You have read shocking exposés in this column about human studies that are so horrendously flawed that their findings are rendered meaningless.

For example, two years ago a report claimed that calcium and vitamin D didn't protect against bone fractures.¹ Our analysis uncovered that a significant percentage of women in the active group of this study did not take their calcium-vitamin D supplement, whereas the placebo group was allowed to take calcium, vitamin D and bone-building hormones on their own. So when there was no difference reported between these two groups, the media proclaimed calcium and vitamin D to be “worthless.”

Interestingly, this study showed that women who actually took their calcium-vitamin D supplement had 29% fewer hip fractures...but this detail was conveniently omitted from most news stories.²³

The headline-hungry media is back at it again, this time with support from the American Medical Association and the FDA.

### Powerful Economic Bias Against Natural Hormones

Pretend for a moment that you work for a pharmaceutical company. You are economically dependent on robust sales of drugs and stents to treat age-related vascular diseases.

An obstacle to your rosy financial future is that increasing numbers of Americans are discovering that vascular disease can be forestalled when youthful hormone balance is restored. If too many people start using these natural hormones, demand for your patented drugs (and stents) will plummet.

Your only hope is to disseminate deceptive information that will frighten the public and turn doctors against natural hormone replenishment.
Flawed Study May Kill Millions

Life Extension long ago recommended that aging men (without prostate cancer) restore their free testosterone to youthful levels. The data were compelling when we first suggested natural testosterone replacement. A flurry of new studies now fully substantiates the longevity benefits that occur in aging men who maintain higher levels of their sex hormones.4-25

A terribly flawed study, published in the Journal of the American Medical Association (JAMA), questioned the value of testosterone replacement. This led the media to print headlines like:

"Testosterone Supplementation for Older Men Appears to Have Limited Benefit"24,25

and

"Testosterone Does Not Improve Function in Older Men"26

Before we get into specific defects of this flawed study, the following astounding quote—written by the study authors—should cause even a novice to question how something this unscientific could ever be published in a medical journal:

"At 6 months, total testosterone was unchanged from baseline in the testosterone group and increased slightly in the placebo group."27

No, you have not lost your sanity. What you just read above said that at the end of the study, the placebo group had higher levels of testosterone than the active group who took testosterone tablets. While the study authors devised some pathetic excuses to explain this egregious discrepancy, the fact is that these testosterone tablets (that are not approved in the United States) failed to increase testosterone levels in the men who took them.

Despite this obvious flaw that renders the study's findings totally useless, it was instead published in a medical journal (Journal of the American Medical Association), which has a huge impact on physician prescribing practices and public perception.27

How many Americans will die from testosterone deficiency because of this horrendously flawed study? Just look at findings released by the American Heart Association in November 2007 about testosterone blood levels in men and subsequent incidences of disease and death (see table on this page).28

Each year, more than one million men die in the United States.29 If we assume that just a small percentage of these men would have restored their testosterone were it were not for this disinformation campaign, tens of thousands of lives could be spared every year.

The cruelest aspect of this sham study is that men who can most benefit from natural testosterone will be told by their cardiologist that it might increase their risk of a heart attack. While this is a total fabrication, the fact that the Journal of the American Medical Association allowed the study's authors to speculate this way will cause hurried doctors to ignore hundreds of positive published studies and caution their cardiac patients against using natural testosterone cream and injections.

| Testosterone Blood Levels and Subsequent Incidences of Disease and Death.28 |
|---------------------------------|-----------------|-----------------|-----------------|------------------|
|                                | Highest Testosterone | Next to Highest Testosterone | Next to Lowest Testosterone | Lowest Testosterone |
| All-Cause Mortality            | 41% reduction      | 38% reduction      | 25% reduction      | Highest rate of Death |
| Coronary Heart Disease         | 48% reduction      | 41% reduction      | 29% reduction      | Highest rate of Death |
| Cancer                         | 29% reduction      | 23% reduction      | 26% reduction      | Highest rate of Death |
Natural Hormones Slash Heart Disease Mortality!

