

## Partnering for Prevention: Protecting Bone Health in Persons with Epilepsy

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### Abstract

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**Purpose:** The purpose of this paper is to propose nursing strategies for the maintenance of bone health in persons with epilepsy due to current risk-associated pharmacotherapy. Because of potentially serious consequences following loss of bone mineral density (BMD), action cannot be delayed. **Methods:** An extensive literature search was conducted utilizing peer-reviewed research articles. Results yielded articles that pertain to research surrounding osteoporosis prevention in persons with epilepsy. Each article was evaluated based on its applicability to the purpose of this paper. **Findings:** Loss of BMD is recognized as a possible consequence of epilepsy and treatment with antiepileptic drugs (AEDs). Length of time on AEDs and use of multiple, concurrent AEDs are recognized as risk factors contributing to loss of BMD. Furthermore, inadequate intake of specific nutrients, insufficient weight-bearing exercise, comorbid conditions, and personal characteristics can further increase risk. **Implications/Conclusions:** The associations between AED use and loss of BMD in persons with epilepsy, as well as the associations among demographics, lifestyle factors, and comorbid conditions to loss of BMD, provide nurses with fundamental strategies for prevention. Nurses are in a key position to assess their patients' current level of risk and to assist them in becoming active partners in the maintenance of bone health.

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**Keywords:** antiepileptics, epilepsy, osteoporosis, bone health, fracture

### Introduction

The maintenance of bone health is recognized as a concern for persons with epilepsy. Fractures occur more often in those who have seizure disorders (Souverain, 2005; Samaniego & Sheth, 2007), and alterations in bone metabolism have been noted for all but the newest generation of antiepileptic drugs (AEDs). Furthermore, alterations in bone health have been found in persons with epilepsy of both sexes and all ages, including young adults, adolescents, and children (Pack, Morrell, Marcus, Holloway, Flaster et al., 2005; Verotti, Pascarella, Trotta, Giuva, Morgese et al., 2000; Verotti, Greco, Latini, Morgese, & Chiarelli, 2002). Given the repeated associations between AEDs and altered bone health found across multiple studies, taking preventative measures is mandated (Sheth, Herman, & Drezner, 2006; Trevathan, 2008).

However, the evidence on specific interventions to prevent loss of bone mineral density (BMD) in persons with epilepsy is virtually nonexistent. The purpose of this paper to propose strategies for the maintenance of bone health in persons with epilepsy, keeping in mind that practices will change as more evidence becomes available. Because of the potentially serious consequences following loss of bone mineral density (BMD), prompt action is important. Nurses must monitor the literature frequently and update their practice as new information becomes available.

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## Background

Older AEDs that have been implicated in loss of BMD include phenobarbital, phenytoin, carbamazepine, and valproate (Fitzpatrick, 2004; Mattson & Gidal, 2004). Several of these medications have been used for decades. Relationships between BMD and newer AEDs have not been studied extensively. It is assumed that newer AEDs may be less harmful to bone, but limited research is available on these agents, specifically lamotrigine, levetiracetam, and topiramate. Two studies suggest that lamotrigine may be less harmful to bone when compared to older AEDs (Pack et al, 2005; Sheth & Herman, 2007), but sample sizes were small in both studies and more research needs to be carried out before results can be generalized.

Although there are theoretical explanations of the mechanism by which bone is affected by AED therapy, research supporting these theories is equivocal at best. Drugs with different mechanisms of action yield similar results regarding bone mineral density, a fact that complicates untangling the etiology (Sheth, 2004). However, not every study separates participants by the AED; multiple studies have clustered participants on different AEDs in the same group (Petty, O'Brien, & Wark, 2007). The lack of evidence regarding the etiological link between AED use and loss of BMD makes it difficult to prescribe prevention strategies. The associations between AED use and loss of BMD in person with epilepsy, as well as the associations among demographics, lifestyle factors, and comorbid conditions to loss of BMD, must provide health care practitioners with guidelines for prevention until data supporting interventions are available.

