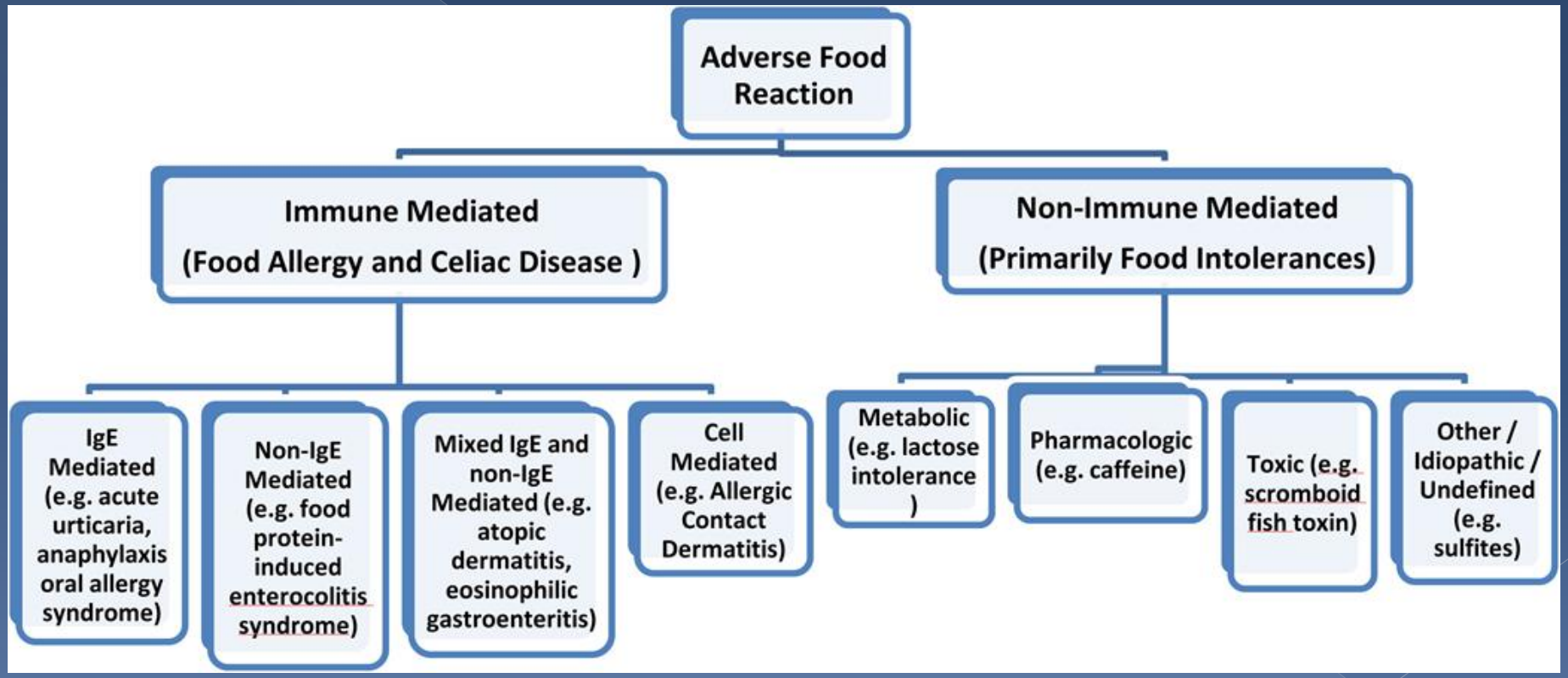
Food allergy. Atopic dermatitis. Acute urticaria.

Julita Chądzyńska

Adverse food reactions

an adverse health effect arising from a specific immune or non-immune response that occurs reproducibly on exposure to a given food.


Adverse Food Reaction
Immune Mediated (Food Allergy and Celiac Disease)
Non-Immune Mediated (Primarily Food Intolerances)
IgE Mediated (e.g. acute urticaria, anaphylaxis oral allergy syndrome)
Non-IgE Mediated (e.g. food protein-induced enterocolitis syndrome)
Mixed IgE and non-IgE Mediated (e.g. atopic dermatitis, eosinophilic gastroenteritis)
Cell Mediated (e.g. Allergic Contact Dermatitis)
Metabolic (e.g. lactose intolerance)
Pharmacologic (e.g. caffeine)
Toxic (e.g. scromboid fish toxin)
Other / Idiopathic / Undefined (e.g. sulfites)

Food allergens

- -specific components of food or ingredients within food
- - typically proteins that are recognised by allergen specific immune cells and elicit specific immunologic reactions, resulting in symptoms

Sensitization

- presence of allergen-specific IgE to food allergens without having clinical symptoms on exposure to those foods,
- an sIgE-mediated FA requires *both* the presence of sensitization and the development of specific signs *and* symptoms on exposure to that food.

