"Natural" or "Bioidentical"
Hormone Replacement: 
What Makes the Difference?
An Interview with Christopher B. Cutter, MD

Jane Vail

Christopher B. Cutter, MD, an associate professor of medicine at UCLA School of Medicine in Los Angeles, is affiliated with Valley Health Care Group in Burbank, California. Dr. Cutter is board-certified in family medicine. He provides a broad spectrum of care for patients who range in age from newborns to the very old, and much of his practice is devoted to bioidentical hormone replacement therapy (BHRT). In the following interview, Dr. Cutter explains his choice of bioidentical hormones as the primary treatment for hormone deficiencies.

Which types of hormone replacement do you provide?
I've been prescribing compounded testosterone for about 5 years and compounded estrogens for about 4 years. For the last couple of years, the hormone treatments that I have prescribed (progesterone, dehydroepiandrosterone [DHEA], testosterone, and estradiol) have been exclusively bioidentical, with the exception of those for a few patients whose insurance won't cover compounds. For women in those circumstances who require hormone replacement, I use Premarin, a manufactured progesterone, which is not a bad product. Premarin, however, releases all its progesterone over just a few hours; that can cause breakthrough bleeding and can negatively affect mood by not providing progesterone throughout the day. Compounded progesterone, on the other hand, can be made in a slow-release form so that breakthrough bleeding is prevented.

Why are bioidentical hormones more effective than other types of hormones?
Bioidentical hormones seem to be safer and more effective than conjugated equine estrogens (Premarin) and medroxyprogesterone acetate (Provera). Premarin does provide relief from hot flashes and urogenital symptoms, but it is a nonhuman formulation. It consists of about 11 compounds, each of which is further broken down and metabolized into several other compounds. You end up with a large mishmash of estrogens circulating through the body that, although it does have some benefit, also exerts other effects that are not well defined and may be harmful. In addition, we cannot monitor the level of Premarin because it is a complex mixture. When I use Bi-Est and Tri-Est, I can measure estradiol after the initiation of therapy to accurately determine the level of that hormone in the blood. That way, I know I'm not prescribing an insufficient dose or a possibly toxic dose (estriol in very high doses can be harmful).

The chance of having a malignancy develop or a thromboembolic event occur exists even when bioidentical estrogens are used; we can monitor the blood level of bioidentical hormones and keep their concentration in a physiologic (normal) range. Some studies indicate that Premarin builds up bone and protects the vagina, but others show that estradiol, estriol, and estrone, which are derived from plants and are identical in structure to endogenous human hormones, also provide benefits.

Why use estrogen from horse urine in humans when plant-based derivatives are identical to human estrogens?

Which benefits are noted by patients taking bioidentical hormones for the relief of menopausal symptoms?

Hot flashes sometimes disappear with the first dose, although more time may be required and the dosage may have to be adjusted. When I prescribe BHRT, I start with a low dosage and work up. An improvement in bone density may require 3 to 6 months.

Most patients treated with estrogens feel that they experience an improvement in memory and in generalized mood, and treatment with progesterone reduces irritability and emotional lability.

Is progesterone safe to use in BHRT?
There has been good evidence for many years that progesterone is a safe hormone and that it should be the preferred progestin for use in hormone replacement. It is a complete mystery to me why so many physicians have neglected it. Many practitioners were taught that progesterone is not absorbed through the gastrointestinal tract and that it can be administered only intravaginally. Actually, progesterone is absorbed by the gastrointestinal tract (although it does undergo some first-pass metabolism), and it works very well when applied in a cream to the trunk or the arms.

We are still lacking large double-blinded studies on the use of progesterone in hormone replacement, but there is a great deal of compelling evidence that it may protect the breast against cancer and benefit the bones, the mind, and the mood. It also does not seem to exert negative effects on the heart. When the flurry of phone calls came in regarding the results of the Heart and Estrogen/Progestin Replacement Study Follow-up (HERS II) trial, I was able to tell all my patients not to worry, because they had not been taking Prem-Pro. That was a tremendous relief.

Even before the HERS II study results were published, what had prompted you to prescribe bioidentical hormones as opposed to other types of hormones?
I obtained a very good education when I was invited to speak on testosterone replacement therapy at a symposium sponsored by the Professional Compounding Centers of America. I had the privilege of attending lectures by Dr. Jean Lorentzen and Dr. David Zava, who provided excellent information about the biochemistry of BHRT, its effects, and the details of precisely how to prescribe it to benefit patients.

Which dosage forms of compounded estrogens do you prescribe?
I tend to give the estrogen in a capsule, but some women (especially those with a
When it comes to creams and gels, it's important to be aware of their potential side effects. Use of creams and gels can lead to irritation, burning, or sensitivity. Always read the label and instructions carefully.

