GI CASES

Dr Judy Huang

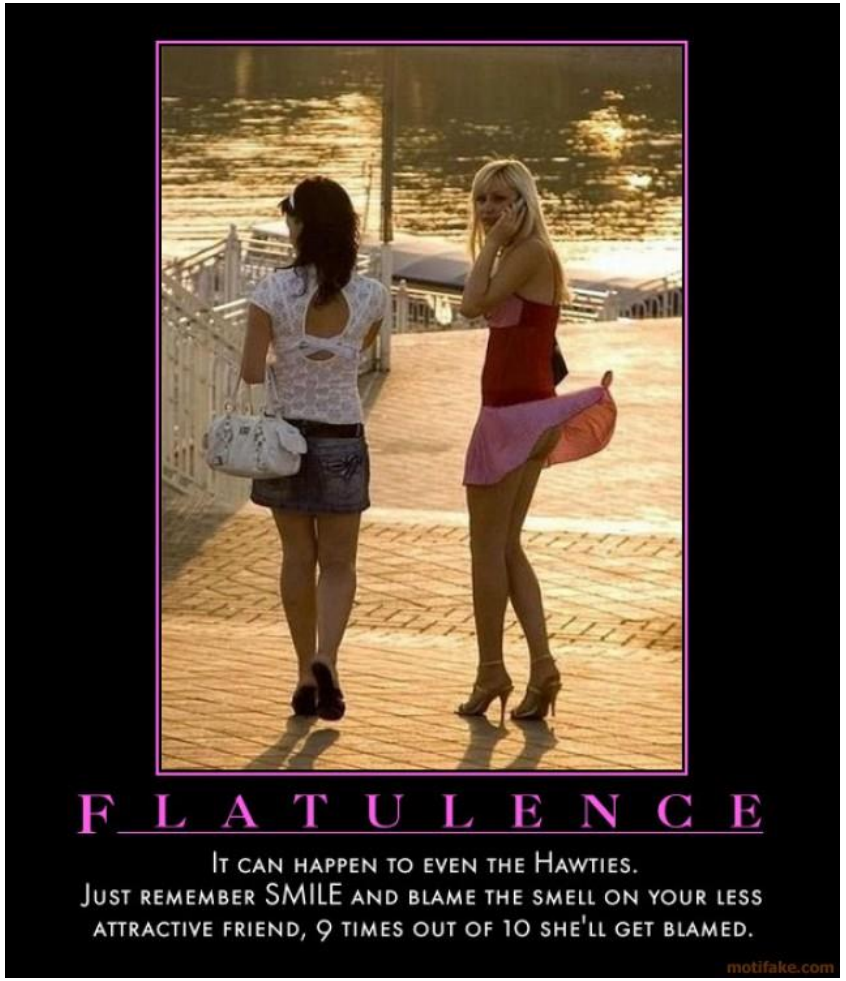
Gastroenterologist

- Diarrhoea
  - Approach and management
- Weight loss
  - Approach and management
- Coeliac disease
- Use of faecal calprotectin: IBD vs IBS

QUESTION

- Upper limit of normal- episodes of flatus per day?

- A 10
- B 15
- C 20
- D 25



CASE 1

- 18 year old Dutch female
- 3 months history of change of bowel habit with urgency
- Diarrhoea

WHAT IS DIARRHOEA?

- 10% of primary care consultation are GI related
  - 5% are diarrhoea related. Usually self limiting or functional
  - 1700 patients/year, approx 85 patients with diarrhoea
- What is normal bowel motion?
- Definition:
  - > 3 loose or watery bowel motions/day *or*
  - Decreased absorption or increased secretion or both *or*
  - > 200mls of stool/day
- Duration:
  - Acute < 14days, Persistent >14days, chronic >30 days

