

# Vitamin Deficiency After Gastric Bypass Surgery: A Review

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**Abstract:** More than 60% of the adult US population now meets the criteria for being overweight or obese. Gastric bypass surgery has become a popular and effective way to combat this medical problem. Despite the success of these procedures, they are associated with many complications, including malnutrition, neurological compromise, and vitamin deficiency. Research has determined that even with multivitamin supplementation for life, a large percentage of bypass patients develop vitamin deficiencies. We present a case of beriberi after Roux-en-Y bypass that illustrates the importance of close follow up. A thorough review of vitamin deficiencies in this unique patient population is explored. Vitamin supplementation and treatment recommendations are compiled from the most up-to-date sources. Even patients on regular supplements should be closely monitored for vitamin deficiencies. Patient education regarding vitamin supplementation is vital; it should begin prior to surgery and continue throughout the postoperative period and beyond.

**Key Words:** bariatric surgery, gastric bypass surgery, nutritional supplementation complications, vitamin deficiency

Obesity has reached epidemic levels, and its incidence continues to rise. More than 60% of the adult US population now meets the criteria for being overweight or obese.<sup>1</sup> Bariatric surgery has become a popular and effective way to combat this medical problem, with more than 100,000 procedures performed annually.<sup>2</sup> It is estimated that over the next few years the total number of obesity surgery patients in the United States will exceed 1 million.<sup>3</sup>

Gastric bypass surgeries, such as Roux-en-Y (RYGBP) and biliopancreatic diversion, reconfigure the gastrointestinal

tract to achieve weight loss by gastric restriction and intestinal malabsorption.<sup>4,5</sup> Typically, a long-term loss of one third of body weight and resolution of many comorbid conditions are achieved.<sup>6</sup> Despite successes, these procedures have multiple inherent risks and complications, including malnutrition, neurological compromise, and vitamin deficiency.<sup>7-9</sup>

A 37-year-old female with morbid obesity underwent RYGBP 3 months prior to presentation. Her operation was uncomplicated, but she received no follow-up care. Two weeks prior to presentation, the patient developed mild paresthesia of the anterior right leg. Two days prior to presentation, her paresthesia worsened and began to involve the left leg as well. She also noted progressive weakness of the lower extremities bilaterally. One day later, she experienced acute problems walking, fell down after her knees buckled under her weight, and was unable to stand due to weakness. She noted persistent nausea and vomiting and a 60-pound weight loss since her surgery.

On admission, bilateral lower extremity proximal muscle weakness was noted from the thighs distally. Bilaterally decreased sensation to light touch from the knees distally was noted, and reflexes were diminished. Neurological examination revealed intact cranial nerves and no upper extremity abnormalities. There were no signs of cardiac disease. A computed tomography scan of the head, and magnetic resonance imaging of the brain and spine, showed no abnormalities. Complete blood count, comprehensive metabolic profile, sedimentation rate, and C-reactive protein levels were unremarkable.

## Key Points

- Gastric bypass surgery is associated with serious vitamin deficiencies.
- Primary care physicians and others should be diligent in vitamin supplementation and treatment in this population to prevent serious complications.
- Vitamin supplementation should be continued for life, and even patients on regular supplements should be closely monitored for vitamin deficiencies.
- Patient education is paramount, and emphasis regarding the importance of vitamin and other nutrient supplementation should begin prior to surgery and continue throughout the postoperative period and beyond.

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The research reported here was conducted using only departmental support. Dr. Marc Matrana has no conflicts of interest to report and no financial disclosures to declare. Dr. William Davis has received honoraria from Wyeth as a consultant and from Takeda as a speaker.

Accepted March 13, 2009.

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0038-4348/0-2000/10200-1025

able. Vitamin levels revealed undetectable thiamine levels (<0.5 nmol/L). B12 and other vitamin and mineral levels were normal.

Aggressive thiamine replacement was started immediately, with 100 mg of intravenous (IV) thiamine followed by 100 mg of intramuscular thiamine daily. After three days, the patient showed little improvement and was still unable to walk. Physical therapy was initiated, and the patient was transported to our rehabilitation facility, where she received daily physical therapy and oral thiamine replacement. After three weeks, she had slowly but progressively improved and was able to ambulate 150 feet with a rolling walker.