## 2. Methods

An extensive search of the Cochrane databases, CINAHL Plus, MEDLINE, Google Scholar, and UpToDate was performed. Results yielded peer-reviewed articles that pertain to research surrounding osteoporosis prevention in persons with epilepsy. Each article was evaluated based on its applicability to the purpose of this paper. Search terms included: antiepileptics, epilepsy, osteoporosis, bone health, and fracture.

### 1.1 Risks Related to AEDs and Other Medications

Length of treatment with a single AED is inversely correlated with lower BMD; that is, the longer that a person takes AEDs, the more likely that his or her bone density will be affected. Furthermore, AED polytherapy has a more deleterious effect on bone than monotherapy (Farhat, Yamout, Mikati, Demirjian, Saway, & El-Hajj, 2002). Those individuals who have been on multiple drugs over years may be at the highest level of risk. Individuals expected to be on AEDs for long periods, perhaps for life, will need to be monitored carefully at intervals (Lado, Spiegel, Masut, Boro & Haut, 2008).

Drugs other than AEDs have also been associated with loss of bone health. Many people with epilepsy have concomitant medical conditions and are taking medications for these conditions in addition to AEDs. Although evidence may be lacking, it is reasonable to hypothesize that the combination of multiple classes of drugs known to result in loss of bone density may accelerate the loss of mineral in persons taking drugs from two or more of these classes concurrently. Examples of these drugs may include steroids (used for many inflammatory conditions including Crohn's disease and asthma) and Depo-provera for contraception (Hulisz & Henak, 2006).

More recently, selective serotonin reuptake inhibitors have been associated with lower BMD (Saag, 2007). This finding has significance for many individuals with have also been implicated in lower BMD (Targownik, Lix, Metge, Prior, Leung, & Leslie, 2008). A comprehensive health history, including a record of all medications taken, is imperative to assess bone health vulnerability in persons who have epilepsy.

### 1.2 Other Comorbidity Risks

**1.2.1 Mobility considerations.** Cerebral palsy and hemiparesis have been associated with loss of bone density (Henderson, Kairalia, Barrington, Abbas, & Stevenson, 2009). These conditions with limited mobility characteristics can co-exist with epilepsy, and the combination could accelerate loss of mineral from bone when compared to having either condition alone. Depression also can result in low levels of physical activity, although, even non-depressed persons with epilepsy may not be exercising optimally to maintain healthy bones. Several studies have found that individuals with epilepsy do not spend enough time performing physical exercise (Ablha, Haug, Konda, Tinius, Ram, Sadler, & Liow, 2008; Steinhoff, Neusus, Theger, & Reimers, 1996; Yu, Lee, Wirrell, Shermann, & Hamiwka, 2008).

This finding is a concern because research has suggested that exercise may be more crucial than diet in creating and maintaining strong bones, especially in young women aged 12 to 22 years (Bouchard, Tremblay, LeBlanc, Lortie, Savard et al, 1983).

**1.2.2 Dietary considerations.** Though the importance of dietary intake compared to exercise is somewhat controversial, the role of nutrition, especially vitamin D and calcium intake, influences bone mineral density and bone turnover. There is no absolute agreement on the ideal intake of these nutrients for adults with epilepsy, but Pack and Shane (2013) describe doses of approximately 1200 milligrams of calcium and 800 International Units (IU) of vitamin D daily as typical. They point out that 800 IU of vitamin D may be inadequate for those on AEDs, especially enzyme inducers. Similarly, the National Osteoporosis Foundation (2010) supports daily intake of 1200 milligrams of calcium and 800 to 1000 IU of Vitamin D for postmenopausal women and men more than 50 years of age. Higher vitamin D doses may be required to maintain a normal serum 25-hydroxyvitamin D (25 OH D) level at a minimum of 30 nanograms per milliliter (National Osteoporosis Foundation, 2010; Pack et al., 2013). The NOF Clinical Guide (2010) provides a tool to assess the amount of calcium in a patient's diet. If dietary intake is inadequate, supplementation may be necessary (National Osteoporosis Foundation, 2010; Pack & Shane, 2013).

