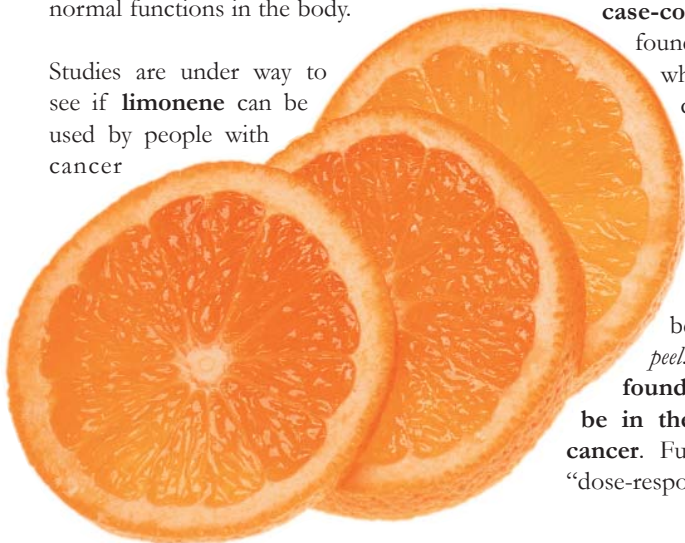


Eat Your Orange Peel!

Everyone knows that citrus fruits -- oranges, lemons, and grapefruits -- are a healthy food. Packed with **vitamin C** and **bioflavonoids**, citrus fruits are to many of us the fresh, sunny taste of good health. But while many people may enjoy the *flesh* of oranges as a regular part of their healthy diet, few of us eat the intensely-flavored *peels* of these fruits. That might turn out to be a major error in judgement. New research suggests that we may have been throwing away the best part of the fruit!

For some years now, scientists have been quietly investigating **limonene**, the major component of the essential oil in orange peels, as a potential anti-cancer nutrient.¹ In animal models, **limonene powerfully prevents tumors of the breast, liver, stomach, skin, and lung**, whether given before exposure to a cancer-causing agent, or even after the first cancerous cells have formed. Partly, **limonene** seems to work by **enhancing the body's phase II detoxification enzymes**, which make cancer-causing chemicals more readily excreted by the body in the urine or bile; as well, **limonene** appears to **induce programmed cell suicide (apoptosis)** and to block a step (**isoprenylation**) required for the proteins made by cancer genes (**oncogenes**) to wreak their havoc. Most excitingly, **limonene appears to somehow induce "redifferentiation,"** forcing rogue cancer cells to settle down and return to their normal functions in the body.

Studies are under way to see if **limonene** can be used by people with cancer



to actually treat their disease. A preliminary study² designed to test its safety in cancer patients concluded that **"limonene is well tolerated in cancer patients at doses which may have clinical activity"** and that its **"favorable toxicity profile supports further clinical evaluation."** It's too early to suggest that people with *existing* cancers take the high doses being used in the preliminary human studies, unless their doctor counsels them to do so. But what about consuming **limonene** in smaller amounts, to reduce the long-term risk of developing "the big C" in the first place?

Some people do use citrus peels in their cooking, using the grated outer peel ("spritz") in cookies and cheesecakes, or making such old-fashioned Southern delicacies as candied orange peel. Citrus peels even feature in some ultra-secret recipes for sweet-and-sour barbecue sauces. People eating these foods regularly get small but significant doses of **limonene** in their diets. One is tempted to ask, *What impact does the consumption of citrus peel have on a person's risk of developing cancer?*

Recently, a group of researchers with the University of Arizona's Cancer Prevention and Control Center decided to find out. The study looked at the eating habits of older people in the Southwestern US, comparing people who had developed **squamous cell carcinoma of the skin** (a form of skin cancer) with another group which had not (a **case-control study**). The researchers found that, as compared to people who had been struck with this skin cancer, people who did not develop the disease were neither more nor less likely to have been big eaters of either citrus fruits or their juices. But about a third of the total group (34.7%) reported themselves to be regular consumers of citrus *peel*. And **citrus peel eaters were found to be one third less likely to be in the group that developed skin cancer.** Further, the researchers found a "dose-response relationship" at work: that is,

the more citrus peel a person consumed, the less likely he or she was to be a cancer patient.³

People wanting to include more **limonene** in their diets don't need to take up a regimen of continuous baking. Many people, once they try it, find that they *prefer* the intense flavor of an orange when it's simply cut up in sections and eaten, peel and all. Another way to enjoy orange peels is to cut a whole orange up and throw it into the blender as part of a morning smoothie, lending the drink a surprising citrus burst and a dose of **limonene**. Just remember to *scrub* the peel — a new habit to get into, after years of simply tossing it out.

