QUADERNI ENPAB

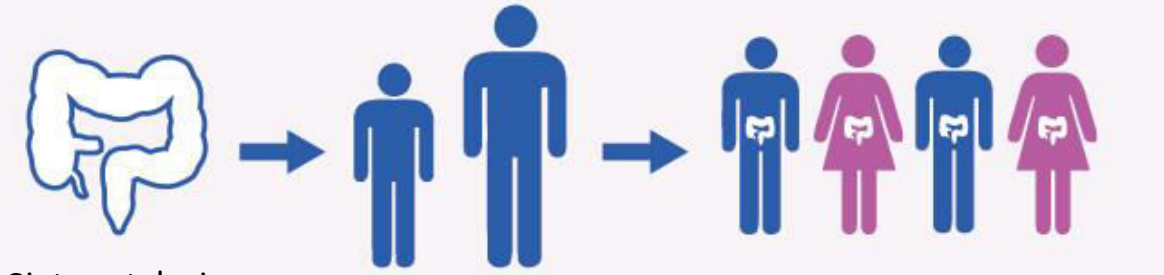
PER UNA NUOVA CULTURA PROFESSIONALE

Enpab

Il Laboratorio nelle MALATTIE INFIAMMATORIE CRONICHE INTESTINALI (MICI - IBD)

a cura di
Mauro Amato (detto Mario)

MALATTIE INFIAMMATORIE CRONICHE INTESTINALI (MICI - IBD)



Sintomatologia

Usualmente diagnosticati tra 15-30 anni

- Malattie croniche
- Colpiscono uomini e donne 50%
- Non ci sono cure specifiche

- Incidenza in deciso incremento in Europa e USA

Inflammatory Bowel Disease

Irritable Bowel Syndrome (**IBS**)

Il digerente appare normale ma non ha sempre una funzionalità corretta

Malattie infiammatorie con bersaglio a livello digestivo in cui il sistema immunitario sembra svolgere un ruolo di base nella infiammazione e danno alla struttura intestinale.

Caratteriste:
- Tendenza alla familiarità
- Decorso cronico recidivante
- Manifestazioni extraintestinali

The goal of inflammatory bowel disease treatment is to reduce the inflammation that triggers your signs and symptoms.
In the best cases, this may lead not only to symptom relief but also to long-term remission and reduced risks of complications. IBD treatment usually involves either drug therapy or surgery.
There is no cure for IBD.

(Mayo Clinic)

SINTOMATOLOGIA (MICI - IBD)

Anemia
Uveite
Febbre
Sudorazione
Ittero

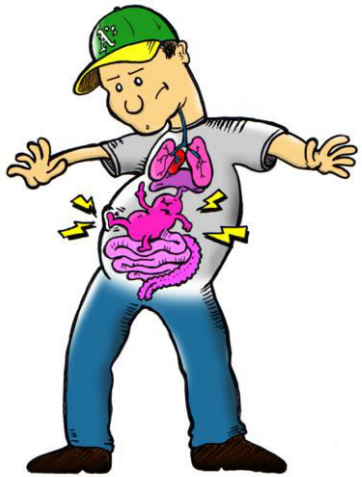
Ulcere orali aftose

Colangite sclerosante primaria

Artrite
Artralgia

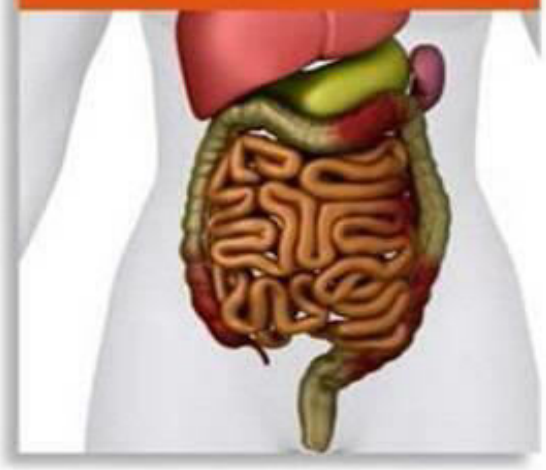
Eruzioni cutanee

Dolori addominali
Evacuazioni dolorose
Diarrea con sangue e mucopus
Malassorbimento
Perdita di peso



MALATTIE INFIAMMATORIE CRONICHE INTESTINALI (MICI - IBD)

Morbo di Crohn



- Può interessare tutto il canale alimentare dalla bocca all'ano.
  Sedi più frequenti sono la **parete** dell'**Ileo distale** e del **Colon**;
- Lesioni a distribuzione segmentaria e **decorso cronico** con tendenza alle **recidive**;
- Sintomi più frequenti:
  - Diarrea cronica intermittente
  - Dolori addominali
  - Calo ponderale

Rettocolite Ulcerosa

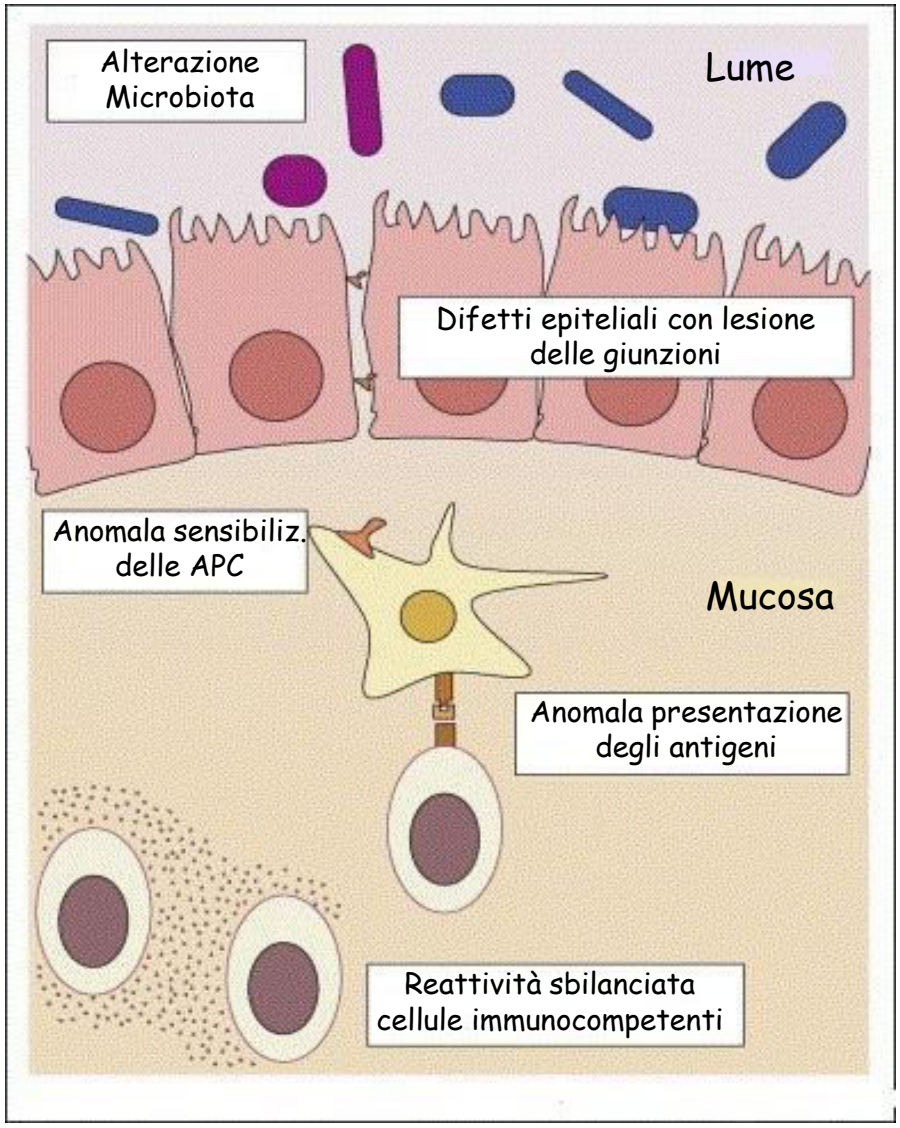
- Detta anche **Colite Ulcerosa** interessa selettivamente la **mucosa** del **Colon discendente** e del **Retto** senza interruzioni con ulcere emorragiche;
- Sintomi più frequenti:
  - Diarrea muco-ematica
  - Emorragia del retto
  - Dolori addominali
  - Tenesmo rettale
  - Muco nelle feci

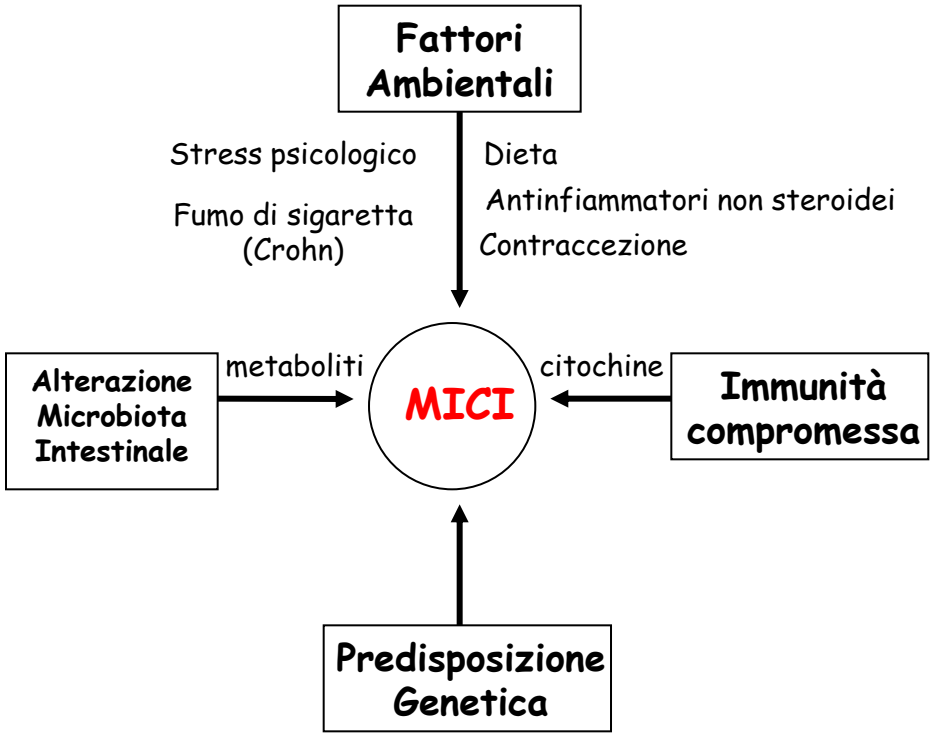
Altre Coliti (10%)

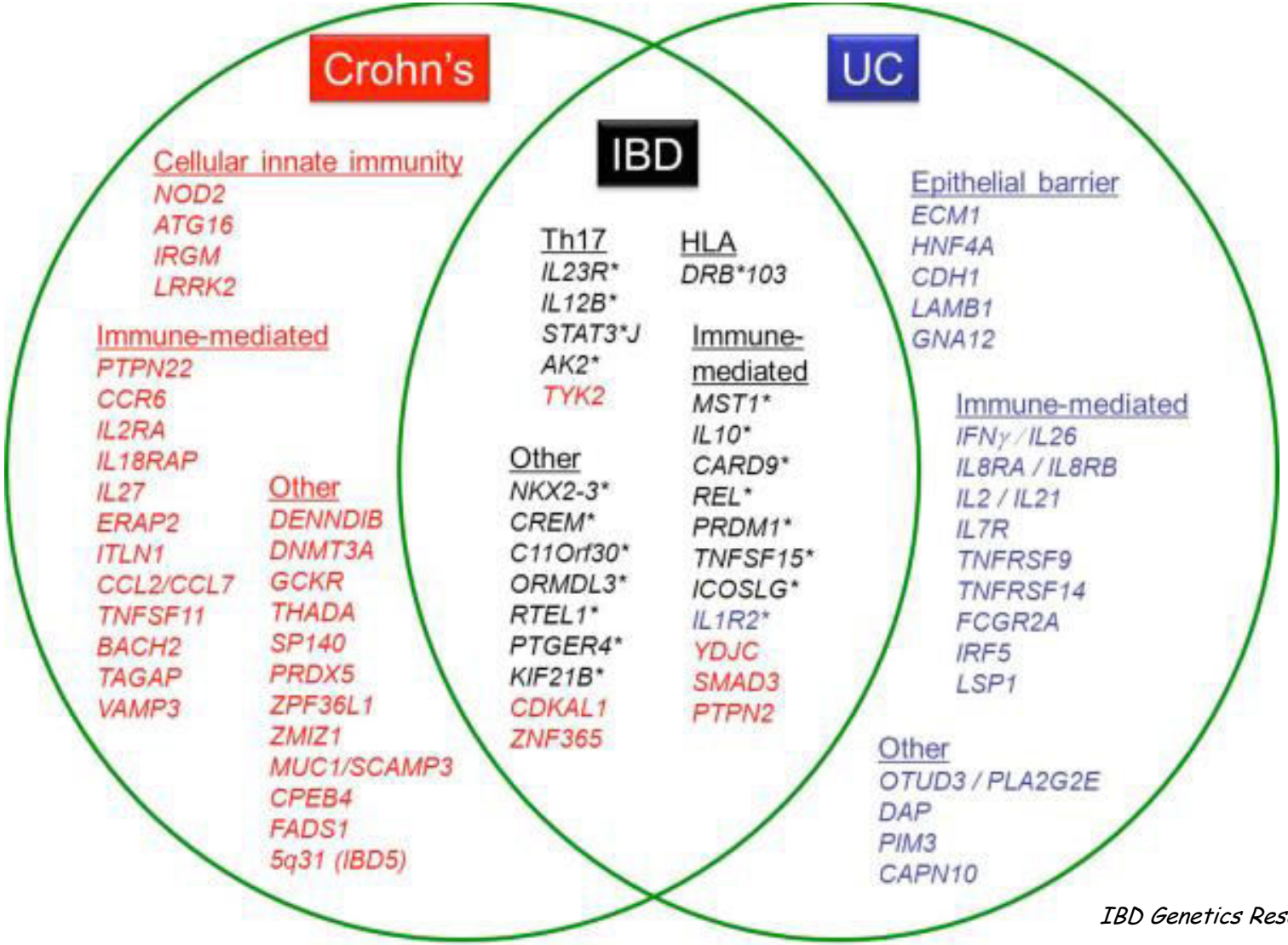
Collagenosica
Linfocitica
Ischemica
Infettiva
Indeterminate

