



## THE ILLUSION OF BONE DRUGS

OSTEOPOROSIS IS A SERIOUS HEALTH PROBLEM. Having strong bones and preventing the loss of bone are important health issues. Drug companies, which seek to use pharmaceuticals for prevention, see the aging baby-boomer population as a target market. In the case of bone-loss drugs, this preventive strategy is aimed at forty million baby boomers, primarily at women. This is a new type of drug use—drugs targeted at healthy people, not at illness.

It is interesting to note that fluoride gives the appearance of increased bone density, yet evaluation shows that the bone is clearly inferior. The actual bone hardness as a result of fluoride intake is diminished, and the mineral content of bone is lessened. The appearance of improved bone density is little more than chaotically growing swollen bone.

In a fascinating and rare display of public battle, the two makers of the best-selling bone drugs squared off. On September 28, 2004, Merck, the maker of Fosamax, published a study stating that its drug was better than its leading competitor's drug (Procter and Gamble's Actonel) at increasing bone density. Procter and Gamble countered by stating that increased bone density isn't necessarily better and claimed Actonel reduces non-spine fractures fifty-nine percent better than Fosamax does.

So, why do many doctors proudly wave x-rays in front of their

patients as proof that their bone drugs are working. What is Procter and Gamble saying? Isn't it interesting that Merck's number-one competitor claims that the appearance of increased bone density isn't necessarily better?

## Drugs That Kill Normal Bone Cells

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Fosamax and Actonel are in a class of drugs known as *bisphosphonates*. They work by killing osteoclasts, which are a type of cell that removes bone. In normal bone growth, maintenance, and healing, osteoclasts act as the remodeling crew. They are cells that do the demolition work. They remove the oldest and most stressed pieces of bone so that these can be replaced with new bone. Osteoclasts are vital to normal bone function.

Osteoclast activity is balanced by osteoblast activity. Osteoblasts are carpenter cells in the bone-building business. They take raw materials like protein and calcium and construct them into new bone. In growing bones there is very high activity on the part of both osteoclasts and osteoblasts.

In bone loss and osteoporosis, the rate of osteoclast activity is higher than the ability of osteoblasts to build new bone; in other words, the demo crew has gone wild. The function of Fosamax and Actonel is to kill the demo crew. By killing the demo crew the hope is that bone loss will be slowed down (true enough) and that bone-building activity will catch up and actually increase the mineral content and strength of the bone. Evidence now suggests that this may be wishful thinking.

## Bone Drugs Were Never Tested for Safety or Proven Effective

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The use of these bone drugs for preventive health raises many questions:

1. How do bisphosphonate drugs kill osteoclasts? Are they damaging other parts of the body?
2. If osteoporosis is a condition of osteoclasts gone wild, why are

they going wild? What is the real cause of the problem?

3. Is it a good idea to kill osteoclasts, since they are a normal part of healthy bone function? What if a person needs them for something, like healing a broken bone?
4. Are bisphosphonates safe for prevention or for early stages of bone loss (osteopenia)? What are the long-term effects in bone and elsewhere in the body when these drugs are used as a preventive strategy?

Any individual who thinks these questions were well thought through before millions of people were put on these drugs is gravely mistaken. In fact, almost nothing was known about these questions before the FDA approved these drugs for osteoporosis.

Normally, when a drug is designed it must meet certain use and safety standards. This was not done with Fosamax or Actonel. Rather, these drugs were initially used for diseases of rapid bone destruction, such as bone cancer. Researchers stumbled upon their potential use for osteoporosis in the early 1990s. They have been in widespread commercial use for twelve years, and only recently are we learning the specifics of how they work—the type of information usually required for drug approval in the first place.

In September 2004, Merck published a review of information stating how they believe bisphosphonates work at the molecular level. A few years earlier, research supported by Procter and Gamble shed many new insights into the molecular workings of these drugs. These sources paint a much clearer picture of how these drugs work.

1. The primary mechanism of “therapeutic action” is to deform and/or kill the osteoclast. The drugs block an enzyme (farnesyl diphosphate synthase) responsible for assembling the gene signals that relate to energy production in the osteoclast. Once the osteoclast runs out of energy, it dies. The drugs induce death by disrupting energy production.
2. These drugs have a preference for bone because their chemical structure binds calcium. They are cleared from the blood

within two hours, going to bone, where they stay for the life of the bone. They layer themselves in and among bone cells. They occupy space at the site of bone mineralization, under osteoclasts, and in osteoclasts. Once the drugs stick to calcium they are there indefinitely, as there is no enzyme in the human body that can take them apart.

