



Bio-Identical Hormone Replacement Therapy (transcribed from a lecture given by Dr. Biddle in Fall 1997)

What are natural hormones? I actually use the term “identical to natural” hormones, or BioIdentical Hormones, because I want to recreate what nature does in a perfectly functioning healthy body. Nature is the template. When I give a therapy, if I’m not just treating symptoms temporarily, I want to replace what the underlying deficit is.

For example, in menopause, the underlying deficit is a relative lack of progesterone as well as the 3 different estrogens that women make. Yes, there are three different estrogens. There is E1 which is Estrone, E2 which is Estradiol, and E3 which is Estriol, and there is Progesterone and of course the androgens such as testosterone.

Currently in conventional medicine, what is most prescribed is Premarin, which you may know, stands for Pregnant Mare’s Urine. It is a mixture of something that doesn’t occur at all in the human body, plus some Estrone and Estradiol. It doesn’t have Estriol. The other Estrogen that is commonly used in conventional medicine is Estradiol, under the trade name Estrace. Estrace is used because the way it is delivered has been patented.

There is a theory that in conventional medicine doctors are taught to use medications because medications are patented, and doctors learn what’s in the pharmaceutical-sponsored medical journals. When I get the Annals of Internal Medicine, I flip through and I see six-page glossy ads for the new drugs coming out. When I first heard this theory about 5 years ago I was very resistant to the idea because I did not want to think that I was being duped and that basically I was being spoon-fed what the pharmaceutical industry wanted me to know. Gradually I came around to realizing that it is true. Physicians basically learn what they learn in medical school and residency and they learn to do what the doctors before them have done. And what the doctors before them have done has been led by the pharmaceutical industry. Therefore they are only taught to use medications which are patentable and the pharmaceutical industry can make a lot of money off of. In spite of evidence showing the advantages of natural compounds, physicians for the most part still aren’t educated to use them.

For example, you can read a study showing that 500 mg of Vitamin C reduces by 50% the rate of re-occlusion after angioplasty, which is published in the American Journal of Cardiology last December, 1996. If that had been a patentable medicine, the study would be front page on the New York Times. When some patentable medicine gets a 5% result, it is front-page news. But when a natural compound gets a 50% result you’ll never hear about it.

For Progesterone, what's generally used is medroxy progesterone or Provera rather than the actual Progesterone that occurs naturally in the human body. The reason I like to use the term "identical to natural" hormones is because the ones that I use are in fact semi-synthetic. They are taken from soy beans or the wild yam as a precursor. The precursor is called diosgenin. It takes one biochemical step in a test tube to go from diosgenin to progesterone. Several other biochemical steps are needed to produce the different estrogens and testosterone. These are "natural" in that the biochemical molecule looks exactly like what the human body makes. They are semi-synthetic in that it has to be made in a test tube. That's why I call them identical to natural, so there is less confusion.

Let's talk about Estriol, or E3, because it is very important. Most people know more about the estrone and estradiol. Estriol is considered a weaker estrogen than the first two. The estrone and estradiol, E1 and E2, are very strong estrogens. They are very good for stopping the symptoms of hot flashes and vaginal dryness. Because they are so strong, they also increase the risk of breast cancer because they stimulate breast cell proliferation. Estriol, on the other hand, is a weaker estrogen internally but still strong externally. In other words, it treats the skin and genitalia very well. It helps prevent vaginal dryness and aging. But, it has actually been shown in several studies to be protective against breast cancers. It has even been used as a treatment for breast cancer in Europe. E3 is much like phyto-estrogens. Phyto-estrogens are estrogen-like compounds from plants, like soybeans. You may have heard about them. They basically are weak estrogen stimulators; if you are low in estrogen they will stimulate your receptors and if you are high in estrogen they will sit in the receptor site and block the stronger estrogens.

Most Americans are estrogen dominant, both men and women. They have too much estrogenic stimulation of their receptors. One reason is because Americans are overweight and our fat cells convert the adrenal hormones into strong estrogens. The second reason is because we live in a "sea of estrogens". All the pesticides, plastics and petro-chemicals look like estrogens to our cell-membrane receptors. For example, DDT was outlawed because of its effects of being an estrogen-mimic.

