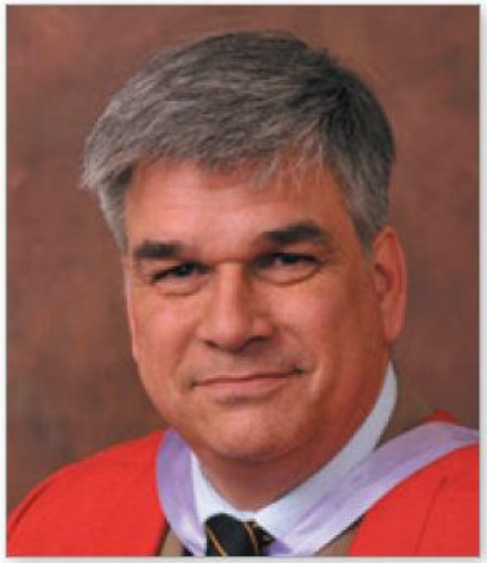


Professor Michael Schultz

Professor

Gastroenterologist and

Head of Department Dunedin School of Medicine

Saturday, August 10, 2019

(Plenary)

16:30 - 16:50 Update on Coeliac Disease - Changes to the ESPGHAN Guidelines

Update on Coeliac Disease
Changes to the ESPGHAN Guidelines

Michael Schultz

University of Otago
Te Whare Wānanga o Otāgo
New Zealand

Southern District Health Board

Background

European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Guidelines for the Diagnosis of Coeliac Disease

*S. Husby, †S. Koletzko, ‡I.R. Korponay-Szabó, §M.L. Mearin, ||A. Phillips, ¶R. Shamir, #R. Troncone, **K. Giersiepen, ††D. Branski, ‡‡C. Catassi, §§M. Lelgeman, ||||M. Mäki, ¶¶C. Ribes-Koninckx, ###A. Ventura, and ****K.P. Zimmer, for the ESPGHAN Working Group on Coeliac Disease Diagnosis, on behalf of the ESPGHAN Gastroenterology Committee

(*JPGN* 2012;54: 136–160) - new guidelines in preparation

UNITED EUROPEAN GASTROENTEROLOGY ueg journal SAGE

European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders

Abdulbaqi Al-Toma,[1] Umberto Volta,[2] Renata Auricchio,[3,*] Gemma Castillejo,[4,*] David S Sanders,[5] Christophe Cellier,[6] Chris J Mulder,[7] and Knut E A Lundin[8,9]

United European Gastroenterol J. 2019 Jun; 7(5): 583–613.

World Gastroenterology Organisation Global Guidelines

Celiac Disease

July 2016

Review Team

Julio C. Bai (Chair, Argentina), Carolina Ciacci (Co-chair, Italy), Gino Roberto Corazza (Italy), Michael Fried (Switzerland), Carolina Olano (Uruguay), Mohammad Rostami-Nejad (Iran), Andrea González (Argentina), Peter Green (USA), Javier Gutierrez-Achury (UK/Netherlands), Michael Schultz (New Zealand), Elena Verdú (Canada), Kassem Barada (Lebanon), Peter Gibson (Australia), Sibylle Koletzko (Germany), Thierry Coton (France), Chris Mulder (Netherlands), Govind Makharia (India), Anton LeMair (Netherlands)

Case

19 year old student is complaining of a subtle but annoying change in bowel habit. Previously just once per day, now several times. Also variable and sometimes not at all.
Complains also of tiredness.

Moved to Dunedin 6 months ago to study.

What blood test would you request?

Case

anti TTG IgA 137 Units HH (0 - 20)

Comment

Comment

Validated by PJ, MLSci

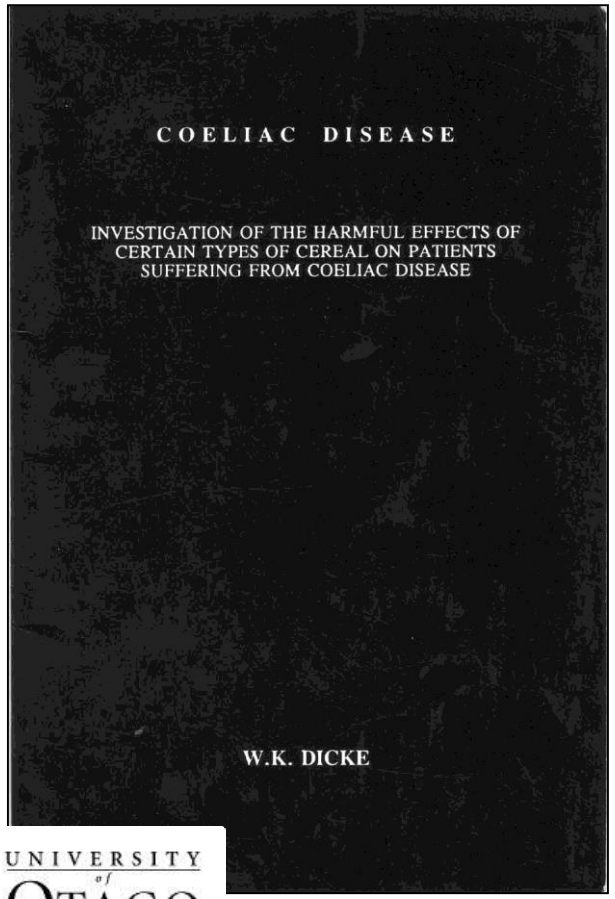
What now?