A landmark study analyzed the relationship of natural hormones (free testosterone, DHEA, and insulin-like growth factor-1 [IGF-1]) to death rates in men suffering from chronic heart failure. The findings from this study are tabulated on the chart in this box. As one can easily see, more men die when any of these hormones is deficient. This same chart shows catastrophic mortality when two or more of these hormones are deficient.

A large number of studies reveal that higher testosterone or dehydroepiandrosterone (DHEA) levels are associated with reduced heart attack risk. DHEA is a low-cost dietary supplement, while IGF-boosting nutrients and natural testosterone cream are available to Americans at affordable prices.

Cardiac drugs generate more profit for pharmaceutical companies than any other class of medication. Pharmaceutical companies thus face huge economic losses if too many Americans use natural hormones to reduce their reliance on expensive prescription drugs.

To give you an idea of the magnitude of financial loss faced by drug companies, this landmark study showed that higher DHEA levels resulted in improved ejection fractions (a measurement of the heart’s pumping capacity) and lower levels of a blood marker that indicates serious congestive heart failure. Widespread use of these natural hormones would slash demand for mediocre cardiac drugs.

<table>
<thead>
<tr>
<th>Hormone Status</th>
<th>Three-Year Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>High levels of DHEA, testosterone, and IGF-1</td>
<td>83%</td>
</tr>
<tr>
<td>Deficiency in one hormone (DHEA, testosterone or IGF-1)</td>
<td>74%</td>
</tr>
<tr>
<td>Deficiency in two hormones (DHEA, testosterone or IGF-1)</td>
<td>55%</td>
</tr>
<tr>
<td>Deficiency in all three hormones (DHEA, testosterone and IGF-1)</td>
<td>27%</td>
</tr>
</tbody>
</table>

Why Testosterone Tablets Are a Poor Choice

If all men had to do was swallow a testosterone tablet once or twice a day, it would become a more popular drug. The problem is that when testosterone is ingested into the stomach, it first passes through the liver where most of it is metabolized and rapidly degraded. Furthermore, the liver itself can be damaged by drugs that undergo extensive liver processing.

To bypass liver degradation of oral testosterone tablets, a new delivery system was developed that is designed to absorb through the lymphatic system rather than by the blood. In theory, this strategy offers the advantage of bypassing liver metabolism. This was the delivery strategy employed with the oral testosterone (undecanoate) drug used in this flawed study.

The problem is that clinical studies as far back as 1984 clearly show that testosterone undecanoate causes wildly inconsistent levels of testosterone in blood plasma. Furthermore, duration of action of testosterone undecanoate is wildly variable not only among individuals but also within the same person hour by hour, and day by day.

To add further embarrassment to the choice of this form of oral testosterone drug, the researchers used a lower dose than clinical experience indicates is necessary to yield measurable increases in testosterone. Clinical experience suggests a dose of at least 240 mg daily is needed to raise blood testosterone levels.

The men in this flawed study who showed no increase in blood testosterone after six months were taking 160 mg a day of testosterone in tablet form and this dose provided no measurable increase in testosterone.

The proper way to restore testosterone is to administer it through the skin, preferably as a 50 mg natural testosterone cream that is applied three to seven days out of the week. The use of this lower dose of transdermal-delivered
natural testosterone normally restores blood free testosterone levels to youthful ranges (which are 20-24 pg/mL of blood according to LabCorp's method).

