

FEATURED TESTS IN AUTOIMMUNITY

Calprotectin

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FECAL CALPROTECTIN

Overview

- Inflammatory Bowel Disease
- Fecal inflammatory biomarkers
- Utility of fecal calprotectin

What is Calprotectin

- Calprotectin is a 24 kDa dimer of calcium binding proteins S100A8 and S100A9.
- Calprotectin accounts for up to 60% of the soluble protein content of the neutrophil cytosol (liquid portion of the cytoplasm).
- Calprotectin is ***released during inflammation*** in the gut.
- Calprotectin complex is resistant to enzymatic degradation making it stable and easy to transport
- Calprotectin levels change with disease activity

What is Inflammatory Bowel Disease (IBD)

- Inflammatory Bowel Disease (IBD) is a term that describes conditions with chronic immune response and inflammation of the gastrointestinal tract
 - Crohn's disease (CD)
 - Ulcerative colitis (UC)
- IBD affects between 0.5-1% of the population
- Both illnesses are marked by an abnormal response of the body's immune system in which it mistakes food, bacteria, and other materials in the intestine for foreign substances and it attacks the cells of the intestines
- White blood cells are sent into the lining of the intestines where they produce chronic inflammation
 - When this occurs, the patient experiences symptoms of IBD

Abraham, C. and J. H. Cho (2009). "Inflammatory bowel disease." N Engl J Med **361(21): 2066-2078.**

Molodecky, N.A., et al. (2012). "Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review." J Gastro 142(1):46-54.

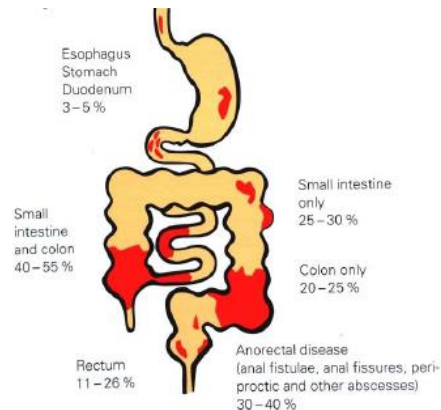
Inflammatory Bowel Disease (IBD)

- The cause of IBD is unknown. Environmental, infectious, genetic and autoimmune triggers have been suspected
- Chronic stress can lead to flare ups and increased inflammation but it is not the cause of the disease
- Patients with IBD have an increased risk of colon cancer
- Treatment can be significant in terms of:
 - Cost of therapy
 - Cost of Surgery
 - Quality of life
- IBD is not curable and requires a lifetime of care

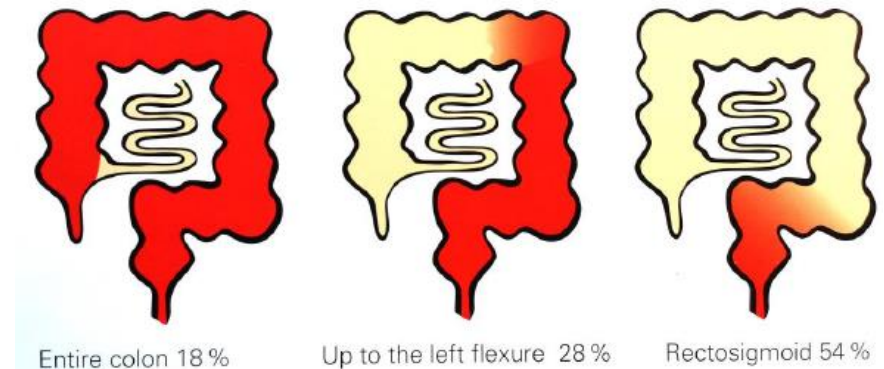
Inflammatory Bowel Disease (IBD)

- Inflammatory Bowel Diseases (IBD) are characterized by chronic recurrent, destructive inflammation of the gastrointestinal tract

Crohn's disease(CD)



Ulcerative colitis(UC)



- IBD affects between 0.5-1% of the population
- Substantial morbidity and health care utilization costs
- Diagnosis/Differentiation- combination clinical history, physical examination, laboratory tests, endoscopic findings, radiographic studies, histology
- overlapping forms

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Rasenack J, IBD Practice Manual, DrFalk Pharma

