

# HORMONE REPLACEMENT THERAPY (HRT) AND CONTRACEPTIVES

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# What is HRT?



HRT is hormone replacement therapy and is used for balancing hormones in women around menopause. (1)

The HRT drugs used in our presentation include: Levothyroxine and estrogen (Estradiol).

Levothyroxine has been a standard treatment for results and resolutions for hyperthyroidism for several years (2)

Estrogen was approved in 1942 by the F.D.A. It is used to help diminish symptoms of menopause and was once thought that it could be used to extend life. (3)

Estradiol is the head intracellular human estrogen. (4)



# Contraceptives



Contraceptives are known to help prevent pregnancy (5)

**Provera** (medroxyprogesterone acetate) and **Minera** (levonorgestrel) include progesterone and are different methods of contraception used to help prevent pregnancy (6)

Kennedy Campbell



# Dental professional importance

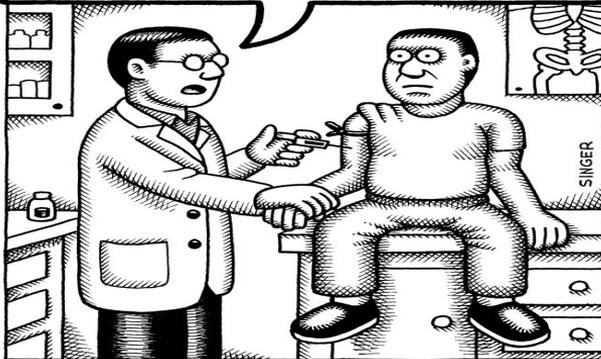
Drugs can have several effects on a person's body due to side effects and that is why this can be an important topic for the dental professional. As dental hygienists, it can be helpful to be aware of any side effects the patient may experience should they be a patient in our seats. This way we will be prepared to take any needed next steps should any side effect ranging from non-life threatening to life threatening occur. (7)

Kennedy Campbell

NO EXIT

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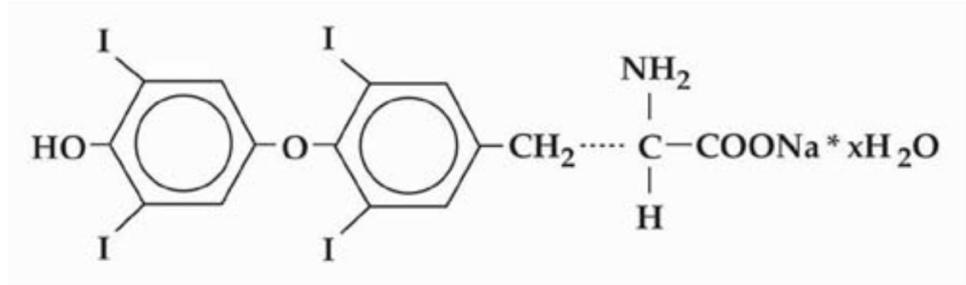
THIS MEDICATION'S SIDE EFFECTS MAY INCLUDE MEMORY LOSS, DIZZINESS, NAUSEA AND FEELINGS OF BEING HIT BY A TRUCK.



# How Does it Work??



## Levothyroxine



**Pharmacodynamics:** Levothyroxine sodium is a synthetic T4 hormone that mimics the action of an endogenous T4. Thus, when levels are lower than normal ranges, Levothyroxine helps to maintain balance by increasing T4. (10)

**Pharmacokinetics:**

- Absorption – 40-80 percent is absorbed from the gastrointestinal tract, most of it is from the jejunum and upper ileum. It will absorb better under fasting conditions and will lower absorption with the consumption of food.
- Distribution – greater than 99% bound to plasma proteins, including thyroxine-binding globulin (TBG), thyroxine-binding prealbumin (TBPA), and albumin (TBA).
- Metabolism – elimination of T4 occurs through deiodination, which 80 percent of T4 intake is deiodinated.
- Excretion – most of thyroid hormones will be eliminated by the kidneys, with a small portion being eliminated through the feces. (10)

**What is hypothyroidism?**

The thyroid produces hormones that influence the control of vital functions, such as body temperature and heart rate. With low levels of these hormones, hypothyroidism occurs. This can be the result of autoimmune disease, hyperthyroidism treatments, radiation therapy, thyroid surgery, and certain medications. Hypothyroidism is a condition when the thyroid is not producing enough T3 and T4. It may not show any significant signs in the beginning, but if not treated it can be a source of many health problems. Some problems can be expressed as: obesity, joint pain, infertility and heart disease. (9)