Rather than applying testosterone to the skin as a cream in the way testosterone replacement is normally prescribed, these researchers irrationally loaded study subjects with oral testosterone tablets known to yield wildly variable pharmacological results. It comes as no surprise that this flawed study did not show any evidence of an increase in testosterone levels in men receiving the oral drug.\textsuperscript{27}

Furthermore, although testosterone undecanoate theoretically avoids liver damage through bypassing liver metabolism (lymphatic absorption), one subject in the active testosterone group had to discontinue because his liver enzymes shot up three times above the upper limit of normal, indicating that this small dose of oral testosterone was damaging his liver.\textsuperscript{27}

What gave the researchers ammunition to attack the safety of testosterone, however, was the reduction in HDL levels that occurred in the group given oral testosterone (with a synthetic carrier) for 26 consecutive weeks. This enabled the authors of this flawed study to speculate that testosterone might increase heart attack risk.

This flies in the face of a huge volume of published studies showing that higher testosterone levels are associated with dramatic reductions in heart attack.\textsuperscript{28,36-53} No published human study shows that testosterone restoration causes heart attacks.

### Role of Testosterone in Facilitating Reverse Cholesterol Transport

A new term that Life Extension members might want to start paying attention to is reverse cholesterol transport (RCT). Reverse cholesterol transport is how HDL removes cholesterol from the arterial wall and returns it to the liver.

While one can reduce their arterial wall exposure to cholesterol through healthier diets and by taking certain medications, the average person still synthesizes about 650 mg every day of cholesterol in their peripheral tissues (outside of the liver). If there is any distortion in the HDL-mediated removal (the reverse cholesterol transport) of cholesterol from the arterial wall, the consequence is atherosclerosis.

Testosterone enhances the beneficial HDL-induced reverse cholesterol transport from the arterial wall. That is one of testosterone's unique and life saving anti-atherosclerotic effects.\textsuperscript{54}

Said differently, testosterone is required for optimal transport of excess cholesterol from our tissues and blood vessels to our liver for processing and disposal. In the testosterone-deficient state, reverse cholesterol transport is compromised, and excess cholesterol cannot be removed from the arterial wall.

HDL and free testosterone levels often plummet in aging humans.\textsuperscript{55} This combination of low HDL and low testosterone virtually guarantees an explosion in demand for vascular stents and drugs that earn tens of billions of dollars in profits each year for pharmaceutical behemoths.

Armed with this knowledge, you can now see past the charade perpetrated on practicing physicians and the public vis-a-vis this horrifically flawed study that implies that increasing testosterone levels may somehow increase heart attack risk.\textsuperscript{27} Numerous well-controlled human studies show the opposite to be true, i.e. higher testosterone levels play a critical role in maintaining healthy blood flow throughout the body by accelerating reverse cholesterol transport and thereby helping to prevent atherosclerosis.\textsuperscript{54,56-62}

### High Testosterone Associated With Improved HDL Function

HDL, or high-density lipoprotein, is commonly referred to as "good cholesterol." Low blood levels of HDL increase vascular disease risks.\textsuperscript{55-59} As you'll read next, a number of studies show that higher blood levels of testosterone correlate with higher HDL, while low testosterone and low HDL are hallmark features of the lethal metabolic syndrome.\textsuperscript{50-90}

When men are given high doses of testosterone drugs, a reduction in HDL levels has been reported in some studies.\textsuperscript{91,92} Authors of these studies are quick to point out that
the beneficial effect of testosterone in enhancing HDL functionality might account for the reduction in absolute HDL count.

For years, we have been told that very high HDL levels are desirable. The facts are that while low HDL is an independent risk factor for vascular disease, HDL levels that are very high are not necessarily a reassuring sign, and could mean that reverse cholesterol transport is suboptimal. That’s because very high HDL levels might serve as a signal that HDL is not doing an efficient job in removing cholesterol from arterial walls and is instead accumulating in the bloodstream and not being disposed of in the liver.

Under optimal circumstances, HDL efficiently removes cholesterol from arterial walls and then transports (reverse cholesterol transport) this cholesterol to the liver for eventual elimination (mostly through the bile duct into the intestines). When there is a deficiency of testosterone, HDL is less efficient in removing debris from the arterial wall and the liver is less efficient in breaking down cholesterol-laden HDL from the bloodstream.