Having a drug stuck in bone indefinitely, as part of the bone structure, is no small issue. The fact that we now know they work by killing osteoclasts is also no small issue. Osteoclasts are a normal part of healthy bone function—these drugs are not.

### **Smoke and Mirrors**

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The fact that a bone picture may show the appearance of improved bone density is not an accurate reflection of truly healthy bone.

In August 2004, researchers published the results of an experiment with rats, fusing the spinal region known as L4-L5. There was a control group, a group given the standard dose of Fosamax, and a group given ten times the standard dose. Pictures of the spine in standard-dose treatment showed an apparent increase in density compared with the control group. The animals were killed and a detailed analysis of the bone was performed. In the standard-dose treatment group the function of osteoclasts and osteoblasts was significantly reduced and there was poor quality of bone remodeling. In the group that was given ten times the standard dose, the effect of Fosamax on bone cells and bone healing was described by researchers as “deleterious.”

This study showed that even at normal treatment levels of Fosamax, the behavior of the bone-building cells is adversely affected, resulting in poor bone formation and healing. Since high doses of Fosamax have deleterious effects on bone, how is that different from the progressive accumulation of Fosamax in bone for fifteen or more years? No one knows.

In May 2004, a study was published in which beagles were given five to six times the normal dose of Fosamax for one year. This study sought to prove that the increase in bone density shown by x-

ray pictures was reflective of truly improved calcified bone matrix. The study was unable to show improved integrity of bone from Fosamax. Instead, a detailed analysis of spinal sections showed that the visual increase in density was actually due to disorganized bone structure. The matrix became bigger because it was abnormal, similar to the idea of a swollen sprained ankle.

The most alarming study to date was published in May 2004. An oral surgery facility started noticing an unusual number of patients with dead jawbones. Normally, the facility only had two patients per year with such a problem. A review of patients' charts concluded that sixty-three patients over a three-year period had this problem, and all of those patients had taken injectable bisphosphonates. Most of the patients required surgical removal of the dead jawbone, meaning the condition was non-responsive to other approaches such as debridement and antibiotic therapy. The researchers urged medical practitioners to pay attention to this problem, as early detection might prevent drastic surgery. Here is evidence in humans that something which is supposed to be helping bone is instead killing it. Like fluoride, high doses of bisphosphonates are deadly to bone. Like fluoride, lower doses of bisphosphonates appear to increase bone density but in reality are damaging the bone.

In August of 2004, the FDA told Merck to put a warning on its Fosamax label. It took Merck until July of 2005 to warn consumers of the dead jawbone side effect. On April 10, 2006, attorneys filed a suit in Florida for class-action status to sue Merck for failure to disclose this side effect to the public. The \$3 billion a year Fosamax scam now teeters on thin ice, adding to the woes of Merck, which has decided to fight every Vioxx case (10,000 are pending). On April 12, 2006, the *Wall Street Journal* published an article by John Carreyrou, titled, "Fosamax Drug Could Become Next Merck Woe":

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In the past two years, some oral surgeons have become convinced that oral bisphosphonates such as Fosamax can also cause jawbone death when taken for a long period of time.... Salvatore Ruggiero, chief of oral surgery at the Long Island Jew-

ish Medical Center in New York, says of the 155 ONJ cases [osteonecrosis of the jaw—dead jawbone] he has come across, 22 involve patients who were taking Fosamax and other oral bisphosphonates. Some of these patients took Fosamax for seven or eight years, he says. “With the oral drugs like Fosamax, exposure time is the key,” Dr. Ruggiero says....

David Tundell, a 61-year-old former aircraft maintenance officer in the Air Force and a plaintiff in the Florida suit, says the Fosamax he took for a year helped alleviate the osteoporosis in his hips. But he believes it also landed him in the emergency room earlier this year when his jaw swelled to the point where he could no longer eat. During a three-day hospitalization, all his teeth were taken out and part of his jaw was shaved off to remove dead bone. He says his doctor recommended he stop taking Fosamax.

