به نام خدا

Food Allergy : Diagnosis & Management

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فوق تخصص آلرژی وایمونولوژی بالینی

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معرفی بیمار (1)

کودک یکساله ای باخوردن بیسکویت دچار علایم خس خس سینه وکهیر منتشر شده است. بیسکویت حاوی شیر، کره، تخم مرغ و گندم بوده است.

اقدامات تشخیصی در این بیمار چیست؟

اقدامات درمانی چیست؟

معرفی بیمار(2)

نوجوانی درحین ورزش دچارعلایم زیرشده است و به اورژانس بیمارستان آورده شده است

فلاشینگ وکهیر منتشر و بی حالی

خس خس سینه

افت فشار خون

چه اقدام درمانی باید انجام داد؟

اقدامات لازم جهت تشخیص چیست؟

Optimizing the Diagnosis of Food Allergy

- Accurate diagnosis of food allergies is vital to identify patients who may have severe, life threatening allergic reactions, and to exclude suspected allergies that could lead to unnecessary dietary restrictions.

Adverse Food Reactions

Immunologic

IgE-Mediated (most common)

- Systemic (Anaphylaxis)
- Oral Allergy Syndrome
- Immediate gastrointestinal allergy
- Asthma/rhinitis
- Urticaria
- Morbilliform rashes and flushing
- Contact urticaria

- Eosinophilic esophagitis
- Eosinophilic gastritis
- Eosinophilic gastroenteritis
- Atopic dermatitis

Non-IgE Mediated Cell-Mediated

- Protein-Induced Enterocolitis
- Protein-Induced Enteropathy
- Eosinophilic proctitis
- Dermatitis herpetiformis
- Contact dermatitis

Allergens

- Proteins or glycoproteins (not fat or carbohydrate)
  - Generally heat resistant, acid stable
- Major allergenic foods (>85% of food allergy)
  - Children: milk, egg, soy, wheat, peanut, tree nuts
  - Adults: peanut, tree nuts, shellfish, fish, fruits and vegetables

Signs and Symptoms

	IgE	Non-IgE	Acute	Chronic
Skin				
Urticaria	✓		✓	
Angioedema	✓		✓	
Atopic dermatitis	✓	✓	✓	✓
Respiratory				
Throat tightness	✓		✓	
Rhinitis	✓		✓	(✓)
Asthma	✓		✓	✓
Gut				
Vomit	✓	✓	✓	✓
Diarrhea	✓	✓	✓	✓
Pain	✓	✓	✓	✓
Anaphylaxis	✓		✓	

Food Allergy Disorders

Anaphylaxis Syndromes

- Food-induced anaphylaxis
  - Food allergy = #1 cause of anaphylaxis in the ED
  - Rapid-onset, up to 30% biphasic
  - May be localized (single organ) or generalized
  - Potentially fatal
  - Any food, highest risk:
    - peanut, tree nut, seafood (cow's milk and egg in young children)
- Food-dependent, exercise-induced: 2 forms
  - Specific foods (wheat, celery most common)
  - Any food (post-prandial)

Fatal Food Anaphylaxis

- Frequency: ~ 150 deaths / year
- Clinical features:
  - Biphasic reaction can contribute –initially better, then recurs
  - Cutaneous symptoms may not be present
  - Respiratory symptoms prominent
- **Risk factors:**
  - **Underlying asthma**
  - **Delayed epinephrine**
  - **Symptom denial**
  - **Previous severe reaction**
  - **Adolescents, young adults**
- History: known food allergen
- Key foods: ***peanuts and tree nuts dominate (~90% of fatalities)***, fish,crustaceans
- Most events occurred away from home

Cutaneous Reactions

- Acute urticaria/angioedema – common
- Contact urticaria - common
- Food allergy rarely causes chronic urticaria/angioedema
- 1/3 of children with moderate to severe atopic dermatitis may have food allergy (especially cow's milk, egg, soy, wheat). Morbilliform rashes may be seen in these children upon food challenge.
- Contact dermatitis (food handlers)

Respiratory Responses

- Upper and lower respiratory tract symptoms may be seen (rhinoconjunctivitis, laryngeal edema, asthma)
- Rarely isolated, usually accompany skin and GI symptoms
- Inhalational exposure may cause respiratory symptoms that can be severe
  - Occupational
  - Restaurants
  - Kitchen/Home

