

Hormone Therapy and Oral Health

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Approximately 46 million women in the United States are postmenopausal, having experienced spontaneous cessation of menses or surgical removal of both ovaries.¹ Hormone therapy (HT)—estrogen alone (ET) or estrogen with progestin (EPT)—is often prescribed on a short-term basis to alleviate the uncomfortable symptoms associated with menopausal estrogen loss, such as hot flashes, night sweats and vaginal dryness.

Recent clinical trials have confirmed the protective effects of HT with regard to the prevention of osteoporotic fractures and colorectal cancer.^{2,3} These trials have also confirmed the negative effects of HT on venous thromboembolism and breast and endometrial cancer, while raising questions about the use of HT for prevention of heart disease and stroke.^{2,3} Other limited research suggests the possibly beneficial effect of HT on oral health in postmenopausal women, which is the subject of this article.

Systemic Osteoporosis, Oral Bone Resorption and Tooth Loss

Tooth loss and resorption of alveolar bone (the bony sockets in which teeth are attached) are significant oral health problems of older adults in the US. The mean number of missing teeth increases with age, from 1.4 teeth in adults under age 30 to 8.6 teeth in those 60 years and

older.⁴ The incidence of tooth loss in postmenopausal women is about 3%-10% per year.⁵⁻⁷ Although the overall rate of edentulism in the US is 10%, the rate increases with age; by age 65 a woman has a 1 in 3 chance of having no teeth remaining.⁸ Denture replacement or adjustment because of bone resorption is common. Americans spend \$1.5

billion each year to treat the loss of tooth support, although only a fraction of the people needing treatment actually receive it.⁹

Although there are many causes of tooth loss (eg, dental caries, periodontal disease, orthodontic treatment and trauma), and some can be prevented by regularly brushing and flossing teeth and consuming a good diet, bone loss surrounding the tooth due to osteoporosis is a contributing factor.⁹⁻¹¹ Measures of bone mineral density (BMD) suggest that osteoporotic changes affect the jaws in a qualitatively similar fashion to the remainder of the skeleton. Patients with osteoporosis have reduced bone mass in the jaws and loss of alveolar bone height, and mandibular BMD correlates with BMD at the spine, hip and radius.¹¹⁻¹³ Similarly, the number of remaining teeth correlates with BMD at skeletal sites, such as the forearm, spine, hip and whole body, and osteoporosis.^{13,14} Women with severe osteoporosis are three times more likely to have no teeth than are healthy, age-matched controls.¹⁴ When osteoporosis affects the jawbone, bone around teeth may be lost, the thinner bone may create a less sturdy foundation for teeth, and teeth may become loose.

Postmenopausal bone loss is clearly associated with a deficiency of estrogen, and HT is an effective method for retarding bone loss, staving off osteoporosis and preventing fractures.^{2,3,15,16} Studies have also demonstrated that HT reduces menopause-associated mandibular alveolar bone loss and, in some instances, promotes an increase in BMD (Table 1).¹⁷⁻¹⁹ A longitudinal study of 41 postmenopausal women who had received HT for 1-23 years found a positive effect of HT on mandibular bone mass.¹⁷ A 1-year longitudinal study of 24 postmenopausal women with a history of periodontitis found that estrogen-deficient (as measured by estradiol serum levels) women displayed a mean net loss in alveolar bone density compared with estrogen-

sufficient women, who had a mean net gain.¹⁸ The only randomized placebo-controlled trial of HT and oral health demonstrated that use of HT for 3 years benefits alveolar bone mass as well as the postcranial skeleton.^{19,20} These studies suggest that estrogen plays an important role in determining alveolar bone mass, and that HT affects oral bone in a manner similar to the way it affects other skeletal sites.

