

# ***Celiac disease the adult story***

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# GLUTEN RELATED DISORDERS

- CELIAC DISEASE

GLUTEN ATAXIA, DERMATITIS HERPETIFORMIS

- WHEAT ALLERGY

- GLUTEN SENSITIVITY (NON-CELIAC)

# WHEAT ALLERGY

- RESPIRATORY (baker's asthma, rhinitis)
  - FOOD ALLERGY
  - EXERCISE INDUCED WHEAT ALLERGY
  - CONTACT URTICARIA
- 
- IgE mediated
  - Peak at 1 year of age
  - Decreases with age

# NON CELIAC GLUTEN SENSITIVITY

Gluten free product consumption has increased over time and currently is higher than low carb and low fat diet

- Only 8% to 12% due to celiac disease or gluten sensitivity
- Not recognized as an entity by physicians

## DEFINITION

- Symptomatic response to gluten withdrawal after both celiac disease and wheat allergy excluded
- Normal biopsy (minimally abnormal)
- May have positive anti-gliadin antibodies

# NON CELIAC GLUTEN SENSITIVITY

- We have no idea how common this is
- Evidence from the GF market place
- Increasing “diagnosis” by non-traditional medical practitioners
- Increasing public awareness



ELSEVIER

Contents lists available at ScienceDirect

## e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism

journal homepage: <http://www.elsevier.com/locate/clnu>



Original article

### Awareness of gluten-related disorders: A survey of the general public, chefs and patients<sup>☆</sup>

S. Simpson<sup>a,\*</sup>, B. Lebwohl<sup>a,c</sup>, S.K. Lewis<sup>a,c</sup>, C.A. Tennyson<sup>a,c</sup>, D.S. Sanders<sup>b,d</sup>, P.H. Green<sup>a,c</sup>

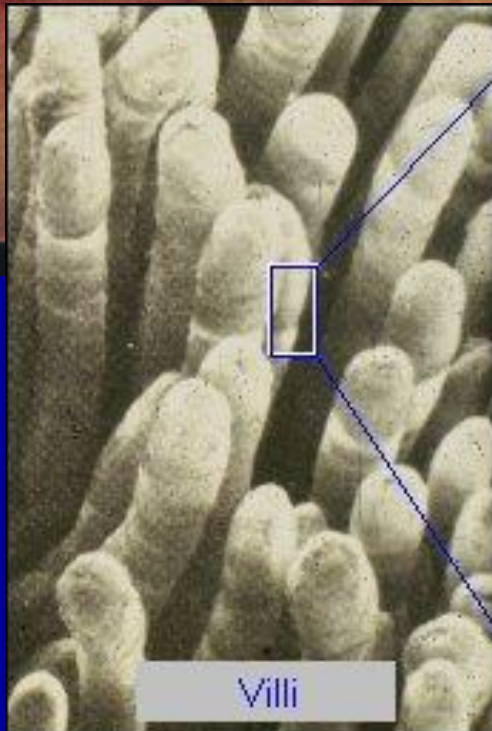
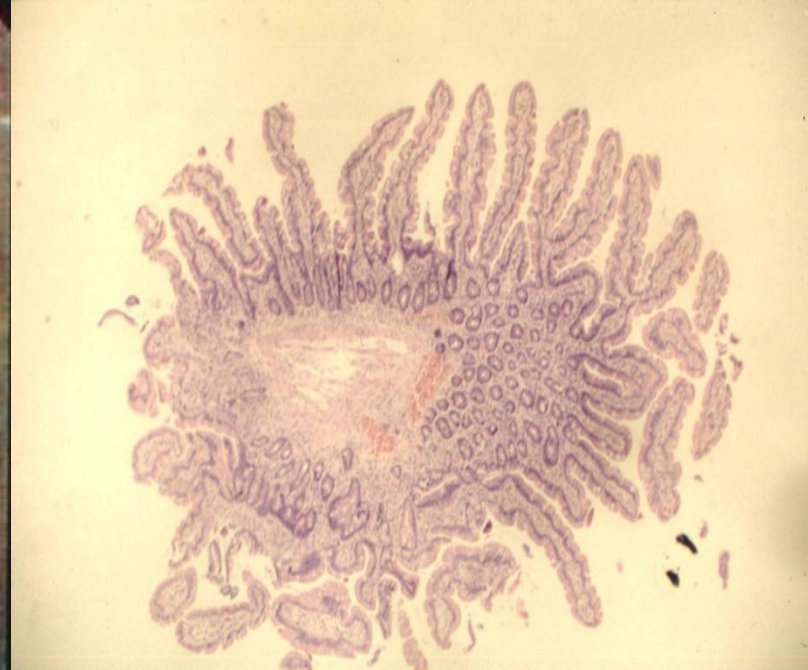
<sup>a</sup> Celiac Disease Center at Columbia University, 180 Fort Washington Avenue, Room 936, NY 10032, USA

<sup>b</sup> Royal Hallamshire Hospital and the University of Sheffield, Glossop Road, Sheffield, South Yorkshire S10 2JF, UK

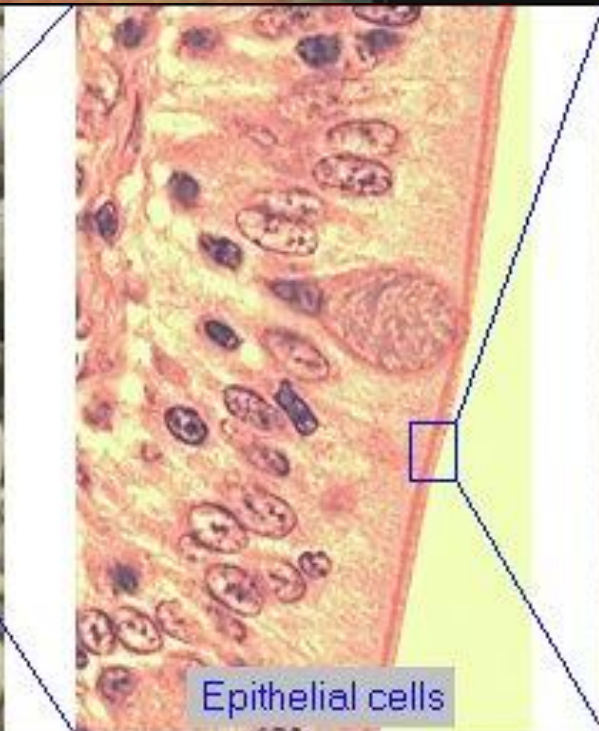
**Results:** Among 861 persons from the general public 47% had heard of CD, 67% of GS and 88% of peanut allergy. Chefs were more likely than the general public to have heard of CD (77% vs. 47%,  $p < 0.0001$ ), though greater proportions in both groups had heard of GS (89% vs. 67%,  $p < 0.0001$ ). 63% of patients ( $n = 790$ ) reported that they avoid restaurants because of the gluten-free diet and ate take-out food and restaurant food significantly less often than the general public. Trained chefs had more knowledge than untrained chefs (83% vs. 52%,  $p < 0.0001$ ). There was a direct relationship between the average check price and chefs' awareness ( $< \$25$ : 64% vs.  $> \$65$ : 94%,  $p < 0.0001$ ).

# NON CELIAC GLUTEN SENSITIVITY

- Mechanism is not clear
- Relationship to the innate immune system
- Why the systemic symptoms
- Why more sensitive to gluten than celiac patients
- Relationship between +AGA and psychiatric diseases



Villi



Epithelial cells



Microvilli

# CELIAC DISEASE

inflammation and villous atrophy



Marked reduction in surface area of the intestine

# PREVALENCE OF CELIAC DISEASE

- **Common**, affects ~1% of the population
- Evidence from serologic screening studies