BRISTOL STOOL CHART

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. **Entirely Liquid**

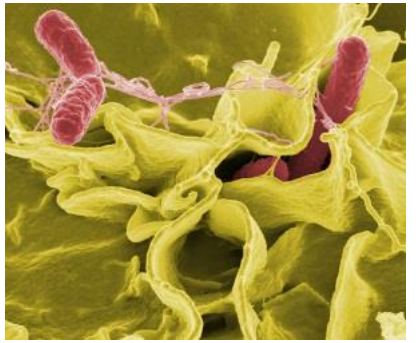
ACUTE DIARRHOEA

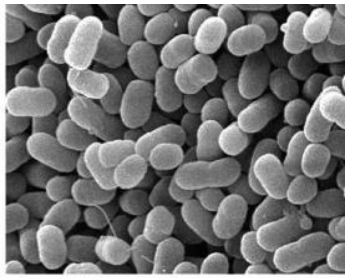
- 80% Infection
  - Faecal – Oral route
  - Viruses, Bacteria, Helminths, Protozoans
- Non Infective
  - Medications, Poorly absorbed sugars, Faecal impaction, Pelvic inflammation
- Most self limiting

Infective	Non Infective
Fever	Afebrile
Pus	No Pus
Blood	No Blood
Travel History	Sporadic without travel history

ACUTE DIARRHOEA

- Bacterial – More Severe
  - E. Coli 0157 (most common)
    - 2 strains 0157 117 (1982 on), 0104 114 (5/2011)
    - No antibiotics - HUS
  - Salmonella
    - Animal faeces, Rx Cotrixmoxazole / Ciprofloxacin
  - Campylobacter
    - Uncooked poultry, 10% bloody, Rx Azithromycin
  - Shigella
    - Fever, chills, cramps; Headache, Rx Azithromycin





ACUTE DIARRHOEA

- Viral – Most Common
  - Calciviruses (Norovirus & related), Rotavirus, Adenovirus, Astrovirus
- Protozoan - Uncommon
  - Cryptosporidia, Giardia, Cyclospora, Entamoeba histolytica
  - Giardia
    - Watery foul smelling greasy stools
    - Rx Tinidazole / Metronidazole
- Females x20 times risk of Listeriosis
  - Fever, systemic unwellness, Pregnancy
- Some conditions Notifiable to MOH

CHRONIC DIARRHOEA

- Cancer
- Inflammation: Crohns, UC
- Malabsorption: coeliac disease, lactose deficiency
- Maldigestion: pancreatic insufficiency
- Functional disease: IBS-D, Post infectious IBS
- Neuroendocrine tumours

Major causes of chronic diarrhea classified by typical stool characteristics

Osmotic diarrhea
Mg, PO4, SO4 ingestion
Carbohydrate malabsorption
Fatty diarrhea
Malabsorption syndromes
Mucosal diseases
Short bowel syndrome
Postresection diarrhea
Small bowel bacterial overgrowth
Mesenteric ischemia
Maldigestion
Pancreatic exocrine insufficiency
Inadequate luminal bile acid
Inflammatory diarrhea
Inflammatory bowel disease
Ulcerative colitis
Crohn's disease
Diverticulitis
Ulcerative jejunoileitis
Infectious diseases
Pseudomembranous colitis
Invasive bacterial infections
Tuberculosis, yersinosis, others
Ulcerating viral infections
Cytomegalovirus
Herpes simplex
Amebiasis/other invasive parasites
Ischemic colitis
Radiation colitis
Neoplasia
Colon cancer
Lymphoma

Secretory diarrhea
Laxative abuse (nonosmotic laxatives)
Post-cholecystectomy (from bile salts)
Congenital syndromes (chloridorrhea)
Bacterial toxins
Ileal bile acid malabsorption
Inflammatory bowel disease
Ulcerative colitis
Crohn's disease
Microscopic (lymphocytic) colitis
Collagenous colitis
Diverticulitis
Vasculitis
Drugs and poisons
Disordered motility
Postvagotomy diarrhea
Postsympathectomy diarrhea
Diabetic autonomic neuropathy
Hyperthyroidism
Irritable bowel syndrome
Neuroendocrine tumors
Gastrinoma
VIPoma
Somatostatinoma
Mastocytosis
Carcinoid syndrome
Medullary carcinoma of thyroid
Neoplasia
Colon carcinoma
Lymphoma
Villous adenoma
Addison's disease
Epidemic secretory (Brainerd) diarrhea
Idiopathic secretory diarrhea

Reprinted with permission from: Fine KD, Schiller LR. AGA technical review on the evaluation and management of chronic diarrhea. Gastroenterology 1999; 116:1464.

