

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

على خمسة

Food protein-induced allergic proctocolitis (FPIAP)

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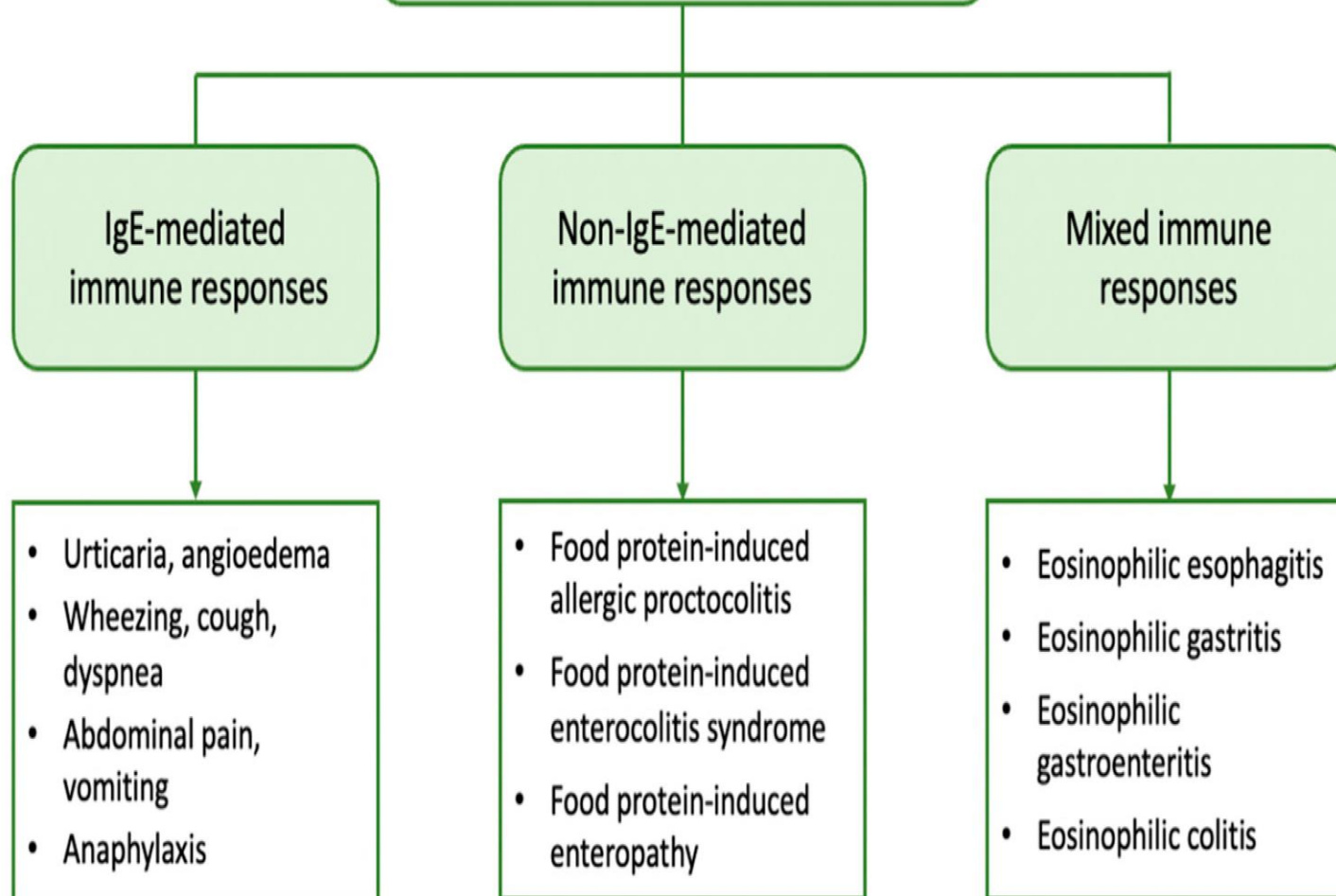
Formerly allergic or eosinophilic proctocolitis or "protein intolerance
first described by Rubin in 1940 and later by Gryboski in 1966 and 1967

- ▶ Is a **common** problem and **benign** condition in young infants.
- ▶ One of the most common etiologies of **rectal bleeding** in infants.
- ▶ Inflammation of the **distal colon** in response to **one** or **more** food proteins.
- ▶ Mechanism that does **not** involve **IgE**.
- ▶ **Cow's milk** (Major component of diet is milk) and **soy** are the **most** common triggers.

