



LABletter

PATHOLOGY & LABORATORY MEDICINE NEWSLETTER

FEATURE ARTICLE HIGHLIGHTS>>

Screening for Allergic Disorders

James Faix, M.D.

Director of Chemistry

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Laboratory Update:

Stanford Clinical Laboratory New Web Site

www.stanfordlab.com

Q&A: Critical / Panic Values

Michael Petzar, M.D.

Pathology Department

James Faix, M.D.

Director of Clinical Chemistry and Immunology at Stanford Clinical Laboratory and



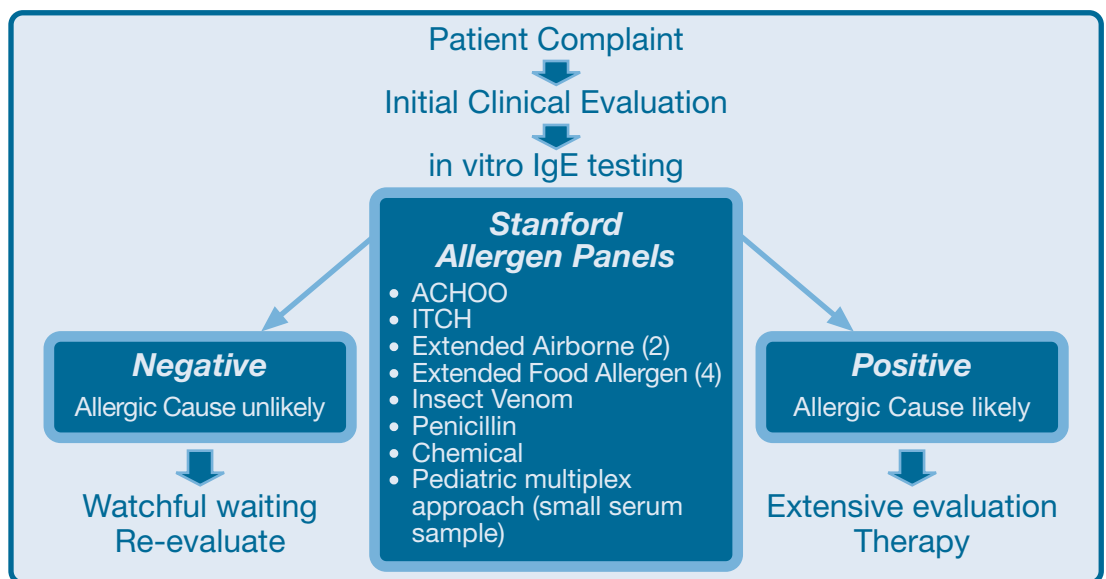
Associate Professor of Pathology at Stanford University School of Medicine. Dr. Faix directs the allergy, automated chemistry, blood gas, endocrinology, immunology, lipid, toxicology and tumor marker sections of the diagnostic laboratory.

Screening for Allergic Disorders

To treat or not to treat – that is the question.

All of the common symptoms seen in allergic disorders may have other causes. **Rhinitis, sinusitis** and **upper airway problems (including asthma)** may be due to infections or irritants. **Urticaria and eczema** may be caused by a variety of skin diseases. A history of intermittent symptoms (especially if related to seasonal change) and specific triggers help point to allergy. But the physician needs to know whether allergy is really behind the patient's symptoms before beginning potentially expensive therapies that may not work if it is not.

The traditional approach has been in vivo skin testing. Small amounts of allergen solutions are introduced into the patient's skin (usually the forearm). A "wheal-and-flare" reaction (edema surrounded by vascular congestion) due to the immediate release of histamine is indicative of the presence of specific IgE on the patient's mast cells. Skin testing requires significant expertise (both to perform and interpret) and may be problematic when the patient is taking antihistamines, has extensive skin disease, or is at risk of serious reactions to the allergen. Consequently, **in vitro** methods that correlate with the results of skin testing (and that could be performed on serum specimens) have been eagerly pursued.