Testosterone elevates the hepatic lipase enzyme that the liver needs to safely clear the body of excess cholesterol. All of this explains why the administration of testosterone can lower HDL, while simultaneously protecting against atherosclerosis by accelerating HDL-mediated reverse cholesterol transport...which is essential in protecting against occlusive arterial disease.

When reviewing population studies of aging men who are not given supplemental testosterone, there is a striking and consistent correlation between low HDL, low testosterone and a host of other vascular disease risk markers. The data on coronary artery disease risk and testosterone levels are even more definitive. One study evaluated men under age 45 who presented with coronary artery disease compared with an age-matched control group. The findings revealed that even moderately reduced free testosterone blood levels (below 17.3 pg/mL of blood) in these younger men resulted in a 3.3-fold greater risk of developing premature coronary artery disease compared with men who had values above 17.3 pg/mL.

To put this testosterone blood reading in perspective, aging men who don’t use testosterone-boosting nutrients or drugs often have very low free testosterone blood levels (less than 10 pg/mL of blood). These same men often have low HDL blood test readings in the danger zone (less than 40-50 mg/dL). Is it any wonder that despite aggressive use of statin drugs and other advances in cardiac medicine, heart attack and stroke are still today’s leading killers?

How Testosterone Affects HDL

The liver contains a receptor called scavenger receptor B1 that acts to stimulate cholesterol uptake for processing and disposal. Testosterone beneficially increases scavenger receptor B1.

Furthermore, a liver enzyme called hepatic lipase functions to remove phospholipids from the surface of HDL and helps enhance the uptake of these HDL-derived lipids by scavenger receptor B1. Testosterone increases the activity of hepatic lipase.

By increasing both scavenger receptor B1 and hepatic lipase activities, testosterone therefore facilitates an increase in reverse cholesterol transport, a process that removes excess cholesterol from the tissues and carries it to the liver for processing and disposal.

The important point here is that the exact mechanism by which testosterone decreases HDL (reverse cholesterol transport) may very well protect against atherosclerosis. In fact, reverse cholesterol transport is itself a key process by which HDL protects against atherosclerosis.
also promoted the benefits of natural testosterone drugs in men. So within a period of one week, the public heard from the American Medical Association and the FDA that there is no scientific basis, and even a potential for harm for men or women who use natural hormone drugs.

This was quite a public relations coup for whoever economically benefits by Americans suffering epidemic deficiencies of their youth hormones. In fact, in June 2007, a study on men over age 70 published that evaluated testosterone levels and found that just about every known vascular risk factor correlates with deficient testosterone. The authors of this study concluded:

"Total testosterone level is significantly related to metabolic and inflammatory factors in elderly men. Low total testosterone may be a significant indicator for development of metabolic syndrome in elderly men."”

So who benefits if Americans are denied access to non-patented natural hormones? The obvious answer is pharmaceutical companies who sell tens of billions of dollars of patented drugs to the aging American population. Please don’t think I am being overly conspiratorial about all this. The drug companies are not shy about colluding with the FDA in order to keep natural hormones out of American’s bodies. The FDA’s press release mentioned that financial interests were involved in its attack on compounding pharmacies that provide lower-cost natural hormones to Americans. Here is exactly what the FDA’s press release stated:

"FDA also responded today to a citizen petition from Wyeth, Madison, NJ, asking FDA to take regulatory action against compounding pharmacy operations that produce compounded "BHRT" (bioidentical hormone replacement therapy) drugs. Other stakeholders, including health care providers and consumer groups, have also raised concerns about “BHRT drugs.””

In case you don’t know who Wyeth is, it is the maker of Premarin® and Prempro®—the unnatural hormone drugs that were shown to increase cancer and vascular disease risks. If you go to Google and type in “Wyeth and hormone drugs,” you’ll see hundreds of articles such as:

When Life Extension first exposed the insidious relationship between FDA and drug companies, we were vilified by the media (and attacked by the FDA). In today’s apathetic world, the FDA openly admits it is helping pharmaceutical “stakeholders” to sell dangerous drugs to Americans. It does this while purporting a mission statement that the FDA “is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs.””

