

# Ophthalmopblem

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Photo credit: Ophthalmic Photography Laboratory of Queen's University, Hotel Dieu Hospital, Kingston, Ont.

A 30-year-old woman had been admitted to hospital in infancy with diarrhea, steatorrhea, and failure to thrive. During late childhood, she developed atypical retinitis pigmentosa involving the retina and a progressive ataxic neuropathy. Investigations showed her serum lacked beta-lipoprotein and her red corpuscles had a spiky shape. Recent ophthalmic examination revealed substantial choroidal atrophy around the disk and a speckled peripheral fundus.

## Which vitamins should this patient be given as therapy for her disorder?

1. Vitamin A
2. Vitamin E
3. Vitamin C
4. Vitamin B

*Answer on page 1085*

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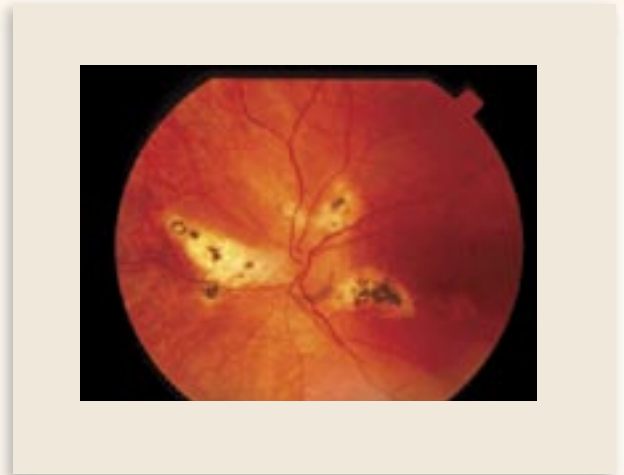
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### 1. Vitamin A and 2. vitamin E

This patient has abetalipoproteinemia (ABL), sometimes called Bassen-Kornzweig syndrome,<sup>1</sup> a disease characterized by malabsorption of fat. The condition is treated with supplements of the two fat-soluble vitamins A and E. Abetalipoproteinemia manifests itself through signs of lipid malabsorption, dense contracted red blood cells with multiple thorny projections, degeneration of the pigment of the retina, and ataxia with hypocholesteremia. The characteristic absence of lipoproteins with beta-electrophoretic mobility led to the name “abetalipoproteinemia.”

Abetalipoproteinemia is a rare autosomal recessive disorder caused by an abnormality in a microsomal triglyceride transfer protein normally present in the liver and intestines.<sup>2-4</sup> A good portion of children with the disorder are born of consanguineous marriages.<sup>2</sup> This inbred error in lipid metabolism adversely affects the cells throughout the body, including the retina. People with ABL are asymptomatic when they are born. With an enriched lipid diet, patients display signs of celiac disease, including diarrhea, vomiting, and abdominal swelling.<sup>2,5</sup> Chronic malabsorption of lipids leads to a lipid-soluble vitamin deficiency. Since the plasma transport of vitamin E depends solely on lipoproteins containing apolipoprotein B, levels of vitamin E are markedly diminished in the body.<sup>2</sup> Vitamins A, D, and K are also diminished, but less so than vitamin E because these vitamins have alternative modes of transportation.<sup>2</sup>

During the first two decades of life, the vitamin deficiencies result in neuro-ophthalmologia, the dominant manifestation of the disease and a determinant of the morbidity associated with ABL.<sup>2,4</sup> The first ophthalmologic signs are alterations in night and colour vision. Reductions in visual acuity and visual fields typically follow. Fundoscopic examination reveals an atypical pigmentation of the retina characterized by small white spots irregularly distributed. Angioid streaks or small breaks



in the elastin-filled tissue of the retina have been reported,<sup>2,4,6</sup> as have ophthalmoplegia, ptosis, and anisocoria.<sup>2,4</sup>