CLASSIFICATION AND TERMINOLOGY

- ▶ Immunologic reactions to dietary *proteins* may be classified :
- ▶ **IgE-mediated**
- ▶ **Non-IgE-mediated**
- ▶ **Mixed**

Cow's milk allergy phenotypes



EPIDEMIOLOGY

- ▶ The real prevalence of AP is not known. (upon the case definition).
- ▶ Frequency appears to be **increasing**(especially in breastfed infants **56.8–60%**).
- ▶ Worldwide, estimates of food allergy prevalence range from 1–10%.

PATHOPHYSIOLOGY

- ▶ The **exact** mechanism for this disorder is **unknown**.

The transfer of maternal dietary protein via breast milk was first demonstrated in 1921.

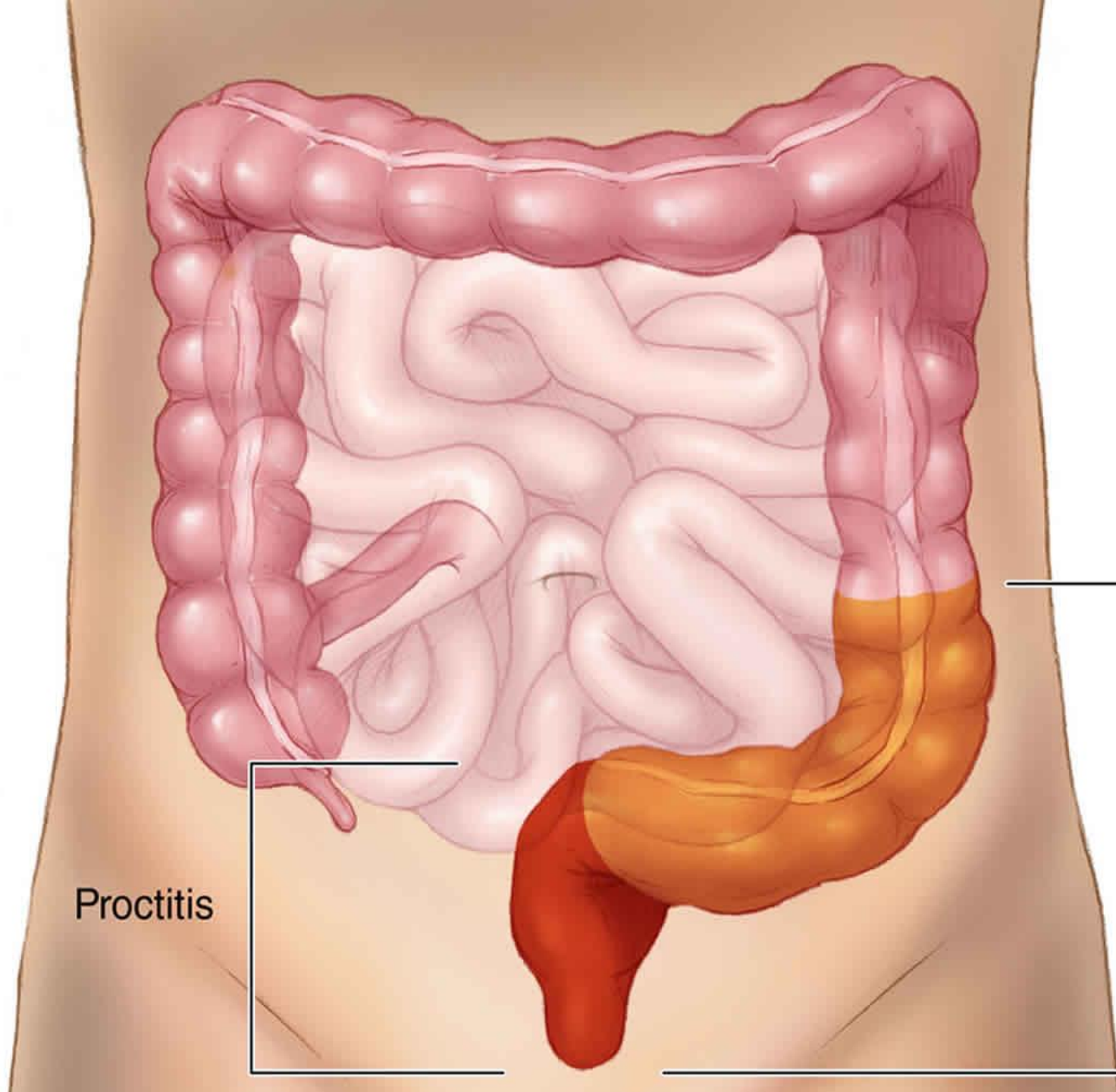
More recently, the presence of cow's milk antigens in breast milk has been established.