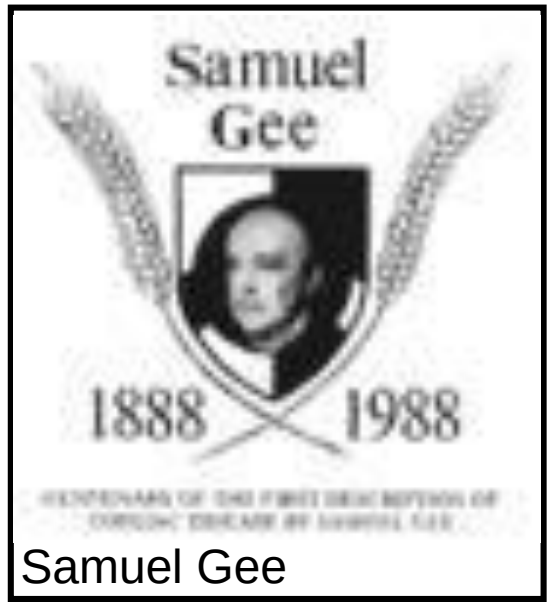
- ✓ Commence on a gluten-free diet?
- ✓ Refer for a gastroscopy with duodenal biopsies?
- ✓ Request additional blood tests?

First mentioned by Samuel Gee in 1887:

→ diarrhea, faintness and growth retardation

→ possible relation to food intake





Samuel Gee

Willem Karel Dicke in 1950:

→ proposed wheat was to be the cause of celiac disease.

→ during World War II (when wheat grains were scarce in Holland), children with CD who had otherwise failed to thrive, improved on a wheat-poor diet.

Definition:

Coeliac disease is caused by a reaction to gliadin

wheat

↓

gluteins/gliadin

several fragments (α-gliadin)

rye

↓

hordeins

barley

↓

secalins

oats

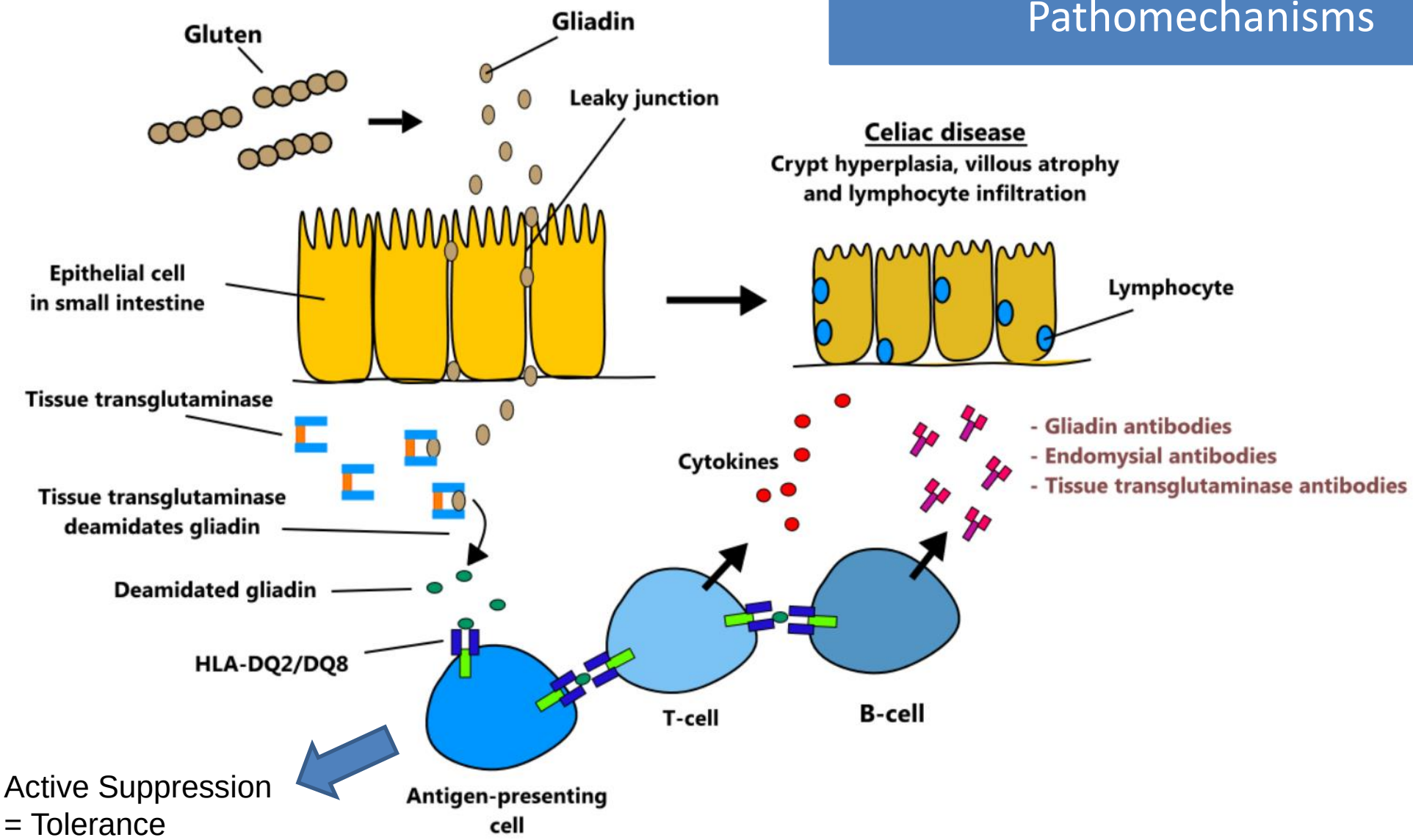
?

