

A 37 –year –Old Woman
with Adult -onset
psychosis

Case vignette.

- 37/Female
- **No known co-morbidities**
- Admitted to Psychiatric hospital with symptoms *s/o Adult onset Psychosis.*
- **Symptoms: a strong belief** that people are talking abt her, conspiring secretly which also involves her friends, family members and neighbors, giving threat calls to family members x since 3 months
- Thinking abt changing her institute where she is currently getting training

symptoms

- No auditory or third person hallucinations
- No visual hallucinations, No affect changes
- No e/o anxiety or depression, No symptoms s/o focal neurological deficit
- **Unintentional weight loss** (9kgs) over unspecified period of time despite **self –described polyphagia**,
- no h/o Vomiting or diarrhea, hematemesis or malena,jaundice
- **Hair thinning** since 2 months
- **mild exertional dyspnea**

Past history

- Was **healthy** most of the time
- No significant past history or h/o hospitalization
- Past h/o RTA with left foot fracture
- h/o right oophorectomy in view of ovarian torsion at the age of 17
- No h/o head injury or seizure
- **No h/o Drug exposure**
- **Bad habits:** Alcoholic beverage once a month,
- Non smoker, had used **marijuana** once,takes two cups of coffee daily

Family history

- **Mother** -SLE
- **Sister** -Hypothyroidism with hyperparathyroidism
- **Maternal grand father** - Diabetes mellitus
- **Aunt** -Breast cancer
- **No family h/o Psychiatric disease**

Social history

- **Unmarried** - reason unknown
- **Irregular** menstrual cycles with adequate flow
- Living **alone** and working at HR department
- **Perfectionist** as per mother
- **Diet: Pescatarian** (*Pescatarians do not eat any land animals or birds, such as beef, pork, chicken or turkey; however, they do eat fish and other seafood, such as shrimp and clams. **Vegetarian foods**, such as fruits, vegetables, beans, grains and nuts, are also allowed on a pescatarian diet.*)
- **no remote travel history** ,lives in North east US

O/E

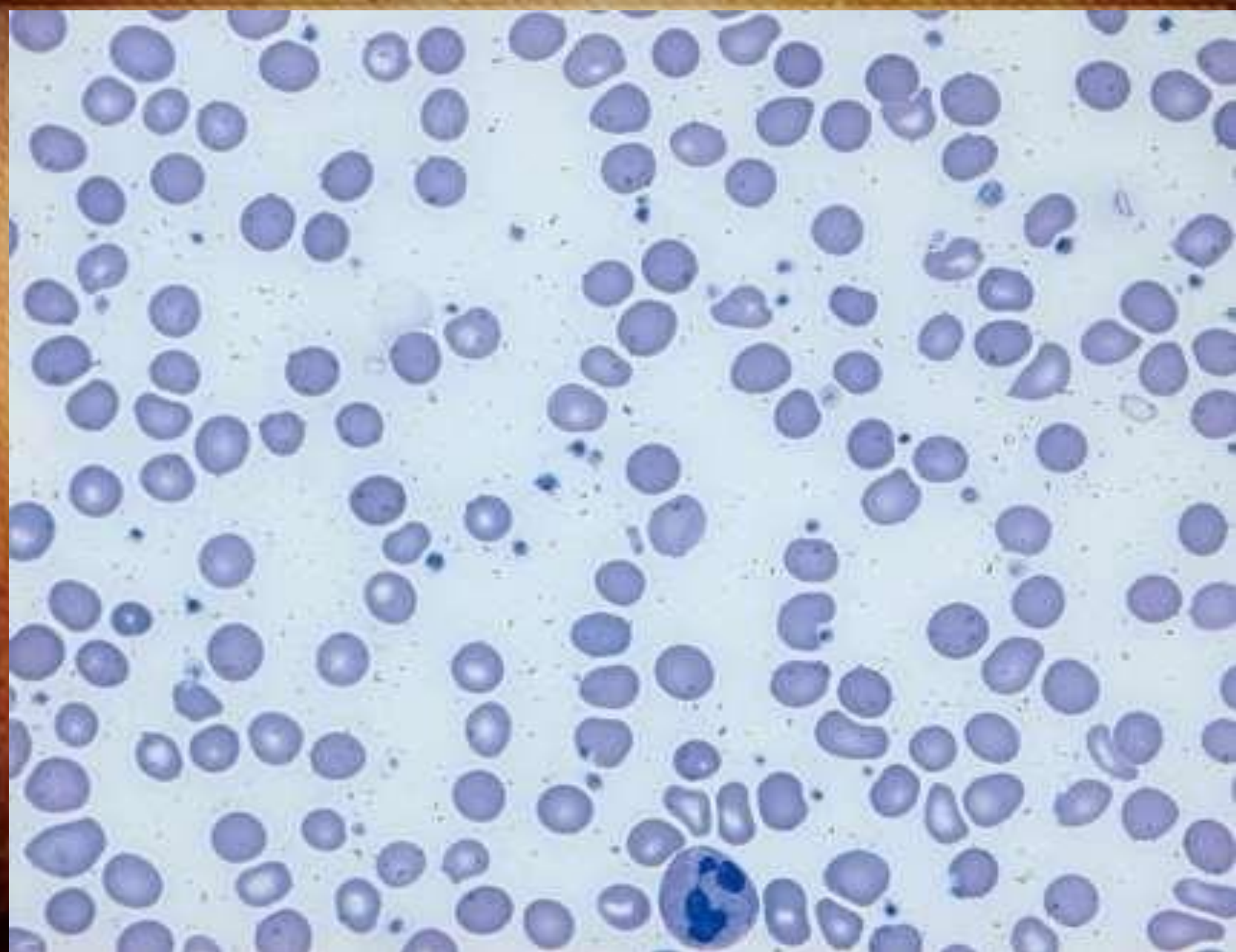
- Pale, thin built, ill-looking
- Ht-167 cm, Wt -45 Kgs(BMI-16.1)
- No icterus/Cyanosis/clubbing/LAP/pedal edema/JVP normal/rash
- Platynychia with brittle nails, angular cheilosis
- Afebrile, well hydrated,
- BP 90/60 mmHg, Pulse-regular at 75 BPM
- respiratory rate 20/min, Spo2: 96% on RA
- Other physical and neurologic examination findings were unremarkable.



| Parameter | Levels |
|----------------|--------------------------------------|
| Hemoglobin | 6.6 g/dl |
| Hematocrit | 18 % |
| MCV | 102 fl |
| MCH | 22.8 pg |
| RDW | 22.2% |
| Retic count | 0.59 % |
| WBC | 4500 /cmm |
| N/L/M/E/B | 45/47/7/1/0 |
| Platelet count | 1,80,000/cmm |
| Serum iron | 23 µg/dL (normal 50-170 µg/dL), |
| TIBC | 534 µg/dL (normal 280-400 µg/dL), |
| serum ferritin | 2.5 ng/mL (normal 20-320 ng/mL) |

| Parameter | Levels |
|--------------------------|--|
| Serum vitamin B12 | 60 pg/mL (normal 211-911 pg/mL) |
| serum folic acid | 11.3 ng/mL (normal >5.4 ng/mL). |
| Peripheral smear | normocytic hypochromic anemia, marked anisocytosis, mild poikilocytosis, hypersegmented neutrophils, and mild thrombocytopenia |
| S.E | 136/4.7/98 |
| Calcium/phosphorus/Vit D | 8.3/3.4/ 10 ng/ml |
| BUL/S.Creat | 16/0.8 |
| TP(Alb/Glob) | 6.8(4.1/2.7) |
| S.Bili(D/I) | 0.8(0.6/0.2) |
| SAP | 161 |

| Parameter | Levels |
|--------------|-------------------------|
| SGPT/SGOT | 36/33 |
| LDH | 535 |
| TSH,ft4 | 2.8(0.4-5)/1.4(0.8-1.9) |
| FSH/LH | 4(2-9)/3.5(1.5-9) |
| Testosterone | 0.43 (3.5 -9.7) |



Managed with..