Possible causal factors have included:

- ▶ *Immaturity of the immune system.*
- ▶ *Impaired intestinal permeability , not be mature for the first few months of life.*
- ▶ *Genetic predisposition.*
- ▶ *Gut microbiome (as it does in some other GI inflammatory disorders).*

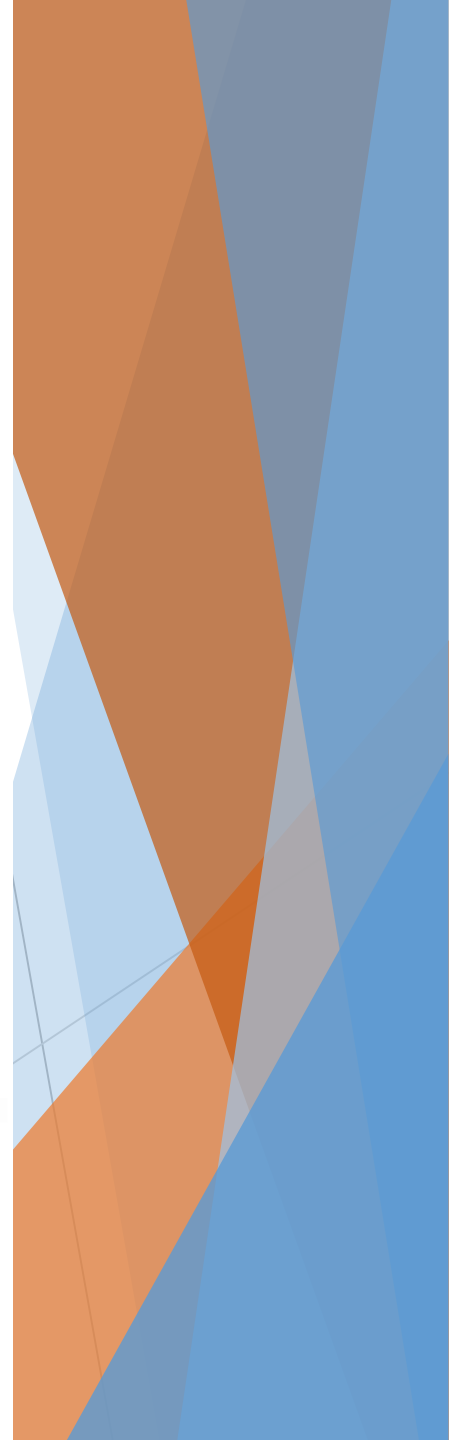
DIETARY TRIGGERS

- ▶ **Cow's milk** is the **most** common trigger in most series.
- ▶ May be exposed to the protein through **breast milk or formula**.
- ▶ Why an orally ingested protein **induces** an inflammatory response limited to the *rectum and distal sigmoid colon*.
- ▶ Offending protein is bound to Ab in the breast milk until **colonic bacterial enzymes** cleave or release the Ag.
- ▶ AI mechanism has been raised by one study's of p-ANCA .



Proctitis

Proctocolitis



CLINICAL PRESENTATION

- ▶ FPIAP is diagnosed almost **exclusively** in young infants .
- ▶ The disorder typically presents within a few months after birth, although symptoms occasionally begin as early as the **first** week of life.