Citicoline Heals Brain Damage

Cytidine diphosphate choline, or **Citicoline** for short, is an orthomolecule with a vital job to play in manufacturing the brain's **phospholipids** (like **phosphatidylserine [PS]** and **phosphatidylcholine [PC]**). In a recent article (see "PS: Remember Your Citicoline!" in *The Holistic Lifestyle 1[5]*), we reviewed some of the evidence that **Citicoline** provides powerful nutritional support in many serious disorders of the brain, as well as in the loss of memory associated with "normal" aging.

Much of the research on **Citicoline** has focussed on its ability to help restore healthy brain function after a stroke. Animal studies⁴ show that **Citicoline reduces the size of the brain injury** which results when an experimental stroke cuts off the brain's oxygen supply. The question is, *how?*

Experiments on animals^{5,6} have suggested that **Citicoline** has both *preventative* and *regenerative* effects on the brain injuries which follow a stroke. On the one hand, strokes usually force brain cells to release some of the fatty acids out of their membranes, a process which can increase the damage inflicted on neurons by free radicals. Animal studies have shown that **Citicoline reduces this release of free fatty acids, preventing excess free radical damage during a stroke.**⁵ On the other hand, because

Citicoline is needed to produce *new* cell membranes, it's no surprise when other studies report that **Citicoline helps damaged brains to repair themselves after a stroke.**⁶

The first study to peer into the brains of *humans* given **Citicoline** after a stroke confirms its ability to speed brain healing, while suggesting that the prevention of the initial stroke damage may also be at play.⁷

The doctors running the trial randomized 100 patients who had been caught within 24 hours of a stroke to take either **Citicoline** (500 milligrams per day) or a dummy pill (**placebo**) for six weeks. The study used **magnetic resonance imaging (MRI)** to examine the brains of the 81 people who followed through for the whole study, looking for signs of brain injury on the day of the stroke, one week later, and at the end of twelve weeks.

The scientists found that the patients taking Citicoline had significantly smaller areas of injured brain tissue at twelve weeks as compared to one week after the stroke: while the size of the injury in people who had received the dummy pills had been reduced by an average of 6.9 cubic centimeters of brain tissue, the people who took **Citicoline** experienced a reduction of 17.2 cubic centimeters. This was interpreted to confirm that **Citicoline helps to speed the healing of brain injuries after a stroke.** Further, the scientists found that the reduction in injury size was associated with improvements in the patients' real-world functionality: **the greater the reduction in the size of the injured area, the greater the improvement patients showed on the National Institutes of Health Stroke Scale,** a measure of things like sensation and the ability to speak and control the muscles.

There was also an impressive-looking reduction in the initial *growth* in the injury size in the period immediately following the stroke: people taking the sugar pill suffered a 180% increase in the size of the initial injured area, whereas people taking **Citicoline** only had a



34% increase in injury size in the same time period. This result was not found to be "significant" in the statistical sense, despite the huge difference in the numbers; the scientists who ran the trial suggest that this

might just be due to a low number of participants; alternatively, it might just be because the final figures were difficult to compare statistically, because the group taking the dummy pill had a wider *variation* in the number and size of their brain injuries, and because of the difficulty in properly measuring smaller-sized injuries. *If* the difference in numbers is a real effect, it would confirm in humans what has already been shown in animals: that **Citicoline** prevents much of the *initial* damage after a stroke, too.

A New Treatment for MS?

Multiple Sclerosis (MS) is a disease in which the body's immune system attacks the **myelin sheaths** which insulate the nerves of the brain and spinal cord. The older therapies for MS are not very effective: powerful anti-inflammatory drugs are used to reduce the frequency and severity of flare-ups, while individual symptoms are be treated with symptom-specific drugs (like **oxybutynin (Ditropan®)** for incontinence, antidepressants for depression, etc). More hopefully, new synthetic versions of the immune-system chemical **interferon beta** are being used to not only cut down on symptoms, but to reduce number of nervous system injuries induced by the disease.

