

# Abstract

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## Choline deficiency increases lymphocyte apoptosis and DNA damage in humans.

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**BACKGROUND:** Whereas deficiency of the essential nutrient choline is associated with DNA damage and apoptosis in cell and rodent models, it has not been shown in humans.

**OBJECTIVE:** The objective was to ascertain whether lymphocytes from choline-deficient humans had greater DNA damage and apoptosis than did those from choline-sufficient humans.

**DESIGN:** Fifty-one men and women aged 18-70 y were fed a diet containing the recommended adequate intake of choline (control) for 10 d. They then were fed a choline-deficient diet for up to 42 d before repletion with 138-550 mg choline/d. Blood was collected at the end of each phase, and peripheral lymphocytes were isolated. DNA damage and apoptosis were then assessed by activation of caspase-3, terminal deoxynucleotide transferase-mediated dUTP nick end-labeling, and single-cell gel electrophoresis (COMET) assays.

**RESULTS:** All subjects fed the choline-deficient diet had lymphocyte DNA damage, as assessed by COMET assay, twice that found when they were fed the control diet. The subjects who developed organ dysfunction (liver or muscle) when fed the choline-deficient diet had significantly more apoptotic lymphocytes, as assessed by the activated caspase-3 assay, than when fed the control diet.

**CONCLUSIONS:** A choline-deficient diet increased DNA damage in humans. Subjects in whom these diets induced liver or muscle dysfunction also had higher rates of apoptosis in their peripheral lymphocytes than did subjects who did not develop organ dysfunction. Assessment of DNA damage and apoptosis in lymphocytes appears to be a clinically useful measure in humans (such as those receiving parenteral nutrition) in whom choline deficiency is suspected.

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