Diagnosis

- careful history
- confirmation by tests including skin prick tests
- serum tests for food-specific IgE
- elimination diets
- oral food challenges(OFC)

Food allergy- epidemiology

- **2.5%** of the general population.
- Up to **8%** of children under 3 years , **2%** of adults
- Children with eczema- 30%.
- About 2.5% of newborn infants have hypersensitivity reactions to **cow's milk** in the first year of life
- approximately 80% outgrow the allergy by the 5th birthday
  - ~ 60% of milk allergic reactions are IgE-mediated.

http://www.worldallergy.org/professional/allergic_diseases_center/foodallergy/

- Prevalence of food allergy(children/adults)

Prognosis

allergies to peanut, tree nuts, fish, and shellfish are likely to persist.

20% of cases of peanut allergy resolve by age 5.

Non-IgE-mediated gastrointestinal food allergies (enterocolitis, proctocolitis) typically resolve in childhood, but food-induced eosinophilic esophagitis appears to be more likely to persist.

Risk factors of development of food allergy:

- Age
- FHx of atopy
- FHx of food allergy
- Atopic dermatitis
- Transdermal food exposure
- Immaturity of the mucosal barrier plays role in the increased prevalence of food allergy in the first few years of life

Ig-E mediated allergic conditions(acute onset)

- **Acute urticaria**
- Contact urticaria
- Anaphylaxys
- Food -asscociated exercise induced anaphylaxys
- **Oral allergy syndrome**

Wheat, shellfish, cellery

Combined IgE-mediated and cell-mediated

- **Atopic dermatitis**
- **Eosinophilic esophagitis**
- **Eosinophilic gastroeteritis**

Cell mediated allergic conditions(delayed onset)

- **Food protein induced enterocolitis syndrome(FPIES)**
- **Food protein induced allergic proctocolitis(FPIAP)**
- **Food protein indcuced enterocolitis**
- Allergic contact dermatitis
- Heiner Syndrome

Pulmonary infiltrates,
Failure to thrive,
Iron defficiency anemia
Cow's milk allergy

Oral Allergy Syndrome

- affects patients with allergic rhinitis who are sensitive to airborne allergens
- homologous proteins(panallergens) in pollens and fresh fruits and vegetables.

Risk factors for OAS:

- Sensitization to tree pollens (particularly birch pollen).
- Sensitization to multiple pollens.
- Severe symptomatic allergic disease.
- Higher pollen-specific IgE levels.
- High-risk areas where pollens are prevalent (e.g. birch, LTP).
- Sensitization to LTPs.

OAS- symptoms

- oropharyngeal symptoms such as lip, mouth, throat, ear itching and swelling after eating fresh fruits or vegetables
- onset within 5 minutes after exposure. Heated fruits or vegetables are generally well tolerated.
- symptoms more pronounced during the associated pollen season.

OAS cross-reacting allergens

Birch	Ragweed	Grass
Apple Cellery Carrot Cherry Pear Hazelnut	Banana Cucomber Melon	Tomato Orange Melon

Management of OAS

Avoidance

- Fresh, raw fuits and vegetables
- Tolerated foods should be continued in the diet
- OFC for the foods which have not been introduced
- SCIT/SLIT???

Acute tretment

- Oral antihistamines
- Hot drink
- In 2% evolution to anaphylaxys- epinephrine i.m.

Atopic dermatitis(AD)

- Atopic dermatitis (AD) chronic, relapsing, inflammatory skin disorder
- Defective epidermal barrier and cutaneous inflammation , IgE and T-cell-mediated responses
- Diagnosis of AD is based on clinical features.
- A complete allergy investigation is required in patients with moderate to severe AD or a history of exacerbation after food ingestion.
- Foods trigger AD in young children(<3ys)
- Goals of treatment are to reduce symptoms, prevent exacerbations, minimize side effects, and provide adequate psychological support
- Common triggers in AD include food proteins, aeroallergens, stress, climate, irritants, and microbes

AD

- Exacerbation of AD can occur with exposure to aeroallergens such as house dust mites, animal danders, and pollens.
- Pruritus is the only symptom of AD
- Physical examination reveals xerosis and typical eczematous lesions with different morphologic aspects
- Typical localisation of the skin lesions
- Allergic investigations are usually not indicated for patients with mild AD.

