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TOP SECRET

• INSIDE THIS EDITION •



The Secrets of Estrogen

NEWS, IDEAS &
INSIGHTS

VOLUME 11 - OCTOBER 2022

3 Different Forms

BY DR. GAYLE FLANNELLY, R.PH., PHARM.D

Estrogen, that ubiquitous substance of female existence, the stuff that makes us who we are. We know that, in many ways, we are governed by this hormone, but do we know to what extent? As it affects us in an ethereal manner from beginning to end, in ways both seen and unseen, it is best to try to dispel some of its secrets.

Estrogen is a sex hormone that is necessary for maintaining sexual and reproductive health in women. It is found in both sexes, but a woman's body produces the most estrogen. It is produced in three different forms: Estrone (E1); the primary form of estrogen that your body makes after menopause, Estradiol (E2); the primary form of estrogen produced by your body during your reproductive years and the most potent form of estrogen and finally Estriol (E3); the primary form of estrogen produced during pregnancy.

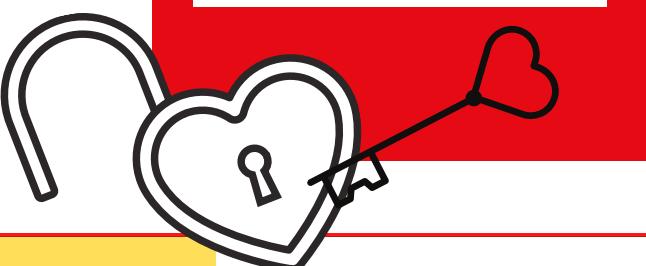
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TABLE OF CONTENTS

Three Different Forms of
Estrogen • P. 1

Healthy Bones • P. 3

Mammograms • P. 7



THE SECRETS OF ESTROGEN

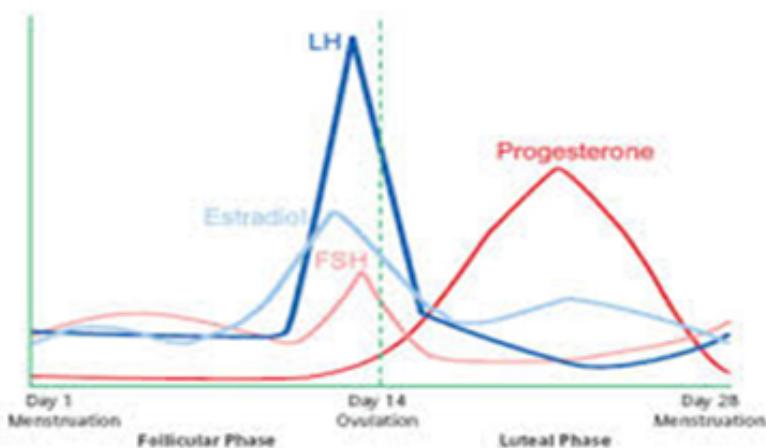
continued from page 1

Estrogen is responsible for the development of the characteristics that make us women. It is responsible for the development of a woman's breasts, a woman's hips, for menstruation and menopause. In addition to regulating the menstrual cycle, estrogen affects the reproductive tract, the urinary tract, the heart and blood vessels, bones, breasts, skin, hair, mucous membranes, pelvic muscles, immune system and the brain.

Here, estrogen begins to exert its powers. These characteristics begin to express the essence of a woman at the very onset of puberty and may persist past menopause.