UK adults (*Gut*, 2003) 1/100

UK children (*BMJ*, 2004) 1/100

Finland children (*NEJM*, 2003) 1/99

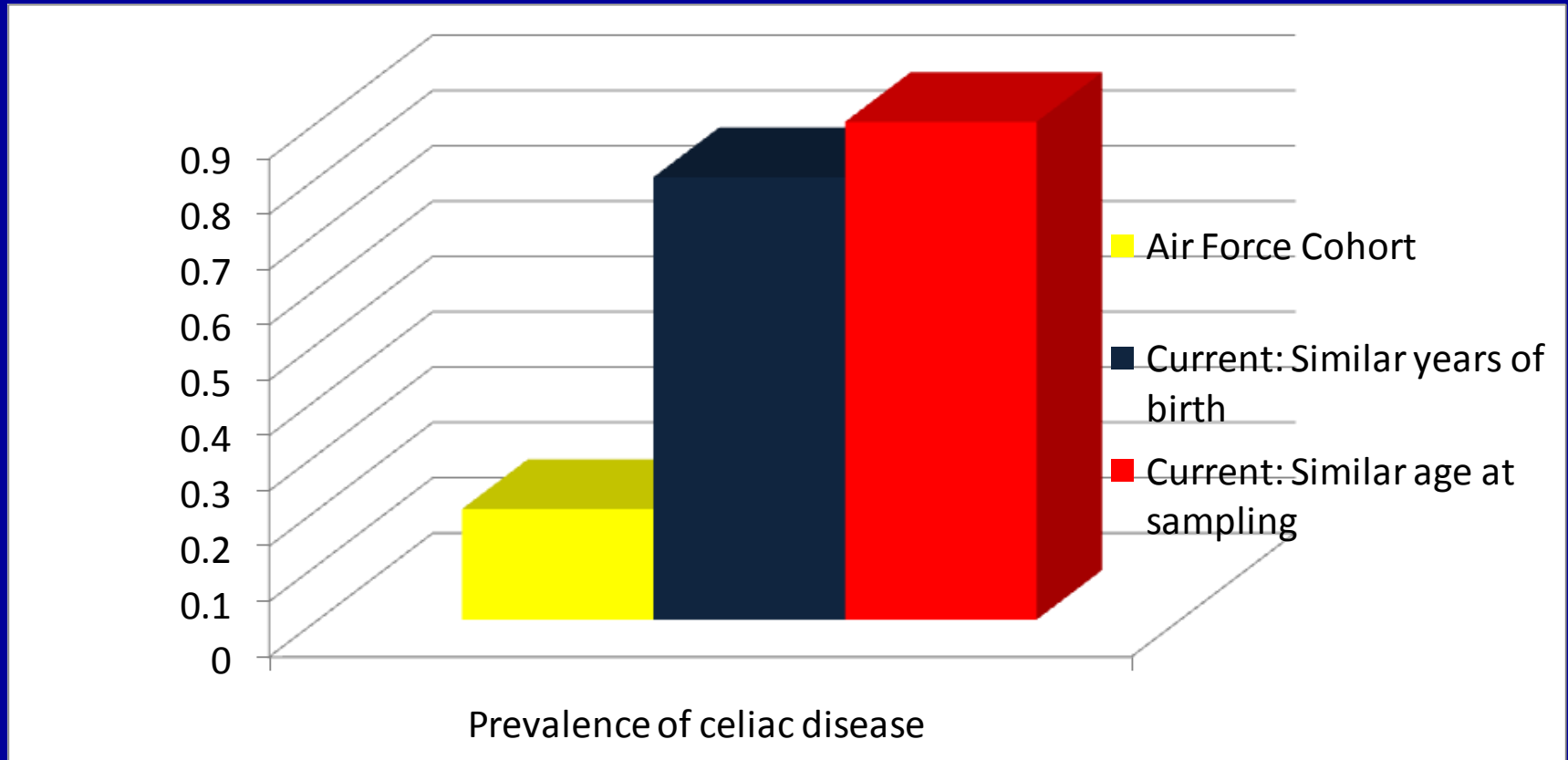
Turkey children (*J Clin Gastroenterol*, 2005) 1/115

Turkey adults (*J Clin Gastroenterol*, 2005) 1/99

North Africa children (*Lancet*, 1999) 1/18

USA adults & children (*Arch Int Med*, 2003) 1/133

# Increasing Prevalence of Celiac Disease



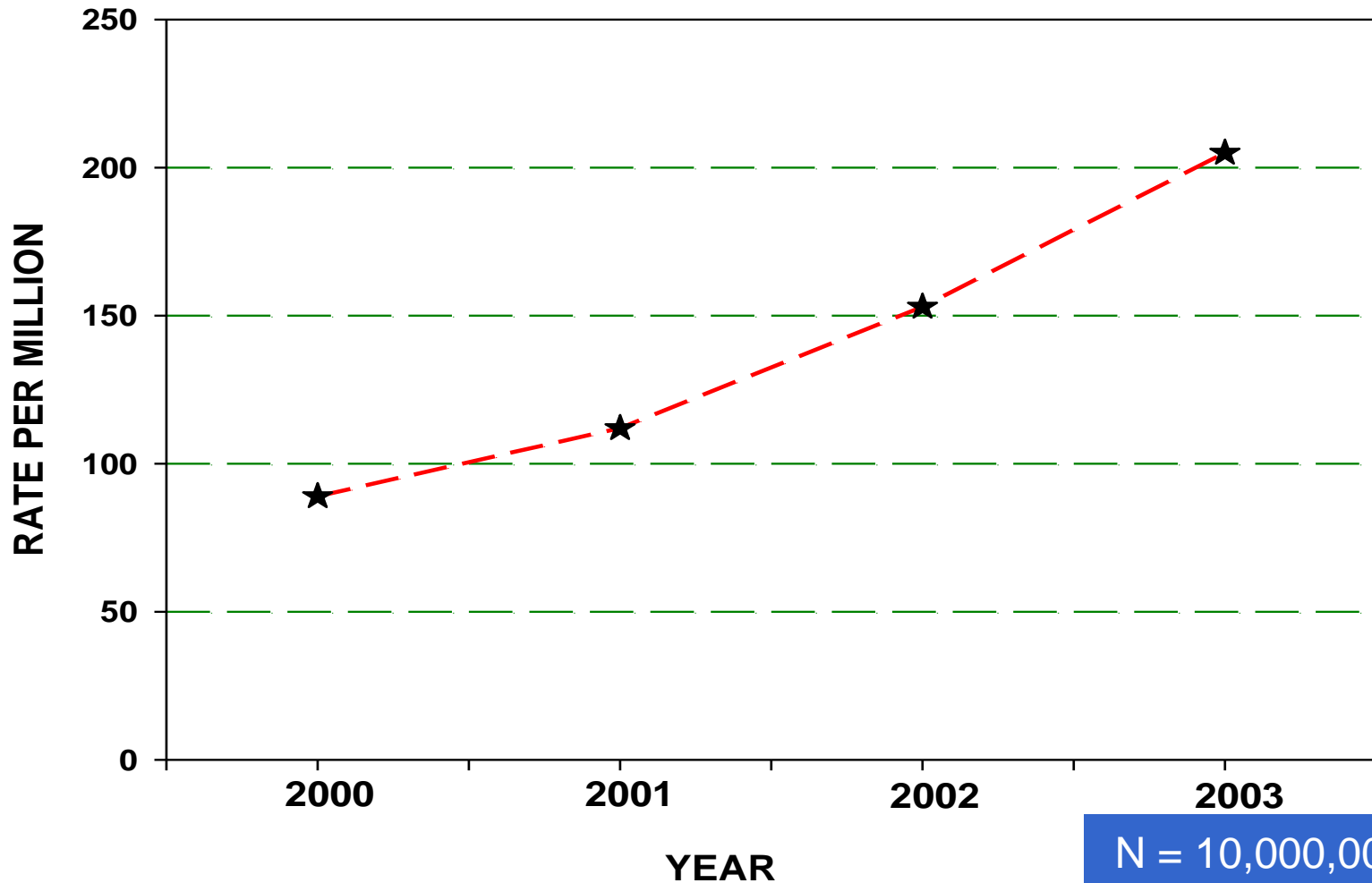
Positive: +TTG, +EMA

# INCREASING PREVALENCE OF CELIAC DISEASE

- Finland 2.4% elderly
- Sweden 3% children aged 12
- United States 0.2% 1950s  
1% 2008

**MOST PEOPLE WITH CELIAC  
DISEASE ARE STILL  
UNDIAGNOSED**

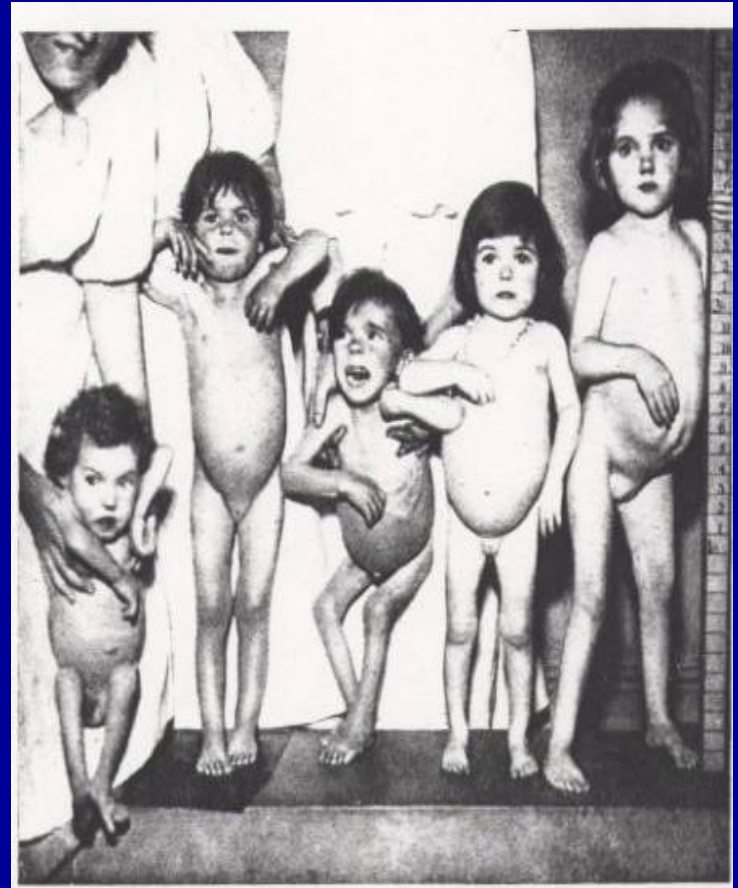
# RATE OF CELIAC DISEASE DIAGNOSIS (CIGNA 2000 – 2003)