There is a lake in Florida you may have heard about where there was a pesticide spill. The next generation of crocodiles in that lake, the males, all had little micro-penises and they could no longer reproduce because of estrogen dominance. The estrogen dominance came from a pesticide.

The sperm count of the average American male is now half of what it was at World War Two because of estrogen dominance. If this happened in a wild population, we would go extinct in three generations. So, everything we put out into our world comes back to us, and becomes part of our bodies. This is why I'm a member of an intentional community called EarthHaven. We have 325 acres south of Black Mountain. We are building a demonstration ecovillage based upon permaculture principles, working on educational outreach about how people can live in harmony with the earth and each other so that 10 generations from now our offspring will still be healthy and alive. Permaculture is a term that means how you live in harmony with the earth and still live in a way that's good for yourself too. (see <http://www.earthaven.org>)

So, back to hormones. In an intact menstruating female, the three estrogens are present in an approximate ratio of 10%, 10% and 80% respectively of E1, E2, and E3. The latest I heard at a conference last week shows it is probably more like 3%, 7% and 90%, so even more E3 than the other estrogens. It is thought that the protective effect of Estriol or E3 is one of the reasons why premenopausal females have a normal or baseline rate of breast cancer, which is less than postmenopausal females.

Measuring what the ratio is of estriol to (estrone and estradiol combined) has been shown to predict the risk of breast cancer. Several studies show that if your ratio of E3/ E1+E2 is too low, you have increased risk for breast cancer. In other words, if you have too much strong estrogen relative to weak estrogen, it puts you at increased risk for breast cancer.

The next topic is Progesterone. There is really only one Progesterone, and that's the natural Progesterone that your body makes. Physicians inappropriately use the work progesterone for the other compounds that they prescribe, such as Provera, that are actually progesterone mimics, or progestins. Synthetic progestins have been shown to increase the risk of birth defects if taken while pregnant, while progesterone is the natural hormone that supports pregnancy. The word progesterone comes from "Pro-Gestational Hormone".

Synthetic progestins cause adverse side effects because they can't go down the normal metabolic pathways of detoxification and de-activation. Our body has complex pathways in order to metabolize away hormones and other compounds, so it can regulate how much you have. If you have a little bit too much you can speed up the metabolic pathway and get rid of it. If you don't have enough, it can slow down the pathway and let it build up some. With synthetic compounds, it's my theory that it can't do that.

Let's talk more about estrogen dominance. Most people know that in menopause, women stop making enough estrogen. However, the production of progesterone can start to drop off long before menopause. Women can get a decrease in the production of progesterone long before they start dropping off the production of estrogen. When they are in their early 30's, women have a balance of estrogen and progesterone. As they go into their 40's, the progesterone starts to fall off some, but they don't have concrete signs like hot flashes and such. What happens in somebody when they are dropping off the production of progesterone but still making enough estrogen is they start to get worsening PMS, fibrocystic breast disease, uterine fibroids, weight gain, depression, and their risk for breast cancer goes up.

What does it feel like to be in estrogen dominance? Estrogen effects include breast stimulation (so breasts are often more swollen), increased body fat (getting you ready to carry a baby), and salt and fluid retention, although it actually improves the lipid panel. Estrogen excess interferes with thyroid hormone function by decreasing how thyroid is received at the receptor site and also by decreasing the conversion of T4 and T3 (T3 is the more active thyroid hormone).

Another example of the contrasting effects of estrogens and progesterone on the female body is pregnancy. A healthy 30-y/o female makes approximately 30 mg progesterone a day in her bloodstream. At the third trimester of pregnancy she makes 300-400 mg progesterone a day, and most women feel great then. That's because of progesterone. Then, they give birth, the placenta comes out, and they have no progesterone until they ovulate and go into the luteal phase and start making progesterone again. So what do women typically experience during this transition? With high progesterone they feel great, then with no progesterone they have 2 weeks of postpartum depression or the baby blues.