Example: crabs to be boiled

Evaluation: History & Physical Exam

- History: most important
  - Symptoms, timing, reproducibility, treatment and outcome
  - Concurrent exercise, NSAIDs, EtOH
- Diet details / symptom diary
  - Subject to recall
  - “Hidden” ingredient(s) may be overlooked
- Physical exam: assess for other allergic and alternative disorders
- Identify general mechanism
  - Allergy vs intolerance
  - IgE versus non-IgE mediated

Evaluation of Food Allergy

- Suspect IgE-mediated
  - Panels/broad screening should NOT be done without supporting history because of high rate of false positives.
  - Prick skin tests (prick-prick with fresh food if pollen-food syndrome)
  - In vitro tests for food-specific IgE
- Suspect non-IgE-mediated
  - Consider biopsy of gut, skin
- Suspect non-immune, consider:
  - Breath hydrogen
  - Sweat test
  - Endoscopy

Evaluation: Interpretation of Laboratory Tests

- Positive prick test or specific IgE
  - Indicates presence of IgE antibody NOT clinical reactivity
  - ~90% sensitivity
  - ~50% specificity
  - ~50% false positives
  - Larger skin tests/higher IgE correlates with likelihood of reaction but not severity

- Negative prick test or specific IgE
  - Essentially excludes IgE antibody (>95% specific)

Specific IgE Levels Associated with 95% Risk of Reaction

Age Group	Food	Serum IgE (kU/L)
Child	Egg	≥ 7
<2 years	Egg	≥ 2
Child	Cow Milk	≥ 15
<2 years	Cow Milk	≥ 5
Child	Peanut	≥ 14
Child	Fish	≥ 20

Evaluation: Elimination Diets & Food Challenges

- Elimination diets (1 - 6 weeks) most useful for chronic disease (eg. AD, GI syndromes)
  - Eliminate suspected food(s) or
  - Prescribe limited “eat only” diet or
  - Elemental diet
- Oral challenge testing (MD supervised, emergency meds available)
  - Open
  - Single-blind
  - Double-blind, placebo-controlled (DBPCFC)

Diagnostic Approach: IgE-Mediated Allergy

- If test for specific-IgE antibody is
  - Negative: reintroduce food*
  - Positive: start elimination diet
- If elimination diet is associated with
  - No resolution: reintroduce food*
  - Resolution
    - Open / single-blind challenges to “screen”
    - DBPCFC for equivocal open challenges

** Unless convincing history warrants supervised challenge*

Diagnostic Approach: Non-IgE-Mediated Disease or those with unclear mechanism

- Elimination diets (may need elemental diet)
- Oral Challenges
  - Timing/dose/approach individualized for disorder
    - Enterocolitis syndrome can induce shock
    - Eosinophilic gastroenteritis may need prolonged feedings before symptoms develop
  - DBPCFCs preferred
  - May require ancillary testing (endoscopy/biopsy)

Molecular Allergy Diagnosis

component-resolved diagnostics (CRD)

- Peanut reactivity and tolerance : Ara h 2
- Hazelnut allergy : Cor a 1

- Exercise-induced wheat anaphylaxis : Omega-5 gliadin

Management of Food Allergy

- Complete avoidance of specific food trigger
- Ensure nutritional needs are being met
- Education
- Anaphylaxis Emergency Action Plan if applicable
  - most accidental exposures occur away from home

This frozen dessert could have peanut, tree nut, cow's milk, egg, wheat

Management: Dietary Elimination

- Hidden ingredients in restaurants/homes (peanut in sauces,egg rolls)
- Labeling issues (“spices”, changes, errors)
- Cross contamination (shared equipment)
- Seeking assistance
  - Food allergy specialist
  - Registered dietitian: (www.eatright.org)
  - Food Allergy & Anaphylaxis Network (www.foodallergy.org; 800-929-4040) and local support groups

Management: Infant Formulas

- Soy (confirm soy IgE negative)
  - <15% soy allergy among IgE-CMA
  - ~50% soy allergy among non-IgE CMA
- Cow's milk protein extensive hydrolysates
  - >90% tolerance in IgE-CMA
- Partial hydrolysates
  - Not hypoallergenic!
- Elemental amino acid-based formulas
  - Lack allergenicity