MALATTIE INFIAMMATORIE CRONICHE INTESTINALI (MICI)

IBD (Inflammatory Bowel Deseases)







IBD Genetics Research - UK

- Identificati più di 90 loci genici per richio IBD
- Nessun beneficio per il paziente ne è ancora derivato

MICI – Indagini di Laboratorio

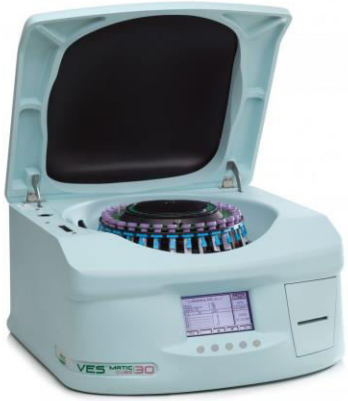
- **VES e PCR**
- **Anticorpi anti-Saccharomyces Cerevisiae (ASCA)** (anticorpi anti-glicano)
- **Anticorpi anti-citoplasma dei neutrofili (ANCA): P-ANCA e C-ANCA**
- **Calprotectina e Lactoferrina fecale**
- **Altri Anticorpi anti-glicano:**
  - **Anticorpi anti-Laminaribioside (ALCA)**
  - **Anticorpi anti-Chitobioside (ACCA)**
  - **Anticorpi anti-Mannobiodide (AMCA)**
- **Anticorpi anti-antigeni batterici:**
  - **Anticorpi anti-Proteica C della membrana esterna E.coli (AOmpC)**
  - **Anticorpi anti-Pseudomonas fluorescens (anti-I2)**

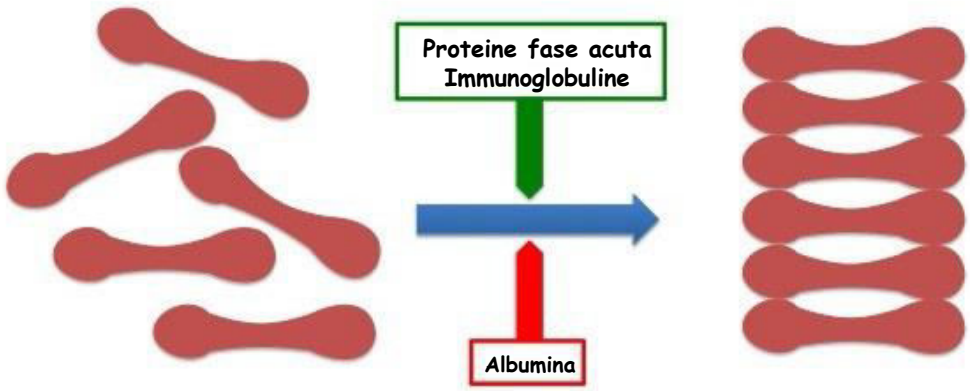
Si associano:

- **Emocromocitometrico**
- **Ricerca sangue occulto e leucociti fecali**
- **Test di permeabilità intestinale**
- Fibrinogeno
- Coprocoltura e parassitologico feci
- Ferro, Zinco e Magnesio
- Vit. B12 e Acido Folico

VES – Velocità di eritrosedimentazione

(Indagine aspecifica di flogosi)





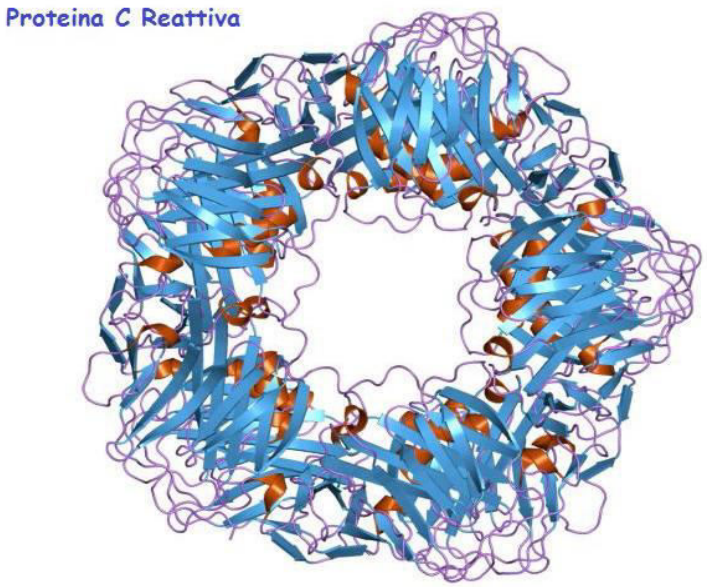
- Anticoagulante citrato di sodio a 3.8%.
- Sospensione in opportune provette graduate su un piano in posizione verticale.
- Trascorsa 1 ora si legge la misura della sedimentazione delle emazie.
- Può essere fatto in automazione

Valori normali:
-uomini fino 50 anni **0-10 mm/h**
- uomini sup. 50 anni **0-15 mm/h**
- donne fino 50 anni **0-15 mm/h**
- donne sup. 50 anni **0-20 mm/h**

Si può anche calcolare l' **Indice di Katz** :
in questo caso si registra anche la seconda ora di sedimentazione e si applica la seguente formula:

Indice di Katz= (1 ora + 2 ora/2)/2

hs PCR – PROTEINA C REATTIVA (alta sensibilità)



- **Alfaglobulina** sintetizzata da **fegato** in risposta a **IL6**, **TNFa** e **IL1β** con netto incremento in **fase acuta reattiva**.
  Può essere prodotta anche dagli **adipociti**
- **Test aspecifico** (non fornisce informazioni sull'origine del processo)
- **Marcatore di flogosi più sensibile nelle MICI**
  70- 90% per il MC
  50- 60% per la RCU
- **Diagnosi differenziale MICI-Patologia funzionale**

I test di nuova generazione sono **hs-PCR** (PCR quantitativa ad alta sensibilità) con metodica immunoturbidimetrica o nefelometrica.

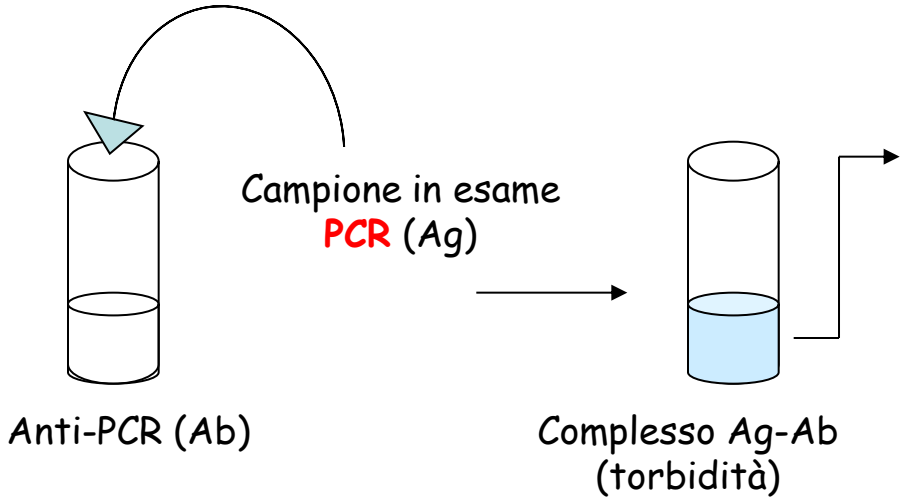
Valori normali di hs-PCR **3-4.5 mg/l**

Oltre che nelle **IBD** la **Proteina C Reattiva** aumenta significativamente in:
- Infezioni di origine batterica e virale
- Infarto miocardico
- Neoplasie maligne
- Reumatismi articolari acuti
- Ascessi, peritoniti e LES

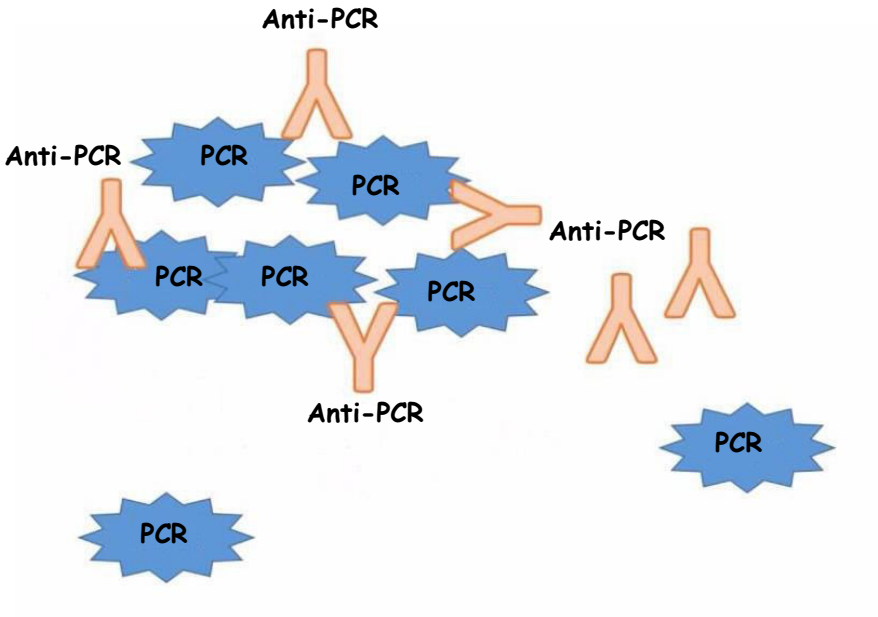
In risposta ad uno stato infiammatorio acuto la **PCR** può aumentare anche alcune centinaia di volte.

