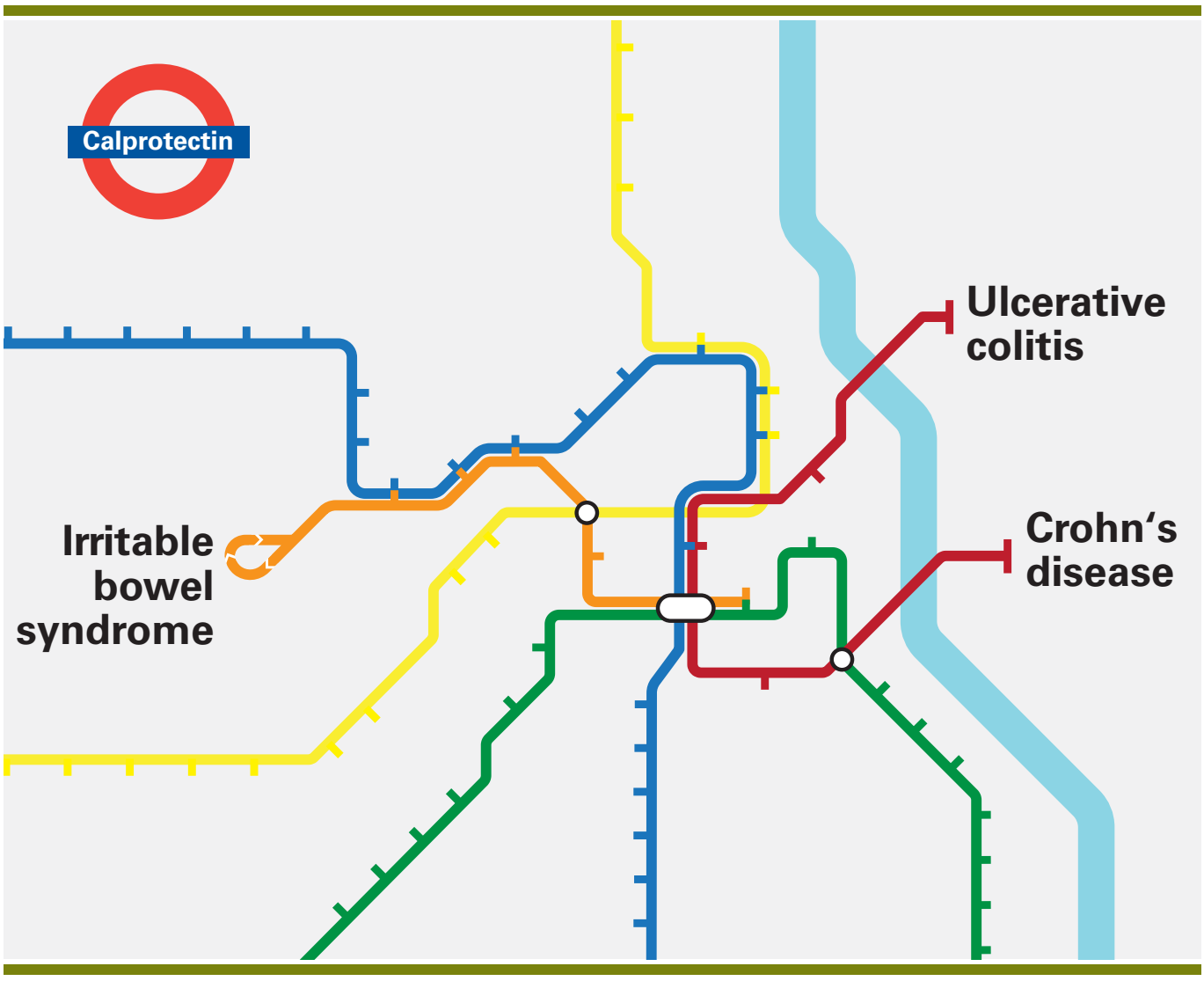
Calprotectin

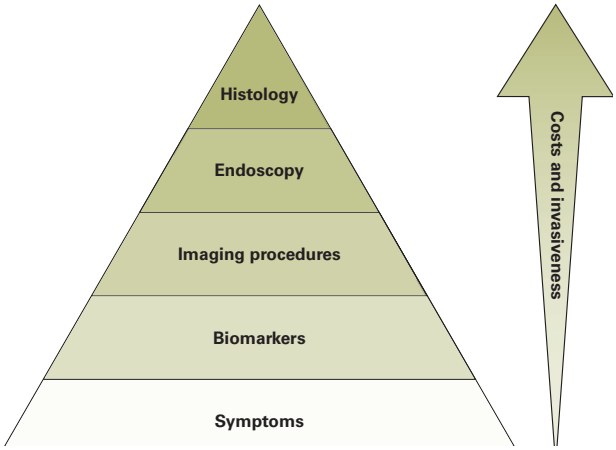
Marker for inflammatory activity in the intestine



- Quick and efficient determination of calprotectin in stool
- Clear differentiation between chronic inflammatory bowel diseases (IBD) and irritable bowel syndrome
- IBD diagnostics in accordance with current international guidelines
- Fully automated processing possible

Diagnosing chronic inflammatory bowel diseases

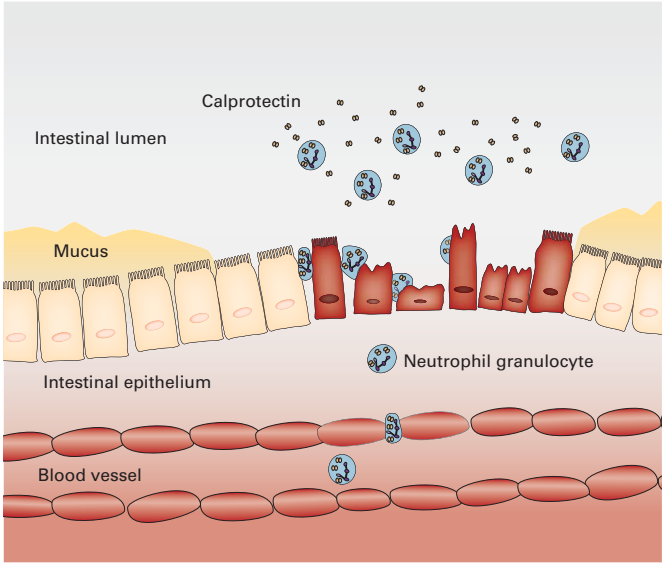
Patients exhibiting symptoms such as stomach ache or diarrhoea represent a large part of patients in gastro-enterological practices. These symptoms may be caused by, for instance, chronic inflammatory bowel diseases (IBD), such as Crohn's disease (CD) or ulcerative colitis (UC), or a functional intestinal disorder such as irritable bowel syndrome (IBS). Differentiation between IBD and IBS based only on the symptoms is not possible. Therefore, for definitive diagnosis, the inflammation of the intestinal epithelium is generally assessed using invasive imaging procedures such as endoscopy. However, these procedures are very cost-intensive and unpleasant for the patient. Besides, more than half of the adults and up to 70 % of paediatric patients show inconspicuous endoscopic results. Test systems for the detection of inflammatory-associated faecal biomarkers are an economical and non-invasive alternative.



modified from Schoepfer AM et al. Gastroenterology 148(5):889-892 (2015)