Irritable Bowel Syndrome (IBS) vs. IBD

- IBD and IBS can have common symptoms and differentiation is critical
- IBS is a relapsing functional bowel disorder defined by symptom-based criteria (abdominal pain, altered bowel function), in the absence of detectable organic causes
- IBS is not associated with intestinal inflammation or cause damage to the intestines
- An estimated 15-20% of the US population suffers from IBS, 10-15% worldwide¹

Need for non-invasive markers of intestinal inflammation

- Inflammatory Bowel Disease (IBD)
 - Optimized patient outcomes require:
 - Direct assessment – Endoscopy
 - Frequent monitoring
 - Evaluate treatment efficacy
 - Severity
 - Risk for potential complications
- Gold Standard
 - Direct assessment of mucosal inflammation - (Endoscopy)
 - Invasive
 - Time-consuming
 - Expensive
 - Associated risks
 - Patient Discomfort

Clinical utility of fecal calprotectin

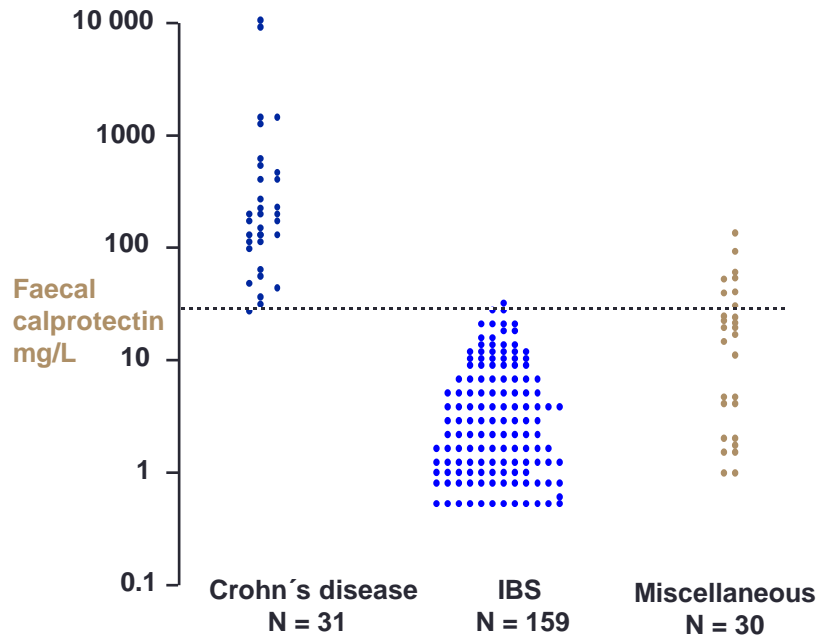


- Calcium and Zinc binding protein
- 60% of cytosolic protein in neutrophilic granulocytes
- Stable in stool 7 days @ room temp
- Measurement is simple, non-invasive, inexpensive

Fecal Calprotectin and Disease Activity

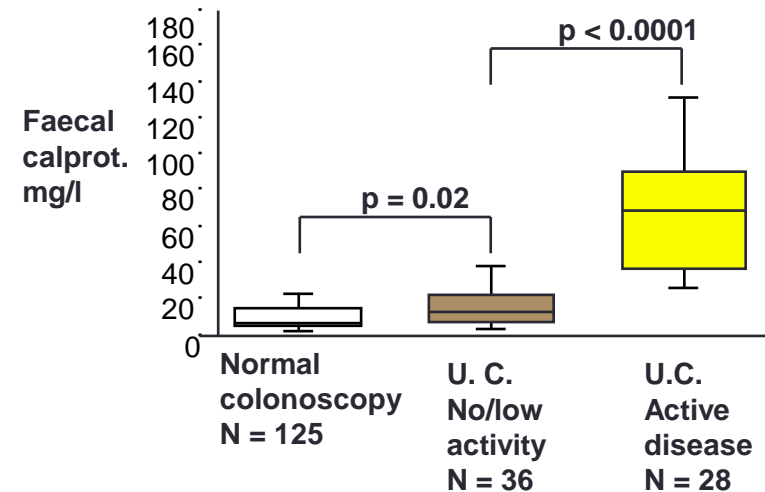
- Differentiating active from inactive disease
- Differentiating IBD from IBS
- Does NOT differentiate Crohn's disease from UC

