Wheeze & Sneeze

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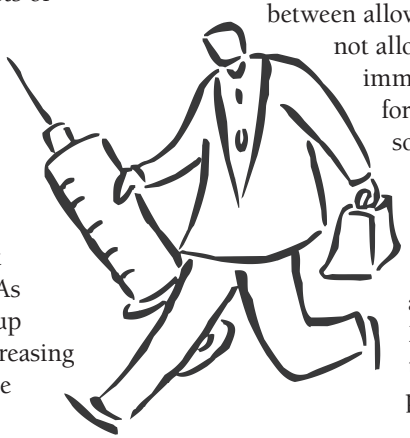
A 'Beta' Take on Beta Blockers, the Latest Poop on Pet Allergy, New Asthma Guideline & More

A Beta Take on Beta Blockers

The importance of beta adrenergic responsiveness in recovery from respiratory manifestations of anaphylaxis was historically regarded as a reason not to give skin tests or immunotherapy to patients who cannot safely interrupt beta blockers. Historically, the only option to offer both was to interrupt the beta blocker in patients with strong enough indications for skin tests or allergy shots.

Allergists began to make exceptions for patients with both life-threatening insect sting allergy and life-threatening cardiac indications not to stop beta blockers. As these patients as a group have done well, an increasing trickle of allergists have also given skin tests and allergy shots for inhalant allergens to patients needing continuous beta blockade.



I probably deserve either credit or blame for provoking the "beta take" that's currently in progress among the policy-makers of my specialty. Several years ago I volunteered to chair a project to survey the immunotherapy practice patterns of allergists in the U. S. Our initial findings, published in 2007, found allergists almost equally divided between allowing and not allowing immunotherapy for at least some classes of patients needing oral beta blockers, and about 2/3 skin testing patients on beta blockers. In my practice we give allergy shots to beta blocker patients with life-threatening insect sting allergy who can't safely interrupt beta blockers. We now skin test patients on beta blockers for inhalant and food allergens and in highly selected cases have given some of them immunotherapy for inhalants.

Major allergy specialty societies periodically survey their members for immunotherapy fatalities. I personally estimate this risk to be ~1 / 12.5 million shots or 8 per year per million patients each receiving 2 allergy shots every week. This is 18 times less than the Harvard Center for Risk Analysis estimate of the annual risk of the average American dying in a motor vehicle accident, which is 1 / 6745. While an average of 2-3 immunotherapy fatalities are reported per year, none have

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Beta Blockers, Pet Allergy, Asthma

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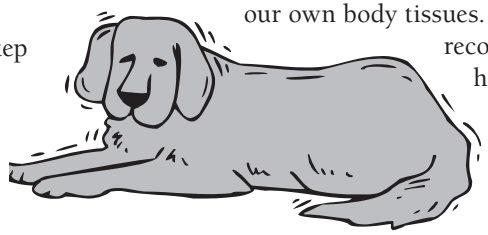
been reported in patients taking oral beta blockers since 1990, one from 1985-89 and two from 1973-84. Skin test fatalities are very rare and none have been reported in patients taking beta blockers in the above three surveys. If half of US allergists are giving allergy shots to at least some patients taking oral beta blockers and with the standardized major allergens that have been available since the late 1980's none of them are turning up on fatality lists, it's likely that they aren't quite as dangerous as originally hypothesized.

I proposed to the leaders of my specialty that with 50% of allergists giving at least some shots to patients taking beta blockers it should be possible to collect real time fatality risk data over time. If allergists will report the number of practice parameter-compliant doses given to these patients with no fatalities or with rare fatalities, we can estimate the resulting fatality risk. If we can document 1,000,000 such shots without a fatality, for example, we can estimate that the fatality risk is not greater than ~ 1 per 1.3 million doses which is half the annual risk of a motor vehicle fatality. If we continue to collect data and can document 2,000,000 doses with (let's suppose) one fatality, we can estimate the risk to be 3.5 times less than that of a motor vehicle fatality. Until we have the data for an evidence-based guideline I'm asking our practice parameters task force for more explicit guidelines based on anecdotal evidence and expert consensus for the management of allergic patients needing beta blockers. Needless to say, management of this condition is evolving but your patients under our care will receive the best evidence-based treatment at every step of the process.

