OPTIMIZING CARE OF ALLERGY PATIENTS: PRACTICE PARAMETER YEAR IN REVIEW

EDITOR’S NOTE: We’re pleased to be able to bring you this special supplement to AllergyWatch, presenting succinct reviews and expert commentaries of five important updated or new Practice Parameters. These guidelines were developed by The Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma & Immunology; the American College of Allergy, Asthma & Immunology; and the Joint Council of Allergy, Asthma & Immunology.

Each Practice Parameter presents recommendations for diagnosis and management of clinical conditions of high interest to every practicing allergist, based on the best available research evidence and expert opinion. The complete Practice Parameters can be freely accessed at www.allergyparameters.org.

We thank the ACAAI Board of Regents for enabling us to bring you this special supplement to AllergyWatch. We hope the information presented will prove to be of value in meeting our specialty’s primary goal: to provide the best possible care for patients and families affected by asthma, allergy, and immune disorders.

S.A.T.

Practice Parameter for Primary Immunodeficiency—Major Update

Primary immunodeficiency diseases (PIDDs) are inherited disorders of immune function occurring in up to 1 of 2,000 live births. More than 200 diagnoses have been identified to date; they may be classified based on a combination of mechanistic and clinical characteristics, or by characteristic phenotypes.

Increased susceptibility to infection is the main clinical manifestation of PIDDs, but the involved organ systems and characteristic pathogens vary depending on the type of immune defect. Autoimmune diseases and malignancies may be seen as well. The evaluating physician should carefully document the infectious foci, organisms involved, and response to treatment. Other predisposing conditions should be evaluated as well.

Initial evaluation for suspected primary immunodeficiency is guided by the clinical presentation (see Figure, p. 5). The Practice Parameter specifies screening and advanced laboratory tests for a stepwise approach to identifying the mechanism of the underlying immune defect. The differing organ systems and the characteristic pathogens involved with various types of immunodeficiency disorders are summarized as well (see Table, p. 6).

Severe combined immunodeficiency (SCID) is associated with complete absence of specific immunity and extreme susceptibility to pathogens. Chronic diarrhea and failure to thrive are a common presentation, with laboratory findings depending on the specific molecular defect. Early intervention for this urgent medical condition improves the chances of survival; definitive hematopoietic stem cell therapy should be performed as soon as possible.

For other immunodeficiency syndromes, the pree...
sentation depends on the specific disorder and host, genetic, and environmental factors. Treatment is generally supportive, with some patients requiring gammaglobulin replacement or antimicrobial prophylaxis; stem cell transplantation is sometimes used. The Practice Parameter also summarizes the findings associated within combined immunodeficiencies and syndromes, various antibody deficiencies, and complement deficiencies.

It also includes algorithms for disorders of immune dysregulation, phagocytic cell defects, and the rare disorders of innate immunity and autoinflammatory syndromes. Diagnosis and treatment should be guided by or in consultation with physicians and centers with knowledge and experience in treating a wide range of PPIDs, in order to achieve consistent evaluation and management and to improve outcomes for the patient and family.

COMMENT: The 2015 PIDD parameter is a significant update from 2005, with an additional 35 pages of information. The classification has changed to follow the World Health Organization and International Union of Immunological Societies. This has resulted in the addition of several new sections on diseases involving defects of innate immunity, autoinflammatory disorders, noninflammasome defects, and immunodeficiency associated with autoantibodies. In total, over 180 additional diseases are discussed. Other specific updates include a section on newborn screening for SCID, antimicrobial prophylaxis regimens, and Internet resources on PIDD. This comprehensive document is specifically targeted to assist the consultant allergist/immunologist in evaluating and managing patients with suspected or known PIDD.

Latest Update on Contact Dermatitis

Several changes in practice related to contact dermatitis (CD) have taken place over the past decade, including increased referrals to allergists, expanded use of preloaded commercially available patch tests, and advances in understanding of different types of reactions. Updated guidelines for evaluation and management of CD in adults and children are presented, based on research evidence and consensus expert opinion.