Contamination

Cross-reactivity

Avenin

Pathomechanisms



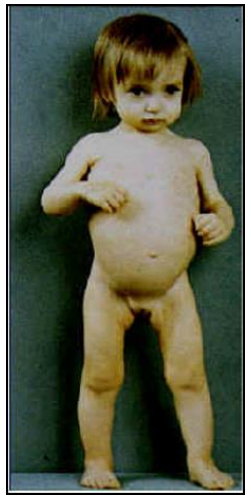
Active Suppression
= Tolerance

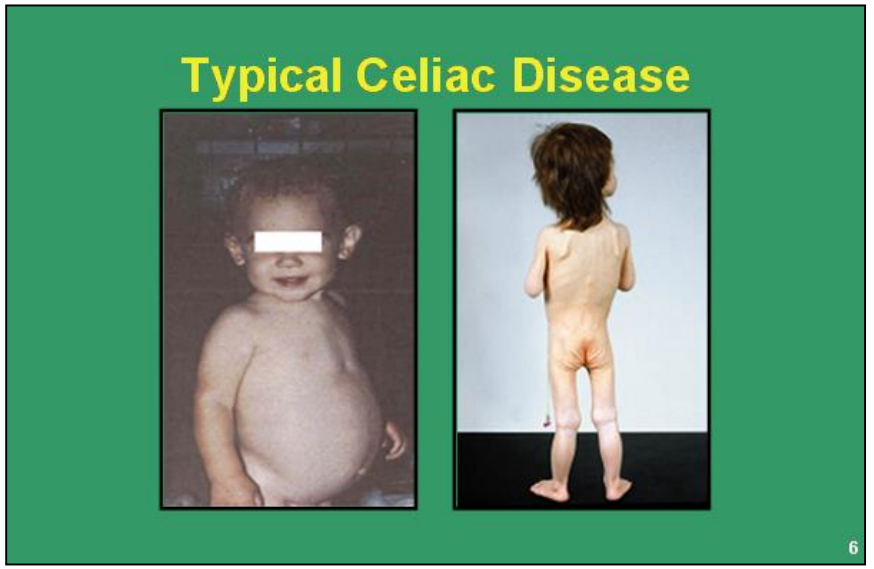
Symptoms

...in young children (6-24 mths)

(following supplementary feeding)

- distended abdomen
- unhappiness
- lack of appetite
- nausea
- vomiting
- explosive, offensive diarrhea
- constipation
- failure to thrive
- growth retardation



