

# Vitamin A deficiency in a newborn resulting from maternal hypovitaminosis A after biliopancreatic diversion for the treatment of morbid obesity<sup>1-3</sup>

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## ABSTRACT

**Background:** Biliopancreatic diversion (BPD) has been advocated for the treatment of morbid obesity. This procedure has the theoretical advantage that patients retain normal eating capacity and lose weight irrespective of their eating habits. However, vitamin deficiencies may develop because BPD causes malabsorption.

**Objective:** This report describes a 40-y-old mother and her newborn infant, who developed vitamin A deficiency as a result of iatrogenic maternal malabsorption after BPD. Our primary objective is to show that BPD patients need close follow-up and lifelong micronutrient supplementation to prevent nutrient deficiencies in themselves and their offspring.

**Design:** The medical records of the mother and infant were reviewed, and their clinical course was followed until 10 mo postpartum. The mother was also interviewed on several occasions about her medical care, follow-up, and supplemental vitamin use.

**Results:** The mother developed night blindness with undetectable serum vitamin A concentrations in the third trimester of her pregnancy. Her vitamin A deficiency was untreated until she delivered her infant. At delivery, the infant also had vitamin A deficiency. He may have permanent retinal damage, but this is still unclear because the ophthalmologic examination performed at 2 mo of age was inconclusive.

**Conclusions:** Complications of BPD may take many years to develop, and the signs and symptoms may be subtle. Because of the malabsorption that results from BPD, patients need lifelong follow-up and appropriate vitamin supplementation to prevent deficiencies. These nutrient deficiencies can also affect the offspring of female BPD patients. *Am J Clin Nutr* 2002;76:426-9.

**KEY WORDS** Vitamin A deficiency, biliopancreatic diversion, night blindness, malabsorption, morbid obesity, neonatal nutrition, hypovitaminosis A

## INTRODUCTION

The prevalence of obesity is constantly rising, and this has led to a parallel increase in the number of surgical procedures performed to treat clinically severe (morbid) obesity. Seventy-five to eighty percent of patients who have surgical treatment for morbid obesity are female (1-3). Some physicians have advocated biliopancreatic diversion (BPD) for the surgical management of obesity. Because most women who choose BPD are of childbearing age (2-4), pregnancy is a frequent event after the surgical intervention. In fact, resolution of infertility is a beneficial effect of BPD (5). However, BPD

patients are at risk of developing deficiencies of protein and fat-soluble vitamins because this procedure relies on intestinal malabsorption. In pregnant women, this becomes an even greater concern because of the physiologic stress associated with pregnancy. Therefore, women who have had BPD need additional prenatal nutritional support. Prenatal vitamins alone are insufficient for preventing severe vitamin deficiencies during pregnancy in BPD patients (6).

In 1973, Scopinaro et al (3) described BPD for the treatment of morbid obesity. In BPD, a distal gastrectomy is performed and the ileum is divided 200 cm proximal to the ileocecal valve. The distal ileum becomes the alimentary limb and is anastomosed to the gastric pouch, which is the intestinal segment that carries the food for absorption. The proximal bowel is known as the biliopancreatic limb because it carries the biliopancreatic secretions to the alimentary limb. The distal end of the biliopancreatic limb is anastomosed to the alimentary limb 50 cm proximal to the ileocecal valve. Thus, absorption of nutrients only takes place in the last 50-cm segment of the intestine (**Figure 1**). Long-term weight loss independent of the patient's eating behaviors has been cited as the major advantage of BPD compared with gastric-restrictive procedures.

In patients who have had BPD, the fat-soluble vitamins (A, D, E, and K) are poorly absorbed because of fat malabsorption in the distal intestine. Six percent of patients develop deficiencies of the fat-soluble vitamins after BPD (7). Consequently, patients who have had surgery to induce intestinal malabsorption and thereby treat obesity are at risk of developing night blindness from vitamin A deficiency, bone loss from calcium malabsorption coupled with vitamin D deficits, bleeding disorders from lack of vitamin K, and both ataxia and dry pruritic skin from vitamin E deficiency. Several cases of vision disorders secondary to vitamin A deficiency after BPD have been reported (2, 7-9). Night blindness (impaired dark adaptation resulting from slowed regeneration of rhodopsin) is the first ocular symptom observed with vitamin A deficiency (10), but late symptoms also occur. In addition, vitamin A is