Dosaggio della Proteina C Reattiva

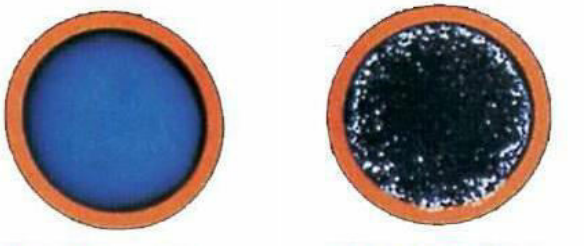
Immunoturbidimetrico/Agglutinazione Latex



- **Torbidità dovuta alla formazione degli immunocomplessi** (Ag-Ab)
- Intensità, letta da strumento dedicato, funzione della quantità di antigene presente nel campione

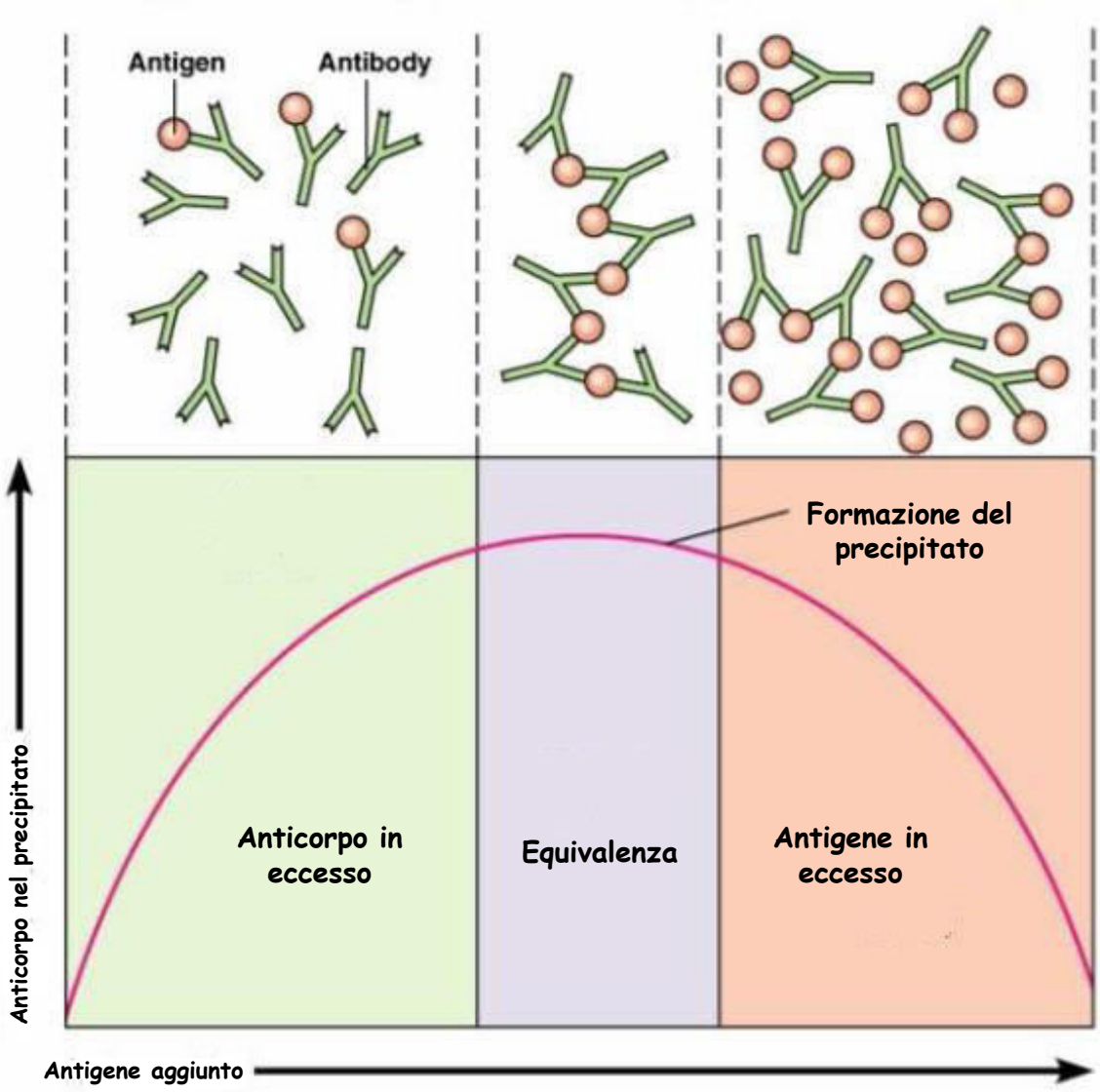


Valutazione qualitativa/semiquantitativa

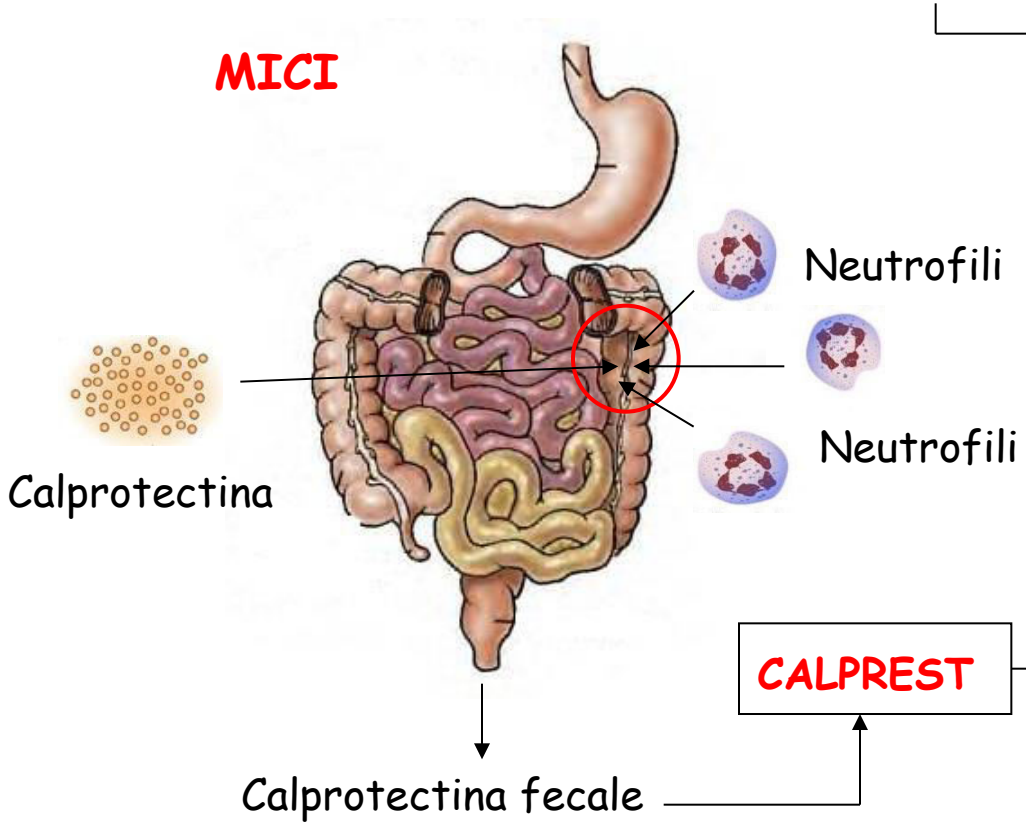


Test NEGATIVO Test POSITIVO

TEST DI AGGLUTIAZIONE



CALPROTECTINA FECALE



- Proteina antimicrobica (legante il calcio), essenzialmente presente nei neutrofili e la sua presenza nelle feci è utilizzata come **indice di infiltrazione di neutrofili** nel lume intestinale.

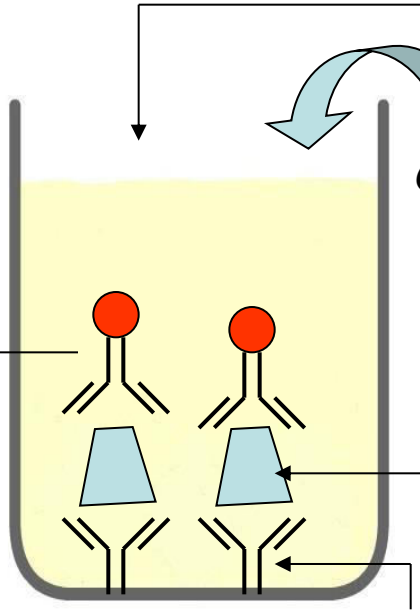
CALPREST

Test per la determinazione della calprotectina fecale quale **marker di flogosi intestinale**.
Verifica, in modo non invasivo, la presenza di uno stato infiammatorio intestinale.

- La **calprotectina fecale aumenta** in oltre il 95% dei **pazienti con MICI**.

- Il **Calprest differenzia** (in modo affidabile) i soggetti con **MICI** da quelli con **IBS**
- Il **Calprest negativo esclude** (con quasi certezza) **una infiammazione della mucosa intestinale**
- Usato anche in casi pediatrici

CALPREST (Immunoenzimatico quantitativo)

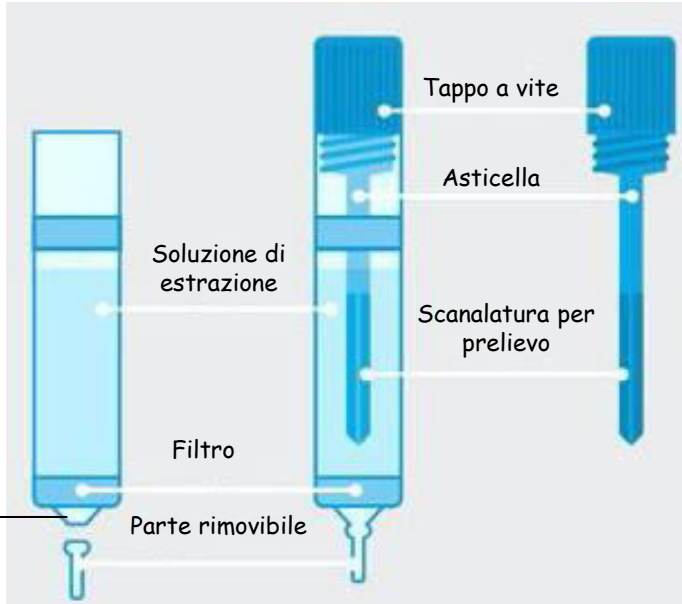


Anti-calprotectina policlonale

Calprotectina fecale

Anti-calprotectina marcata

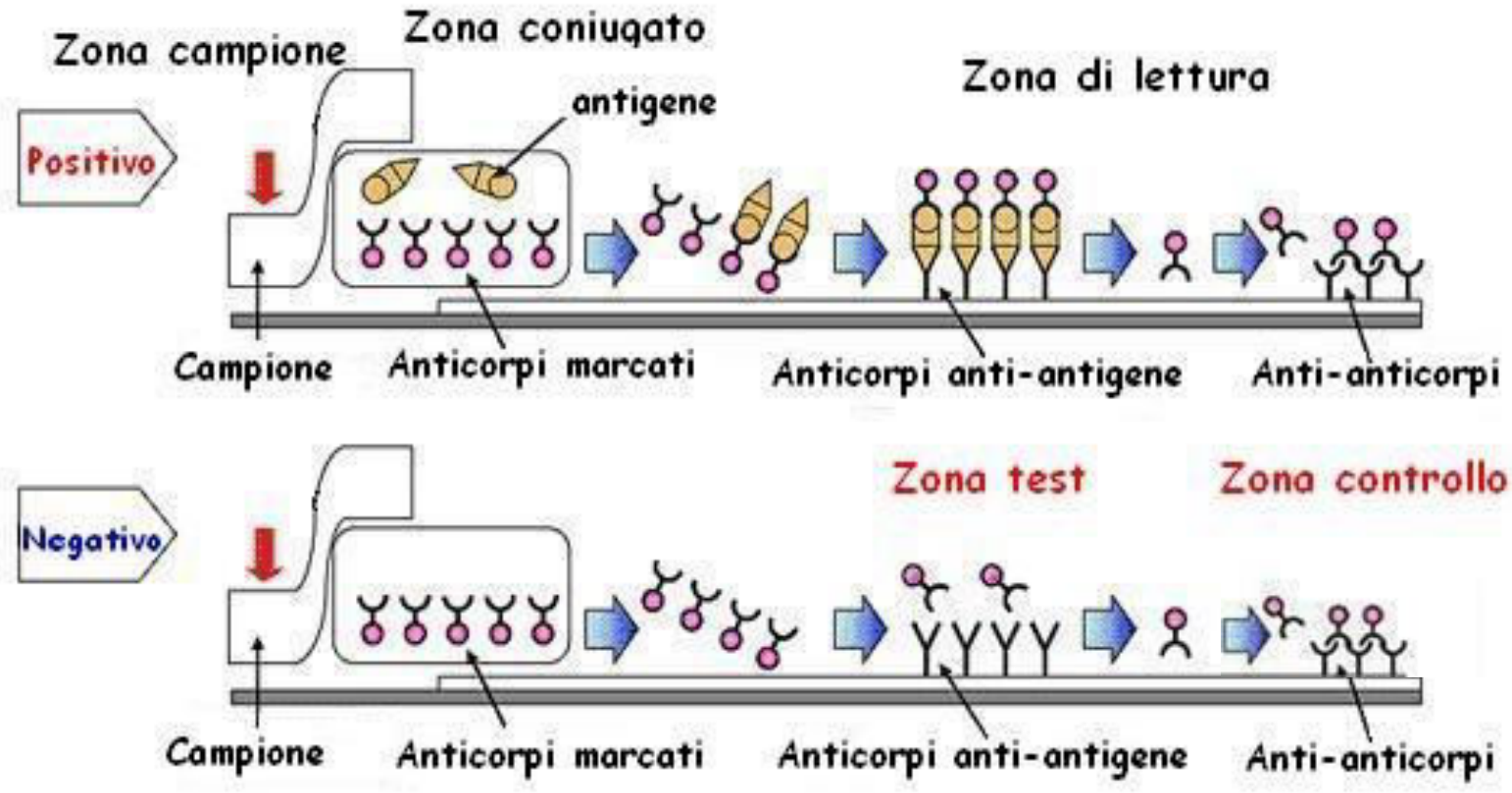
Valori riferimento: border-line **25-50 ug/g feci**



