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Calcium, Vitamin D and Bisphosphonates. Oh My!

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John Fan, MD, Hutchinson Clinic, Hutchinson, Kansas, reminded polio survivors at PHI's 10th International Conference (June 2009) that there was research justification for "taking a holiday" from bisphosphonates. His message was heard, and polio people started asking more questions. Using research data and in consultation with Frederick M. Maynard, MD, I offer the following answers to frequently asked questions.

Question 1: *When I had my DEXA* (Dual Energy X-ray Absorptiometry) *scan, they scanned my spine and my good hip assuming that my polio hip would be worse. My friend's experience was the opposite – her polio hip was scanned because the technician thought it was important to know how bad it was, so "the physician will know what to do." Which is the most logical thinking?*

One recent study found a significant relationship between bone density of the hip and muscle strength of the affected leg of polio survivors. Participants with osteoporosis of the hip had weaker leg muscles than other patients in the study. The weaker a patient's leg muscles were, the more likely they were to have osteoporosis of that hip.

This retrospective clinical study also reported that about 19 percent of polio survivors (n=164) who had bone density scans had them performed only on their stronger hip. If they only had osteoporosis in their weaker hip this would not have been apparent in their bone scans, and they would be assessed as not having osteoporosis.

The researchers directly answer your question. They recommend that all post-polio patients be evaluated for osteoporosis at both hips (or less preferably at the hip of the weaker lower extremity) and at the lumbar spine. (Osteoporosis in a post-polio clinic population, Haziza M, Kremer R, Benedetti A, Trojan DA, *Archives of Physical Medicine and Rehabilitation*, 2007: 88:1030-1035.)

Dr. Maynard cautions polio survivors and health professionals about the pitfalls of interpreting scan scores. "Remember that for polio people who were left with significant lower limb weakness during childhood, a 'normal' maximum bone density was never attained by early adulthood. A low bone-density DEXA score for one's age when done at age 50 to 60 does indicate an increased risk of fracture prevalence for the tested bone compared to peers of the same age, but it does not mean a person has an accelerated rate of bone mineral loss compared to able-bodied peers of the same age.

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"Only serial DEXA scans can show that new loss is occurring and how fast. This is an important distinction because new treatments for osteoporosis have only been shown to be effective among people who have *accelerated bone mineral loss* by slowing down the rate of loss. They rarely actually increase bone density in a specific bone."

Dr. Maynard concludes, "To me, there is value in scanning both hips. The hip DEXA score of the weaker leg will indicate how easily that hip may fracture due to localized osteoporosis of that hip bone. The DEXA score of the stronger leg will be a better indicator of the generalized diagnosis of osteoporosis and the possible value of systemic treatments."

Question 2: *After a blood test, my physician advised 50,000 units of vitamin D a week for a month. Have you ever heard of that? It seemed like a lot. I now take 600 IU (International Units) of Vitamin D and 600 mg of calcium each day. I consume orange juice and yogurt each day that has been fortified with calcium.*

Yes, I have heard of it and, in fact, have taken 50,000 units of vitamin D a week for a month as prescribed by my primary care physician. Research has shown that calcium and vitamin D are important for strong bones and most people (including polio survivors) don't take in enough of either on a daily basis. The current recommendation for adults over 50 is to take in 1,200 mg per day of calcium.

Experts recommend a daily intake of 600 IU of vitamin D. (Recent guidelines from The Endocrine Society state, "People older than 70 years should get a minimum of 800 IU of vitamin D a day.") Sources include sunlight, supplements or vitamin D-rich foods such as egg yolks, saltwater fish, liver and fortified milk. The Institute of Medicine recommends no more than 4,000 IU of vitamin D as a regular daily intake.

Your blood test must have been to measure the 25-hydroxy vitamin D level. It is the most practical method to assess how much vitamin D is in your body. It requires a blood draw. The normal range is 30.0 to 74.0 nanograms per milliliter (ng/mL), with 40-50 as optimal. Physicians may prescribe higher doses, such as 50,000 IU, to increase levels quickly to the normal range. (MedlinePlus)

Dr. Maynard reminds polio survivors that symptoms of low levels of vitamin D are similar to PPS symptoms – fatigue and muscle pain. "I would discourage survivors from taking doses of vitamin D above 4,000 IUs daily for time periods greater than one month without monitoring of blood levels and physician oversight."