The report of a consensus panel for the supplementation of Vitamin D in childhood and adolescence recommends 400 IU of vitamin D daily as a starting dose for young people on anticonvulsants with periodic monitoring of 25 (OH) D levels (National Institutes of Health, 1994)

**1.2.3 Other considerations.** Besides the factors outlined above, the special risks related to epilepsy and AED therapy are superimposed on the other individual risk factors. These include genetics and demographics. Those who have a family history of osteoporosis and/or are thin may have greater risk for developing osteoporosis than those who have a larger frame. Asking about diagnosis of osteoporosis in relatives may offer a clue about genetic risk. Stage of life is also important; accelerated loss of BMD has been associated with the years immediately following menopause for women and at age 50 and older in men (National Osteoporosis Foundation, 2010).

## **2. Nursing Strategies**

### **2.1 Assessing Risk**

As described above, the threat for alterations in bone health is multifactorial. Nurses are uniquely qualified, based on their holistic perspective of their patients, to assess patient risk for low BMD from several vantage points. Several of these have been described above. However, a more detailed guide is described below. Figure 1 describes a guide for assessment of bone health in persons with epilepsy.

**Figure 1: Identifying Risk Factors for Low Bone Mineral Density in Persons with Epilepsy.  
An Assessment Guide for Nurses**

<p><b>Personal, Family History</b></p> <ul style="list-style-type: none"> <li>• Ethnicity</li> <li>• Sex, Age</li> <li>• Height, Weight, Body Mass Index</li> <li>• Personal History of Fracture</li> <li>• Family member with history of fracture</li> <li>• Family member with history of osteoporosis</li> <li>• Personal history of ETOH use</li> <li>• Personal history of tobacco use</li> </ul>	<p><b>Increased Risk with</b></p> <ul style="list-style-type: none"> <li>• Caucasian or Asian ethnicity</li> <li>• Post-menopausal women</li> <li>• Taller height, lower weight</li> <li>• Personal history of fracture</li> <li>• Family history positive for fracture or osteoporosis</li> <li>• ETOH use more than occasionally</li> <li>• Positive smoking history</li> </ul>
<p><b>Medications</b></p> <ul style="list-style-type: none"> <li>• Current AED(s)</li> <li>• Past AED(s)</li> <li>• Medical conditions other than epilepsy</li> <li>• Medications other than AEDs</li> </ul>	<p><b>Increased Risk with</b></p> <ul style="list-style-type: none"> <li>• AED marketed before 1990</li> <li>• Long- term use of AED(s)</li> <li>• Polytherapy</li> <li>• History of depression, kidney disease, thyroid disease</li> <li>• SSRI use, steroid use, Depo-Provera</li> </ul>
<p><b>Mobility</b></p> <ul style="list-style-type: none"> <li>• Presence of physical impairment</li> <li>• Amount of time in sedentary activities</li> <li>• Exercise Patterns</li> <li>• Type of usual exercise</li> </ul>	<p><b>Increased Risk with</b></p> <ul style="list-style-type: none"> <li>• Any impairment or comorbidity that decreases activity</li> <li>• Majority of waking hours spent in sedentary activity</li> <li>• Less than ½ to 1 hour daily spent on exercise</li> <li>• Predominance of non-weightbearing exercise</li> </ul>
<p><b>Diet</b></p> <ul style="list-style-type: none"> <li>• Calcium Intake - # of dairy servings daily or supplements</li> <li>• Vitamin D Intake – Fortified foods or supplements</li> <li>• Patient understanding of nutrients needed for bone health</li> </ul>	<p><b>Increased Risk with</b></p> <ul style="list-style-type: none"> <li>• Less than 3 servings of dairy/day</li> <li>• Less than 800 IU of Vitamin D daily for adults, 400 IU daily for children</li> <li>• Lack of awareness re: important of nutrients for bone health</li> <li>• Inability to read food labels</li> </ul>
<p><b>Results of Previous Screening</b></p> <ul style="list-style-type: none"> <li>• DEXA results indicating Osteoporosis</li> <li>• DEXA results indicating Osteopenia</li> <li>• Results indicating low Vitamin D levels</li> </ul>	<p><b>Increased Risk with</b></p> <ul style="list-style-type: none"> <li>• Results indicating osteoporosis or osteopenia (low bone mass)</li> <li>• Patient does not understand results</li> </ul>