# How Does it Work??

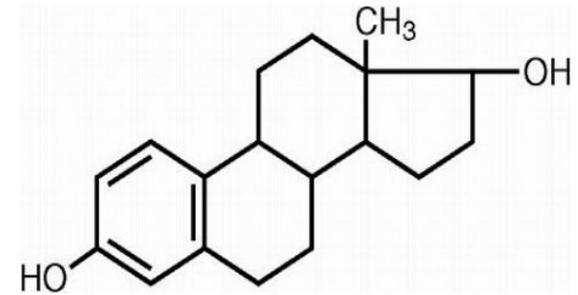


## Estradiol

**Pharmacodynamics:** Estradiol is the main intracellular human estrogen and it is more sustainable than other hormones, estrone and estriol, at the receptor level. Consuming this drug will act through binding to the nuclear receptors in estrogen-responsive tissues. The drug will decrease the raised levels of these hormones that women experience in a later stage in their lives during postmenopause. (11)

**Pharmacokinetics:**

- Absorption – Estradiol is rapidly absorbed with oral administration. This increases the stability of metabolism and the bioavailability.
- Distribution – Estrogens circulate in the blood largely bound to sex hormone binding globulin (SHBG) and albumin.
- Metabolism – Exogenous and endogenous estrogens are metabolized very similarly in the liver. It is first converted reversibly to estrone, which can also convert to estriol. Then, it goes through an enterohepatic recirculation in the gut and reabsorbed.
- Excretion – Estradiol, estrone, and estriol are removed from the body through the filtration of the kidneys in the form of urine. (11)



**What is Estrogen?**

Estrogens are female hormones. They are naturally made by the body and are needed for the normal sexual development of the female and for the regulation of the menstrual cycle. This hormone is responsible for the production of ovaries, which decreases after menopause. Prescription drugs, such as Estradiol, help to reduce the signs of menopause by producing estrogen. Such drugs also help with physical signs of hot flashes, unusual sweating, chills, faintness, or dizziness. (11)

# How Does it Work??

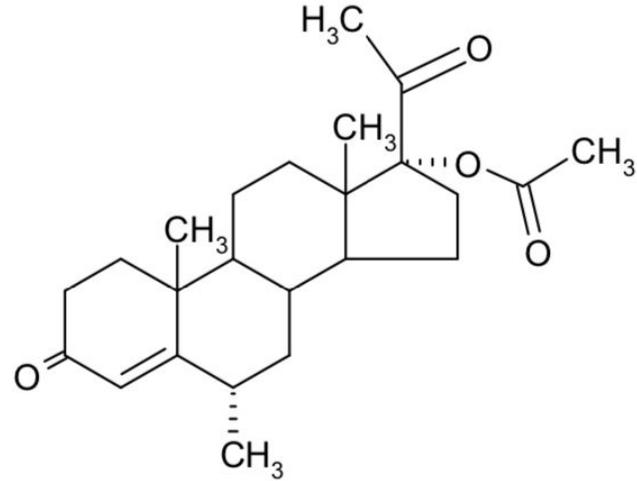


## Provera

**Pharmacodynamics:** No specific data available on the way this drug affects the body. (8)

**Pharmacokinetics:**

- Absorption – intramuscular injection is administered.
- *Distribution* – eighty six percent of plasma protein binding of medroxyprogesterone acetate, MPA, occurs. MPA binding is mainly to serum albumin, but no binding of MPA happens with sex-hormone-binding globulin (SHBG).
- Metabolism – MPA is metabolized in the liver by P450 enzymes.
- Excretion – The concentrations of MPA is substantially reduced to the point that its undetectable between 3-7 months. Most MPA metabolites are removed via filtration of the kidneys in the form of urine. (8)



### What are contraceptives?

Contraceptives are drugs that are used to avoid pregnancy during sexual encounters. There are different drugs that are used to prevent a pregnancy by either stopping the menstrual cycle or not allowing the egg and the sperm to meet and fertilize.