The Latest Poop on Pet Allergy

All of us are familiar with animal allergy. My favorite true story is that of a narcotics swat team police officer who before allergy shots couldn't go into a house on a drug bust unless a fellow officer confirmed that there were no cats inside. However, several studies report that growing up in a home with pets is associated with reduced risk of developing asthma, allergic sensitization and eczema. Pets are only associated with risk reduction if they're in the home before the child is born, suggesting that any immunomodulating effect occurs within the first few months of life. The studies show association rather than cause, but endotoxin is believed to be a major mediator of this effect. Should we recommend that prospective parents become pet owners first? A cautionary note is the fact that dogs bite ~5 million Americans every year, 70% of them children, causing 1000 emergency department visits per day and 15 to 20 deaths per year (MMWR 2003;52:605).

Some individuals have positive cat or dog skin tests but no symptoms from close contact with their own pets of these species. This reflects a balanced response involving both allergic antibody and protective blocking antibody. Children with this pattern who go away to college may show allergy for the first time when they return home for vacation because allergic antibody lasts longer than blocking antibody. Allergy shots for cat, dog or horse help patients transition from allergic to blocking antibody responses and finally to a suppressor immune response, similar but not fully identical to the immunologic tolerance we normally have for our own body tissues. Animal shots are normally recommended for patients who have only occasional contact with the offending animal, like the police officer described above, but they



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Guidelines and More

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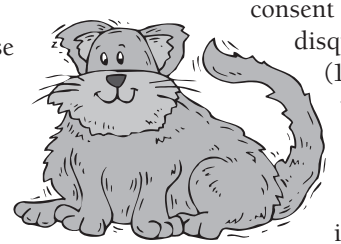

also help most patients who choose to keep the pets to which they are allergic. We have seen patients in whom ongoing exposure to their pets appears to have helped maintain a state of immune suppression or immunologic tolerance after it was achieved with the aid of immunotherapy. Tolerance is more likely to be maintained if shots are continued, but they can usually be spaced out to monthly intervals. The bottom line: We all have the same immunologic switches, but their settings vary between us on the basis of genetics and past exposure.

A complicating factor in cat allergy is that cat allergen sticks to any cloth surface and can be transferred from one cloth surface to another. If your house has lots of cloth surfaces it will be a reservoir of cat allergen even when the cat is out. Cat allergen was the major allergen measured in surveys of many hospitals, getting onto the carpet from the clothing of patients, staff and visitors. Cases of indirect cat exposure include the patient who runs an upholstery business and before immunotherapy couldn't work on a couch from a home with cats, and the clothing boutique manager who would sneeze every time she inspected returned merchandise from a home with cats.

56% of US Asthma Allergic

Newly released data from the Third National Health & Nutrition Examination Survey (NHANES III) correlates skin test positivity to 10 common environmental allergens with the presence of asthma in a subset of 10,508 subjects selected to be representative of the U.S. Population age 6-59, chosen from the 31,311 subjects age 2 mos. to 90 years in the full NHANES III study by randomization (n = 12,106) less those refusing consent for skin testing (1069) less those disqualified for complicating medical conditions (174). This study found 56.3% of asthma to be associated with atopy, defined as skin test positivity to at least one of the 10 allergens tested. Cat allergy had the strongest association with asthma, followed in decreasing order by alternaria (a mold), white oak, short ragweed and dust mite.

This study only covered the age range from 6 to 59 years. A smaller population survey in Cincinnati, with a climate and allergen exposure similar to ours, found a high frequency of positive skin tests often to pollens, in children with asthma as young as 12 months. This was unexpected, as significant pollen allergy was previously thought to take about 3 seasons of exposure to develop. We've started to look for it in our patients, but numbers to date are too small to estimate significance.