Are you concerned about the effects of creams and gels on your skin? Consider the following:

1. Read the label carefully.
2. Use a small amount on a small area.
3. Monitor for any signs of irritation or sensitivity.
4. Discontinue use if any adverse reactions occur.

When using creams and gels, always follow the instructions provided by the manufacturer. Contact a healthcare professional if you experience any unusual reactions.

In summary, while creams and gels can be beneficial for skin care, it's important to be cautious and use them appropriately.
out intervention, they would have died. I explained to each of those patients that because of his or her age, the use of BHRT would be controversial, but many of them were willing to try it. The results of that therapy (an improvement in memory after 1 month of treatment and an increase in overall strength, balance, and mood) have been positive. For example, one of my patients (an elderly woman with osteoporosis) had been falling. She had been taking Fosamax, but we wanted to do everything we could to improve those bones. It has been shown that intensive hormone therapy can lead to an improvement in bone strength after 3 to 6 months of treatment. Adding estrogen to bone-building medications like Fosamax has a very positive effect. I decided that (at the very least) I would be increasing that patient’s bone strength so that if she fell 6 months after she had started therapy with BHRT, her bones would be a bit stronger than they had been before treatment. The ideal effects of BHRT include an improvement in outlook, clarity of thinking, and balance. In an elderly patient, a fall can be the beginning of the end. The events that follow a broken hip are often terminal; many such patients die within a year. I’ve used BHRT to treat a very small number of elderly patients. As I gain experience with that type of therapy in that population, I feel more and more comfortable prescribing bioidentical hormones if the patient understands that the treatment may produce some unknown effects.

Which type of BHRT do you prescribe for younger women?

I have found that many perimenopausal women or those in their 30s have a relative progesterone deficiency, and their life is terribly affected by premenstrual tension. Those women sometimes ask for antidepressants. They notice a worsening of mood just before they menstruate (during the luteal phase of their menstrual cycle). I have prescribed 200 mg of compounded progesterone as a trial to be taken by women with that symptom at bedtime 2 weeks before their menstrual period. Several women treated with that protocol have told me that they no longer need antidepressants and that they feel so much better! Some noted a positive response to progesterone just a few days after therapy was initiated. If the options for treating depression are Prozac or progesterone, I’d rather administer progesterone. It, unlike Prozac or other selective serotonin reuptake inhibitors, does not diminish libido.

In which cases do you prescribe testosterone replacement therapy?

During the last 5 years, I have screened more men for testosterone deficiency than I did during the prior 15 years. Usually, that type of deficiency is not discovered unless a specific blood test is requested. Many men have a mild-to-moderate testosterone deficiency, and a significant number have a severe deficiency. Physicians should screen men for a low testosterone level much more frequently than they now do. The test is simple: A blood sample is obtained in the morning, because that’s when the serum level of testosterone is highest. Screening with a saliva sample is also reliable and inexpensive.

Will you continue to prescribe only BHRT?

Yes. There’s a lot of good that we as physicians can do to help patients who have a sometimes subtle hormone deficiency. Some women experience severe symptoms of premenstrual tension or menopause, and with the right treatment they feel immeasurably better. Many men who are treated for a testosterone deficiency also have a much-improved quality of life. I’ve realized how different my practice is now; it’s very rewarding, because using compounded formulations enables us to carefully adjust the dosage of those very effective preparations to achieve maximum benefit. It’s great to have patients so happy with their treatment.