N = 10,000,000  
JIM, 2009

# The “old” CD epidemiology

- A rare disorder typical of infancy
- Malabsorption
- Ricketts
- Growth failure



G. 2.—Photograph of five cases of coeliac disease showing the general clinical features

early onset osteoporosis

irritable bowel syndrome

vitamin deficiencies

weight loss

abdominal pain

constipation

gas

bloating

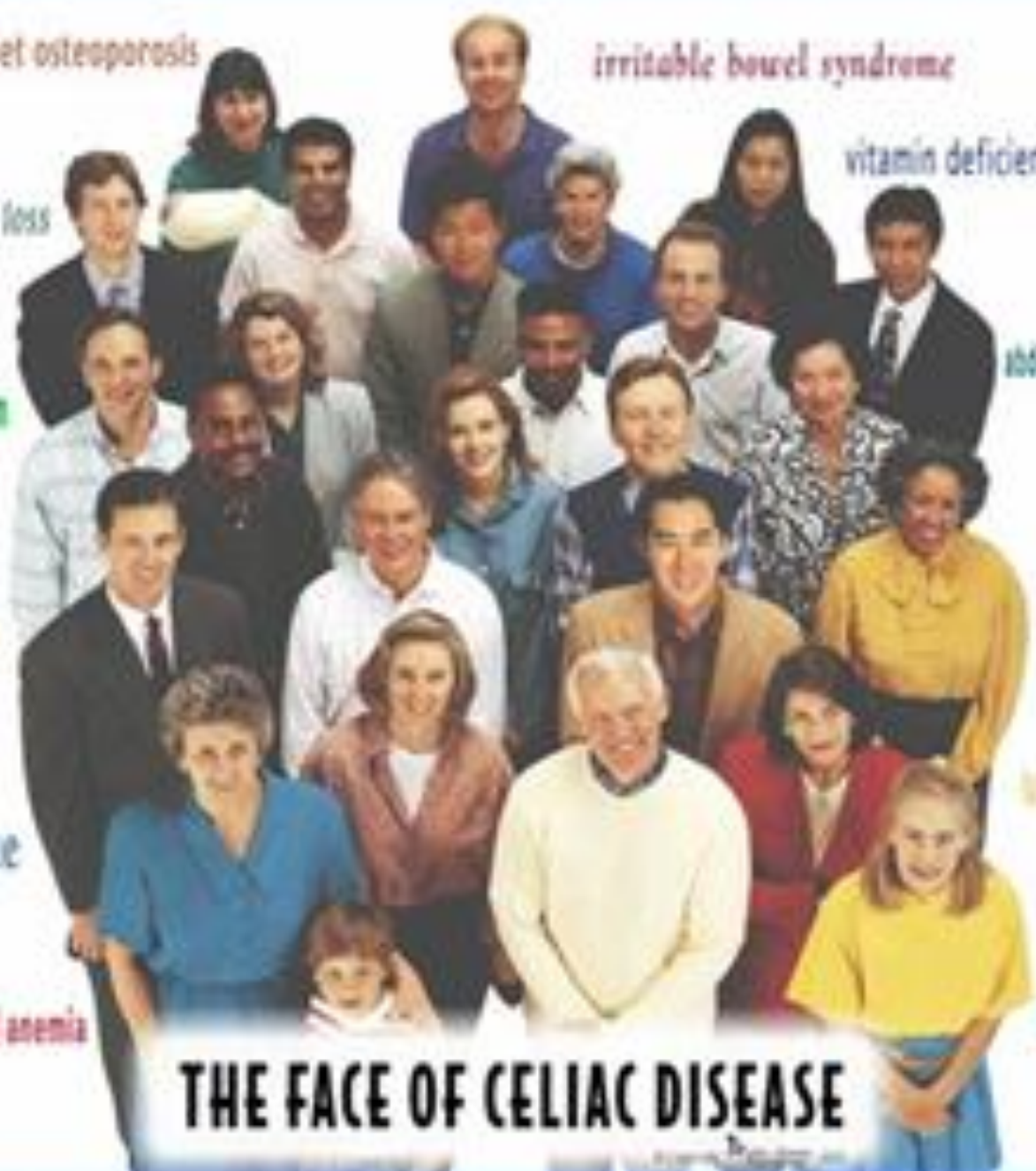
weakness

fatigue

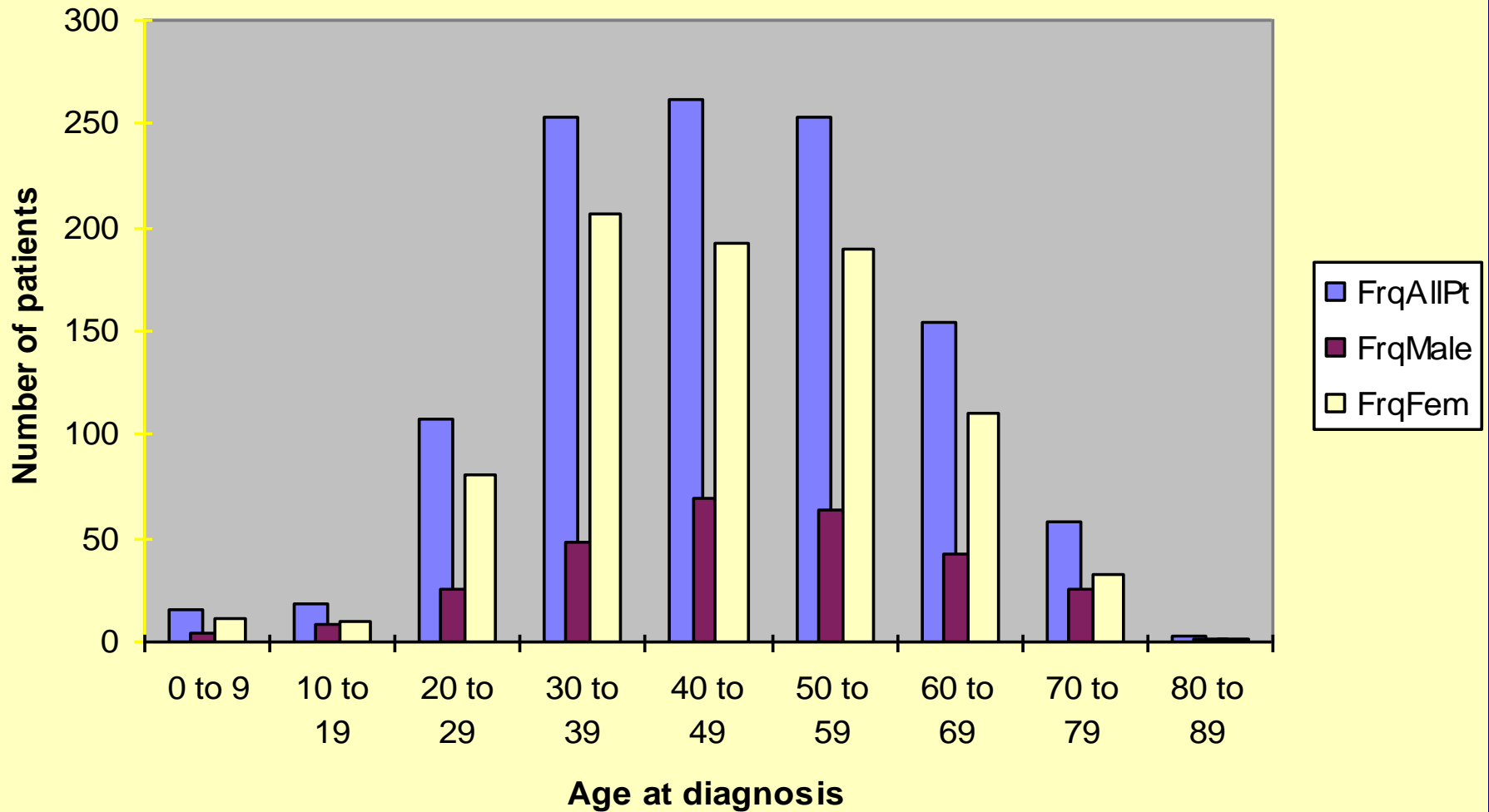
diarrhea

unexplained anemia

# THE FACE OF CELIAC DISEASE



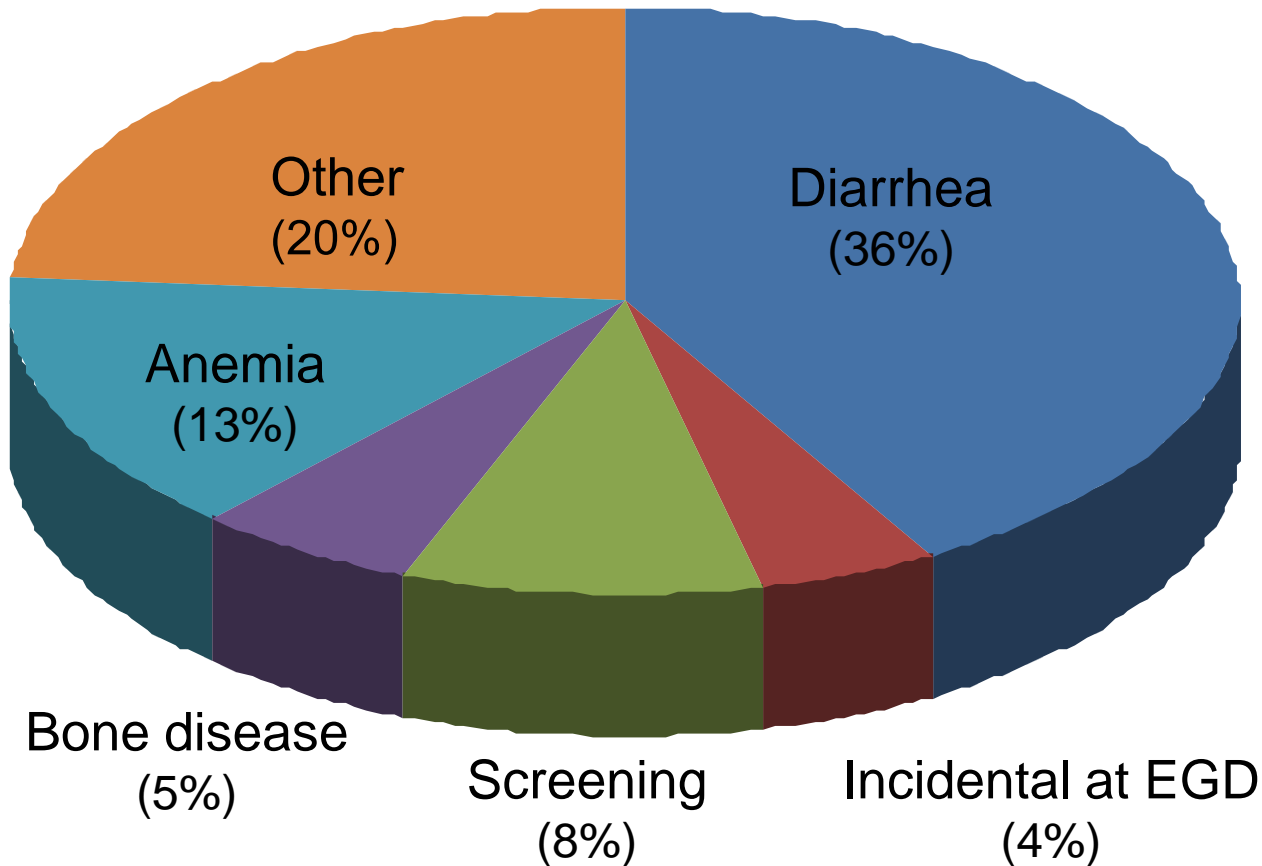
# AGE AT DIAGNOSIS



# GENDER

- Women diagnosed 2 – 3X more commonly than men
- Exceptions children and elderly
- Screening studies show celiac disease is present in both men and women equally

# PRESENTATION OF CELIAC DISEASE (ADULTS)



N = 1499

# OTHER PRESENTATIONS

## (20% n = 306)

- Dermatitis herpetiformis
- Weight loss
- Bloating
- Neurological presentations (neuropathy, ataxia)
- Thyroid disease
- Dental enamel abnormalities
- BLOOD TEST ABNORMALITIES
  - Abnormal LFTs, low ferritin
  - Hypocholesterolemia, low HDL
  - Hyperamylasemia (macroamylasemia)
  - Hypoalbuminemia
  - Elevated ESR, vitamin E deficiency
  - Hypocalcemia, secondary hyperparathyroidism

# DERMATITIS HERPETIFORMIS (DH)



Anti tTG3

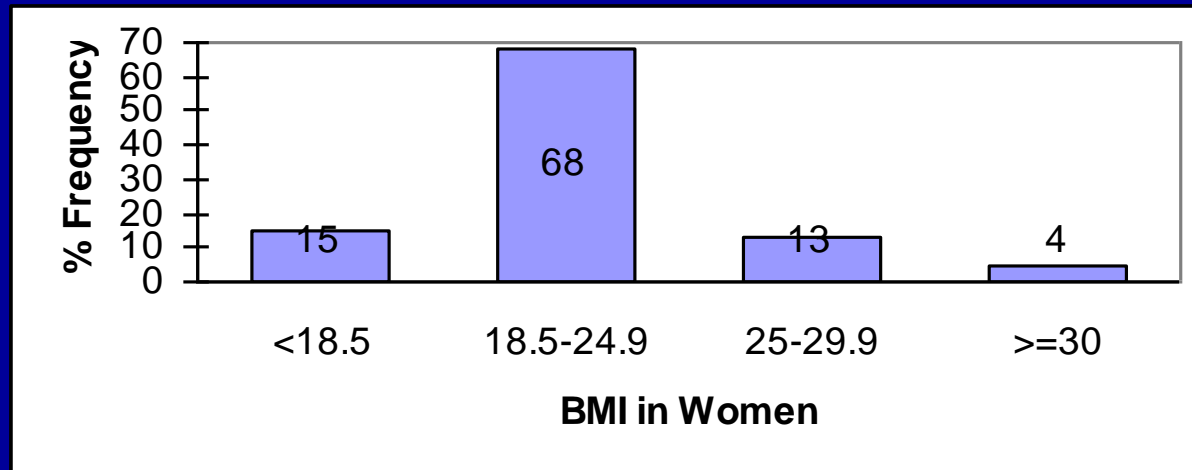
# DERMATITIS HERPETIFORMIS (DH)

- Occurs in ~8% celiacs
- Extremely gluten sensitive