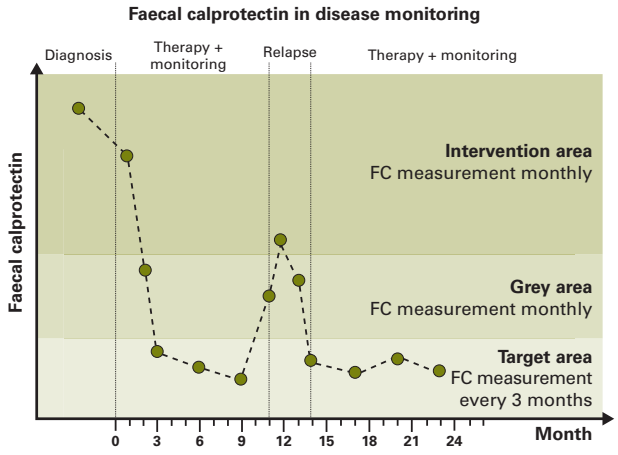
Faecal calprotectin in IBD diagnostics

When the gastrointestinal tract is inflamed, neutrophil granulocytes migrate through the intestinal mucosa into the lumen, where they release calprotectin. This stimulates an immune response and has an antimicrobial effect. Calprotectin that is released into the intestinal lumen accumulates, and is then excreted, in the stool. Faecal calprotectin (FC) can therefore be used as a marker for inflammatory processes that affect only the gastrointestinal tract. The FC level is proportional to the extent of the inflammation. Thus, FC is superior to clinical indicators and classical serological markers in IBD diagnostics, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and leukocyte number. A concentration of < 50 µg/g is considered as inconspicuous and excludes an inflammatory cause of gastroinestinal disorders with great certainty. At higher concentrations, the inflammation of the intestinal epithelium should be investigated further using imaging procedures. If patients are selected for endoscopy based on their increased FC levels, the number of endoscopic examinations is significantly reduced.



Correlation with disease activity

IBD proceeds in episodes. Symptomatic phases (relapses) alternate with remission phases, in which the disease is unapparent. Several studies have demonstrated that FC correlates with the level of inflammatory activity. Accordingly, current guidelines recommend the determination of FC to monitor disease progression in IBD patients under drug therapy. In addition, it is recommended to monitor FC levels at regular intervals even if the disease is in remission phase. With increased FC values, further investigations should be performed, and adapted therapy measures taken. The regression in the epithelial inflammation (mucosal healing) correlates with the normalisation of the FC values.



modified from van Rheenen PF. Inflamm Bowel Dis 20(8):1416-1417 (2014)

Risk marker for post-operative relapses

Studies suggest that FC can also be used as a risk marker for post-operative relapse:

- CD patients after surgical removal of inflamed intes-tinal sections have a higher risk of a relapse if their FC values are increased.
- FC correlates to a higher extent with the likelihood and degree of a relapse than CRP and CDAI (Crohn's disease activity index).

Calprotectin in paediatrics

FC is also suited for paediatrics to avoid unnecessary endoscopy particularly in small children.

- FC normal values are significantly increased in small children. Nevertheless, in case of IBD, the inflam-mation values correlate with the severity of the disease.
- From the age of 4 years, children exhibit values in the normal range of adults (up to 50 µg/g).

Calprotectin in IBD guidelines

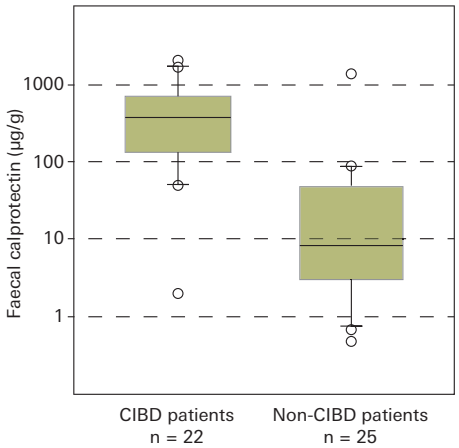
Current guidelines on IBD diagnostics recommend measuring FC for differentiation between IBD and IBS and underline the good correlation between the FC concentration and the degree of disease activity. Furthermore, important organisations such as the German Association for Gastroenterology, Digestive Illnesses and Metabolic Disorders (DGVS) and the European Crohn's and Colitis Organization (ECCO) make a recommendation regarding the monitoring of IBD by means of FC.