The average patient maintains food consumption between 600 and 900 kcal daily after gastric bypass surgery.<sup>10</sup> Without supplementation, such dietary restriction often leads to nutri-

tional deficiencies. Deficiencies also develop secondary to the loss of gastrointestinal segments where nutrients are absorbed. Vitamin deficiencies are among the more common nutritional problems in bariatric surgery patients, and they present in a variety of ways. Inadequate vitamin levels lead to serious neurological, hematological, and other manifestations. No firm guidelines for vitamin supplementation exist in this patient group, and data are relatively scarce. Research has found wide variations in vitamin supplementation and monitoring among surgeons who treat postgastric bypass patients (Table).<sup>11</sup>

**Vitamin A**

Vitamin A refers collectively to a number of retinoids that are essential for visual acuity, immunological func-

**Table. Summary of vitamin supplementation recommendations for postgastric bypass patients**

|                           | <b>Major natural dietary sources</b>   | <b>Deficiency-associated symptoms</b>   | <b>Recommended daily allowance (RDA) in healthy adults</b>   | <b>Recommended daily oral supplementation in gastric bypass patients</b>                             |
|---------------------------|--|---|--|--|
| Vitamin A                 | Liver, leafy green vegetables, carrots, sweet potatoes, and pumpkins   | Night blindness, xerosis, impaired immunity, and changes in epithelial tissues and teeth                            | Adult male: 900 µg/d. Adult female: 700 µg/d   | 10,000 IU/d <sup>14</sup> (approx 3,000 µg/d) <sup>a</sup>   |
| Vitamin B1 (thiamine)     | Fortified breads, cereals, pastas, whole grains, dried beans, peas, and soy  | Wernicke encephalopathy, Korsakoff syndrome, and beriberi   | Adult male: 1.2 mg/d. Adult female: 1.1 mg/d   | 50–100 mg/d <sup>b</sup>   |
| Vitamin B9 (folate)       | Liver, leafy green vegetables, dried beans, and cereals  | Macrocytic megaloblastic anemia, diarrhea, anorexia, weight loss, weakness, headaches, and behavior changes         | Adults: 400 µg   | 0.5–1 mg/d   |
| Vitamin B12 (cobalamin)   | Meat, milk, shellfish, and eggs  | Macrocytic megaloblastic anemia, peripheral nerve damage, coordination disorders, ataxia, and cognitive impairments | Adults: 2.4 µg/d   | 350–500 µg/d (some patients may require monthly intramuscular B12 injections of 1,000–3,000 µg/dose) |
| Vitamin C (ascorbic acid) | Citrus fruits, green peppers, strawberries, tomatoes, broccoli, leafy greens, and melons   | Scurvy (bleeding and bruising, hair and tooth loss, and joint pain and swelling)                                    | Adult male, nonsmoker: 90 mg/d. Adult male, smoker: 125 mg/d. Adult female, nonsmoker: 75 mg/d. Adult female, smoker: 110 mg/d | No clear consensus. Patients should consume foods and supplements rich in vitamin C                  |
| Vitamin D                 | Some fatty fish (mackerel, salmon, and sardines), fish liver oils, and eggs, as well as fortified milk, formula, orange juice, and cereals | Increased incidence of certain cancers, heart disease, and osteoporosis   | Adults ages 19–50: 5 µg/d. Adults ages 51–70: 10 µg/d. Adults ages ≥71: 15 µg/d <sup>c</sup>                                   | 800–1,200 IU/d (20–30 µg/d) along with at least 1,200–1,800 mg/d of calcium citrate                  |
| Vitamin E                 | Avocados, nuts and seeds, olives, green leafy vegetables, and vegetable oils   | Ataxia, peripheral neuropathy, myopathy, and pigmented retinopathy  | Adults: 15 mg/d  | Supplement with standard multivitamin formulation rich in vitamin E                                  |
| Vitamin K                 | Green leafy vegetables and in some vegetable oils, including soybean, cottonseed, canola, and olive oils                                   | Stomach pains, bleeding, cartilage calcification, malformation of developing bone, and atherosclerosis              | Adult male: 120 µg/d. Adult female: 90 µg/d <sup>c</sup>   | At least 300 µg/d  |

<sup>a</sup>The exact conversion between international units and micrograms is dependent on the source of vitamin A.