RED FLAGS IN GASTROENEROLOGY

General Red Flags

- Unexplained weight loss
- Onset in older patients
- Family history of CRC/IBD
- Severe unremitting symptoms
- Rectal bleeding
- Nocturnal symptoms

IBD Red Flags

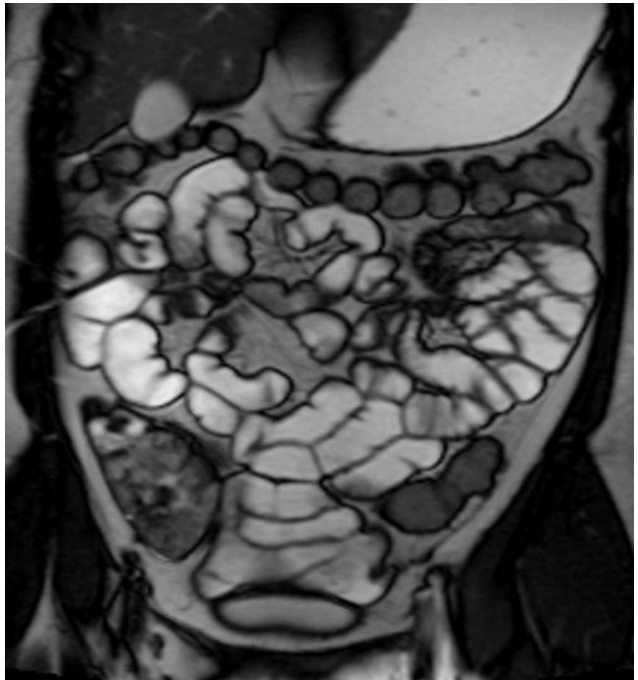
- Mouth ulcers
- Peri-anal disease
- Relationship of onset to smoking
- Extra-intestinal manifestations

HISTORY

- Definition, duration, description
- Presence of Blood
- Exposure
  - Travel, Sick Persons, Pets, Farm animals
  - Food: Unpasteurised milk, raw / uncooked meat, heavy coffee or fruit drink intake
  - Water ? Tank Water
- Diet
- Systemic Illness
  - Mouth, eyes, skin
  - Carcinoid
  - HIV
- Family History
  - Cancer, Coeliac, IBD
- Medical Problems
  - Thyroid, pancreas
- Medications
  - Antibiotics / NSAID's

INVESTIGATION

- Stool
  - MC&S, parasites, C.diff
  - Calprotectin
  - Pancreatic elastase
- Yersinia, E. Coli 0157, Crypto, Microscopy
- Bloods:
  - FBC, ESR, CRP, U&Es, TFTs, Coeliac
- Endoscopic Evaluation
  - Gastroscopy for Small Intestinal Biopsy
  - Colonoscopy for colonic Biopsy
  - Capsule endoscopy
- Hydrogen Breath Test: SIBO, lactose
- Gastrin, VIP, Chromogranin A, 24hr Urine 5-HIAA



MANAGEMENT

- Dependent on Results of Investigation
- Treat appropriate causes
- Stop implicated Medications
- Empiric Antibiotics
- Bile Acid Sequestrant
  - Cholestyrmine, colestipol
- Creons
  - Pancreatic insufficiency
- Symptomatic Treatment
  - Buscopan
  - Loperamide