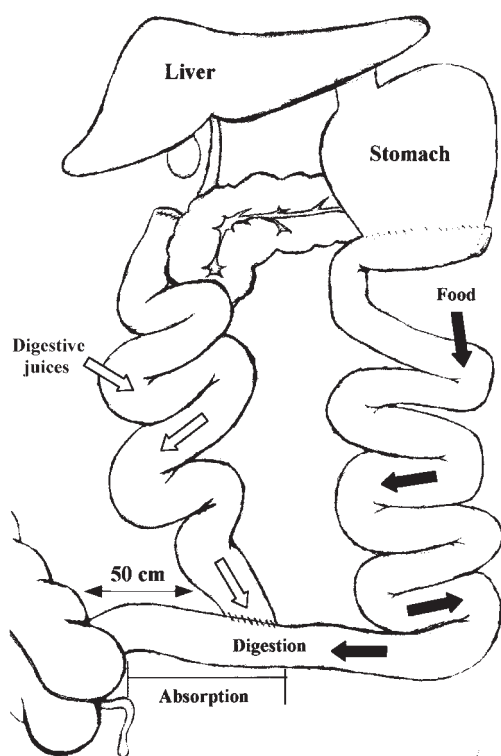
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**FIGURE 1.** Diagram of biliopancreatic diversion, showing that the only intestinal segment available for digestion and absorption is the last 50 cm of the small intestine, where the alimentary limb meets the biliopancreatic segment.

required for the differentiation and growth of epithelial cells during embryonic development (11), and thus it is an important micronutrient during pregnancy.

Although BPD is often performed in women of reproductive age (3), and vitamin A deficiency is common after BPD, adverse effects resulting from hypovitaminosis A have not been reported previously in the offspring of BPD patients. The present report was written to describe the need for close follow-up in patients who have undergone BPD. Close follow-up is especially important in pregnant women because their micronutrient deficiencies may also affect their offspring.

## SUBJECTS AND METHODS

### Data collection methods

We reviewed the medical care received by the mother and infant from the date of admission to the UCLA Medical Center at 12 d postpartum until 10 mo postpartum. Information was obtained from the medical charts and from interviews conducted in person and by telephone with the mother. We also collected data regarding her medical condition, vitamin supplementation, and physician follow-up from the time of her BPD surgery until 10 mo postpartum (1987–2000). The patient provided written, informed consent for both herself and her child.

### Case report

The patient had a history of obesity, which was treated surgically with BPD at a community hospital in 1987. Her weight

before surgery was 127 kg, with a body mass index (in kg/m<sup>2</sup>) of 50. She lost 68 kg during the first year after her surgery, but eventually regained 13.6 kg. Postoperatively, she had a good appetite and did not experience nausea or vomiting. The patient had mild chronic diarrhea, with loose bowel movements 3–4 times/d for the first few months after surgery.

She was in good health until 1994, when she developed fatigue and weakness. At this time, iron deficiency anemia was diagnosed by her primary care physician. The anemia did not improve with oral iron supplementation. The patient eventually required parenteral iron (3 doses/y), which she received for 3 y from 1994 to 1997. She did not undergo further testing for other micronutrient deficiencies and she had no follow-up care from either a surgeon or a nutritionist from the time following BPD surgery until she was admitted to the UCLA Medical Center. The only supplements she took during this time period were one children's multivitamin and 600 mg calcium carbonate/d. In addition, she received routine prenatal vitamins during her pregnancies.

The patient first became pregnant in 1995. This pregnancy was complicated by preeclampsia, but ultimately resulted in the delivery of a healthy infant. In 1999, a second pregnancy ended in spontaneous abortion at 10 wk gestation. In 2000, during a third pregnancy, the patient developed fatigue, lightheadedness, persistent dizziness, and night blindness during the second trimester. At this time, she was taking one children's multivitamin containing 2500 IU vitamin A (50% of the RDA) daily, 600 mg calcium carbonate/d, and 325 mg ferrous sulfate 3 times/d.