** CMA=cow's milk allergy*

Management: Emergency Treatment of Anaphylaxis

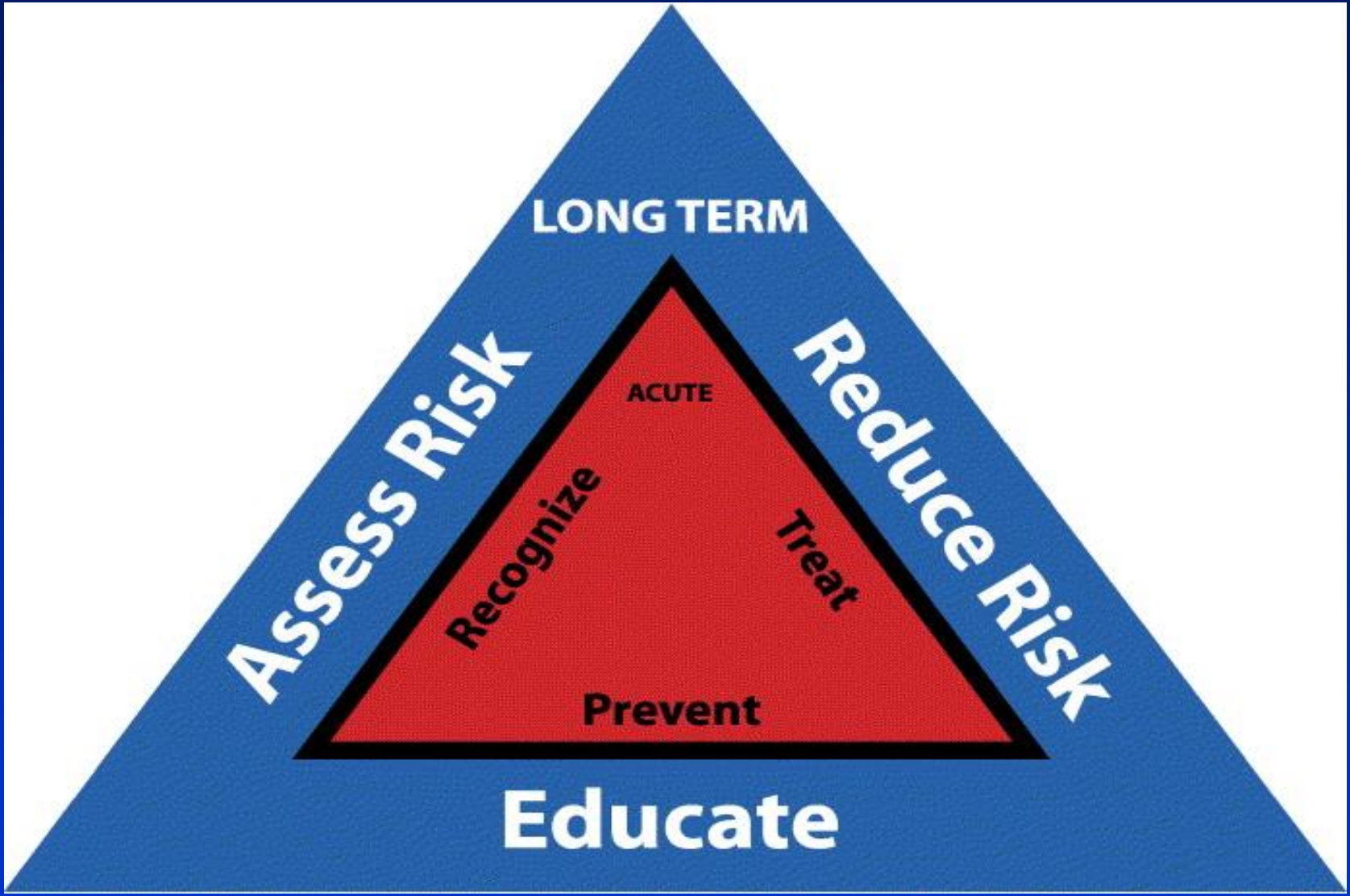
- Epinephrine: drug of choice
  - Self-administered epinephrine readily available at all times
  - If administered, seek medical care IMMEDIATELY
  - Train patients, parents, contacts: indications/technique
- Antihistamines: secondary therapy only: WILL NOT STOP ANAPHYLXAXIS
- Written Anaphylaxis Emergency Action Plan
  - Schools, spouses, caregivers, mature sibs / friends
- Emergency identification bracelet

Accidents Are Never Planned

Emergency medications and a treatment plan must be immediately available and accessible at all times!