<sup>b</sup>Represents standard maintenance dose in patients who have been treated for thiamine deficiency or beriberi.

<sup>c</sup>RDA has not been established. Recommendations based on Institute of Medicine’s Adequate Intake (AI) levels.

tioning, and cell proliferation and differentiation. Retinoids also function to protect tissues from oxidative stress caused by free radicals. Found as provitamin carotenoids in most plant sources and mostly as retinyl palmitate in animal sources, vitamin A is an important part of the human diet.

The recommended daily allowance (RDA) of vitamin A for the adult male is 900  $\mu\text{g}$  and for the adult female is 700  $\mu\text{g}$ . Major sources of vitamin A include liver; leafy green vegetables; and yellow and orange carotenoid-containing foods such as carrots, sweet potatoes, and pumpkins. Deficiencies in vitamin A can lead to night blindness, xerosis (that can progress to total blindness), impaired immunity, and detrimental changes in epithelial tissues and teeth.

The incidence of vitamin A deficiency after gastric bypass surgery varies widely in published reports. In 2006, Clements et al<sup>12</sup> noted an incidence of vitamin A deficiency of 11% and 8.3% of patients at one- and two-year follow up, respectively. They hypothesized that intestinal absorption may adapt, thereby overcoming the decreased surface area, but also noted that fewer patients follow up at two years, skewing most analyses. Even with supplementation, vitamin A deficiency may still occur; Brolin et al<sup>13</sup> reported a vitamin A deficiency rate of 10% in post-RYGBP patients despite supplementation. Biliopancreatic surgeries are associated with a higher incidence of vitamin A deficiency; Slater et al<sup>14</sup> reported an incidence of vitamin A deficiency of 69% at four-year follow up after biliopancreatic surgery.

Several case reports have noted night blindness and other visual complications associated with vitamin A deficiency after bariatric surgery.<sup>15–18</sup> In 2002, Huerta et al<sup>19</sup> reported a case of vitamin A deficiency in a female patient who later gave birth to an infant with greatly reduced vitamin A levels and possible visual complications.

No consensus about appropriate prophylactic vitamin A supplementation in bariatric surgery patients currently exists. Slater et al<sup>14</sup> recommend at least 10,000 international units (IU) daily. It is clear that routine measurement of vitamin A levels prior to and after surgery is warranted in many cases. Oversupplementation of vitamin A is associated with systemic toxicities that can present as a wide variety of symptoms, including gastrointestinal complaints, irritability, altered mental status, blurry vision, and weakness. In addition, teratogenic malformations in infants have been associated with hypervitaminosis A in mothers.<sup>19</sup>

### Vitamin B1 (Thiamine)

Thiamine, or vitamin B1, acts as a coenzyme in the metabolism of carbohydrates and branched-chain amino acids and in the formation of glucose via the pentose monophosphate pathway.<sup>20</sup> It is vital for the proper functioning of the nervous system. Thiamine is found in fortified breads, cereals, pastas, whole grains, dried beans, peas, and soy. The

RDA of 1.2 mg for men and 1.1 mg for women is normally exceeded in the average American diet.<sup>21</sup>

Thiamine deficiency is associated with Wernicke encephalopathy, Korsakoff syndrome, and beriberi. Wernicke encephalopathy is characterized by ataxia, ophthalmoplegia, confusion, and short-term memory impairment. Patients with Korsakoff syndrome manifest anterograde and retrograde amnesia, confabulation, apathy, ataxia, and tremors. Beriberi is subdivided into two distinct clinical entities in the adult population. Dry beriberi is usually associated with caloric restriction and relative inactivity and is the type reported in post-gastroectomy patients.<sup>22</sup> It is defined by a predominance of neurological symptoms, including weakness, peripheral neuropathies, paresthesias, and other sensorimotor deficits. Listlessness and other personality shifts are common.<sup>23</sup> Wet beriberi (involving predominantly cardiac symptoms) is associated with vigorous exercise and high carbohydrate intake. No cases of wet beriberi have been reported in patients after bariatric surgery; they typically avoid carbohydrates because of the risk of dumping syndrome.<sup>24</sup>

