Introduction

Feeling full quickly when eating, experiencing bloating during and after meals, or suffering from acid reflux may all be signs of low stomach acid — clinically referred to as hypochlorhydria. Hypochlorhydria occurs when the parietal cells in the gastric mucosa do not produce sufficient amounts of hydrochloric acid (HCl). There are numerous underlying causes of parietal dysfunction of psychological, physiological, and infective origin. An underproduction of HCl causes the gastric environment to lack acidity, leading to a number of symptoms relating to malabsorption, digestive disturbances, and decreased lower esophageal sphincter tone.[1] A decrease in stomach acidity can potentially lead to bacterial overgrowth, acid reflux, and nutrient deficiencies.[2, 3] In turn, nutrient deficiencies caused by hypochlorhydria can contribute to a variety of conditions, including depression, osteopenia/porosis, and acne.[1]

Evaluation of hypochlorhydria involves clinical case–taking, as well as interpretation of routine bloodwork. Several specific tests to evaluate stomach acidity are available, but are not regularly performed. In individuals with diagnosed conditions associated with hypochlorhydria, screening for hypochlorhydria is especially prudent.

The Role of Stomach Acid

Stomach acid plays a pivotal role in the digestive process, and is crucial for the appropriate breakdown and utilization of dietary protein.[2] Along with protein, stomach acid is required for absorption of a number of micronutrients. Notably, appropriate gastric secretions of intrinsic factor and stomach acid are required to separate and absorb vitamin B\textsubscript{12} from food sources, making B\textsubscript{12} deficiency a common manifestation of low gastric secretion.[4] Hypomagnesemia (low magnesium) and iron deficiency are also common in cases of hypo- and achlorhydria.[4, 5] Beyond its role in digestion, stomach acid acts as a
barrier to many pathogenic bacteria. Low stomach acid conveys susceptibility to colonization by unwanted bacteria lower in the digestive tract.[2] Low stomach acid, and specifically the use of stomach acid–lowering agents, is associated with serious infections including C. difficile.[6] Stomach acid also plays a mechanistic role in our digestive tract, by acting to signal the lower esophageal sphincter (LES) to close properly. When working improperly, the LES keeps stomach contents from entering the esophagus. If the LES remains poorly closed, gastric contents can ascend into the esophagus, causing irritation known as acid reflux, GERD, or heartburn.[1]

Causes of Hypochlorhydria
There are a number of direct causes of decreased secretion of stomach acid, including:

Autoimmunity: Various autoimmune conditions, including Hashimoto’s, hyperthyroidism, and type 1 diabetes, are associated with hypochlorhydria.[1, 7] In autoimmune atrophic gastritis, the development of autoantibodies against parietal cells leads to their destruction and to a consequential underproduction of stomach acid.[4] Autoantibodies against intrinsic factor may also be present, causing malabsorption of vitamin B$_{12}$ — a common finding in hypochlorhydria.[4] Commonly, pernicious anemia develops and can be recognized through routine screening. In individuals with autoimmune conditions, autoimmune gastritis and pernicious anemia occur as much as three to five times more often as in the general population.[4]

H. pylori: Helicobacter pylori (H. pylori) is a bacteria linked to gastric and peptic ulcers, gastritis, and stomach cancer. H. pylori can produce proteins which interfere with the parietal cells’ ability to secrete appropriate quantities of stomach acid.[8, 9] Infection with H. pylori has been demonstrated to decrease vitamin B$_{12}$, iron, folic acid, and vitamin A levels via a reduction in stomach acidity.[10, 11, 12] After eradication of H. pylori in affected individuals, parameters relating to vitamin and mineral absorption have been shown to improve.[10, 11]
**Food Sensitivity:** Histamine is a modulator of HCl release in the gut. In some individuals, exposure to certain foods leads to a decrease in histidine (needed to make histamine), which leads to a decrease in HCl release.[1]

**Medications:** Proton-pump inhibitors are one of the most commonly utilized class of drugs, and are specifically used to decrease stomach acid. This intentional induction of hypochlorhydria is associated with various micronutrient deficiencies, including vitamin B$_{12}$, iron, folic acid, vitamin D, calcium, and zinc.[13] Although controversial, there is a noted association between osteopenia/-porosis and the use of PPIs.[14] Perhaps most alarmingly, serious community-acquired infections, such as pneumonia and *C. difficile*, are associated with use of PPIs in the elderly.[6]

**Consequences of Hypochlorhydria**

**Vitamin/Mineral Deficiencies** As noted previously, deficiencies of folic acid, vitamin B$_{12}$, vitamin D, vitamin A, calcium, iron, and zinc are associated with low stomach acid.[1, 7, 10] These deficiencies are due to a decreased ability to disassociate minerals and vitamins from food stuffs, as well as related effects on gastric secretions other than hydrochloric acid that facilitate absorption.[4]