Respond Quickly!

- Administer epinephrine quickly
- Activate EMS – 911
- Then, call emergency contacts


LONG TERM
Assess Risk
Reduce Risk
ACUTE
Recognize
Treat
Prevent
Educate

Management: Follow-Up

- Re-evaluate for tolerance periodically
- Interval and decision to re-challenge:
  - Type of food allergy (IgE vs non-IgE)
  - Severity of previous symptoms
  - Allergen/Prognosis (cow's milk vs peanut)
- Ancillary testing
  - Skin prick test/in vitro specific IgE may remain positive
  - Decline in concentration of food specific-IgE is suggestive of development of tolerance

تشخیص بیماران

- Case 1: Food allergy to wheat flour protein
- Case 2: Food-dependent exercise-induced anaphylaxis

Food Allergy Therapy

- **Allergen specific** (native food allergen, modified food allergen)

- **Allergen nonspecific** (Chinese herbs FAHF-2, anti-IgE, probiotics & prebiotics, anti-IL-5, Trichuris suis ova , TLR agonists)

Native Food Allergen IT

- Extensively heated milk or egg diet
- SQ cross-immunotherapy with pollen
- Oral IT
- Milk OIT + anti IgE
- Sublingual IT
- Epicutaneous IT

Modified Food Allergen IT

- Heat killed E-coli expressing modified Arah1,2,3 rectal vaccine
- Peptide IT
- Plasmid DNA IT
- Human Fc-Fc fusion protein
- Mannoside – conjugated food allergen IT