# How Does it Work??

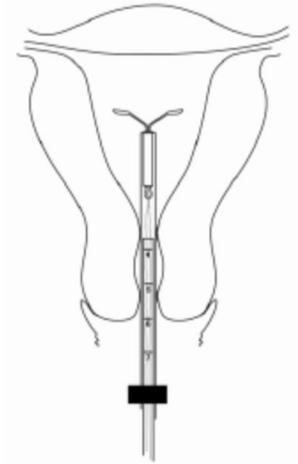
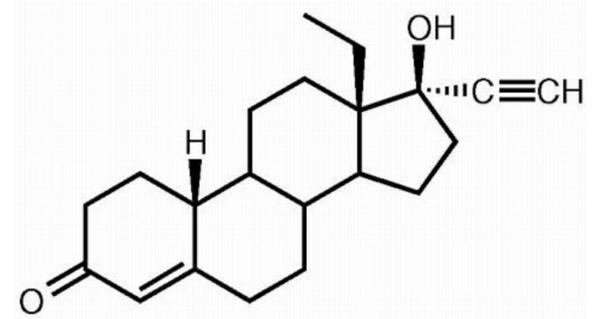


## Minera

**Pharmacodynamics:** Mirena has a targeted progestogenic effect in the uterine cavity. The release of levonorgestrel induces a stromal pseudodecidualization, glandular atrophy, a leukocytic infiltration, and a reduction in glandular and stromal mitoses. (12)

**Pharmacokinetics:**

- Absorption – levonorgestrel is administered to the uterine cavity. It's being released very slowly, 20 mcg per day.
- Distribution – 1.8 liter per kilogram is the amount that levonorgestrel is being distributed. Which is about 97.5 to 99% protein-bound, principally to sex hormone binding globulin (SHBG) and, to a lesser extent, serum albumin.
- Metabolism – after the absorption of levonorgestrel, it conjugated at to form sulfate conjugates and glucuronide conjugates in serum. A large amount of conjugated and unconjugated 3 $\alpha$ , 5 $\beta$ - tetrahydrolevonorgestrel will be found in the serum with very small amounts of 3 $\alpha$ , 5 $\alpha$ -tetrahydrolevonorgestrel and 16 $\beta$ hydroxylevonorgestrel.
- Excretion – about half of levonorgestrel and its metabolites are filtered by the kidneys and extracted in the form of urine, a third is excreted in feces. (12)



# Hormone replacement therapy drugs

**Levothyroxine** is a hormone drug, used to treat an underactive thyroid gland (hypothyroidism). It replaces or provides more thyroid hormone, which is normally produced by the thyroid gland (13).

- Having enough thyroid hormone is important for normal mental and physical activity. In children, having enough thyroid hormone is important for normal mental and physical development.
- This medication should not be used to treat infertility unless it is caused by low thyroid hormone levels.
- The dosage is based on your age, weight, medical condition, and response to treatment.
- Do not stop taking this medication without consulting your doctor. Thyroid replacement treatment is usually taken for life.

## Brand names

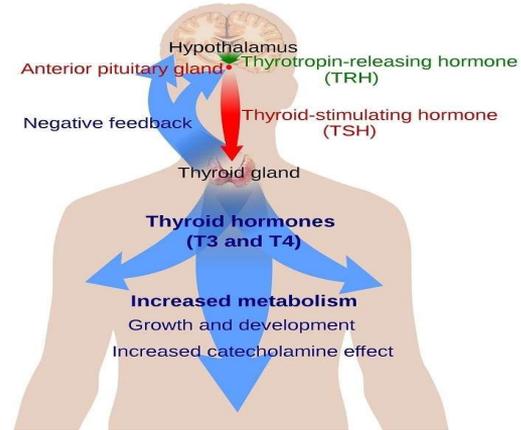
- Synthroid Most common
- Lavanthroid

## Side effects:

- Hair loss ▶ may occur in the first month of the treatment.
- Sweating
- Mental/mood changes
- Diarrhea
- Tremor
- Easily broken bone

**MOA:** Levothyroxine is a synthetic version of the principal thyroid hormone, thyroxine (T4) that is made and released by the thyroid gland. Thyroid hormone increases the metabolic rate of cells of all tissues in the body. In the fetus and newborn, thyroid hormone is important for the growth and development of all tissues including bones and the brain. In adults, thyroid hormone helps to maintain brain function, utilization of food, and body temperature, among other effects (14).

