<u> </u>Mass General Brigham

Pamphlet #4: ASTHMA AND INHALED STEROIDS

Introduction

"Steroids" are a family of chemicals normally made within the body. They serve as hormones — chemical signals that help to regulate the body's growth and function. Some steroid hormones, like testosterone, stimulate formation of protein and growth of muscle. Competitive athletes have been known to take illicit derivatives of these "body-building" steroids in large amounts to improve their athletic performance. A very different category of steroid hormones are the corticosteroids, steroid hormones made in the cortex (hence, "cortico-") of the adrenal glands, which sit adjacent to the kidneys. Corticosteroid hormones have many different effects on body function, including influences on how we use our energy stores (fat, protein, and sugar) and how we adjust the salt and water content of our body.

Early in the 20th century it was discovered that corticosteroid hormones, if purified and taken in large amounts as a medicine, have powerful anti-inflammatory effects. Ever since this discovery, corticosteroids have been used to treat a great variety of diseases where inflammation (not infection and not cancer) is the major problem—from arthritis to psoriasis to asthma. When you and your medical provider talk about steroids to treat your asthma, it is these anti-inflammatory corticosteroids about which you are speaking.

Steroids Swallowed or Steroids Inhaled

To treat the inflammation of asthma within the bronchial tubes, steroids can be taken in tablet or liquid form or by inhalation. Occasionally, steroids are given by injection or—in hospitalized persons—directly into the veins (intravenous infusion). Taken as tablets, liquid, injection, or intravenous infusion, the steroid medication travels in the blood and is carried throughout the body, including to the bronchial tubes. Used in this way, steroids have their most powerful effects—both for the good (relieving asthmatic symptoms) and for the bad (undesirable side effects). On the other hand, inhaled steroid medications deposit directly on the bronchial tubes, where they act locally; very little medication is carried into the bloodstream. Although not as powerful in their immediate effects, steroids by inhalation are better suited for long-term use in the treatment of inflamed bronchial tubes because they are free of major undesirable side effects.

Examples of steroids in tablet form are prednisone (brand name: *Deltasone*[®]) and methylprednisolone (*Medrol*[®]). Examples of steroids by inhalation are beclomethasone (*Qvar*[®]),

budesonide (*Pulmicort*^{*}), ciclesonide (*Alvesco*^{*}), fluticasone furoate (*Arnuity*^{*}), fluticasone propionate (*Armonair*^{*}, *Flovent*^{*}), and mometasone (*Asmanex*^{*}).

More information about steroids in tablet form is available in a separate pamphlet prepared by Mass General Brigham Asthma Center, entitled <u>Asthma and Steroids in Tablet Form.</u> The remainder of this pamphlet focuses on the use of steroids by inhalation.

The Concept

Inflamed bronchial tubes are an important part of the problem in asthma. The cause of the inflammation is not always known, although for many persons a persistent, low-grade allergic-type reaction is probably the culprit. If severe enough, the inflammation and swelling of the bronchial tubes makes it difficult to breathe, with cough and chest congestion, wheezing and chest tightness. More recently, it has been learned that even when a person with asthma feels perfectly well, a mild degree of inflammation persists in the bronchial tubes and contributes to making them hyperreactive, that is, hypersensitive to the triggers of asthma attacks.

To reduce the inflammation of the bronchial tubes, one can identify and then seek to avoid those things that stimulate the inflammation, whether it is cigarette smoke or allergic triggers ("allergens") such as animal danders, dust, mold, etc. At the same time, one can take antiinflammatory medications to reduce the bronchial inflammation. For long-term use these are the inhaled corticosteroids and leukotriene modifiers, such as montelukast (*Singulair*[®]) and zafirlukast (*Accolate*[®]). For many persons with asthma, inhaled corticosteroids are the most effective of these currently available anti-inflammatory medications. Some patients benefit from allergen immunotherapy ("allergy shots") to address specific allergic sensitivities. And a novel approach to reducing airway inflammation in those with severe, refractory asthma involves injection of highly specialized monoclonal antibodies, referred to as "biologics," as addressed in a separate Mass General Brigham Asthma Center pamphlet, <u>Use of "Biologics" to Treat Severe Asthma</u> (*in preparation*).

Regular Use of Inhaled Steroids

Inhaled steroids are safe to be taken every day for months and years. The traditional approach to the treatment of asthma, still widely and appropriately employed, is the daily use of an inhaled steroid and the as-needed use of a quick-acting bronchodilator, such as albuterol. Most of the inhaled steroids are administered once or twice daily. They are available as dry-powder inhalers (medication released by the force of your inhalation), metered-dose inhalers (medication released as a spray from a pressurized canister), and a solution for nebulization. They do not bring about instant relief of symptoms, but with time they make asthma gradually less troublesome — for example, less cough, fewer asthma attacks, less often awakened at night with asthma, and less often needing your bronchodilator medication for the quick relief of symptoms.