- **Diagnosi differenziale MICI/IBS**
- Controllo del decorso della patologia
- Monitoraggio della strategia terapeutica
- Previsione ricadute cliniche

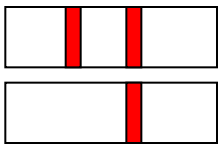
CALPREST (Qualitativo/Semiquantitativo)

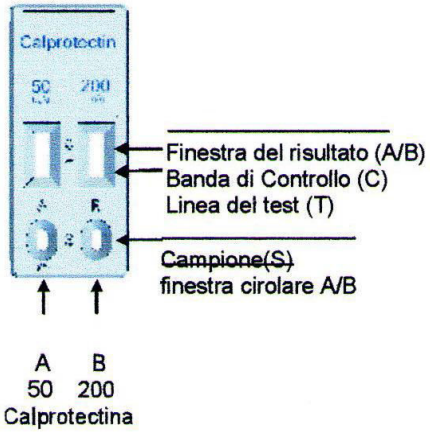
Immunocromatografia a flusso laterale (dispositivo CARD)



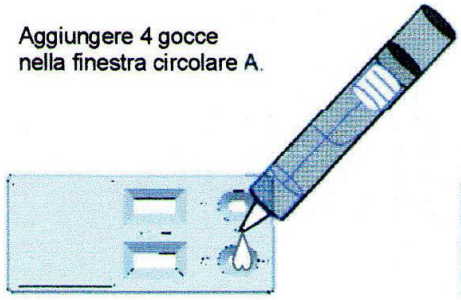
Test Positivo: due bande colorate in rosso

Test Negativo: una sola banda rossa





(3)



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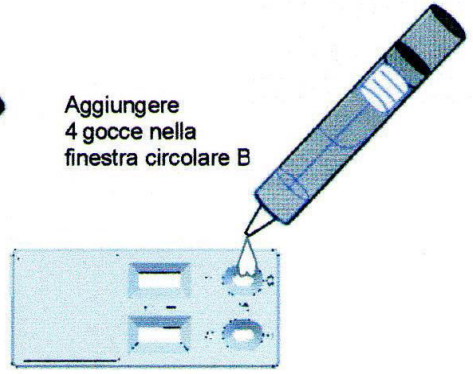


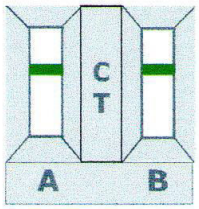
(5)

CALPREST
Card semiquantitativo

INTERPRETAZIONE DEI RISULTATI (riferirsi all'illustrazione sotto)

NEGATIVO

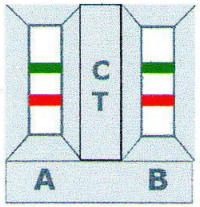
1.



A: Verde→Calprotectina 50 negativa
B: Verde→Calprotectina 200 negativa

POSITIVO

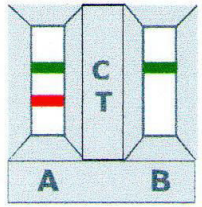
2.



A: Verde-Rosso→Calprotectina 50 positiva
B: Verde-Rosso→Calprotectina 200 positiva

POSITIVO

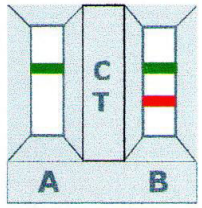
3.



A: Verde-Rosso→Calprotectina 50 positiva
B: Verde→Calprotectina 200 negativa

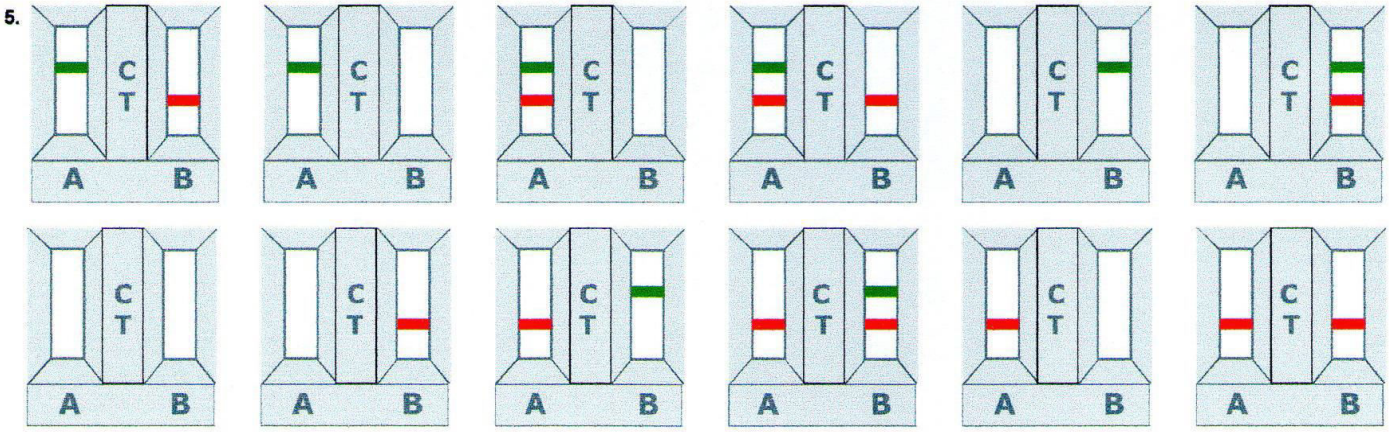
INVALIDO

4.



INVALIDO

5.



http://www.meridianhealthcare.it/wp-content/uploads/2014/05/Calprotectina-Flyer.pdf

http://www.meridianhealthcare.it/wp-content/uploads/2014/05/Calprotectina-ITA.pdf

Inflamm Bowel Dis. 2017 Jun 20. doi: 10.1097/MIB.0000000000001173. [Epub ahead of print]

Noninvasive Fecal Immunochemical Testing and Fecal Calprotectin Predict Mucosal Healing in Inflammatory Bowel Disease: A Prospective Cohort Study.

Ma C[1], Lumb R, Walker EV, Foshaug RR, Dang TT, Verma S, Huang VW, Kroeker KI, Wong K, Dieleman LA, Fedorak RN, Halloran BP.

Author information

Abstract

BACKGROUND: The noninvasive biomarkers fecal immunochemical testing (FIT) and fecal calprotectin (FCP) are sensitive for prediction of mucosal inflammation in inflammatory bowel disease. However, neither test has yet been shown to independently and accurately predict mucosal healing (MH). We aimed to assess the specificity of noninvasive FIT and FCP for MH prediction.

METHODS: In this prospective cohort study of adult inflammatory bowel disease outpatients presenting for colonoscopy, stool samples for FIT and FCP were collected 48 hours before endoscopy. Using MH defined by Simple Endoscopic Score for Crohn's disease (SES-CD = 0), Rutgeert's score (i0), and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS = 3), receiver operator characteristic curves were plotted, and sensitivity, specificity, positive and negative predictive values, and areas under the curve were calculated. Multivariate logistic regression analysis was used to develop a clinical model for noninvasively predicting MH.

RESULTS: Eighty patients (40 Crohn's disease and 40 ulcerative colitis) were enrolled. The specificities of FIT <100 ng/mL and FCP <250 µg/g for MH were 0.57 (95% confidence interval, 0.38-0.74) and 0.77 (0.57-0.89), respectively. Positive predictive values for MH for FIT <100 ng/mL and FCP <250 µg/g were 0.78 (0.64-0.87) and 0.77 (0.58-0.90), respectively. In multivariate modeling, combining FIT, FCP, and clinical symptomatic remission improved specificity for MH to 0.90 (0.72-0.97) with positive predictive values of 0.84 (0.60-0.96). Areas under the curve for FIT was higher for patients with ulcerative colitis (0.88) than for patients with Crohn's disease (0.69, P = 0.05).

CONCLUSIONS: FIT and FCP have similar performance characteristics for identifying MH. Combined, low FIT, low FCP, and clinical remission are specific for MH.

https://www.ncbi.nlm.nih.gov/pubmed/28644184

frontiers in Pediatrics

ORIGINAL RESEARCH
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Impact of Fecal Calprotectin Measurement on Decision-making in Children with Inflammatory Bowel Disease

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Background: The use of fecal calprotectin (FCal) as a marker of intestinal inflammation, in the management of inflammatory bowel disease (IBD) is increasing. The aim of this study was to examine the impact of FCal measurements on decision-making and clinical care of children with IBD.

Materials and methods: In a retrospective cohort study, FCal, clinical activity indices, and blood markers were measured in children with established diagnoses of IBD. Pearson correlation coefficient analysis was performed to examine association between FCal and other markers. Decisions based on FCal measurements were prospectively documented and participants were evaluated 3–6 months later.

Results: A total of 115 fecal samples were collected from 77 children with IBD [median age 14, interquartile range (IQR) 11–15.6 years, 42 females, 37 with Crohn's disease]. FCal positively correlated with clinical activity indices ($r = 0.481$, $P < 0.05$) and erythrocyte sedimentation rate ($r = 0.40$, $P < 0.05$) and negatively correlated with hemoglobin ($r = -0.40$, $P < 0.05$). Sixty four out of 74 (86%) positive FCal measurements (≥250 μg/g of stools) resulted in treatment escalation with subsequent significant clinical improvement while in the FCal negative group, 34 out of 41 (83%) measurements resulted in no change in treatment and were associated with remission on follow-up.

Conclusion: Based on high FCal, the majority of children had treatment escalation that resulted in clinical improvement. FCal measurements were useful and reliable in decision-making and clinical care of children with IBD.

OPEN ACCESS

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http://journal.frontiersin.org/article/10.3389/fped.2017.00007/full

CALPREST/LACTOFERRINA

Immunocromatografia a flusso laterale (qualitativo)

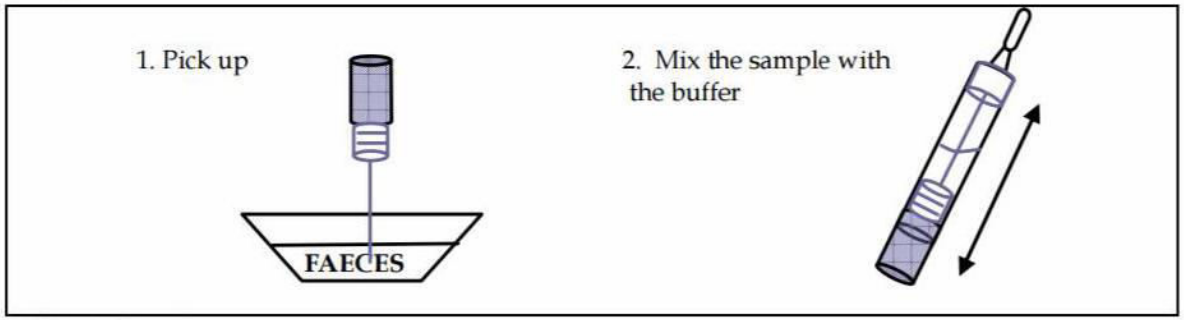
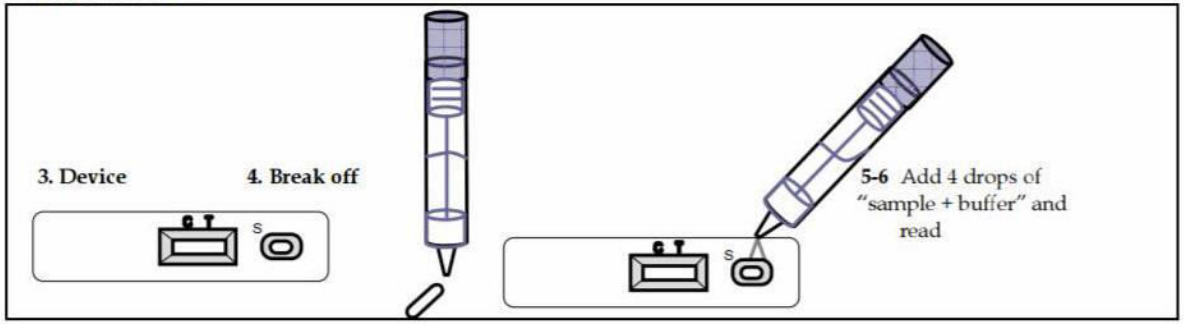
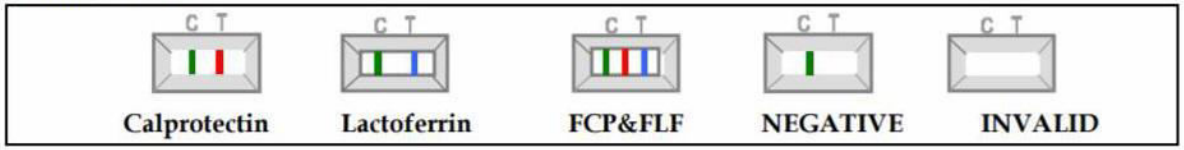