Crohns and IBS



UC Active vs inactive disease

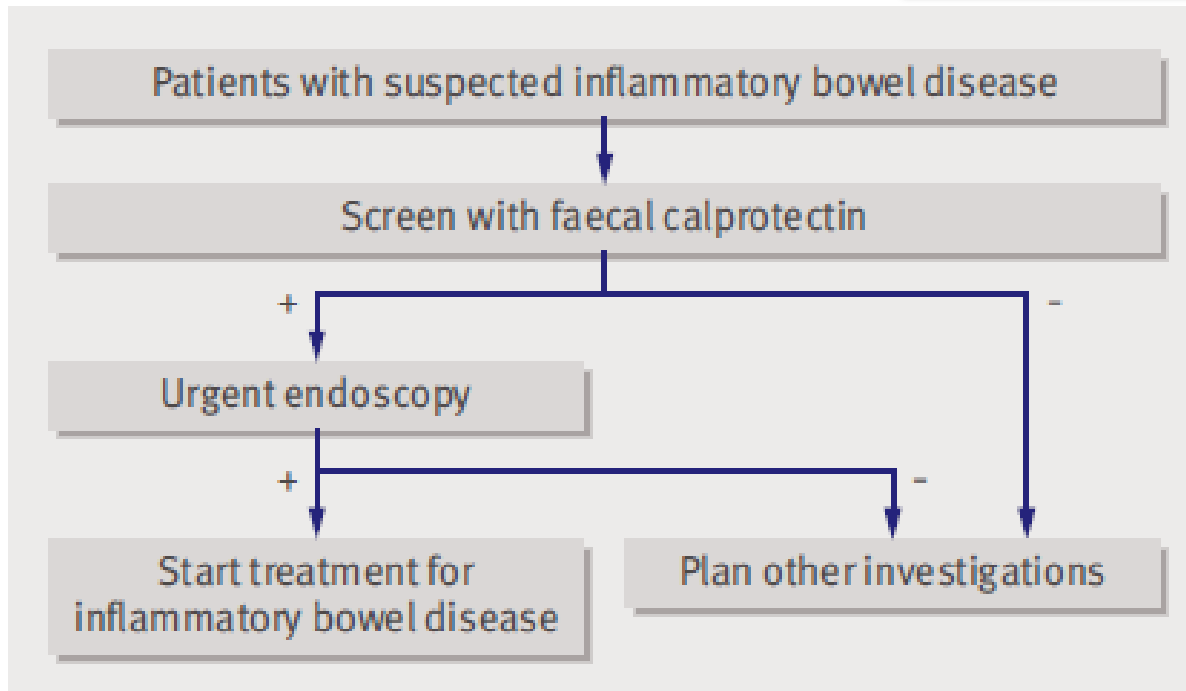
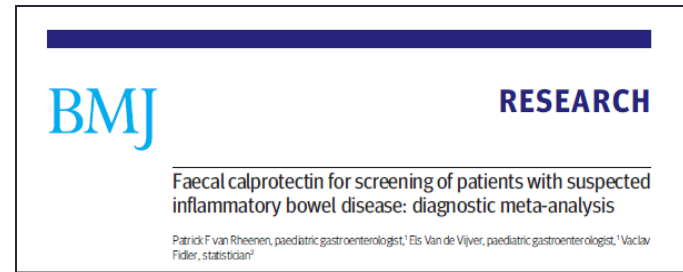
Calprotectin as marker of disease activity in UC assessed according to histology



