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# Carotenemia

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*Carotenemia is a common benign pediatric condition of yellowing of the skin and elevated beta-carotene levels in the blood. The condition is usually caused by excessive beta-carotene intake but is also more rarely associated with a few serious metabolic disorders. Carotenemia caused by high beta-carotene intake does not have serious sequelae; discoloration remits with dietary modification.*

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**C**arotenemia is a clinical entity characterized by yellowing of the skin and increased serum beta-carotene levels. This condition can occur in any age group but typically occurs in children. Although carotenemia is generally benign, it is also rarely associated with a few serious metabolic disorders such as jaundice—making differentiation of carotenemia from potentially more consequential clinical signs very important.

## Background

Pigmentary skin changes characteristic of carotenemia were noticed in healthy infants in 1908. Yellowish discoloration occurred after carrots were introduced into the infants' diet.<sup>1</sup> The plant substances responsible for the change in pigmentation were found to be carotenoids.

Carotenoids are pigments that impart the red-orange or yellow colors found in many fruits and vegetables. In addition, carotenoids are in many green plants, though these pigments may be masked by the green pigment imparted by chlorophyll.

Foods with a high concentration of carotenoids include carrots, mangoes, sweet potatoes, spinach, kale, cantaloupe, and papaya.<sup>2</sup> Of the carotenoids, the carotenes, particularly beta carotene, are most important in the development of carotenemia.

After ingestion, a fraction of beta carotene is converted to vitamin A in the mucosal cells of the small intestine; then it enters the lymphatic system. Approximately 10% of the ingested beta carotene enters the portal circulation unchanged.<sup>3,4</sup> Beta carotene is transported in the serum by lipoproteins, concentration of which remains relatively constant even in a carotenemic individual.<sup>5</sup> Beta carotene is eliminated primarily through the colon and the epidermis<sup>6</sup> (in sweat and sebaceous material<sup>7</sup>). Reabsorption of excess beta carotene occurs in the stratum corneum.<sup>8</sup> Accumulation of beta carotene in the skin lags behind serum accumulation by approximately 2 weeks.<sup>9</sup>

## Clinical Features

Carotenemic individuals are usually aware of excessive beta-carotene intake, as would be seen with a vegetarian diet, but some caregivers may inadvertently feed infants foods rich in beta carotene (carrots are a major constituent of commercial meat and vegetable baby foods<sup>10</sup>). If routine questioning does not uncover a high beta-carotene food source, taking a more detailed history of food consumption is warranted to determine if carotenemia is due to excessive dietary intake. If diet is found not to be responsible for the condition, the physician should consider a few metabolic disorders that include carotenemia as a feature (Table). Diabetes mellitus and hypothyroidism can be associated with elevated beta-carotene levels. The pathophysiologic mechanism responsible was postulated to be decreased conversion of beta carotene into vitamin A as a result of increased concentration of  $\beta$ -lipoproteins, which are the serum carrier proteins of the carotenes.<sup>11-14</sup> Later, however, carotenemia was determined not to

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produce an increase in serum lipoprotein concentration,<sup>5</sup> which may suggest that saturation of lipoproteins is incomplete in nonhyperlipidemic states and therefore that the postulated mechanism of action may be erroneous. Carotenemia occurs in liver disease as well. In addition, an association was found between carotenemia and hypothalamic amenorrhea in patients with a predominantly vegetarian diet. Dietary modification that reduced beta-carotene levels also helped to normalize the menstrual cycle.<sup>15</sup>

The yellow pigmentation that characterizes carotenemia is most obvious in areas of thickened stratum corneum, including the palms and soles. The pigmentation also is usually evident on the nasolabial folds, tip of the nose, forehead, chin, knuckles, and behind the ears and may occasionally appear on the palate.<sup>7,16</sup> Notably, the sclera are spared. Laboratory test results usually indicate normal liver function and elevated serum beta-carotene levels ranging from 250 µg/110 mL to 500 µg/100 mL.<sup>12</sup>

### Differential Diagnosis

When considering the diagnosis of carotenemia, it is most important to exclude jaundice, which also produces a yellowish discoloration of the skin. Three differences are important in diagnosis. First, unlike carotenemia, jaundice involves the sclera. Second, scleral icterus is an early clinical sign of jaundice, thereby abolishing any window during which the clinical conditions may be confused. Third, carotenemia caused by excessive beta-carotene intake is asymptomatic, whereas jaundice may be accompanied by fever, pruritus, malaise nausea, vomiting, stool color changes, or liver enlargement.

Yellowish skin also may be produced by percutaneous absorption or ingestion of chemicals, including quinacrine hydrochloride, saffron, 2,4-dinitrophenol, and picric acid.<sup>10</sup> In addition, a condition similar to carotenemia—lycopenemia—occurs in individuals whose intake of lycopene is excessive. Lycopene, another carotenoid, is found in high concentration in tomatoes. Lycopenemia, not as common as carotenemia, gives the skin a deeper orange hue.<sup>17</sup>

### Course and Treatment

Isolated carotenemia not associated with a metabolic disorder is a benign condition. Although beta carotene is a precursor to vitamin A in humans, excessive intake of beta carotene has not been proved to result in hypervitaminosis A. Presumably, vitamin-A toxicity does not occur because conversion of beta carotene to vitamin A may be regulated

## Causes of Carotenemia

- Diabetes mellitus
- Dietary excess of beta carotene
- Hypothalamic amenorrhea
- Hypothyroidism
- Liver disease

by feedback inhibition. In addition, excessive beta carotene can be eliminated from the body without conversion to vitamin A.<sup>9</sup> Therefore, hypervitaminosis A in a carotenemic individual would be caused by simultaneous overdose of the vitamin.

Treatment of carotenemia involves reassuring the patient of the benign nature of the condition and having the patient decrease beta-carotene intake. With appropriate dietary modification, the yellow discoloration remits, though it may persist for 2 to 3 months because of the lipophilic nature of beta carotene.<sup>10</sup>

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