Illustration 2



INTERPRETAZIONE DEI RISULTATI

Illustration 3



http://www.iamconsultingsrl.it/wp-content/uploads/2013/12/Calpro-Lacto.pdf

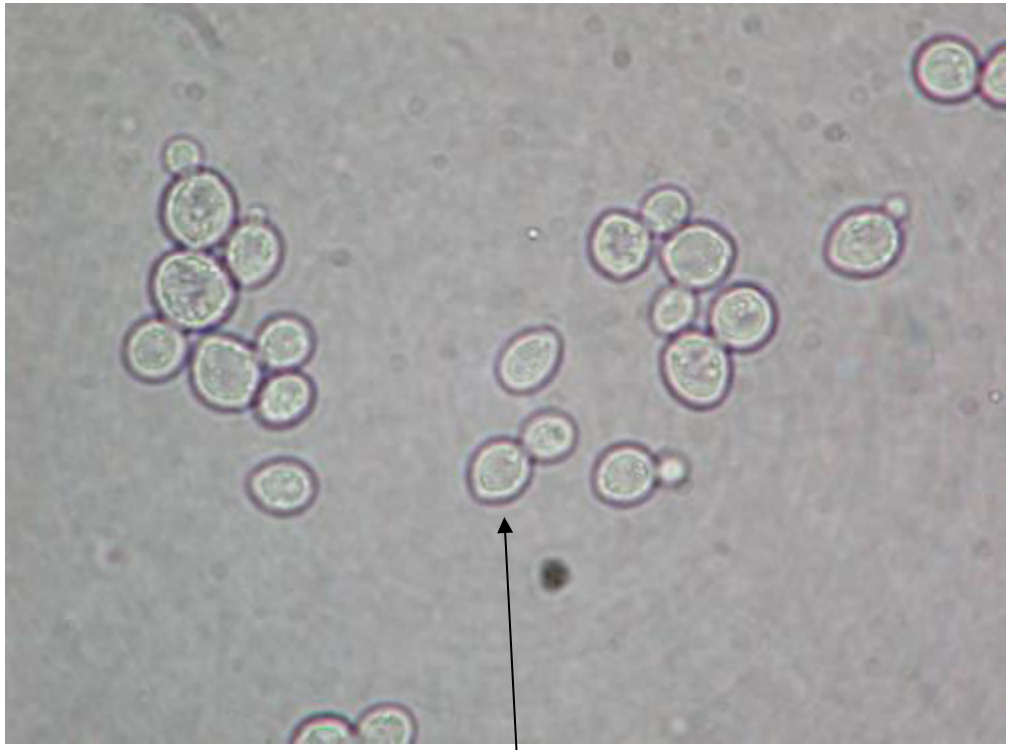
Lactoferrina proteina legante il ferro presente come "scorta" nei granuli dei neutrofili.

La presenza nelle feci di Calprotectina, Lactoferrina, leucociti e sangue occulto suggerisce una **intensa reazione infiammatoria intestinale**.

Le indicazioni cliniche suggeriscono l'**uso di questo test come verifica della infiammazione intestinale**, delle infezioni batteriche, delle infezioni parassitarie e per il **monitoraggio dello stato nel Morbo di Crohn e Rettocolite ulcerosa**.

Come per la Calprotectina è possibile anche il **dosaggio della Lactoferrina con tecnica immunoenzimatica**.

Anticorpi anti-Saccharomyces Cerevisiae (ASCA)



- Nella parete cellulare del **Saccharomyces Cerevisiae** è presente il **Mannano** (fosfopeptide contenente mannosio).
  Sembra che nelle **MICI** (**soprattutto Crohn**) il mannano sicomporti da antigene stimolando la produzione di anticorpi IgA e IgG.

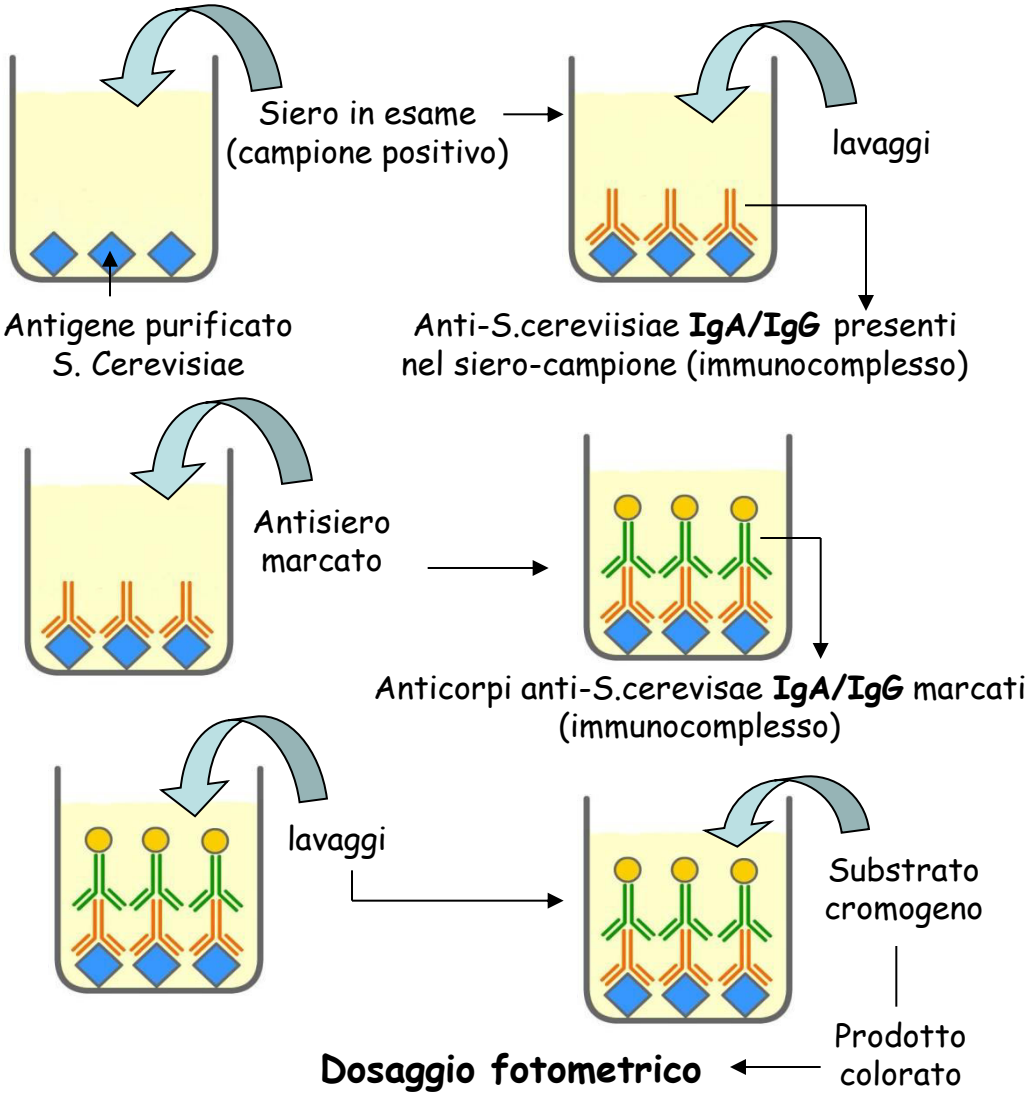
- Con il test **ASCA (Anti-Saccharomyces Cerevisiae Antibody)** si indaga sulla presenza di questo tipo di anticorpi.

ASCA IgA/IgG (immunoenzimatico)

- Presenza di **ASCA** IgG o IgA è **significativa nella diagnosi del Morbo di Crohn** con incidenza del 60-70%.
- **Presenza** di **ASCA sia IgG che IgA** sembra **indicativa** al 90-100% del Morbo di **Crohn**.
- Tutte le probabili IBD dovrebbero essere esaminate per gli ASCA.
- La loro presenza può essere **utile per la diagnosi differenziale del Morbo di Crohn rispetto alla Colite Ulcerosa**.
- Positività più **rara** anche nella **Celiachia**.
- La presenza degli ASCA sembra essere **indice di predisposizione genetica**.

Valori di riferimento:

- **ASCA IgA** valori di cut-off **7-10 U/ml**
- **ASCA IgG** valori di cut-off **10-15 U/ml**



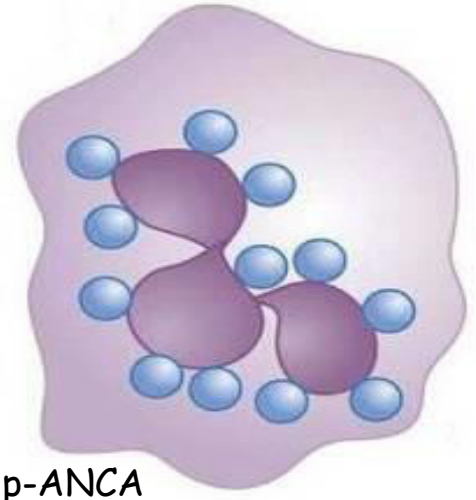
Anticorpi anti-Citoplasma dei Neutrofili (ANCA)

- **ANCA** autoanticorpi contro le proteine contenute nei lisosomi dei neutrofili e dei monociti.
  Antigeni bersaglio ANCA più importanti sono:
  -- **Proteinasi 3** (PR3)
  -- **Mieloperossidasi** (MPO).

- ANCA **anti-PR3** (**c-ANCA**) e **anti-MPO** (**p-ANCA**) **strettamente alle Vasculiti ANCA-associate**.

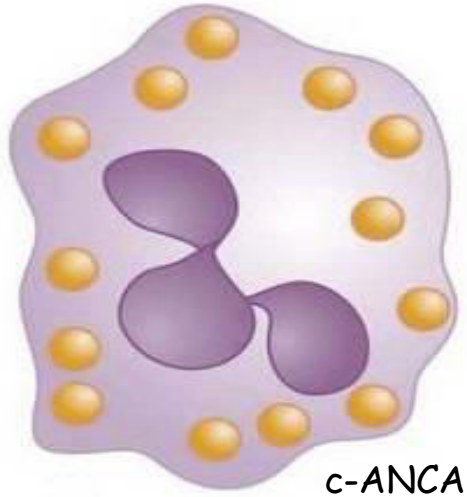
- **ANCA presenti anche nel 50-70% dei pazienti con Rettocolite Ulcerosa** e **10-30%** di pazienti affetti da **Crohn** e può essere così elemento di diagnosi.

- Presenti più raramente in altre patologie gastro-intestinali (**celiachia**)



p-ANCA

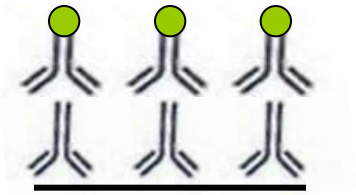
Leucociti Neutrofili



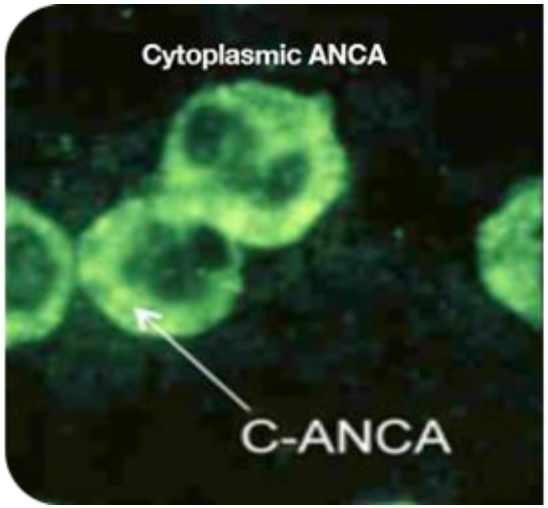
c-ANCA

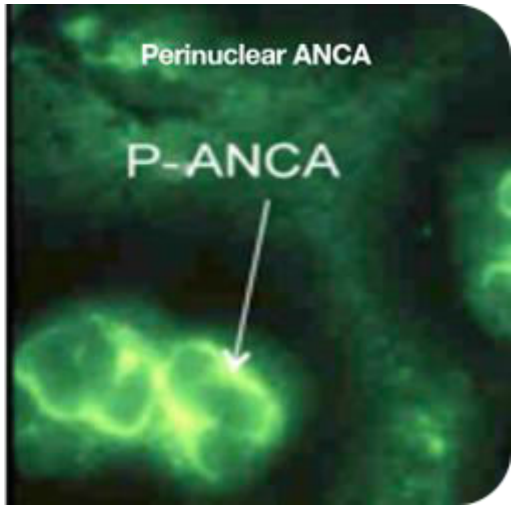
Anticorpi anti-Citoplasma dei Neutrofili (ANCA)
Immunofluorescenza indiretta

Microscopio fluorescenza



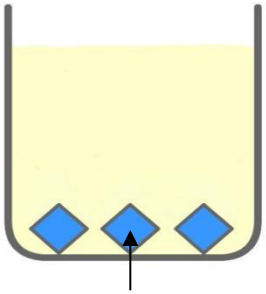
Granulociti fissati in etanolo o formalina





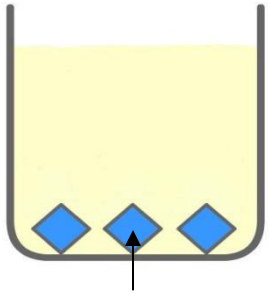
Valori di normalità **inf. 1/20**

Anticorpi anti-Citoplasma dei Neutrofili (ANCA)
Immunoenzimatico



PR3 umana da neutrofili purificata

c-ANCA
Cut-off **5-8 U/ml**



MPO umana da neutrofili purificata

p-ANCA
Cut-off **5-8 U/ml**

Biomed Rep. 2017 Apr;6(4):401-410. doi: 10.3892/br.2017.860. Epub 2017 Feb 17.