The Practice Parameter provides action-based summary statements to guide identification of potential sensitizing substances in CD, based on clinical presentation in specific skin areas. Allergic CD should be considered in patients with chronic eczematous or noneczematous dermatitis. Other skin conditions can have a similar appearance, and should be considered in the differential diagnosis.

Contact dermatitis is suspected from the clinical appearance and distribution of the skin lesions, along with the absence of other causes. A scattered/generalized distribution is the most common location, followed by the hands and the face. Personal products used by the patient should be reviewed along with home and workplace factors.

Specific types of exposures to consider are discussed for patients with rashes in the periorbital, perioral, scalp and neck, hand, • • •
Update on Anaphylaxis Addresses Questions and Controversies

Since the last Practice Parameter in 2010, there have been developments in several areas affecting evaluation and management of patients with anaphylaxis. An evidence-based update on anaphylaxis is presented, with new sections including “controversies and unsettled issues.”

The new document includes summary statements concerning the evaluation and management of patients with a history of anaphylaxis (see Figure, p. 7). There is a strong recommendation that patients should be supplied with and instructed in the use of auto-injectable epinephrine (AIE), including advice to carry two AIEs at all times. Other recommendations address the anaphylaxis action plan, individualized avoidance measures, and education about hidden allergens and cross-reactivity. Counseling about future episodes should include information about beta-blockers or other medications that might worsen an event or lead to complications.

The Practice Parameter discusses the roles of pharmacologic prophylaxis and desensitization. It also provides information on specific aspects of diagnosis and treatment of anaphylaxis, including a protocol for treatment of anaphylaxis in the physician’s office.

There is continued debate over the use of AIEs in certain clinical situations—including patients receiving subcutaneous immunotherapy, large local reactions to insect stings, oral allergy syndrome (fruit pollen syndrome), and children with facial contact urticaria from food allergens. In all of these situations, the decision is left to physician discretion.

The potential risks of Hymenoptera venom immunotherapy in patients taking angiotensin-converting enzyme inhibitors should be discussed with the patient’s other specialists (cardiologist, nephrologist). Unsettled issues include the use of epinephrine in patients with mild systemic symptoms or in elderly patients with hypertension and/or arteriosclerotic heart disease. While there is a lack of data on the proper dosage of epinephrine in children weighting less than 15 kg, the recommendations conclude that prescribing an AIE is “prudent” for small children at risk of anaphylaxis.

COMMENT: This newest iteration of the Practice Parameter goes beyond an evidence-based document regarding the diagnosis and treatment of anaphylaxis. Dr. Lieberman and colleagues also grapple with “controversies and unsettled issues related to patients at risk for or being treated for anaphylaxis.” They tackle questions including whether AIE should be provided to patients undergoing immunotherapy or those with large local reactions to Hymenoptera or with oral allergy syndrome (fruit-pollen syndrome). Other controversies include the use of AIE in patients with cardiac disease, dosing in small children and exclusion of Hymenoptera immunotherapy in patients receiving an ACE inhibitor. This is a must-read—although no firm answer can be had in most of these issues, the authors bring to light several gaps in knowledge that allergists face in caring for patients with anaphylaxis and explore what literature is available.

J.J.O.


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axillary, anogenital, and lower extremity areas. It is important to consider the possibility of coexisting atopic dermatitis and allergic CD. Irritant CD should be considered especially for patients with hand dermatitis.

Patch testing is the standard for diagnosis, including core or baseline allergens along with others based on the patient’s specific exposures. Testing may be performed using a preloaded thin-layer testing kit or a panel of antigens loaded in a chamber system. The T.R.U.E. Test system is standardized and provides highly reproducible results. Recommendations for reading and interpretation are discussed, including possible causes of false-positive and false-negative reactions.

Considerations for evaluating sources of clinically relevant allergen exposure include skin contact with seasonal pollen allergens, the types of chemicals most commonly involved in reactions to cosmetics and personal care products, special issues related to hair and nail products, and possible reactions to topical medications. Other topics include suspected photo-allergic CD, in vitro tests for delayed hypersensitivity to contact allergens, use of the repeated open application test, and evaluation and management of pediatric and occupational contact dermatitis.