Although quite common after weight loss surgery, thiamine deficiency is usually mild and rarely symptomatic in these patients. Symptomatic beriberi is seen in only 0.0002–0.4% of gastric bypass patients.<sup>13,25</sup> Urine and serum thiamine levels are screening tests, but normal levels have been observed even in those with symptomatic deficiency. The erythrocyte transketolase activation assay is the gold standard test for accurate diagnosis in the face of normal urine and serum levels.<sup>13</sup> Methods for using high performance liquid chromatography to measure thiamine levels have also been proposed.<sup>14,26</sup>

Beriberi should be aggressively treated with thiamine replacement. Glucose infusion should be avoided prior to replacement to avoid acute Wernicke encephalopathy. The standard dose of thiamine is 100 mg IV for one day, followed by 100 mg intramuscularly each day for five days, and then permanent oral maintenance of 50–100 mg daily. Symptoms of dry beriberi may persist for weeks to months following the replacement of thiamine, but wet beriberi typically responds quickly to treatment.<sup>12</sup>

### Vitamin B12 and Folate

Vitamin B12 refers to a group of closely related molecules, including cyanocobalamin, that are essential in cell metabolism, nervous system functioning, DNA synthesis, and blood formation. Vitamin B12 is found naturally in meat, milk, shellfish, and eggs. Folate (folic acid, or vitamin B9) is a molecule related functionally to vitamin B12. It is essential in the formation of DNA bases and in erythropoiesis. It is found in liver, leafy green vegetables, dried beans, and cereals. The RDA of vitamin B12 is 2.4  $\mu\text{g}$  in adults; the RDA of folate is 400  $\mu\text{g}$  in adults.

Vitamin B12 and folate deficiencies can lead to macrocytic, megaloblastic anemia. B12 deficiency can also lead to

neurological sequelae: peripheral nerve damage, coordination disorders, ataxia, and cognitive impairments. Folate deficiency may present with a wide variety of systemic symptoms, including diarrhea, anorexia, weight loss, weakness, headaches, and behavior changes. Folate deficiency in pregnant women has been associated with neural tube defects in developing fetuses.

Vitamin B12 deficiency is one of the most common nutritional deficiencies occurring after obesity surgery. Studies have estimated the prevalence of vitamin B12 deficiency at one-year follow up after gastric bypass surgery to be as high as 30%.<sup>27</sup> The long-term prevalence of vitamin B12 deficiency after gastric bypass surgery ranges widely, from 36–70%.<sup>28,29</sup> It is clear that standard supplements alone are not sufficient to prevent deficiencies. Most authors recommend 350–500  $\mu\text{g}/\text{day}$  of oral cobalamin, though some patients will require monthly intramuscular B12 injections (1,000–3,000  $\mu\text{g}/\text{dose}$ ).<sup>30</sup>

Folate deficiency following obesity surgery is rare. A study by Mallory and Macgregor<sup>31</sup> of 1,067 post-RYGBP patients found only a 1% prevalence of folate deficiency. Deficiencies can be prevented with 400–500  $\mu\text{g}/\text{day}$  of oral folate, although most experts recommend supplementing with 1 mg of daily folate. Folate supplementation may correct anemia associated with low B12 levels, but it can also mask underlying B12 deficiency, leading to the progression of neurological damage.

### Other B Vitamins

Researchers have found other B vitamins to be reduced after gastric bypass surgery. Riboflavin (B2) and pyridoxine (B6), along with other B vitamins, are essential for normal cell metabolism. B complex vitamins are found in a range of foods, but especially in some fruits, vegetables, liver, tuna, and yeast. Deficiencies result in a wide array of disorders, including various skin manifestations and neurological complications. Clements et al<sup>12</sup> found vitamin B2 deficiencies of 13.6% and 7.1% at one- and two-year follow up, respectively, and vitamin B6 deficiencies of 17.6% and 14.2% at the same intervals. Boylan et al<sup>32</sup> found that only 36% of their subjects had adequate vitamin B6 levels prior to surgery.

### Vitamin C

Vitamin C, or ascorbic acid, is a water-soluble vitamin that is essential in the synthesis of connective tissues and bone. It plays a role in the synthesis of norepinephrine and carnitine. Its potent antioxidant functions protect a large variety of molecules from oxidative damage caused by free radicals. Research has also suggested that vitamin C plays a role in the metabolism of cholesterol to bile acids.<sup>33,34</sup>

Vitamin C can be found naturally in a wide variety of fruits and vegetables, especially citrus fruits, green peppers, strawberries, tomatoes, broccoli, leafy greens, and melons.