Three ongoing cohort studies have examined the relationship between HT and tooth loss in postmenopausal women.^{6,13,21-24} The first investigation asked 3,921 elderly women (52 to 109 years; median age, 81 years) participating in the Leisure World Cohort Study to report the number of remaining teeth.²¹ Use of ET was self-reported

on the baseline health survey (1981-1985) before the dental survey in 1992. In the Nurses' Health Study,⁶ 42,171 women, 46 to 71 years of age, were asked if they had lost any teeth in the previous 2 years. Their status with regard to HT was determined from questionnaires in 1990 before the tooth loss was reported in 1992. In the Framingham Heart Study,²³ a trained observer recorded the number of teeth remaining and their location in 488 women, 72 to 95 years of age (mean age, 81 years). History of ET use was obtained from self-reports kept since 1960 until the dental examination in 1994-1995.

Each study demonstrated a benefit of HT on tooth retention (Table 2, page 35).^{13,21} Users of HT have about a 25% lower risk of tooth loss

Table 1. Effect of Serum Estrogen Levels and Hormone Therapy (HT) on Alveolar Bone Mass in Three Studies

| | Number | Bone Mass Change | | |
|--|--------|--|--|------------------------------------|
| Jacobs¹⁷ Postmenopausal women ages 32-64 years Treated with HT for average 5 years | 41 | <i>Change per year in mandibular bone mass between exams 1 and 2</i> +2.67% | | |
| Payne¹⁸ Postmenopausal women with periodontitis | | <i>Change in alveolar bone density over 1 year</i> | | |
| Estrogen-sufficient women | 10 | +0.30 ± 0.07 | | |
| Estrogen-deficient women | 14 | -0.44 ± 0.07 | | |
| Civitelli¹⁹ 3-year randomized controlled trial of postmenopausal women ages 41-70 years | | <i>Change in alveolar bone mass</i> | <i>Change in alveolar crest height</i> | <i>Change in femoral bone mass</i> |
| HT | 68 | +1.84% | +4.83% | +3.59% |
| Placebo | 67 | +0.95% | +3.46% | +0.22% |
| <i>P</i> -value for difference between HT and placebo groups | | <i>P</i> = 0.04 | <i>P</i> = 0.34 | <i>P</i> = 0.001 |

compared with nonusers. These findings are consistent despite differences in prevalence of tooth loss (<10%-30%), use of HT (38%-63%), socio-

economic and educational status (primarily high school graduates, to trained nurses, to affluent, primarily college-educated women), age and

methods of obtaining hormone data and tooth count. Although the Nurses' Health Study suggested that the most substantial decrease

Table 2. Effect of Hormone Therapy (HT) on Tooth Loss in Three Cohort Studies

| <i>Leisure World Cohort Study</i> ^{13,21} (n = 3291) [*] | Ever taken HT | | Duration of HT (years) | | | | How recently HT taken | | | | |
|---|---------------|-----------|--|--------------------------|-----------|-----------|-----------------------|-----------|-----------|-----------------------|-----------|
| | No | Yes | | ≤ 3 | 4-14 | 15+ | Past | Current | | | |
| Mean number of teeth | 19.5 | 21.2 | | 20.0 | 21.2 | 21.9 | | | | | |
| Relative risk for <25 teeth | 1.00 | 0.76 | | 0.87 | 0.74 | 0.70 | 0.75 | 0.73 | | | |
| 95% CI | | 0.67-0.87 | | 0.72-1.05 | 0.62-0.87 | 0.58-0.84 | 0.65-0.87 | 0.61-0.87 | | | |
| Relative risk for edentulism | 1.00 | 0.64 | | 0.85 | 0.57 | 0.49 | 0.70 | 0.51 | | | |
| 95% CI | | 0.51-0.79 | | 0.64-1.13 | 0.43-0.76 | 0.36-0.68 | 0.56-0.88 | 0.37-0.70 | | | |
| Relative risk for dentures | 1.00 | 0.81 | | 0.86 | 0.82 | 0.74 | 0.81 | 0.81 | | | |
| 95% CI | | 0.71-0.93 | | 0.71-1.05 | 0.69-0.97 | 0.61-0.89 | 0.67-0.97 | 0.69-0.94 | | | |
| <i>Nurses' Health Study</i> ^{6,22} (n = 42,171) [†] | Ever HT | | Duration of HT (years) for current users | | | | | | | How recently HT taken | |
| | No | Yes | <1 | 1 | 2 | 3-4 | 5-9 | 10-14 | 15+ | Past | Current |
| Relative risk for loss of 1 or more teeth | 1.00 | | 0.80 | 0.78 | 0.67 | 0.81 | 0.72 | 0.77 | 0.73 | 0.91 | 0.76 |
| 95% CI | | | 0.67-0.94 | 0.67-0.91 | 0.59-0.76 | 0.73-0.89 | 0.66-0.79 | 0.69-0.87 | 0.65-0.83 | 0.85-0.96 | 0.72-0.80 |
| Relative risk for <25 teeth | 1.00 | | | | | | | | | 0.90 | 0.62 |
| 95% CI | | | | | | | | | | 0.85-0.94 | 0.59-0.65 |
| <i>Framingham Heart Study</i> ^{23,24} (n = 488) | Ever HT | | Duration of HT (years) | | | | | | | | |
| | No | Yes | | 1-4 | 5-8 | >8 | | | | | |
| Mean number of teeth (excluding third molars) [§] | 10.7 | 12.5 | | 11.8 | 12.2 | 14.3 | | | | | |
| Percent edentulous | 33 | 26 | | 29 | 23 | 21 | | | | | |
| Relative risk of edentulism | | | | 0.94 for year each of HT | | | | | | | |
| 95% CI | | | | 0.90-0.99 | | | | | | | |