Calprotectin in international guidelines on IBD diagnostics							
Year	2015	2018			2019	2020	2021
Organisation	WGO[1]	JSGE[2]	ACG[3]	ECCO[4]	BSG[5]	DGVS[6]	DGVS[7]
Country / Region	Worldw.	JP	USA	EU	UK	D	D
Disease	IBD	IBD	CD	CD	IBD	UC	UC
Differential diagnostics for IBD / IBS	■	■	■	■	■	■	■
Correlation with disease activity	□	□	□	■	■	■	■
Prognosis of a relapse			□	■	■	■	■
Marker for mucosal healing				■*			□
Marker for post-operative relapse				■	■		■

■ recommended; □ mentioned; * only UC

Reliable diagnosis of IBD using the EUROIMMUN Calprotectin ELISA

Quantification of faecal calprotectin by means of the EUROIMMUN Calprotectin ELISA allows non-invasive and clear differentiation between IBD and IBS. Values < 50 µg/g should be evaluated as negative and values > 120 µg/g as positive. Values that lie in between should be considered as borderline or suspicious. The results obtained with this assay correlate excellently with the clinical diagnosis. In a study with IBD patients and patients with gastroenterological disorders the test achieved a **sensitivity of 94.1%**, with a **specificity of 95.5%**, taking into account the threshold area. The median calprotectin level in the IBD group was significantly higher than that obtained with the non-IBD group.



Sample preparation using stool dosage tubes

The manual weighing and extraction of stool samples in clinical routine diagnostics is very time-consuming. Stool dosage tubes (SDT) from EUROIMMUN allow the extraction of a defined amount of stool with one work step. This reduces the time for preanalytics to a minimum. Calprotectin values obtained after extraction with SDTs have an excellent correlation with values yielded after manual weighing and extraction of the stool sample. Transfer of the sample after centrifugation is unnecessary. SDTs can be used directly in manual or automated processing.

Automation

The EUROIMMUN Calprotectin ELISA is compatible with all open ELISA platforms. It has been validated for fully automated processing on the EUROIMMUN Analyzer I and EUROIMMUN Analyzer I-2P. There is no risk of contamination when using stool samples.

Analyzer I

Further IBD diagnostics

FC allows quick and very reliable identification of IBD as well as differentiation from functional intestinal disorders. A differentiation between ulcerative colitis and Crohn's disease, however, is not possible. In these cases, disease-specific markers must be investigated. Antibodies against intestinal goblet cells and granulocyte antigens (DNA-ANCA) are pathognomonic for UC. Specific markers for CD are antibodies against exocrine pancreas (acinus cells) and Saccharomyces cerevisiae (ASCA). These can be serologically determined in an uncomplicated way.

ORDERING

Product	Order number
Calprotectin ELISA	EQ 6831-9601 W
Stool dosage tubes, prefilled with extraction buffer, 45 pieces	ZE 6010-4501-2
Stool dosage tubes, not filled with extraction buffer, 100 pieces	ZE 6010-0100-3

References

[1] Bernstein C, et al. World gastroenterology organisation global guidelines inflammatory bowel disease: Update August 2015. J Clin Gastroenterol 50:803-818 (2016). [2] Matsuoka K, et al. Evidence-based clinical practice guidelines for inflammatory bowel disease. J Gastroenterol 53:305-353 (2018). [3] Lichtenstein GR, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol 113:481-517 (2018). [4] Maaser C, et al. ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: Initial diagnosis, monitoring of known IBD, detection of complications. J Crohns Colitis 13(2):144-164 (2019). [5] Lamb CA, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut 68: s1-s106 (2019). [6] Kucharzik T, et al. Aktualisierte S3-Leitlinie Colitis ulcerosa. Z Gastroenterol. 58:241-326 (2020). [7] Sturm A, et al. Aktualisierte S3-Leitlinie – „Diagnostik und Therapie des Morbus Crohn" der Deutschen Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten (DGVS). Z Gastroenterol. 60:332-418 (2022).