- DX::PSYCHOTIC DISORDER possibly PARANOID SCHIZOPHRENIA with nutritional deficiency
- She was treated at Psy hospital for 1 month
- Discharged with:
 1. **Risperidone,**
 2. **Sertraline,**
 3. **ferrous sulphate**
 4. **Calcium with Vitamin D**
 5. **Vitamin C with other Multivitamin Capsules**

after 6 weeks on follow up visit

- **Excessive thinned out (Wt- 34 kgs) with poor control over psychiatric symptoms**
- **Thyroid nodule was palpable → underwent Bx and Dx as: Hashimoto's thyroiditis and Papillary carcinoma of Thyroid → patient has opted for Surgical thyroidectomy → kept on escalating doses of oral L-thyroxine supplemets (50 → 75 → 100 mcg/day)**
- **4 weeks after: TSH and f T4 were: 15/0.75, dose escalated to 150 mcg/day**
- **4 weeks later : TSH and f T4 were: 10/0.8**

**??? Cause of psychosis and
hypothyroidism
not responsive to replacement therapy**

- A primary psychaitric disorder
- Or Any associated endocrine disorder
- Or underlying medical condition: based on the h/o PCT,Hashimotos , multiple deficinecies,clinically significant wt loss
- Or illicit drug abuse
- Or Diet associated
- Or Cancer cachexia
-

Lets elaborate...

1.Iron and vit def:

- **Fe deficinecy** : irregluar but normal menses, no meat consumption
- **Vitamin B12 deficiency** – vegeeterian diet,sea food exposure,?pernicius anemiav,generally does not cause psychosis(ataxia,T and N and confusion)
- **Vitamin D deficinecy** : northeast US with winter season –can cause psychosis but despite adequate correction, may be contributory here..
- All these nutrients are low: post **bariatric** surgeries

- **2.weight loss:**
- Was perfectionist with irregular menses - **anorexia nervosa** but had binging too
?Bulimia
- 9 kg wt loss: >>sec to **cancer** or psychosis sec to brain mets or primary brain malignancy
- ?Wt loss due to **malabsorption**



- **3. Thyroid disease:** brittle thinned out hairs, wt loss, polyphagia → ? **hyperthyroidism** –can cause psychosis, but lab s/o Hypothyroidism
- **Severe hypothyroidism** can cause psychosis
- h/o Hashimoto and PCT –? Incidental
- **4. Malabsorption :** Despite escalating doses of L-thyroxine –TSH remained high: ?**impaired oral absorption** of L-thyroxine (calcium and Iron with L-thyroxine)
- **Poor control of Psychotic symptoms despite antipsychotics:** s.o Malabsorption of antipsychotics as well
- **5. ?Affective disorder with psychosis-**
- **6. delusional disorder**

Medical conditions that may present as psychotic disorders

- Hypoglycemia.
- Diabetic Ketosis or non-ketotic
- Wernickes-Korsakoff's syndrome: acute thiamine (vitamin B1)
- DT's (delirium tremens): drug withdrawal from alcohol or other sedative hypnotics.
- Hypoxia (low blood oxygen)
- Meningitis.
- Subarachnoid hemorrhage
- Subdural hematoma
- Anticholinergic (atropine) poisoning
- Progressive neurological diseases: Multiple sclerosis
- Drugs-illicit

Medical conditions that may present as psychotic disorders

- Huntington's chorea
- Alzheimer's disease and Pick's disease.
- Central nervous system infections: Encephalitis
- Neurosyphilis (syphilis of the central nervous system).
- HIV encephalopathy.
- Space occupying lesions within the skull Brain tumors, bleeding within skull, Brain abscesses, mets
- Metabolic encephalopathy and Disturbances in electrolytes
- Acute intermittent porphyria
- Endocrine disorders: Myxedema, Cushing's syndrome
- Thiamine deficiency: Wernicke-Korsakoff amnestic syndrome;
- Pellagra (nicotinic acid deficiency) and other B complex deficiencies;
- Zinc deficiency
- Temporal lobe epilepsy (or partial complex seizure disorder)

- **To summarise:**
 - Young female without comorbidities, has thyroid disease, strong f/h/o autoimmunity and different mineral and vitamin deficiency and reduced absorption of medications with psychosis
- 
- Some disorder associated with **autoimmunity**
- 
- Combination of malabsorption with autoimmunity strongly suggests the possibility of: **Celiac disease**
 - **But there is absence of gastrointestinal symptoms (diarrhea, flatulence, abdominal pain etc)**

Gastroenterologist and Endocrinologist consultations sought

- **IgA t-TG levels : strongly positive(179 U/ml,Normal range is < 20)**
- **Diagnosis also confirmed on OGD scopy and on HPE of duodenal biopsy.**
- **Adv:Gluten free diet**
- Patient thought her practitioner became deceitful regarding the diagnosis and refused to adhere to gluten free diet—psychosis persist and worsened—lost her job,attempted suicide once, became homeless wandering on streets,lost all family support.

Further follow-up

- Readmitted in psychiatric hospital and now treated with gluten free diet with antipsychotics for at least 3 months
- Her symptoms started regressing gradually ,weaned off from the antipsychotics and became symptom free for 7 months ,meanwhile serological tests and repeat Endoscopic Bx were also became normal.
- After 7 months she had inadvertently ingested gluten → **became delusioanl,IgA tTG levels raised,became anemic,had wt loss ,and now not willing to follow gluten free diet as has strong delusion of not having celiac disease at all!**

celiac disease

- aka: Celiac Sprue/Gluten sensitive enteropathy
- **Celiac(Greek): suffering in the bowels**
- Chronic disorder of digestive tract that results in inability to tolerate gliadin, the alcohol –soluble fraction of gluten commonly found in wheat, rye, barley.
- It's an immunological response against gluten proteins results in release of chemicals which destroy small intestinal villous structure → malabsorption
- It has diverse systemic manifestations than purely a GI system disease.

Epidemiology

- About **1 case in 3000** persons
- More common in **western** than eastern population
- Strong associations with **genetic** factors (**HLA-DQ 2 and HLA-DQ8** heterodimers binds more tightly with gliadins)
- **F>>>M**
- Age distribution: **bimodal**
 - 1.8-12 months
 - 2.third to fourth decade

Facts!!