The current RDA of vitamin C is 90 mg for adult male nonsmokers and 75 mg for adult female nonsmokers. Daily allowances are higher for smokers (125 mg for adult males and 110 mg for adult females) due to increased oxidative stress.

Deficiencies in vitamin C lead to bleeding and bruising, hair and tooth loss, and joint pain and swelling—a condition known as scurvy. The 18th century British Navy was aware that scurvy could be cured by eating citrus, even though vitamin C was not isolated in the laboratory until the 1930s.

Little is known about the effects of bariatric surgery on vitamin C levels. To our knowledge, no cases of overt scurvy have been reported in postoperative patients. In the only study examining serum vitamin C deficiency after obesity surgery, Clements et al<sup>12</sup> found an incidence of 34.6% at one-year follow up and 35.4% at two-year follow up after RYGBP in a series of 318 and 141 patients, respectively. No clear consensus can be drawn regarding the optimal vitamin C supplementation in postsurgery patients.

### Vitamin D

Vitamin D refers to fat-soluble substances that are synthesized by human skin upon exposure to ultraviolet-B radiation (cholecalciferol) or obtained from the diet (ergosterol) and activated in the skin upon light exposure. Vitamin D receptors are found in many tissues. Vitamin D is essential for maintaining normal calcium metabolism, and low levels have been associated with increased incidence of certain cancers, heart disease, and osteoporosis.<sup>35–37</sup>

Dietary sources of vitamin D include some fatty fish (such as mackerel, salmon, and sardines), fish liver oils, and eggs. In the United States, certain foods are fortified with vitamin D, including milk, infant formula, orange juice, and some cereals. The Institute of Medicine's Adequate Intake (AI) levels for vitamin D are 5  $\mu\text{g}/\text{day}$  for ages 19–50, 10  $\mu\text{g}/\text{day}$  for ages 51–70, and 15  $\mu\text{g}/\text{day}$  for those 71 years and older.<sup>38</sup>

Vitamin D deficiency is common after bariatric surgery, and many patients have low levels prior to surgery.<sup>39–41</sup> Vitamin D deficiency further exacerbates calcium malabsorption, causing an increase in parathyroid hormone (PTH) and, eventually, osteoporosis in postsurgery patients.<sup>42</sup> Coates et al<sup>43</sup> studied bone metabolism in 25 patients at 9 months following RYGBP and found that bone mineral density and content were significantly diminished compared to 30 obese control patients.

Slater et al<sup>14</sup> found vitamin D deficiencies in 57% of patients at one-year follow up and 63% at four-year follow up. Brolin et al<sup>13</sup> found that 51% of postoperative patients had significant vitamin D deficiencies at two-year follow up, and Dolan et al<sup>44</sup> measured low vitamin D levels in 50% of subjects at 28 months after surgery. Johnson et al studied 243 gastric bypass patients and found that beyond five years of

follow up, few patients had adequate vitamin D levels ( $\geq 30$  ng/mL). They also found an inverse relationship between vitamin D and PTH levels, such that lower levels of vitamin D correlated with higher levels of PTH.<sup>45</sup> Currently, most authors recommend supplementing postgastric bypass patients with at least 800–1,200 IU of vitamin D and at least 1,200–1,800 mg of calcium citrate daily (the bioavailability of calcium carbonate is reduced in the absence of stomach acid).<sup>14,45</sup>

### Vitamin E

Vitamin E refers to a related set of tocopherols and tocotrienols, which act as fat-soluble, antioxidant vitamins. These substances are essential for normal neurological functioning, protecting neuronal cell membranes from oxidative damage.<sup>46</sup> The role of vitamin E as a signaling molecule has also been suggested.<sup>47</sup> In addition, at least five large observational studies suggest that an increased consumption of vitamin E is associated with a decreased risk of myocardial infarction or death from heart disease, although clinical trials have not substantiated these hypotheses.<sup>48–51</sup> Several major studies have failed to show significant associations between tocopherol intake and the incidence of cancer.<sup>52–54</sup>

Vitamin E can be found naturally in a variety of foods, including asparagus, avocados, nuts and seeds, olives, green leafy vegetables, and vegetable oils. The RDA of vitamin E is 15 mg in adults.<sup>55</sup> Deficiencies in vitamin E have been associated with ataxia, peripheral neuropathy, myopathy, and pigmented retinopathy.