If you read what the FDA pretends to do, and then see how the agency really functions, it becomes apparent that this concept of “drug regulation” is largely a hoax perpetrated against the health of the American public.

The Journal of the American Medical Association (JAMA) is funded by prescription drug advertising. The FDA has intentionally expended public resources to financially benefit pharmaceutical giants. This “trilogy of death” involving the American Medical Association, the FDA, and phar-
maceutical industry is the subject of numerous books authored by alternative health investigative journalists. This sordid alliance is obviously alive and well in 2008.

Pathetic Excuses of JAMA Authors

Aging humans can safely benefit from natural hormone drugs if they are prescribed the dose that meets their individual needs. Low-cost blood tests can measure one's levels of testosterone, estrogen, and other sex hormones. Once the results of these blood tests come back, youthful hormone balance can be individually restored using inexpensive natural compounds.

In the atrociously flawed study published in the *Journal of the American Medical Association, 27* each man in the active group was given the same dose of testosterone pills. No attempt was made to customize the dose on based on blood readings. It does not require a person with a medical education to understand that the dosing of hormone drugs varies considerably among individuals. One size clearly does not fit all!

Based on our abundant wealth of clinical experience, the idea of blindly giving a group of aging men the same dose (160 mg/day) of oral testosterone, without factoring in individual variability factors mounts to medical malpractice. The doctors who conducted the study acknowledged the desirability of topically administered testosterone when they stated:

"Finally, when this study was designed, patches and gels that provide more steady testosterone levels were not available in the Netherlands." 927

Can you imagine that these doctors had the audacity to state that testosterone creams were not available in the Netherlands, a place where you can legally buy a host of substances like marijuana and hashish and where just about any drug imaginable is available? This study was conducted between January 2004 and April 2005, a time when testosterone creams were widely sold throughout the world. Yet curiously, these medical doctors based in the Netherlands claimed they had to rely on testosterone "pills."

When seeking to explain why the men receiving these testosterone pills did not show increases in their blood testosterone levels, they claimed blood readings were not important since the testosterone pill group had an increase in lean body mass, a decrease in fat mass, along with increased insulin sensitivity. All of this, they say, is consistent with the findings from other studies showing that testosterone produces these beneficial changes. This statement, of course, is preposterous in that testosterone drugs are supposed to boost testosterone blood levels.

While these testosterone pills might have induced temporary spikes in systemic testosterone, we know that when natural testosterone strategies are properly employed, there is a consistent level of testosterone in the blood that does not depend on "timing of the blood draw" to obtain an accurate result. Men in this flawed study were taking testosterone pills twice a day, yet no increase was observed in their blood testosterone levels. Natural testosterone strategies only require once a day or only once every-other-day dosing to achieve increased and steady blood testosterone levels.

We again raise the question why this study that showed no increase in testosterone blood levels was used to question the value of restoring blood testosterone levels in aging men, and how it could ever be published.
It has no scientific value, other than to show that testosterone tablets are ineffective, something that those in the anti-aging medical community long ago realized and published.97

**Don't be Victimized by This Deception**

The body count is mounting as drug company influence continues to mislead the public about proven means of reducing disease risk.

In searching the scientific literature to write this article, I purchased an expensive textbook titled "Androgens in Health and Disease." While the book is somewhat dated and does not reflect the more recent studies documenting the life-saving benefits of natural hormone restoration, the preface of the book made the following prophetic statement:

"Although the lay public tends to view androgens primarily as agents of virility and muscularity, androgens actually regulate nearly every physiologic system in some way..."98

If androgens are involved in the regulation of nearly every system in our body, then how can one expect to enjoy healthy aging if there are not enough androgens to regulate our body's systems?