Patients with celiac disease have increased risk of **intestinal lymphoma or adenocarcinomas of the intestine**, oropharynx, esophagus, pancreas, small and large bowels

- Risk of NGL + increased
- Frequently extraintestinal manifestations are more in adolescents

Symptoms:

Could be **Asymptomatic** (30%)

GI system:

- Diarrhea (45-85%)
- Flatulence (25%)
- Borborygmus(35-70%)
- Weight loss: 45%
- Severe abdominal pain(35- 65%)
- Acute pancreatitis(5%)

Extraintestinal

- **Neurological** -peripheral neuropathy,Ataxia,seizure,psychosis ,short term memory loss,anxiety and depression,chronic headache
- **Dental:** enamel defects,apthous ulcers
- **cardiovascular:** myocarditis ,atrial fibrillation
- **Cutaneous:** Dermatitis
herpetiformis,urticaria,eczema,psoriasis,brittle nails,hair thinning
- **Pulmonary:** Idioapthic pulmonary hemosiderosis(Lane hamilton sundrome)
- **Renal:** Increased risk of Glomerulonpehritis
- **Hematological** -anemia
- **Hepatic:** Hepatitis
- **Musculoskeletal system:** joint pains,osteopenia, osteoporosis



Dermatitis herpetiformis



characterized by grouped excoriations, erythematous, urticarial plaques, and papules with vesicles. The classic location for dermatitis herpetiformis lesions is on the extensor surfaces of the elbows, knees, buttocks, and back. It is extremely pruritic, and the vesicles are often excoriated to erosions by the time of physical examination, as shown in the image.

Celiac disease as a multiorgan autoimmune disease

General:

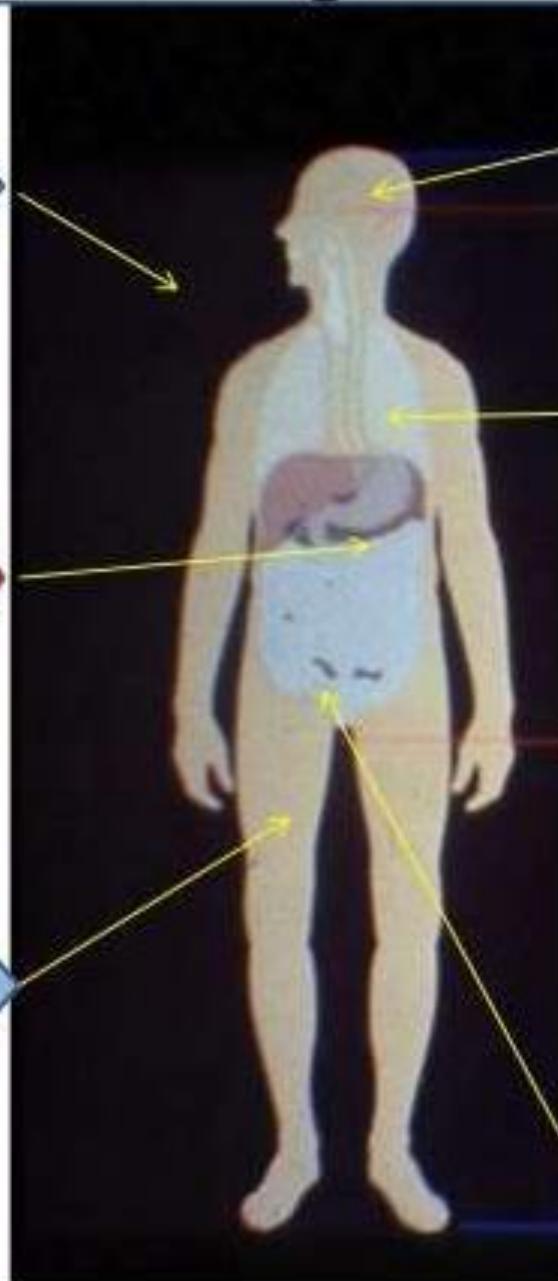
Puberty & growth delay
Malignancies
Anemia

GI system:

Diarrhea, vomiting
Distension, pain
Malnutrition, weight loss
Hepatitis, cholangitis

Bone:

Osteoporosis, fractures
Arthritis
Dental anomalies



CNS:

Ataxia, seizures
Depression

Heart:

Carditis

Skin & mucosa:

Dermatitis herpetiformis
Aphthous stomatitis
Hair loss

Reproductive system:

Miscarriage
Infertility

differentials

- Anorexia nervosa
- Autoimmune enteropathy
- Bacterial overgrowth
- Collagenous sprue
- Crohn's disease
- Giardiasis
- HIV enteropathy
- Hypogammaglobulinemia
- Infective gastroenteritis
- Irritable bowel syndrome
- Ischemic enteritis
- Lactose intolerance
- Pancreatic insufficiency
- Soy protein intolerance
- Tropical sprue
- Tuberculosis
- Whipple's disease
- Zollinger-Ellison syndrome
- Intestinal lymphoma