COMMENTS: The 2015 Practice Parameter on CD has been updated since the 2006 parameter in many important ways. Several new allergens are discussed including methylchloroisothiazolinone or methylisothiazolinone, important as a cosmetic and toiletry contact allergen; and essential oils (e.g., tea tree oil) and propolis in cosmetic dermatitis. There are new sections on drug allergy, including the baboon syndrome, and the role of drug patch testing in severe cutaneous adverse drug reactions. There is a very in-depth discussion on metal implants, and the role and interpretation of preoperative patch testing in patients with a history of metal allergy are reviewed. An expanded discussion on patch testing in children has also been updated. A new table highlights those allergens which appear early versus those with late peak reactions. Finally, several new appendices contain very practical information such as patch test forms, where to obtain contact allergens, and corticosteroid cross-reactivity charts. This is a helpful and practical resource for allergists seeing patients with potential contact reactions.

D.A.K.

J Allergy Clin Immunol Pract. 2015;3(suppl);S1-39.  ●
Anaphylaxis in the Emergency Room—What ED Physicians Need to Know

Emergency department (ED) physicians and allergists both recognize the importance of timely epinephrine administration for patients with anaphylaxis. However, epinephrine may be underused if anaphylaxis is not recognized, or sometimes even when it is recognized. This new Practice Parameter provides recommendations on ED diagnosis and management of anaphylaxis.

Diagnosis of anaphylaxis in the ED relies on the history and physical examination, but must recognize the wide variation in clinical presentations. Immediate triage and monitoring are essential, as anaphylaxis can rapidly become life-threatening. The Practice Parameter includes recommendations to place patients in a supine position; to administer oxygen, especially when respiratory and cardiovascular conditions are present; and to consider other possible causes besides anaphylaxis. Risk factors for severe or potentially fatal anaphylaxis include delayed epinephrine administration, asthma, history of biphasic reactions, and cardiovascular disease.

As soon as anaphylaxis is diagnosed, epinephrine is administered intramuscularly in the anterolateral thigh (see Figure, p. 8 ). If there is no response, monitored intravenous epinephrine should be given; if intravenous access is not readily available, intraosseous administration is a safe and effective alternative. The Practice Parameter includes a discussion of airway management, including the difficult decision whether to intubate. Aggressive fluid resuscitation is needed for patients with circulatory collapse, followed by glucagon if necessary. Antihistamines or corticosteroids should not be routinely used instead of epinephrine—the Practice Parameter states, "There is no substitute for epinephrine in the treatment of anaphylaxis."

The anaphylaxis trigger should be identified, but may be obscure. Observation for at least 4 to 8 hours should be considered for patients with anaphylaxis, and longer for those with risk factors for severe anaphylaxis. The consensus statement recommends prescribing auto-injectable epinephrine and instructions to follow up promptly with an allergist. COMMENT: This Practice Parameter was developed by allergists as well as emergency medicine physicians, and is directed toward ED physicians’ treatment of anaphylaxis. Several of the summary statements deserve mention—including one reinforcing that intramuscular epinephrine is the first-line treatment for anaphylaxis. In patients who don’t respond, the next line of therapy (beyond copious fluids and basic CPR) would be epinephrine via the intravenous route. The authors reinforce that antihistamines and corticosteroids, should not be considered first-line and should solely be used as adjunctive therapy. They recommend that patients should be observed for at least 4 to 8 hours following an anaphylactic episode. Patients with prior biphasic or protracted anaphylaxis should be observed for even longer. Finally, the

Practice Parameter recommends prescribing of an auto-injectable epinephrine as well as an allergy consultation at discharge from the ED.


Food Allergy—Update on Classification, Diagnosis, and Management

Food allergies involve specific and reproducible immune responses to foods, including not just IgE-mediated immunologic reactions but also other types of sensitivity reactions. The prevalence of food allergies may be increasing, although self-reported rates are higher than confirmed rates. The 2014 Practice Parameter presents an extensive update on the classification, diagnosis, and management of food allergies.