Symptomatic vitamin E deficiency is rare, found mostly in individuals with lipoprotein disorders, such as abetalipoproteinemia, and in those with disorders of fat absorption such as cholestatic liver disease and cystic fibrosis. Symptomatic vitamin E deficiency after gastric bypass surgery is also rare but has been reported in a few cases.<sup>56,57</sup> One study has shown a significant increase in serum levels of alpha-tocopherol (the most active form of vitamin E) at 24 weeks after vertical banded gastroplasty in a survey of 22 patients. This was thought to be secondary to a decrease in the generation of free radicals after surgery.

In a study of 22 patients who underwent RYGBP at the Medical College of Virginia, researchers found that 77% of subjects had normal vitamin E levels prior to surgery. They noted no statistically significant differences in plasma tocopherol levels prior to and at 6 and 12 months after surgery in subjects taking vitamin E supplements. The data did indicate a significant correlation between a dose of vitamin E supplement intake and total plasma tocopherol levels.<sup>32</sup>

### Vitamin K

Vitamin K is a fat-soluble vitamin, essential for coagulation. It also acts as a cofactor in the gamma-carboxylation of glutamic acid residues of proteins involved in bone min-

eralization and cell growth.<sup>58–61</sup> Vitamin K refers to two distinct categories of substances: phyloquinone synthesized by plants (known as vitamin K<sub>1</sub>) and menaquinone synthesized by bacteria (known as vitamin K<sub>2</sub>).<sup>62</sup> Vitamin K is found at its highest levels in green leafy vegetables and in some vegetable oils, including soybean, cottonseed, canola, and olive oils. Recommended dosages are 120  $\mu$ g/day in adult males, and 90  $\mu$ g/day in adult females.<sup>63</sup> Vitamin K deficiencies are associated with stomach pains, bleeding, cartilage calcification, malformation of developing bone, and atherosclerosis.<sup>64</sup>

In 2004, Slater et al reported the follow-up results of 202 patients who had undergone biliopancreatic diversion for obesity. All of these patients had been prescribed 300  $\mu$ g of vitamin K daily. Among these patients, 51% had vitamin K deficiencies at one-year follow up; the prevalence increased to 68% by the fourth year after surgery. By the fourth year, 42% of patients studied had undetectable vitamin K levels ( $< 0.1$  nmol/L) despite supplementation.<sup>14</sup>

Although no incidence of bleeding secondary to vitamin K deficiencies after bypass surgeries has been reported, Van Mieghem and colleagues published a case in 2008 of severe fetal hemorrhage due to maternal vitamin K deficiency after gastric banding.<sup>65</sup> Postgastric bypass patients require at least 300  $\mu$ g/day of supplemental vitamin K.<sup>14</sup>

### Conclusions

In 2007, Colossi et al<sup>66</sup> concluded that the continuous use of a multivitamin supplement for life is necessary after RYGBP. Gasteyer et al conducted a retrospective study that included a two-year follow up of post-RYGBP patients and noted that despite supplementation with a standard multivitamin, 98% of patients required additional specific vitamin supplements by 24 months. On average, each of their patients required  $2.9 \pm 1.4$  specific supplements in addition to a multivitamin.<sup>67</sup> Recent studies have suggested the benefit of systematic assessment of the micronutrient status of all gastric bypass candidates prior to surgery, and regular monitoring of vitamin levels is strongly encouraged in the postoperative period and for several years beyond.<sup>68</sup>

Because the number of gastric bypass surgery patients is increasing substantially, and because many patients do not follow up with their surgeons as advised, it is vital for all primary care physicians and others to be aware of the medical complications of weight loss surgery. It is especially important to be cognizant of vitamin deficiencies and their various presentations in this unique patient population. Patient education is paramount, and emphasis regarding the importance of vitamin and other nutrient supplementation should begin prior to surgery and continue throughout the postoperative period and beyond.

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“Habits of thought persist through the centuries; and while a healthy brain may reject the doctrine it no longer believes, it will continue to feel the same sentiments formerly associated with that doctrine.”

—Charlotte Perkins Gilman