Many of you may have heard about the latest resveratrol clinical study (Timmers et al., Cell Metabolism, 14: 612-622, 2011). After all, it has been widely publicized in places like The Wall Street Journal, the Huffington Post and your local newspapers.

Let me start with a bit of background:

Caloric restriction in the range of 30-50% has been shown to extend the lifespan in every species studied (Of course, lifespan studies are impossible in humans because we live too long). Human clinical studies have shown that both caloric restriction and endurance exercise exert many of the same metabolic effects in humans as caloric restriction in animals.

The effects of endurance training is particularly interesting.

Endurance training increases the activity of mitochondria (the power packs of our cells), especially the ability of our mitochondria to use fat as an energy source. In addition, endurance training increases the ability of the muscle cells responsible for endurance exercise to store fat. This increased ability of those muscle cells to store and utilize fat makes them more efficient and less dependent on carbohydrates as an energy source.

All of this is fascinating, but not very practical. **Very few people want to starve themselves half to death just so they can live longer. And, as for the effects of endurance training, we are talking about the metabolic effects observed in elite endurance athletes - not just the casual jogger or cyclist.**

That makes the question about whether **resveratrol and other naturally occurring polyphenols could exert some of the same beneficial effects particularly interested**. Studies in mice have suggested that possibility.

Mouse studies have shown that resveratrol exerts many of the same effects on longevity as caloric restriction, and it does that by affecting the activity of genes associated with the aging process - genes that affect the diseases associated with aging.

**For example, mouse studies have shown that both caloric restriction and resveratrol decrease inflammation (which is thought to be a root cause of many diseases) and production of the free radicals (reactive oxygen species) that damage DNA and lead to aging at a cellular level.**

**Mouse studies have also shown that both caloric restriction and resveratrol lower blood pressure and triglycerides (which decreases the risk of heart disease), lower blood glucose levels and improve insulin sensitivity (which decreases the risk of type 2 diabetes) and increase the number and activity of mitochondria (the power packs of the cell) which improves exercise endurance.**

So is all of the hype about this recently published clinical study true?

It was a relatively small study, but it was very well designed.

11 obese men (average age 52, average weight = 220 pounds, average BMI = 31) were enrolled in the study.

The study was what scientists call a randomized, double-blind crossover study.

In plain English that means that half of the men received 150 mg of resveratrol during the first 30 days and the other half received a placebo. This was followed by a four week washout period to remove resveratrol from the bloodstream. Then in the final 30 days of the trial the groups were switched. Those that received the placebo during the first 30 days were given resveratrol and vice versa.

The strength of this kind of study is that each subject serves as their own control - which eliminates a lot of individual variability.

The result of just 30 days on resveratrol were impressive:

1**) The same gene regulators (AMPK, SIRT1 and PGC-1a) were activated in this study as are activated by caloric restriction and resveratrol in mice and endurance training in humans.**

**2) Blood glucose levels and blood insulin levels were decreased and insulin sensitivity was improved.**

**3) Triglyceride levels and levels of inflammation markers (eg IL-6 and TNFa) were decreased.**

**4) Systolic and average blood pressure was decreased.**

**5**) Both gene expression and metabolic studies showed that mitochondrial efficiency was increased - especially the ability of mitochondria to generate energy from fat stores. In addition, fat stores in the muscle fibers responsible for endurance exercise were increased.

**6) Fat stores in the liver (a pathological condition associated with obesity that can lead to liver damage) were decreased and blood markers of liver health were improved.**

**7) <u>No adverse effects of resveratrol supplementation were observed.</u>**

The authors concluded "[This study] shows that resveratrol supplementation exerts favorable metabolic adaptations that in many aspects mimic the effects of caloric restriction and/or endurance training."

And these results are fully consistent with two other human clinical studies published just this year.

Wong et al, (Nutrition, Metabolism & Cardiovascular Diseases, 21: 851-856, 2011) have already reported that resveratrol at doses as low as 30 mg/day improves arterial blood flow.

Similarly, Ghanim et al (The Journal of Clinical Endocrinology & Metabolism, 96: 1409-1414, 2011) have shown that 100 mg of resveratrol plus polyphenols from muscadine grapes was sufficient to blunt the inflammatory response and free radical damage caused by a high fat meal.

So, what is the bottom line for you?

1) Clearly, more human clinical trials are needed, but evidence is starting to accumulate that resveratrol supplementation may provide some substantial health benefits.

**2) Many of the metabolic effects of resveratrol seen in this and other studies (improved blood sugar control, decreased blood pressure, lower triglycerides, decreased markers of inflammation, decreased free radical damage and decreased fat stores in the liver) have the potential to reduce the risk of many of the diseases associated with aging.**

3) The improvement in mitochondrial efficiency and ability to utilize fat as an energy source should be of interest to many athletes - especially endurance athletes.

4**) While the dose of resveratrol used in this study was 266 fold lower than the highest dose used in mouse studies, the blood levels of resveratrol were two times higher than the highest blood levels achieved in those studies.**

This puts to rest the argument by some experts that if we were to extrapolate from the mouse studies to humans it might take thousands of mg/day of resveratrol to exert a beneficial effect in humans.

Based on the published clinical studies to date doses in the range of 30 to 150 mg/day appear to be effective in humans.

**5) Not only was 4 weeks without supplementation sufficient return blood resveratrol levels to baseline, but it also returned all of the improved metabolic parameters to baseline. This means that continuous resveratrol supplementation is likely to be required to achieve long term health benefits.**

6) While long term clinical studies are clearly needed, the available data suggest that doses of resveratrol in the 30 to 150 mg/day range are safe in humans - which is in **sharp contrast to the side effects observed in clinical trials of the synthetic resveratrol derivatives being developed by the pharmaceutical industry.**

7) Finally, I would like to point out that other naturally occurring polyphenols exert health benefits that resveratrol does not. And, if we have learned anything over the last 10 or 20 years it is that high potency individual nutrients can sometimes cause more harm than good - probably by interfering with the absorption of closely related nutrients.

So until the safety of high dose, high purity resveratrol has been unequivocally demonstrated, my personal recommendation would be to use supplements with resveratrol plus a blend of related polyphenols rather than with resveratrol alone. (Shaklee Vivix)

To Your Health!
Dr. Stephen G Chaney