

Common Allergic Diseases in Primary Care

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Objectives

- Discuss allergic conditions that often present diagnostic or therapeutic uncertainty
- Outline initial approaches to evaluation and management
- Discuss first steps in treatment of these conditions
- Review criteria for referral to an allergist

Case #1

- 47 year old male
- History of hypothyroidism, hypertension
- Presents with 8 weeks of rash
- Diffuse, pruritic, erythematous
- Raised papules and confluent plaques
- Migratory, individual lesions last for 1-2 hours
- No new foods, topical products, medications

Case #1

- No relief with Benadryl
- Taking ibuprofen for joint pain associated with lesions
- Cell phone photo



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Urticaria

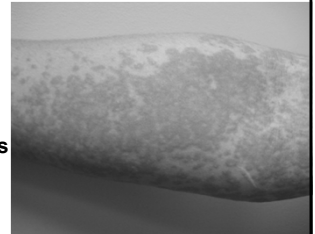
- Pruritic wheals
- Develop rapidly
- Central edema with surrounding erythema
- Generally last <24 hours
- Frequently associated with angioedema



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Urticaria

- Acute (< 6 weeks)
 - Often with allergic trigger
 - Medication, food, environmental, illness
- Chronic (>6 weeks)
 - Majority symptomatic days
 - Chronic inducible (CindU)
 - Chronic spontaneous (CSU)



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Chronic Inducible Urticaria

- Recurrent hives after specific stimuli
- Dermatographism
- Cold urticaria
- Cholinergic urticaria
- Delayed pressure urticaria
- Vibratory urticaria
- Lower rates of remission than spontaneous hives



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<https://www.publicdomainpictures.net/en/view-image.php?image=164892&picture=ice-cubes>

Chronic Spontaneous Urticaria (CSU)

- Hives independent of external stimuli
- Affecting 0.1-0.8% population
- Often presenting in 30s-50s
- High morbidity
- Majority self-limited
- Average duration of 2-5 years
- 30-50% with spontaneous remission at 1 year

Chronic Spontaneous Urticaria

- Exacerbating factors
 - Physical - temperature, pressure, vibration
 - NSAIDs
 - Stress
 - Alcohol
 - Opiates
- Associated conditions
 - Autoimmunity – celiac, SLE, thyroid
 - Malignancy

Chronic Spontaneous Urticaria

- Evaluation
 - History and physical
 - Medications
 - Bruising, lesions lasting multiple days
 - CBC, CMP, CRP/ESR, TSH
 - G6PD function
 - Skin biopsy if vasculitic concern
- Testing low yield if no clear risk factors
- Skin testing for foods, aeroallergens not recommended

Treatment

Second Generation H1 antihistamine (4x approved dosing)

H2 antihistamine twice daily

Montelukast 10 mg daily

- If not improving, consider cyclosporine, Xolair, dapsone

Our Patient

- Diagnosis of chronic spontaneous urticaria
- CBC, CMP, TSH, ESR/CRP unrevealing
- Cetirizine 20 mg BID, famotidine 20 g BID; ibuprofen held
- Modest improvement, montelukast added
- Improved, but still flaring twice weekly
- Starts Xolair 300 mg monthly with marked improvement
- At 12 months, no further significant flares
- Medications are held with no recurrence of symptoms

Chronic Urticaria Take Home Points

- Chronic urticaria require >6 weeks duration
- Generally without food or aeroallergen triggers
 - Food eliminations are unlikely to be beneficial
- Patients may have autoimmune background but often no clear trigger
- Generally require high dose antihistamines for adequate control
- Majority of patients with spontaneous resolution
- Referral to allergy if unresponsive to antihistamines, montelukast

Case #2

- 35 year old healthy female
- Recurrent abdominal pain, then hives and wheezing
- Has required treatment in ED, epinephrine injector provided
- Two episodes in the middle of the night
- No symptoms within 2 hours of meals
- No changes in diet, new medications



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Case #2

- Food diary reviewed
 - Beef brisket, pork chops on evenings of episodes
- Anaphylaxis of unclear etiology
- Girl Scout troop leader
- Camping trip to Tennessee 4 months ago
- Had to remove tick from sock line



Source: <https://www.publicdomainpictures.net/en/view-image.php?image=53766&picture=tent-by-the-lake>

Another Medical Mystery

- 2005 – Severe anaphylaxis reported to cetuximab
- Monoclonal antibody for metastatic colorectal cancer
- Occurred with initial exposures
- Similar episodes reported throughout southeastern US
- Antibody analysis showed IgE toward oligosaccharide
- Galactose-alpha-1,3-galactose (alpha-gal)
- Severe allergic reactions generally attributed to proteins

Another Medical Mystery

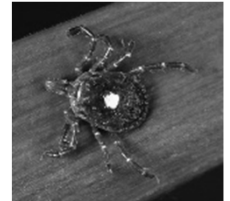
- Concurrent reports of patients with repeated anaphylaxis
- Patients often spent large amount of time outdoors
- History of mammalian meat ingestion 3-5 hours prior
- Several reported tick bites in preceding months
- Similar geographic distribution to cetuximab patients