Still, none of these therapies address the underlying *cause* of the disease: the ongoing "belief" of some of the body's immune cells that the myelin which shields the brain and spinal cord is "the enemy" and must be wiped out. One promising therapy, which has been supported in clinical trials,^{8,9} is to actually give patients capsules containing myelin itself — a therapy known as **oral tolerization**. The theory behind this

therapy has been that, that by providing the immune system with constant exposure to myelin, may gradually become "used" to its presence and cease to regard it as a threat.

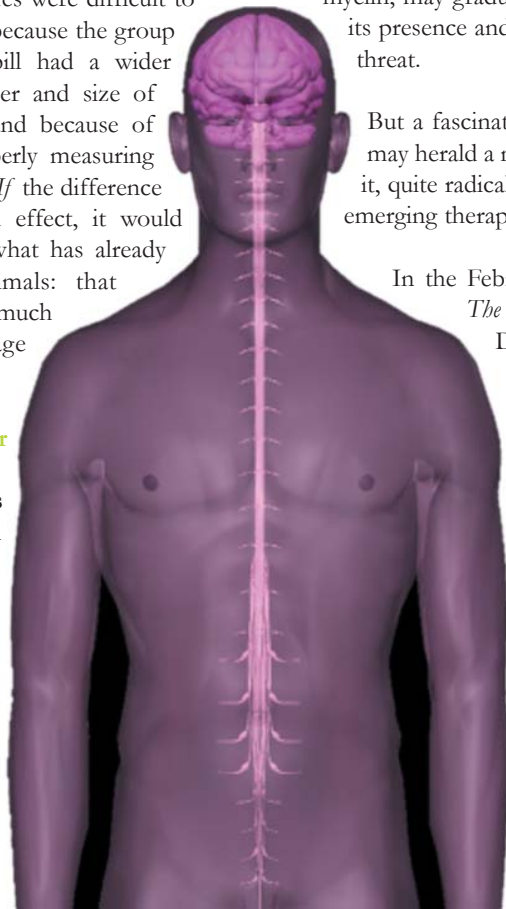
But a fascinating animal experiment may herald a new and, on the face of it, quite radical understanding of this emerging therapy.

In the February 1, 2001 issue of *The Journal of Immunology*,¹⁰

Dr. Hugh McFarland and his colleagues report experiments on marmoset monkeys whose immune systems had been sensitized to attack their myelin sheaths, just as is seen in human MS. Then the researchers divided the animals into three groups. One group received a high dose of a synthetic version of the two main proteins present in myelin through an

IV catheter; a second group of monkeys received a smaller dose of the same proteins; the third group received no myelin proteins, thus serving as a control group.

The scientists made several important discoveries. First, the new animal model of the disease may, in itself, turn out to be a breakthrough in scientists' ability to explore the disease, as it more closely resembles "the real thing" than does the standard mouse model. Second, and more important, **giving the monkeys myelin proteins prevented many of the symptoms of the disease, and reduced damage to the myelin sheaths** seen on an MRI. In fact, the more myelin proteins an animal received, the better off it was: while all control monkeys showed symptoms of the disease (including incontinence, an inability to coordinate muscle movements, and paralysis), only two thirds of the animals receiving the moderate dose of myelin proteins showed symptoms (and those symptoms were delayed significantly by the treatment). Most impressively, **none of the animals receiving the high dose of myelin proteins showed any disease**



symptoms.

But we already knew, from controlled trials in humans, that even *oral* myelin is helpful in MS patients. What's really new about this study is the suggestion that **administering the proteins in myelin may actually cause the body to destroy the renegade immune cells which cause the disease.** The scientists believe, based on previous research, that the therapy works because when a significant increase in myelin presents itself to the immune system, the body simply won't let itself be overwhelmed by an immune response so potent that it might flat-out kill the organism (as opposed to the long, drawn-out degeneration seen in MS). Rather than allowing the deranged immune cells to run amuck through the body in response to the higher load of myelin, the body somehow causes the

bringing new hope that substances containing myelin proteins may indeed emerge as potent medicine against this crippling disease — while giving new insight into the surprising nature of that medicine.

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anti-myelin immune cells to commit cellular suicide (**apoptosis**). It's an imprecise analogy, but one might recall the use of dynamite to extinguish forest fires.

The effect has actually already been seen using other antigens. This study extends it to an excellent animal model of MS,

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