Distribution of skin lesions

Infants
Generalized, the face and extensor surfaces

Children and adults
Peri-orbital area, flexor surfaces of the joints, and about the wrists and ankles

Diagnostic crteria (Hanifin and Rajka)

3MA+3MI

Major

- Pruritis
- Typical distribution and morphology
- Chronic or chronically relapsing dermatitis
- Personal or family history of atopy

Minor

- Xerosis
- Periauricular fissures
- Ichtyosis
- Hyperlinear palms
- Keratosis piliaris
- Elevated IgE
- Palm/foot dermatitis
- Scalp dermatitis
- Susceptibility to skin infections(S. aureus)
- Dennie Morgan suborbital folds
- Nipple egzema
- Food intolerance
- White dermatographism

SCORAD INDEX

SEVERE	>40
MODERATE	15-40
MILD	<15

Treatment

Eosinphilic esophagtis(EoE)

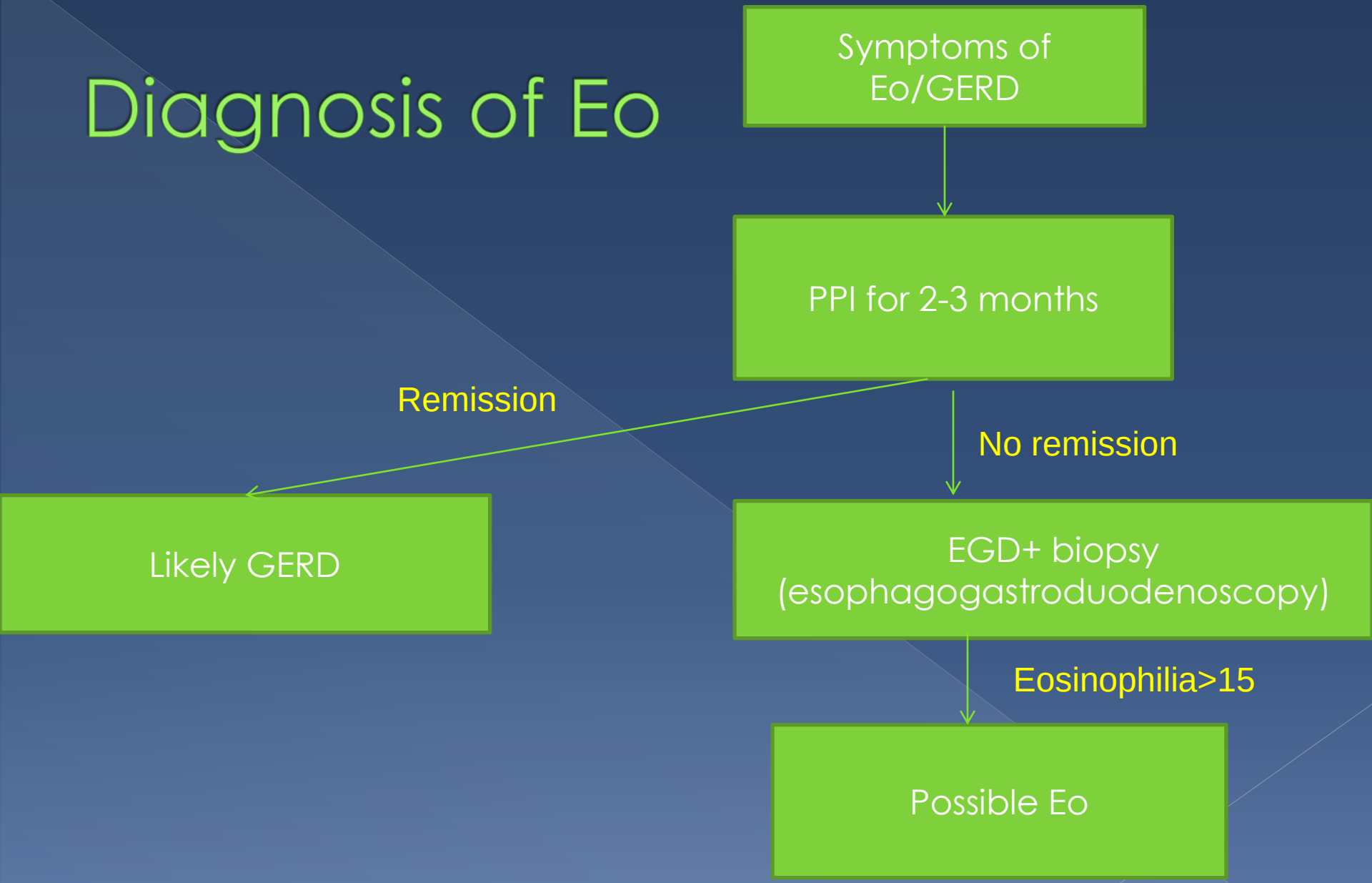
- Triggered by multiple foods, and possibly aeroallergens.
- Symptoms related to esophageal dysfunction