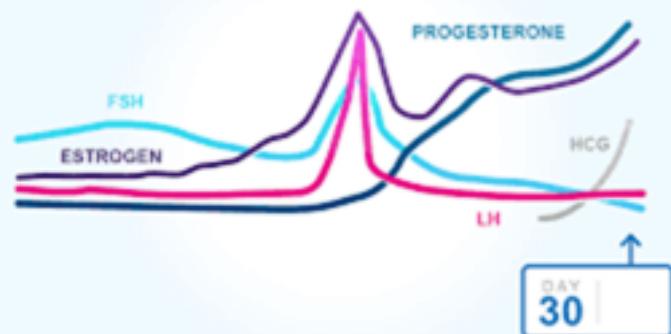
Estrogen is produced in many places in the human body. In females, it is produced and secreted by the ovaries during your reproductive years, it is also produced in adipose tissue or fat and the pituitary gland. The female body is exquisitely attuned to concentrations of estrogen, with levels rising as we approach puberty and diminishing with menopause. During childbearing years, the hormone's concentration rises each month in preparation for fertilization and should that occur, plays an integral part in maintaining uterine health along with progesterone for the fertilized egg. If fertilization does not take place, the level drops and menstruation begins.

Monthly cycle



Estrogen levels are at their highest during pregnancy, affecting many changes in the female body. Other hormones are surging and declining throughout a woman's reproductive years including FSH (follicle stimulating hormone) and LH (luteinizing hormone) and progesterone. Estrogen leads this cohort of hormones as estrogen makes them possible.

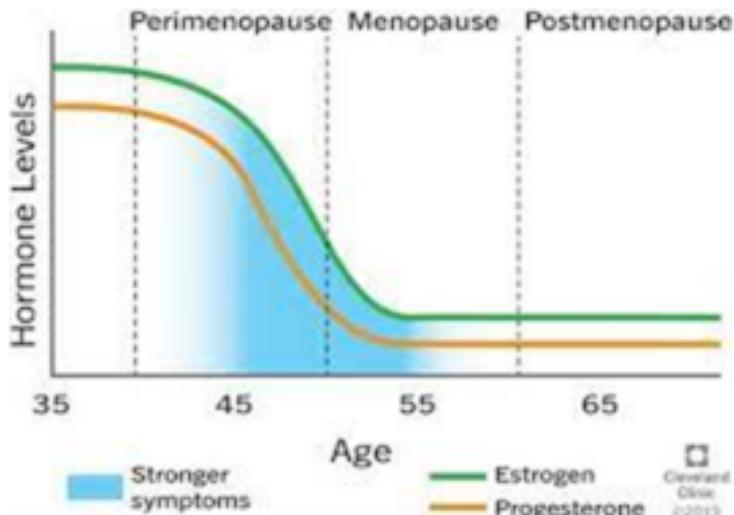
...Or for pregnancy



THE SECRETS OF ESTROGEN

continued from page 2

Estrogen affects many other parts of the female body. Its levels continue to play important roles well into post-menopausal life. Its powers can be felt by its existence or its absence.



Estrogens have been used in FDA approved medications to treat symptoms associated with menopause, pills to prevent pregnancy, medications to moderate acne vulgaris and treatments for prostate cancer. The presence or absence of estrogen in the human body can be a powerful trigger for change, but an imbalance can result in problems also.

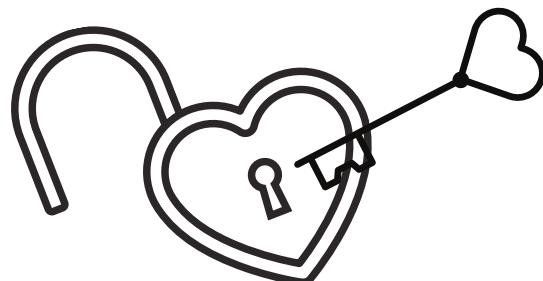
As women, we are familiar with that pre-teen female anxiety that accompanies the bodily changes signaling the beginning of becoming a woman. She may begin to develop breast and show a curvature of the waist and hips as the concentration of estrogen rises. Later, the pituitary gland in the brain begins to release other hormones previously mentioned and menses begins. We are familiar with the effects of estrogen in puberty, but we seem to know less of estrogen's effects on a woman's body as we go through life.



BONE DEVELOPMENT

Estrogen is responsible for bone development and health in both females and males. In the young skeletal structure, it is needed for proper construction of bone and the closing of growth plates. Estrogen aids in maintaining healthy bones throughout one's life. In a young person, estrogen deficiency can lead to weaker bones. As menopause approaches and estrogen levels decrease, bone structure can be weakened by bone resorption and breakdown.

