal dysregulation, and dysglycemia. Gastroparesis is common in diabetics. Low CNS glucose, either from hypoglycemia or from insulin resistance, can yield under-fueled motor neurons, including poorly fueled vagal motor neurons. This yields diminished vagal outflow to signal stomach emptying.

With hyperglycemia, over-fueling of mitochondria in nerve cells can lead to increased ROS, NFkB and inhibition of autophagy, impairing nerve cell repair. If insulin (and thus c-peptide) levels are high or normal, the c-peptide-mediated component of neuronal repair would be intact. If insulin and c-peptide levels are low, the c-peptide-mediated neuronal repair would be diminished. This is a major reason that patients with diabetes have neuropathy. If a diabetic patient has neuropathic changes that affect vagus nerve function, that can have a major impact on gastric emptying. This perhaps makes clearer the association between diabetes and gastroparesis.

In patients with reflux, one would expect inflammation of esophageal epithelial lining cells. The inflamed epithelia generate TSLP, IL-33, and IL-25, driving a shift toward Th2. The IL-4 made by Th2 cells is known to inhibit autophagy. Autophagy is necessary for the repair of nerve cells in both the CNS and peripheral nervous system. Mitophagy (the autophagy of mitochondria) is also inhibited by IL-4. Interferon gamma (IFNγ) is required for autophagy and mitophagy. This suggests that support for adequate Th1/NK cell response and inhibition of Th2 dominance are suitable to consider here.

Supplements to Consider:

DGL Plus (Pure Encapsulations) – 1 to 3 per meal, taken before meal. A combination of DGL, aloe, slippery elm and marshmallow. This is likely to be first line for most patients. Dose needs to be high enough to match the level of need.

Th1 Support (Pure) – 2 breakfast, 2 lunch. Support for adequate Th1 response, to drive IFNγ production in support of autophagy. The berberine in Th1 support also diverts excess fuel from mitochondria, protecting the mitochondria and improving metabolic regulation, in support of glycemic control. Note: Because berberine increases AMPK, it can give the patient more energy, so it's useful for doses to be taken earlier than 4pm.

Perilla Extract (Pure) – 2 BID. To downregulate IL-4, so autophagy can go forward, so vagus nerve repair can go forward, if the need for neuronal repair is part of the case.

Renual (Pure) – 2 to 3 BID, a source of urolithin A, which promotes mitophagy. Recycling damaged mitochondria makes way for a healthier population of mitochondria that make more ATP and less ROS.