  Histologically- eosinophil-predominant inflammation.
- Approximately 1% of children and adults with GERD symptoms prove to have EoE.
- Approximately 12–15% of adults referred to endoscopy for dysphagia are eventually diagnosed with EoE.
- Male predominance (2 : 1 to 3 : 1)

Symptoms of Eo

Children	Adults
Abdominal pain Chest pain Cough Decreased appetite Dysphagia Food refusal Chocking/gagging Nausea Regurgitation Sleeping difficulty Throat pain	Dysphagia Food inpaction Chest pain

Diagnosis of Eo



Treatment

- Elemental diet (AA-based formula, at times with continued ingestion of only 1–2 foods),
- An allergy test-directed elimination diet (removing foods that test positive on skin prick tests and atopy patch tests),
- Empiric elimination diet (milk, wheat, egg, soy, nuts, and seafood).
- Dietary elimination therapies- clinical and histologic disease remission 50% - 95%.
- Inhaled glucocrticosteroids(fluticasone, budesonide)

Untreated Eo progressess from an inflammatory disease into a fibrostenotic disease

Eosinophilic gastroenteritis(EGE)

- constellation of clinical symptoms in combination with gastric, small intestine, and/or large intestine infiltration of eosinophils
- esophagal involvement possible
- symptoms relate to the depth of tissue that the eosinophils infiltrate.

Eosinophilic gastroenteritis

- **Mucosal** disease manifests with abdominal pain, emesis, and diarrhea;
- **Muscular** disease leads to obstructive symptoms;
- **Serosal** disease is associated with ascites.

- Growth failure, anemia,hypoproteinemia, hypoalbuminemia
- History of atopy, including allergic rhinitis, asthma, and/or atopic

dermatitis.

- The diagnosis of mucosal EG (the most common type) is confirmed by **esophagogastroduodenoscopy (EGD) with biopsies**, demonstrating gastric and/or duodenal eosinophilia

Eosinophilic gastroenteritis(EGE)

- An **elemental diet** is highly effective in children.
- Food allergy test-directed dietary elimination therapy has not been successful
- **Oral corticosteroids** are effective
- Cromolyn and montelukast have been reported to be successful
- Anti-IgE therapy may be a potential candidate for future therapeutic trials in EG patients,

Food protein-induced proctocolitis

- FPIES is a non-IgE-mediated food hypersensitivity in which patients present in infancy with profuse vomiting, sometimes accompanied by diarrhea, resulting in dehydration, lethargy, weight loss, and failure to thrive.
- FPIES is very rare in exclusively breastfed infants

FPIES

- Typical presenting symptoms, which improve with removal of the offending food from the diet
- Infants with FPIES often appear dehydrated and l ethargic, infants with chronic FPIES may additionally have failure to thrive.
- Elevated WBC with neutrophilia and methemoglobinemia following food ingestion and vomiting are consistent with FPIES.
- OFC is not be necessary for the initial diagnosis if the child presents with recurrent symptoms consistent with typical FPIES.

Differental diagnosis

Chronic FPIES	Acute FPIES
Frequent ingestion	Intermittent ingestion
Emesis, watery or mucus-/blood containing diarrhea	Profuse emesis(10-20x/day) 1- 3 h after ingestion
Poor weight gain	Lethargy, pallor, hypotension, hypothermia
Dehydration	
Hypoproteinemia, Increased WBC, Eosinophilia, Anemia	Hypoproteinemia Increased WBC Increased PLT

History

- Detailed history regarding the timing and number of vomiting episodes, diarrhea, and association with feeding changes
- Growth
- Choking, breathing difficulty, cyanosis, abdominal distension

Physical examination

- Signs of dehydration: lethargy, depressed fontanelle, sunken eyes, dry mucous membranes, poor skin turgor, prolonged capillary refill, pallor.