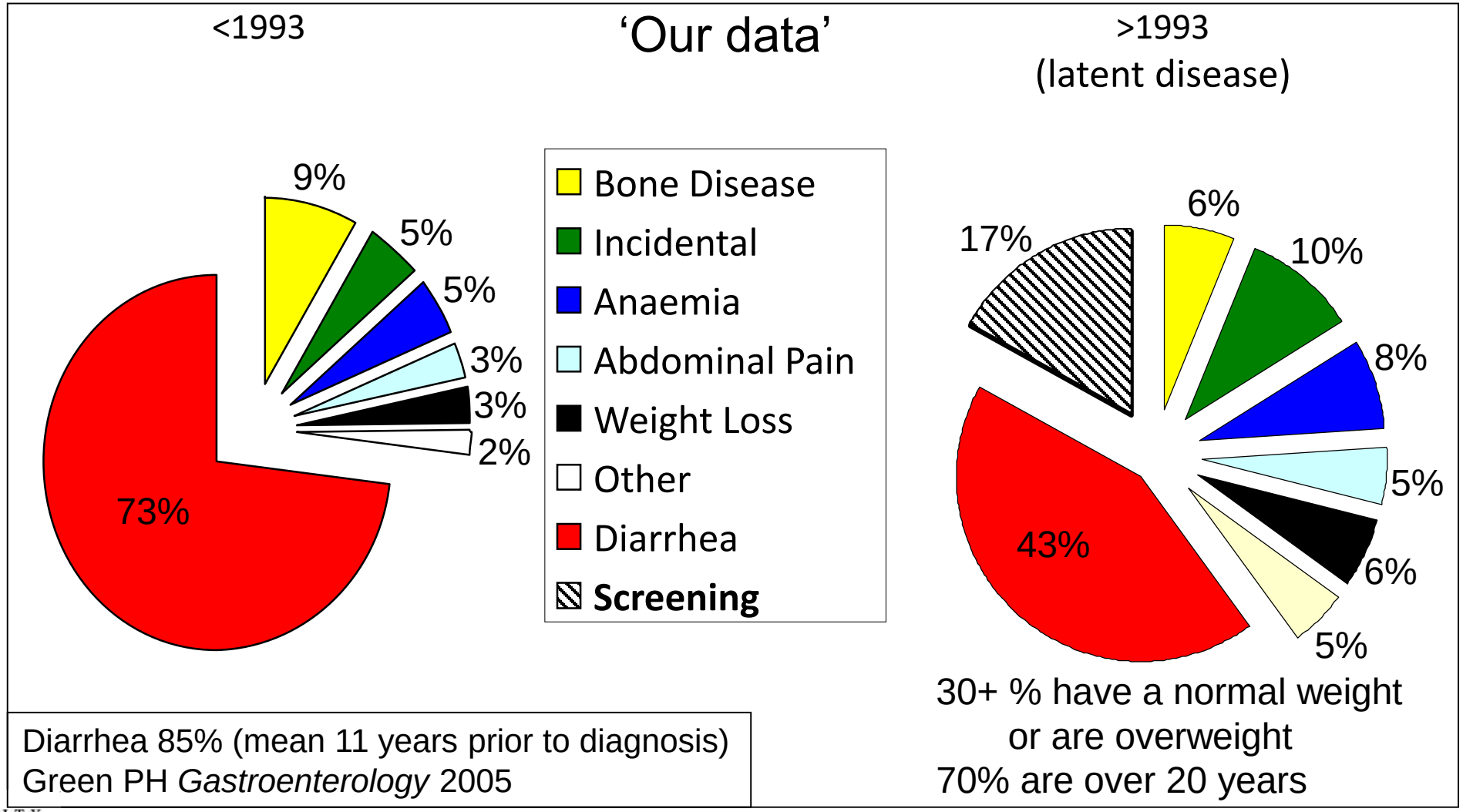


…in older children (5-7 yrs)

- symptoms of malabsorption
  - ➢ growth retardation
  - ➢ dental enamel defects
- relapsing abdominal complaints

Classic disease – diarrhea predominant
Silent disease

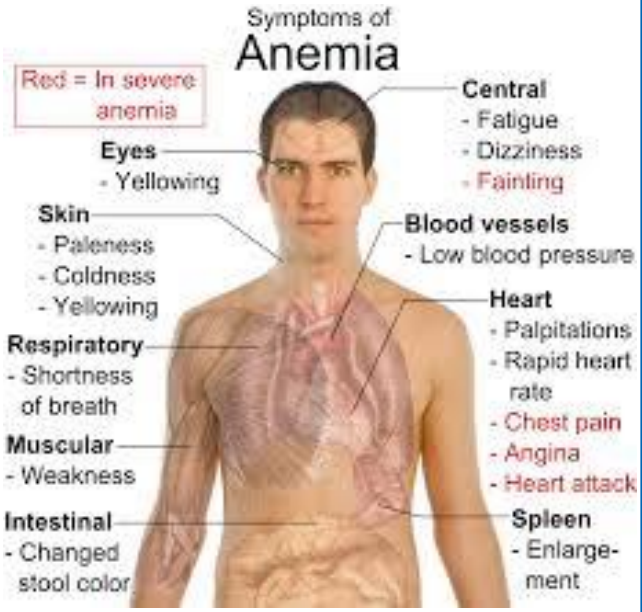
Symptoms

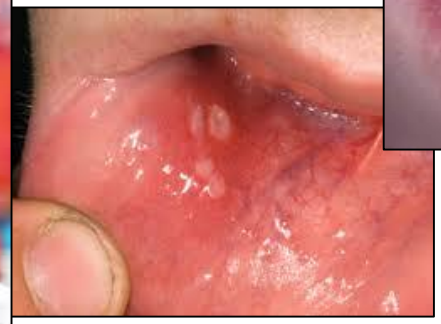


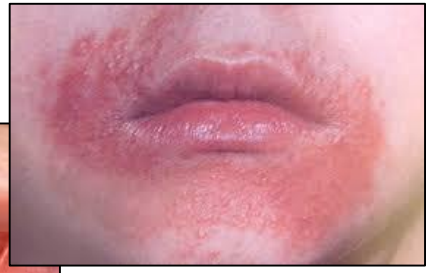
Diarrhea 85% (mean 11 years prior to diagnosis)
Green PH *Gastroenterology* 2005

Diagnosis

- iron deficiency anaemia (prevalence of 3-12%)
- osteoporosis and osteopenia (prevalence approximately 5%)
- diarrhea
- positive family history (in monocygotic twins ~70-75%, FDR 5-10%, 25% FH)
- thyroid diseases (autoimmune thyroiditis, prevalence 6-8%)
- type I diabetes (prevalence of 1-7%)
- dermatitis herpetiformis Duhring (prevalence 2-3%)
- aphtous oral lesions
- Down syndrome
- various neurological disorders (calcification of the brain)
  - ataxia of the cerebellum
  - peripheral neuropathy → 8%
  - epilepsy?
- Autoimmune disorders in 30% (3% in gen pop)







Diagnosis

anti TTG IgA 137 Units HH (0 - 20)

Comment

Comment

Validated by PJ, MLSci

What now?

