“STEROID” is often used as a generic term to refer to medicines that treat a variety of inflammatory conditions. Most commonly, steroid is used as a shortened name for corticosteroids, also known as glucocorticoids. These medications play important roles in reducing the inflammation that plagues individuals with primary immunodeficiency (PI), as well as helping with side effects that may accompany some of the treatments for PI. Corticosteroids should not be confused with the banned “anabolic steroids” used illegally by athletes to gain advantage in competition. Instead, corticosteroids are legitimately used steroids that offer no athletic advantage, but rather are very helpful for the treatment of inflammatory disorders. Commonly prescribed corticosteroids include prednisone (sold under many brand names such as Deltasone and Sterapred), methylprednisolone (Medrol), prednisolone (Prelen, Pediapred), dexamethasone (Decadron, Hexadrol) and hydrocortisone (Acticort, Cortef). These products are most typically prescribed to treat diseases that cause inflammation such as multiple sclerosis, lupus, rheumatoid arthritis and other autoimmune diseases, as well as skin conditions and cancers.1

Corticosteroids were once considered miraculous when, in 1948, the first patients with rheumatoid arthritis were treated with daily injections and thought to be cured. Subsequently, between 1954 and 1958, six synthetic steroids were introduced for systemic anti-inflammatory therapy. But, by the 1960s, it was discovered that corticosteroids given in high doses over prolonged periods cause serious side effects, and the term “scare-oids” was coined. As such, physicians began prescribing corticosteroids more conservatively, and some fearful patients even declined treatment. But despite the possible harmful effects, corticosteroids administered within proper guidelines can be very therapeutic. So, understanding how they work and how to reduce harmful effects is essential.2,3
What Are Corticosteroids and How Do They Work?

Corticosteroids are drugs that mimic the effects of endogenous cortisols, hormones that are naturally produced in the adrenal cortex (the outer layer of the adrenal gland). Cortisols help to control salt and water balance in the body and regulate carbohydrate, fat and protein metabolism, and, in particular, they are secreted each day to help reduce the inflammation naturally accumulating in the body. The adrenal glands typically produce about 20 milligrams of cortisol a day, but when the body is stressed by situations such as infection, trauma, surgery or emotional problems, they can produce five times that amount to allow the body to cope with the metabolic needs and need for reduction in inflammation.

Treatment with higher doses of corticosteroids — much higher than what the body normally produces — may also suppress the immune system. As such, treatment with higher doses of corticosteroids may help control an autoimmune disease caused when the immune system mistakenly attacks its own tissues. However, they can also impede the normal function of white blood cells, which could increase susceptibility to infections.3,4

The use of corticosteroids, then, may seem to be counterproductive for treatment of PI patients. Why treat someone with a compromised immune system with medications that can result in immunosuppression? Terry O. Harville, MD, PhD, medical director of the Special Immunology Laboratory at the University of Arkansas for Medical Sciences and a consultant for immunodeficiencies, autoimmunities and transplantation, explains that when corticosteroids are prescribed for PI patients, “the dosages being used are for reducing inflammation, trying to keep the dose low enough to not further add to immune system compromise.” In general, he says, taking low doses of corticosteroids once a day in the morning doesn’t result in much immune system impairment in most people. At other times, though, higher doses may be required, which actually may result in some decrease in immune system activity, especially when trying to control some autoimmune manifestations. According to Dr. Harville, it’s like fighting fire with fire — deliberately raising small controllable fires, which are called “backfires,” to remove any flammable material to deprive it of fuel. Yet, even though low-dose treatment with corticosteroids may not further impair already compromised immune systems, it is recommended to employ a team approach by joining the skills of the immunologist with those of a specialist in treating the organ system involved (i.e., gastroenterology, rheumatology, pulmonology, endocrinology, nephrology, dermatology or hematology).5

Corticosteroids Prescribed for PI Patients

Corticosteroids are sometimes needed in conjunction with PI patients’ primary treatment — immune globulin (IG) therapy — that causes side effects such as hives, rashes, difficulty breathing, headache, diarrhea, chills, body aches and other symptoms. Many of these side effects can be reduced or eliminated by pretreating patients prior to IG infusions with a low-dose oral corticosteroid such as prednisone, or the shorter-acting hydrocortisone. In some cases, higher dosing may be required for amelioration of more serious side effects.