* Adjusted for age (similar results after adjustment for age, smoking, alcohol consumption and education)

† Adjusted for age, smoking

§ Adjusted for age, smoking and education

CI = confidence interval.

occurred among current users and that duration had little influence on risk,⁶ the other studies found that risk of tooth loss decreased with increasing duration of estrogen use,^{21,23} and was present, although less substantial, in past users. The Nurses' Health Study also found that the risk of tooth loss was similar in current users of all dosages of conjugated estrogen and all types of hormones (oral conjugated estrogen with and without progestin, patch estrogen with or without progestin, vaginal estrogen, and progestin).⁶ The Framingham Study found an association of tooth loss with duration of use among different types of teeth (incisors, canines and premolars, but not molars).²³ These data suggest that, in addition to being susceptible to osteoporosis, alveolar bone also shares in the benefits of HT with regard to preventing osteoporosis, and postmenopausal women are less likely to suffer tooth loss or need dentures if they receive HT.

Periodontal Diseases

Periodontal diseases are infections caused by bacteria in the dental plaque that forms on oral surfaces. The basic periodontal diseases are gingivitis, which affects the gums, and periodontitis, which affects the soft tissue and bone supporting the teeth. Severe periodontal disease (≥ 6 mm loss of attachment at one or more sites) increases with age; it affects fewer than 7% of adults under 45 years of age, but affects 14%, 19%, 23% and 30% of those ages 45-54, 55-64, 65-74, and 75+ years, respectively.⁸ Several investigations

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have found that skeletal BMD is related to clinical attachment loss,^{25,26} implicating osteoporosis as a risk factor for periodontal disease in postmenopausal women.

The effect of estrogen on the periodontium has been the subject of several clinical studies (Table 3, page 38).²⁷⁻²⁹ One small study found that, among nonsmoking, osteoporotic, early-menopausal periodontitis patients, estrogen-deficient women had nearly twice the gingival bleeding on probing and a higher frequency of clinical attachment loss than estrogen-sufficient women.²⁷