Serologic testing of a panel of five antibodies in inflammatory bowel diseases: Diagnostic value and correlation with disease phenotype.

Wang ZZ[1], Shi K[2], Peng J[1].

Author information

Abstract

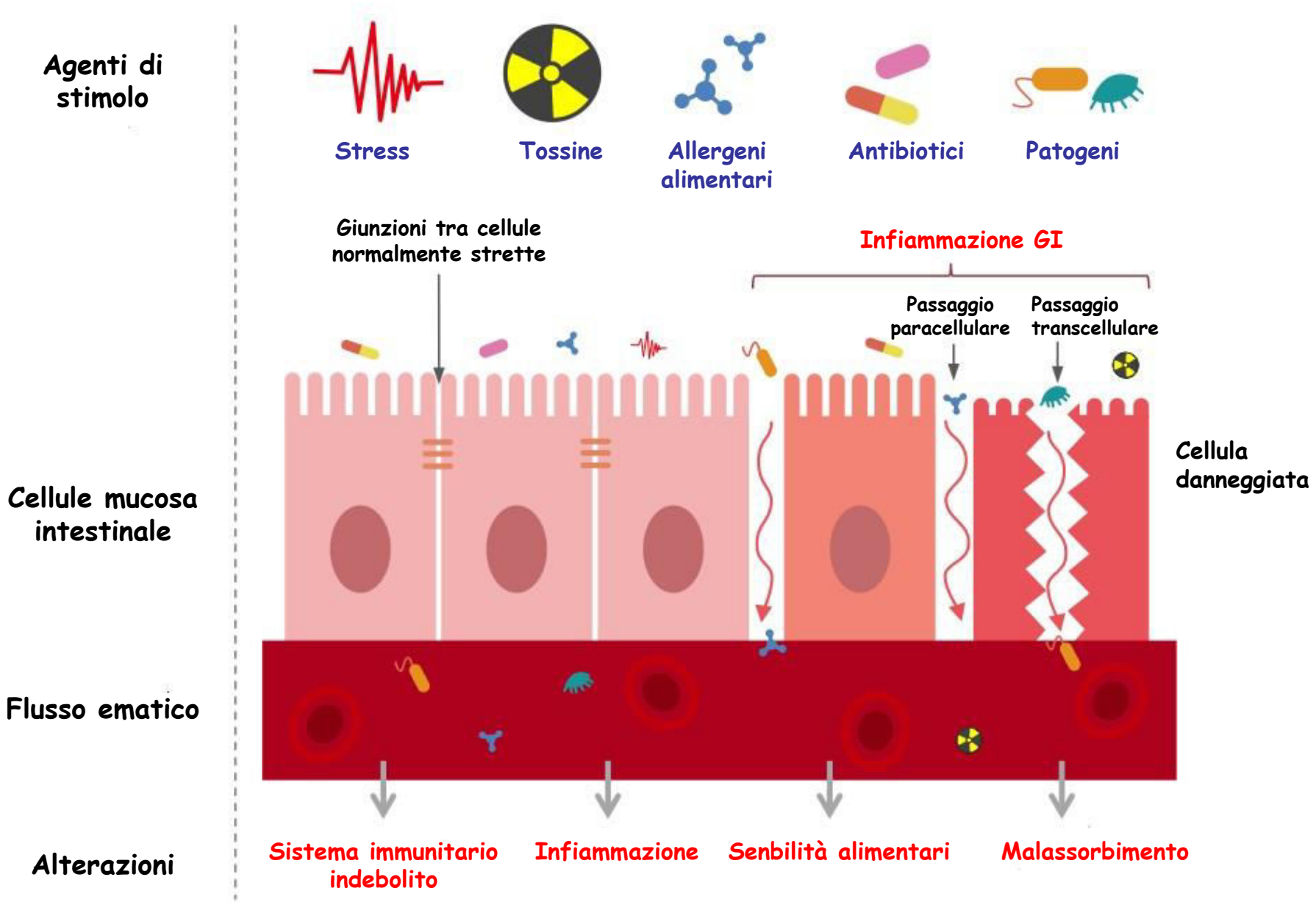
The aim of the present study was to evaluate the diagnostic value of five serological antibodies, perinuclear antineutrophil cytoplasmic antibody (pANCA), anti-*Saccharomyces cerevisiae* antibodies [ASCA; ASCA-immunoglobulin (IgG)and ASCA-IgA], *Escherichia coli* outer membrane porin C antibody (anti-OmpC) and CBir1 flagellin antibody for detection in inflammatory bowel diseases. Whether the antibody status correlated with the disease phenotype was also evaluated. Sera from 71 patients with Crohn's disease (CD), 41 patients with ulcerative colitis (UC), 78 patients with other gastrointestinal diseases and 31 healthy control subjects were investigated. Clinical data were gathered at the time of serum sampling and enzyme-linked immunosorbent assay was used to determine titers of the above mentioned five antibodies. The pANCA test exhibited a sensitivity of 53.7% for UC and the ASCA test had a sensitivity of 66.2% for CD. The prevalence of anti-OmpC was significantly higher in CD than in intestinal tuberculosis (TB), indicating that anti-OmpC may be a serologic marker distinguishing CD from TB. The $pANCA^+$/ASCA- exhibited the best specificity for differentiating between CD and UC. In UC, the presence of pANCA was greater in the patients with moderate to severe activity than in those with mild activity. ASCA was more positive in ileal CD. Furthermore, positive ASCA-IgG or anti-OmpC implied that complicated CD and pANCA was associated with colonic CD. Seropositivity of anti-CBir1 was lowest in colonic CD.

KEYWORDS: CBir1 flagellin antibody; Crohn's disease; anti-Saccharomyces cerevisiae antibodies; anti-outer membrane porin C; inflammatory bowel disease; perinuclear antineutrophil cytoplasmic antibody; serological antibodies; ulcerative colitis

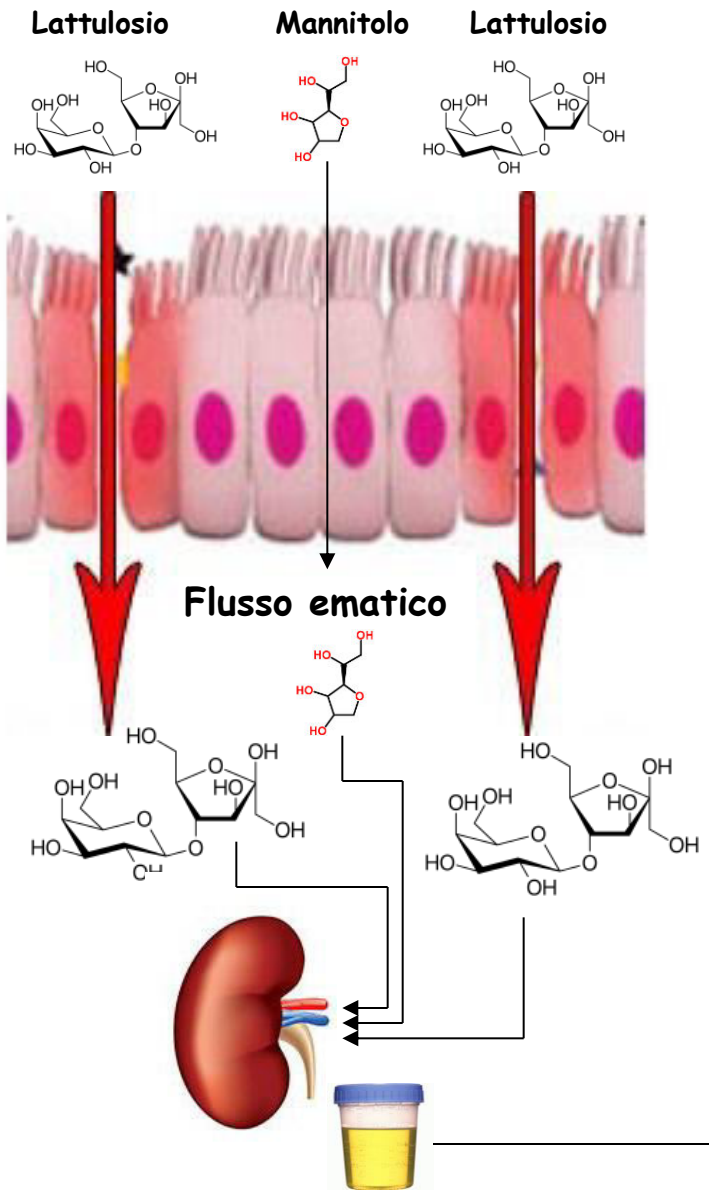
PMID: 28413638 PMCID: PMC5374894 DOI: 10.3892/br.2017.860

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5374894/

PERMEABILITA' INTESTINALE (Leaky Gut)



TEST DI PERMEABILITA' INTESTINALE
(Rapporto Lattulosio/Mannitolo)



- **Test diretto più comune per una Leaky Gut** in quanto utilizza il **Lattulosio** con una grossa molecola e il **Mannitolo** con una piccola per cui normalmente il Lattulosio viene assorbito soltanto per l'1% mentre il Mannitolo per circa il 14%.
- Essendo zuccheri non metabolizzabili si ritroveranno escreti nelle urine.

- Dopo aver fatto osservare alcune precauzioni, al paziente vengono somministrati 5 gr. di Lattulosio e 1 gr. di Mannitolo.
- Dopo **6 ore** si dosano, in un campione di urine dello stesso paziente, questi due composti.

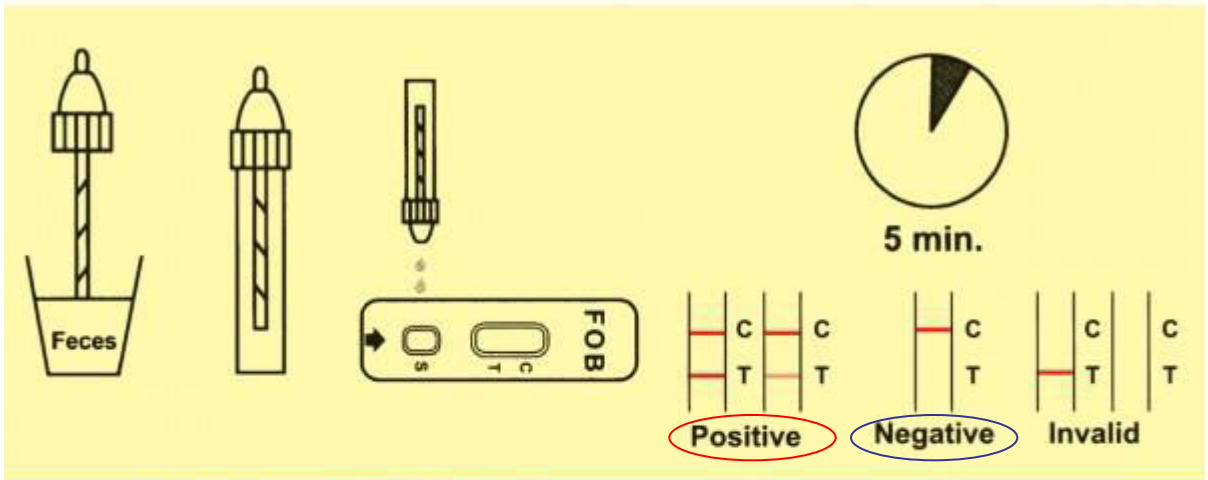
- Il **rapporto Lattulosio/Mannitolo deve essere inferiore a 0.03** visto che in un intestino sano passeranno nel flusso ematico e saranno escrete solo le molecole di mannitolo.