Calprotectin Utility in Diagnosis¹

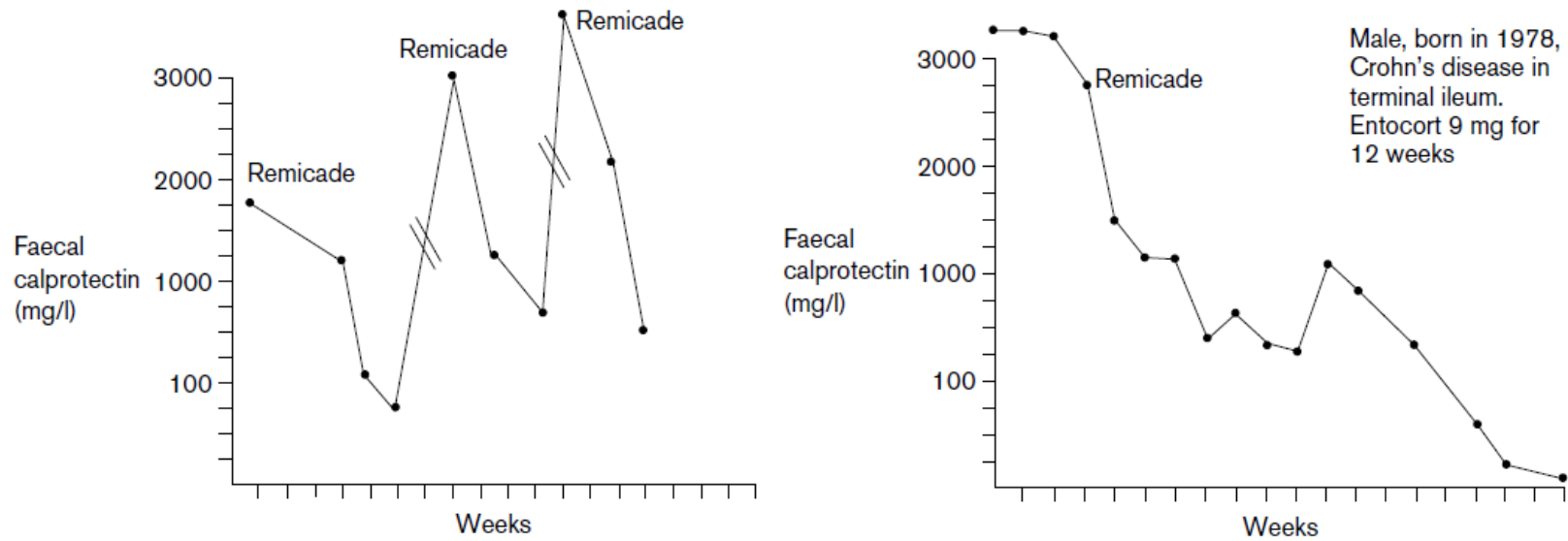
- **Key Findings:**

- Calprotectin is useful for screening patients most likely to need endoscopy for suspected inflammatory bowel disease



