Physiological and therapeutic factors affecting cholesterol metabolism: does a reciprocal relationship between cholesterol absorption and synthesis really exist?

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Abstract

Cholesterol absorption and synthesis contribute to maintaining cholesterol homeostasis. Several physiological and therapeutic factors affect cholesterol homeostasis, including: genetics, circadian rhythm, body weight, plant sterols, ezetimibe, and statin therapy. The present objective is to determine the main vector, i.e. cholesterol absorption or synthesis, affected by each of these factors, and to examine whether an alteration in one vector is linked to a reciprocal change in the other. Current techniques used to assess cholesterol absorption and synthesis are also reviewed. Review of physiological factors affecting cholesterol metabolism suggest a reciprocal relationship between these two vectors. Carriers of the E2 isoform of apolipoprotein E and ATP binding cassette (ABC) G8 19H (exon 1 mutation) show a decrease in cholesterol absorption accompanied by a corresponding increase in synthesis. Circadian rhythm affects cholesterol synthesis, however, its effect on absorption has yet to be established. Obese subjects show an increase in cholesterol synthesis with a subsequent decrease in cholesterol absorption. Weight loss down regulates cholesterol synthesis, but has little or no effect on absorption. In the case of therapeutic factors, plant sterols and stanols inhibit cholesterol absorption, which results in a compensatory increase in synthesis. Ezetimibe also decreases intestinal absorption, while reciprocally increasing synthesis. Statin therapy down regulates synthesis, which is accompanied by a rise in absorption. These findings suggest that a change in one vector, fairly consistently, results in a compensatory and opposing change in the other. An understanding of this reciprocal relationship between cholesterol absorption and synthesis may allow for the development of more effective interventions for dyslipidemic disorders.