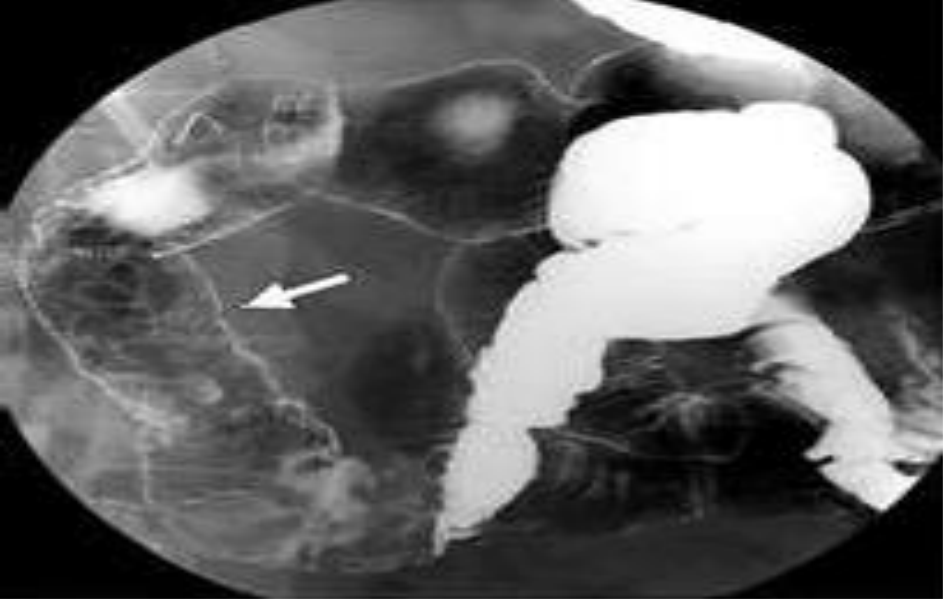
Diagnosis

Labs

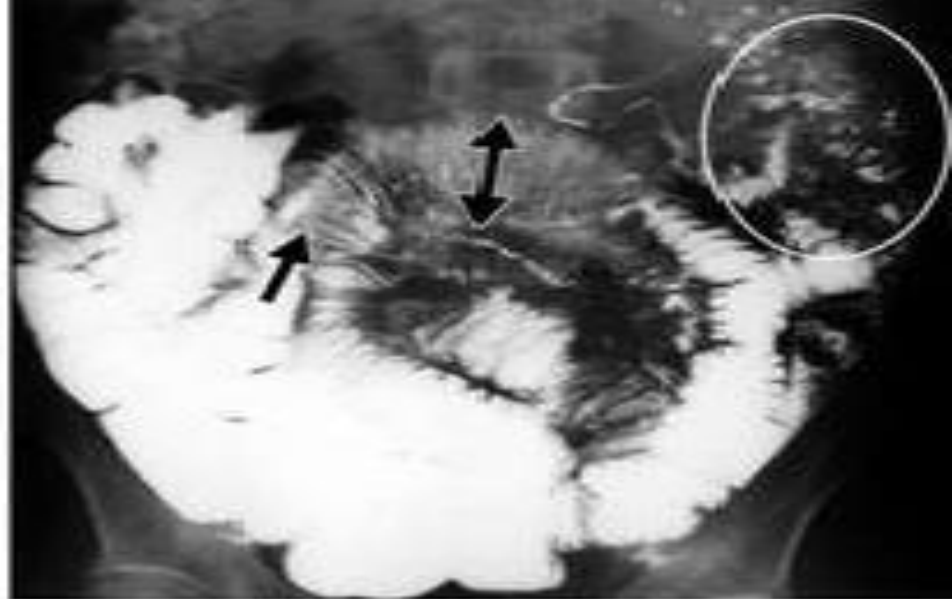
- ACG recommends: IgA anti tissue transglutaminase
- In Children < 2 years: ACG recommends IgA TTG should be combined with IgG –DGP
- SI biopsy for confirmation- Bx of at least 6 sites
- Stool examination
- Oral lactose tolerance
- Hematologic test –anemia ,low serum iron ,prolonged PT/INR(Vit K def)
- Genetic testing
- Bone density

Malabsorption

- A 72 hours fecal fat estimation-steatorrhea ,Sudan stain
- D-xylose for carbohydrate intolerance
- Excretion of breath Hydrogen s/o lactase intolerance
- Imaging: barium meal- dilatation of small intestine ,a coarse or obliteration of normal mucosal pattern and fragmentation/flocculation of barium in the gut lumen



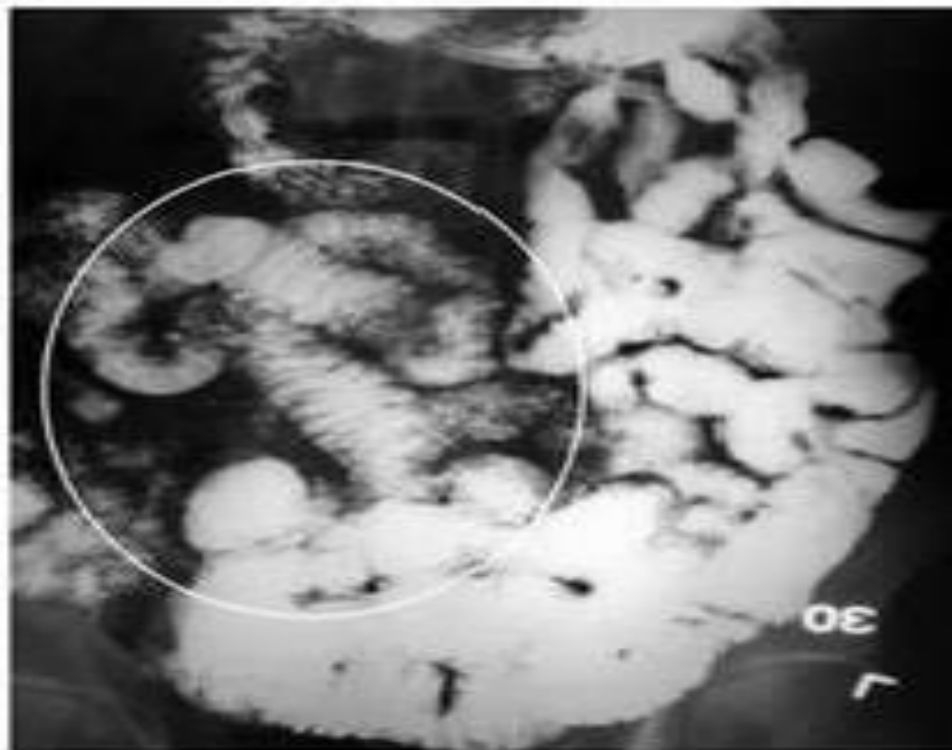
a.



b.



c.