When panels are properly constructed and assay performance is carefully monitored:

- **Negative results** can help reassure physicians that an allergic component to the patient's symptoms is unlikely to be present.
- **Positive results** indicate that allergy is more likely to be involved. These patients should be considered for referral to allergy specialists who can perform a more extensive evaluation (including confirmatory skin testing, if needed) and who can also expertly advise the patient regarding available treatment (including immunotherapy).

“Specific IgE *in vitro* allergy testing is a convenient way to perform screening of patients seen by primary care physicians.”

The major *in vitro* tests utilized include total IgE levels and specific IgE anti-allergen assays. Total IgE (measured by immunoassay) has relatively limited predictive value. Although it is probably true that patients with severe allergic disease have very elevated total IgE levels, the test is too insensitive to be used to exclude allergy as a cause of the patient’s symptoms. Also, a variety of non-allergic disorders may elevate total IgE levels, especially parasitic infections. ***Immunoassays that detect the presence of specific IgE antibody in the patient’s serum are more sensitive and specific.***

The major allergens tested are ***airborne allergens*** (those implicated in respiratory symptoms) and ***food allergens*** (either gastrointestinal or skin disease). *Airborne allergens* are usually classified as *either outdoor or indoor*; *food allergens* are usually classified as *either primarily affecting children or primarily affecting adults or both*.

Other important types of allergens include *drugs, insect venom and chemical agents*.

The Stanford laboratory can look for IgE antibody against a large number of allergens. But we have created a number of screening panels for ordering convenience.

ACHOO and ITCH

These panels were designed to include the major airborne and food allergens.

- The **“Air-Carried House & Outdoor Option” (ACHOO)** includes **16 airborne allergens**, comprising 12 outdoor pollen allergens and 4 indoor allergens. The outdoor allergens include three trees (Alder, Oak and Olive); three grasses (Bermuda, Rye and Timothy); three weeds (Dock, Sage and Western ragweed); and three molds (Alternaria, Aspergillus and Cladosporium). The indoor allergens are: cockroach, dog and cat dander, and dust mites.

The **“Ingested Things Causing Hives” (ITCH) panel** includes **all of the common food allergens** causing problems in both children and adults: egg white and milk; almond; peanut and soy; oat, corn and wheat; codfish and shrimp; orange and tomato; and chicken.

Both **ACHOO and ITCH** also include total IgE, which, if elevated, can help suggest that low or moderately elevated specific IgE levels may be significant.

Extended Airborne Allergen Panels

- There is a specific panel for **bird allergy (canary, finch, parakeet and parrot)**.
- We also offer a panel that includes most of the **important mold allergens**, including the three offered in the ACHOO screen as well as eleven others:
 - Auerobasidium; Candida; Chaetomium; Epicoccum; Fusarium; Helminthosporium; Mucor; Penicillium; Rhizopus; Trichophyton and Ulocladium.

Extended Food Allergen Panels

We have also grouped the commonly requested food allergens into additional panels for ordering convenience. The most popular are

- **Nuts** (almond, Brazil nut, cashew, chestnut, hazelnut, macadamia, pecan, pistachio and, even though it’s not actually a tree nut, peanut);
- **Fish** (codfish, halibut, herring, three types of mackerel, plaice,

salmon, sardine, sole, swordfish, trout and tuna);

- **Seafood** (abalone, clam, crab, lobster, mussel, octopus, oyster, scallops, shrimp, snails and squid).
- **Berry** panel includes blackberry, blueberry, cranberry, raspberry and strawberry.

Other Panels:

- Panels for insect venom (bee, yellow jacket, wasp and hornet);
- Penicillin (Penicillin G and V as well as amoxicillin and ampicillin);
- Chemical allergy (including both the isocyanates used in the manufacture of polyurethane and anhydrides found in resins).

We would be happy to discuss your specific needs (and customize a panel for your practice).