CASE CONTINUE

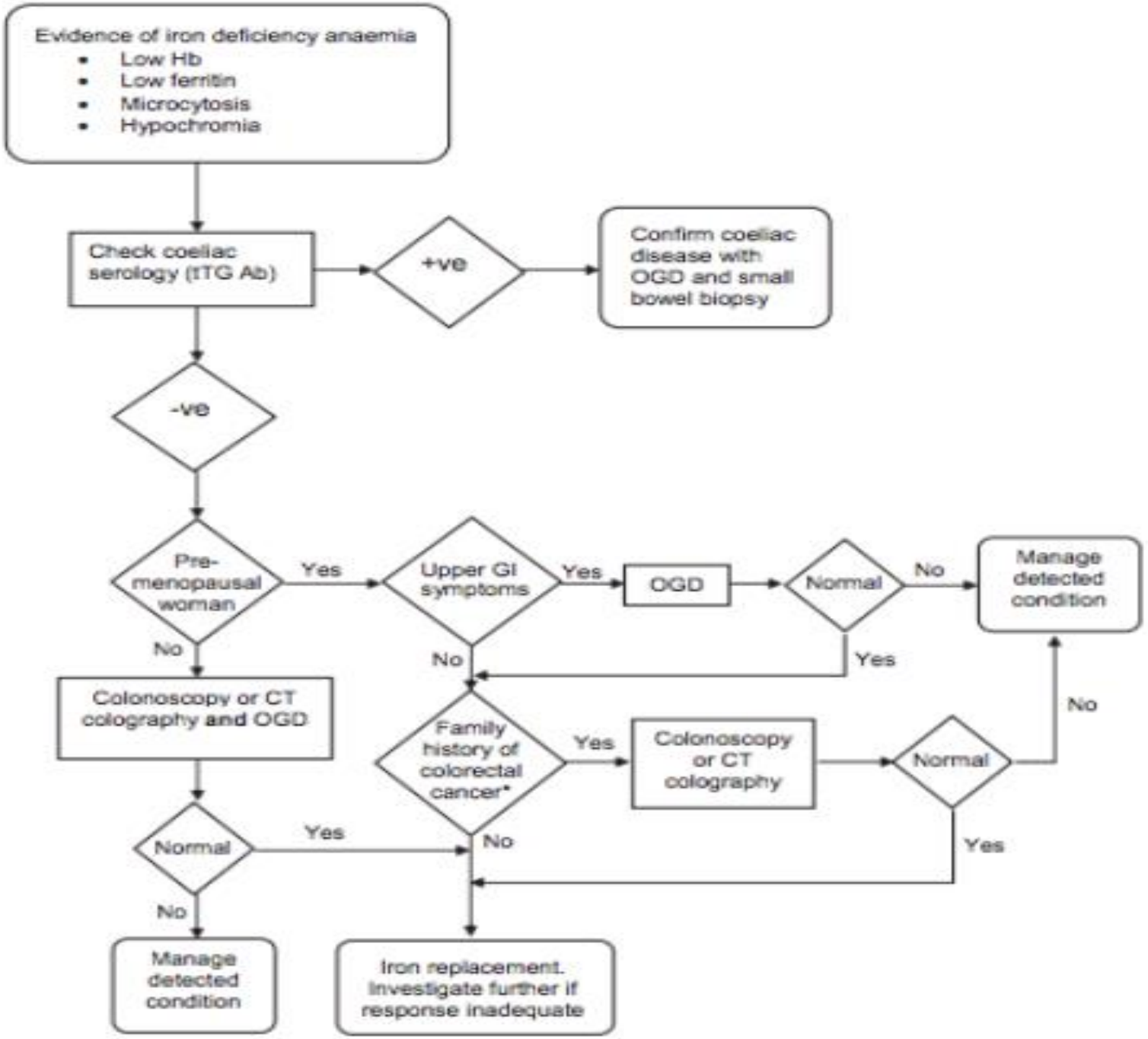
- Usual bowel motion: once daily. Bristol stool chart type 4
- Recent change
- Loose bowel motion, increased frequency, Bristol stool chart type 6
- After return from holiday in Fiji
- No antibiotics used
- Worse with certain type of food

INVESTIGATION

- LFTS, U+E, Cr normal
- FBC: Hb115 MCV 78
- Iron study: ferritin 19
- Stool
  - Microbiology –ve for E. coli, shingella, giardia, crytosporium
  - Faecal calprotectin: 80
- Coeliac serology
  - TTG IgA Ab: >250
  - IgA: 1.4
  - Endomysial Antibody: positive

IRON DEFICIENCY ANAEMIA

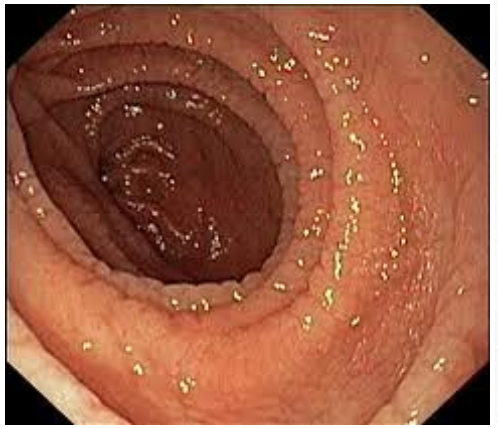
Occult GI blood loss	Malabsorption	Non-GI loss
Common	Common	Common
• Aspirn/NSAID 10-15%	• Coeliac disease. 6%	• Mensturation. 30%
• Colon cancer 10%	• Gastrectomy <5%	• Blood donation. 5%
• Gastric cancer. 5%	• H. Pylori <5%	
• Benign gastric ulcer. 5%		
• Angiodysplasia 5%		
Uncommon	Uncommon	Uncommon
• Oesophagitis 2-4%	• Gut resection. <1%	• Haematuria 1%
• Oesophageal cancer. 1-2%	• Bacterial overgrowth. <1%	• Epistaxis 1%
• GAVE		