During her third trimester, the night blindness worsened, prompting her to seek medical care at the Jules Stein Eye Institute at UCLA. Ophthalmologic examination revealed a visual acuity of 20/30 in the right eye and 20/40 in the left eye with normal ocular motility in both eyes. The intraocular pressure measured by tonometry was normal at 16 mm Hg in both eyes. Dark adaptometry (SST-1 Scotopic Sensitivity Tester; LKC Technologies, Gaithersburg, MD) revealed a prolonged dark adaptation time in both eyes, which is consistent with vitamin A deficiency. An electroretinogram (Visual Evoked Response Imaging System; LKC Technologies), which measures the electrical response of the retina to flashes of light, revealed panretinal abnormalities of both rod- and cone-mediated systems. Rod responses were not detected, suggesting that the visual loss was a result of vitamin A deficiency. Vitamin A concentrations were not measurable in her serum, leading to a diagnosis of night blindness secondary to vitamin A deficiency. After the diagnosis of vitamin A deficiency, water-miscible vitamin A was recommended. However, the patient declined medications because of her fear that they might harm the fetus.

The patient delivered a premature male infant via normal spontaneous vaginal delivery at 34 wk and 5 d gestation. He weighed 1935 g (25th percentile; weight-for-age *z* score = -0.674) and was 45 cm in length (30th percentile; length-for-age *z* score = -1.056). His head circumference was 30 cm (20th percentile; head circumference-for-age *z* score = -0.704) and his APGAR scores were 7 and 9 at 1 and 5 min, respectively. At 2 d of age, he had a plasma vitamin A concentration <0.1 mg/L (normal range: 0.3–0.9 mg/L). The patient's postpartum course was unremarkable except that she did not breast-feed her infant because she was unable to lactate.

The patient was discharged from the hospital on the second day after delivery. She was discharged to home with the following medications: 600 mg ibuprofen every 6 h as needed for pain and 325 mg ferrous sulfate 3 times/d. She was given a prescription for oral vitamin A (50 000 IU/d), but she did not fill the prescription.

**TABLE 1**

The mother's laboratory values during her hospital admission at 12 d postpartum showing evidence of severe anemia; hypoalbuminemia; low plasma concentrations of vitamin A, 25-hydroxyvitamin D, vitamin E, calcium, and zinc; and elevated liver function tests<sup>1</sup>

Complete blood count	Chemistry profile	Vitamins	Minerals	Liver function tests
WBC = $9.6 \times 10^3/\mu\text{L}$ (3.28–9.29 $\times 10^3/\mu\text{L}$ )	Sodium = 138 mmol/L (136–146 mmol/L)	Vitamin A <0.1 mg/L (0.3–0.9 mg/L)	Iron = 18 $\mu\text{g/dL}$ (17–156 $\mu\text{g/dL}$ )	AST = 63 U/L (15–50 U/L)
RBC = $2.98 \times 10^6/\mu\text{L}$ (3.76–4.93 $\times 10^6/\mu\text{L}$ )	Potassium = 3.7 mmol/L (3.6–5.0 mmol/L)	25-hydroxyvitamin D = 6 ng/mL (15–57 ng/mL)	TIBC = 379 $\mu\text{g/dL}$ (250–450 $\mu\text{g/dL}$ )	ALT = 84 U/L (5–50 U/L)
Hemoglobin = 6.9 g/dL (11.4–14.1 g/dL)	Chloride = 108 mmol/L (97–110 mmol/L)	Vitamin E <2.0 mg/L (5.6–22 mg/L)	Copper = 81 $\mu\text{g/dL}$ (80–155 $\mu\text{g/dL}$ )	Alkaline phosphatase = 199 U/L (35–110 U/L)
Hematocrit = 24.2% (34.0–42.1%)	CO <sub>2</sub> content = 25 mmol/L (25–32 mmol/L)	Vitamin K = 143 pg/mL (80–1160 pg/mL)	Zinc = 45 $\mu\text{g/dL}$ (65–256 $\mu\text{g/dL}$ )	Total bilirubin = 0.4 mg/dL (0.3–1.5 mg/dL)
Platelets = $256 \times 10^3/\mu\text{L}$ (143–398 $\times 10^3/\mu\text{L}$ )	Glucose = 90 mg/dL (65–110 mg/dL)	Thiamine = 3.4 $\mu\text{g/dL}$ (1.6–4.0 $\mu\text{g/dL}$ )	Calcium = 8.1 mg/dL (8.4–10.2 mg/dL)	Total protein = 5.3 g/dL (5.8–8.1 g/dL)
	Urea nitrogen = 13 mg/dL (5–20 mg/dL)	Vitamin B-6 = 5.3 ng/mL (5.0–30 ng/mL)	Ionized calcium = 1.07 mmol/L (1.09–1.29 mmol/L)	Albumin = 2.8 g/dL (3.4–4.7 g/dL)
	Homocysteine = 10 $\mu\text{mol/L}$ (15–20 $\mu\text{mol/L}$ )	Vitamin B-12 = 153 pg/mL (160–840 pg/mL)		
		Folate = 7.8 ng/mL (5.6–19.3 ng/mL)		