That's what it feels like to be in progesterone deficiency. That's what women come to me and say they feel like when they're put on Premarin but no progesterone because they simply don't have a uterus. The uterus is not the only place in the human body that has progesterone receptors. Just because a woman doesn't have a uterus doesn't mean she doesn't need progesterone.

The next topic is the delivery of hormones, which generally involves pills, patches, or creams. In the past I've used mostly creams and I've been reviewing that now because I've had clinical results of testing showing creams to be overdosing some people. The other problem is that you can't cycle creams very well. The creams are very well absorbed into the subcutaneous fat layer; it takes a couple of weeks to reach steady state and then you reach steady state or slowly continue to build some. You can't use it for cycling women because you can't turn off the subcutaneous release of the hormones. After you stop using the cream, it can release for weeks for weeks or even months So we're starting to use more of the oral. One of the original reasons progesterone wasn't used orally was because it is very quickly metabolized, but the compounding pharmacies have been doing a lot of research on how to improve the absorption using micronized oral progesterone. Most women can use it just once a day; but sometimes you have to go to twice a day.

Let's talk about the effects of hormones on lipids. In the PEPI Trial, the estrogen that they were using was actually horse estrogen in the form of premarin, but it still showed that estrogens improved women's lipid profiles. It raised their HDL significantly. However if they gave a synthetic progestin, Provera, it almost completely eliminated that gain, losing 80% of the increase in HDL. On the other hand, if they gave natural progesterone they only lost about 10-20% of the gain. So, that natural progesterone shows a much better lipid profile effect. Natural progesterone has also been shown to protect from endometrial hyperplasia, or the overgrowth of the uterine lining potentially caused by unopposed strong estrogens. There are several studies that show that the oral natural progesterone can control endometrial proliferation when used against estradiol.

Unfortunately, there is no evidence, no studies done, showing the progesterone creams do the same thing. I don't expect those studies to be done, because who is going to fund them? Nobody has a stake in making any money off of this. Progesterone creams are cheap and available without a patent. It's not tangible. I don't expect anybody to study the effects of transdermal natural progesterone because there are 2 reasons most studies are done. The most common reason is when a drug company looks at the possibility of eventually making a bunch of money off of a product by having a patent on that product for fourteen years. That's who funds most studies. The other reason is when enough public outcry occurs concerning an issue that the NIH funds a study. Eventually that may happen with things like this. But it hasn't happened for things like chelation therapy.

So, the next hormone to discuss is DHEA. I use DHEA some, usually just in conditions for which it has been well studied. Usually I just bring DHEA back into the therapeutic zone, which I usually measure.

I mentioned measuring hormones a couple times. How do I measure it? There are two good ways to measure: Saliva testing and 24-hour urines. Saliva testing is the only real good way for a cycling female because you have to figure out what's happening each stage, so on the saliva test the patient simply takes home a kit and every 3 days collects some saliva, freezes it, does it for a whole cycle, has 10 different samples and the lab plots out a very nice graph. I see many examples where women are not ovulating at all, so that's why they are having symptoms of bloating, weight gain, PMS, fibrocystic breast disease, uterine fibroids, etc. Those are signs of estrogen dominance because if women don't ovulate, they are not going to have a corpus luteum, and they won't produce any progesterone. Therefore they get progesterone deficient and in estrogen excess. They then have the adverse effects of estrogen excess. In that case I give them oral micronized progesterone from days 18-28 and they do very well. I get to be their best friend. It's nice.

How many of you have ever been tested to see if your estrogen and progesterone levels are appropriate? Do you think every woman in the country needs either a 0.6 or 1.25 mg dose of premarin? What is the natural dose of horse urine for a human? I don't know. I don't think you can measure it. It's a totally different estrogen.

I'm not particularly in favor of mammograms because there is two sides of the story on mammograms. On one side, there is a voice that makes a lot of money off of doing them.

There's a whole other side to the debate. I don't talk people out of mammograms, or into them. I counsel them about the risk-to-benefit ratio and go over their family history, and tell them about how they can decrease their risk of breast cancer. I generally ask them to check their intuition about whether they need a mammogram.

