Breath of Fresh Air

E-Volume 1, No. 2 *Information, news and advice for improving asthma well-being* **Autumn 2013**

Intermittent Inhaled Steroids for Mild Asthma

For decades now, guidelines for asthma care have recommended that persons with persistent asthma should take daily anti-inflammatory medication, preferably an inhaled steroid, to lessen their symptoms of asthma and reduce the frequency of flare-ups of their disease (asthma "attacks"). At the same time, it has been suggested that persons who have very mild disease and few symptoms ("intermittent asthma") can use their quick-relief bronchodilator as needed and need no other medication for their asthma. Inhaled steroids have not been recommended for persons with mild and intermittent asthma because: 1) infrequent symptoms do not seem to warrant daily medication, and 2) evidence indicates that long-term use of inhaled steroids does not improve lung function over time or affect long-term outcomes in asthma.

Panels of experts write the asthma guidelines based on their experience and available scientific information. (The guidelines are not divinely inspired or carved in stone tablets!) Asked to define "persistent asthma," the experts reached the following consensus: anyone who has two days or more of asthma symptoms each week **or** wakes up two or more times with asthma symptoms each month **or** has lung function that is below normal **or** has had two or more attacks of asthma (requiring oral steroids) in the past year. Taken as a whole, patients with persistent asthma who are treated with regular (daily) inhaled steroids have fewer symptoms of their asthma, less need for their "rescue" bronchodilator, better lung function, fewer asthma attacks, and an overall improved sense of well-being.

But a fair question – and one that has now been addressed by recent clinical research – is exactly where one should draw the line between "intermittent" and "persistent" asthma. Did the experts get it right, or are there patients with persistent (as defined above) but mild asthma who do not in fact need to take an anti-inflammatory medication daily for relief of symptoms and prevention of asthmatic attacks? If you have mild persistent asthma and your symptoms are sufficiently few (more than two days out of the week but less than every day), prior asthma attacks have been sufficiently rare, and breathing tests are for the most part normal, might you take inhaled steroids only during periods when your asthma is troublesome but stop them when during times when

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your asthma is no longer bothering you? It is very likely that many patients with asthma have been following this practice for years – because daily medication use can be onerous – but is it safe and advisable?

Two studies – one in adults [Boushey et al., *New England Journal of Medicine* 2005; 352:1519] and one in young children [Zeiger et al., *New England Journal of Medicine* 2011; 365:1990] – have indicated that the strategy of using inhaled steroids intermittently, only during periods of increased symptoms, is indeed safe for persons with *mild* persistent asthma. These studies found that among persons with mild persistent asthma there was no difference in the frequency of asthma attacks, including severe or dangerous attacks, and very little overall difference in sense of well-being whether they used their inhaled steroids every day vs. used them only when symptoms became troublesome … as long as everyone had a plan regarding how to deal with an asthma attack.

Let's be specific. Based on these recent studies, if your asthma has been mild, your medical provider might prescribe for you an albuterol (ProAir, Proventil, or Ventolin) or levalbuterol (Xopenex) inhaler to use whenever you need it. If you find yourself using your quick-relief bronchodilator a lot, or if you feel congested at the start of a "cold," or if you are visiting your in-laws who own a cat to which you are allergic, you would begin your steroid inhaler, such as fluticasone (Flovent), budesonide (Pulmicort), beclomethasone (Qvar), mometasone (Asmanex), or ciclesonide (Alvesco). You would probably take at least *four* inhalations morning and night every day for approximately ten days, and then when you felt better, didn't need your rescue bronchodilator so often, had gotten over the cold, or were no longer exposed to the pet cat, stop your steroid inhaler. And you would be prepared with the knowledge that if your symptoms worsened despite taking the inhaled steroid, you would need to begin oral steroids (e.g., prednisone) and be in contact with your medical provider.

Two important caveats before one puts this approach into practice. First, it is not intended for persons with more severe forms of asthma. Our emergency departments routinely treat persons with asthma who had been doing well until they stopped taking their preventive asthma medication (their inhaled steroids), thinking that they no longer needed them, and then developed severe asthma symptoms. In persons with moderate and severe persistent asthma, evidence is unequivocal that stopping inhaled steroids is associated with more asthma attacks and worse asthma control. Second, intermittent use of inhaled steroids does not mean "as needed" or "p.r.n." For this new strategy to work, the inhaled steroids need to be taken not here and there, trying to relieve symptoms, but every day, usually twice a day, for a period of 10 days or more. Intermittent use of inhaled steroids refers to regular, daily administration, but for a limited period of time rather than year-round indefinitely.