It may present with any of the following symptoms:

in apparently healthy, regularly growing infants

- ▶ Frequent visible blood in normal or loose stools
- ▶ Loose stools with mucus, with or without gross or occult blood
- ▶ Constipation, usually with occult blood (**uncommon** presentation)

visible blood in normal or loose stools



At least 25 immunogenic proteins in cow's milk, (beta-lactoglobulin and casein).

CLINICAL PRESENTATION

- ▶ The symptom is nonspecific.
- ▶ A **minority** of patients may also present with refusal to eat and irritability, abdominal pain, pain on defecation.
- ▶ A **family history** of *atopic disease* is **more common** among FPIAP.

CLINICAL PRESENTATION

- ▶ **Warning signs** that suggest a diagnosis other than FPIAP include:
- ▶ Unwell appearance or fever
- ▶ FTT
- ▶ Severe diarrhea
- ▶ Forceful vomiting
- ▶ Abdominal distension
- ▶ Perianal disease
- ▶ Severe rectal bleeding
- ▶ Significant anemia

EVALUATION

- ▶ **General evaluation** for all patients :

For most patients

- ▶ A focused History
- ▶ Physical Exam **is sufficient** to establish a **clinical** diagnosis.
- ▶ Followed by treatment with dietary restriction.

History

- ▶ Combination of **rectal bleeding**, increased streaks of mucus, and/or stool output.
- ▶ **Atypical symptoms** : irritability, pain, vomiting, and weight loss or FTT.
- ▶ If breastfed, mother's diet, cow's milk or dairy products, soy, eggs, corn and wheat.
- ▶ If the infant is fed formula, the history should document the type of formula :

Standard cow's milk-based formula

Soy-based formula

Formulas with extensively hydrolyzed proteins

Physical examination

- ▶ Infants are **usually** remarkably well appearing **but** can be *ill* appearing.
- ▶ When **visible** bleeding, inspection of the **anus** for *fissures*.
- ▶ Should examine one or more stools directly.
- ▶ Stools are soft ,loose, blood *specks or streaks* distributed stool, with / without mucus.
- ▶ **Weight and height** and tracking on a growth chart.

**Among the atopic comorbidities, eczema is present in 22% - 52% of patients with AP.
An atopic family history is also present in 25% to 50% of patients .**



We are covering non-IgE allergic reactions today

Laboratory testing

- ▶ Not necessary in *well-appearing infants* with typical symptoms .
- ▶ S/E and a CBC may be useful when the diagnosis is **unclear**.
- ▶ Fecal calprotectin, may be elevated, its **clinical** utility has **not** been established.
- ▶ Levels are generally higher in infants < 7 months than in older individuals.
- ▶ Not indicated in most cases, considered who haven't responded to dietary changes.

Further evaluation for selected patients

- ▶ **Allergy testing:** Skin prick test and IgE aren't recommended. (usually negative).
- ▶ The presence of food-specific IgE and will be inconclusive in non-IgE disorders.
- ▶ May be considered if there are factors suggestive of IgE-mediated allergy, such as **rashes, hives, or acute reactions.**

Endoscopy

- ▶ Colonoscopic evaluation with biopsy :for evaluation of **selected** patients.
- ▶ Is usually reserved for patients with unusual or **atypical** symptoms:
 - ❖ Constipation
 - ❖ Diarrhea with mucus-streaked stools but without **grossly** visible bleeding.
 - ❖ Severe rectal bleeding **or** anemia despite a trial of milk elimination diet .
 - ❖ Families who desire a definitive diagnosis before making treatment .

Endoscopy

- ▶ Usually confined to the distal colon, occasionally extend proximally.
- ▶ Mild colitis patchy erythema, erosions, ulcerations, edema with **loss** of vascularity.
- ▶ Biopsies typically reveal high numbers of eosinophils (eosinophilic abscesses).
more than 60 eosinophils on 10 high-power fields is sufficient to diagnose AP
- ▶ LNH is **frequently** observed in these infants.
- ▶ Findings may be **patchy**, so that care should be taken to examine **many** levels.
- ▶ Features are **not** typical :cryptitis, neutrophilic crypt abscesses, glandular distortion, Paneth cell metaplasia; suggest an alternate diagnosis (IBD).