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The real issue here is not when Merck knew and failed to warn; the real issue is that the FDA allows this drug to be sold for preventive bone health to millions of Americans. It does this when it has no proof showing the drug builds healthy bones but it has specific proof that the drug can kill jawbone. Doctors expect people to stay on Fosamax for the rest of their life. Here we see that the longer this poison accumulates in bones the greater the chance for serious bone disease. This is further evidence that the FDA is incapable of protecting the American public.

In September of 2000, Japanese researchers specifically warned about such dental problems resulting from the use of bisphosphonates. They demonstrated in mice that gram-negative bacteria (the type commonly found in people with poor dental health) exaggerated the inflammatory side effects of bisphosphonate drugs, leading to potentially serious dental problems. They urged extreme caution in prescribing these medications. The FDA should have acted on this information six years ago.

### **The “Known” Side Effects of Bone Drugs Are Understated**

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The primary recognized side effect of bisphosphonate drugs is

esophageal inflammation and ulceration. This has led to explicit directions from drug companies that people should stand upright for thirty minutes after taking them. Doctors are told to have patients take these drugs properly in order to avoid these problems, and this is considered an adequate warning. However, doctors routinely give bisphosphonates to people with serious digestive problems; I see this happening regularly.

All other side effects are considered trivial. Here is the actual story: Japanese researchers first reported in 1993 that bisphosphonate drugs activate inflammatory processes of the immune system. Their further research demonstrated increases in histamine release, increased activity of inflammatory immune cells, and increased inflammatory messages coming from immune cells. The researchers continually reported their concerns over the use of bisphosphonates by anyone with a gram-negative bacterial infection.

Australian researchers also helped to publicize the inflammatory problem of these drugs. They pointed out that osteoclasts, which gobble up old bone, and macrophages of the immune system are both members of the same trash-engulfing cell type. They also documented that the production of inflammatory signals from these macrophages is induced by bisphosphonates. Additionally, they showed that this inflammation could induce activity of cell-adhesion molecules on cells of the cardiovascular system, the exact problem which leads to plaque formation and cardiovascular disease.

A more recent animal study shows that bisphosphonates induce plaque to rupture from the lining of arteries. As bisphosphonates travel through the blood on their way to bone, they may yank calcium out of plaque in the arteries, causing the plaque to rupture. Such a study should be vigorously pursued by the FDA, as rupturing of plaque is a cause of heart attacks and stroke. This means that women who take bisphosphonates are being exposed to undue cardiovascular risk. Yet, the drugs carry no such warning.

The known issue of gastrointestinal inflammation is now undergoing closer scrutiny. There are 213 studies in science literature relating to this very serious side effect. Fosamax can dam-

age the esophagus simply by its direct-contact toxicity, and it can provoke secondary inflammatory mechanisms as well. Esophageal tissue damage by Fosamax can be very severe, both at the site of ulceration and in neighboring cells. Generally, the severe esophageal damage can heal when the drug is stopped. However, in one case the esophageal problems developed after only ten months of use and caused a closure of the esophagus that was unresponsive to treatment. Researchers are warning arthritis patients, who may be taking steroid drugs that already adversely affect bones and the GI tract, to be extremely careful with these drugs, and they highly recommend other options.

Because these drugs cause inflammation in immune cells, problems will surface in organs based on an individual's genetic weakness or existing health conditions. Indeed, severe inflammatory problems from bisphosphonate drugs are now being reported, in addition to the GI tract inflammation.

These include:

1. Severe eye inflammation
2. Severe acute hepatitis (liver inflammation)
3. Pancreatitis (pancreatic inflammation)
4. Acute polyarthritis (intense general inflammation)
5. Seizures
6. Inflammatory skin reactions

These studies should be setting off alarm bells at the FDA. How can the FDA sit by and allow a drug that stays in bone indefinitely—on the flawed theory that it builds better bone—with an undefined side-effect profile, to be given to millions of people for general prevention and mild bone loss?

It is clear that bisphosphonate drugs add to the inflammatory burden of an individual and thereby contribute to immune inefficiency. They work by poisoning the energy system in a bone cell; they are clearly an anti-health poison. Yet the FDA allows their use for prevention of bone loss.

All diseases of aging, including bone loss, have as a common

denominator an increase in inflammation. Immune system inefficiency is the hallmark of the aging immune system. Bisphosphonate drugs make both issues worse.