**Osteopenia and Osteoporosis** As with other minerals, calcium requires adequate levels of stomach acid to dissolve from its salt form in order to be properly absorbed.[13] It is postulated that low levels of stomach acid, leading to a decreased ability to absorb calcium, may increase the risk of osteopenia and osteoporosis.[13] Similarly, long-term use of proton-pump inhibitors has been associated with an increased risk of bone fracture associated with decreased bone mineral density.[14]
Skin Conditions
Numerous skin conditions are associated with inadequate stomach acid. Acne roseacea, alopecia, eczema, lupus, and vitiligo have all been linked to deficiency in HCl production.[1, 15] Studies as early as 1945 showed that individuals with roseacea improved when supplemented with HCl.[16]

Depression
Not only is stomach acid required for proper digestion and absorption of vitamins and minerals, but it is also required to adequately digest protein. Without adequate protein digestion, individuals can become deficient in specific amino acids.[1] A deficiency in tyrosine and tryptophan can lead to deficiencies in norepinephrine and serotonin, leading to depression.[1] Vitamin B₁₂ deficiency is also correlated with depression and anxiety, and has a well-established relationship to hypochlorhydria.[4, 17]

Acid Reflux
Acid reflux is caused by the presence of stomach contents in the esophagus. The lower esophageal sphincter (LES), located between the stomach and esophagus, when adequately closed prevents the movement of gastric contents into the esophagus. Although routinely treated as a condition of excess stomach acid, reflux is more commonly caused by insufficient stomach acid, as the LES needs adequate stomach acid to prompt proper closing.[1]

Digestive Upset
Constipation, bloating, feelings of fullness, and abdominal discomfort are all associated with hypochlorhydria. Often, individuals with hypochlorhydria will describe a quick onset of fullness when they begin eating, and feel as if food “sits” in their stomach.

Management
Diagnostics
Hypochlorhydria can be assessed through clinical symptoms in conjunction with information from regular laboratory work and specialty tests.[1] Due to the associated micronutrient deficiency in hypochlorhydria, often routine blood test abnormalities, such as vitamin B₁₂ deficiency and iron deficiency, may suggest hypochlorhydria.[1, 4] Special tests to directly measure stomach acid are available, but not commonly used. These tests include the gastrotest and Heidelberg
gastric pH test.\cite{1, 18} The Heidelberg test involved the use of a small pH electrode that is swallowed and transmits information via radio transmitter to assess gastric pH.\cite{1, 18} The gastrotest utilizes a stomach acid–provoking agent such as caffeine, followed by the ingestion of a long string attached to an inert pill. The string is removed and the pH at several lengths is measured to assess gastric pH.\cite{1} Less invasive and able to be done at home is the betaine HCl challenge test; this test utilizes a titration method to assess how much exogenous stomach acid–mimicking supplement an individual can tolerate.

**Treatment**

The priority in any therapeutic plan is to identify and treat the underlying cause of disease. In the case of hypochlorhydria, identifying related and contributing factors is crucial in treatment. Eradicating \textit{H. pylori}, eliminating food sensitivities, and modifying pharmaceutical use can each be fundamental in reversing the underlying cause of low stomach acid. Along with treating the underlying cause of hypochlorhydria, there are several strategies that are useful in raising stomach acid and repleting nutrients that may be deficient after long-term low stomach acid:

\textbf{i) Betaine HCl:} Along with being a useful supplement to assess stomach acid, betaine HCl is useful in increasing digestive function in individuals with low stomach acid. Supplemented before and during meals, betaine HCl mimics stomach acid, aiding in nutrient absorption and digestion. Protocols using betaine HCl often utilize a titrating dose strategy to find the appropriate replacement dose for individuals.\cite{1}

\textbf{ii) Niacin:} There is some evidence that niacin may impact production of stomach acid, although the exact mechanism remains unclear.\cite{1}

\textbf{iii) Bitters:} Herbalists and other medical practitioners often use bitter herbs, such as gentian, dandelion, wormwood, and yarrow, to stimulate digestion and increase gastric secretions. The bitter taste of these herbs is thought to be partly responsible for their effects on digestion.\cite{18}

\textbf{iv) B vitamins, iron, multiminerals, amino acids:} As discussed, hypochlorhydria can decrease absorption of \textit{B}_{12}, iron, and a number of other nutrients.\cite{4} Supplementing with nutrients suspected deficient in individuals with hypochlorhydria can improve related health conditions and overall health.

**Conclusion**

Hypochlorhydria is a complex health condition which is associated with and contributes to a number of chronic health conditions. Screening of at risk individuals can improve outcomes and quality of life.
References