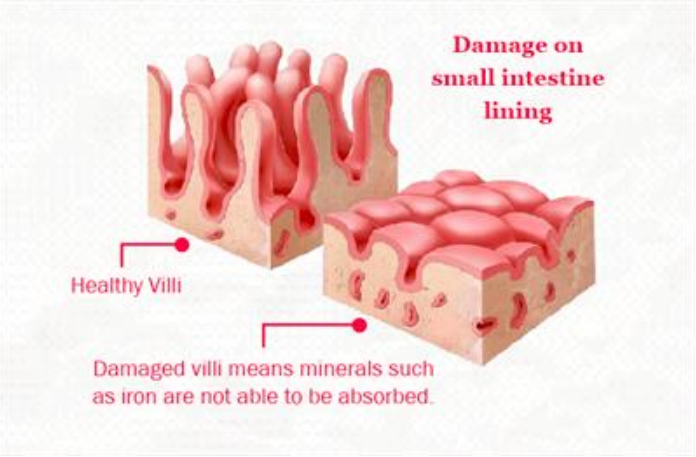

Evidence of iron deficiency anaemia
Low Hb
Low ferritin
Microcytosis
Hypochromia
Check coeliac serology (tTG Ab)
+ve
Confirm coeliac disease with OGD and small bowel biopsy
-ve
Pre-menopausal woman
Yes
Upper GI symptoms
Yes
OGD
Normal
No
Manage detected condition
No
No
Yes
Colonoscopy or CT colography and OGD
Family history of colorectal cancer*
Yes
Colonoscopy or CT colography
Normal
No
Normal
Yes
No
Yes
No
Manage detected condition
Iron replacement. Investigate further if response inadequate

COELIAC DISEASE

- Immune mediated small intestinal enteropathy that is triggered by exposure to gluten (enviromental) in genetically predisposed individual (genetic).

- First described in 1887 by Samuel Gee, " On the Coeliac affection"
- Although mentioned in 1st century. ? Chronic malabsorptive disorder
- But unexplained until WWII, recognised by Dutch paediatrician
- Coelac pathological changes was only seen after war: mucosal inflammation, intraepithelial lymphocytosis, cyrpt hyperplasia, villous atrophy