Killing osteoclasts with a drug is similar to killing cancer cells with chemotherapy. Such approaches fit neatly into the theory of Western medicine, which is to identify a disease and eliminate it with poison. While it is relatively easy to grasp the idea that a cancer cell should be killed, it is far harder to buy into this logic when the cell being killed is a normal part of bone. Furthermore, no one would undergo chemotherapy as a preventive approach to reducing cancer risk. Fosamax and Actonel are essentially chemotherapy for osteoclast bone cells—poison used for prevention.

### **The True Cause of Excess Bone Loss**

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Thankfully, new science is shedding light on the true cause of bone loss. Researchers are now answering the question, “What causes there to be so many osteoclasts that eat away at bone?” Bisphosphonate drugs do not address the source of the problem.

Researchers are now finding an unexpected and completely interwoven relationship between the immune system, nervous system, and bones. Of particular interest on the subject of bone loss are two cells—the osteoclast of the skeletal system and the macrophage of the immune system. Both these cells actually develop from the same parent or precursor cell. This means that as new cells are forming inside of bone, there is a point where these cells can become either osteoclasts or macrophages.

The body creates both types of cells in the amount needed for natural and healthy function. In the condition of osteoporosis, the body is making too many osteoclasts, causing bone loss. The true source of the bone-loss problem is the cellular decision to make too many osteoclasts instead of macrophages.

Researchers have now identified the gene signal that is making the faulty decision. It is called NF kappaB. In my book *Mastering Leptin*, I have explained in great detail the workings of NF kappaB in health and disease. Excessive NF kappaB is an inflammatory signal at the genetic level of cell function. Excess NF kappaB

production in bones, along with its pro-inflammatory best friend TNF $\alpha$ , stresses bone. It can be naturally balanced to support normal and healthy function.

Anything that helps a person achieve a state of natural balance—improved quality of sleep, less stress, better fitness—will help cool off excess NF kappaB and support the healthy function of bones. Bone stress is a reflection of the emotional stress, physical demands, and chemical poisons that the person has experienced over the course of a lifetime. There is no quick fix for bones, but bones can be improved. The human body makes a significant effort to function normally when provided with helpful nutrition.

## **How Exercise Helps Bones**

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The new science shows a complex interaction between cells that build bone and cells that take bone down. This process is coordinated by the nervous system and the immune system. Most people understand that physical fitness, especially weight-bearing exercise, can increase bone density: As muscle use sends force vectors through bone, the force creates “microdamage” in the bone. In response, osteoclasts take down the microdamaged bone, and osteoblasts remodel the bone. This is a harmonious relationship between osteoclasts (remodeling demo crew) and osteoblasts (remodeling building crew).

Fosamax and Actonel work by killing osteoclasts. While this may slow down bone loss in serious osteoporosis, the usefulness of this principle for general health or prevention of bone loss is highly questionable. These drugs directly interfere with the repair of microdamage. People who exercise will induce a certain amount of small damage to bone that needs to be repaired, stimulating bone fitness. When people take bisphosphonates, the ability to repair the small damage to bone is reduced or blocked, depending on the dose. The net result is that microdamage to bone accumulates and bone fitness is lost, replaced by abnormal bone with disorganized structure.

There is not a single shred of evidence that bisphosphonates build strong bone. Indeed, they were recently tested in military

training where stress fractures are common. In young healthy people, bisphosphonates did nothing to reduce bone fractures.

Within three years of taking bisphosphonates the appearance of a better bone picture begins to go away. The misleading pictures of swollen bone are now replaced with the reality of microdamaged bone that is difficult to fix. The drug companies and the FDA know about this information. The legions of doctors handing out these medications are in the dark.

## **Bone-building Nutrients**

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The human body is composed of water, fat, carbohydrates, protein, minerals, and various nutrients that act through enzymes to assemble or regulate the structure and function of the body. Bones have nutrient requirements that are essential to proper healthy function. Nutrients like calcium, protein, vitamin D, vitamin K, boron, silica, strontium, and manganese are vital to constructing bone.