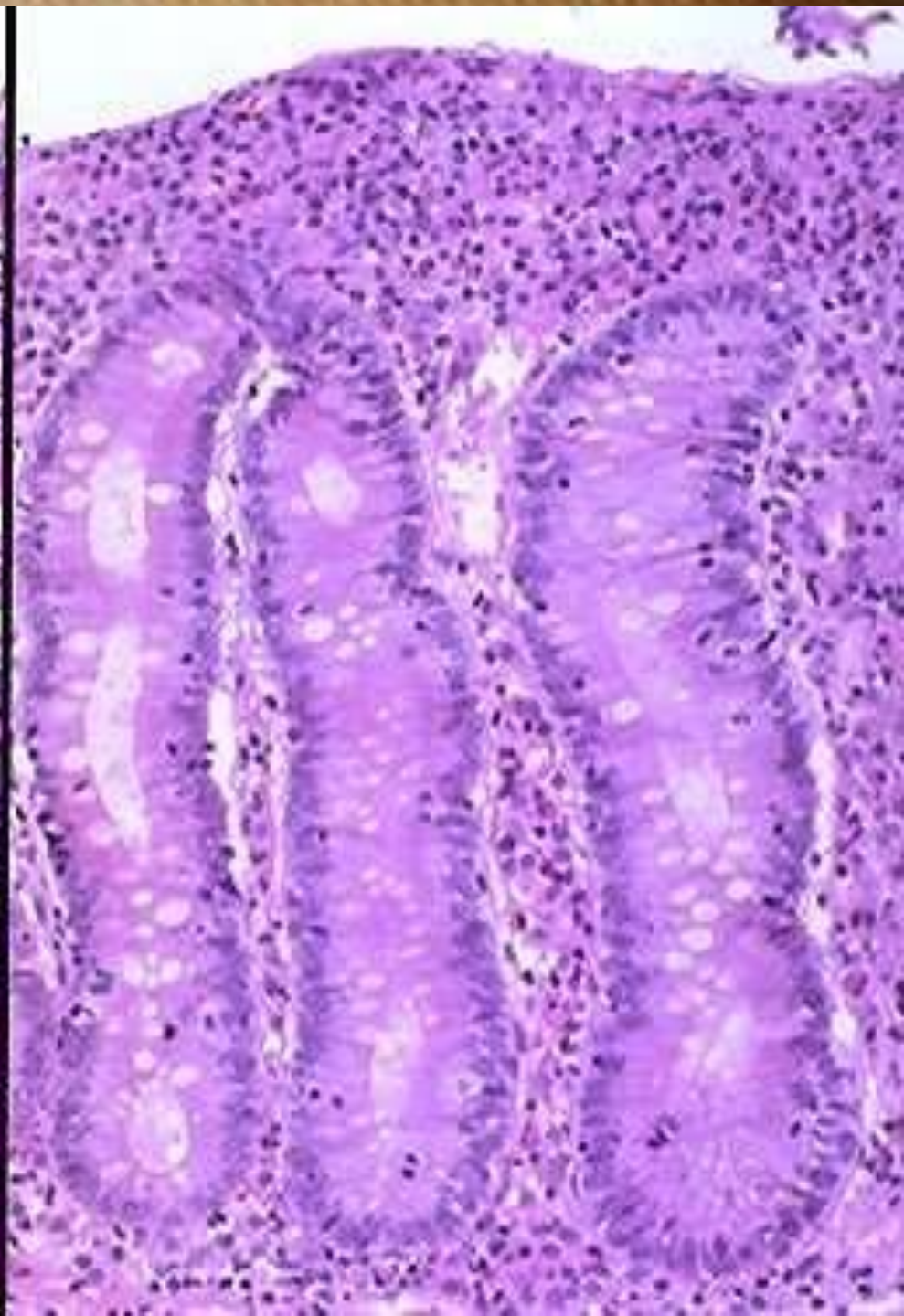
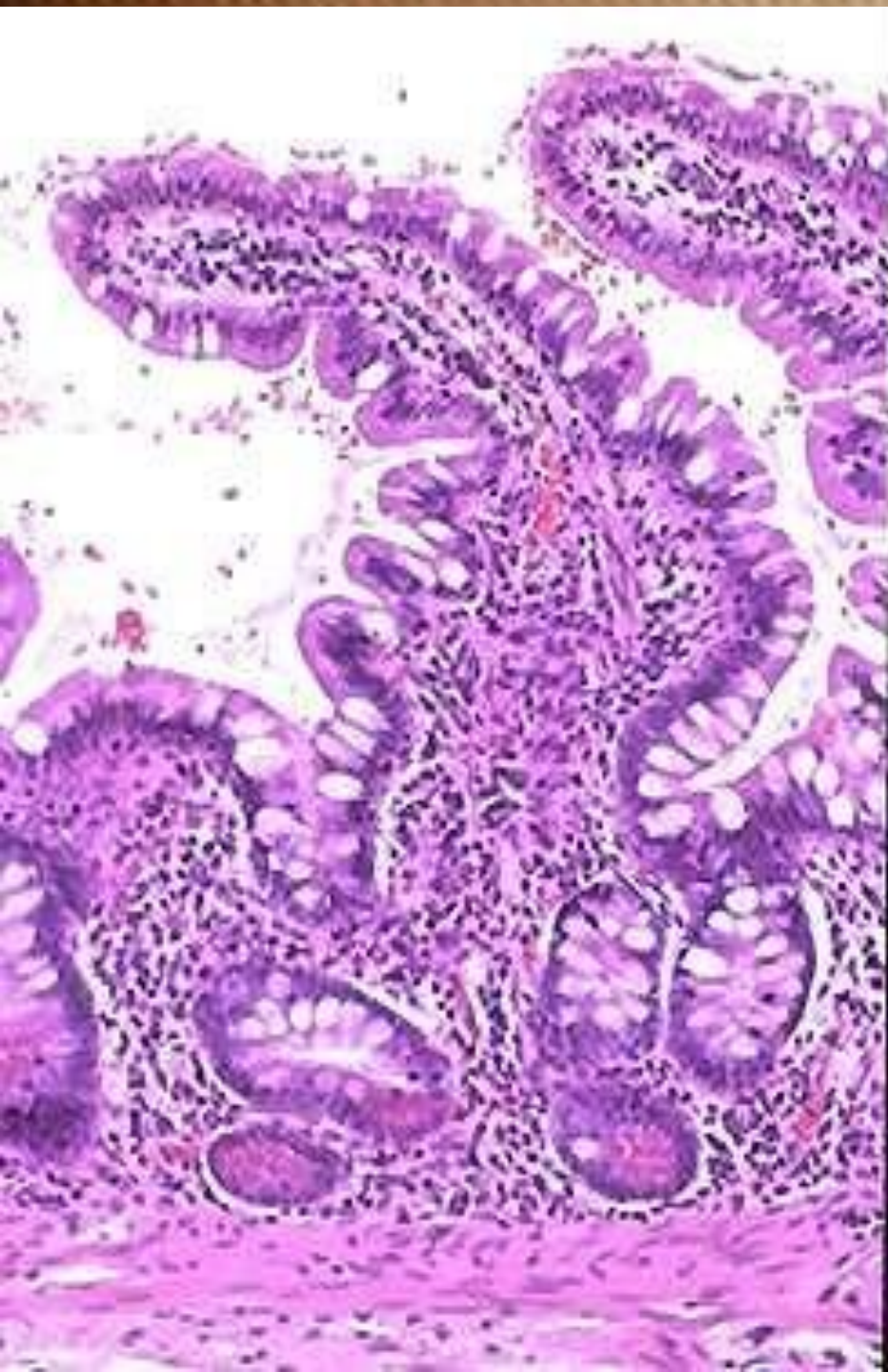


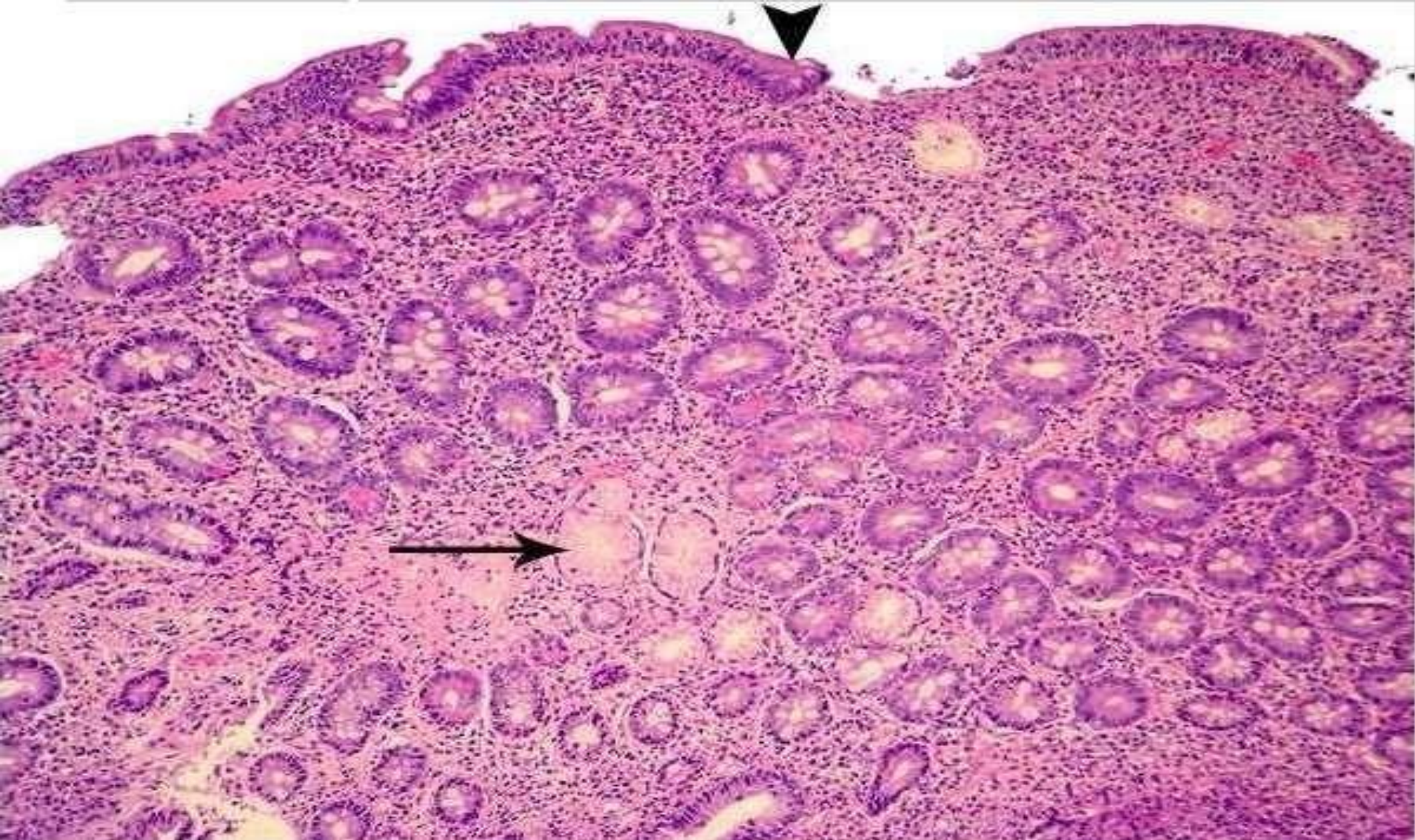
d.