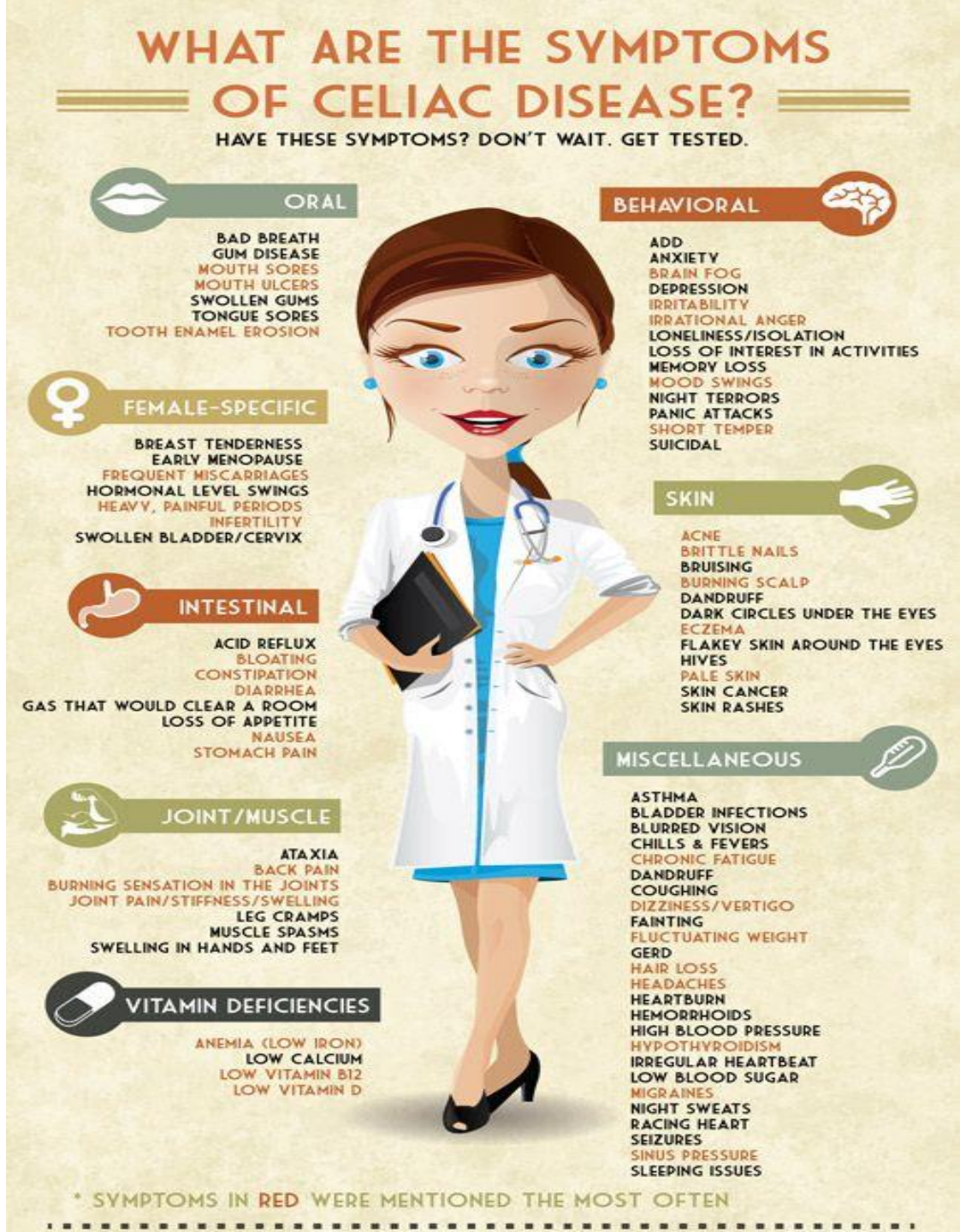


COELIAC DISEASE

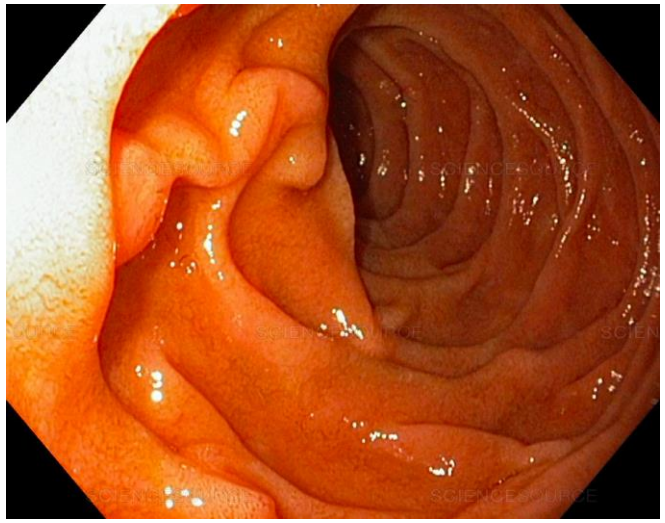
- Rare?
- Large scale study in Europe, 1%
- More common in woman, M:F= 1:1.5-2
- Increasing prevalence of coeliac disease with age
  - 15% newly diagnosed CD are > age 65
- Ethnicity
  - Predominantly Caucasian: 1% in Europe and USA
  - Increasing incidence in others. ? Immigration ? Underdiagnosed
  - Low incidence in Asia
- High prevalence among 1st degree relatives, 75% in monozygotic twins