Question 3: *In years past, we were encouraged to take hormone replacement therapy (HRT) because it helped "prevent osteoporosis." Why don't we hear about that anymore?*

Menopause is the time in a woman's life when her menstrual periods stop. It is a normal part of aging. In the years before and during menopause, the levels of female hormones can go up and down. This can cause symptoms such as hot flashes and vaginal dryness. Some women take HRT to relieve these symptoms. HRT may also protect against osteoporosis by preventing a sudden decline in estrogen levels, which is known to be associated with increased loss of bone mineral and can often occur during menopause, especially during an abrupt or relatively young-age onset of menopause.

The reason you hear less about HRT for osteoporosis prevention is that researchers have found that HRT also has risks. It can increase your risk of breast cancer, heart disease and stroke. Certain types of HRT have a higher risk, and each woman's own risks can vary depending upon her health history and lifestyle. Another reason you hear less is because additional, and possibly more effective, drug treatment options have become available in addition to HRT.

PHI's Research Fund supported work by a team from the University of Michigan, and in 2003, they concluded that "HRT did not confer substantial benefits in these postmenopausal polio survivors to warrant their

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using HRT at a higher rate than their non-disabled peers."
(Hormone replacement therapy and health behavior in postmenopausal polio survivors, Kalpakjian CZ, Riley BB, Quint EH, Tate DG, Maturitas, *The European Menopause Journal,* Elsevier Ireland, Ltd., 2003:1-13.)

You and your health care provider need to discuss the risks and benefits for you. If you do decide to take HRT, lower doses for shorter time periods are safer. Taking hormones should be re-evaluated every six months.
(MedlinePlus.NIH: National Heart, Lung, and Blood Institute)

Question 4: *My family physician is pressuring me to take Fosamax®. I have read about the side effect of jaw necrosis (deterioration and cell death). But I have fallen in the past, so shouldn't I take bisphosphonates to be sure I don't break anything? I am not sure what to do. HELP!*

Before I share some of the research findings, Dr. Maynard wisely points out that, "first of all polio survivors should address the causes of the falls and learn all they can about falls prevention strategies. Fosamax® may decrease the risk of a fracture from occurring; it does not prevent fractures." (See first question.)

A recent study conducted in Ireland of 50 post-polio patients (30 women, 20 men) reported that, based on bone mineral density data, 28 (56%) were diagnosed with osteoporosis and 20 (40%) had osteopenia, but only eight (16%) received antiresorptive therapy. Of the 19 patients who had a fracture, 14 (74%) had osteoporosis and five (26%) had osteopenia, of whom only six (32%) received antiresorptive therapy. Fractures of the hip were more common in the weak leg.
(High incidence of osteoporosis and fractures in an aging post-polio population, Mohammad AF, Khan KA, Galvin L, Hardiman O, O'Connell PG. Department of Rheumatology, Beaumont Hospital, Dublin, Ireland. *European Neurology,* 2009; 62(6):369-74.)

In a study reported in the *Journal of the American Medical Association,* healthy women (not those who had polio) who discontinued alendronate (a bisphosphonate) after five years showed a moderate decline in bone mineral density (BMD). In the study that measured total hip BMD and at other sites, the cumulative risk of a non-vertebral fractures, after five years, was not significantly different for those continuing or discontinuing alendronate.
(Effects of Continuing or Stopping Alendronate after 5 years of Treatment: The Fracture Intervention Trial Long-term Extension (FLEX): A Randomized Trial, Black D, et.al. *JAMA*, December 27, 2006, 296 (24):2927-37.)

In an editorial in the same issue, the authors find it reasonable to conclude that women who are at high risk of vertebral fracture because of previous vertebral fractures might be considered for continued therapy. They further state and their answer to your question is, "Decisions about additional treatment should consider the individual fall risk, individual fracture risk, response to previous therapies and remaining life expectancies."
(Ten vs Five Years of Bisphosphonate Treatment for Postmenopausal Osteoporosis; Enough of a Good Thing, Colón-Emeric, C. *JAMA,* December 27, 2006, 296(24):2968-69.)

The FRAX® tool has been developed by the World Health Organization (WHO) to evaluate fracture risk of patients. It is based on individual patient models that integrate the risks associated with clinical risk factors as well as bone mineral density at the femoral neck. It can be accessed at www.shef.ac.uk/FRAX. The FRAX® models have been developed from studying population-based cohorts from Europe, North America, Asia and Australia.

Dr. Maynard points out that there have not been any studies that show that bisphosphonates actually help polio survivors, "and there are side effects that should not be ignored, such as the ones mentioned in the question."