Although virtually any food can elicit reactions, most cases of food allergy involve a relatively small number of allergens, such as cow’s milk, hen’s egg, soy, wheat, peanut, tree nuts, fish, and shellfish. Patients should be evaluated for and understand the risk of cross-reactivity to other allergens. The Practice Parameter includes information on the low risk of reactions to genetically modified foods along with recommendations related to potential adverse reactions to food additives.

The physician must assess whether food allergy can be diagnosed from the history and laboratory findings, or whether oral food challenge is needed. Follow-up should be individualized, including consideration of which childhood food allergies tend to resolve more quickly (eg, milk and egg) and which do not (eg, peanut and tree nuts). Mothers should be encouraged to breast-feed exclusively during the first 4 to 6 months of life; partially or extensively hydrolyzed formula can be considered if needed. Dietary supplementation with probiotics is not routinely recommended.

Recommendations for diagnosis of food allergy include the appropriate roles of specific IgE tests, component resolved testing, open and blinded food challenges, and specific tests for food protein-induced enterocolitis (FPIES), eosinophilic esophagitis, and other disorders.

A targeted elimination diet is the treatment for known or strongly suspected food allergy, with education about anaphylaxis and the use of epinephrine for IgE-mediated allergic reactions. Patients should understand that severe allergic reactions almost always result from ingestion, rather than skin exposure or close proximity. The Position Paper addresses treatment recommendations targeting specific disorders and follow-up for children and adults. It calls for all patients to receive a written action plan, and to be asked about bullying related to food allergies.
**COMMENT:** The 2014 Food Allergy Practice Parameter has been extensively updated from the 2006 parameter. It also includes advances since the 2010 NIAID Guidelines. This parameter was authored by many of the most prominent food allergy experts in the United States, under the leadership of Hugh Sampson. Many new items and sections may be found in this update, including delayed mammalian meat allergy due to alpha-gal, recommendations regarding prevention of food allergy, genetically modified foods, new food additive allergy, and use of component-resolved testing. In addition to IgE-mediated food allergies, there are detailed sections on diagnosis and management of non-IgE mediated food reactions including FPIES and eosinophilic esophagitis. Emerging therapies including baked milk and egg diets and oral immunotherapy are also discussed. Finally, the update includes many useful and practical tables on topics including food cross-reactivity and predictive values for skin tests and specific IgE to selected foods.


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**General approach for the diagnosis of primary immunodeficiency.**

For complete legend and other algorithms and tables referred to in this figure, see the full Practice Parameter.