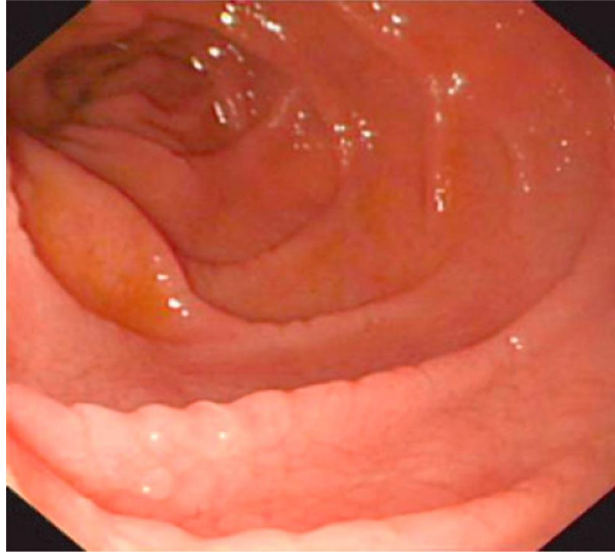
- Classic disease
  - Malabsorption
  - Villous atrophy
  - Resolution of the 2 above when on GFD

- Wide range of symptoms
  - Malabsorption, diarrhoea, steatorrhoea,
  - Weight loss, failure to thrive
  - Vague GI symptoms
  - Dermatitis herpetiformis, arthritis, epilepsy
  - Iron deficiency anaemia
  - Deranged liver functions
  - Asymtopmatic

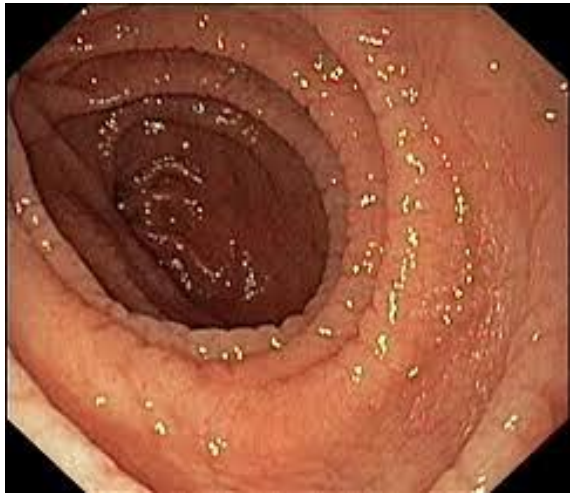


DIAGNOSIS





- Coeliac serology
  - TTG IgA Ab, endomysial Ab
  - Seronegtive coeliac disease:6-22% in all cases



- Duodenal biopsy (gold standard) via gastroscopy
  - D1+D2
  - Villous atrophy
- Gluten containing diet: 4 slices of wheat bread/day for 2 weeks
- HLA DQ2 and DQ8

HLA DQ2 AND DQ8

- Genes causing CD CELIAC1 on chromosome 6 (*HLA-DQ2* and *HLA-DQ8*)
- Highly associated with CD
- 90% of Coeliac patients in Europe and USA has DQ2 positive
- In family screening, DQ2 or DQ8 +ve: 16x increase risk
- High negative predictive value, low positive predictive value
  - **used to rule out CD**

- For patients on GFD already, no appropriate testing prior GFD. Reluctant to have gluten challenge

- Recent ESPGHAN proposed new guidelines in children

- If symptomatic on gluten containing diet. +
- Strongly positive coeliac serology. +
- HLA DQ2 or DQ8 positive
- **→ No Duodenal biopsies required**

- **But Duodenal biopsies remain gold standard for diagnosis and follow up**

- if sign of malabsorption or family history of CD, even if serolgy –ve, should still consider duodenal biopsy

ASSOCIATED CONDITIONS

- Dermatitis herpetiformis: HLA DQ
- Type I Diabets mellitus and autoimmune thyroiditis: share multiple genetic loci
  HLA DQ2, DQ3, DQ8
- Selective IgA deficiency
- Down syndrome
- Liver disease: elevation of AST/ALT. normalised with GFD
- ? Increase in Eosinophilic oesphagitis, IBD, microscopic colitis
- GI malignancy, small bowel lymphoma

MANAGEMENT

- Gluten Free Diet
- -mucosal healing and symptoms remission
- Can usually feel the difference within 2 weeks
- Bone density in those with high risk

- Seeing Dietician help the adherence and positive outcome
- Regular specialist follow up help the adherence: 97.5% vs 40%
- Baseline Bone density in those with high risk
- Monitoring the response to GFD
  - Repeat serology and biopsies in 12 -18 months
  - Repeat biopsies in 12-18 months

- Non-responsive CD: refractory, something else?