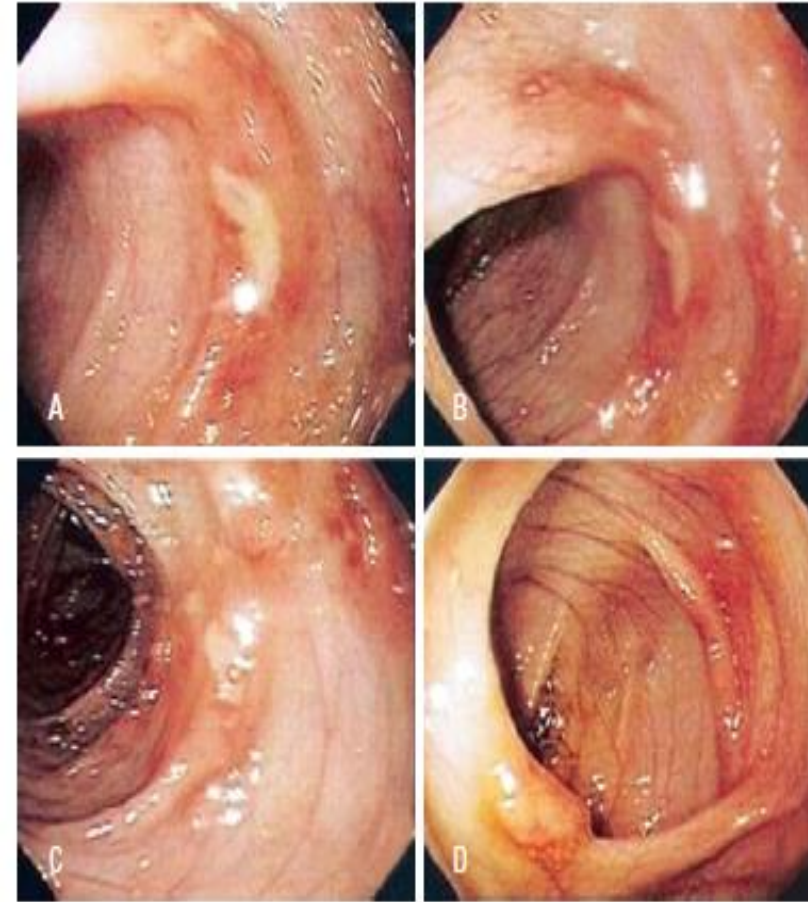


Figure 3. Colonic mucosa showing ulceration (A, B and D) and lymphoid nodules (C)

DIAGNOSIS

- ▶ Is almost always a **clinical diagnosis**, based upon typical symptoms in **early** infancy that resolve upon withdrawal of the food antigen.
- ▶ *Although the most **accurate** diagnosis would include either a **sigmoidoscopy** with biopsy demonstrating an allergic colitis or a food challenge (withdrawal of the offending antigen[s] and resolution of symptoms, followed by the reintroduction of the antigen[s] with a recurrence of symptoms), these diagnostic tools are not utilized by the majority of clinicians, due to the **benign** course of this disorder.*
- ▶ **Atypical** features, diagnosis is **uncertain, not respond** to elimination should undergo further evaluation.

Diagnostic criteria

- ▶ Although there are no validated diagnostic criteria in the literature, European Academy of Allergy and Clinical Immunology (EAACI) which are as follows:
 - ▶ mild rectal bleeding in an otherwise healthy patient;
 - ▶ resolution of clinical manifestations after elimination of trigger food(s)
 - ▶ reappearance of symptoms on reintroduction of the trigger food(s);
 - ▶ exclusion of other causes of rectal bleeding.
-
- ▶ A diagnostic confirmation may not be necessary in some milder cases of AP.

DIFFERENTIAL DIAGNOSIS

- ▶ **Anal fissure** –**Most** common cause of rectal bleeding younger than one year.
- ▶ **Intussusception**-Sudden-onset, severe, crampy, progressive abdominal pain, inconsolable crying and drawing up of the legs toward the abdomen. It is most common in between 6 and 36 months (uncommon prior to 3 months).
- ▶ **Infection**-Bacterial enteric pathogens (fever, abdominal pain, and tenesmus).
- ▶ **Meckel's diverticulum** -Presentation before 6 months of age is rare.
- ▶ **FPIES** –Acute or chronic symptoms and may include vomiting, diarrhea (with / without blood), and weight loss .Infants with FPIES are generally **sicker**.