(Clinical attachment is a measure of periodontal tissue surrounding and supporting a tooth.) In another study of 228 middle-aged postmenopausal women, estrogen users had a significantly lower proportion of gingival bleeding (30% versus 39%) than nonusers.²⁸ The proportion of estrogen users with established periodontitis was also lower, but not statistically significant, than that in nonusers (21% vs. 26%). In addition, seven of eight periodontal pathogens were found at lower levels in the estrogen users, although only the mean level of *Capnocytophaga-ssp* was significantly lower. After adjustment for age, education, dental habits, plaque and pathogens, the significant difference in gingival bleeding remained (31% vs. 38%, $P = 0.04$). In another study in which periodontal disease was assessed in 236 postmenopausal women (59 on ET) and 176 premenopausal women, postmenopausal women who did not take ET were 1.5 times more likely than their ET-using counterparts, and 3 times more likely than premenopausal women, to exhibit severe attachment loss (19%, 12%, 6% in postmenopausal women not on ET, postmenopausal women on ET, and premenopausal women, respectively) and severe alveolar bone loss (34%, 20%, 10%).²⁹ Thus, ET appears to have a protective effect on the periodontium and on the severity of periodontal disease.

Other Oral Manifestations of Menopause

In addition to osteoporotic jaws, periodontal disease and tooth loss, clinical findings of postmenopausal

problems on dental examination include decreased saliva flow, increased dental caries, dysesthesia, altered taste, dry mouth and burning mouth.^{12,30-34} While 6% of premenopausal women report oral discomfort (oral ulceration, dry mouth, burning sensation or altered/bad taste),³⁴ 20%-90% of postmenopausal women report the same.^{12,30,34} Among 52 menopausal women, 29% complained of dry mouth, 6% burning mouth, 15% oral ulceration, and 4% altered/unpleasant taste.³⁴ In the Boston Longitudinal Study of Aging (153 pre-, peri- and postmenopausal women) salivary gland flow was lower in postmenopausal compared with premenopausal women (Table 4).³⁵ This decreased salivary gland flow

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The oral mucosa is, in many ways, similar to the vaginal mucosa,

and HT may influence oral mucosa in the same way it affects vaginal mucosa. In one clinical study evaluating the efficacy of HT in 32 postmenopausal who complained of oral dryness or burning, after 3 months of HT two-thirds of the women showed noticeable improvement in the subjective symptoms and the clinical appearance of the oral mucosa.³⁷ Similarly, 4-8 weeks of HT improved oral discomfort without an apparent local physical cause in 17 postmenopausal women.³⁴ Another study also reported estrogen deficiency as a risk factor for dry mouth, and found that patients taking estrogen had an increase of secretory performance of the palatal (minor salivary) glands.³¹ By 12 weeks, the flow rate increased 10

Table 3. Effect of Estrogen on Periodontal Disease in Three Studies

| | Number | | | | | | | |
|---|--------|-------------------------------------|-----------------------|-----------------------------|----------------------|--|--|----------------------------------|
| Reinhardt²⁷ <i>Non-smoking early-menopausal osteoporotic women with periodontitis</i> | | <i>Gingival bleeding on probing</i> | | | | <i>Clinical attachment loss ≥ 2 mm</i> | | |
| Estrogen-sufficient women | 8 | 24% | | | | 1.2% | | |
| Estrogen-deficient women | 9 | 44% | | | | 3.8% | | |
| | | <i>P<0.04</i> | | | | <i>P<0.01</i> | | |
| Norderyd²⁸ <i>Postmenopausal women ages 50-64 years</i> | | <i>Gingival bleeding</i> | <i>Visible plaque</i> | <i>Subgingival calculus</i> | <i>Periodontitis</i> | <i>Clinical attachment level (mm)</i> | <i>Alveolar bone height (mm)</i> | |
| Estrogen users | 57 | 30% | 60% | 29% | 21% | 2.1 | 2.7 | |
| Nonusers | 171 | 39% | 69% | 38% | 26% | 2.3 | 2.8 | |
| <i>P-value</i> | | 0.009 | 0.03 | | | | | |
| Grossi²⁹ <i>Postmenopausal women ages 50-74 years and premenopausal women ages 25-49 years</i> | | | | | | <i>Clinical attachment loss (mm)</i> | <i>Clinical attachment loss ≥ 3 mm</i> | <i>Alveolar bone loss ≥ 3 mm</i> |
| Premenopausal | 176 | | | | | 1.8 | 6.30% | 9.70% |
| Postmenopausal estrogen users | 59 | | | | | 2.1 | 12% | 20% |
| Postmenopausal nonusers | 177 | | | | | 2.4 | 19% | 34% |

times over baseline (Table 4). HT also is effective in ameliorating oral dysesthesias irrespective of whether the tissues appear atrophic, normal or erythematous.³⁸