Additionally, nutrients are needed to help the body perform its regulatory functions of bone. Specifically, the presence of certain nutrients inside bone turns down the excess production of NF kappaB, which turns off the excess formation of osteoclasts. This approach to solving the problem of bone loss is not achieved by killing osteoclasts; it is achieved by returning bone function to normal. NF kappaB requires proper nourishment in order to work correctly and to properly decide how many osteoclasts to produce. Nutritional deficiencies handicap healthy bone function and can easily be corrected by fortifying the diet with foods and supplements that contain the helpful nutrients.

Recently, several studies have analyzed the specific action of nutrients on NF kappaB and osteoclasts, testing the ability of nutrition to fortify healthy bone building.

In May 2004, researchers at the University of Texas tested the function of curcumin, a natural spice. Using a cellular model and advanced genetic testing they were able to conclusively prove that curcumin can turn off NF kappaB, promoting the normal level of osteoclast activity.

It has been known for some time that individuals with diets higher in fruits and vegetables have healthier bones. Recently, the bioflavonoid content of these foods has been proposed as the reason for this benefit. The main bioflavonoid under investigation is called quercetin. In May 2004 French researchers tested quercetin and found, like the curcumin study, that quercetin naturally balances NF kappaB and promotes healthy osteoclast function. This research has been confirmed by numerous recent studies.

Many other nutrients are proving to be beneficial in building healthy bones. Tocotrienols are a special form of vitamin E which contain a high level of antioxidants, superior to regular vitamin E (d alpha tocopherol). They have been shown to be an important factor for bone growth, whereas regular vitamin E is not. Tocotrienols balance NF kappaB function, whereas regular vitamin E does not.

It has been known for years that magnesium is an important nutrient for bones. Researchers, trying to understand why magnesium alone helps bones, placed rats on a controlled diet lacking only magnesium for one year. After that year, detailed analysis of their bones showed the loss of bone, simply from a deficiency of magnesium. Magnesium deficiency, like sulfur deficiency, occurs because these important minerals are depleted from our soil. Magnesium helps bones maintain their healthy function.

Omega 3 oils, especially DHA, accumulate in bone. DHA reduces or blocks the improper production of NF kappaB. Second-generation rats bred to be deficient in DHA exhibit poor bone integrity. By supplying DHA to them, the bone deficiency is corrected and bone strength returns to normal. In a rather amazing study, DHA was shown to maintain bone health in ovariectomized mice (meaning they produce no estrogen). Detailed analysis showed that DHA prevented macrophages in bone from releasing NF kappaB, thereby helping to maintain the normal function of osteoclasts. This is good news for any woman whose ovaries have been removed or who is going through menopause.

Human genetics has evolved in a survival mode. The fact that so many nutrients commonly found in the diet can directly work to support healthy bone is a testament to the human body's ability

to adapt to the environmental food supply. Unfortunately, many of these nutrients are no longer at optimal levels in our food. They require supplementation.

Quercetin is found in fruit; however, an optimal amount is obtained only in vine-ripened fruit. Another source is onions. Curcumin is found in turmeric, a cooking spice. While tocotrienols are found in rice oil or palm oil; it is easiest to take them as a supplement.

Magnesium is in fruits, vegetables, nuts, and grains: However, due to the farming methods that now predominate, many soils are lacking in magnesium. This leads to lower levels in fresh food than what was historically available. Magnesium is also the mineral most easily lost by stress. Few Americans get the advised daily requirement of 400 milligrams, an amount that is probably not adequate for people under high stress or who exercise often (magnesium is lost in sweat).

DHA occurred in animal fat when animals ate grass. Now DHA is mainly found in deep-water fish like salmon and tuna. When taking a DHA supplement, look for those that are molecularly-distilled to avoid the mercury contamination that may be present in such fish.

While healthy individuals may be able to extract these needed bone nutrients from a good diet, supplements can also be used to fortify and boost the natural bone-building process.

### **The FDA Is Irresponsible**

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The FDA would like to see all the helpful nutritional support for bones eliminated from the market. The FDA will not even inform the public of the most basic and obvious risks of bone drugs—risks that are clearly evident in the scientific literature.

The drug companies are doing nothing to explain what their bone research actually means. If they did, their drug sales would decline. However, the FDA has all this information at their fingertips and also does not inform the public.

The FDA has sold out the American public through a combination of vested-interest pressure, negligence, and gross incompe-

tence. Instead of doing its job, the FDA is now obsessed with preventing you from understanding natural options for your health.