A smaller study reported by JH Krouse in the ENT literature in 2000 found a similar association between the disease burden of chronic & recurrent rhinosinisitis and respiratory allergy. He found degree of allergic disease to be a better indicator of symptom severity and impairment in quality of life among chronic rhinosinusitis patients than CT stage. He concluded that careful evaluation and treatment of allergic disease is critical in the treatment of chronic rhinosinusitis.

The bottom line regarding the above studies is the simple jingle: *"If you wheeze or sneeze, come see us, pleeze."*

New NAEPP Asthma Guidelines

A newly revised 440 page expert panel report from the National Asthma Education & Prevention Program of the NHLBI (naepp-epr3) was published in August 2007 and is available on line at www.nhlbi.gov. This compares with 153

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pp for naepp-epr2 in 1997. With knowledge still incomplete about its primary pathophysiology, asthma remains a chronic inflammatory disease that cannot be cured but can be managed to minimize morbidity, disability, risk of severe exacerbations and complications and cost of care. The panel's consensus seems to be that while the two simple tables used to classify severity and need for treatment in the 1997 guidelines were easy enough for most PCP's to follow, they didn't provide enough individualization to optimize disease management. In 2007 the pendulum swung in the opposite direction, with an assessment matrix involving 8 separate tables for each of 3 age ranges, a treatment matrix of 4 additional tables for each age range and 5 additional tables of guidelines for acute exacerbations.

If you want to treat asthma in compliance with current guidelines, download the PDF file and skim through it on your computer. If you don't trust yourself to memorize your way through 41 tables of evaluation and treatment criteria, we think it's a good idea to find an asthma specialist you trust, to collaborate with you for the following: 1) Set-up and periodically review protocols for management in your office of those patient groups you see in significant numbers, and 2) Set up criteria and intervals for his or her specialty evaluation and periodic follow-up to interface smoothly with your own capabilities and resources. This will increase costs of physician care and specifically specialist physician care, but if done right should result in healthier patients and reduce their total cost of care. I personally still have the best track record in the peer-reviewed English language medical literature for keeping previous asthma "frequent fliers" out of hospitals and emergency rooms, improving their quality of life and reducing their total cost of care. If you elect to consult us for this purpose we'll be happy to collaborate in coordination-of-care relationships to benefit each of the four parties: you, us, your patients and those who pay for their hospital and pharmacy as well as physician care.

What Do We Do That's Different?

A difference in our global approach to patient care became apparent when my wife asked one of her physicians if he could switch two of her costly brand name medicines to $4 per month Wal-Mart generics of the same classes. He replied that if it ain't broke, don't fix it. For our own patients, we're always looking for fixes that are safer, more effective or more efficient (the latter category including less costly). Once long term management is truly optimized and in the absence of interval exacerbations we try to schedule patients who are doing well for annual evaluation. Up to that point or if their interval course is rocky, we want to see them more frequently. We document a broader range of quantitative and semi-quantitative assessments, on a spread-sheet medical record that reflects my engineering background and orientation. Every time we see a patient we try to leave him (or her) doing at least one thing with greater safety, effectiveness &/or efficiency than before that visit. We believe our outcomes justify the effort.

Update On Sublingual Epinephrine Study

We asked the FDA to let us begin dose-ranging equivalency trials with the same lot of drug to be assayed for uniformity, following demonstration that it has the physical characteristics associated in published studies with reliably high bio-availability. The FDA wants to see physical and uniformity data first, and also wants us to begin dose-ranging trials with a lower dose tablet than we had requested. Funding this pre-clinical research will require applying to different grant programs than those that cover clinical trials, and to date I just haven't had time to do it.

Do you have colleagues who aren't on our mailing list and would like their own copies? If so, ask them to contact us by phone (856.825.4100) fax (206.202.2105) or e-mail (crsj@crsj.net) with their name, degree, medical specialty, mailing address, phone, fax & e-mail.