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Cushing's Synrome

AN OVERVIEW OF EQUINE CUSHING'S SYNDROME

Janet Hall

A disease of the bovine adrenal glands, diabetes mellitus, and Cushing's syndrome have been reported in horses. These conditions are most likely to occur in older horses and are usually identified by a decrease in appetite, loss of weight, and an increase in thirst. The diagnosis of Cushing's syndrome is often difficult because the symptoms are similar to those of other diseases. The syndrome is caused by an overproduction of adrenocorticotropic hormone (ACTH) by the pituitary gland, which stimulates the adrenal cortex to produce cortisol. The increased cortisol production results in increased glucose metabolism and protein catabolism, leading to a decrease in the production of insulin and other hormones that regulate blood glucose levels. The increased cortisol levels also cause an increase in the production of aldosterone, which increases the amount of sodium and water retained by the kidneys. This can lead to an increase in blood pressure and a decrease in blood flow to the kidneys, which can result in kidney failure. The increased cortisol levels also cause an increase in the production of corticotropin-releasing hormone (CRH), which stimulates the production of ACTH. This can lead to a vicious cycle of increased cortisol production and increased CRH production, which can result in a chronic state of hypercortisolemia. The symptoms of Cushing's syndrome are usually seen in older horses and can include weight loss, increased appetite, decreased exercise tolerance, muscle weakness, and a decrease in the production of testosterone and other sex hormones. The diagnosis of Cushing's syndrome is usually made by the detection of hypercortisolemia, which can be measured in blood or urine samples. The treatment of Cushing's syndrome is usually aimed at reducing the cortisol production, which can be achieved by the administration of adrenocorticosteroids or by surgical removal of the adrenal glands. However, the long-term prognosis for horses with Cushing's syndrome is usually poor, and the disease is usually progressive, leading to a decreased quality of life and a decreased lifespan.
Cushing’s Disease or Cushing’s Syndrome?
Philip J. Johnson, BVSc(Hons), DVM, MS, Diplomate ACVIM, MRCVS, a professor of internal medicine in the College of Veterinary Medicine at the University of Missouri-Columbia, is a specialist in the treatment of disorders such as equine Cushing's syndrome. He differentiates the human form of the disease from the type that occurs in horses. "Cushing's disease' refers to the clinical manifestations of excess glucocorticoids (adrenal gland steroids) resulting from a pituitary tumor in humans. In horses, that condition is called 'equine Cushing's syndrome.' The type of pituitary tumor and the resultant hormone abnormalities that occur in horses differ from those in humans. The cause of the tumor that produces equine Cushing's syndrome is unknown. Horses of all breeds and both genders are affected, and the disease is not endemic to a particular geographic area. No known environmental conditions trigger it, and it is not transmitted by any known vectors. Until we know the cause of classic pituitary-dependent equine Cushing's syndrome, we can suggest no precautionary action. It can be attributed to other nonpituitary causes such as the administration of steroids, primary adrenal gland disease, diseases of the hypothalamus, and cancers that produce hormonally active substances, but those occurrences are very rare."

Supportive Management and Drug Therapy Produce Optimal Results
Dr. Johnson noted that a combination of appropriate management ( hoof care, hair-coat management, dental care) and the use of an effective drug (cyproheptadine or pergolide) produces the best response. "Pergolide acts like dopamine (a neurotransmitter in the pituitary gland), and cyproheptadine inhibits serotonin (another neurotransmitter in the pituitary gland)," he explained. "However, many cushingoid horses do not respond to cyproheptadine. Pergolide is more effective in inhibiting the hormonal activity of the pituitary tumor. Usually, low-dose orally administered pergolide therapy is prescribed; most horses respond to 0.5 to 1.0 mg/day. Adverse effects from treatment with pergolide have not been reported to a meaningful extent, although the bioavailability of the orally administered drug varies among horses. Pergolide has not been specifically approved for use in horses, so the drug prescribed in pill form for humans is often crushed and mixed with the horse's feed. However, the dose of pergolide for horses is quite low when compared with that prescribed for humans.

"Improvement from pergolide therapy, which is usually noted in 3 to 4 weeks, is manifested in the reduction of water consumption to a more normal level, improved diagnostic test results, appropriate shedding of the hair coat, less lamination pain, and fewer infections. Without treatment, some affected horses succumb to secondary effects of equine Cushing's syndrome; for example, disease-related neurologic impairment or laminitis. Treated horses, however, are less likely to be affected by complications caused by the disorder. They are also more comfortable and have a better quality of life."

Angel DePuy, DVM, a veterinarian in the equine division of the veterinary hospital that managed Silver's treatment, has also identified Cushing's syndrome in many horses and ponies. "If we suspect that a horse has Cushing's syndrome, we measure the amount of ACTH in its blood. The ACTH test involves a one-time blood draw and, unlike the dexamethasone suppression test, it does not require the administration of steroids that can induce laminitis in a cushingoid horse. The sensitivity of the plasma ACTH concentration as an indicator of equine Cushing's syndrome is 90.9% in horses and 81.8% in ponies, and the specificity of the test is 100% in both groups. Hyperglycemia and sometimes an elevation in alkaline phosphatase or an increase in triglyceride or cholesterol levels can also occur. Surgery is not an option for the type of tumor that causes the problem, and the tumor will never go away. It might enlarge and impinge on other areas of the brain, but usually it simply persists and causes no problems other than Cushing's syndrome."

Dr. DePuy also relies on pergolide as a first-line treatment. "Pergolide, a type 2 dopamnergic agonist, is now the most commonly used therapy for equine Cushing's syndrome," she said. "Pergolide replaces dopamine, which many cushingoid horses lack. It's more effective than cyproheptadine, which is an antiserotonergic and antihistamine, and it provides better control of the disease. Horses just don't seem to respond as fully to cyproheptadine; some symptoms may improve with treatment but others do not. For example, skin infections may resolve, but the hair coat may not shed well. I prescribe 1 mg of pergolide administered