<sup>1</sup>Normal ranges are shown in parentheses. WBC, white blood cell count; RBC, red blood cell count; TIBC, total iron-binding capacity; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

At 12 d postpartum (19 October 2000), the patient was admitted to the UCLA Medical Center. Her symptoms included fatigue, lightheadedness, dizziness, dyspnea with minimal exertion, and bilateral lower-extremity edema. She was only taking ferrous sulfate and one children's vitamin/d. On physical examination, her body temperature, blood pressure, heart rate, and respiration were all normal (37°C, 140/80 mm Hg, 78 beats/min, and 16 breaths/min, respectively). She weighed 73.5 kg (body mass index of 29). She was pale with dry skin, very fine and crispy hair, and pitting nails. On examination, her lungs were normal with good air movement. Her cardiac exam revealed a regular heart rate and rhythm with a mild systolic murmur at the left sternal border radiating to the base. Her abdominal exam was also normal without masses or tenderness. Bilateral pedal edema and tenderness at both shins were noted. Mild ataxia and unsteadiness were present on the neurological examination.

The patient's laboratory results (Table 1) revealed severe anemia; hypoalbuminemia; low plasma concentrations of vitamin A, 25-hydroxyvitamin D, vitamin E, calcium, and zinc; and elevated liver function tests.

An abdominal ultrasound showed hepatomegaly and an abdominal computed tomography scan showed a low-attenuation lesion in the left hepatic lobe, most likely consisting of fat, and a right renal angiomyolipoma. A liver biopsy indicated mild microvesicular steatosis. An echocardiogram was unrevealing. No evidence of osteomalacia was found on femoral and tibial radiographs.

On the basis of all of the tests performed, the following diagnoses were made: vitamin E deficiency resulting in ataxia, vitamin B-6 deficiency resulting in neuropathy, and vitamin A deficiency with a history of night blindness.

During the hospitalization, the patient was transfused with 2 units of packed red blood cells. Parenteral multivitamins containing thiamin, folic acid, and vitamin D (calcitriol; Abbot Laboratories, Chicago) were administered, and oral vitamin B-6, vitamin E, and ferrous sulfate were provided. In addition, the patient received intramuscular vitamin A (100 000 IU) 3 times during her hospital admission and follow-up for outpatient therapy.

After these interventions, the patient's hemoglobin and hematocrit improved. The dizziness, mild neuropathy, dyspnea, and lower extremity edema resolved. Her night blindness corrected soon after vitamin A was administered. She was then discharged with the following medications: 325 mg oral ferrous sulfate 3 times/d, 15 IU tocopherol (vitamin E)/d, 250 mg ascorbic acid (vitamin C)/d, 2  $\mu\text{g}$  calcitriol (vitamin D)/d, 250  $\mu\text{g}$  cyanocobalamin (vitamin B-12)/d, and protein-rich nutritional shake meal replacements. At a 2-wk follow-up after her hospitalization, she was asymptomatic.

The child's course of treatment was as follows. At 9 d of age, he received 50 000 IU vitamin A intramuscularly. At 1 mo of age, the child's eyes were fully formed and the mother thought that he could see to some extent, although probably below the normal acuity for his age. The mother also stated that he blinked at light and performed some tracking. At this time, he was evaluated for retinopathy of prematurity, a proliferative disorder of the retinal blood vessels. This disorder was excluded as a potential cause of his visual impairment. At 2 mo of age, his values for plasma retinol,  $\alpha$ - and  $\gamma$ -tocopherol, and 1,25-dihydroxyvitamin D were all within the normal ranges. At 7 mo of age, the infant was below the 10th percentile for length (length-for-age *z* score = -1.282), at the 25th percentile for weight (weight-for-age *z* score = -0.674), and at the 50th percentile for weight-for-length (weight-for-length *z* score = 0). The infant may have permanent retinal damage, but this is still unclear because the ophthalmologic examination performed at 2 mo of age was inconclusive.