- Location        classical  
                         anywhere

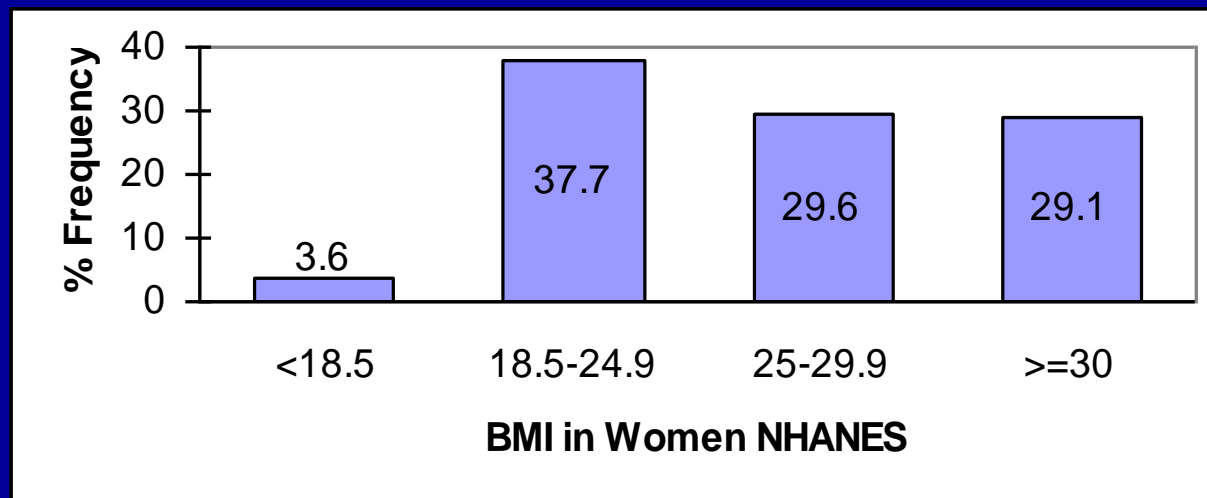
DIAGNOSIS biopsy 1mm away from a  
lesion, immunofluorescence studies

TREATMENT GFD, restrict iodine, NSAIDs  
dapsonsone

# BMI (WOMEN) CELIAC DISEASE Vs US NATIONAL DATA



N=232



NHANES

# BMI CHANGES

- Low BMI improved
- Obese pts lost weight
- Maybe related to being followed in a Celiac Center



# The Association Between Celiac Disease, Dental Enamel Defects, and Aphthous Ulcers in a United States Cohort

*Ted Malahias, DDS,\* Jianfeng Cheng, MD, PhD,\* Pardeep Brar, MD,†  
Maria Teresa Minaya, DDS,† and Peter H. R. Green, MD†*

**Results:** Among patients (n = 67, mean age 34.8 ± 21.6y) compared with controls (n = 69, mean age 28.1 ± 15.7 y), there were significantly more enamel defects [51% vs. 30%,  $P = 0.016$ , odds ratio (OR) 2.4, 95% confidence interval (CI) 1.2-4.8]. This was confined to children (87% vs. 33%,  $P = 0.003$ , OR 13.3, 95% CI 3.0-58.6), but not adults (32% vs. 29%,  $P = 0.76$ , OR 1.2, 95% CI 0.5-2.8). This was reflected in defects being observed in those with mixed dentition compared with those with permanent dentition (68.4% vs. 29.6%,  $P < 0.0001$ ). The degree of agreement between the 2 dentists was good ( $\kappa$  coefficient = 0.53,  $P < 0.0001$ ), aphthous ulcers were more frequent in CD than controls (42.4% vs. 23.2%,  $P = 0.02$ ).

