

is limited and primarily focused on dosing; little to no attention is given to how and when the medication should be taken with meals and drug interactions.² If physicians are going to dispense samples, they must also take on the responsibility of fully educating the patients about their use.

Finally, we must also consider the long-term effect on our patients. Samples will be available for branded, newer, more expensive medications. If this is the most appropriate medication, samples might be a reasonable way to assess the efficacy and tolerance of a new medication in an individual patient. However, this must be done with the knowledge that when we can no longer supply the patient with samples of that medication, they might be left with a more expensive long-term treatment plan.

Alternatively, Dr Wolf suggests a percentage of the pharmaceutical samples be tithed to pharmacies that serve indigent populations. Advantages of this option include the availability of a pharmacist to help with the education and instruction of the patient and more efficient tracking of dispensed samples, as required by law. However, is it in the best interests of our indigent patients to switch medications according to availability? What will be the effect on the overall health of our indigent patients if we repeatedly switch their medication regimen on the basis of the availability of samples. Will there be effects on compliance, patient knowledge, and understanding of their medications and potential side effects? Furthermore, pharmacies that supply samples to patients will need to keep samples separate from retail inventory to avoid possible diversion.

Although the use of samples in the office setting might be an appropriate choice for a given patient, we must be aware that the decision of which drug to use is influenced by which samples are available. The difficulty in remaining unbiased in our choice of therapy has contributed to many large multispecialty group practices to remove samples from their practices. Boltri et al³ compared 2 time periods: January through February 1997, when drug samples were available, and January through February 1998, when sample distribution was prohibited. They observed that after the prohibition of sample distribution, there was an increase in first-line antihypertensive use from 38% to 61%. Similarly, the use of samples through a tithing program to outside pharmacies will also influence the medication prescribed for our indigent patients. Ideally, we should prescribe a medication for a patient on the basis of our perception of what is the best drug for the overall clinical situation. However, reality dictates that the economics of these decisions also have to be considered. Prescription drugs account for only 11% of medical costs but an increasingly large share of out-of-pocket costs to patients.⁵ How and where pharmaceutical samples are incorporated into this decision process needs to be carefully considered.

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Atopy and asthma: An epidemic of unknown cause

To the Editor:

In the Detroit Children's asthma study, the number of cases of asthma that have developed by the age of 5 to 7 years is too small to draw most conclusions.¹ The authors recognize this but have published their finding that fathers with continuing symptoms present a greater asthma risk for their children. They conclude that persistent symptoms indicate a stronger genetic susceptibility. Had they considered it possible that atopy might be caused by a transmissible agent, they could have concluded that a symptomatic parent might be more contagious.

The specific abnormal T_H2 clones responsible for driving atopy not only have become immortal but also produce less IL-10 than normal T_H2 cells in the same subject. Once boosted to a manifested level, these cells remain active for years, even in the absence of further allergen exposure. The cause of the abnormal specific clones is unknown. Some viruses immortalize T_H2 clones to preserve themselves and avoid the host's immune defenses (eg, herpes simplex virus and human T-cell leukemia virus 1). Atopy susceptibility is reduced by half in subjects with antibody to hepatitis A and an insert at Tim1 (an area where viral uncoating and entry are facilitated).² In view of the current epidemic of atopic disease, epidemiologists must consider every possibility.

It is also important for epidemiologists to know that it is normal to make IgE to some things. All positive skin test results, especially to mites, which after all are parasites, are not signs of atopy. They may indicate only current exposure. (For example, positive skin test results to mites were common in rural Ethiopia, where asthma was rare.)

Susceptibility of the very young with widespread immunity in adults is a common pattern in many infectious

diseases. A study presented at the 2004 American Academy of Allergy, Asthma and Immunology meeting was a study of a community in which households accommodate several unrelated families. The risk for atopy in children depended on the household rather than on genetic relationships.

Adoptees adopted as infants by atopic families have been found at increased risk for atopic diseases. Pulmonary therapists have a low but very significant increased risk for asthma compared with physiotherapists and x-ray technicians. In our studies in the late 1950s and a recent German study, marital partners of people with atopic disease have shown about the same increased risk. It is possible to explain away these results as recognition problems, but the numbers are remarkably similar.³

As laboratory tools improve and more is learned about the properties of viruses and treatment, the need to consider the possibility of a viral cause for atopy becomes increasingly important. The subject is sensitive, but good evidence that most adults have become immune with casual exposure should allow ample reassurance.

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Reply

To the Editor:

The correspondence from Dr Jeanne Smith¹ regarding our recently published manuscript² from the Detroit

Childhood Allergy Study highlights the conundrum of allergy research and supports the need for large prospective cohort studies, which have the power to tease apart the environmental and genetic contributions. Although the data from the Detroit Childhood Allergy Study are not sufficient to answer Dr Smith's question directly, ideally we will be able to address the hypothesis of transmissibility in our new birth cohort, which is expected to enroll 3000 families.

In Dr Smith's review,³ she and Dr Hussain suggest that the close contact of mothers, as the primary caregivers, with infants increases the opportunity for transmission. Speaking somewhat against the transmissibility hypothesis, our data show a stronger paternal effect for atopy, seroatopy, and current asthma. In addition, childhood-only disease in the father, which would not allow for exposure to his offspring, conferred a increase of 6-fold to 8-fold in risk that was statistically significant. In addition, we tested to see whether exposure to a parent reported to have adult allergy conveyed an increased risk for the other parent to have reported disease. This analysis resulted in a nonsignificant result ($P > .05$).

Dr Smith's comments further highlight the complexity of the relationship between genetic susceptibility to diseases and the environment, which may include transmissible infectious agents as well as the allergens, pollutants, and immunomodulatory exposures such as endotoxin that are most commonly analyzed in current epidemiologic studies of asthma and allergy.

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