**2.1.1 Personal and family history.** Begin by verifying basic demographic information. If relevant, ask about pregnancies, breastfeeding, and/or menopausal status. Ask about family history of osteoporosis, and personal history of traumatic and atraumatic fracture. Inquire about smoking history and consumption of alcohol; both of these social habits have been associated with lower bone density (National Osteoporosis Foundation, 2010). List all current and past health problems.

**2.1.2 Medications.** Note all AEDs taken, both current medications and those prescribed in the past. Also note the length of time that each was taken, as well as length of AED polytherapy.

Next, note medications taken for all other conditions. Go back at least two years in the history, as even discontinued medications may have an effect on the patient's current BMD. Ask specifically about birth control pills and the birth control "shot," as well as medication delivered by patches or inhalers. Some patients will only think of medications taken by the oral route when asked to name every drug they take.

**2.1.3 Mobility.** Note any mobility problems. Ask how much the patient exercises, how often, and what activities are included. Ask about activities encountered in the work setting, as applicable. Ask the patient to estimate the percentage of each day that is spent in sedentary activities.

**2.1.4 Diet.** Ask about diet, focusing on sources of Vitamin D and calcium. Also ask about sunlight exposure, another source of Vitamin D. Assess the patient's level of understanding about diet and exercise and how they can affect health. Does the patient read labels of food consumed? Do they understand how their dietary choices influence their health?

Discuss the results of the nursing assessment with the patient. Are they aware of their risk for low bone density? Have they ever had a DEXA scan to measure their bone density? Has their primary care provider or neurologist discussed bone health with them?

## 2.2 Nursing Interventions

**2.2.1 Resources.** Provide and direct the patient to appropriate educational resources. Nurses who educate patients regarding their risk for low bone density should review their educational materials and websites to properly evaluate them for readability and usability. With the limitations placed on the amount of time spent with each patient, it is imperative for nurses to ensure that the information given to each patient is tailored and accessible. There are numerous resources online, and printed materials are available from the National Osteoporosis Foundation.

**2.2.2 Screening.** Encourage the patient to ask their provider about bone health screening (e.g., DEXA scanning). Patients should also be encouraged to ask their provider about screening for Vitamin D level deficiency. Advanced practice nurses may be able to order BMD screening and lab work independently following the assessment.

**2.2.3 Healthy habits.** Encourage exercise, healthy sun exposure, and balanced diet. Some patients may have the skills to monitor milligrams and international units as they pertain to key nutrients. Others do better by monitoring the intake of certain foods and/or, number of servings. Explain that weight-bearing exercise is preferable to non-weight-bearing activity in the maintenance of bone health. Weight bearing exercise includes such activities as walking, running, and step aerobics and non-weight bearing exercise includes swimming and bicycle riding. For some patients, a pedometer may motivate them to spend more time on their feet each day.

## 3. Summary

Loss of bone mineral density is recognized as a possible consequence of epilepsy and treatment with AEDs. Both length of time on AED treatment and use of multiple, concurrent AEDs have been recognized as factors increasing the risk of loss of BMD. In addition, inadequate intake of specific nutrients and insufficient weight-bearing exercise can further increase risk, as can comorbid conditions and their treatment, as well as the personal characteristics of the patient. Nurses are in a key position to assess their patients' current level of risk and to assist them in becoming active partners in the maintenance of bone health.

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