- ✓ Commence on a gluten-free diet?
- ✓ Refer for a gastroscopy with duodenal biopsies?
- ✓ Request additional blood tests?

Additional information:

- Patient is horrified by the thought of a gastroscopy
- She has heard that perforation is possible
- She demands general anaesthesia

Case

anti TTG IgA	> 150 Units	HH	(0 - 20)
Endomysial Ab	POSITIVE	A	
Deamidated Gliadin Peptide IgG	29 units	HH	(0 - 20)
Comment			
Comment			

Comment
These results support a diagnosis of coeliac disease.

Comment

Validated by PJ, MLSci

Biopsy?

Diagnosis

Sensitivity and specificity of different serological tests.

Antigen	Antibody type	Sensitivity, % (range)	Specificity, % (range)	
Gliadin	IgA	85 (57–100)	90 (47–94)	
	IgG	80 (42–100)	80 (50–94)	
Endomysium	IgA	95 (86–100)	99 (97–100)	Most specific
	IgG	80 (70–90)	97 (95–100)	
Tissue transglutaminase	IgA	98 (78–100)	98 (90–100)	Most sensitive
	IgG	70 (45–95)	95 (94–100)	Best for IgA deficiency
Deamidated gliadin peptide	IgA	88 (74–100)	90 (80–95)	
	IgG	80 (70–95)	98 (95–100)	

Correlation between positive IgA-tTG and EMA results

tTG range	EMA done	EMA positive	EMA percentage positivity
≥150	647	646	99.9%
100 - 149	251	244	97.2%
60 - 99	304	245	80.6%
50 – 59	118	53	44.9%
40 – 49	238	58	24.4%
30 – 39	317	58	18.3%
21 – 29	530	24	4.5%

Unpublished data courtesy of Dr Kristin Kenrick

Biopsy outcomes versus IgA-tTG level

IgA-tTG	Biopsy done	Biopsy CD positive	Positivity Rate	Biopsy normal
≥150	411	400	**97.8%**	6/411 (1.5%)
100 - 149	138	122	**88.4%**	15/138 (10.9%)
60 - 99	143	119	**83.2%**	18/143 (12.6%)
21 - 59	369	196	**53.1%**	152/369 (41.2%)