## Thyroid system



<https://study.com/academy/lesson/levothyroxine-classification-uses-dosage.html>

## Food Interactions

Absorption increased in fasting state and decreased in malabsorption states. Consistent administration in relation to meals is recommended. No iron or calcium carbonate within 4 hours of taking this medication. Oral administration with infant soybean formula, soybean flour, cottonseed meal, walnuts, foods containing large amounts of fiber, ferrous sulfate, and antacids may decrease drug absorption. Take 30-60 minutes before breakfast.

**Estrogen**, is the primary female sex hormone. It is responsible for the development and regulation of the female reproductive system and secondary sex characteristics. **Use** in Contraception, Menopause, hypogonadism, transgender women, prostate cancer, breast cancer (14).

There are different types of hormone medicine medicines:

• **Estrogen-Only Medicines**

Brand Name	Generic name	Product type
Alora *	estradiol	Pach
Cenestin *	<u>Synthetic conjugate estrogens</u>	Pill
Climara	Estradiol	Pach
Estrace	Estradiol	Pill/Vagina cream
Estradermar	Estradiol	Pach
Estring	Estradiol	Vagina cream
Estrasorb	Estradiol	Skim Cream
Evanist	Estradiol	Skim Spray
Fertrace	Estradiol acetate	Pill
Premarin *	Conjugate Estradiol	<u>Pill/Vaginal cream/Injection shot</u>

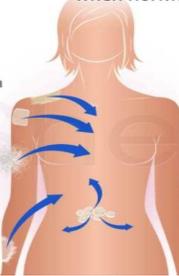
• **Progestin-Only Medicines**

Brand Name	Generic Name	Product Type
Prometrium	Micronized Progesteron	Pill
Provera	<u>Medroxyprogesterone Acetate</u>	Pill

## Hormone Replacement Therapy (HRT)

Hormone replacement therapy is a FDA-approved treatment to **relieve menopause symptoms** and **prevent osteoporosis**. It is used to supplant natural hormones with synthetic hormones during the menopause transition, when hormonal production decreases.

COMMON TYPES:



WHEN IT'S RECOMMENDED TO USE

- **Hysterectomy.** Or any other unnatural decrease in hormonal production.
- **Severely symptomatic.** Where a patient hasn't found relieve with CAM. It will help relieve the symptoms of menopause and prevent osteoporosis.

POSSIBLE RISKS

There are several studies that suggest that the use of HRT may increase the risk of **Breast Cancer** and **Strokes**.

**Euro-American Connections & Homecare**

### Estradiol and Grapefruit

Grapefruit juice may interact with estradiol and cause unwanted side effects.

**MOA:** Estrogen and progesterone are steroid hormones that play a pivotal role in the regulation of mammalian reproduction. One primary action of these hormones is to regulate the development and function of the uterus. These hormones act by regulating the transcription of specific genes in the uterus (14).

• **Combination Estrogen and Progestin Medicines**

<b>Brand Name</b>	<b>Generic Name</b>	<b>Product Type</b>
Climara Pro	Estradiol/Levonorgestrel	Patch
Combipach	Estradiol/Norethindrone Acetate	Patch
Femhrt	Norethindrone Acetate/ Ethinyl Estradiol	Pill
Presfest	Estradiol/Norgestimatee	pill

• **Combination Estrogen and Other Medicines**

<b>Brand Name</b>	<b>Generic Name</b>	<b>Product Type</b>
Duavee	Cojugated Estrogen/Bazedoxifene	Pill

**Do not use if you:**

- have unusual vaginal bleeding
- have or have had certain cancers such as breast cancer or uterine cancer
- have or have had blood clots in the legs or lungs
- have a bleeding disorder
- have had a stroke or heart attack
- have liver problems
- have serious reactions to estrogen medicines
- think you are pregnant

**Serious Side Effects**

- Heart attack or stroke Blood clots
- Breast Cancer
- Dementia in women 65 years and older
- Gallbladder disease or high triglyceride (cholesterol) levels that could lead to problems with the pancreas
- Vision loss caused by a blood clot in the eye
- Liver problems
- High blood pressure
- Severe allergic reactions