Electroretinogram and fluorescein angiography investigations show the retina to be affected in asymptomatic patients.<sup>2,4</sup> Patients with more advanced disease can experience night blindness. A few histologic examinations show a depletion of the photoreceptors and an accumulation of lipofuscin (a brownish pigment left over from the breakdown and absorption of damaged cells) in the retina.<sup>2,4</sup>

Patients with ABL have deposits of lipofuscin in several tissues (skeletal striated muscle, liver, myocardium, spinal cord, and retina), which suggests vitamin E deficiency.<sup>4</sup> Vitamin E normally serves as an antioxidant preventing free radicals from attacking the mitochondrial membrane. Without the protection of vitamin E, lipoperoxidation results in the formation of lipofuscin pigment. In animals, a vitamin E deficiency has been shown to produce the same neuro-ophthalmologic signs as those seen in patients with ABL.<sup>2,4</sup> Patients with ABL also have lesions in the nervous system similar to those observed in vitamin E-deficient experimental animals and in malabsorption syndromes, including tocopherol deficiency.<sup>2</sup>

The role of vitamin A in retinal complications of ABL is unclear. Night blindness found in patients with ABL is a classic sign of vitamin A deficiency; other signs of vitamin A deficiency,

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such as xerophthalmia and keratomalacia, are rarely found in patients with ABL.<sup>2</sup> Vitamin A supplementation alone can sometimes improve night blindness and reduce abnormalities seen on the electroretinogram.<sup>2</sup>

Patients with ABL have been treated with combined vitamin A and E since the 1960s to prevent or delay retinal degeneration.<sup>4</sup> This therapy is based on clinical and laboratory data that show that levels of vitamin A and E are low in patients with ABL and on the important role vitamin A has in photo-transduction.<sup>2,4</sup> Severe impairment of retinal function was found in rats deficient in both vitamin A and E for prolonged periods.<sup>4</sup> It seemed reasonable that supplementation with these vitamins might benefit patients with ABL.

While vitamin supplementation has been the mainstay of treatment for the past four decades, only a few studies have investigated the intermediate and long-term benefits of this treatment.<sup>4,5,7</sup> Studies show that, in the long run, oral vitamin A and E (at recommended levels) given to children before they are 2 years old can markedly hinder the severe retinal degeneration that results from ABL.<sup>4</sup> Fundoscopic and functional retinal changes, however, were seen in a substantial number of patients despite early initiation of treatment.<sup>4</sup> This might be due to a deficiency of essential fatty acids or other nutrients necessary for preserving normal retinal function in some patients, among other factors. The treatment protocol for ABL needs to be further refined.

### Management

As a baby, this patient was given a diet of long-chain triglycerides replaced by medium-chain triglycerides and oral fat-soluble vitamin supplements (D, A, E, and K). Vitamin E was later given by intramuscular injection to help slow her developmental neurologic abnormalities (this maneuver has proven successful over the years). As she approached the age of 10, she developed retinitis pigmentosa and

difficulties adapting her eyes to darkness, despite the vitamin therapy.

Just before she was 20, she developed progressive night blindness, fundus findings resembling bilateral retinitis pigmentosa, and an angiodlike branching chorioretinal atrophy in the peripapillary region of both eyes that threatened the foveal region in the right eye. Her visual acuity is 6/12 in her right eye and 6/60 in her left. She receives vitamin therapy to this day. Her son has a micro-ophthalmia condition likely related to the large doses of vitamin A she took during pregnancy. Otherwise, the son is free of the disease.

### Recommendations

Patients who start vitamin therapy at an older age have markedly worse prognoses.<sup>4</sup> Therefore, as soon as patients present with signs of ABL they should be referred to a neurologist and an ophthalmologist for assessment and management. Because a lipid-rich diet exacerbates the syndrome, parents should be encouraged to give their children a lipid-poor diet. Because ABL is a lifelong disease, patients need to be educated, monitored, and supported with regard to the disease. Genetic counseling might be beneficial for parents and for patients with ABL wanting to have children of their own. ❁

### References

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