Unpublished data courtesy of Dr Kristin Kenrick

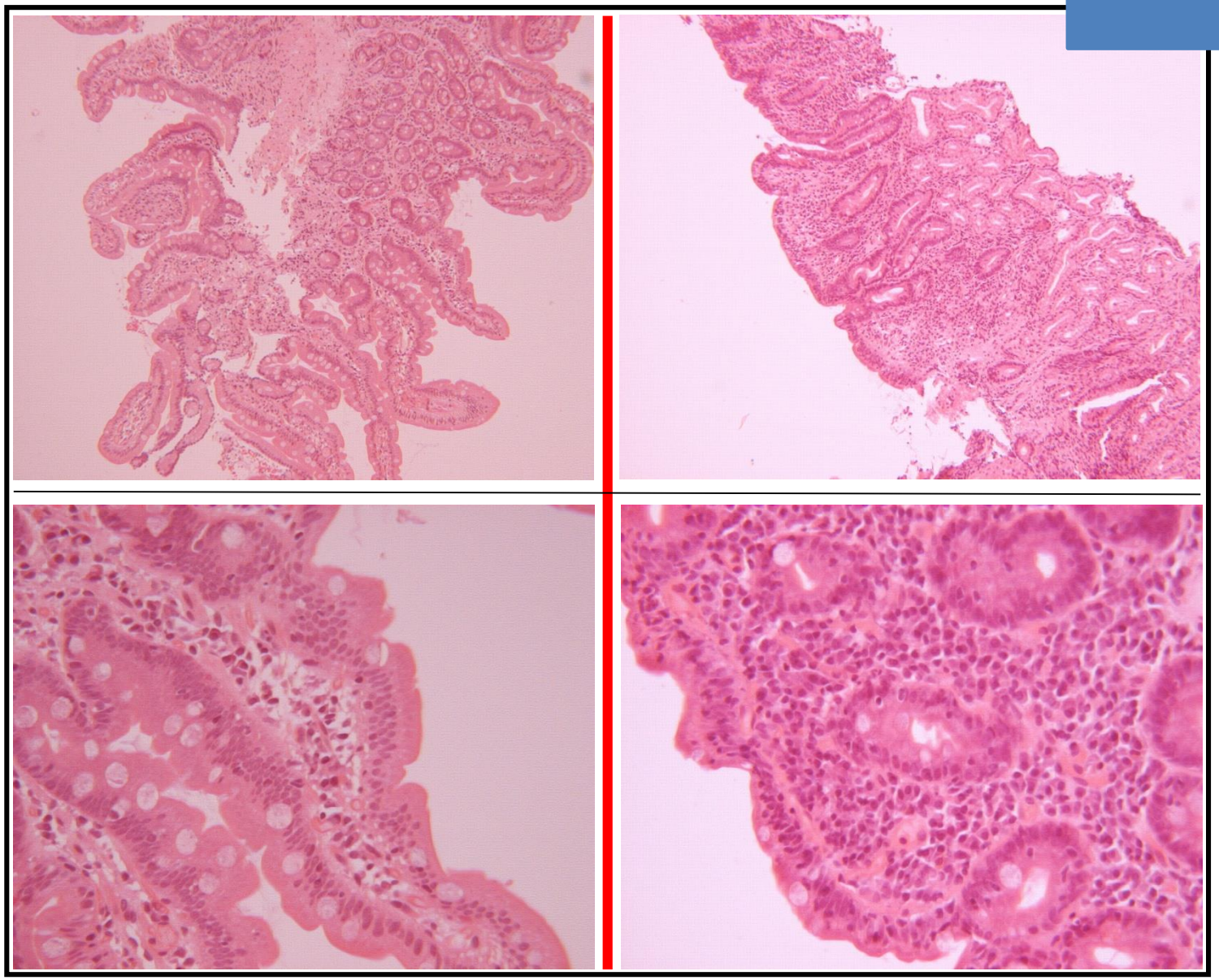
Rates of biopsy per IgA-tTG level

Year	Biopsy rate IgA-tTG > 150	Biopsy rate IgA-tTG 100 - 149	Biopsy rate IgA-tTG 60 - 99	Biopsy rate IgA-tTG 21 - 59
2007	73.3%	57.9%	50%	24.6%
2008	68.9%	90.5%	77.8%	42.9%
2009	65.1%	54.5%	50%	41.8%
2010	83%	80%	52.9%	43.3%
2011	81.3%	75%	50%	30%
2012	80.9%	85.7%	66.7%	35.6%
2013	72.7%	47.6%	76.9%	45.2%
2014	73.2%	52.9%	70.4%	51.4%
2015	75.4%	71.4%	77.8%	45.1%

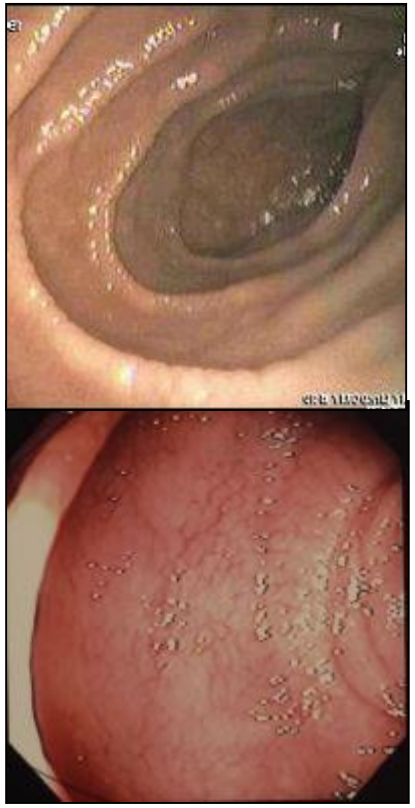
Unpublished data courtesy of Dr Kristin Kenrick

Histology

normal



Coeliac Disease



Southern District Health Board

Causes of histological mimics of CD in seronegative patients.

Differential diagnosis of CD with or without villous atrophy

Normal villous architecture and increased IELs	VA ± increased IELs
Food hypersensitivity (cow's milk, soy, fish, eggs, etc.) Peptic ulcer disease *Helicobacter pylori*-associated gastroduodenitis Drugs (NSAIDs, proton pump inhibitors) Infections (e.g., viral enteritis, *Giardia, Cryptosporidium*) Immune dysregulation (rheumatoid arthritis, Hashimoto's thyroiditis, SLE, multiple sclerosis, autoimmune enteropathy) CVID Graft-versus-host disease (GVHD) Inflammatory bowel disease (IBD) Bacterial overgrowth Blind loop syndrome Microscopic colitis (lymphocytic and collagenous) IBS NCGS	Infections (tropical sprue, *Giardia*, Whipple disease, *Mycobacterium avium* complex, AIDS enteropathy) Collagenous sprue Autoimmune enteropathy CVID GVHD IBD (Crohn disease) Drugs (mycophenolate mofetil, colchicine, olmesartan, losartan) Chemoradiation therapy Immunomodulatory therapy (anti-CTLA4 antibody) Eosinophilic gastroenteritis Bacterial overgrowth Enteropathy-associated T cell lymphoma (EATL) Nutritional deficiency Amyloidosis

Case

SITE:
Duodenum 2nd part

MACROSCOPIC:
The specimen consists of five fragments of pale tissue 4, 3, 3, 2 and 2 mm in diameter. AI/3L (SF)

MICROSCOPIC:
Sections show small intestinal mucosa with normal architecture. There is a mild chronic inflammatory infiltrate within the lamina propria and increased intraepithelial lymphocytes. There is no evidence of villous atrophy, infectious organisms, dysplasia or malignancy. These changes in association with the positive serology are diagnostic of coeliac disease. In addition, both flow cytometry and immunohistochemical stains show a normal intraepithelial T-cell phenotype (CD3, CD8 positive) with no aberrancy seen on flow cytometry.