## DISCUSSION

BPD reduces the intestinal capacity to absorb fat and starch, thereby limiting energy absorption and promoting weight loss (2). In addition, BPD patients are at risk of malabsorption of the fat-soluble vitamins, calcium, iron, and proteins. Complications of long-term malabsorption occurring many years after the procedure have been described; these complications include steatohepatitis, hepatic failure (7, 12), and secondary hyperparathyroidism resulting from vitamin D and calcium malabsorption (13). Micronutrient malabsorption after this operation has also been

reported. Vitamin A deficiency is relatively common in BPD patients, who often present with night blindness (2, 7–10). In a large series of 1356 patients who underwent BPD, Scopinaro et al (2) reported that 37 patients (2.7%) developed night blindness.


In addition to its role in the visual system, vitamin A plays an essential role in gestation and the normal development of the embryo. In normal gestation, vitamin A is transported rapidly across the placenta from the mother to her fetus (11, 14, 15) by way of retinal-binding-protein receptors (16). Because an increasing number of women of childbearing age are undergoing surgical treatment for obesity, it is important to establish the risk factors for this patient population to avoid hypovitaminosis A and possible adverse effects on the fetus. In a series of 1136 BPD patients, there were 239 pregnancies including 73 abortions, 152 term pregnancies, and 14 women who were pregnant at the time of the report. In this 18-y follow-up, 32 patients required parenteral nutrition and the rest received standard prenatal care (5). Twenty-two infants (15.3%) were born prematurely and 40 (27.8%) were born small for gestational age (5). It is possible that nutritional deficiencies contributed to the high rates of preterm deliveries and small-for-gestational-age newborns, but the role of vitamin A in these cases is unclear. The incidence of vitamin A deficiency in pregnant women after BPD has not been reported.

The present case shows the consequences of iatrogenic vitamin A deficiency after BPD. Because the patient was eating normal amounts of food, she was not aware that she might be developing micronutrient deficiencies. Her medical follow-up was inadequate, which contributed to the delay in diagnosing her deficiencies. In addition, the signs and symptoms of vitamin A deficiency are often subtle. The first symptom noted in the present case was night blindness, which could have been precipitated by the patient's pregnancy.

The plasma concentration of vitamin A generally does not decrease during pregnancy, despite fetal uptake (15). This is probably a result of the increased metabolism of fat that occurs during pregnancy (15, 17–19). However, in the BPD patient, this physiologic mechanism is impaired because of fat malabsorption, and therefore vitamin A deficiency may develop in both the mother and fetus, with adverse effects on the fetus. Animal studies of vitamin A deficiency during pregnancy have found fetal malformations, intrauterine growth retardation, and spontaneous abortion (19, 20). Infants of mothers with hypovitaminosis A have a higher mortality rate, which may be associated with decreased immune function (21). In the present case, the mother delivered prematurely and the infant was born small for gestational age. Whether this association can be attributed to vitamin A deficiency, other nutritional deficits, or both is unclear.

Currently, advocates of BPD recommend 2 g oral calcium carbonate daily, 400 000 IU vitamin D intramuscularly each month, 325 mg ferrous sulfate 3 times/d, and both thiamin and vitamin A as needed for nonpregnant patients to avoid deficiencies of these micronutrients. There are currently no standard guidelines for vitamin supplementation in pregnant women who have undergone BPD. Some vitamins, particularly vitamin A, may even be teratogenic in high doses (> 25 000 IU). Excessive vitamin A during early pregnancy has been associated with congenital obstructive lesions of the ureter and malformations of the urinary tract (22). Thus, it is absolutely imperative for a pregnant woman who has undergone BPD to have close follow-up to assess nutritional deficiencies and the appropriate supplementation.

This case study describes a severe, late complication of a procedure used to treat morbid obesity. To our knowledge, this is the first case of vitamin A deficiency in an infant resulting from iatrogenic, induced malabsorption in the mother. This case shows the

importance of life-long, close follow-up and vitamin A supplementation after BPD for the treatment of morbid obesity. 

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