I do a lot of testing for osteoporosis and there is a urine test for this too. Basically the bone tests tell you where you are right now. If you get another one two years later it will tell you how your bone density changes. Of course you have that inevitable variability of standard deviation going on where you will have a 5% change by statistics. The urine test tells you at this moment whether you are losing bone mass and how fast. What is your risk for developing further osteoporosis right this moment? With that you can see the rate of change of bone loss or bone gain right now and make interventions such as progesterone, estrogen, strontium, boron, magnesium, and zinc. You know, a woman with osteoporosis does not have a total body deficiency of calcium. It's just in the wrong places. It is in her arteries, in her kidneys, her brain, making everything else not work so good. What you have to do is keep it in her bones. There was a great study done showing that getting magnesium and zinc reversed osteoporosis better than giving calcium. Because Mg and Zn keep the Ca in the bones. Also, weight bearing exercise. We have our patients lift weights and get rid of soda pop because phosphate and sugar leech calcium out of the bones. This is how you do it.

Does estrogen prevent heart disease? There is only one study I know of that actually has done a control of giving people placebos VS estrogen. The ones given the horse estrogen had an increased risk of heart disease compared to the other. It's a simplistic idea to think that since women have less heart disease than men, it must be estrogen that prevents it. It's actually because women bleed and get rid of excess iron. Iron overload is why men have an increased risk of heart disease. We all take antioxidants to prevent heart disease. Iron rusts; it is a strong oxidant. There was a great study done showing that men who donate blood 3 times a year decrease their risk of heart disease to equal that of menstruating female. Very nice study.

I test the ferritin level to check iron status, and if it is low I do recommend iron. I'm shooting for a ferritin of about 100 or less. The lab values goes from 20-350, but if your ferritin gets up to about 200 you can double your risk of heart disease. I don't want my patient's to have a risk factor of 200%. So I want them down around 100 and if they can't donate blood for some reason I order therapeutic phlebotomies or we do it my office. As part of the conclusion, I want to talk about what else to do with a patient besides balance their hormones, including a program of diet, supplementation, exercise, stress reduction. I consider myself a holistic physician when I look at a person. I don't look at a person as a case of menopause, but as a woman with menopause.

I'll give you my dietary philosophy in a nutshell because I think it's healthy for everybody. However, it's going to look different for everybody.

First, you need adequate protein. Not high protein. Not low protein. Adequate protein. We figure out the protein requirement the same way that a hospital nutritionist does: lean body mass X activity level.

For example, approximately 140-lb woman with 20-25% body fat is going to have 110 lbs of lean body mass. If she is exercising occasionally, she's going to have a conversion factor of 0.7. If you multiply 110×0.7 , she needs about 70 grams of protein a day just to maintain muscle mass.

What does 70 grams of protein look like? Well, it's very close to the minimum US-RDA of 60 grams. Knowing that one ounce of meat, fish or cheese is 7 grams protein, then that's only 10 oz of high-density protein food spread throughout a day. So that's not high protein. An egg has 6 grams and an egg white has 4 grams of protein.

Next, you need healthy fats. The low-fat diet is killing Americans, especially diabetics. During the last 15 years, obesity has increased by 50% and adult-onset diabetes has tripled while Americans have been following the low-fat diet. Not simply advised to follow it but actually followed it. I'll go into why just briefly. Fats are not to be avoided, fats are our friends. You should eat a lot of them, but you certainly need to know what is a good fat versus a bad fat. Please stay away from hydrogenated fats, which are artificially saturated. Also decrease saturated fats. These are solids at room temperature and they make your cell membranes stiff, which is one of the definitions of premature aging. Basically if your cell membranes are stiff and rigid, the cells of your immune system and your nervous system can't communicate with each other, causing lots of problems there. You should eat a lot of monounsaturated fat, which are in olive oil and avocados, hence the benefits and the so-called paradoxes of the Mediterranean diet. Please eat lots of polyunsaturated fats such as Omega-3 and Omega-6 fats, which are essential fatty acids. Most Americans are deficient in Omega-3 fatty acids because these fragile fats go rancid very easily and are therefore removed from processed foods. Right now the wheat growers are developing strategies to grow strains of wheat that are deficient in omega-3 fatty acids to extend the shelf life. But we need Omega-3 fats. So we supplement them with flax oil, cod-liver oil, and cold-water fish like salmon, sardines, and mackerel. Essential fatty acids are like antifreeze, liquid at very low temperatures. For example, flax is a cold weather grain, so it has a lot of healthy fats. When you take polyunsaturated fatty acids you have to take a lot of antioxidants like Vitamin E, Vitamin C and Lipoic acid. Because those fats can go rancid not only outside your body but also inside your body, so you have to have anti-oxidants.