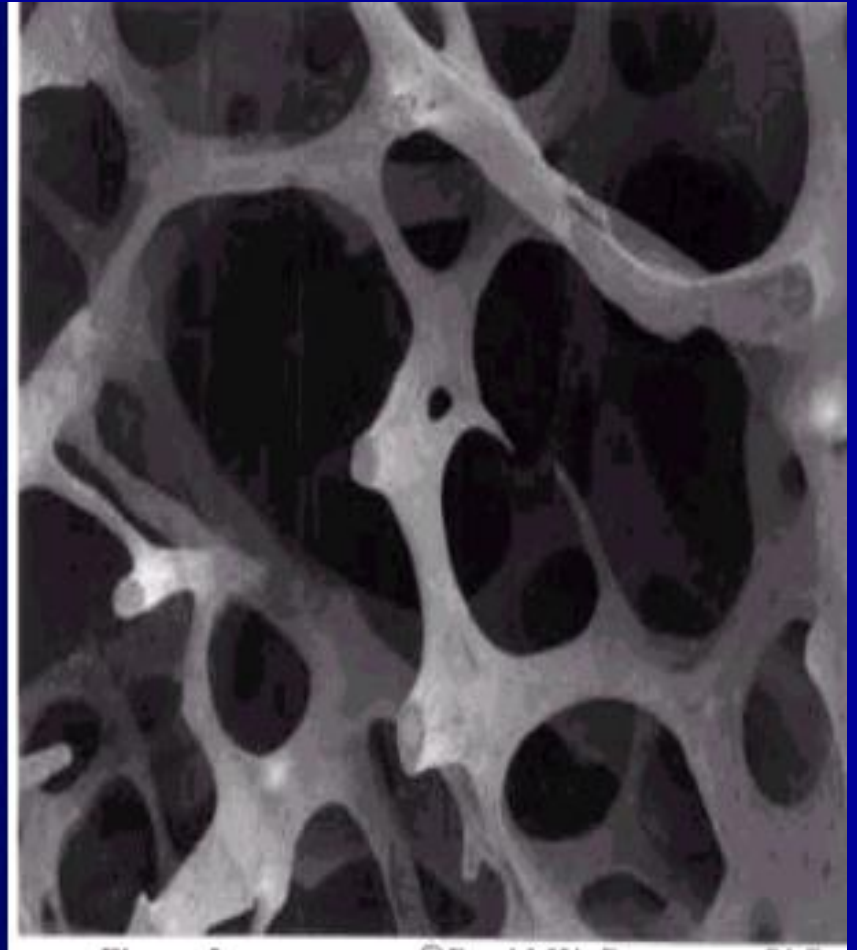
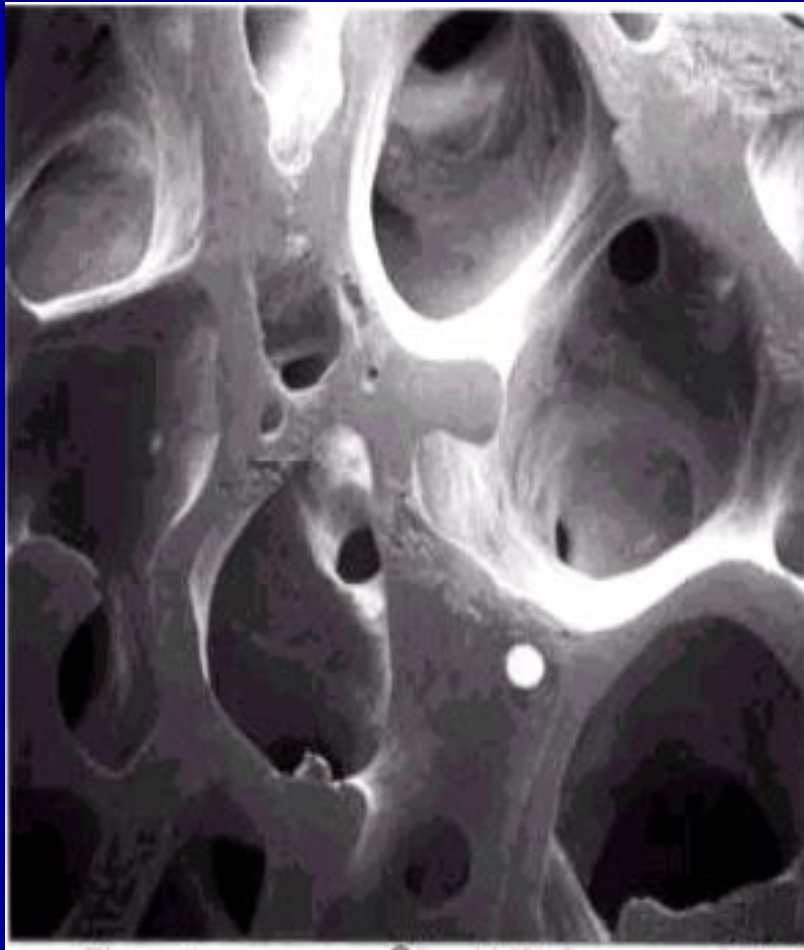


Celiac children 22.7% (61/269) vs 7.1% (41/575)  
( $p < 0.0001$ , OR 4.3; 95% CI 2.7-6.7).  
71% (33/46) reported significant improvement on  
gluten-free diet, ( $p = 0.0003$ )

# Common manifestations

- Iron deficiency anemia
- Osteoporosis

# Normal bone versus osteoporotic bone



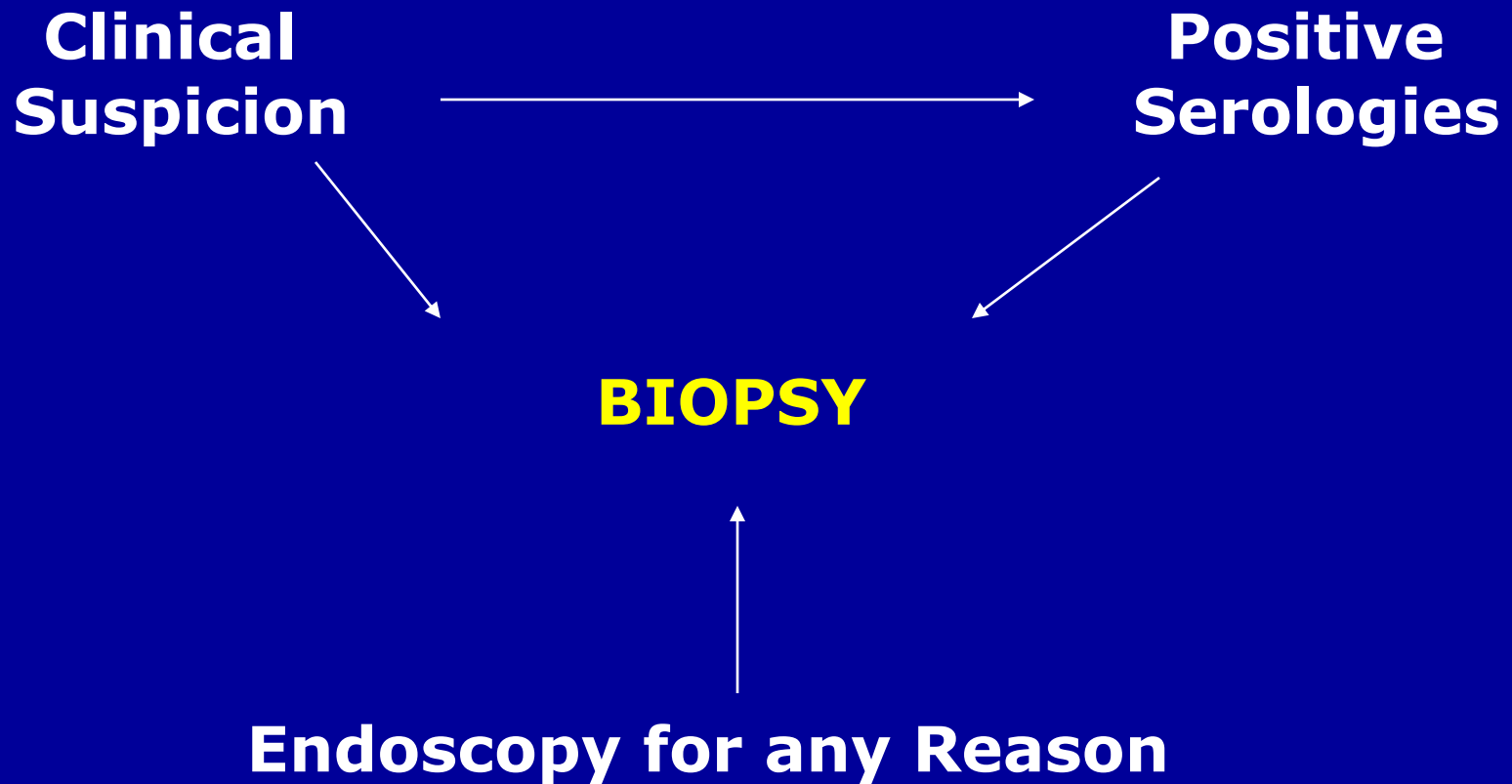
# OSTEOPOROSIS

- Reduced bone density is common
- Increased fracture risk
- Osteoporosis Improves on gluten-free diet
- Consideration of the need for drug therapy
  - not necessary
  - ?dangerous