Question 5: *I read that drinking tomato or papaya juice is beneficial in reducing the risk of osteoporosis. Is this true?*

A small study (n=23) of postmenopausal women (presumably none were polio survivors) aged between 50 and 60 were asked to stick to a diet free of lycopene for one month. For four months, one group took two 15 mg lycopene supplements daily; another group drank two glasses of regular tomato juice (enough for a daily intake of 30 mg of lycopene); a third group drank a special Japanese tomato juice high in lycopene (70 mg daily); and a control group took placebo capsules. The researchers compared the effects on chemical signs of bone loss in

the women. Women taking lycopene from either juice or pills had lower levels of the chemical by-product associated with osteoporosis.

(Dietary restriction of lycopene for a period of one month resulted in significantly increased biomarkers of oxidative stress and bone resorption in postmenopausal women, Mackinnon, ES, Rao AV, Rao LG. Department of Medicine, Division of Endocrinology and Metabol-ism Sr. Michael's Hospital, Toronto, Ontario, Canada. *Journal of Nutrition Health and Aging*, 2011, Feb; 15(2);133-8.)

As usual, further and larger studies need to be done, but until it is proven without a doubt, there isn't any harm in drinking tomato juice or eating foods that contain lycopene, e.g., tomato products, watermelon, pink grapefruit, guava, papaya and rose hips.

Question 6: *I got the impression from Dr. Fan at the conference that he is not too keen on our taking the bone building medications for years and years. Did I get the right impression? Why is he hesitant?*

Dr. Fan explains his reluctance this way. Bone is a living tissue. Bisphosphonates work by "forcing" calcium into the bone. This is analogous to filling the bone with concrete. It makes the bone solid and brittle, not flexible and living. When it is damaged in a fall, it may crack or crumble. Dr. Maynard, too, has reservation about the quality of bone that results from use of these medications, especially when used for long periods of time. A more recent study, cited below, suggests this to be true.

(Bisphosphonate Use and the Risk of Subtrochanteric or Femoral Shaft Fractures in Older Women, Laura Y. Park-Wyllie, PharmD, MSc; Muhammad M. Mamdani, PharmD, MA, MPH; David N. Juurlink, MD, PhD; Gillian A. Hawker, MD, MSc; Nadia Gunraj, MPH; Peter C. Austin, PhD; Daniel B. Whelan, MD, MSc; Peter J. Weiler, MD, MASc, P Eng; Andreas Laupacis, MD, MSc. *JAMA,* February 23, 2011, 305(8):783-789.)

Conclusion: I wrote this article because the topic is personal. I have had scans every few years for the last 15 years and have osteopenia-type scores. I have taken Evista® and Fosamax®, but am currently on my "holiday." Articles say that "Decisions about additional treatment should consider the individual fall risk, individual fracture risk, response to previous therapies and remaining life expectancies."

Well, I have fallen twice in the last year. One was a legitimate accident. The other might have been from new left leg weakness. I cracked my sacrum in the legitimate fall. My scan scores maintained and improved slightly with Fosamax® use. My parents lived to the ages of 88 and 92, so I presumably have genes for a longer life, and I am in otherwise very good health. For now, I take my calcium, vitamin D, eat yogurt with calcium, drink orange juice

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GLOSSARY

Alendronate, a bone resorption inhibitor (resorption is the process of calcium from the bone being reabsorbed into the blood), is a nonhormonal medication for the treatment of osteoporosis that builds bone, restoring some of the bone loss.

Antiresorptive therapy is one of two primary types of drug therapy for osteoporosis. Antiresorptive drugs, such as calcium and vitamin D supplements, reduce bone loss as do antiresorptive therapies such as bisphosphonates and estrogen.

Bisphosphonates are a class of drugs that prevent the loss of bone mass, used to treat osteoporosis and similar diseases.

DEXA stands for dual energy X-ray absorptiometry. It is an imaging test that measures bone mineral density by passing X-rays with two different energy levels through the bone and is used to diagnose osteoporosis.

FRAX® is a web-based calculation that assesses the 10-year risk of osteoporosis fracture based on an individual's risk factors and femoral neck bone mineral density if available. The values are entered into the website tool, followed by clinical risk factors. The FRAX® tool then provides a figure indicating a 10-year fracture probability as a percentage, which, together with a clinical assessment, provides guidance for determining access to treatment in healthcare systems. As of July 2010, the tool was available for 26 country models and in 11 languages.