That leaves us carbohydrates. Americans have been there are two types of Carbohydrates (CHO): simple and complex. We've been told to eat a lot of complex carbohydrates. But I'll tell you that there are actually three groups of carbohydrates. There are simple sugars, starches, and fibrous carbohydrates. You've been taught that both the starches and the fibrous groups are all complex CHO. I say that's a lie. Only the fibrous CHO are truly complex. Those are the green and leafy vegetables: broccoli, asparagus, kale, cabbage, and things that you get out of your garden. All the sugar in there is so bound up in fiber that you don't get a high glycemic index, instead you get a slow release into your blood stream so you don't get a big insulin surge. The starches are just one glucose molecule hooked onto another, so as soon as you chew it the amylase in your saliva breaks it down into glucose. Starch has a glycemic index usually in the 90's. White potatoes, bread, rice, pasta, and bananas - the very things we're telling our diabetics to eat are killing them by raising their insulin levels. Of course we should avoid simple sugars. Everybody knows that. What we also have to do is have people cut down on starchy foods.

So there are several main keys to the dietary approach we recommend: high fiber, low starchy and simple carbohydrates, healthy fats, and adequate protein. It changes per individual because the amount of carbohydrates you can eat without getting an insulin surge is different depending on your genetics, your weight, your age, your gender, how much you exercise, and what you've been eating recently.

When I agreed to come give this talk, I was reluctant. Because I've gone through internal medicine residency, I'm Board Certified, I've been a cynic, and I've been a critic. I did not get into this "alternative" stuff until my last year of residency. I did not believe most of it at that time. I even talked my mother's boyfriend out of getting chelation therapy and into a bypass surgery and 6 years later, he needed a second bypass surgery. I'm ashamed of that particular fact. If he had made dietary changes and gotten chelation therapy he would have done much better. So I agreed to come to share with you what I do and to share with you my passion about trying to mimic nature as much as possible.

Questions....?

Estrogen helps decrease the rate of bone loss for about 5-6 yrs. After that it loses its effectiveness. It does not reverse osteoporosis, it slows it down. It inhibits osteoclasts, so it slows bone loss, but does not promote bone growth. Look in your basic physiology textbooks. Progesterone activates osteoblasts. You can increase bone density by 5% a year with natural progesterone. It will build bone back so you can get reversal of osteoporosis, not just slowing. So, Progesterone and testosterone are much more important for osteoporosis than estrogen ever will be.

I don't think all women need hormones after menopause. If you look at indigenous cultures, they go through menopause very easily, they don't have symptoms, they simply stop menstruating, they have a ritual of cronehood and are respected for their wisdom. Everybody looks up to them and they become teachers. In the USA, less than 18% of postmenopausal women in the U.S. stay on estrogen therapy. That means that over 80% of women are either doing fine with out it or else missing out on something; probably both. I think there are many women who will do fine without hormone therapy and I think it depends on how slender they are, how naturally they live, how much they exercise, and what their history has been. If they are living on organic foods, they are getting less pesticides and therefore less estrogen dominance, then they may do better. If they are exercising and not overweight then they may do better. The more estrogen dominance you have before menopause, the more symptoms you're going to have after menopause. The more we eat phyto-estrogens and avoid xeno-estrogens, then the less we will be in estrogen dominance before menopause, so can go through menopause more easily. Many herbal remedies can get women through menopause just fine. I'm not an expert in herbal remedies, but I use a few. For example, Vitex works at the hypothalamic level to increase LH and therefore help the production of progesterone.