- a) Image shows duodenitis with nodularity in a fold-free duodenum (arrow).
- (b) Image shows flocculation (within oval at upper right), dilution (single arrow), and dilatation (double arrow).
- (c) Image shows moulage (within oval), which is a featureless bald appearance of the jejunum caused by atrophy of folds and wall edema.
- (d) Image shows reversal of the fold pattern (within oval), with more prominent folds in the ileum than in the jejunum.

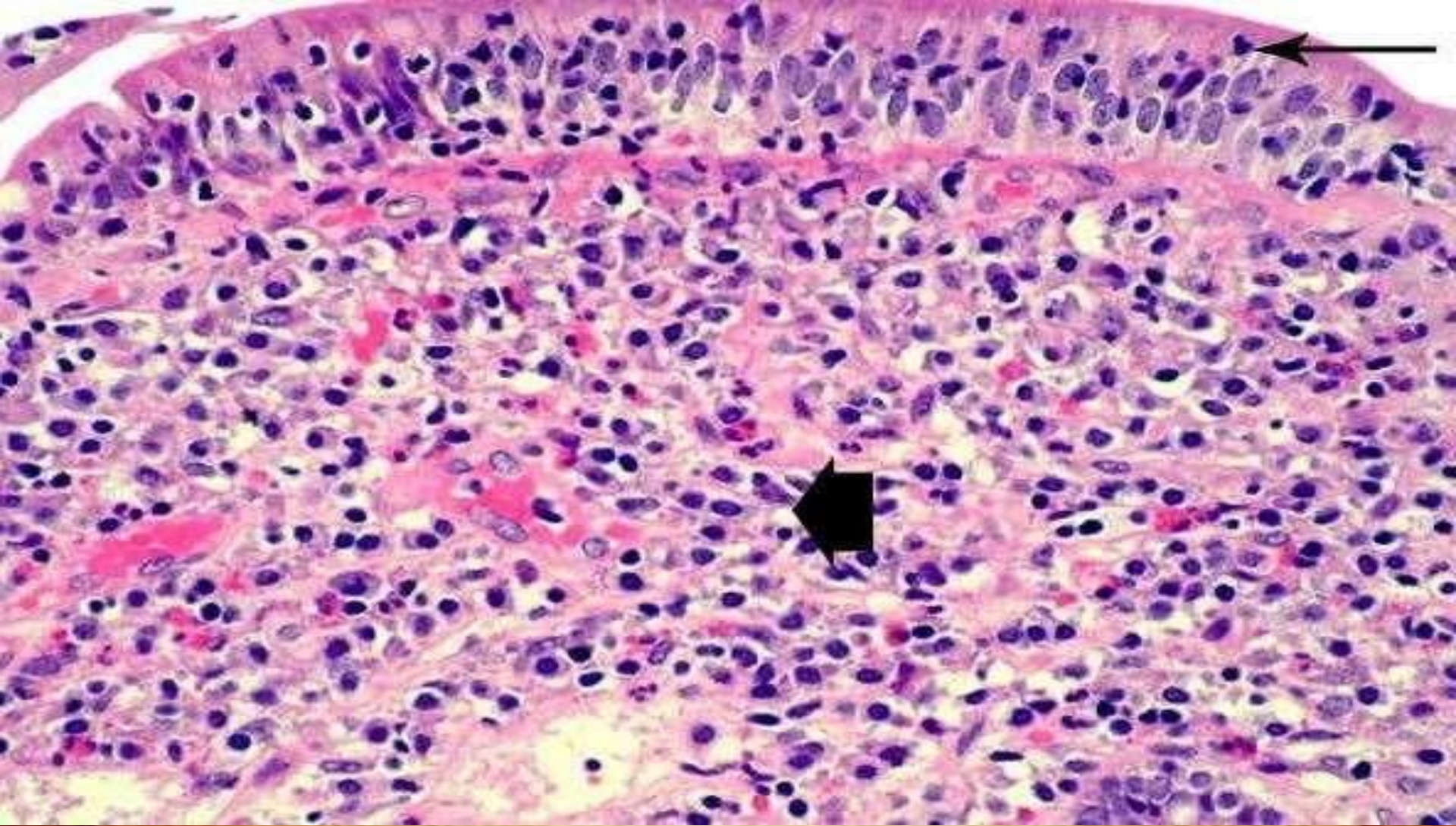


The Classical scalloping of duodenal mucosa seen in established disease at endoscopy





Celiac disease is a malabsorptive syndrome of the small intestine which shows characteristic morphologic changes in the proximal small intestine. The most visible feature is the total or subtotal loss of villous architecture imparting an appearance akin to colon. The loss of villous architecture is the result of an inflammatory and autoimmune damage to the epithelial cells. Note the flattened top of the duodenal mucosa (top arrowhead) and the presence of a few remaining Brunner's gland.