DIAGNOSIS:
Gluten-sensitive enteropathy (coeliac disease)
T58200
M43000

AUTHORISED: Dr Michael Lau, Consultant Pathologist
michael.lau@sclabs.co.nz
DDI: (03) 4748322

Treatment

Criteria Details - Please enter relevant application criteria:

FORM SA1729 - Application for subsidy

Initial application - all patients from dietitian, relevant specialist or vocationally registered general practitioner

Term: patient's lifetime
Application details:

☐ Gluten enteropathy has been diagnosed by biopsy **or**

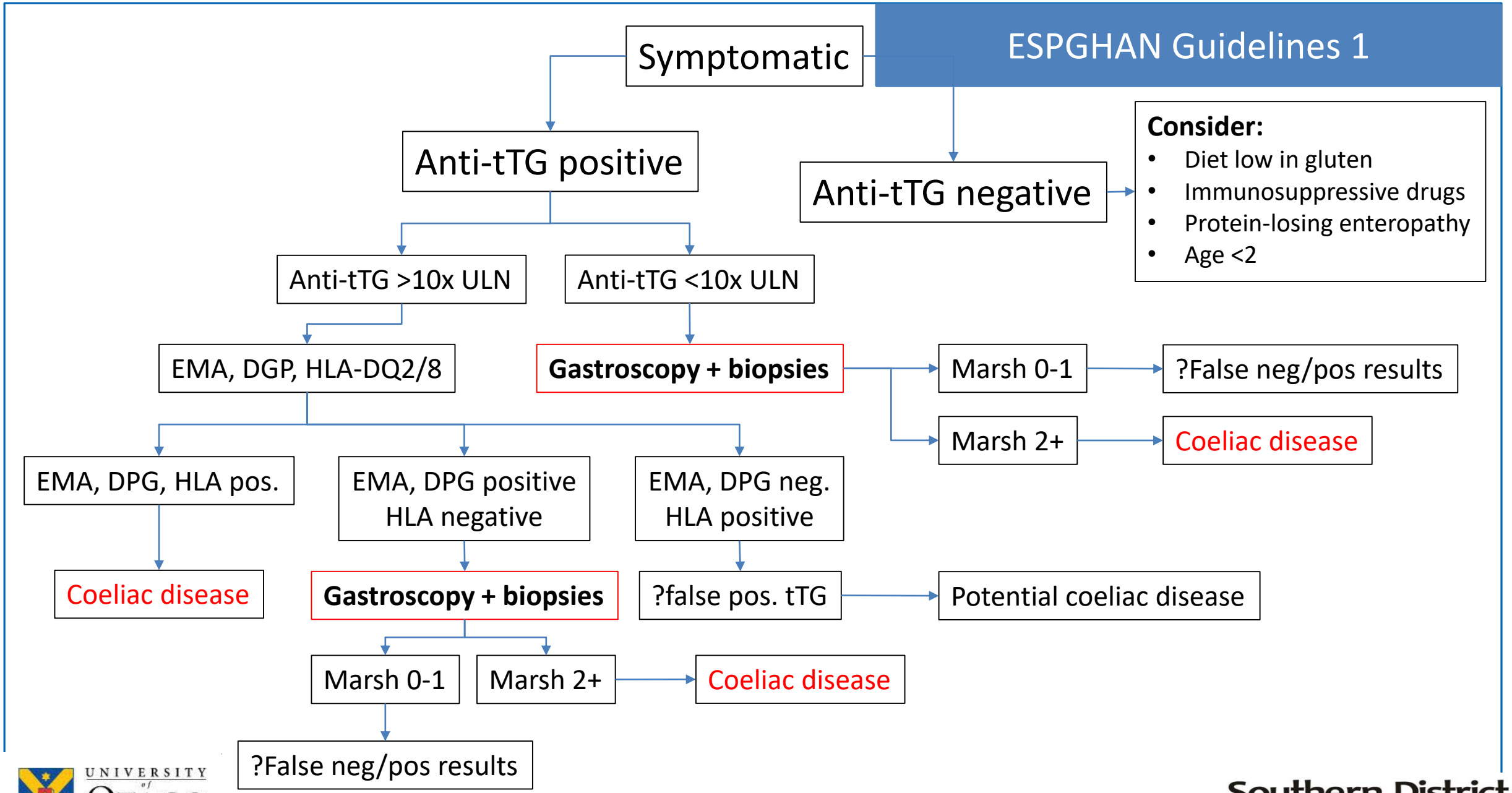
☐ Patient suffers from dermatitis herpetiformis