New Pediatric Panel “multiplex” approach

Allergic disease often presents in infancy and early childhood. There is a well-established pattern (called the “allergy march”) in which children who are likely to develop significant upper respiratory disease (including asthma) first exhibit IgE antibodies to food allergens, becoming sensitized to airborne allergens only later. For this reason, we **include egg white whenever an airborne allergen panel is ordered on a patient who is less than five years old.**

One particular problem often encountered when screening for allergy in young patients is **the need to utilize only small amounts of serum**. Most of the individual specific IgE assays require 40-50 microliters of serum, and the automated instrument we use requires a 100-200 microliter “dead” volume in order to pipette each aliquot. This can significantly limit the number of different allergens that can be tested.

One alternative is the use of “mixes” (specific IgE assays that employ a number of different allergen on the solid-phase). However, if this “mix” is positive, individual assays must still be run to determine which of the allergens are being recognized by the patient’s IgE antibodies.

Another approach being pursued at the current time is the use of individual beads, each with a different allergen and a different fluorescent color; using flow cytometry and a fluorescent-labeled anti-IgE antibody, a large number of different allergens may be tested simultaneously. This so-called **“multiplex” approach** (using the xMAP® technology developed by the Luminex Corporation) has been successfully used to measure many different cytokines and have recently been used to measure different anti-nuclear antibodies. But development of this technique for specific IgE measurement has been difficult.

Future Developments: New Multiplex Immunoassay Approach

We recently completed an evaluation of a different approach to multiplex immunoassay specifically designed (by Hitachi Chemical Diagnostics) for allergy testing. This method uses a disposable solid phase with twenty different allergens, each bound to a different portion. A small stream of sample is allowed to interact with these and, after washing, anti-IgE is added. A chemiluminescent detection system allows individual measurement of each of the twenty areas. This method (which agreed well with our individual automated assays) requires only 300 microliters of serum to perform the 20 assays and they include the common airborne and food allergens seen in children. We hope to be able to offer this new panel soon.

Especially given the rising prevalence of allergic disease, it is increasingly important to consider allergy when patients present with a variety of respiratory and cutaneous symptoms. Serum testing for specific IgE antibodies is a convenient way to screen the large numbers of such patients seen by primary care physicians.

Laboratory Update: Stanford Clinical Laboratory launches www.stanfordlab.com

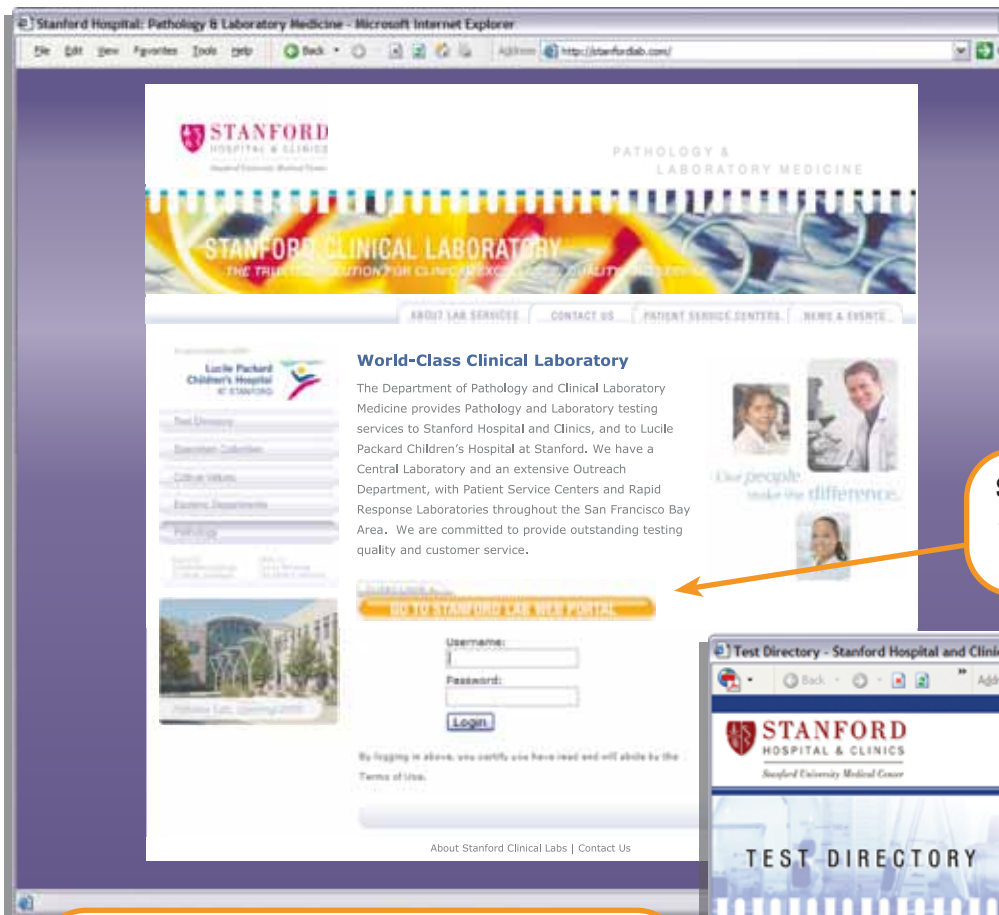
Dedicated to providing an easy to navigate resource for internal and out patient services.