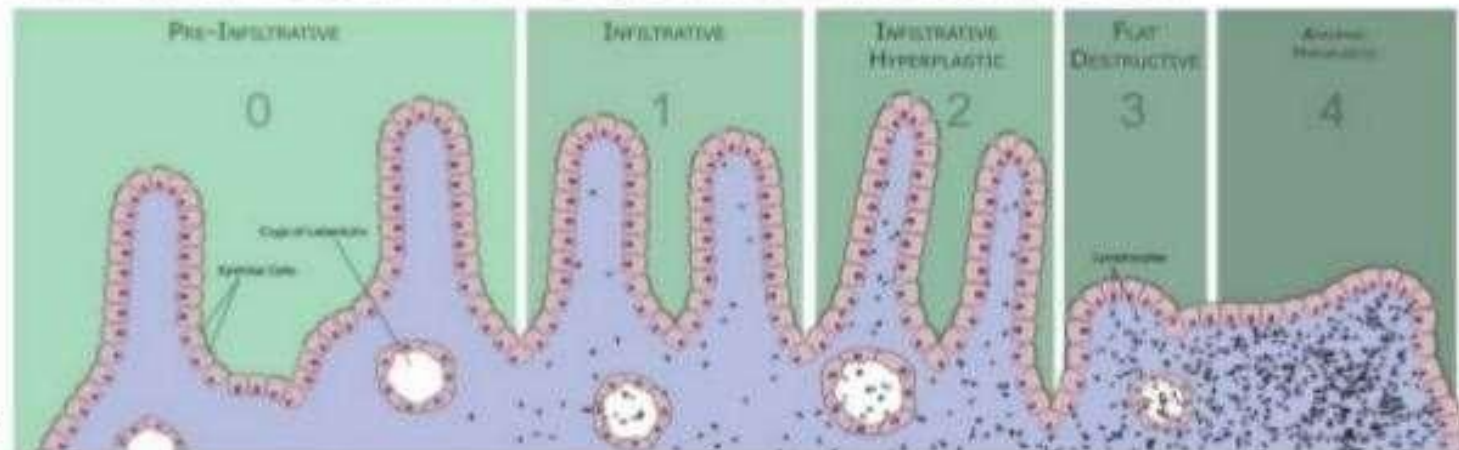
varying degrees of chronic inflammation is present in the lamina propria and surface epithelium. The long arrow at the top shows intraepithelial lymphocytes with loss of brush border. The broad arrow at the bottom shows moderate chronic inflammation with small lymphocytes, plasma cells, and eosinophils.

Pathological spectrum of small intestine

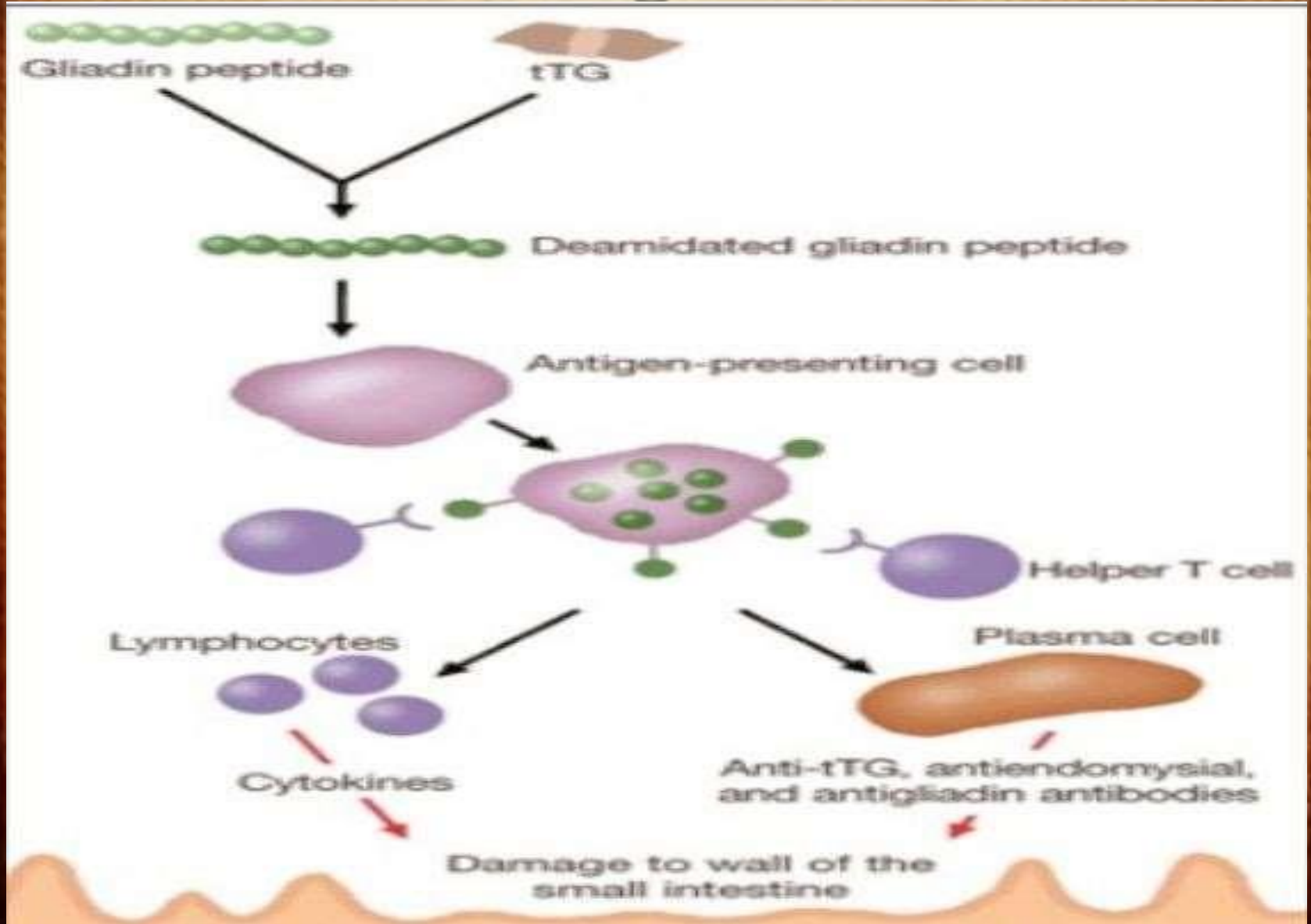
The classic pathology changes of celiac disease in the small bowel are categorized by **"Marsh Classification"**:

- **Marsh stage 0:** normal mucosa
- **Marsh stage 1:** ↑ intra-epithelial lymphocytes >20/100 enterocytes
- **Marsh stage 2:** proliferation of the crypts of Lieberkuhn
- **Marsh stage 3:** partial or complete villous atrophy
- **Marsh stage 4:** hypoplasia of the small bowel architecture