DIFFERENTIAL DIAGNOSIS

- ▶ **EOG**-Tissue eosinophilia in any or all of the intestinal mucosa, muscularis, or serosa.
- ▶ **NEC**– Approximately 90 percent of infants with NEC are born prematurely.
- ▶ **Very early-onset inflammatory bowel disease** -IBD of infancy, is a **rare** cause .
- ▶ **Other** –swallowed maternal blood, intestinal duplication cysts, vascular malformations.
- ▶ **Hirschsprung disease** with enterocolitis, or malrotation with volvulus.

MANAGEMENT

- ▶ Diagnosed and managed by primary care clinicians or pediatric GI.
- ▶ Dietary elimination in mild cases.
- ▶ Referral to a pediatric GI in cases of diarrhea, bleeding, and weight loss.
- ▶ If symptoms don't **quickly** improve, persist **beyond** 4 to 6 weeks, **other** Ag considered.
- ▶ Referral to an allergist when **comorbid** atopic disease .
- ▶ Dietitians **and** psychologists -for assisting the family with prolonged or multi-food elimination diets or anxiety. (diet sufficient calories, ca, other nutrients).

MANAGEMENT

- ▶ Continued breastfeeding and **completely** eliminate the suspected food from diet.
- ▶ Cow's milk should be eliminated first, **unless** evidence implicating specific food.
- ▶ All dairy products should be completely eliminated diet. (goats, sheep, or camels)
- ▶ Majority respond to elimination of milk.
- ▶ Labels *milk, eggs, fish, crustacean shellfish, tree nuts, peanuts, sesame, wheat, and soybeans* are required to identify **nine** specified food allergen sources.
- ▶ Foods that contain lactose as an ingredient are usually safe to consume.

MANAGEMENT

- ▶ **Clinical** symptoms typically clear within **one** to **two** weeks.
- ▶ OB is not necessary, microscopic blood or PMN may persist for **many weeks**.
- ▶ If symptoms fail to resolve, review **mother's diet** that all sources completely eliminated.
- ▶ Milk eliminated for at least **2 weeks** if symptomatic, then soy, followed by egg, should also be removed.
- ▶ The different frequencies of trigger foods may depend on the different habits found in the geographical areas where the studies are conducted.

Infants Fed with Formula or Mixed Feeding

- ▶ Formula milk should be replaced with an **extensively** hydrolyzed formula.
- ▶ Using soybased formulas is generally not recommended, (15%) who are intolerant of cow's milk also do not tolerate soy (Older studies up to 40%)
- ▶ Approximately 5–10% of patients do not respond to the EH formula and, therefore, must switch to the amino acid formula.

Reintroduction

- ▶ Traditional approach is to reintroduce the protein at approximately **one** year.
- ▶ This approach is **successful** in the **vast majority** of infants.
- ▶ Some begin to reintroduce limited quantities of the offending protein before 1 year and, occasionally, as **early** as six months of age.
- ▶ **Atopic** symptoms or other **risk factors** for IgE-mediated disease, referral to an allergist may be useful.

Reintroduction

- ▶ Reintroduction of cow's milk is generally effective.
- ▶ Hydrolyzed formula can be switched to a cow's milk- or soy formula.
- ▶ AAB formula can either be switched directly to a cow's milk-based formula or can be switched to a EH for 1 to 2 m before advancing to a intact cow's milk protein.
- ▶ Observed for any clinical changes, bloody stools, diarrhea, vomiting, and irritability.
- ▶ If it fails, one option is to attempt introducing "cooked" or "baked" milk products.

Recurrence

*If hematochezia or other symptoms of proctocolitis recur, then resume the diet restriction for an additional **six** months.*

PROGNOSIS

- ▶ The prognosis of FPIAP is **excellent**.
- ▶ Resolution usually in 50% by the age of 6 months, and 95% by 9 months.
- ▶ Nearly **all** infants be able to tolerate cow's milk and soy products by 1 year .
- ▶ Progression to persistent **food allergy** or **colitis** including IBD is **extremely** rare.

Thanks for your attention