Features include:

- Test Results
- Specimen Collection Information
- PSC locations with Mapquest® driving directions
- LabLetter archives, The Stanford Clinical Laboratory Newsletter

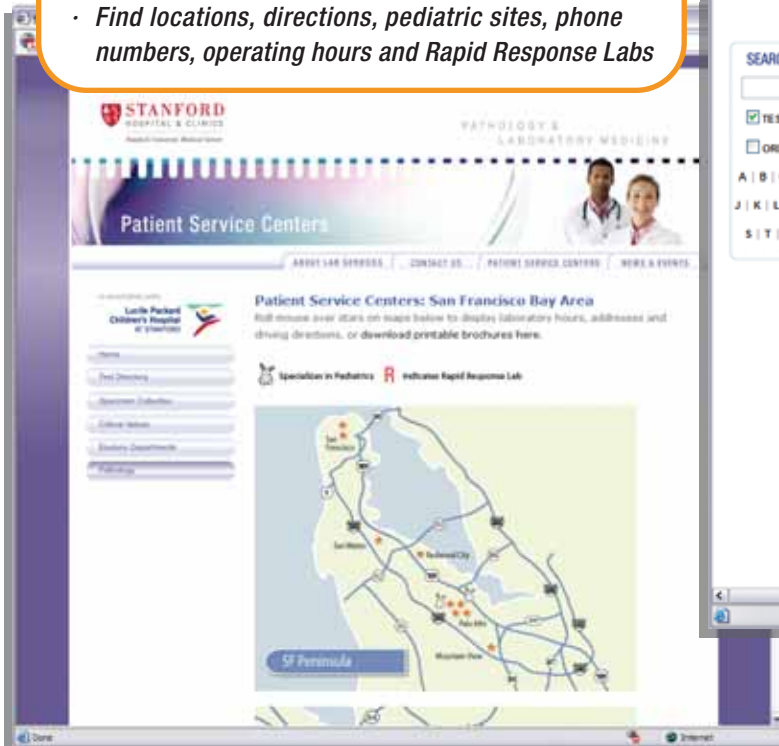
Stanford Lab Web Portal

- Direct access of test results for clients of Stanford Clinical Laboratory



Patient Service Centers

- Find locations, directions, pediatric sites, phone numbers, operating hours and Rapid Response Labs



Test Directory Compendium

- Find test information, specimen requirements and turn around times for specific tests

Q&A: Submit Q&A topics of interest to: labmarketing@stanfordmed.org

An opportunity for the Bay Area Medical Community to request specific Q&A topics to our medical directors that are relevant to patient's clinical needs.



Michael Petzar, M.D.

STANFORD CLINICAL LABORATORY CRITICAL / PANIC VALUES FOR ADULT AND PEDIATRIC POPULATIONS

Q&A with Michael Petzar, MD, Associate Director: Point-of-Care Testing, Coagulation, and Clinical Hematology Laboratories, Stanford Hospital & Clinics / Lucile Packard Children's Hospital.