# NEUROLOGICAL MANIFESTATIONS

- Peripheral neuropathy (small fiber)
- Ataxia
- Seizures
  
- Dementia
  
- Exclusive of vitamin (B12, 6, 1, E) and copper deficiency and vitamin B6 toxicity

# DIAGNOSIS OF CELIAC DISEASE



# SEROLOGIC TESTS IN CELIAC DISEASE

- Antigliadin antibodies IgA, IgG      NOT USED ANYMORE
- Deamidated gliadin peptide (**DGP**) antibodies
- Endomysial antibodies (EMA) IgA
- Tissue transglutaminase antibody (**tTG**) IgA
- Total serum IgA
  
- **BEST COMBO – tTG IgA + DGP**

# WHY BIOPSY?

- Currently the diagnosis requires villous atrophy
- Why not?
- Life long diagnosis requiring an expensive and restrictive diet
- Some people may have + blood tests and not as yet have villous atrophy
- Definition is changing

# BURDEN OF DISEASE IN (DIAGNOSED) CELIAC DISEASE

- Autoimmune diseases  
3-10X the general population

# AUTOIMMUNE DISEASES

IDDM, Sjogren's syndrome

Liver disease (PBC, CAH)

Thyroid disease

Neurologic (neuropathy, epilepsy, ataxia)

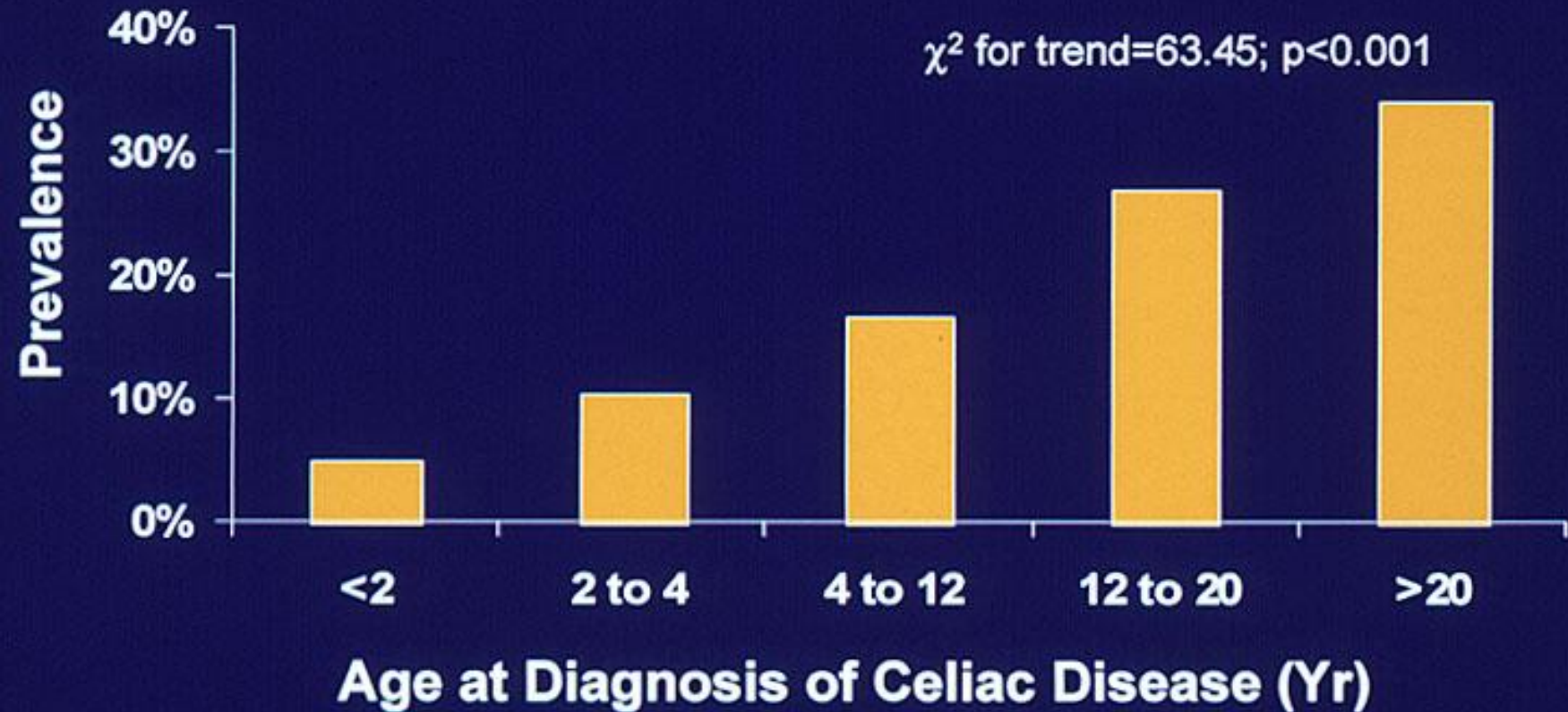
IgA nephropathy, Macroamylasemia

Cardiomyopathy, Addison's disease

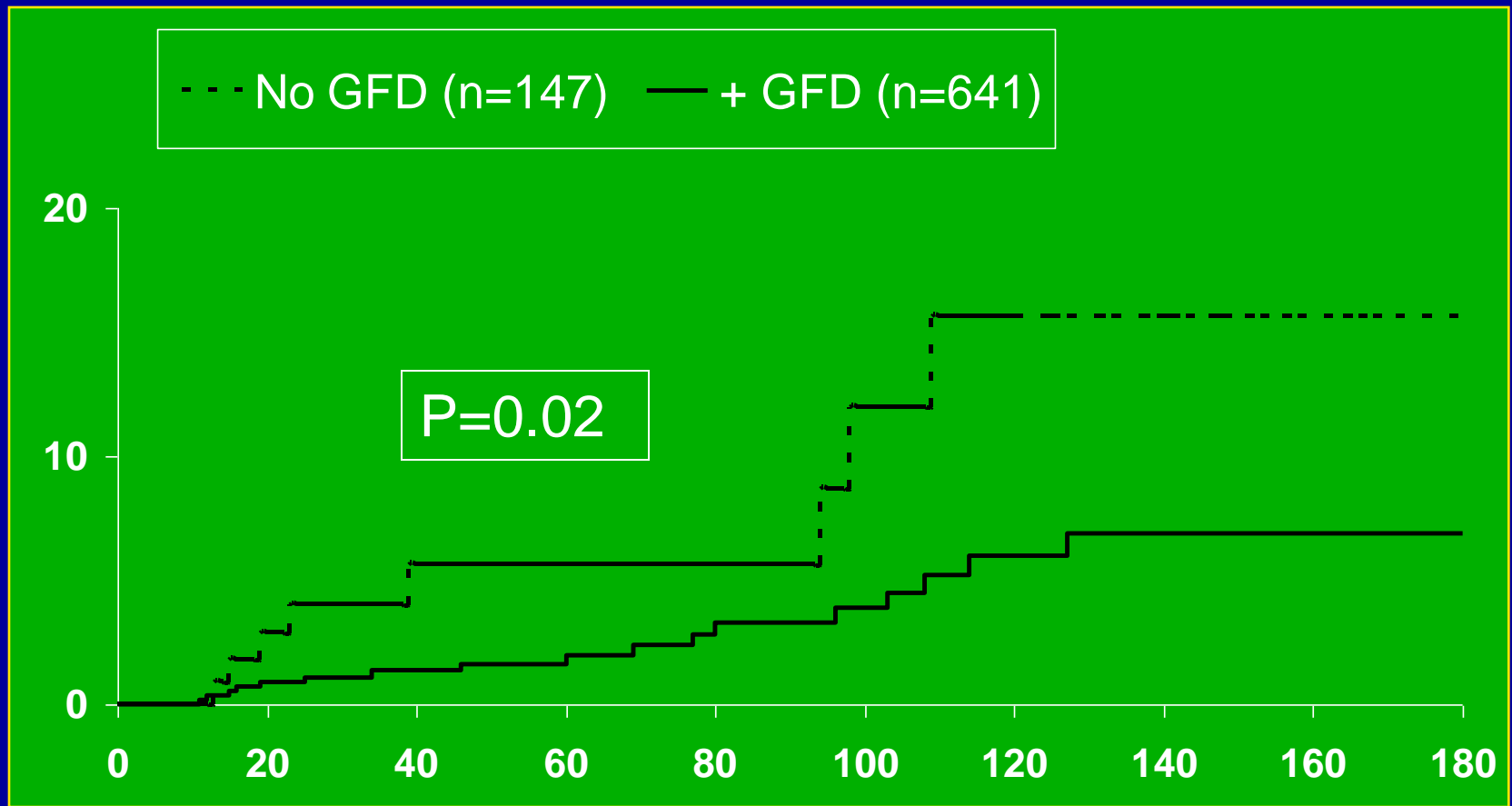
Alopecia, viteligo

Chronic autoimmune urticaria

# Prevalence of Autoimmune Disease in Celiac Disease



**% patients with auto-immune disease**



**P=0.02**

**months after diagnosis of celiac disease**

no. at risk :