Laboratory evaluation FPIES

- CBC with differential- leukocytosis with neutrophilia, anemia, eosinophilia, and thrombocytosis.
- A blood gas assessment should be ordered for infants who are ill-appearing or lethargic, and may reveal non-anion gap metabolic acidosis (with a mean pH of 7.03 in one series).
- Stool studies may reveal elevated leukocytes, frank or occult blood, and/or eosinophils.
- OFC is the gold standard for diagnosis, but may not be necessary for initial diagnosis if

OFC- FPIES

- High-risk procedure (i.v. fluids available, physician supervision)
- 0.06–0.6 g of food protein divided in three equal portions, over 30-45 minutes
- Observation for 4–6 hours prior to discharge.
- Positive OFC:
  - emesis (onset 1–3 hours),
  - lethargy (onset 1–3 hours),
  - diarrhea (onset 2–10 hours, mean 5 hours)
- CBC with differential(prior to and about 6 hours after positive OFC)
- If diarrhea is present, stool guaiac tests
- Continue strict food avoidance, re-evaluate at12–18 months

Treatment FPIES

- Exclusive breastfeedinga or extensively hydrolyzed casein formula
- **>12 months** avoid trigger foods, OFC with reactive food every 18 months
- Delay the introduction of grain, legumes, poultry, as well as cow's and soy milk until the first year (high rate of FPIES to multiple foods)
- Infants with moderate to severe reactions - **intravenous fluids** and other supportive therapies.
- Intravenous methylprednisolone may be used for more severe reactions, although its therapeutic benefit has not been proven in controlled clinical trials.

Food protein-induced proctocolitis (FPIP)

- Food protein-induced proctocolitis (FPIP) should be suspected in well-appearing infants presenting with isolated bloody stools.
- FPIP is characterized by an eosinophil-dominated inflammation limited to the rectum and distal sigmoid colon.
- FPIP typically occurs in breastfed infants and formula-fed infants,
- Cow's milk or soybean allergy

Differential diagnosis of FPIP

History FPIP

- A careful dietary history is essential to diagnose FPIP.
- cow's milk and/or soy proteins are typically incriminated
- Prolonged latent interval between the introduction of food proteins and the initial presentation,
- Elimination diet- complete resolution of the symptoms within 48–96 hours (i.e. up to 2 weeks).

Physical examination

- anal fissures
- evaluation of the growth.

Laboratory FPIP

- Diagnosis is based mainly on the clinical response to a strict elimination diet and exclusion of other etiologies
- Complete blood count (CBC) (eosinophilia, mild anemia)
- Rarely hypoalbuminemia
- SPT and sIgE are not recommended for an initial
- Smears of the fecal mucus- increased polymorphonuclear neutrophils.
- Colonoscopy- persistent bleeding despite implementation of an elimination diet.
- The colonoscopy usually shows a mild colitis with focal erythema, rectal ulcerations, and lymphoid nodular hyperplasia

Diagnosis of FPIP

- The diagnosis is based on a **positive clinical history** (**mild rectal bleeding in an otherwise healthy infant**)

Rresolution of symptoms following elimination of the causative food protein, usually within **48–96 hours**.

- SPT and sIgE are usually negative in FPIP.
- Exclusion of other causes of rectal bleeding (infection, fissure, necrotizing enterocolitis, intussusception)

Treatment of FPIP

Breastfed- strict avoidance of the offending food proteins in their diet.

- Dietary restriction.

Formula-fed children casein hydrolysates(5–10%will need AA-based formulas

- Symptoms resolve gradually within **72 hours-2 weeks.**

- Reintroduction at **8–12 months** of age, usually at home.

Recurrence of bleeding will appear within 6–72 hours if the infant is still allergic to the food.

- If food-specific IgE to the offending food is positive, a supervised oral food challenge in the physician's office may be necessary.

