

## LE Magazine August 1999

## Q &amp; A

A Good Dose of Deprenyl  
How Much is Too Much?

Q I am in contact with an anti-aging physician who takes 5mg of deprenyl daily, as do his patients. He believes the 5 mg of deprenyl twice a week recommended by The Foundation is too low, especially when compared to animal studies of longevity as shown in the abstract I provided. Has the Foundation looked into this dosage controversy lately? I fully understand the conservative philosophy of LEF (and applaud it), but are we missing something here?

P.S. This physician says he has been able to take all his patients off their antidepressants after they go on full hormone replacement therapy (DHEA, testosterone, human growth hormone, estrogen, etc.) with deprenyl 5 mg daily (He is a board certified psychiatrist and very much aware of effects of these psycho-active drugs.)

A The question of optimal dosage for humans of selegiline (deprenyl) based on animal studies is a very difficult one given the wide variation in responses seen based on species, sex and age. This point is demonstrated in the abstract you sent (printed out at the end of this "Q&A"). The optimal dose for increasing these activities, however, differed greatly depending on the sex and age of animals, with a 10-fold lower value for young female than male rats. Interestingly, aging caused an increase and a decrease in the optimal dose in female and male rats, respectively. In addition, treatment for a longer term tended to reduce the optimal dosage in the same animal group. The question is complicated even further by the fact that rats use MAO-A to metabolize dopamine, unlike humans who use MAO-B. This might make comparisons of rat studies with humans suspect, although Dr. Joseph Knoll - the researcher who first discovered the life-extending properties of selegiline in rats - claims that life span extension by selegiline is due to the anti-oxidant enzyme induction effects rather than the MAO-B inhibition effects.

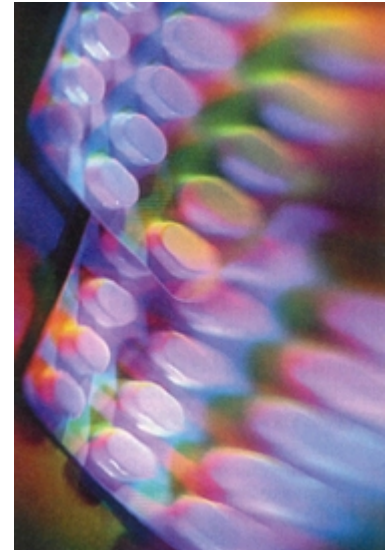
Anti-oxidant enzyme induction follows a bell-shaped curve, with too much or too little selegiline being suboptimal. But the problem is complicated by the fact that optimal dose varies so extremely, depending on species, sex and age. Knoll claims that Kitani failed to increase maximum life span (increasing only average life span) because Kitani used double the dose of deprenyl that Knoll had used. The bottom line of all this is that the animal data cannot be relied upon to determine optimal dose for humans. There are a few constraints and parameters that should be considered for humans, however.

Dosages above 20 mg/day are likely to seriously elevate blood pressure due to MAO-A inhibition. Blood pressure elevation may occur in some people with much lower doses. Since selegiline binds to MAO-B irreversibly, a single 5 mg dose can cause 90% reduction in dopamine for 5 days and does not return to baseline for 2 weeks. However, past the age of 45 there is a dramatic increase in the levels of MAO-B synthesized by glial cells, so optimal MAO-B inhibition may require higher doses of selegiline.

These last points are not really relevant, however, if Knoll is correct that selegiline extends maximum life span primarily through anti-oxidant enzyme induction rather than MAO-B inhibition. Based on the above constraints and the results on elderly beagle dogs [Life Sciences 61:1037-1044 (1997)], which may be more comparable to humans than rats, I would say that 5 mg per day is not unreasonably high for a person in their 40s. When taking 5 mg a day of deprenyl over an extended period of time, it is important to make sure there is no problem with increasing or decreasing blood pressure. If anti-depressant drugs are being used, deprenyl (especially in higher doses) is contraindicated. That is why The Foundation continues to recommend a conservative dose of 5 mg of deprenyl to be taken twice a week. Some of the Foundation's advisors, however, recommend that people over age 45 take 5 mg a day of deprenyl based on the large body of evidence showing that this drug protects against brain aging in many unique ways and may extend life span.