**Less Serious, Common Side Effects**

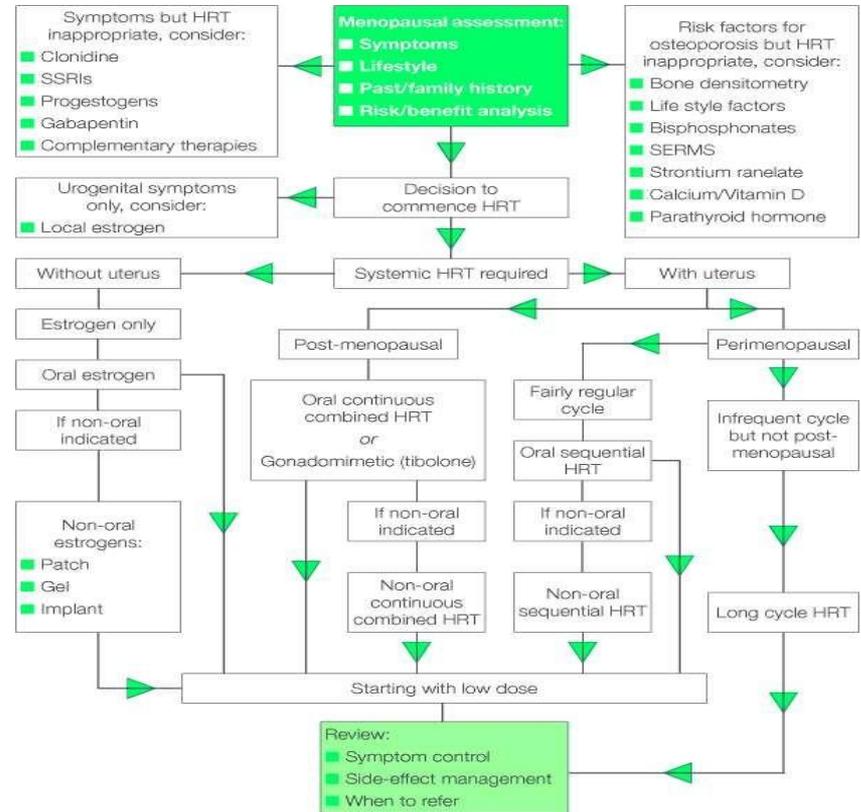
- Headaches
- Painful or tender breasts
- Vaginal spotting
- Stomach cramps/bloating
- Nausea and vomiting
- Hair loss
- Fluid retention
- Vaginal yeast infection

# Estrogen/Progesterone/Progestin Hormone Therapy

- This is often called combination therapy, since it combines doses of estrogen and progesterone, the synthetic form of progesterone.
- It's meant for women who still have their uterus.
- Taking estrogen with progesterone lowers your risk for cancer of the endometrium, the lining of the uterus.

**Oral progestins** – Taken in pill form, progestin medications include medroxyprogesterone acetate **Provera** and the synthetic progestin pills (norethindrone, norgestrel). Many experts now treat the majority of their menopausal patients with natural progesterone rather than synthetic progestins.

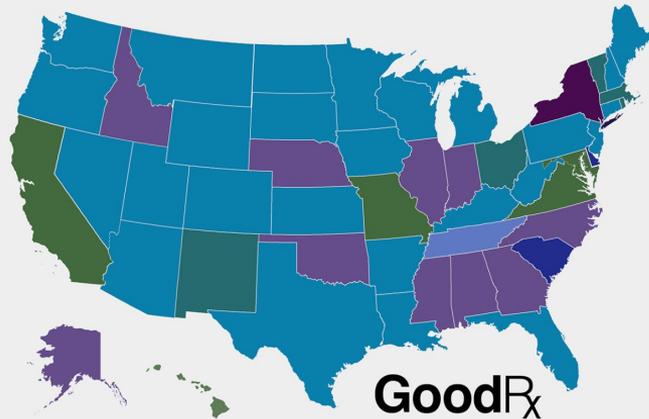
**Intrauterine progestin** – Not approved for this use in the United States, the low-dose intrauterine devices (IUD) **levonorgestrel** are sold under the brand names: **Liletta**, **Kyleena**, **Mirena** and **Skyla**.