Food protein induced enteropathy (FPIE)

- Small-bowel injury with malabsorption
- **Protracted diarrhea**, typically the first 1 to 2 months, and typically within weeks after introduction of cow's milk formula.
- Other assocciated allergens: soybean, wheat, and egg
- **vomiting** and **failure to thrive**, abdominal distension, early satiety.
- Moderate anemia (typically caused by iron deficiency) is present in 20% to 69% of infants with cow's milk protein–induced enteropathy.
- Occult blood can be found in 5% of patients.
- hypoproteinemia, steatorrhea, sugar malabsorption, and deficiency of vitamin K–dependent factors
- Resolution of symptoms 1 to 4 weeks

FPIE

- Food protein–induced enteropathy is diagnosed by the confirmation of **villous injury, crypt hyperplasia, and inflammation on small-bowel biopsy** specimens obtained from a symptomatic patient who is being fed a diet containing the offending food allergen.
- Gastrointestinal evaluation with **endoscopy and biopsy** is necessary for the conclusive diagnosis of enteropathy

	Vomiting	Diarrhea	Growth	Foods
FPIP	-	Minimal, bloody	Normal	Milk/soy
FPIES	+++	+++	Poor	Milk/Soy/ Egg/ rice/oat
FPIE	+/-	Moderate	Poor	Milk/soy

Food associated exercise-induced anaphylaxis

- Occurs when patient exercises within 2-4 hours of ingesting a food
- In the absense of exercise, the patient can ingest the food without any apparent reaction
- Most common in female patients 15 to 35 years of age

- Food allergy is the most common trigger of anaphylaxys in children

Cross-reactions between food allergens

Acute urticaria

- Urticarial lesions (“hives”) are vascular skin reactions, extremely pruritic, circumscribed, raised, erythematous plaques or papules, often with a pale center.
- Individual lesions are transient and generally **resolve within 24 hours.**
- does not exceed **6 weeks** in duration.
- affects **up to 20%** of the population at some point in their lives
- Acute urticaria is less likely to progress to chronic

urticaria in children, but overall 20–30% of

patients with acute urticaria will progress to chronic or recurrent urticaria.

- Photo

Urticaria/angioedema?

URTICARIA	ANGIOEDEMA
Pruritis, burning sensation	Pain
Resolution 1-24 h	Up to 72 hours
Superficial swelling of the dermis	Swelling of the lower dermis and subcutis

Etiology of acute urticaria

- Viral and bacterial infections, parasitic infections, reactions to medication, vaccination, stinging or biting insects, allergen exposure, blood transfusion
- In children, **infectious causes** are believed to be the most common etiology for acute urticaria.
- Urticaria can also be triggered by **specific physical stimuli**(dermatographism, delayed pressure urticaria, cholinergic urticaria, adrenergic, urticaria, solar urticaria, aquagenic urticaria, and vibratory urticaria)
- Urticaria is often an early manifestation of a systemic disorder such as urticarial vasculitis,autoimmune disease, mastocytosis/mast cell disorder, or malignancy

History

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

EAACI

POSITION PAPER

The EAACI/GA²LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update

T. Zuberbier[1], W. Aberer[2], R. Asero[3], C. Bindslev-Jensen[4], Z. Brzoza[5], G. W. Canonica[6], M. K. Church[1], L. F. Ensina[7], A. Giménez-Arnau[8], K. Godse[9], M. Gonçalo[10], C. Grattan[11], J. Hebert[12], M. Hide[13], A. Kaplan[14], A. Kapp[15], A. H. Abdul Latiff[16], P. Mathelier-Fusade[17], M. Metz[1], A. Nast[1], S. S. Saini[18], M. Sánchez-Borges[19], P. Schmid-Grendelmeier[20], F. E. R. Simons[21], P. Staubach[22], G. Sussman[23], E. Toubi[24], G. A. Vena[25], B. Wedi[15], X. J. Zhu[26] & M. Maurer[1]

Examination

- Vital signs, circulatory, neurologic, respiratory, and gastrointestinal systems
- Resolution of urticaria without residual skin marks
- H1-blocking antihistamine medications may cause that the lesions appear flat.
- Angioedema may also be present
- Note any non-urticarial exanthem, other rash, pigment changes, ecchymosis, or purpura
- No urticaria at the time of examination (photographs may be helpful)

Vasculitis

- Photo

Urticaria pgmentosa

Serum Sickness- like disease

Shonlein- Henoch purpura

Erythema multiforme

Spontaneous urticaria

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Inducible urticaria

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UAS-7 Urticaria activity score

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Treatment

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