آلرژی به گندم

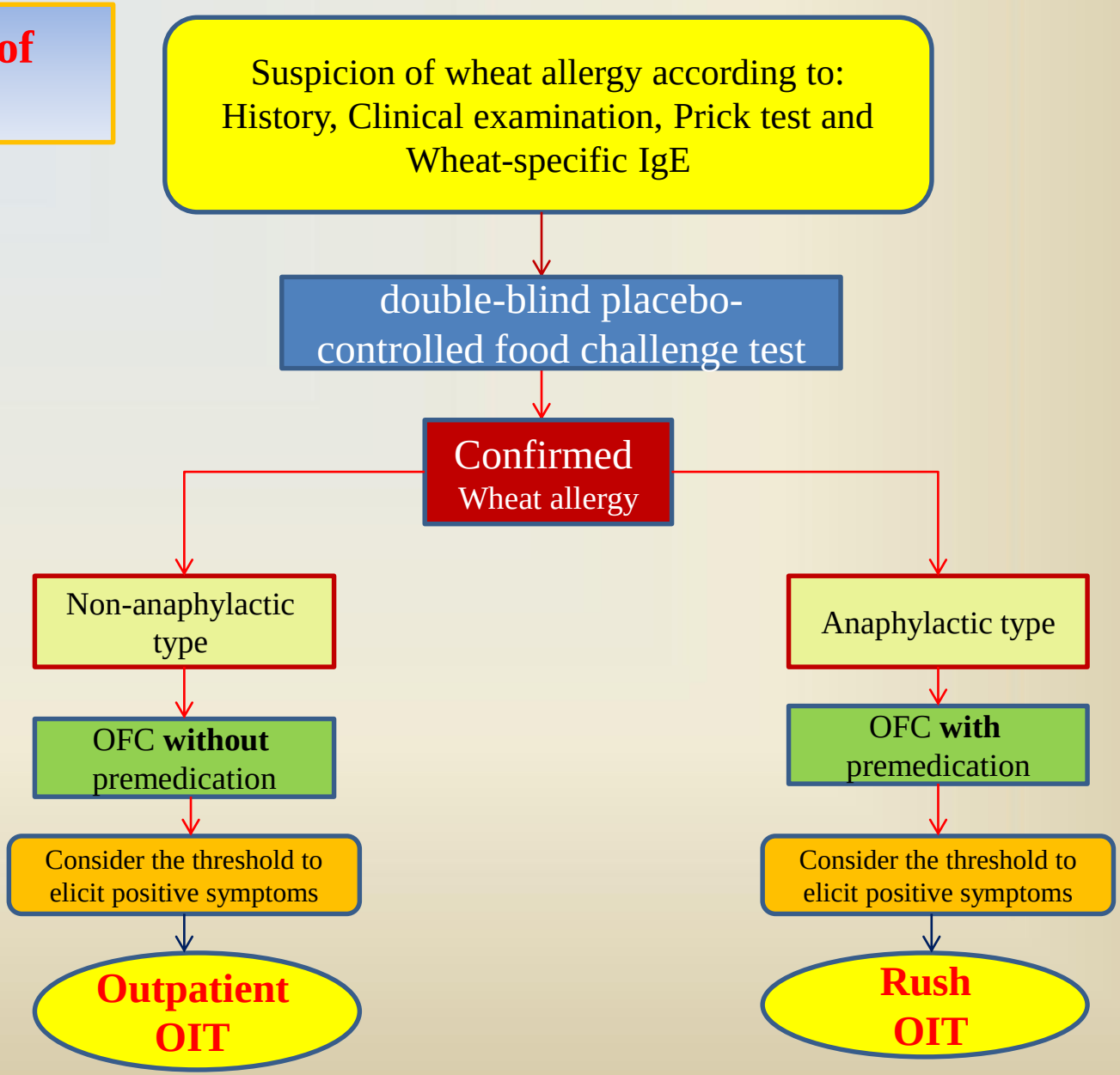
- آلرژی به گندم یکی از شایعترین حساسیت های غذایی است که بعلت مصرف زیاد گندم شیوع بالایی دارد
- شیوع آلرژی به گندم حدود ۰.۲ تا ۰.۹٪ در بزرگسالان و ۰.۴ تا ۱.۳٪ در کودکان گزارش شده است
- گندم وسایر غلات نشاسته ای حاوی تعدادی پروتئین هومولوگوس هستند که در ایجاد واکنش های آلرژیک نقش دارند
- اجزای گلوبولین و گلوتنین آلرژن های اصلی در ایجاد واکنش های وابسته به IgEو گلیادین عامل اصلی در بیماری سلیاک و آلبومین عاملی در ایجاد آسم نانواها (baker's asthma) می باشد

ایمونوتراپی خوراکی

- در حال حاضر ایمونوتراپی خوراکی یکی ازبیشترین راهکارهایی است که فعالانه جهت درمان آلرژی غذایی در حال تحقیق و بررسی می باشد

- در ایمونوتراپی خوراکی ماده غذایی حساسیت زا با یک حامل (غذای بی ضرر) ترکیب شده و بتدریج و با دوز افزاینده به بیمار داده می شود.
- مرحله افزایش دوز (dose escalation) معمولا با نظارت انجام می شود و مقادیری از غذا که تحمل می شود در مراحل ساخت (build-up) و نگه دارنده (maintenance) در منزل ادامه می یابد

Summary of protocol



ایمونوتراپی خوراکی سفیده تخم مرغ و ایجاد حساسیت زدایی و تولرانس نسبت به آن در بیماران مبتلا به آلرژی به سفیده تخم مرغ