CASE CONTINUE

- Gastroscopy: Duodenal biopsies confirmed coeliac disease
- GFD
- Symptoms largely improved first 2 months then slowly 6 months

- Oral iron 3/12 was given.
- Ferritin improved.

- Repeat biopsy and serology in 12 months time
  - Normalised.

FAECAL CALPROTECTIN

- Zinc/calcium binding protein belonging to the S100 protein family
  - Light polypeptide chain and two heavy polypeptide chains, with a molecular weight of 36,5 kDa
- Very stable, unaltered in stool for 7 days
- Occurs in large amounts in neutrophil granulocytes
- Inflammation
  - Degranulation of neutrophil granulocytes releasing Calprotectin

- BUT, it cannot differentiate the type of inflammation
- Normal range: <50 µg/g, evidence showed rare organic cause < 150 µg/g

USE OF FAECAL CALPROTECTIN

- Can not differentiate type of inflammation
- IBS vs IBD
- IBD disease monitoring

CASE 2

- 55 year old woman
- Recently move to Auckland
- 6 months history of abdominal discomfort and possibly change of bowel motion
- Weight lost of 6 kg
- Previously surgical treated low grade ovarian tumor

- Investigation
  - FBC/U+E/Cr normal
  - Faecal spec normal. Faecal calprotectin normal

- History?

UNINTENTIONAL WEIGHT LOSS

- More than 5% of body weight loss over 6 months time
- 27% of community dwelling elderly people
- 50% of nursing home resident
- 5% of general population

- Important to investigate
  - Associated with increased morbidity and mortality

CAUSES OF UNINTENTIONAL WEIGHT LOSS

- 10 **D**s
  - **D**ementia
  - **D**epression
  - **D**isease
  - **D**ysphagia
  - **D**ysgeusia
  - **D**iarrhoea
  - **D**rugs
  - **D**enitions
  - **D**ysfunction
  - **D**ON'T KNOW (25%)

CAUSES OF UNINTENTIONAL WEIGHT LOSS

- Malignant
  - Gastrointestinal, lung, lymphoma, renal, prostate cancer
  - Cachexia
- Non-maligant
  - Peptic ulcer, coeliac, IBD, malabsorption
  - Psychiatric: depression, eating disorder, other psychiatric disorders
  - Endocirnopathies: diabetes, hyperthyoridism, adrenal insufficiency
  - Infectious disease: HIV, hepatitis, Tb, chronic infection
  - Advanced chronic disease: COPD. CKD, CHF, CLD
  - Neurologic disease: stroke, dementia, parkinsion's
  - Rhuematologic disease
  - Chronic vigorous exercise
  - Medication/substance abuse

No clinical guideline

- History
  - Intentional?
  - Documenting weight loss
  - Pattern
  - Associated symptoms!?

- Physical examination
  - General, CVS, Head and Neck, Abdominal exam
  - Lymph nodes
  - Cognitive assessment

- Basic diagnostic tests
  - FBC, electrolyte, renal function, liver function, glucose and Hb1Ac, thyroid functions
  - ? Viral hepatitis, HIV

What if all normal?

WHAT TO DO NEXT?

- Observation
  - More weight loss?
  - New symptoms?
- Gastroscopy and Colonoscopy
- CT body
  - Helpful or unhelpful?
  - Disadvantages: cost, yield, incidental-mass
  - Scottish Study in 2012: n=440
    - Cancer n=72 (16.4%), non-cancer n =4 (0.9%), normal n= 364 (82.7%)
    - Stratified to previous imaging finding, 42.4% if abnormal Xray/USS, 2.1% if normal Xray/USS

CASE CONTINUE

- Abdominal/pelvic ultrasound
  - 2cm para-aortic lymph node
  - Small hypoechoic dots in the liver which are consistent of haemangioma
- Examination
  - Palpable supraclavicular lymph nodes
  - Normal abdominal examination

- Urgent gastroscopy and colonoscopy= normal
- Urgent CT body: Multiple lymph nodes involvement
  - Lymph node biopsy: metastatic ovarian cancer

TAKE HOME MESSAGES

- Approach for Diarrhoea
  - History!
  - Acute vs Chronic
  - Red flags
  - Baseline investigation
  - Use of faecal calprotectin
  - Specialists' investigation
- Coeliac disease: serology, biopsy and symptoms are still the MAINSTREAM!
- Weight loss: documentation. Amount and duration. Tailored the management!