Initial application - paediatric patients diagnosed by ESPGHAN criteria from paediatric gastroenterologist

Term: patient's lifetime
Application details:

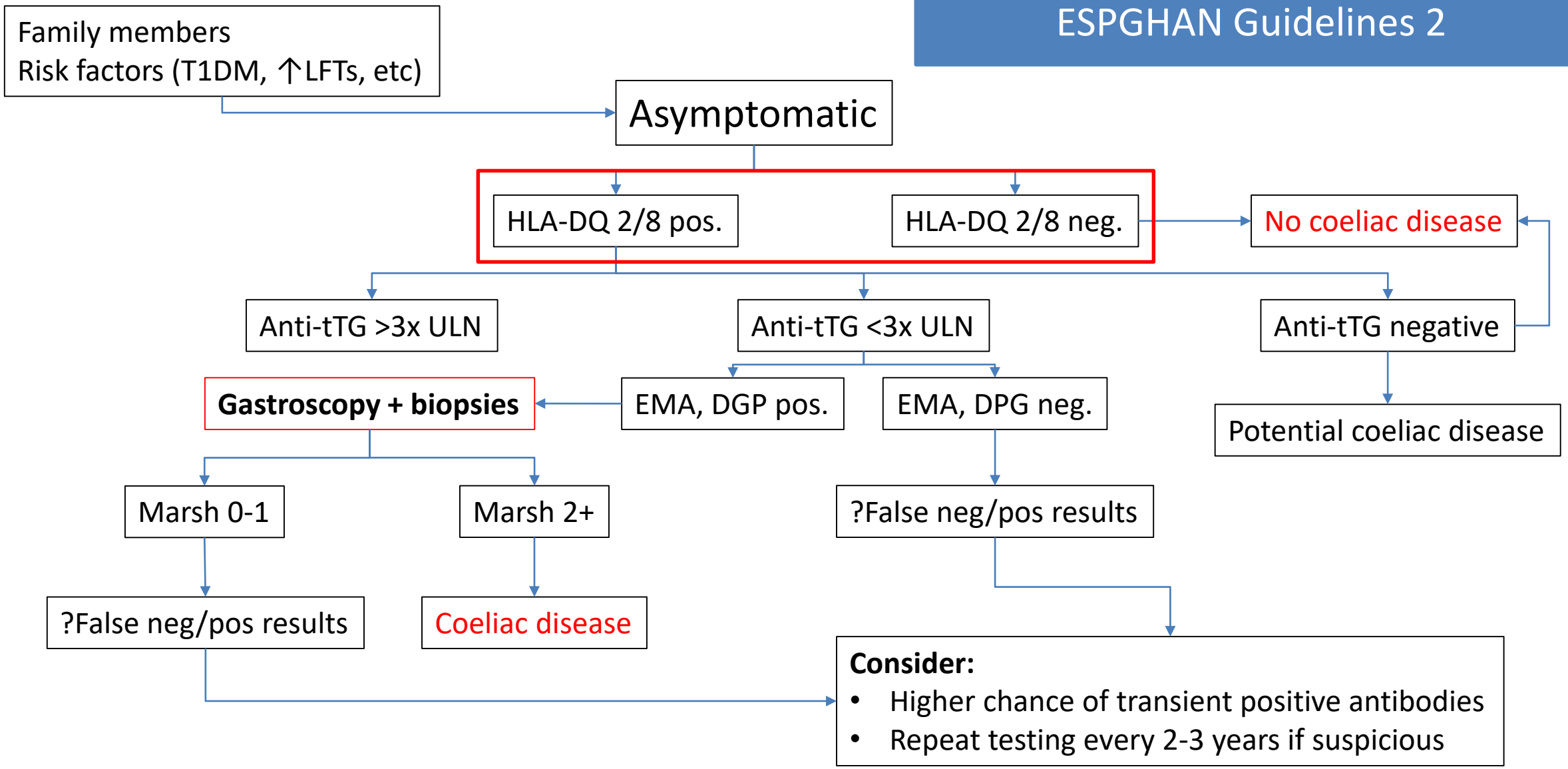
☐ the paediatric patient fulfils ESPGHAN criteria for biopsy free diagnosis of coeliac disease

ESPGHAN Guidelines 1



Neg. serology within 6-12months in 80%

ESPGHAN Guidelines 2



Coeliac disease - Treatment

Gluten-free Diet

live-long + strict !

- beer
- pasta
- breads
- sauces
- processed foods
- …

→ emulgation
→ stabilisation
→ carrier
→ …

Dietary advice
Coeliac support groups
Internet

Serology in 12months
No need to routinely re-biopsy

Coeliac disease - Summary

→ Otago: we should have 1800 – 5400 patients

→ NZ: we should have 40 - 120.000

→ But the MoH only knows of about 6000!

- Remember to test for coeliac disease (active case-finding)
- Duodenal biopsy remains the gold standard
- In children follow the algorithm to avoid gastroscopy