International Units (IU) and **milligrams** (mg) are not equivalents. IUs are a measure based on the biological activity of a substance in the body. They are set by a research committee commissioned by the World Health Organization and provide a measure of the effect on the body a substance will have regardless of its mass. Milligrams are a measure of mass or weight.

Lycopene is an antioxidant compound that gives tomatoes and certain other fruits and vegetables, such as watermelons and papayas, their color.

Osteoporosis is a disease, most common in postmenopausal women, in which bones are less dense and more fragile and thus at greater risk for fracture. This disease often affects bones in the hip, spine and wrist.

Osteopenia is the term used for bones that have become somewhat less dense than normal, but not as severe as in osteoporosis. Not everyone who has osteopenia progresses to osteoporosis.

to attain "good sleep" without just dangerously taking higher doses of prescribed sleeping pills.

Question: ***I have a severe rotator cuff tear and an orthopedic surgeon has recommended a shoulder replacement because of the severity of the tear and the presence of significant arthritis. I had polio in my right leg and use my left leg to lift/stabilize myself on crutches. Apparently the increased dependency has weakened my arms and, perhaps, injured them. The surgery may help or may create complications. Can you share any knowledge to help me make an informed decision?***

A: You raise several important issues related to the pros and cons of shoulder replacement in polio survivors. First of all, if you never had any significant residual weakness in your shoulder muscles as part of your original polio, then it is unlikely that your shoulder problems are, anatomically at least, related to polio. You may have worn them out and/or injured them as you suggested, and the shoulder problem can be surgically treated like anyone else's.

Definitely get a second opinion about whether the best treatment is arthroplasty (replacement). In addition to a second opinion from a shoulder surgeon specialist, I recommend a second opinion from a non-surgeon, such as a physical medicine and rehabilitation specialist in post-polio. That person cannot only advise about non-surgical alternatives for the shoulder problem, but also advise you on preparations for the post-operative period, if you do elect to have the shoulder replacement.

Certainly, you should at least practice transferring and walking and caring for yourself with only one arm, since you will not have much use of the arm after surgery for at least three months. You are facing a difficult and important decision. Don't make a hasty one, especially if you are not suffering severely. Take all steps possible to inform yourself about the pros and cons. ▲

SEND YOUR QUESTIONS FOR DR. MAYNARD TO INFO@POST-POLIO.ORG.

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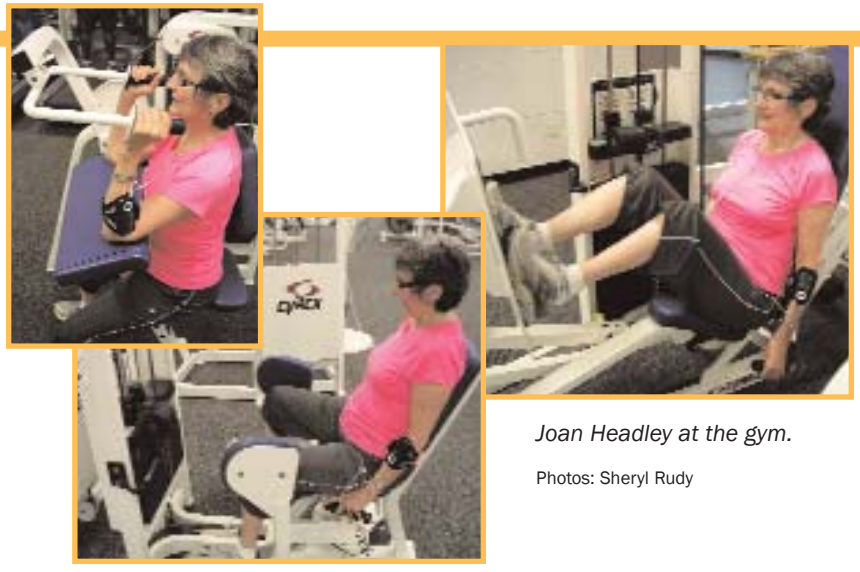
with calcium added and tomato juice. Because my polio effects are mostly in my left leg and because I can, I participate in specific targeted exercises at least three to four times a week at the gym in order to maintain my strength and therefore decrease my risk of falling, and weight-bearing exercises also help deposit calcium into bone. I will decide soon if I should end my holiday. ▲



Joan Headley at the gym.

Photos: Sheryl Rudy