- La **presenza di molecole di Lattulosio** (più grandi) **nelle urine è indicativa di una Leaky Gut**

FOB (Qualitativo/Semiquantitativo)

Sangue Occulto Fecale

Immunocromatografia a flusso laterale (dispositivo CARD)



Zona Campione

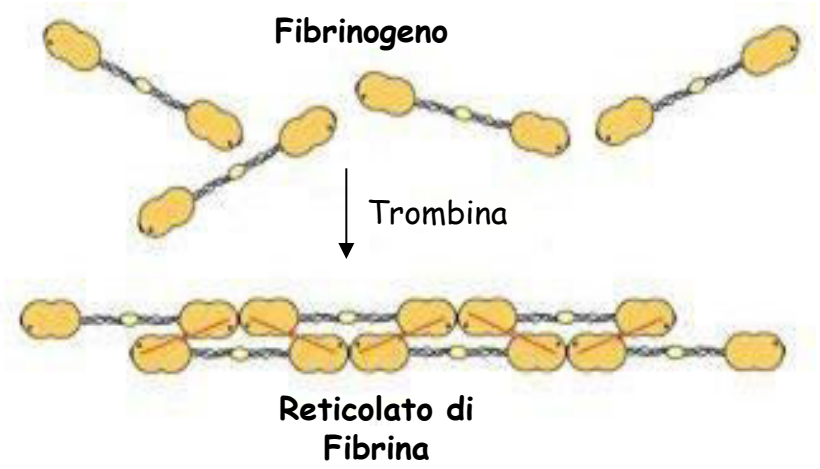
Zona Coniugato

Zona Lettura

http://www.medicalbabilon.com/lang-en/diagnostics/312-test-fob-sangue-occulto-nelle-feci-conf-25-test.html

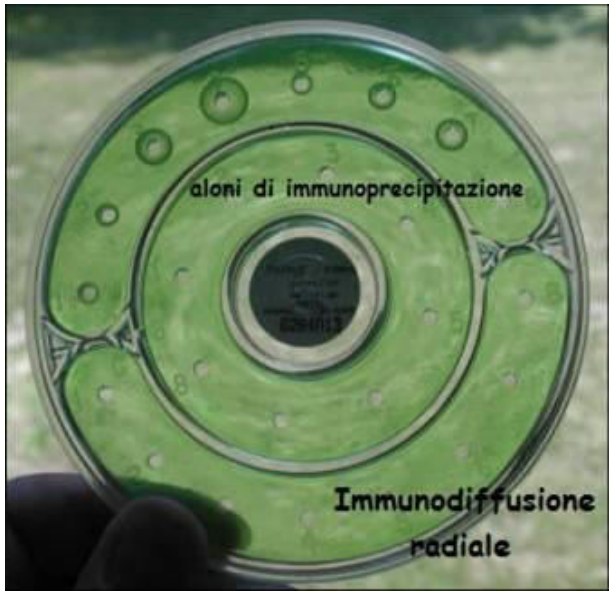
FIBRINOGENO

- **Fattore I** della coagulazione
- **Glicoproteina** sintetizzata dal fegato
- Come la PCR aumenta durante al **fase acuta infiammatoria.**



Viene dosato con metodica coagulativa, immunoturbidimetrica e in immunodiffusione radiale

Valori normali 150-430 mg/dl



Oltre che nelle MICI il **Fibrinogeno aumenta** in:
- Malattie cardiovascolari
- Infarto miocardico, ictus e angina pectoris
- Gravidanza
- Reumatismi articolari acuti
- Ascessi e peritoniti
- Altre patologie infiammatorie

Diminuzione:
- Epatopatie gravi
- Deficit ereditari
- Emorraggie

BMC Neurol. 2017 May 19;17(1):101. doi: 10.1186/s12883-017-0865-7.

Association of fibrinogen level with early neurological deterioration among acute ischemic stroke patients with diabetes.

Lee SJ[1], Hong JM[1], Lee SE[1], Kang DR[2], Ovbiagele B[3], Demchuk AM[4], Lee JS[5].

Author information

Abstract

BACKGROUND: Diabetes mellitus (DM) is a risk factor for early neurological deterioration (END) in acute ischemic stroke. The prothrombotic protein fibrinogen is frequently elevated in patients with diabetes, and may be associated with poorer prognoses. We evaluated whether fibrinogen is associated with END in patients with diabetes after acute ischemic stroke.

METHODS: We included 3814 patients from a single hospital database admitted within 72 h of onset of ischemic stroke. END was defined as an increase in the National Institutes of Health Stroke Scale (NIHSS) ≥2 within 7 days post-admission. In the total population (END, n = 661; non-END, n = 3153), univariate and multivariate analyses were performed to assess fibrinogen as an independent predictor for END. We then performed propensity score matching and univariate analyses for DM (END, n = 261; non-END, n = 522) and non-DM populations (END, n = 399; non-END, n = 798). Multiple logistic analyses were performed after matching for fibrinogen as a risk factor in each subgroup.

RESULTS: Fibrinogen levels were higher in the END group than in the non-END group (367 ± 156 mg/dL vs. 347 ± 122 mg/dL, p = 0.002), though they were not associated with END in logistic regression analyses. Fibrinogen levels were found to be an independent predictor for END, but only in the DM population (fibrinogen levels 300-599 mg/dL, odds ratio: 1.618, 95% confidence interval: 1.037-2.525, p = 0.034, fibrinogen levels ≥600 mg/dL, 2.575, 1.018-6.514, p = 0.046; non-DM population, p = 0.393). The diabetes-fibrinogen interaction for the entire cohort was p = 0.101.

CONCLUSIONS: Elevated fibrinogen is dose-dependently associated with END in patients with diabetes following acute ischemic stroke.

KEYWORDS: Cerebral infarction; Diabetes mellitus; Disease progression; Fibrinogen; Intracranial thrombosis

https://bmcneurol.biomedcentral.com/articles/10.1186/s12883-017-0865-7

- Livelli di fibrinogeno persistentemente alti rappresentano un segno di aumentata probabilità di infarto e ictus soprattutto nei pazienti diabetici.

- Partecipa attivamente alla aterosclerosi

MICI – Indagini di Laboratorio in età pediatrica

I livello

- VES, PCR e Fibrinogeno
- Emocromocitometrico
- Enzimi epatici e pancreatici
- Nutrizionali: Albumina, Ferro, Zinco, Proteine totali, Calcio, Fosfatasi alcalina e a1-antitripsina
- Microbiologia, Calprotectina e Sangue occulto fecale

II Livello

- ANCA
- ASCA

Giada

- Anni 8
- Frequenti episodi di diarrea muco-ematica con 2-3 evacuazioni/die
- Dolori addominali localizzati a livello periombelicale
- Calo ponderale e pallore congiuntivale
- Padre con RCU

Dalle indagini ematochimiche richieste dal pediatra di base si rileva:

- Emocromo: Hgb 9.2 g/dl con leucocitosi neutrofila
- Ves 18 mm, PCR 5.8 mg/l
- Calprotectina fecale 105 µg/g
- Permeabilità intestinale 0.15

In seguito a visita specialistica e ricovero:

- Peggioramento dei dati ematochimci
- pANCA (IIF) positivo 1/80 – ASCA Negativo
- Ecografia ed Endoscopia consistente

con diagnosi di **RCU**

Armando

- Anni 18
- Alvo stitico ed episodi di rettoraggia
- Presenza di escrescenze perianali
- Dolori addominali localizzati ipocondrio destro
- Calo ponderale e pallore congiuntivale
- Anamnesi familiare negativa

Dalle indagini ematochimiche richieste dal medico di base si rileva:

- Emocromo: Hgb 9.8 g/dl con evidente leucocitosi neutrofila
- Ves 68 mm, PCR 19.8 mg/l
- Calprotectina fecale 180 µg/g
- Permeabilità intestinale 0.10

In seguito a visita specialistica e ricovero:

- Peggioramento dei dati ematochimci
- ASCA IgG e IgA (elisa) aumentati – pANCA negativo
- Endoscopia, colonscopia e istologia consistente

con diagnosi di **Crohn a localizzazione perianale**

MICI – Ricapitolando:

- Risultato della combinazione di: **Predisposizione genetica**, **Fattori ambientali**, **Immunità compromessa** e **fattori legati ad Alterazion del Microbiota intestinale**.
- **PCR** e **Calprotectina e Lactoferrina** rappresentano i **migliori marcatori**.
- **PCR** più efficace nel Crohn meno nella CU. Decremento indica buona risposta alla terapia.
- **Calprotectina fecale** efficiente nella **differenziale con IBS**; presenta una elevata **correlazione** con il grado istologico dei **danni alla mucosa**.
- Dosaggi elevati di **Calprotectina predittivi sulla comparsa dei sintomi**.
  Valori di **150 ug/g o superiori** è predittivo di **ricadute nei successivi 12-14 mesi**.
- Con **PCR > 20 mg/l** e **VES > 15 mm** significativa **probabilità di ricaduta**.

- La presenza di **ASCA IgG** o **IgA** è significativa per il **Morbo di Crohn**.
- La presenza di **ANCA** è significativa per la **Rettocolite Ulcerosa**.
- La **combinazione ASCA** e **p-ANCA** è più accurata nella **differenziazione Crohn/RCU**:
  - **ASCA positivo/p-Anca negativo tipica del Crohn** con sensibilità del 50-70%
  - **ASCA negativo/p-ANCA positivo tipica per RCU** con sensibilità del 40-65%
- **Alterazioni ematologiche**: Leucociti↑ Piastrine↑ Emoglobina e serie rossa↓
- **Alterazioni biochimiche**: VES↑ PCR↑ Albumina↓ Sideremia↓ Alfa1-glicoproteina acida↑ Proteine totali↓ Acido folico e vit. B12↓ Magnesio↓

The Gut Microbiota in Inflammatory Bowel Disease

Donal Sheehan, MB, Fergus Shanahan, MD, DSc*

KEYWORDS

• Ulcerative colitis • Crohn's disease • Microbiota • Fecal microbial transplantation
• Inflammatory bowel disease

KEY POINTS

- Environmental factors that shape the composition and function of the microbiota are maximally active during the earliest perinatal and postnatal phase of life.
- The neonatal and infant microbiota shapes the development and maturation of the immune system.
- Most of the genetic risk factors for inflammatory bowel disease code for proteins that sense or regulate the host response to the microbiota.
- The molecular mechanisms by which genes, microbes, and the immune system interact in the pathogenesis of inflammatory bowel disease are becoming clarified.
- Strategies for manipulating the microbiota have been remarkably effective in experimental animals but attempts to translate these to the human context have been resoundingly disappointing.

http://www.sciencedirect.com/science/article/pii/S0889855316300899

INTRODUCTION

Therapeutic strategies for inflammatory bowel disease (IBD) have increased over the past decade, but considerable unmet needs remain. Increasingly, patients seek safer, long-term options and alternatives to immunomodulatory and immunosuppressive drugs. The prospect of modulating the microbiota in both Crohn's disease and ulcerative colitis is conceptually appealing and is based on sound rationale.[1–4] However,

Conflict of Interest Statement: F. Shanahan is a founder shareholder in Atlantia Food Clinical Trials and Alimentary Health Ltd. He is director of the *APC Microbiome Institute*, a research center funded in part by Science Foundation Ireland (APC/SFI/12/RC/2273) and which is/has recently been in receipt of research grants from Abvie, Alimentary Health, Cremo, Danone, Janssen, Friesland Campina, General Mills, Kerry, Mead Johnson, Nutricia, 4D pharma and Second Genome, and Sigmoid pharma.

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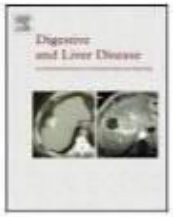
gastro.theclinics.com

Digestive and Liver Disease 44 (2012) 185–194

Contents lists available at SciVerse ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld



Review Article

Diet and risk of inflammatory bowel disease

Vibeke Andersen[a,b,*], Anja Olsen[c], Franck Carbonnel[d], Anne Tjønneland[c], Ulla Vogel[e,f]

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[d] Liver and Gastrointestinal Unit, University Hospitals of Paris Sud in Bictre, Assistance Publique Hpitaux de Paris, University Paris Sud, France
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Keywords:
Animal protein
Crohn's disease
Fish
Food
Intestinal inflammation
Meat
Ulcerative colitis

ABSTRACT

Background: A better understanding of the environmental factors leading to inflammatory bowel disease should help to prevent occurrence of the disease and its relapses.
Aim: To review current knowledge on dietary risk factors for inflammatory bowel disease.
Methods: The PubMed, Medline and Cochrane Library were searched for studies on diet and risk of inflammatory bowel disease.
Results: Established non-diet risk factors include family predisposition, smoking, appendectomy, and antibiotics. Retrospective case–control studies are encumbered with methodological problems. Prospective studies on European cohorts, mainly including middle-aged adults, suggest that a diet high in protein from meat and fish is associated with a higher risk of inflammatory bowel disease. Intake of the n-6 polyunsaturated fatty acid linoleic acid may confer risk of ulcerative colitis, whereas n-3 polyunsaturated fatty acids may be protective. No effect was found of intake of dietary fibres, sugar, macronutrients, total energy, vitamin C, D, E, Carotene, or Retinol (vitamin A) on risk of ulcerative colitis. No prospective data was found on risk related to intake of fruits, vegetables or food microparticles (titanium dioxide and aluminium silicate).
Conclusions: A diet high in protein, particular animal protein, may be associated with increased risk of inflammatory bowel disease and relapses. N-6 polyunsaturated fatty acids may predispose to ulcerative colitis whilst n-3 polyunsaturated fatty acid may protect. These results should be confirmed in other countries and in younger subjects before dietary counselling is recommended in high risk subjects.