Absorption of dietary calcium, a mineral required for healthy bones, is as high as 60% in infants and young children, but it decreases to about 25% in adults and continues to decline with age in both sexes. But as estrogen levels begin decreasing in perimenopause and the ability to absorb calcium decreases with age, a woman's risk of osteoporosis and its untoward consequences can be more apparent.



As we approach menopause, a woman should pay more attention to the health of her bones to decrease her risk of osteoporosis. Calcium can be found in a healthy diet and dietary supplements. The Recommended Dietary Allowance (RDA) of Calcium can be found in the attached chart and is enough to meet the nutritional requirements of most healthy individuals.

THE SECRETS OF ESTROGEN

continued from page 3

DIETARY ALLOWANCE (RDAs): IMPORTANCE OF CALCIUM

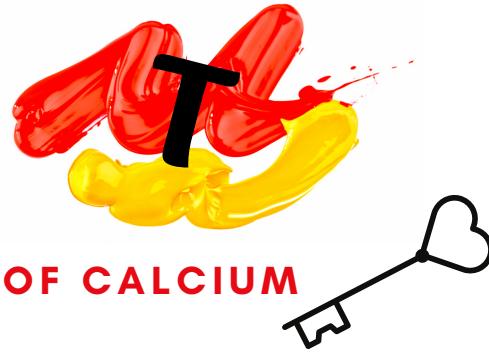


Table 1: Recommended Dietary Allowances (RDAs) for Calcium [1]

Age	Male	Female	Pregnant	Lactating
0–6 months*	200 mg	200 mg		
7–12 months*	260 mg	260 mg		
1–3 years	700 mg	700 mg		
4–8 years	1,000 mg	1,000 mg		
9–13 years	1,300 mg	1,300 mg		
14–18 years	1,300 mg	1,300 mg	1,300 mg	1,300 mg
19–50 years	1,000 mg	1,000 mg	1,000 mg	1,000 mg
51–70 years	1,000 mg	1,200 mg		
71+ years	1,200 mg	1,200 mg		

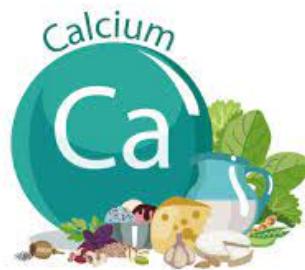
Top 10 Calcium rich foods - for Building strong bones.



Varying levels of calcium can be found in different foods. Approximately 72% of calcium comes from the intake of dairy products in The United States. Other sources of calcium can be found in the food we eat such as canned sardines and salmon with bones as well as certain vegetables, such as kale, broccoli, and Chinese cabbage (bok choi). One absorbs about 30% of calcium from dairy products and fortified foods. However certain compounds in plants (e.g., oxalic acid, phytic acid) can decrease calcium absorption by forming indigestible salts with calcium. Studies have found that absorption of calcium is only about 5% from spinach, whereas it is much higher, at 27%, for milk. In addition to spinach, other foods with high levels of oxalic acid include collard greens, sweet potatoes, rhubarb, and beans. Caffeine and phosphorus can decrease absorption of calcium.

If one has difficulty eating a well-balanced diet, your doctor may advise you to take a calcium supplement. Calcium comes in different salts that make varying amounts of calcium available for absorption. Calcium carbonate and calcium citrate are the most common salts found in dietary supplements. Calcium carbonate can be found in brand name supplements such as Oscal® and calcium citrate in Caltrate ®.