0 GFD	147
+ GFD	641

49
279

23
118

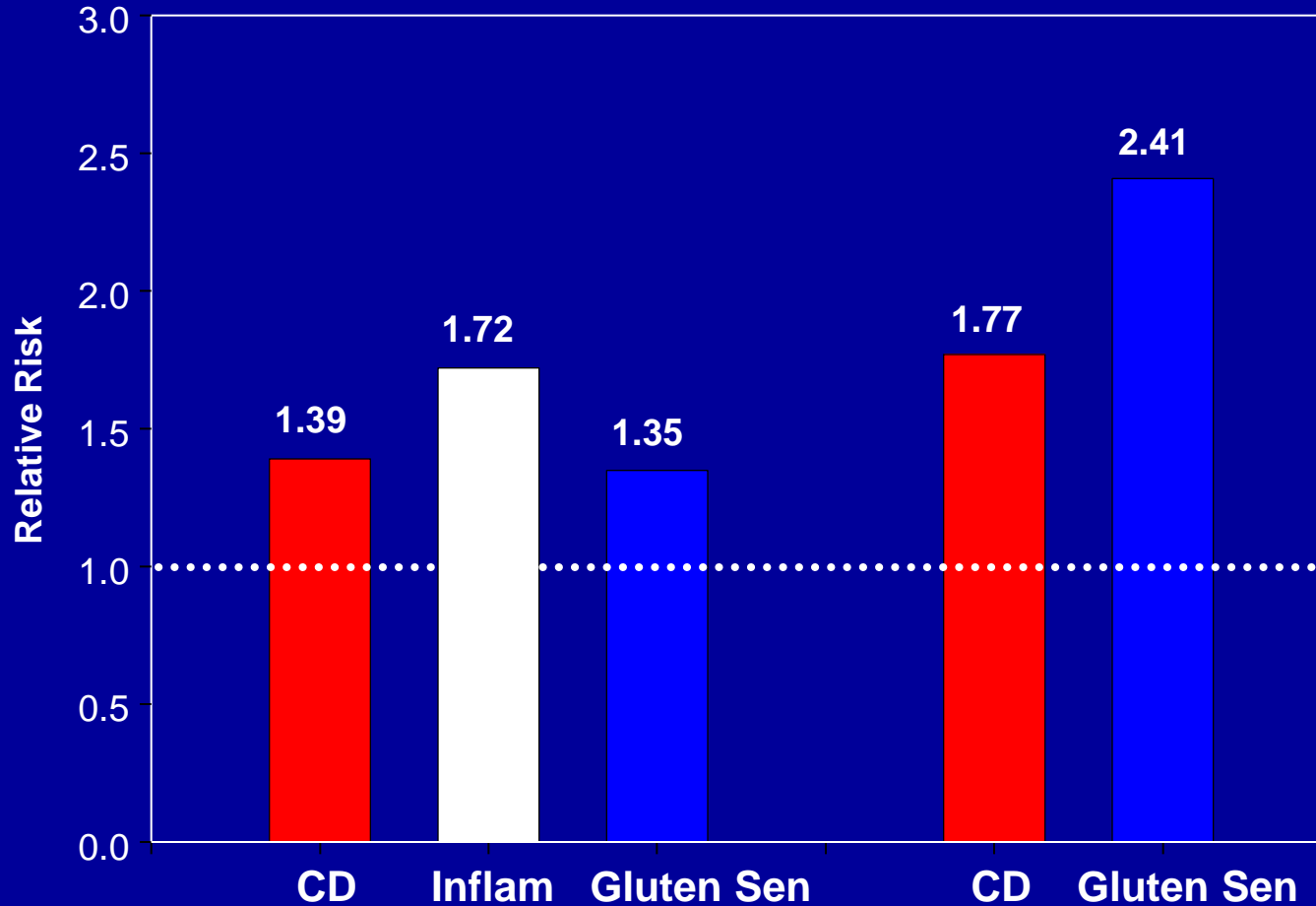
10
57

**Cosnes et al, CGH 2008**

# AUTOIMMUNE DISEASES

- Early diagnosis (< age 20 yrs) reduces risk of developing autoimmune diseases
- Adherence to GFD reduces the development of autoimmune diseases (does not eliminate the risk – lessens it)

# STANDARDIZED MORTALITY RATES



SWEDEN

JAMA , 2009

N. IRELAND

WJG, 2007

# Causes of Death in People With Celiac Disease Spanning the Pre- and Post-Serology Era: A Population-Based Cohort Study From Derby, UK

Matthew J. Grainge, PhD<sup>1</sup>, Joe West, PhD, MRCP<sup>1,2</sup>, Timothy R. Card, PhD, MRCP<sup>1-3</sup> and Geoffrey K.T. Holmes, MD, PhD, FRCP<sup>4</sup>

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The American Journal of GASTROENTEROLOGY


**Table 2. Observed and expected deaths by disease heading for celiac disease patients diagnosed in Derby, UK**

	Observed	Expected	SMR (95% CI)
<i>Deaths in postdiagnosis period (after 2 years)</i>			
All deaths	142	103.45	1.37 (1.16–1.62)
Cardiovascular (I00–I99)	45	40.02	1.12 (0.82–1.50)
Malignancy (C00–D48)	49	30.44	1.61 (1.19–2.13)
Accidents/suicide (S00–Y98)	5	3.02	1.65 (0.54–3.86)
Respiratory (J00–J99)	21	13.37	1.57 (0.97–2.40)
Digestive (K00–K93)	10	4.57	2.19 (1.05–4.02)
<i>Deaths in peridiagnosis period (within 2 years)</i>			
All deaths	32	24.53	1.31 (0.89–1.84)
Cardiovascular (I00–I99)	4	9.61	0.42 (0.11–1.07)
Malignancy (C00–D48)	18	7.41	2.43 (1.44–3.84)
Accidents/suicide (S00–Y98)	0	0.68	0.00 (0.00–5.39)
Respiratory (J00–J99)	2	3.24	0.62 (0.07–2.23)
Digestive (K00–K93)	4	1.05	3.81 (1.04–9.75)

CI, confidence interval; SMR standardized mortality ratio.

# MORTALITY DECREASES WITH TIME AFTER DIAGNOSIS

Years since diagnosis	Total (n = 653)		
	Observed deaths	Expected deaths	O:E
1-2	16	3.89	4.1 <sup>a</sup>
3-4	12	3.80	3.2 <sup>b</sup>
5-9	26	11.66	2.2 <sup>a</sup>
10-14	28	18.33	1.5
15+	19	12.45	1.5
Total	115	61.78	1.9
95% CI	—	—	1.5-2.2



GLUTEN -FREE DIET IS PROTECTIVE

# REASON FOR INCREASED MORTALITY

- Not clear
- Unclear whether
  - Degree of adherence to the diet
  - Persistence of villous atrophy
- Is there an inherent risk, despite being on the diet?

# ***MANAGEMENT - EARLY AND LATE STAGES***

Peter HR Green MD

# POST DIAGNOSIS

- Is the diagnosis correct?
- Were the right tests done? (stool, saliva, gene tests, IgG food sensitivity tests)
- What blood tests?
- Biopsy?
- If unsure, equivocal get another opinion

# EARLY MANAGEMENT

- VITAMIN LEVELS

B12, folate, vitamin D

- MINERAL LEVELS

Iron, calcium

PTH (parathyroid hormone)

copper and zinc

- BONE DENSITY

# EARLY MANAGEMENT

- Gluten free multivitamin with regular daily requirements
- Calcium (citrate in split dosage)
- Vitamin D guided by levels
- Other supplements as guided by levels
- Avoid other OTC supplements (probiotics)

# MANAGEMENT

## GLUTEN-FREE DIET

**Sources** Local support groups  
National support groups  
(CDF, GIG, CSA/USA)

**Dietitian**

**Internet**

**Pitfalls** restaurant foods, preprepared foods,  
fast foods, communion wafers,  
medications

# GLUTEN-FREE DIET

- Be aware of the limitations
- Not a healthy diet
  - low in fiber
  - low in B vitamins
  - low in iron
  - high in fat, calories
- Don't avoid dairy products unnecessarily
- DIET can be healthy if guided by an experienced dietitian

- Worries
  - weight gain
  - elevated cholesterol
- Our studies show that the major factor is being followed by an experienced nutritionist
- **LET THE REFERRING DOCTOR KNOW HOW GOOD HIS NUTRITIONIST REALLY IS**

# FOLLOW UP CARE

- THOSE WITH CELIAC DISEASE NEED SPECIFIC FOLLOW UP MEDICAL AND NUTRITIONAL CARE!!
- Inadequacies of the GF diet
- Risk of associated diseases
- Interval testing (patients and families)
- We offer screening of relatives and advice re attempting to reduce the risk in newly born children