Source: <https://www.publicdomainpictures.net/en/view-image.php?image=211453&picture=double-cheeseburger>

Another Medical Mystery

- Alpha-gal IgE found in patients with delayed meat reactions
- Alpha-gal is found in non-primate mammalian meat
 - Symptoms with beef, pork, lamb, venison
 - No issues with fish, poultry
- Distribution of reactions similar to Lone Star tick
- Alpha-gal IgE titers increased post-tick bite



Source: CDC/ Michael L. Levin, Ph. D

Another Medical Mystery Solved

- Tick bite → alpha gal sensitivity → delayed mammalian meat reaction
- Increased deer populations may account for wider exposure
- Slow metabolism of alpha-gal may result in delayed symptoms
- Unclear sensitizing factor in tick bite
 - Saliva, contamination from prior blood meal?
- Reported internationally, variable tick species
- Alpha-gal IgE can drop if no repeat sensitization/bite

Alpha-gal allergy

- Has been reported outside of the southeastern US
- Can occur in adults and pediatric patients
- Consider diagnosis with recurrent unexplained hives or anaphylaxis
- Careful dietary history, particularly mammalian meat
- Reactions reported to organ meat, gelatin, milk
- Commercially available IgE for alpha-gal
- Patients should avoid mammalian meats, carry epinephrine
- Tick avoidance measures per CDC guidelines

Our Patient

- Alpha-gal allergy suspected given dietary history
- IgE to alpha-gal sent and found to be substantially elevated
- Recommended avoidance of all mammalian meats
- Instructed to carry epinephrine auto-injector at all times
- Significant reassurance in identifying trigger
- No recurrence of episodes

Alpha-gal Allergy Take Home Points

- Consider alpha-gal in patients with recurrent hives/anaphylaxis
- Atypical in causative trigger (carbohydrate) and timing
- Careful dietary history - mammalian meat several hours prior
- May not occur with each ingestion
- History of tick bite exposure
- Epinephrine auto-injector for all affected patients
- Identification of trigger and avoidance with significant quality of life benefit

Case #3

- 18 year old male, works in landscaping
- Digs into yellow jacket nest at work
- Stung multiple times on the hand, swells to elbow
- Also develops scattered hives, lip swelling
- No wheezing, vomiting, loss of consciousness



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No changes made

Case #3

- Co-workers call 911
- He is given epinephrine in the field
- Modest improvement in skin symptoms
- Does not require ED transport
- Treats with antihistamines at home
- Swelling resolves after 4-5 days
- Presents for recommendations on allergy testing



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No changes made

Stinging Insect Allergy

- At least 40 deaths attributed annually to sting reactions
 - Likely underestimate
- Potentially life threatening sting reactions
 - 3% of adults
 - 0.4-0.8% of children
- Identification of at-risk patients potentially life-saving



Source: Author: Jonathunder
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Stinging Insect Allergy

- Stinging insects belong to order Hymenoptera
 - Honeybee, yellow jacket, yellow hornet, white faced hornet, wasps, fire ants
- Most stings occur in defense of insects/nest
- Honeybee – barbed, single sting
- Wasps, hornets, yellow jackets – multiple stings



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Source: <https://en.wikipedia.org/wiki/Stinger#/media/File:Waspstinger1658-2.jpg>

Stinging Insect Allergy

- Typical reaction – local swelling, pain
- Large local reactions (LLR)
 - Progressive gradual swelling contiguous with sting site
 - May last for up to 10 days
 - Often 10 cm or more, may cross joint lines
 - Can cause local compression, not typically dangerous
- Toxic reactions – may occur with multiple stings

Stinging Insect Allergy

- Fire ant stings
 - Sterile pustules can develop days after stings
 - Non-infectious
 - Self-limited



Source: USDA

Stinging Insect Allergy

- Cutaneous systemic reaction
 - Hives, angioedema, flushing, pruritus
 - Limited to skin (no tongue, throat involvement)
- Systemic reaction
 - Hives, angioedema
 - Wheezing
 - Nausea, vomiting, diarrhea
 - Hypotension, syncope

Stinging Insect Allergy

- Risk stratification
- Systemic reactors – up to 75% chance of future systemic
- Immunotherapy can drop risk to 5%
- Baseline tryptase level
- Referral for allergy testing
 - Percutaneous skin testing, intradermals, IgE testing
- Carriage of epinephrine injector x2 at all times
- Avoidance of ACEi, beta-blockers if possible

Stinging Insect Allergy

- Large local reactors – 4-10% chance of systemic
 - Generally not severe
- Cutaneous systemic reactors – low chance severe reaction
- Can be false positive tests, especially after sting
- Do not require epinephrine injectors
- No need for allergy testing, immunotherapy
- May be risk factors that prompt testing

Stinging Insect Allergy

- Testing and treatment for all available venoms
- 3-5 years unless high risk
 - Reaction to a shot/sting on treatment
 - Honeybee allergy
 - Severe initial reaction
 - Elevated tryptase
 - Frequent exposure
- Cluster and rush protocols available, safe