Calcium salt	Elemental calcium (%)
Carbonate	40
Tricalcium phosphate	38
Citrate	21
Lactate	13
Gluconate	9



THE SECRETS OF ESTROGEN

Vitamin D



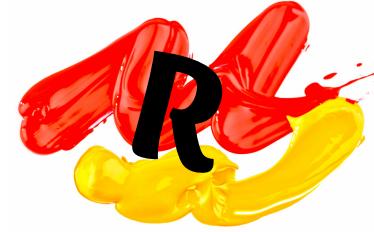
Vitamin D is also necessary for the absorption of calcium. There has been much debate as to how much vitamin D is needed and many people and governing bodies were not in agreement with previously published numbers. Therefore, the United States and Canadian governments requested that the Institute of Medicine (IOM, now called the Health and Medicine Division) review the evidence on vitamin D and calcium to obtain updated recommendations. Published in 2011, the IOM panel increased the RDA for vitamin D to 600 IU (International Units) for people up to age 70 and to 800 IU for those over 70. The IOM also raised the safe upper limit of daily intake for most age groups from 2,000IU (equivalent to 50mcg) to 4,000 IU (100mcg) per day.

Exercise also is important in maintaining healthy bones. Weight bearing exercises and resistance exercises are the best for building and maintaining bone health. They include walking, hiking, jogging, climbing stairs, playing tennis, and dancing. Resistance exercises such as lifting weights can also strengthen bones. This also helps with strengthening muscles as they begin to diminish in one's late thirties along with decreasing estrogen levels.

Women should begin monitoring their bone density as they begin to enter perimenopause. A bone mineral density test, sometimes called a bone density test, detects whether you have osteoporosis, a word that comes from

Greek and literally means "porous bone". An osteoporotic bone is a bone that has become weaker and is more prone to break. A bone density test is an X-ray test that is painless and just a few minutes long. There are two types; DXA (dual-energy X-ray absorptiometry) which measures the spine, hip, or total body. It is considered the most useful and reliable for checking bone density.

QCT (quantitative computed tomography) usually measures the spine, but it can also test other areas. It is not used often because of the cost and the amount of radiation it delivers. The X-rays show the calcium and mineral content of your bone and how dense or thick your bones are. If the number is high, your bones are dense and strong. Conversely, if they are low, you are at a higher risk of developing osteoporosis and breaking a bone.



There are numerous medications available for the treatment of osteoporosis. Some are categorized as estrogen or hormone replacement medications such as Raloxifene (Evista ®) and others such as bisphosphonates like Alendronate (Fosamax ®) that contain no hormones.