In addition to leading to tooth loss, osteoporotic jaws are often unsuitable for conventional prosthetic devices or dental implants.³⁶ Postmenopausal women not taking HT have been found to have the highest failure rates of dental implants.³⁹ Implants placed in the maxilla (but not in the mandible) of post-

menopausal women not receiving HT failed to integrate with bone considerably more often (14%) than implants in those receiving HT (8%) or in premenopausal women (6%) (Table 4).

Healthy User Effect

As virtually all studies of HT and oral health are observational studies, a healthy user bias could explain some or all of these potential benefits. Women who take HT differ from those who do not in many ways

that may alter risk. HT users tend to be more affluent and better educated, to exercise more often and make other healthier lifestyle choices, and to access the healthcare system more frequently.^{40,41} These characteristics may, themselves, lead to better oral health. Only randomized, placebo-controlled clinical trials can rule out these possible confounders and other unknown differences between users and nonusers of HT, and establish HT as a contributing cause of improved oral health.

Table 4. Effect of Estrogen on Other Oral Manifestations in Three Studies

| | Number | | | | |
|---|--------|---|---------------------------|----------------------------|-----------------|
| Streckfus³⁵ <i>Baltimore Longitudinal Study of Aging</i> | | Submandibular/sublingual gland flow rates (mL/min) | | | |
| | | | <i>Unstimulated</i> | <i>Stimulated</i> | |
| Premenopausal (mean age, 39 years) | 51 | | 0.09 | 0.27 | |
| Perimenopausal (mean age, 48 years) | 26 | | 0.09 | 0.22 | |
| Postmenopausal (mean age, 69 years) | 76 | | 0.06 | 0.19 | |
| <i>P</i> -value | | | <i>P</i> <0.03 | <i>P</i> <0.01 | |
| Niedermeier³¹ <i>Women ages 43-77 years</i> | | Flow rates of palatal glands ($\mu\text{L}/\text{cm}^2/\text{min}$) | | | |
| | | <i>Baseline</i> | <i>4 weeks</i> | <i>12 weeks</i> | <i>24 weeks</i> |
| Estrogen users | 34 | 2 | 4 | 19 | 25 |
| <i>P</i> -value for comparison to baseline | | | <i>P</i> <0.05 | <i>P</i> <0.01 | <i>P</i> <0.001 |
| August³⁹ <i>Patients with endosseous implants</i> | | Failure rate | | | |
| | | | <i>Maxillary Implants</i> | <i>Mandibular Implants</i> | |
| Premenopausal women | 114 | | 6.3% | 6.9% | |
| Postmenopausal women with ET | 75 | | 8.1% | 10.0% | |
| Postmenopausal women without ET | 168 | | 13.6% | 9.3% | |
| Men <50 years | 59 | | 6.3% | 3.1% | |
| Men >50 years | 110 | | 7.6% | 6.6% | |
| <i>P</i> -value for comparison of pre- vs postmenopausal women not on ET | | | <i>P</i> = 0.04 | | |

Conclusions

Tooth loss and periodontal disease diminish quality of life by causing loss of function, aesthetics and self-esteem. Progressive loss of bony support for teeth after menopause may result in costly, lengthy, uncomfortable treatments, with eventual tooth loss and the inconvenience of wearing prosthetic devices. The positive results of HT on alveolar bone mass support the conclusions of observational studies of HT on tooth loss and periodontal disease, reinforcing the notion that HT strengthens the tooth attachment apparatus and improves dental health. The additional therapeutic benefit of sustained oral health and better tooth retention may give women who use HT to alleviate menopausal symptoms another reason to smile. ■

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Dr. Paganini-Hill reports no potential conflicts related to the content of this article.

This article discusses off-label drug use.

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