Corticosteroids are also used to treat PI patients who suffer from autoimmune disorders. These include, but are not limited to, autoimmune cytopenias, lung disease (e.g., interstitial lung disease and granulomas in the lung), skin disease (eczema, psoriasis, hair and skin pigmentation changes), gastrointestinal disease (Crohn’s disease [aka granuloma colitis] and inflammatory bowel disease), musculoskeletal disease (e.g., rheumatoid arthritis and dermatomyositis/polymyositis), lupus and Sjögren’s syndrome.3

PI patients may also suffer from allergies and asthma. Corticosteroids in the form of over-the-counter or prescriptive nasal sprays are often prescribed for nasal allergies. For asthma or other respiratory

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Corticosteroids come in many forms, including pills, injections (for joints or muscles, or via intravenous infusion), ointments and inhalers. They are prescribed for short-term and long-term use, and to minimize dosages, they are sometimes used in conjunction with other non-steroidal anti-inflammatory drugs (NSAIDs) or other disease modifying anti-rheumatic drugs (DMARDs) to act as “steroid-sparing” medications.3
problems, inhaled corticosteroids are prescribed. For more serious cases, courses of oral or intravenous corticosteroids may be required.

“One problem with PI is that, depending on the type of disease condition, parts of the immune system may begin working overtime and create more inflammation and damage,” says Dr. Harville. “We give corticosteroids to help slow down the unnecessarily overactive parts of the immune system, as well as to reduce inflammation.”

According to Dr. Harville, dosing of corticosteroids depends on the disease condition and severity. In general, the lowest dose that provides benefit is desired. “Typically, the initial dose may be 1 mg/kg to 2 mg/kg, which is tapered to the lowest successful dosing,” he explains. Tapering generally occurs every three days. “A dose between 0.15 mg/kg and 0.25 mg/kg prednisone equivalent is considered to be ‘physiologic,’ or equivalent to the body’s own production of endogenous cortisols. Thus, doses less than this are felt to be somewhat safer since they are below the body’s production level. Most physicians try to reduce the dose even more to every-other-day dosing to further reduce the adverse effect of the corticosteroid on normal physiologic production of cortisols.” Why sub-physiologic levels of corticosteroids control inflammation is not well understood. “There’s something unique about the synthetic cortisols (i.e., perhaps longer lifespans) versus the natural cortisols that makes them better at controlling disease,” adds Dr. Harville.

Several studies have demonstrated successful treatment of autoimmune disorders with corticosteroids in PI patients. In one study, a 23-year-old man with common variable immunodeficiency and symptoms of chronic diarrhea, malabsorption and weight loss that had been apparent for two years was treated with 30 mg prednisone each day for one month. The prednisone was then tapered weekly by 5 mg until it was discontinued. Three months later, the patient’s clinical symptoms disappeared, and his quality of life improved. During the subsequent nine months follow-up, his body weight increased, and he was able to work without suffering any effects from his illness.

Harmful Effects of Long-Term Corticosteroid Use
Both short-term and long-term corticosteroid use can result in harmful effects in multiple body systems. Short-term effects could include an increase in blood sugar; upset stomach, with stomach ulcers and bleeding; increased hunger; increased risk of pneumonia, thrush and irritability.