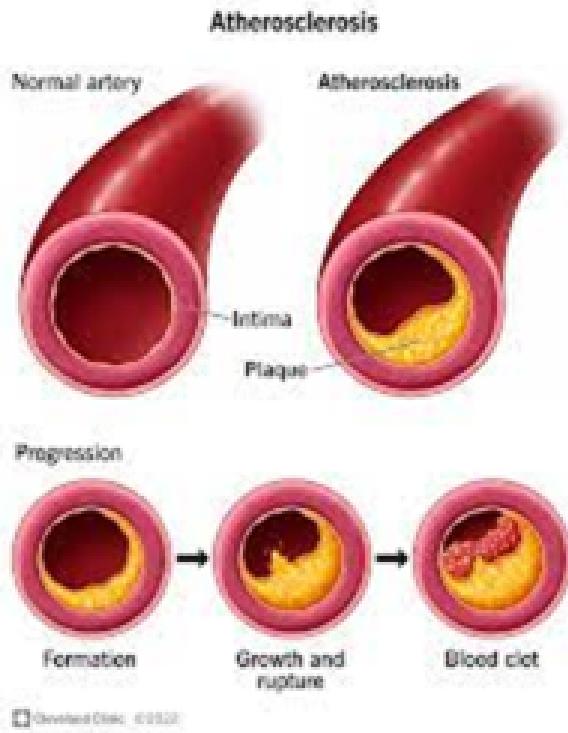
SPINAL DISC WITH NORMAL BONE MATRIX VERSUS DISC WITH OSTEOPOROSIS



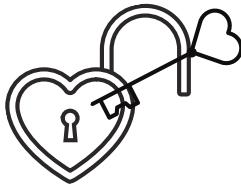
THE SECRETS OF ESTROGEN

Estrogens Role in the Cardiovascular System

Estrogen also plays a major role in the cardiovascular system where it is thought to be cardioprotective. Estrogen has a beneficial effect on a woman's cholesterol levels. It increases high density lipoproteins (HDL), the protein that carries cholesterol from other parts of your body back to your liver. In the liver, cholesterol is removed from your body. Therefore, HDLs have been called the good cholesterol. Estrogen also decreases low density lipoproteins (LDL) levels. LDL, or the bad cholesterol, can build up in blood vessels, creating plaque. The buildup of plaque in blood vessels is called atherosclerosis. It is a destructive lipid deposit that disrupts normal blood flow. It can build up in the blood vessel and obstruct the flow of blood to organs. When plaque dislodged from a blood vessel, it can travel through arteries and become lodged in smaller vessels, blocking oxygenated blood flow to organs such as your heart and brain. Coronary artery disease (CAD) results when the coronary arteries cannot supply enough blood, oxygen and or nutrients to the heart muscle. Cholesterol deposits (plaques) in the heart arteries and inflammation are usually the cause of coronary artery disease. Persons with CAD can experience tightness in the chest, also called angina and shortness of breath. CAD develops over many years, but the best way to avoid this is by eating a heart healthy diet.



A heart attack can also occur if plaque blocks the flow of oxygen rich blood in the coronary arteries from reaching the heart. This blockage of oxygen results in damage to the cardiac muscle and is called a myocardial infarction (MI) or heart attack.



An ischemic stroke is death of an area of brain tissue (cerebral infarction). This can be due to the blockage of an artery by a blood clot and/or a fatty deposit due to atherosclerosis. This fatty deposit, or plaque, can block an artery in the brain thereby starving that area of oxygenated blood. The area in the brain will begin to die within 4.5 hours without blood.

Estrogen has another important function in the heart. The heart contains estrogen receptors. These receptors bind estrogen and help to release nitric oxide which helps to regulate blood flow. It relaxes the blood vessel which may increase blood flow. As menopause approaches, estrogen production decreases which results in a decrease in the beneficial effects of nitric oxide on the heart's blood vessels.

The CDC recommends that persons age 20 or older and at low risk of heart disease have cholesterol levels taken every 5 years or more frequently for people with cardiovascular disease risk factors such as obesity, diabetes, or family history of heart disease or high cholesterol.

THE SECRETS OF ESTROGEN

continued from page 6

As estrogen levels continue to decrease, some women experience side effects of menopause. Hormone replacement therapy was used in the past for the treatment of symptoms of menopause, but many questioned the effects of the therapy on a woman's heart health. So, in 1991 the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) started a large study on the efficacy of hormone replacement therapy called the Women's Health Initiative (WHI). The trial studied estrogen-plus-progestin (HRT) in women with a uterus and estrogen-alone (ERT) in women without a uterus. Both studies were concluded early when the research showed that hormone replacement did not help prevent heart disease and it increased the risk for some medical problems.

A woman's risk of heart disease is less than that of a man's in our childbearing years. However, a woman's risk of heart disease increases as we age as our level of estrogen with its cardioprotective effects decreases. As heart disease is the number one cause of death in women in the United States, it is best to prepare for this normal decrease in estrogen's cardio protective effects as we age by following a heart healthy diet and exercising throughout one's lifetime. Knowing your numbers such as blood pressure, cholesterol and blood sugar levels is important as well your family history. Have a routine physical and speak with your health practitioner to maintain your best heart health.

ESTROGEN & REPRODUCTIVE HEALTH

Estrogen plays a vital role in sexual development and reproductive health. But estrogen is also a carcinogen, which means it has the potential to cause cancer. The effects of estrogen have been studied in many cancers that effect both men and women. Cancers of the breast, endometrium, ovaries, and prostate can be estrogen dependent. This type of cancer is stimulated to grow in the presence of estrogen. Some cancers may also be called hormone-dependent, hormone-positive, hormone receptor-positive or hormone-sensitive.