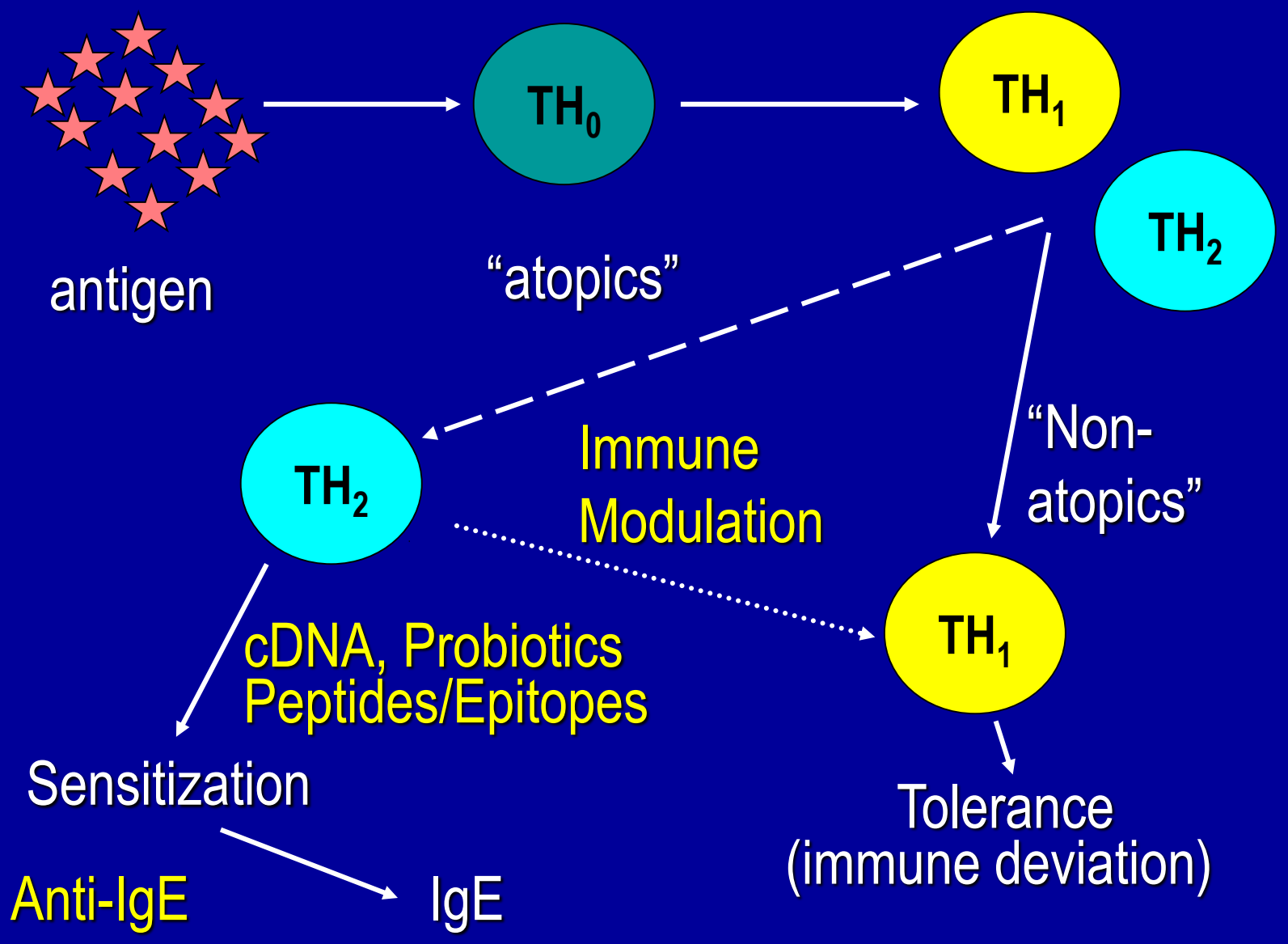
Milk Protein Desensitization

- Challenge tests
- Desensitization
- Oral immunotherapy

Future Approaches

Future Immunomodulatory Approaches

- Recombinant anti-IgE antibody
- Gene (naked DNA) immunization
- Mutated B-cell epitopes
- Minimal T-cell epitopes
- Immune-modulating adjuvants (ISS)
- Probiotics
- T lymphocyte manipulation to induce tolerance
- Chinese herbal remedies (Food Allergy Herbal Formula)


antigen
TH0
TH1
TH2
"atopics"
"Non-atopics"
TH2
Immune Modulation
TH1
cDNA, Probiotics
Peptides/Epitopes
Sensitization
Tolerance
(immune deviation)
Anti-IgE
IgE

Role of the Allergist

- Identification of causative food
- Institution of elimination diet
- Education on food avoidance
- Development of an Anaphylaxis Emergency Action Plan
- Prevention of other allergies
- Follow-up to ascertain tolerance