Calprotectin as indicator of therapy response in Crohn's Disease

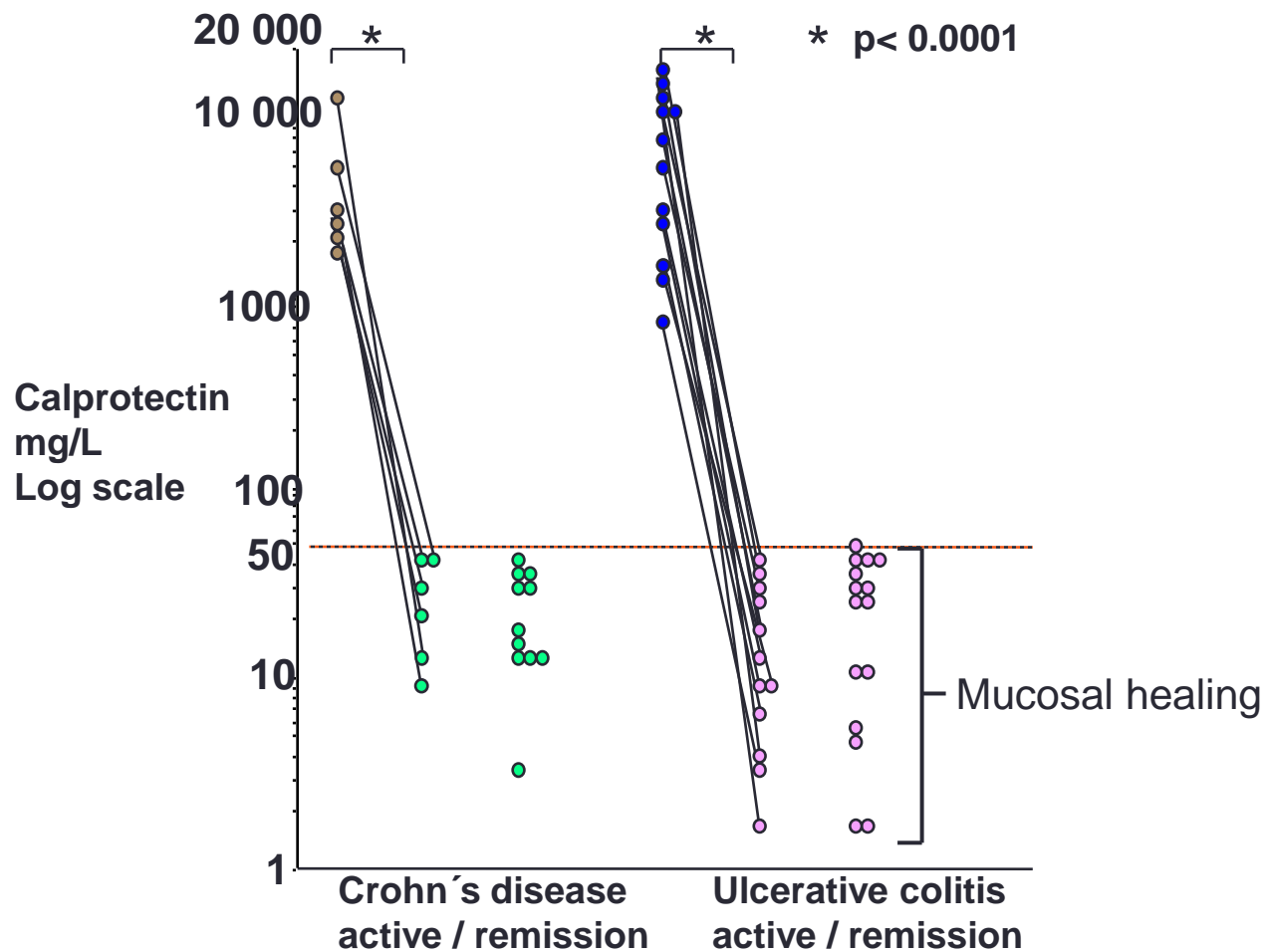
Fig. 1



Two examples of changes in faecal calprotectin levels in patients with Crohn's disease treated successfully with Remicade (infliximab).

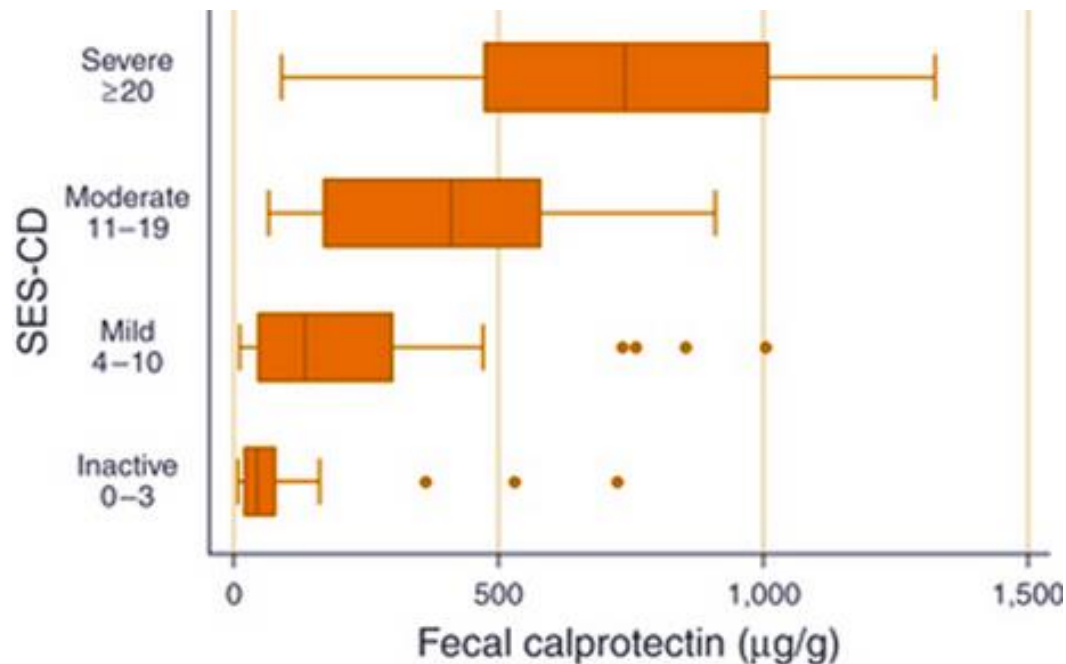
- Calprotectin decreases with successful treatment, increases with relapse
- May help assess early response or non-response to treatment

Calprotectin levels in IBD patients with active disease and during mucosal healing



Calprotectin – Utility in Monitoring

Endoscopic Crohn's disease activity measured by (SES-CD) vs fecal calprotectin concentration



Key Messages

- Non-invasive marker of intestinal inflammation
- Diagnostic utility to differentiate between IBS and IBD
- Use in the selection of patients for endoscopy, reduce unnecessary endoscopy
- Use in monitoring treatment response, adjustment of dosages, and end-point marker for mucosal healing
- Early predictor of relapse allowing early treatment intervention

Thank you!