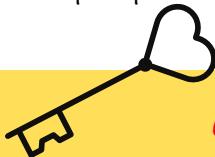
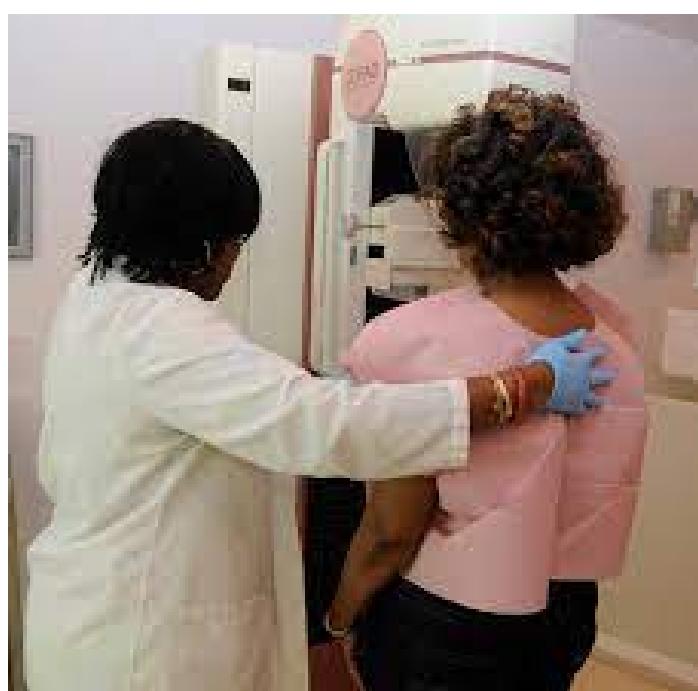


Most breast cancers are sensitive to hormones. If the cancer is hormone-sensitive, its cells have proteins on their surfaces called receptors. The receptors link to hormones like a lock and key. Estrogen receptor + (ER+) accounts for about 80% of breast cancers. Estrogen +/Progesterone+ (ER+/PR+) make up about 65% of estrogen-receptor-positive breast cancers and are also progesterone-receptor-positive.

ER+/PR-, estrogen-receptor-positive and progesterone-receptor-negative account for about 13% of breast cancers. These designations are important and help guide the Physician in their choice of chemotherapy used to manage the disease.

MAMMOGRAMS

Self-examination of the breast and mammograms are your first line of defense against breast cancer as well as knowing your family history. The United States Preventative Service Taskforce recommends that women have mammograms every two years when between ages 50-74 years old and are at average risk for breast cancer. An American woman's lifetime risk of breast cancer is 1 in 8.



THE SECRETS OF ESTROGEN

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Breast cancer has the highest mortality rate of any cancer in women between the ages of 20 and 59. African American women have a 31% breast cancer mortality rate – the highest of any racial or ethnic group in the United States.

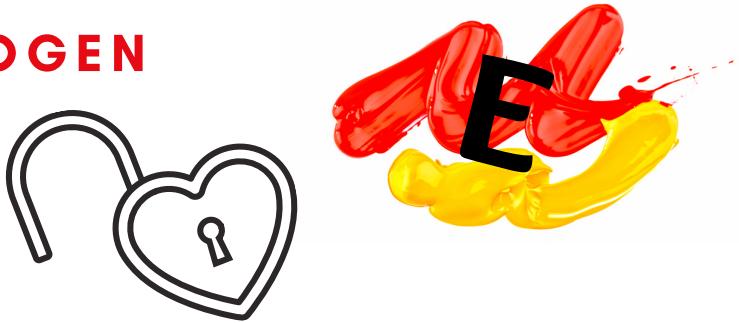
Younger women in general, and younger African American women in particular, are more likely to present with triple negative breast cancer, a more aggressive subtype which is difficult to treat and associated with a higher mortality rate.

It is recommended that women who are 40-49 years old talk to their healthcare provider about when or how often to get a mammogram based upon personal risk and health history. However, over the past 20 years, despite the universal decrease in mortality rates, we have seen an increase in the incidence of breast cancer in African American women. Again, African American women have a 31% breast cancer mortality rate – the highest rate of any U.S. racial or ethnic group. This can be decreased in part by earlier detection.