Deprenyl increases the life span as well as activities of superoxide dismutase and catalase but not of glutathione peroxidase in selective brain regions in Fischer rats

Deprenyl, an MAO-B inhibitor that is also known to be effective for symptoms of Parkinson's disease, when injected subcutaneously (sc) in male Fischer-344 rats at a dose of 0.5 mg/kg per day (3 times a week) from 18 months of age, significantly increased the



remaining life expectancy. The average life span after 24 months was 34% greater in treated rats than in saline-treated control animals.

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Q Has any progress been made in regards to the Life Extension Center effort, as reported in past issues of Life Extension magazine? I recall your piece outlining the need for a comprehensive facility that could offer all the latest life-saving therapies, as well as a follow-up piece that said that many people were willing to invest in the concept. Is there more to report?

A Progress has been limited to negotiating deals with individual hospitals. No definitive arrangements have been made yet, but discussions are continuing. Next year, Life Extension Foundation will have a medical office complex with at least one full time physician at its headquarters. The objective of this pilot project is to initiate treatment of patients on an out-patient basis and use the physician's hospital privileges for patients who require hospitalization.

Q I use your thermogenic enhancing capsules & I am a member of The Foundation. A friend advised me that a television report stated that at least 50 people have died of heart-related problems due to the use of capsules that contain ma huang. What is your position on ma huang & the thermogenic capsules?

A Ma huang, or ephedra, is safe if used as directed, but there are certain precautions to observe. Our Thermogen Tea product, which contains ephedra, carries the following warnings, which also apply to the Thermogenic Enhancing Capsules: "Not for use by children, or pregnant or lactating women. Persons with high blood pressure, cardiovascular disease (especially cardiac arrhythmia), diabetes, prostatic hypertrophy, glaucoma (angular closure), hyperthyroidism, psychosis or thyroid disease must NOT use this product. Do not use this product within 14 days after taking MAO (monamine oxidase) inhibitor drugs, such as certain antidepressants. If symptoms of allergy develop, discontinue use. Elderly persons may be more sensitive to this product. If you are taking asthma medications, prescription anorectics (appetite suppressing drugs), antidepressants or cardiovascular medications, ask your physician before using this product. CAUTION: Keep out of reach of children. Use only as directed. Do NOT exceed three servings per day. Drinking too much tea can result in nervousness, restlessness or insomnia, similar to drinking too much coffee, tea or cola drinks. If this occurs, reduce the amount consumed. Tolerance usually develops rapidly to these effects. This tea may increase the stimulating effects of caffeine. Avoid the use of aluminum containing antacids with this product. Thermogen Herbal Tea II is a dietary supplement. Not to be used in the treatment of disease or medical condition."

Having stated the above, if someone were to abuse it as if it were a recreational drug, the potential for harm does exist. We cannot confirm the report of 50 deaths, but have heard reports of teenagers abusing it on a recreational basis. It would be a shame if these abusers cause the availability of ma huang to adults to be restricted.

Q While reading through a magazine on herbs the other day I came across a very interesting article entitled "Plants at Risk. Some of the plants mentioned are ones many of us take, i.e. echinacea, kava, wild yam and black cohosh. The article suggested that substitutes be used or pressure should be applied to the manufacturers to cultivate the herbs, and not use the remaining wild stands. The concept is very similar to what animal activists are trying to suggest: breed various types of animals instead of using wild caught, which usually leads to extinction or near extinction. I would like to know if LEF is actively engaged in growing herbs at all, or if you have discussed this with your suppliers. It seems that there are two groups trying to alert people: United Plant Savers (UpS) in East Barre, Vt, and The National Center for the Preservation of Medicinal Herbs in Rutland, Ohio. I use all of the above herbs, some only occasionally, and would hate to think that I'd helped deplete our resources. Could you shed some light?

A We have come across some instances in which alternatives to "wild" herbs have been suggested. At an herbal conference we attended in 1997 people were being asked to use alternatives to goldenseal, as it is disappearing. But some people prefer wildcrafted herbs and many are listed as such, so that "wild-crafted" is used as a selling point. Apparently there is a similar situation with black cohosh. What a shame. Organic cultivation should be encouraged. However, one way or the other, we must maintain our support for the herbal industry. If we don't, the herbal industry will weaken, and it needs to remain strong to stand up to the FDA!

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