Coeliac Disease: Diagnosis and clinical features

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Coeliac disease

- Greek: *koiliakos* = of the belly
- = gluten enteropathy, nontropical sprue

Abnormal immune response to gluten in wheat, rye, barley

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Small intestinal inflammation, crypt hyperplasia, villous atrophy

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Malabsorption
Epidemiology

- 0.5-1% prevalence in Western populations
- Increasingly recognised in northern India, Middle East, North Africa
- 80-90% remain undiagnosed
- Usually present in 20-30s
- Uncommon in:
  - Chinese
  - Japanese
  - sub-Saharan Africans
Pathogenesis

Genetics
- HLA DQ2, DQ8
- Other loci

Gluten
- Glut deamidase
  - Cross links glutamine-rich proteins
  - Deamidates glutamine
  - Enhances gluten binding to DQ2/DQ8

Gliadin reactive T cells
- Other immune, extrinsic factors

Intraepithelial lymphocytes
- Crypt hyperplasia
- Villous atrophy
Clinical groups

- **Classic**
  - GI symptoms, malabsorption, histology, resolution with GFD
- **Atypical (largest group)**
  - No GI symptoms
  - Iron deficiency, osteoporosis, short stature, infertility
- **Silent**
  - Asymptomatic, incidentally discovered
- **Latent**
  - Yet to develop (e.g. +ve serology, inconclusive histology)
  - Diagnosed, normalised on GFD, now gluten tolerant
GI symptoms

- Bloating, distension
- Abdominal pain
- Flatulence, wind
- Lactose intolerance
- Diarrhoea, altered bowel habits
- Reflux
- Weight loss
Non-GI symptoms

- Iron deficiency +/- anaemia
- Osteoporosis, osteomalacia
- Vitamin D and calcium deficiency
- Infertility
- Rheumatic disorders
- Hyposplenism
- Neuropsychiatric manifestations
  - Peripheral neuropathy, ataxia
  - Migraine, seizures
  - Depression, anxiety
Associations

- Dermatitis herpetiformis: 10%
- Eosinophilic oesophagitis: SIR =16.0
- Type 1 diabetes mellitus: 5-10%
- Lymphocytic colitis: 3-5%
- Auto-immune thyroid disease
- Immune liver diseases (AIH, PBC, PSC)
- IgA deficiency
- Down syndrome
Genetics

• Concordance:
  – 10% of 1° relatives
  – 30% of HLA identical siblings
  – 70% of MZ twins

• HLA DQ2: 95% of CD, 30% of popn
• HLA DQ8: 5% of CD
• DQ2 (-) and DQ8 (-) excludes CD, 99% NPV
Serology

- IgA anti-tissue Transglutaminase Ab
  - Commonly referred to as TTG
  - Sensitivity 90%, specificity 95% (high titre)
- Useful to exclude coeliac in low risk
  - E.g., irritable bowel syndrome, osteoporosis, infertility
- Useful to monitor response
Diagnosis

- **Histology**
  - Necessary for diagnosis
  - “Gold” standard
    - Patchy, non-definitive
    - Duodenal bulb biopsy now recommended

- **Serology**
  - Confirmatory

- **Resolution with GFD**
  - Not absolutely necessary
Histological differentials

- NSAID enteropathy
- H. pylori duodenitis
- Post-gastroenteritis, viral infections
- Angiotensin receptor blockers (-sartans)
- Crohn
- CVID, other immunodeficiencies

- Giardiasis
- Lymphoma
- Bacterial overgrowth
- GVHD
- TB
- Cow’s milk, soy protein intolerance
- Eosinophilic gastroenteritis
- Tropical sprue
- Z-E
- Autoimmune enteropathy
- Whipple
Diagnostic difficulties

• On gluten free diet
  – 3g/d (2 slices bread) for 4 weeks
• Elevated TTG, normal histology
  – ? False positive
  – Latent/potential coeliac
  – Ultra short coeliac disease
  – Repeat in 1-2 years
• IgA deficiency (2-3% of CD)
  – Biopsy if clinical suspicion
Management

- Gluten-free diet, strict, lifelong
- Education
- Dietitian review
- Identify nutritional deficiencies
- Access to an advocacy group
- Multidisciplinary long-term follow-up
GFD for asymptomatic?

- Reduce micronutrient deficiency
- Decrease malignant potential
- Reduce low birth weight, pre-term
- Reduce autoimmune diseases
Non-responsive coeliac

- Usually sub-optimal compliance
- Other diagnoses:
  - Microscopic colitis, pancreatic insufficiency, lactose intolerance, irritable bowel syndrome
- Refractory coeliac disease: 5%
  - Type I: normal intra-epithelial lymphocytes
  - Type II: aberrant IEL clone
    - 50% progression to ulcerative jejunoileitis, lymphoma
    - High mortality
Malignancy

Risk not as high as previously thought

Strict compliance may reduce risk

- Intestinal T-cell lymphoma (5X risk)
- Other GI (2x risk):
  - oropharyngeal
  - oesophageal squamous
  - small intestinal
  - colorectal
  - hepatocellular

- Reduced risk:
  - Breast (0.35)
  - Lung (0.34)
Summary

- Coeliac disease is common
- Large undiagnosed group
- Classical presentation is uncommon
- Definitive diagnosis requires histology
- Strict gluten exclusion is mainstay of therapy
- Serious complications are rare