

tea extract that delivered 1.3 g/day total polyphenols including 800 mg/day epigallocatechin-3-gallate (EGCG) was given to all subjects in the form of four capsules taken during one meal each day up until the time of surgery (a median of 34.5 days).

**Main Outcome Measures:** Prostate-specific antigen (PSA), insulin-like growth factor I, and additional biomarkers of prostate CA status

**Key Findings:** PSA levels declined by 10.4% ( $P=0.01$ ). In the subgroup of subjects taking the extract for longer than the median time ( $>34.5$  days), 85% experienced a decline in PSA compared with 64% of those taking the extract for shorter periods of time, though this difference did not attain statistical significance.

Insulin-like growth factor I declined by 11% ( $P=0.02$ ). Other prostate CA markers declined by 3–19% and each of these changes also attained statistical significance ( $P$  values varying from 0.03 to  $<0.001$ ).

Cases of hepatotoxicity have previously surfaced in regard to green tea polyphenols. However, liver enzymes and other markers of hepatic function (which were tracked because of this concern) actually *declined* during the trial; five of these reductions reached statistical significance.

**Practice Implications:** EGCG has inhibited prostate CA cells *in vitro*. Though epidemiologic data remain mixed, three years ago, an Italian research group reported that consumption of green tea polyphenols delayed progression of high-grade prostatic intraepithelial neoplasia (*Cancer Res* 2006;66:1234–40).

Why might green tea polyphenols have anticancer effects? Hepatocyte growth factor (HGF)/c-Met signaling pathway is disturbed in a wide variety of cancers including prostate CA. Increasingly, researchers believe that inhibition of this pathway should increase life expectancy in CA patients. Green tea polyphenols had an inhibitory effect in the current trial.

Other markers of prostate CA status or progression have also recently been found to either increase proliferation of CA cells or interfere with apoptosis. The authors of the current trial measured these newer markers along with PSA scores in hopes that green tea polyphenols would alter markers in directions compatible with CA regression. It's exciting to note that

virtually all markers tracked by these researchers moved in the direction of safety and most of these changes attained statistical significance.

What are clinicians to do with these new findings? As long as liver enzymes are monitored to insure the same level of safety reported in the current trial (though not in all previous reports), it may be time for healthcare professionals to tell their prostate CA patients about these new findings, which suggest the potential (though not yet proof of) significant anti-cancer effects from green tea extracts containing appropriate amounts of polyphenols. ♦

## Nutrients for Migraine Prevention

by Alan R. Gaby, M.D.

More than 10% of Americans suffer from migraines. Even the most effective medications prescribed for migraine prophylaxis reduce migraine frequency by no more than 50%, and many of these drugs are associated with significant side effects. Safer and more effective ways of preventing and treating migraines are therefore needed.

Mitochondrial energy production appears to be impaired in people with recurrent migraines, and this impairment might play a role in the pathogenesis of migraines. Nutrients that are involved in energy production might therefore be beneficial. Magnesium is a cofactor for the synthesis of adenosine triphosphate (ATP), the body's main storage form of energy. Riboflavin (in the form of flavin adenine dinucleotide [FAD]) and coenzyme Q<sub>10</sub> are cofactors in the electron-transport chain, a biochemical cascade that culminates in ATP synthesis. Each of these three nutrients has been shown in clinical trials to decrease the recurrence rate of migraines.

## Magnesium

Eighty-one migraine sufferers were randomly assigned to receive, in double-blind fashion, 600 mg per day of magnesium or placebo for 12 weeks. During the last four weeks of the study, as compared with baseline, the mean frequency of migraines was reduced by 42% in the magnesium group and by 16% in the placebo group ( $p < 0.04$  for the difference in the change between groups). Adverse effects of magnesium were diarrhea in 18.6% of patients and gastric irritation in 4.7%.<sup>1</sup> In other research, effective migraine prophylaxis was achieved with a magnesium dose of 360 mg per day,<sup>2</sup>

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