Common sense, along with a plethora of recently published studies, clearly shows that age-related sex hormone decline significantly contributes to degenerative disease and increased mortality.

The good news is that Life Extension members have had free and open access to low-cost blood testing. As greater volumes of hormone blood tests have been ordered, the cost to perform them has gone down.

As you can read on the next page, the member price for the comprehensive Male or Female Blood Test panels is now only $198 during our annual Blood Test Super Sale. That is 50% below our low retail price and about 80% below what commercial labs charge.

I encourage members to take advantage of these extra-discounted prices by ordering their blood tests by June 2, 2008. Once you place your order, we will send you a pre-paid requisition form along with directions to blood-draw stations in your area. Since appointments are almost never necessary, you can have your blood drawn at your convenience.

To order the comprehensive Male or Female Blood Test Panels or any other tests at extra-discounted prices, call 1-800-208-3444.

**Lowest Prices Ever For Blood Tests**

For the past 12 years, Life Extension members have had the opportunity to test male or female hormones to determine whether they are low enough to warrant hormone replacement therapy. The results of these hormone blood tests are not intended to supersede medical advice. However, they provide a starting point that can be supplemented with androgens and other natural hormones if needed.

William Faloon

Credits: This article was independently peer reviewed by Steven Joyal, MD and then by Edward Lichten, MD. Dr. Joyal is the author of a brand new book titled "What Your Doctor May Not Tell You about Diabetes," while Dr. Lichten is the author of the book titled "Textbook of Bio-Identical Hormones" published in November 2007.

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MALE AND FEMALE BLOOD TEST PANELS

Unlike commercial blood tests that evaluate only a narrow range of risk factors, Life Extension's Male and Female Panels measure a wide range of risks that predispose aging humans to the most common age-related diseases. Just look at the huge numbers of parameters included in the popular Male or Female Panels:

<table>
<thead>
<tr>
<th>MALE PANEL</th>
<th>FEMALE PANEL</th>
</tr>
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<tbody>
<tr>
<td><strong>Total cholesterol</strong></td>
<td><strong>Total cholesterol</strong></td>
</tr>
<tr>
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<td><strong>Low-density lipoprotein (LDL)</strong></td>
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<td><strong>Very low-density lipoprotein (VLDL)</strong></td>
<td><strong>Very low-density lipoprotein (VLDL)</strong></td>
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<td><strong>High-density lipoprotein (HDL)</strong></td>
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<td><strong>Triglycerides</strong></td>
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<td><strong>Homocysteine</strong></td>
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<td><strong>C-reactive protein (high-sensitivity)</strong></td>
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<td><strong>Glucose</strong></td>
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<tr>
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<td><strong>Estradiol (an estrogen)</strong></td>
</tr>
<tr>
<td><strong>Total testosterone</strong></td>
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<td><strong>PSA (prostate-specific antigen)</strong></td>
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<td><strong>Immune cell counts</strong> (white cell count, lymphocytes, monocytes, eosinophils, basophils)</td>
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<tr>
<td><strong>Red blood cell counts</strong></td>
<td><strong>Red blood cell counts</strong></td>
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<td>(hemoglobin, hematocrit, red blood cell count, MCV, MCH, MCHC, RDW)</td>
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</tbody>
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Every-day member price: $299
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To obtain these comprehensive Male or Female Panels at the lowest prices ever offered, call 1-800-208-3444 to order your requisition forms.

Then at your convenience, you can visit one of the blood-drawing offices we provide in your area.
Scientists are increasingly recognizing that occlusive arterial disease (atherosclerosis) has multiple underlying causes, and that each one of these independent risk factors (depicted as 14 lethal daggers pointed at the heart above) must be corrected if vascular disease is to be prevented. The only way of finding out if you are at risk for heart attack, stroke, and many other common age-related disease is to have the comprehensive Male or Female Panels performed annually.
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