As black women have a higher risk of breast cancer, some practitioners suggest that having biennial mammograms in your forties is acting as your own best advocate.

In a woman's youth, menstruation signals the beginning of estrogen's effect on the uterus, but varying levels of estrogen can wreak havoc upon a woman during her lifetime. Perimenopause, or the phase of diminishing levels of estrogen leading to the end of menstruation, or menopause, marks an equally important phase in a woman's life as the absence or significant decrease of estrogen in a woman's body has its own significant effects.

Estrogen can be a carcinogen and prolonged exposure to estrogen can cause problems for some women. Ovarian, breast and uterine cancers are estrogen dependent cancers. Uterine cancer is the most common gynecologic cancer in the United States.



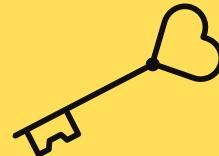
UTERINE CANCER RISK FACTORS

Your risk of uterine cancer increases if:

- You are older than 50
- Are overweight
- Have taken estrogen (buy itself) for hormone replacement during menopause
- Have had trouble getting pregnant or have had fewer than five periods in a year before starting menopause
- Taken tamoxifen, a drug used to prevent and treat certain types of breast cancer
- Have close family members who have had uterine, colon, or ovarian cancer

Uterine cancer can cause vaginal discharge or abnormal bleeding. Other symptoms, such as pain or pressure in your pelvis can occur. Bleeding may be abnormal because of how heavy it is or when it happens, such as after you have gone through menopause or between periods. Any bleeding after menopause (1 year without a period) is **abnormal bleeding**. It is best to see your doctor should you experience any symptoms or any bleeding after menopause.

Again, screening is your best defense. NIH suggests that screening for cervical cancer should begin at 21 with a pap smear. Women ages 30 through 65 should be screened with either a Pap test every 3 years or the HPV (Human Papilloma Virus) test every 5 years. If you or your sexual partner has other new partners, you should have a Pap test every 3 years. Women ages 65 through 70 can stop having Pap tests as long as they have had 3 normal tests within the past 10 years.



The Secrets of Estrogen



continued from page 8

Women who have been treated for precancer (cervical dysplasia) should continue to have Pap tests for 20 years after treatment or until age 65, whichever is longer.

If you have had your uterus and cervix removed (total hysterectomy), and you have not been diagnosed with cervical cancer, you do not need to have Pap smears. Speak with your health care provider to determine your best course for screening given your history.

Taking hormone replacement therapy (HRT) to control the side effects of menopause should be approached cautiously. Any therapy with estrogen should also have a progesterone component. Speak with your health practitioner to weigh the risks and benefits of this approach before starting HRT.



CLICK ON THIS LINK: [HTTPS://WWW.YOUTUBE.COM/WATCH?V=UGWD7QFJKBI](https://www.youtube.com/watch?v=UGWD7QFJKBI)

The effects of estrogen are truly ethereal in the brain yet felt by all women in different ways. It defies scientific measurement, making it impossible to quantify yet scientists are aware of the cause and effect. Fluctuations of estrogen levels are responsible for premenstrual syndrome (PMS), premenstrual dysphoric disorder, and postpartum depression. Conversely it modifies the production and the effects of endorphins, the "I can do anything" chemicals in the brain. Estrogen also increases serotonin, the natural antidepressant, and the number of serotonin receptors in the brain. It is thought to protect nerves from damage and even promote growth. Estrogen also effects the immune system, where we see its effects on the incidence of autoimmune diseases such as MS, RA, and SLE which are higher in women than in men.

Exercise, eating a healthy diet and getting the proper amount of sleep remains our best defense against the normal challenges that life brings our way. It is also best for women to stay current with all screenings and discuss having your pre-teens vaccinated against the Human Papilloma Virus (HPV).



TOP SECRET



The Secrets of Estrogen

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HEALTH AND SOCIAL SERVICE COMMITTEE NEWSLETTER



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VOLUME 11 - OCTOBER 2022

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