Common long-term adverse effects of oral corticosteroids include elevated pressure in the eyes (glaucoma); fluid retention, causing swelling in the lower legs; persistent high blood pressure; problems with mood, memory, behavior and other psychological effects; weight gain with excess fat deposits in certain areas; clouding of the lens in one or both eyes (cataracts); high blood sugar that can trigger or worsen diabetes; increased risk of infections; thinning bones and fractures; suppressed adrenal gland hormone production; and thin skin, bruising or slower wound healing.

Side effects of inhaled corticosteroids include fungal infection in the mouth (oral thrush) and hoarseness. Systemic effects may also occur, and there is some risk for cataracts. Topical corticosteroid side effects include thinning of skin, red skin lesions and acne. And, side effects of injected corticosteroids include skin thinning and loss of skin color at the site of injection, as well as facial flushing, insomnia and high blood sugar.

According to Dr. Harville, whether due to short- or long-term use of corticosteroids, what can be most troubling in some patients are the psychological effects: “Paranoia is one of the major side effects people will experience, resulting in a potential for outbursts, mood swings and other adverse alterations in thought processes. These can be very disturbing to some patients, because they know that it is not them; it seems to be someone else.”

Reducing Corticosteroids’ Harmful Effects
Both physicians and patients can take measures to help minimize the risks of long-term corticosteroid use.

If possible, physicians will opt to prescribe topical or inhaled therapy rather...
than systemic (oral or injected) to reduce the effects. “If a PI patient is having diarrhea or granulomas in their intestines, prescribing a form that doesn’t get absorbed very well into the body will result in fewer systemic side effects, and may bring the symptoms under control,” explains Dr. Harville. “But if someone with common variable immunodeficiency has lung disease, they may need the systemic effects of the corticosteroids to gain control and get improvement of the disease.” In these cases, as mentioned earlier, physicians strive to prescribe the lowest dose that provides the needed benefit.

When stopping corticosteroids, patients should be tapered off treatment. This is so their adrenal glands can once again begin producing cortisols. Stopping corticosteroids without tapering can result in the lack of endogenous cortisols and may cause fatigue, joint pain, muscle stiffness, muscle tenderness, fever and even a flare-up of the condition.7

Unfortunately, there are patients who can never go off low-dose daily corticosteroids. These patients will accumulate damage, which is why self-care is essential. Getting an annual flu shot is important because long-term use may result in some reduction in the normal protective role of the immune system. Taking corticosteroids after a full meal or with an antacid may help reduce stomach irritation that often occurs when they are taken along with NSAIDs such as ibuprofen or aspirin.

Physicians may obtain a bone density test at the start of corticosteroid treatment, which can be repeated to assess the effectiveness of measures to prevent bone loss. They may also prescribe bone-preserving medications such as alendronate (Fosamax), calcitonin (Miacalcin), raloxifene (Evista) and risedronate (Actonel). Measures patients can take include consuming calcium supplements and milk products to increase calcium intake to at least 1,500 mg per day; taking a multivitamin to be sure they get a minimum of 400 IU of vitamin D per day to help absorb the calcium; reducing or eliminating smoking and alcohol use; and conducting weight-bearing exercises such as running, walking and dancing to stabilize bone mass.7

Patients should follow a heart-healthy lifestyle by watching calories and exercising regularly to try to prevent excessive weight gain and the development of atherosclerosis.

Patients should follow a heart-healthy lifestyle by watching calories and exercising regularly to try to prevent excessive weight gain and the development of atherosclerosis. Consuming a low-sodium diet will help reduce fluid accumulation and control blood pressure. And, blood sugar levels should be checked regularly. Those patients who already have diabetes should follow their prescribed medical and dietary regimens.7

For mood changes, physicians can sometimes prescribe another medication. In extreme cases of psychological problems, corticosteroid dosage will have to be decreased.7

Overcoming “Scare-oids”

When used long-term and with high doses, as noted, corticosteroids have many possible adverse consequences. “One major dilemma in some patients fearful of corticosteroids, but become educated about them and their adverse side effects. Then, both patients and their physicians can help to minimize side effects while achieving significant benefits. ■

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References