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Characteristic clinical presentations of some immunodeficiency disorders.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Symptoms and/or clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIDs</td>
<td></td>
</tr>
<tr>
<td>SCID</td>
<td>Failure to thrive, diarrhea, severe disseminated infections, opportunistic infections, rash; abnormal newborn screen*</td>
</tr>
<tr>
<td>CD40L deficiency</td>
<td>Recurrent serious pyogenic infections, opportunistic infections (PCP)</td>
</tr>
<tr>
<td>Immunodeficiency syndromes</td>
<td></td>
</tr>
<tr>
<td>WAS</td>
<td>Thrombocytopenia with bleeding and bruising, eczema, recurrent infection with encapsulated organisms, autoimmunity</td>
</tr>
<tr>
<td>AT</td>
<td>Chronic sinopulmonary disease, cerebellar ataxia, oculocutaneous telangiectasia, malignancy</td>
</tr>
<tr>
<td>DGS</td>
<td>Hypocalcemic seizures caused by hypoparathyroidism, cardiac disease, abnormal facies, infection, abnormal newborn screen*</td>
</tr>
<tr>
<td>Antibody deficiency</td>
<td>Recurrent sinopulmonary infections with encapsulated bacteria, recurrent viral respiratory tract and gastrointestinal infections</td>
</tr>
<tr>
<td>Immune dysregulation</td>
<td></td>
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<tr>
<td>Phagocytic cell defects</td>
<td></td>
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<tr>
<td>CGD</td>
<td>Deep-seated infection, abscess with granuloma formation</td>
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<tr>
<td>LAD</td>
<td>Recurrent serious bacterial infections, delayed separation of the umbilical cord; poor wound healing, lack of pus</td>
</tr>
<tr>
<td>HIES type 1</td>
<td>Chronic dermatitis, recurrent serious infection of the lungs with pneumatoceles; skin infections, bone fragility, failure to shed primary teeth</td>
</tr>
<tr>
<td>MSMD</td>
<td>Severe mycobacterial and Salmonella species infections</td>
</tr>
<tr>
<td>Innate immune defects</td>
<td></td>
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<tr>
<td>NEMO deficiency</td>
<td>Severe bacterial infections, opportunistic infections, anhidrotic ectodermal dysplasia</td>
</tr>
<tr>
<td>IRAK-4 defect</td>
<td>Severe gram-positive bacterial infections in early childhood</td>
</tr>
<tr>
<td>CMCC</td>
<td>Chronic skin and mucous membrane fungal infections</td>
</tr>
<tr>
<td>HSE</td>
<td>Herpes simplex encephalitis</td>
</tr>
<tr>
<td>EV</td>
<td>Severe disseminated cutaneous papillomatosis</td>
</tr>
<tr>
<td>Autoinflammatory disorders</td>
<td>Episodic fever often associated with dermatitis, gastrointestinal symptoms, and arthropathy</td>
</tr>
<tr>
<td>Complement deficiency</td>
<td>Recurrent bacterial infections (encapsulated strains, Neisseria species), autoimmunity</td>
</tr>
<tr>
<td>Immunodeficiency associated with autoantibodies</td>
<td></td>
</tr>
<tr>
<td>Anti--GM-CSF autoantibodies</td>
<td>Cryptococcal meningitis and PAP (alone or together)</td>
</tr>
<tr>
<td>Anti--IFN-γ autoantibodies</td>
<td>Disseminated infections with mycobacteria, Salmonella species, Cryptococcus species, Histoplasma species, Penicillium species, and varicella-zoster virus</td>
</tr>
</tbody>
</table>

*Many states are now screening for SCID (see SS 26). Some infants with DGS (and other disorders) might be detected by this newborn screening. See Table II for abbreviations.

Algorithm for initial evaluation and management of a patient with a previous episode of anaphylaxis.

1. Is the history consistent with a previous episode of anaphylaxis?  
   - NO  
   - Proceed with diagnosis or make appropriate referral

   - YES  
   - Consider consultation with allergist/immunologist

   - YES  
   - Is cause really identified by history?

   - NO  
   - Consider allergic anaphylaxis

   - YES  
   - Are further diagnostic tests indicated? Allergy skin tests or in vitro tests? Anaphylactic shock or IgE antibody detection? Food allergy diagnostic protocols? (See Box 10)

   - NO  
   - Diagnosis established or lack of history
   - Risk of testing
   - Limitation of tests
   - Patient refusal
   - Other management options available
   - Management

   - YES  
   - Reconsider clinical diagnosis
   - Consider allergic anaphylaxis
   - Consider further testing
   - Management (See Box 10)

2. Diagnosis made for specific cause of anaphylaxis

3. Management of anaphylaxis
   - General patient education
   - Risk assessment
   - Consider appropriate discontinuation of drugs which may worsen the event or interfere with the treatment. These might include beta-adrenergic blockers, angiotensin-converting enzyme inhibitors, monoamine oxidase inhibitors, etc.
   - Medication: self-administered epinephrine
   - Specific: Avoidance (e.g., food)
   - Immunotherapy (e.g., hyposensitization)
   - Desensitization (e.g., penicillin)
   - Graded challenge (e.g., local anesthetic)
   - Premedication (e.g., anti-allergy agents)
   - All patients should be prescribed an automatic epinephrine injector and given an anaphylaxis action plan

Emergency anaphylaxis management algorithm.