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PMCID: PMC3915038
NIHMSID: NIHMS533512

Long-term Intake of Dietary Fat and Risk of Ulcerative Colitis and Crohn's Disease

Ashwin N. Ananthakrishnan, M.D., M.P.H.,[1] Hamed Khalili, M.D.,[1] Gauree G. Konijeti, M.D., M.P.H.,[1] Leslie M. Higuchi, M.D., M.P.H.,[2] Punyanganie de Silva, M.B.B.S, M.R.C.P,[1] Charles S. Fuchs, M.D., M.P.H.,[3,4] Walter C. Willett, M.D., Dr.P.H.,[4,5] James M. Richter, M.D.,[1] and Andrew T. Chan, M.D., M.P.H.[1,4]

Introduction

Dietary fats influence intestinal inflammation and regulate mucosal immunity. Data on the association between dietary fat and risk of Crohn's disease (CD) and ulcerative colitis (UC) are limited and conflicting.

Methods

We conducted a prospective study of women enrolled in the Nurses' Health Study cohorts. Diet was prospectively ascertained every four years using a validated semi-quantitative food frequency questionnaire. Self-reported CD and UC were confirmed through medical record review. We examined the effect of energy-adjusted cumulative average total fat intake as well as specific types of fat and fatty acids on the risk of CD and UC using Cox proportional hazards models adjusting for potential confounders.

Results

Among 170,805 women, we confirmed 269 incident cases of CD (incidence 8/100,000 person-years) and 338 incident cases of UC (incidence 10/100,000 person-years) over 26 years and 3,317,338 person-years of follow-up. Cumulative energy-adjusted intake of total fat, saturated fats, unsaturated fats, n-6 and n-3 polyunsaturated fatty acids (PUFA) were not associated with risk of CD or UC. However, greater intake of long-chain n-3 PUFA was associated with a trend towards lower risk of UC (Hazard ratio (HR) 0.72, 95% CI 0.51 – 1.01). In contrast, high long-term intake of trans-unsaturated fatty acids was associated with a trend towards an increased incidence of UC (HR 1.34, 95% CI 0.94 – 1.92).

Conclusion

A high intake of dietary long-chain n-3 PUFA may be associated with a reduced risk of UC. In contrast, high intake of trans-unsaturated fats may be associated with an increased risk of UC.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3915038/

World Journal of Gastroenterology

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Published online 2016 Jan 21. doi: 10.3748/wjg.v22.i3.895
PMCID: PMC4716043

Diet and nutritional factors in inflammatory bowel diseases

Danuta Owczarek, Tomasz Rodacki, Renata Domagała-Rodacka, Dorota Cibor, and Tomasz Mach

Author information ► Article notes ► Copyright and License information ►

Abstract

Go to:

Inflammatory bowel disease (IBD) development is affected by complex interactions between environmental factors, changes in intestinal flora, various predisposing genetic properties and changes in the immune system. Dietary factors seem to play an underestimated role in the etiopathogenesis and course of the disease. However, research about food and IBD is conflicting. An excessive consumption of sugar, animal fat and linoleic acid is considered a risk factor for IBD development, whereas a high fiber diet and citrus fruit consumption may play a protective role. Also, appropriate nutrition in particular periods of the disease may facilitate achieving or prolonging remissions and most of all, improve the quality of life for patients. During disease exacerbation, a low fiber diet is recommended for most patients. In the remission time, an excessive consumption of alcohol and sulfur products may have a negative effect on the disease course. Attempts are also made at employing diets composed in detail in order to supplement IBD therapy. A diet with a modified carbohydrate composition, a semi-vegetarian diet and a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols are under investigation. Due to chronic inflammation as well as side effects of chronically used medications, patients with IBD are also at increased risk of nutritional factor deficiencies, including iron, calcium, vitamin D, vitamin B12, folic acid, zinc, magnesium and vitamin A. It should also be remembered that there is no single common diet suitable for all IBD patients; each of them is unique and dietary recommendations must be individually developed for each patient, depending on the course of the disease, past surgical procedures and type of pharmacotherapy.

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Role of Vitamin D in Inflammatory Bowel Disease.

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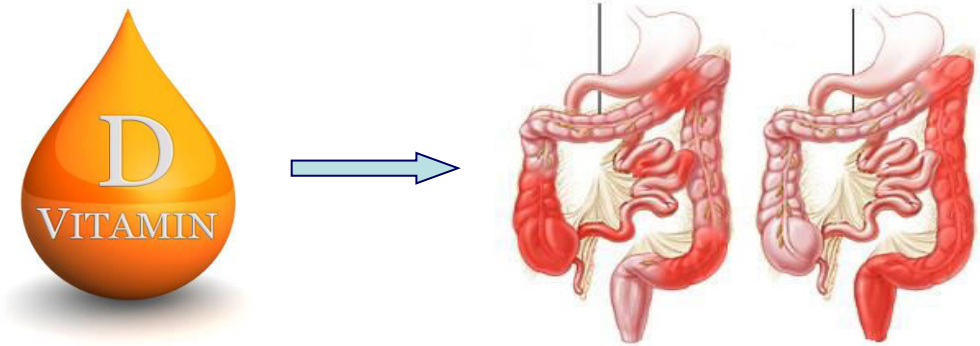
Abstract

Vitamin D is a secosteroid hormone that possesses immunomodulatory properties and has been demonstrated to potentially influence inflammatory bowel disease (IBD) pathogenesis and activity. Epidemiologic data have associated vitamin D deficiency with an increased risk of IBD, hospitalizations, surgery, and loss of response to biologic therapy. Conversely, IBD itself can lead to vitamin D deficiency. This bidirectional relationship between vitamin D and IBD suggests the need for monitoring and repletion of vitamin D, as needed, in the IBD patient. This review discusses the role of vitamin D in IBD and provides practical guidance on vitamin D repletion.

KEYWORDS: Crohn's disease; cholecalciferol; ergocalciferol; inflammatory bowel diseases; ulcerative colitis; vitamin D; vitamin D deficiency



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Review

Curcumin and Inflammatory Bowel Disease: Potential and Limits of Innovative Treatments

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Abstract: Curcumin belongs to the family of natural compounds collectively called curcuminoids and it possesses remarkable beneficial anti-oxidant, anti-inflammatory, anti-cancer, and neuroprotective properties. Moreover it is commonly assumed that curcumin has also been suggested as a remedy for digestive diseases such as inflammatory bowel diseases (IBD), a chronic immune disorder affecting the gastrointestinal tract and that can be divided in two major subgroups: Crohn's disease (CD) and Ulcerative Colitis (UC), depending mainly on the intestine tract affected by the inflammatory events. The chronic and intermittent nature of IBD imposes, where applicable, long-term treatments conducted in most of the cases combining different types of drugs. In more severe cases and where there has been no good response to the drugs, a surgery therapy is carried out. Currently, IBD-pharmacological treatments are generally not curative and often present serious side effects; for this reason, being known the relationship between nutrition and IBD, it is worthy of interesting the study and the development of new dietary strategy. The curcumin principal mechanism is the suppression of IBD inflammatory compounds (NF-κB) modulating immune response. This review summarizes literature data of curcumin as anti-inflammatory and anti-oxidant in IBD, trying to understand the different effects in CD e UC.

REVIEW

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Intestinal dysbiosis in inflammatory bowel disease

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Key words: dysbiosis, microbiota, inflammatory bowel disease, antibiotics, probiotics

The worldwide incidence of inflammatory bowel disease (IBD) is increasing. Abundant literature has suggested that an imbalance between harmful and protective bacteria or dysbiosis, of the intestine is largely responsible for the rising incidence of IBD. In this review, data supporting dysbiosis as a cause of IBD are presented. A comparison of the number of scientific publications in the US vs. Europe on intestinal dysbiosis and microbiota revealed the US scientific community has a lower level of interest in studying dysbiosis and microbiota compared the research community in Europe. The rising trend of antibiotic use in the US provides further evidence of the lack of concern for the effect of dysbiosis on human health. Further research to understand the causal relationship between dysbiosis and IBD are needed to better guide clinical practice in using probiotics.

antibodies has been used for refractory disease. Despite the advent of this new class of medications, however, end-stage inflammation remains the sole target. Novel therapies that target upstream inflammation, or aim to correct intestinal dysbiosis, may provide benefit in reducing complications for patients with IBD.

The worldwide incidence of IBD has increased over the past several years, especially in the rapidly developing countries in Asia.[3-5] Current theories suggest that IBD is a result of (i) innate genetic defects in the intestinal epithelial and mucosal barrier, which may contribute to bacterial translocation; (ii) microbial imbalance or dysbiosis, in the intestine and (iii) dysfunction in the intestinal inflammatory cascade, leading to an eventual pathologic proliferation of inflammatory cytokines.[6] The rising incidence of the IBD suggests that one, if not more, of these causative factors has gained strength over the past several years.

Intestinal dysbiosis has been linked to numerous gastrointes-

Immunopathogenesis of IBD: current state of the art

Heitor S. P. de Souza[1] and Claudio Fiocchi[2]

Abstract | IBD is a chronic inflammatory condition of the gastrointestinal tract encompassing two main clinical entities: Crohn's disease and ulcerative colitis. Although Crohn's disease and ulcerative colitis have historically been studied together because they share common features (such as symptoms, structural damage and therapy), it is now clear that they represent two distinct pathophysiological entities. Both Crohn's disease and ulcerative colitis are associated with multiple pathogenic factors including environmental changes, an array of susceptibility gene variants, a qualitatively and quantitatively abnormal gut microbiota and a broadly dysregulated immune response. In spite of this realization and the identification of seemingly pertinent environmental, genetic, microbial and immune factors, a full understanding of IBD pathogenesis is still out of reach and, consequently, treatment is far from optimal. An important reason for this unsatisfactory situation is the currently limited comprehension of what are the truly relevant components of IBD immunopathogenesis. This article will comprehensively review current knowledge of the classic immune components and will expand the concept of IBD immunopathogenesis to include various cells, mediators and pathways that have not been traditionally associated with disease mechanisms, but that profoundly affect the overall intestinal inflammatory process.

http://www.nature.com/nrgastro/journal/v13/n1/full/nrgastro.2015.186.html

During the past few decades, the main components believed to be responsible for Crohn's disease and ulcerative colitis have been identified: the environment, the genetic make-up, the gut microbiota and the immune response. Chronic inflammation is, ultimately, a dysregulated immune response, and therefore much of the investigation of IBD pathogenesis has been focused on immune abnormalities. The study of such abnormalities was initially concentrated on adaptive immunity and lately on innate immunity. With the realization that many of the relevant antigens were of microbial origin and that most nonimmune cells display active immunoregulatory functions, the investigation of IBD immunopathogenesis has widened to include these components. The discovery of the inflammasome, regulatory RNAs and damage-associated molecular patterns (DAMPs) has further expanded the number of factors involved in mediating IBD. Thus, immune events must be integrated with and interpreted in the context of a larger scenario in which the environment, genetics and the microbiota have equal, or perhaps even more important, roles in the overall pathogenesis of IBD. This topic will be comprehensively discussed in this Review by primarily emphasizing studies relevant to human IBD and referring to experimental and animal models as necessary for supportive evidence.

Evolutionary steps and epidemiology

Profound changes associated with human behaviour have been empirically blamed for the increased incidence of IBD[1]. Among various components of modern lifestyle[1,2], several have emerged as modifiers of systemic and intestinal immunity, such as alterations of the microbiota, antibiotics, diet, smoking and vitamin D. Risk of IBD markedly increases in children repeatedly exposed to antibiotics in early life[3] and in adults after an episode of acute gastroenteritis[4], events probably secondary to changes in the gut microbiota. Western-like diets also modify the composition and function of the microbiota, as do smoking and ubiquitous food additives[5,6]. Availability of vitamin D, an important regulator of mucosal immunity, depends not only on ingestion, but also on sunlight, and low sunlight exposure is a risk factor for Crohn's disease[7]. Another factor is lipolysaccharide, a ubiquitous bacterial product with potent immunoregulatory actions, and lipopolysaccharide levels are lower in house dust samples from children with IBD than from healthy controls[8].

Epidemiological evidence shows a clear correlation between the decrease in infectious diseases, lack of parasites, use of antibiotics, vaccinations and a general improvement in food, water and housing sanitary

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