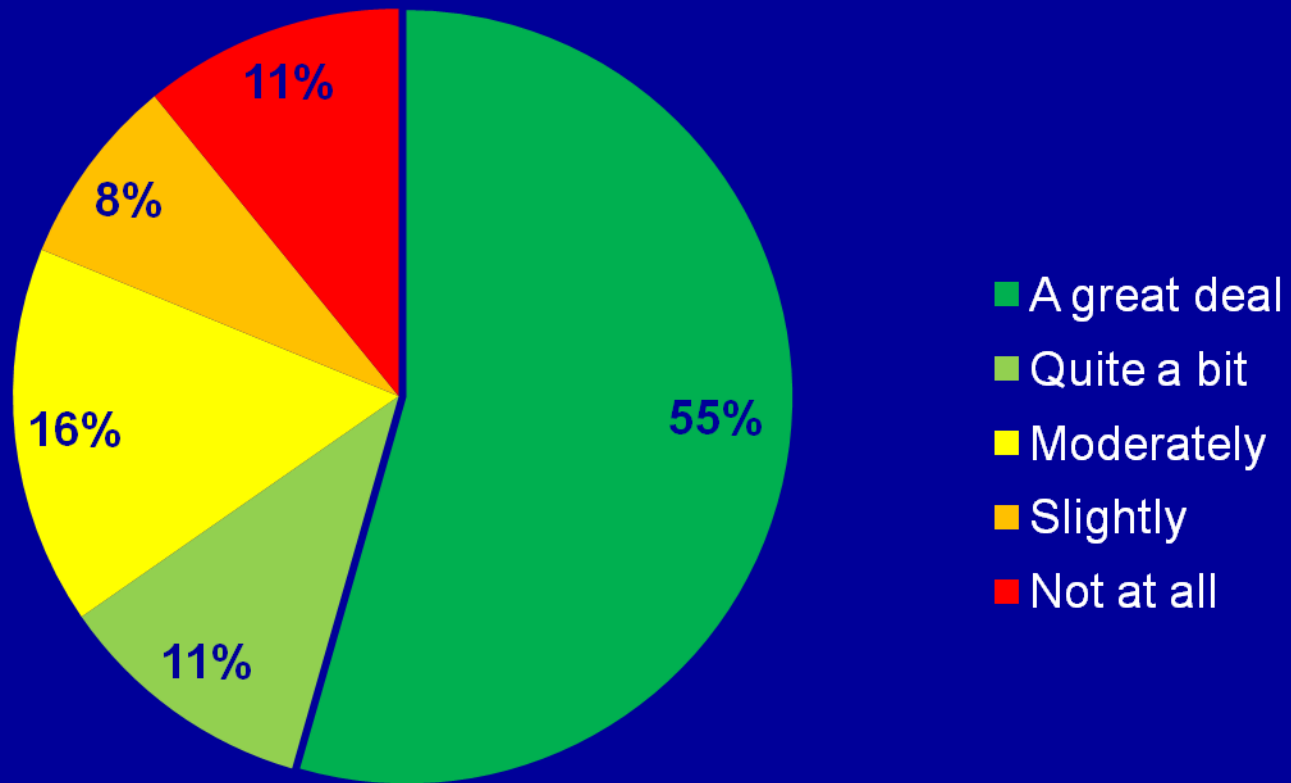
# CELIAC HEALTH QUESTIONNAIRE

“I would take a medicine to treat celiac disease, if available”

C Tennyson, S Simpson, SK Lewis,  
B Lebwohl, PH Green

# INTEREST IN A MEDICATION

Biopsy Proven CD (n=339)



# CONCLUSIONS

- High rate of wanting a medication (if available)
- Older patients and males most interested
- Those that eat out, consider cost an important issue and that are not satisfied with weight
- Those with a lower celiac specific QOL

# POORLY RESPONSIVE PATIENTS

- Wrong diagnosis
- Gluten ingestion
- Microscopic colitis
- Bacterial overgrowth
- Fructose >> lactose intolerance
- (other food sensitivities)
- Pancreatic insufficiency
- IBS
- Refractory celiac disease

# FOLLOW UP

- PHYSICAL EXAM

is my thyroid ok?

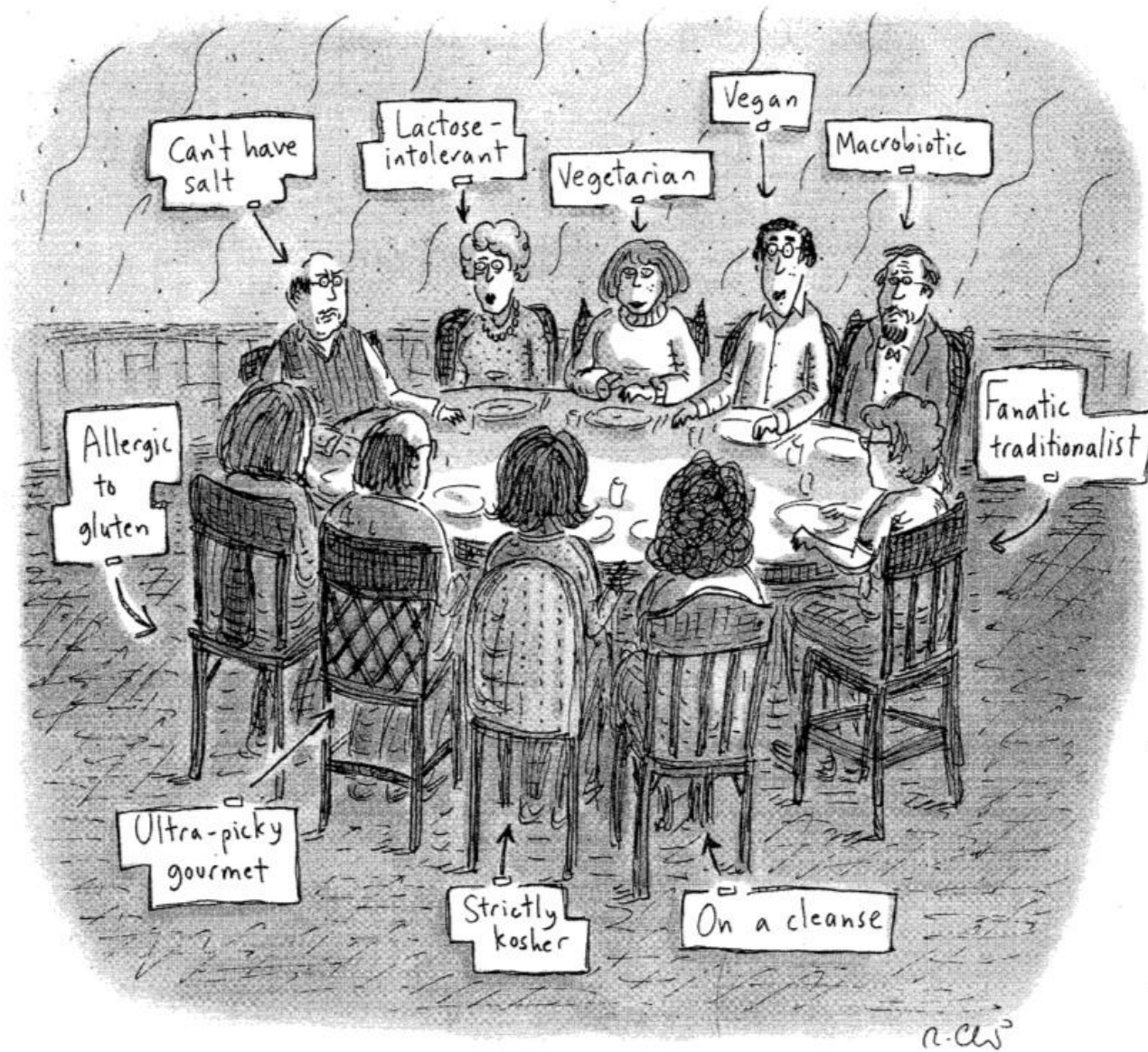
is there blood in my stool?

recent or upcoming colonoscopy is not a substitute for rectal exam and testing for occult blood

# FOLLOW UP

- SEROLOGIC TESTS
- ROUTINE      CBC, chem profile, Thyroid,  
                    iron, vit B12  
                    Zinc and copper levels
- SPECIAL PROBLEMS  
    Fatigue – serum carnitine  
    Neurological symptoms  
    (copper, vitamin B12, E, xs B6)

# THE LAST THANKSGIVING



# SUMMARY

- Gluten related disorders are common
- Celiac disease is important
- Patients need a correct diagnosis
- Diagnosis is easy
- Difficulty appears to be physicians thinking of it!!

Unmasking One of the Most Under-Diagnosed  
Autoimmune Diseases

# CELIAC DISEASE

A HIDDEN EPIDEMIC

- End your medical odyssey and get the right diagnosis
- Treat symptoms and complications
- Get gluten out of your diet –  
and feel better

IS THE  
FOOD YOU EAT  
MAKING YOU  
SICK?

**Peter H.R. Green, M.D.**

Director of the Celiac Disease Center at Columbia University

**and Rory Jones**

**STRICTLY NOT FOR DUMMIES!!!!!!!!!!!!**