

with clomiphene citrate were randomly assigned to receive, in double-blind fashion, 600 mg of N-acetylcysteine (NAC) twice a day or placebo along with clomiphene citrate (100 mg/day) for five days starting at day three of the cycle. Compared with placebo, NAC significantly increased both the ovulation rate (49.3% vs. 1.3%; $p < 0.0001$) and the pregnancy rate (21.3% vs. 0%; $p = 0.00006$). No cases of ovarian hyperstimulation syndrome were reported in the NAC group. Two miscarriages occurred.

Comment: Clomiphene citrate is frequently used to induce ovulation in women with PCOS. Approximately 70% of women treated with this drug experience a return of menstruation and ovulation, and 30% become pregnant within three months of treatment. The results of the present study suggest that the combination of NAC and clomiphene citrate is beneficial for some women with PCOS who have failed to respond to clomiphene citrate alone. While the mechanism of action of NAC is not known, it may work by improving the insulin resistance that is frequently associated with PCOS.

Rizk AY, et al. N-acetyl-cysteine is a novel adjuvant to clomiphene citrate in clomiphene citrate-resistant patients with polycystic ovary syndrome. *Fertil Steril*. 2005;83:367-370.

Flavonoids for menorrhagia

Thirty-six women (mean age, 33.3 years; range, 20-45 years) with a history of idiopathic menorrhagia (excessive menstrual bleeding) for a mean duration of 11.7 months received 1,000 mg/day of Daflon (containing 90% diosmin and ten percent hesperidin) beginning five days prior to the expected onset of menstruation and continuing until the end of bleeding for three cycles. In 70% of the patients, the total amount of bleeding decreased by 50%, and the duration of bleeding decreased by one-third. There was a 50% improvement in associated dysmenorrhea in about 75% of cases.

Comment: Daflon is a commercial preparation that contains two flavonoids, diosmin and hesperidin. A number of different flavonoids have been shown to improve capillary integrity, which appears to be impaired in some women with idiopathic menorrhagia. Studies conducted a half-century ago found that supplementation with citrus flavonoids in combination with vitamin C was frequently beneficial in the treatment of menorrhagia or metrorrhagia (bleeding between menstrual periods). However, these studies attracted little interest, and this simple treatment is virtually unknown to the conventional medical community. Hopefully, there will be greater interest this time around.

Mukherjee GG, et al. Treatment of abnormal uterine bleeding with micronized flavonoids. *Int J Gynaecol Obstet*. 2005;89:156-157.

Cane is not able

One hundred-forty three patients with hypercholesterolemia or combined hyperlipidemia were randomly assigned to receive, in double-blind fashion, sugar cane policosanol (10, 20, 40, or 80 mg/day) or placebo for 12 weeks. In none of the five treatment groups did the mean LDL-cholesterol level decrease more than ten percent from baseline. No statistically significant differences between policosanol and placebo were observed with respect to the mean changes in total-, LDL-, or HDL-cholesterol, the ratio

of LDL-cholesterol to HDL-cholesterol, or triglyceride levels. A test analyzing dose-dependency yielded nonsignificant results.

Comment: Policosanol is a mixture of long chain (C₂₄ to C₃₄) primary alcohols, originally isolated from sugar cane wax. These long-chain primary alcohols are also found in bee's wax, rice bran, and wheat germ. A number of studies have found that sugar cane policosanol lowers serum cholesterol levels as effectively as various statin drugs. However, all published studies demonstrating a beneficial effect of sugar cane policosanol have been authored by a single research group from Cuba. The results of the present study, as well as those of a similar study using wheat germ policosanol that I cited a few months ago in this column, suggest that policosanol is not an effective treatment for hyperlipidemia.

In my review of the wheat germ policosanol study, I requested feedback from readers about their experiences with policosanol. So far, I have received one correspondence, from a doctor who has observed that sugar cane policosanol, usually in doses of 20-40 mg/day, is very effective for lowering lipid levels.

Berthold HK, et al. Effect of policosanol on lipid levels among patients with hypercholesterolemia or combined hyperlipidemia: a randomized controlled trial. *JAMA*. 2006;295:2262-2269.

Stomach acid interacts with thyroid hormone treatment

Two hundred forty-eight patients with multinodular goiter who were receiving treatment with thyroxine were studied. Fifty-three of the patients also had *Helicobacter pylori*-related gastritis, and 60 had atrophic gastritis (31 with evidence of *H. pylori* infection and 29 without such evidence). The daily requirement of thyroxine to maintain a low TSH level (0.05-0.20 mU/L) was 22-34% higher in patients with *H. pylori*-related gastritis, atrophic gastritis, or both conditions than in patients without those conditions. In prospective studies, the development of *H. pylori* infection in 11 patients treated with thyroxine led to an increase in the TSH level ($p = 0.002$), an effect that was nearly reversed after eradication of *H. pylori*. In a similar way, omeprazole treatment, which reduces gastric acid secretion, was associated with an increase in the TSH level in all ten patients treated with thyroxine, an effect that was reversed by an increase in the thyroxine dose by 37%.

Comment: These findings suggest that gastric acid secretion is necessary for effective absorption of thyroxine. Patients who develop conditions that result in reduced acid secretion (such as *H. pylori* infection or atrophic gastritis) and patients who take antacids or acid-blocking drugs may require an increase in their thyroxine dose to maintain an euthyroid state. Conversely, an increase in gastric acidity (as would result from discontinuation of antacids or acid-blocking drugs, from treatment of a hypochlorhydric patient with hydrochloric acid, and possibly from the eradication of *H. pylori*) may require a decrease in their thyroxine dose. Patients being treated with thyroxine should be monitored more closely during periods in which their gastric acidity is expected to change.

Centanni M, et al. Thyroxine in goiter, *helicobacter pylori* infection, and chronic gastritis. *N Engl J Med*. 2006;354:1787-1795.

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