Particularly effective has been the combination of inhaled steroids and long-acting bronchodilators. Inhaled steroids suppress inflammation of the bronchial tubes while long-acting bronchodilators work to prevent the bronchial muscles from tightening around these airways. Because of the effectiveness and safety of these two types of medications used together, several inhalers (both dry-powder and metered-dose) have been developed that combine both an inhaled steroid and a long-acting bronchodilator in one device. Examples include fluticasone propionate + salmeterol (*Advair*[®], *AirDuo*[®], *Wixela*[®]); fluticasone furoate + vilanterol (*Breo*[®]); budesonide + formoterol (*Symbicort*[®]); and mometasone + formoterol (*Dulera*[®]). They are to be taken once or twice daily.

As for any inhaled medication, it is crucially important that you use proper technique to inhale these medicines deep into your lungs. We do not feel that, as a routine, you need to use a bronchodilator before taking an inhaled steroid or that you have to wait one minute between inhalations. In most instances we do encourage the use of spacer devices when your inhaled steroid is delivered from a pressurized canister. These breathing aids, typically shaped as a hollow tube, attach to the steroid metered-dose inhalers and serve to maximize the amount of steroid medicine deposited onto the bronchial tubes while minimizing the amount left behind in your mouth. They are available on-line and at most pharmacies. Examples of these spacer devices include the *Aerochamber*[®], *Optichamber*[®], *Vertex*[®], and others.

Inhaled Steroids Used as Needed

Recently, it has been recognized that using an inhaled steroid together with a quick-acting bronchodilator provides better relief and stronger protection against asthma attacks than use of a quick-acting bronchodilator alone. The concept behind this approach is that when you are having asthma symptoms and seeking relief from your quick-acting bronchodilator (like albuterol), there is active inflammation of the bronchial tubes that is best treated at that moment with an anti-inflammatory corticosteroid. A relatively new recommendation for persons with more than very mild asthma is that you should use an inhaled steroid each time you reach for your quick-acting "rescue" bronchodilator. The concept has been dubbed "antiinflammatory rescue" (or AIR, for brief). It can be achieved with two inhalers (one a quick-acting bronchodilator like albuterol; the other an inhaled steroid like beclomethasone, budesonide, ciclesonide, fluticasone, or mometasone). The same would apply if you were to use a nebulizer for quick-relief. This process has been simplified by the creation of inhalers that combine a quick-acting bronchodilator and an inhaled steroid into one device. At present, available combination inhalers of this type are albuterol + budesonide (AirSupra[®]), formoterol + budesonide (Symbicort[®]), and formoterol + mometasone (Dulera[®]). (Yes, formoterol is one of the long-acting bronchodilators, but because of the rapidity with which it begins to work, it too can be used for guick relief of symptoms.) If your medical provider has recommended combination formoterol + budesonide (Symbicort^{*}) to be taken every day, it can also be used for quick relief, an approach referred to as SMART (single inhaler for maintenance and rescue therapy.) On the other hand, the long-acting bronchodilator, salmeterol, contained in

combination inhalers such as *Advair*[®], *AirDuo*[®], and *Wixela*[®], begins to work more gradually and cannot be used for quick relief as part "anti-inflammatory rescue."

Undesirable Side Effects

The great advantage of corticosteroids by inhalation is that even with long-term use (that is, many years), the undesirable side effects associated with steroids in tablet form (for example, prednisone) do not develop. In conventional doses, the only potential side effects that you are likely to encounter are sore throat, hoarse voice, and a yeast infection in the mouth (oral candidiasis or "thrush"). This latter infection usually manifests as white deposits on the tongue, gums, and/or roof of the mouth. The risk of developing thrush can be reduced by rinsing your mouth with water after each use of the inhaled steroids (the water can be swallowed or spit out) and by use of the spacers mentioned above. Prescription medications are available to clear up thrush, should it develop.

When used in high doses, a small amount of the medication is absorbed into the bloodstream and some side effects beyond the mouth and throat may develop. The most likely to be encountered are easy bruisability of the skin and suppression of the function of the adrenal glands. The significance of adrenal gland suppression is discussed in further detail in the pamphlet entitled <u>Asthma and Steroids in Tablet Form</u>, prepared by the Mass General Brigham Asthma Center. Only after many years of very high doses of the inhaled steroids does one become susceptible to an increased risk of thinning of the bones (osteoporosis), glaucoma, and cataracts. However, it is widely agreed that any side effects associated with long-term use of high-dose inhaled steroids is far less than those resulting from regular or repeated use of steroids in tablet form.