I go by symptoms and testing. The heavier a woman is the less she may need estrogen, in fact she may be in estrogen dominance, so I may just give progesterone. You can have estrogen deficiency and estrogen dominance at the same time because that's a relative aspect in relationship to progesterone. In other words, many women are more deficient in progesterone than they are deficient in estrogen. I want people balanced. And, based on bone density, breast cancer risk, how they feel, symptoms, and testing, you have to work out their individual treatment program.

There is no "typical woman", but if you take your average statistical woman, the statistical woman will end up on about 10-15 mg of transdermal progesterone a day along with about 1.25 - 2.5 mg of BiEstrogen, which is a compound that has 80% E3 (estriol) and 20% E2 (estradiol). Estrone is the one that is the most suspicious for causing breast cancer, so I no longer put E1 in at all. So 2.5 mg of BiEstrogen a day, which is 20% E2, yields 0.5 mg of estrace, which is equivalent to the Estraderm patch. And then some of them need testosterone. If they've had their ovaries removed, they definitely need testosterone. Their husbands will thank you because testosterone is vitally important for libido and bone density and muscle mass.

Question: 'Where do get it from?'

There are 2 compounding pharmacies in town here, Nature's Pharmacy (Bill Cheek and Mike Rogers) and the Medicine Shoppe (John Boff). It's a prescription item, no different than anything else. The best book out now for dietary philosophy is called Protein Power by Michael Eades. We actually sell it at our clinic. There are two problems with that book, the first is the title makes it sound like a high protein diet. It's not. It is an adequate protein diet. The second is the chapter on essential fatty acids. He was confused about the pathways and what happens, and he tells people to avoid omega-3 fatty acids, which is exactly backwards, you need to get a lot of omega-3 fatty acids. And, he knows he's wrong. He has come and visited our clinic to see what we do. He's opening up a new clinic in Colorado and he's modeling it after our clinic to a certain extent. He's writing a second book right now to correct that defect of his first book. The interesting part about this field is it is always changing. I always learn something new. I tell my patients, your other doctor may know everything already but I don't. I'm learning something new every week, so next week I may have to tell you something different.

Autoimmune disease: In general we can calm the immune system by giving the appropriate fatty acids. You have to think about prostaglandins. There are 3 cascades. Series one and three are mostly soothing; series 2 is mostly inflammatory. If you give people NSAIDS or aspirin, it just cuts off all the prostaglandins, including the healing ones. That's why they cause ulcers because your stomach lining needs healing (series 2) prostaglandins to regenerate. That's why NSAIDS increase arthritis in the long run because your cartilage needs the healing prostaglandins to regenerate. It is not wise to cut off all prostaglandins. What you want to do is manipulate the diet so you create more P2, the 2nd series of prostaglandins. The way you do that is two fold. First, you eat the right types of fats; saturated fats and hydrogenated fats cause production of inflammatory prostaglandins. Monounsaturated fats are neutral. The essential fatty acids, especially certain types of omega-6 (like borage oil and evening primrose oil), and then the omega-3s found in flax oil or cod liver oil will help the series 2 prostaglandins be reproduced. The second major dietary thing is to lower insulin. Even if a person is not insulin dominant as in a type-II prediabetic, they may be having insulin surges. The way most of us eat we get insulin surges three or four times a day. That's why we get energy fluctuations throughout the day, mid-morning and mid-afternoon slumps when our blood sugar drops. Each time our insulin surges it pushes our prostaglandins down the wrong path. In addition, we should eat smaller meals more often.

We have good track record of reversing adult onset diabetics, getting over 50% of type-II diabetics off insulin, reversing obesity, and reversing heart disease. I have cancer patients, but I don't do specific alternative anti-cancer therapies. I support their immune systems, digestive systems, and hormonal systems so they can improve their quality of life, fight off infections, live longer, and perhaps increase their chance of a spontaneous remission.

Anti-aging? What does nature want you to be doing?

Oh, by the way, the Latin word for Doctor means Teacher. Not healer. It's our job to educate our patients about how to cure themselves, in my humble opinion.

I appreciate the opportunity to talk to you. Thank you.