# Oral/Dental Side Effects (HRT)

## The United States of Drugs

The most prescribed medication in each of the 50 states (2018)

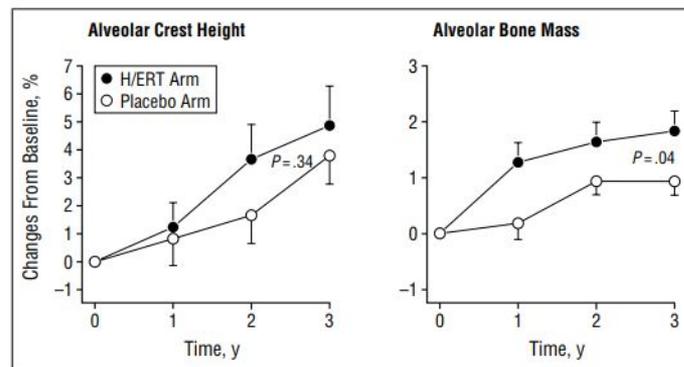


Data represents volume of US prescriptions by state filled at pharmacies during 12 months ending February 2018. Data comes from several sources, including pharmacies and insurers, and provides a representative sample of nationwide US prescription drug volume. For more info, visit [goodrx.com/blog](http://goodrx.com/blog)

- **Levothyroxine** is one of the most commonly prescribed drugs in the U.S. There are no significant effects or complications of levothyroxine on dental treatment (14).
- **Adverse reactions** to be considered: **cardiovascular** (angina pectoris, cardiac arrest, cardiac arrhythmia, cardiac failure, flushing, hypertension, increased pulse, myocardial infarction, palpitations, tachycardia), **CNS** (anxiety, choking sensation, fatigue, headache, heat intolerance, irritability, nervousness), **gastrointestinal** (abdominal cramps, dysphagia, gag reflex, vomiting), **hypersensitivity** (to inactive ingredients, causing rash, angioedema, fever, wheezing), **neuromuscular and skeletal** (decreased bone mineral density, tremor), and **respiratory** (dyspnea)(14).

# Oral/Dental Side Effects (HRT)

- There are no significant effects or complications of **estrogens** on dental treatment (14).
- As with any other medication, it is important to consider possible adverse effects in relation to dental treatment (heart attack, stroke, hypertension, headaches, nausea, vomiting).
- Based on a randomized, double-blind, placebo-controlled trial, estrogen replacement therapy has actually been shown to improve alveolar bone mass in postmenopausal women (15).
- This can have a positive effect on alveolar crest height and tooth retention.



**Figure 2.** Changes in oral bone variables in women treated with hormone/estrogen replacement therapy (H/ERT) or placebo. Data represent mean  $\pm$  SE obtained from 67 women in the placebo arm and 68 in the H/ERT arm and reflect an intention-to-treat analysis. *P* values represent the significance level of treatment effect estimated by multivariate analysis of variance. Treatment arms are described in detail in the “Study Design” subsection of the “Subjects and Methods” section.

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# Effects on Dental Treatment

- Neither **levothyroxine** nor **estrogen** have not been found to have any direct effects on dental treatment. However, it is important to consider possible adverse reactions.
- With HRT for hypothyroidism, dental professionals should warn patients regarding skipping doses or taking lower doses than indicated to save money, as treatment involves a lifelong hormone replacement.
- Many patients requiring postmenopausal HRT tend to be older individuals, whom may present with other conditions such as cardiovascular disease or osteoporosis. These diseases can very well affect dental treatment.

# Oral/Dental Side Effects (contraceptives)

- There are no significant effects or complications of oral progestins (**Provera**) or intrauterine progestin (**Mirena**) on dental treatment.
- “64.6% of patients who discontinued oral contraceptives did so because of adverse effects” (16).
- Educating patients about adverse effects of contraceptives helps establish realistic expectations and prevents unnecessary switching to alternatives (16).



A circular illustration with a dashed blue border containing various dental items: a toothbrush, a dental mirror, a tooth, a dental probe, a tube of toothpaste, and a dental chair. The background is light blue with small circles.

# Dental Treatment for Patients on HRT or Contraceptives

- A thorough medical history assessment must be conducted to evaluate all possible risks or medication interactions.
- The dental professional is responsible for informing/educating the patient about any associated side effects or risks for developing other diseases, as a consequence of HRT or contraceptives.
- In the event a patient presents with persistent symptoms of concern, a referral to a specialist should be made.
- Patients should be advised to maintain recare visits and undergo periodic periodontal screening to evaluate any changes in periodontal status.

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