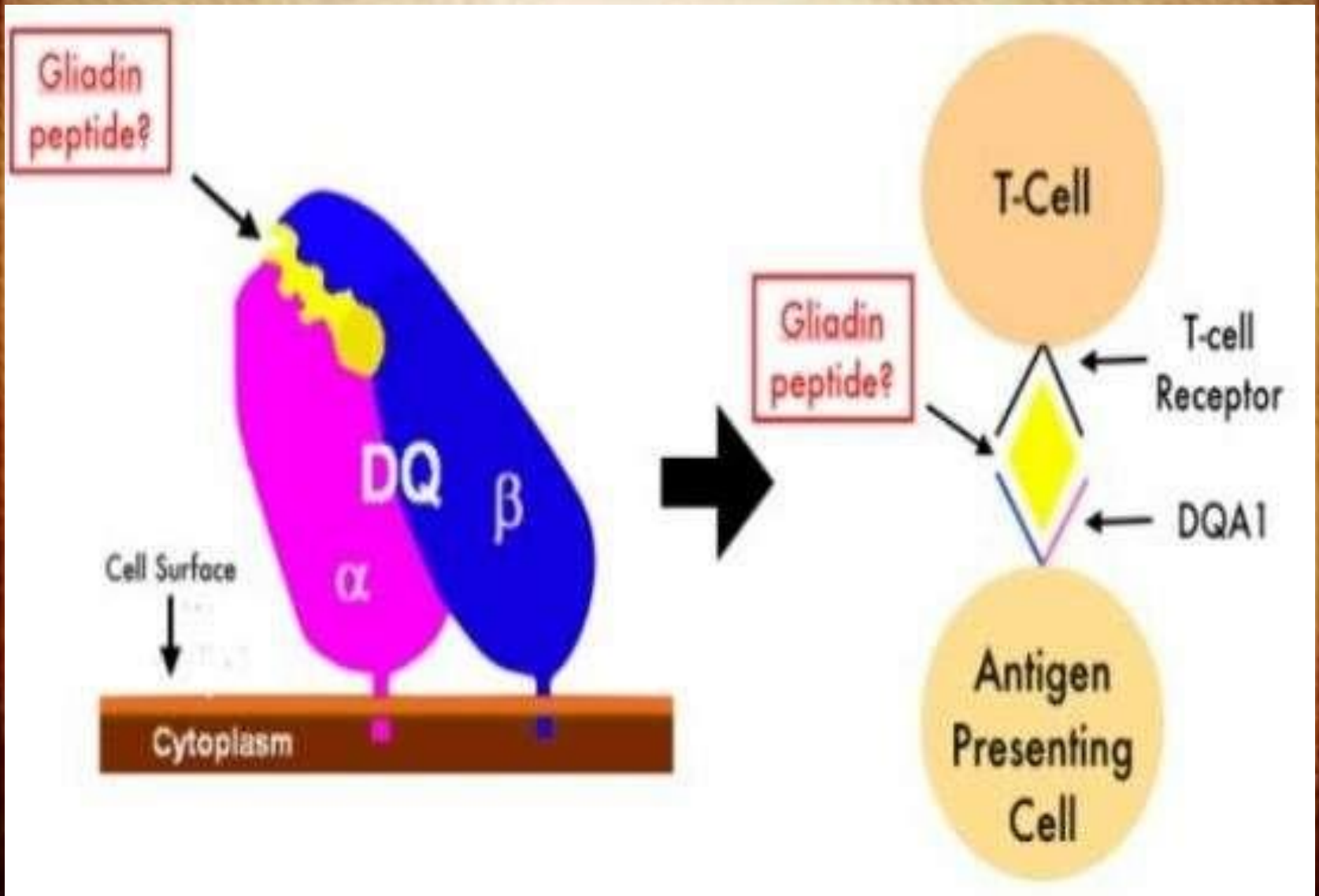
UPPER JEJUNAL MUCOSAL IMMUNOPATHOLOGY



Pathogenesis



Pathogenesis



What is gluten ??



THE Protein flour that form the structure of dough

Specific peptide fraction of Protein Found in:

Wheat

Rye

Barely

↓
Glutenins,
Gliadins.

↓
Secalinus

↓
Hordenis

Different autoantibodies formed

- *Anti-tTG /TG2 (tissue transglutaminase)*
- *Anti-EMA (Endomysial antibody)*
- *Anti- DGP (deamidated Gliadin Peptides)*
 - IgA level should be done with EMA/tTG
- Anti- Gliadin/Anti- Reticulin

Sensitivities and specificities

| Test | % Sensitivity | % Specificity | Age |
|---------|---------------|---------------|----------|
| tTG-IgA | 90-100 | 94-100 | Children |
| | 84-100 | 91-100 | Combined |
| EMA-IgA | 87-95 | 95-100 | Adults |
| | 88-100 | 90-100 | Children |
| | 91-98 | 99-100 | Combined |
| DGP | 91 | 98 | Combined |

Scoring system for diagnosis of Celiac disease

| | Points |
|---|--------|
| Symptoms | |
| Malabsorption syndrome | 2 |
| Other CD-relevant symptom or having T1DM or being a first-degree family member | 1 |
| Asymptomatic | 0 |
| Serum antibodies ^a | |
| EMA positivity and/or high positivity (> 10 ULN) for anti-TG2 | 2 |
| Low positivity for anti-TG2 antibodies or isolated anti-DGP positivity | 1 |
| Serological assessment not performed | 0 |
| Serological assessment performed but negative for all celiac-specific antibodies ^a | -1 |
| HLA | |
| Full HLA-DQ2 (in <i>cis</i> or <i>trans</i>) or HLA-DQ8 heterodimers present | 1 |
| No HLA performed or half DQ2 (only HLA-DQB1*0202) present | 0 |
| HLA neither DQ2 nor DQ8 was present | -1 |
| Histology | |
| Marsh 3b or 3c (subtotal villous atrophy, flat lesion) | 2 |
| Marsh 2 or 3a (moderately decreased villous height/crypt depth ratio) or marsh 0-1 plus intestinal TG2 antibodies | 1 |
| Marsh 0-1 or no biopsy performed | 0 |

CD, celiac disease.

^aIgG deficiency to IgG class EMA, TG2, and DGP antibodies.

Who should be tested for Celiac disease

Group 1:

unexplained symptoms and signs

chronic or intermittent diarrhoea, failure to thrive, weight loss, stunted growth, delayed puberty, amenorrhoea, iron-deficiency anaemia, nausea or vomiting, chronic abdominal pain, cramping or distension, chronic constipation, chronic fatigue, recurrent aphthous stomatitis (mouth ulcers), dermatitis herpetiformis-like rash, fracture With inadequate traumas/osteopenia/osteoporosi, and abnormal liver biochemistry.

Group 2:

Asymptomatic increased risk for CD

Type 1 diabetes mellitus (T1DM)

Autoimmune thyroid disease

Autoimmune liver disease

IgA deficiency

Down syndrome

Turner syndrome

Williams syndrome

First-degree relatives

Treatment

- The best treatment available-

GFD(gluten free diet)

Gluten free diet

| Gluten-free grains and grain products ^a | Serving size |
|--|--------------------|
| Breads | |
| Breads, English muffins and bagels made from rice, potato, bean, soy, corn, sorghum, teff, or other flours | 1 slice or piece |
| Frozen, gluten-free waffles | |
| Gluten-free pizza crust made from a mix or frozen readymade | |
| Homemade breads, biscuits, pancakes, waffles, muffins, or quick breads made from gluten-free flours/corn tortillas | |
| Cereals | |
| Cooked cereal made from corn (hominy, grits), rice, pure buckwheat, amaranth, or quinoa | 1/2 to 1 cup |
| Gluten-free puffed rice/gluten-free cornflakes/rice flakes, amaranth flakes, or other dry cereals | |
| Snacks | |
| Crackers or crisp breads made from rice or corn | 1 oz (check label) |
| Popcorn/rice cakes/pretzels made from gluten-free flours/corn chips | |
| Other | |
| Brown, wild, or white rice | 1/2 to 1 cup |
| Pasta made from rice, corn, amaranth, quinoa, or pure buckwheat | |
| Kasha made with pure buckwheat | |
| Corn/quinoa/flax/millet | |

^aProducts vary by manufacturer, so be sure that they are gluten free.