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A Steroid "Burst"

We recently received an e-mail from overseas commenting that a steroid "burst" does not translate well. It sounds too violent, like an explosion. Now that we think about it, a steroid "burst" does sound like something one might see at a Fourth of July fireworks display! But you know what we are referring to: that time-limited course of prednisone or methylprednisolone (Medrol) taken by mouth to quiet a flare of out-of-control asthma. Most persons with asthma have a love-hate relationship with oral steroids. Love: the medicine helps you breathe normally again, "better than ever," at a time when other medications seem no longer to work. Hate: it often has unpleasant side-effects, such as stomach discomfort, moodiness, agitation, sleeplessness, and, of course, the "hungry horrors."

What may have struck you … as it does us … is that no one seems to know the exactly "right" way to prescribe a steroid "burst." Sometimes you are given 40 mg of prednisone to start, sometimes 60 mg. If you went to the Emergency Department to receive your first dose, it may have been given intravenously at twice the amount, as methylprednisolone (Solu-Medrol) 125 mg. After the first dose you may have been given 5 days of treatment, 14 days, or longer. And the dose may have been reduced from its initial large amount to zero in various ways – by 10 mg/day every day or every two days, by 20 mg every 4 days, by inclusion of the low dose of 5 mg/day or not, etc. Or perhaps your doctor likes the Medrol dose-pack, a pre-programmed 6-day tapering schedule in a package of tablets clearly laid out with each day's decreasing dose. Most recently you may have been sent home with 50 mg/day for 5 days, then stop. No taper to off, just stop.

As you might surmise, such a variety of approaches reflects lack of scientific knowledge. The best way to prescribe a short course of oral steroids has not been carefully studied in scientific trials, and it may be that there is no one "right way" to use steroids. Some people and some exacerbations of asthma may require more medicine for longer periods of time, others may do well with less medicine for shorter duration. A recent experiment among more than 300 people with chronic obstructive pulmonary disease (COPD, the chronic obstructive lung disease of cigarette smokers) found that 5 days of prednisone at 40 mg/day was as effective as a two-week course of treatment [Leuppi, et al., *Journal of the American Medical Association* 2013;309:2223], but COPD is not asthma. It is uncertain whether the same would be true among persons experiencing flare-ups of their asthma.

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What we do know may surprise you. Despite the time-honored approach of reducing the dose of prednisone in stepwise decreases – the "steroid taper" -- research has shown that abrupt discontinuation of oral steroids achieves the same asthma control and prevention of recurrences as a slow steroid taper, *as long as after the oral steroids you continue preventive treatment with inhaled steroids*. When used for a brief period (fewer than 2-3 weeks), there is no medical reason that the dose of oral steroids has to be slowly decreased. It is o.k. to reduce the dose in stepwise fashion, but it is not necessary for biologic reasons.

In the absence of scientific data, we are free to share with you what we think is a reasonable general approach *in the adult*, acknowledging that other recommendations may someday be found to be just as good or even better (in which case we will change our approach!). During a severe asthma flare-up, we begin with prednisone between 40 and 60 mg/day (40 mg/day for smaller people, 60 mg/day for larger people). Then, in the absence of major medication side effects, it makes most sense to continue treatment at this dose until one is all better or almost all better (as guided by symptoms or, even better, by finding that the measured peak flow has returned back to its usual value when one is feeling well), and then stop the prednisone or quickly reduce the dose to zero over a few days. Typically, medical providers make a guess as to how long it will take to recover from this particular asthma attack and prescribe a specific duration of treatment. Sometimes providers will allow their patients to adjust the duration of treatment according to their response to it. Once you are better, we anticipate that you will continue to feel well and maintain good lung function *if you continue taking your inhaled steroid* and, where possible, avoid the triggers that set off your asthma attack in the first place.

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In the future, another group of national and international asthma experts will write an updated set of asthma guidelines and render its opinion regarding this approach to asthma care. In the meantime, our opinion is that this is a safe and reasonable way to treat mild asthma. It is not appropriate for persons whose asthma is more severe, and its implementation requires careful explanation and reinforcement such that everyone is clear as to when to begin the inhaled steroids, how to use them and for how long, and what to do if asthma fails to improve as expected.

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