Federal Regulations require a laboratory to “immediately alert the...entity requesting the test...when any test result indicates an imminent life-threatening condition...” We are currently reviewing our list of critical values to more accurately classify those values which could represent an emergency. You will receive an updated list of critical values when the process is complete.

Q1: How are critical values determined?

A1: The medical director of each section of the laboratory uses their expertise to evaluate available medical literature, the critical values used by other laboratories, and consultations with clinicians, to identify abnormal laboratory values which could indicate medical conditions resulting in significant morbidity or mortality if not evaluated immediately. These values are then submitted for approval to the Medical Director of the laboratory and to the Medical Boards of Stanford University Medical Center and Lucile Packard Children's Hospital which are responsible for setting the medical standards of our care.

Q2: What is the policy for Stanford Clinical Laboratory in calling critical values?

A2: If a result is a critical value, a technologist or customer service representative will call the provider's office or answering service within 30 minutes of result verification to communicate the result. If no provider is available after hours, another attempt to call the result will be made the next morning and if still not successful, again on the next business day. The laboratory report will document when the call was placed, when the provider responded to receive the results, and the reasons for any delay in communication.

Q3: Can I “opt out” of notification or have different thresholds for critical values to be called?

A3: No, you cannot “opt” out of notification or have different thresholds for critical values since *federal regulations require the laboratory to communicate critical values immediately*. A lack of uniformity in what constitutes a critical value will create confusion within our staff and lead to medical error. We consider the needs of the patients of *all* our clients in setting our critical values. This is a difficult process, as the patient's medical condition is key to determining whether a given result is life threatening. The patient's provider is the *best person* to evaluate whether a critical value needs attention. For example:

- An INR of 6 may only require skipping a dose of coumadin in an asymptomatic patient, but could require urgent care in a bleeding patient.

- A low glucose may represent an insulin reaction at the time of the blood draw (long since past), but the laboratory cannot know whether the patient is on a long acting oral hypoglycemic where a low value could require emergent treatment. Our critical values are designed to alert clinicians to the possibility of imminent danger to their patients, but *only you can evaluate whether a true emergency exists*.

Q4: Will I be called if a result is known to be erroneous?

A4: Not usually.

- If a result is known to be erroneous you will not be called. The result will be invalidated and the report will indicate the need to resubmit the specimen.
- If the value cannot be determined to be erroneous, but there is a possibility of a compromised specimen, you will be called and the situation explained so you can decide whether the patient needs to be urgently evaluated.
- If you have a question about the test the technologist can't answer for you, ask them to contact the laboratory physician on-call who has access to the expertise of all the section directors 24 hours a day / 7 days a week. Our goal is to provide you with the best knowledge of laboratory science.

Q5: What can I do to make the critical value notification process effective?

A5: Patient injury due to failures in timely communication of important ancillary test results is a rising source of litigation. Protect your patients, yourself and us by ensuring we are able to reach you urgently when needed.

- Please check with our customer service department to be sure we have the correct contact information or to whom we should call the critical values to, so they can be addressed promptly (*regulations do not permit the technologists to give laboratory values directly to patients*).
- If you are expecting a significantly abnormal result, consider having the patient drawn at our Fremont, Samaritan Drive (San Jose), or Salinas (coming soon) **Rapid Response Laboratories** where Basic Metabolic, Electrolytes, CBC, PT, APTT, and Urinalysis are performed on-site, *or* take advantage of our RUSH services to get your result during business hours or early evening.

References

1. Laboratory critical values policies and procedures: A College of American Pathologist Q-probes study in 623 institutions. *Archives of Pathology & Laboratory Medicine*, Jun 2002 by Peter J. Howanitz, MD; Steven J. Steindel, PhD; Nan V. Heard, MD Copyright College of American Pathologists Jun 2002
2. Clinical Laboratory Improvement Amendments of 1988: final rule (42 CFR Part 405, et al), 57 Federal Register 7001-7186 (1992).
3. Stanford Clinical Laboratory Critical Value Policy and Critical Value List.