Source: No machine-readable author provided. Biggishben-commonswiki assumed - CC BY-SA 3.0

Our Patient

- Classified as cutaneous systemic reaction
- Discussion of low risk of severe systemic reaction
- Skin testing, IgE testing deferred
 - Risk of false positives, limited protective benefit of shots
- Epinephrine autoinjector not strictly indicated
 - He prefers to have this given his exposure

Our Patient

- Stinging insect avoidance measures
 - Avoiding eating outside
 - No straws/cans/open bottles outside
 - Avoid flowering plants
 - Cover trash cans
 - Avoid walking barefoot outside
 - Remove fallen fruit, pet feces
 - Monitor for nests in ground/bushes during yard work

Stinging Insect Allergy Take Home Points

- Careful history is crucial in risk stratification
 - Standard reaction
 - Large local reaction
 - Cutaneous systemic reaction
 - Systemic reaction
- Patients with systemic reactions or large local/cutaneous systemic reactions with risk factors warrant referral for testing
- Risk of false positive tests – only those considered for shots generally tested
- Allergy shots can be life-saving
- Prevention measures key, epinephrine for appropriate patients

Case #4

- 55 year old female with history of recurrent sinusitis
- History of penicillin allergy in childhood
- Developed a rash several days into treatment
- May have had some throat tightness
- Did not require ED visit
- No desquamation, mucosal ulceration, ocular involvement
- No re-exposure



Source: <https://www.publicdomainpictures.net/en/view-image.php?image=24312&picture=medical-pills>

Penicillin Allergy

- Approximately 10% of US population carries label
- More than 90% are not found to be allergic on evaluation
 - If reaction >10 years ago, risk severe allergic reaction 1-2%
- Inappropriate labeling associated with increased costs, risk
 - Side effects/cost of alternative treatments
 - Drug resistant organisms
 - Increased cost/length of hospital stays
 - Decreased cure rates
- IDSA, CDC advocate for de-labeling allergy

Penicillin Allergy

- Non-allergic
 - Family history, side effects
- Immediate hypersensitivity
 - Anaphylaxis
 - Histaminergic symptoms (hives, pruritus, swelling)
 - Rapid onset
- Delayed reactions
 - Morbilliform rash, delayed hives/angioedema
 - DIHS/DRESS, SJS/TEN, AGEP
 - Interstitial nephritis, hemolytic anemia, hepatitis

Penicillin Allergy

- If non-allergic, can re-challenge or de-label
- If strict contraindication, no testing available
 - SJS/TEN, hepatotoxicity, etc
- Reaction unclear or immediate allergy, referral
 - Skin testing
 - Graded dose challenge
 - Desensitization

Penicillin Allergy

- Skin testing
- Assessing for immediate IgE mediated allergy
- Performed with Pre-Pen (penicilloyl-polylysine)
 - Major allergenic determinant
- PCN G (10,000 units/ml)
 - Minor allergenic determinant
- Percutaneous testing
- Intradermal Testing



Author: National Institute of Allergy and Infectious Diseases

Penicillin Allergy

- Histamine and saline controls
- Tests read at 15 minutes
- Positive test – wheal \geq 3 mm negative control
- Approximately 50% PPV
- Approximately 97-99% NPV
 - If false negative, reaction generally mild

Penicillin Allergy

Graded Dose Challenge	Desensitization
Rules out immediate allergy	Induces temporary tolerance
Low risk patients	Higher risk patients
Performed in office	ICU/stepdown setting
2-3 doses (1%, 10%, 90%)	10 or more doses (1:100,000)
Monitoring for 30-60 minutes	15 minutes between doses
Avoid antihistamines, beta blockers	Avoid antihistamines, beta blockers

Our Patient

- Unclear nature of initial reaction
- Brought into allergy clinic for skin testing
- Negative SPT and intradermal testing for Pre-Pen and PCN G
- Challenged with 10% and 90% of treatment dose of amoxicillin
- Monitored for 2 hours without reactivity
- De-labeled as penicillin allergic
- Sinusitis 3 months later, treated with Augmentin without issue

Penicillin Allergy Take Home Points

- Penicillin allergy is much less common than reported
- Unnecessary allergy labeling increases risks, costs
- Careful history can help stratify risk
 - Side effect, possible immediate allergy, absolute contraindication
- Penicillin skin testing is available, high negative predictive value
 - Validated testing not available for other antibiotics
- Graded dose challenges can help rule out allergy
- Desensitization can be used for treatment, but tolerance transient

Conclusions

- Hives are common and often non-allergic
- Can aggressively treat with antihistamines, montelukast
- Consider referral >6 weeks for additional workup and treatment
- Keep alpha-gal allergy on differential for recurrent hives/anaphylaxis
- History is critical for risk stratification of venom allergy
- Refer for systemic reactions or severe large local/cutaneous systemic
- Penicillin allergy frequently reported but rare
- If unable to de-label, refer for skin testing, graded challenge

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