

# Convegno Autismo Forum Consapevolezza. Formazione. Inclusione.

Latina, 25 Maggio 2018

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**U.O.A.D.U. Gastro-Epatologia**  
**Azienda Ospedaliera Universitaria Città della Salute e della  
Scienza di Torino**



# Sintomi Gastrointestinali e Autismo



Dolore  
addominale

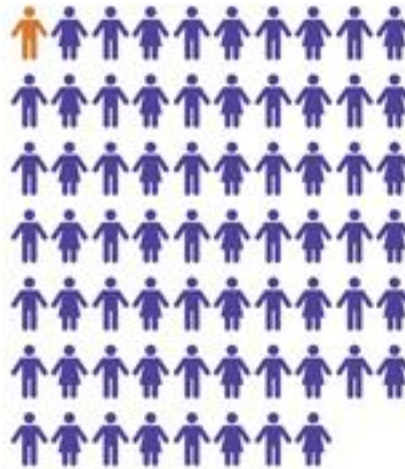
Stipsi/diarrea

Intolleranze  
alimentari



Refusso

## NUMBER OF CHILDREN IDENTIFIED WITH ASD



**1 in 68**



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention





# Prevalenza dei Sintomi Gastrointestinali

- In letteratura è riportata fra il **15 e il 91%** nei pazienti con età 1-18 anni
- Variabilità legata alla metodologia di approccio
- Pazienti con soglia del dolore più elevata
- Pazienti che non comunicano verbalmente
- Emerge però il concetto di possibile secondarietà del comportamento autistico



Andrea 11/05/99

### Come stai Andrea?

Non sto bene. Devo muovermi in continuazione.

Bisogna che assuma sempre delle posizioni per il dolore alla pancia.

Ho lo stimolo continuo ad andare in bagno, ho un dolore sordo inguinale.

Sono confuso e annebbiato, mi è difficile fare tutto.

### Cosa fai per il tuo malessere?

Mi isolo, ho bisogno di calma e di silenzio.

Mangerei sempre per alleviare il dolore all'addome.

Il male mi rende tutto insopportabile e mi devo muovere continuamente



Hans Asperger correlava influenza del cibo, stato nutrizionale e gastrointestinale e disturbo comportamentale

Coury DL et al 2012





# Anamnesi

1. Familiarità per malattie autoimmuni
2. Disturbi durante allattamento o svezzamento
3. Infezioni ORL frequenti, dermatiti, gastroenteriti
4. Evento infettivo acuto
5. Stipsi, dolore, diarrea
6. Disturbo del comportamento



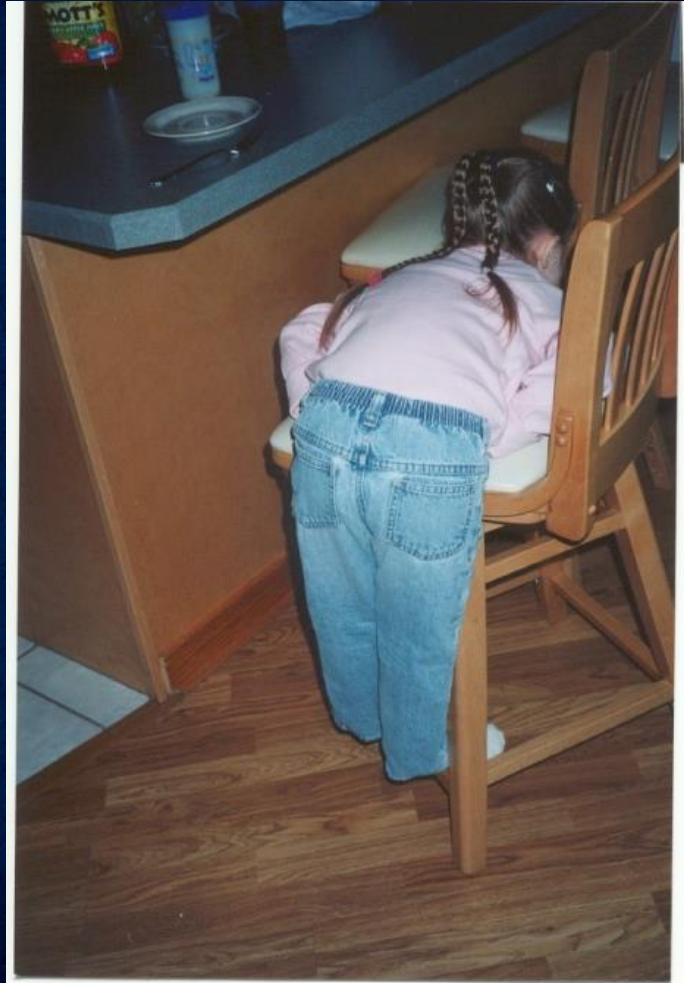
Dolore







Dolore





# Dolore



Dolore





Dolore



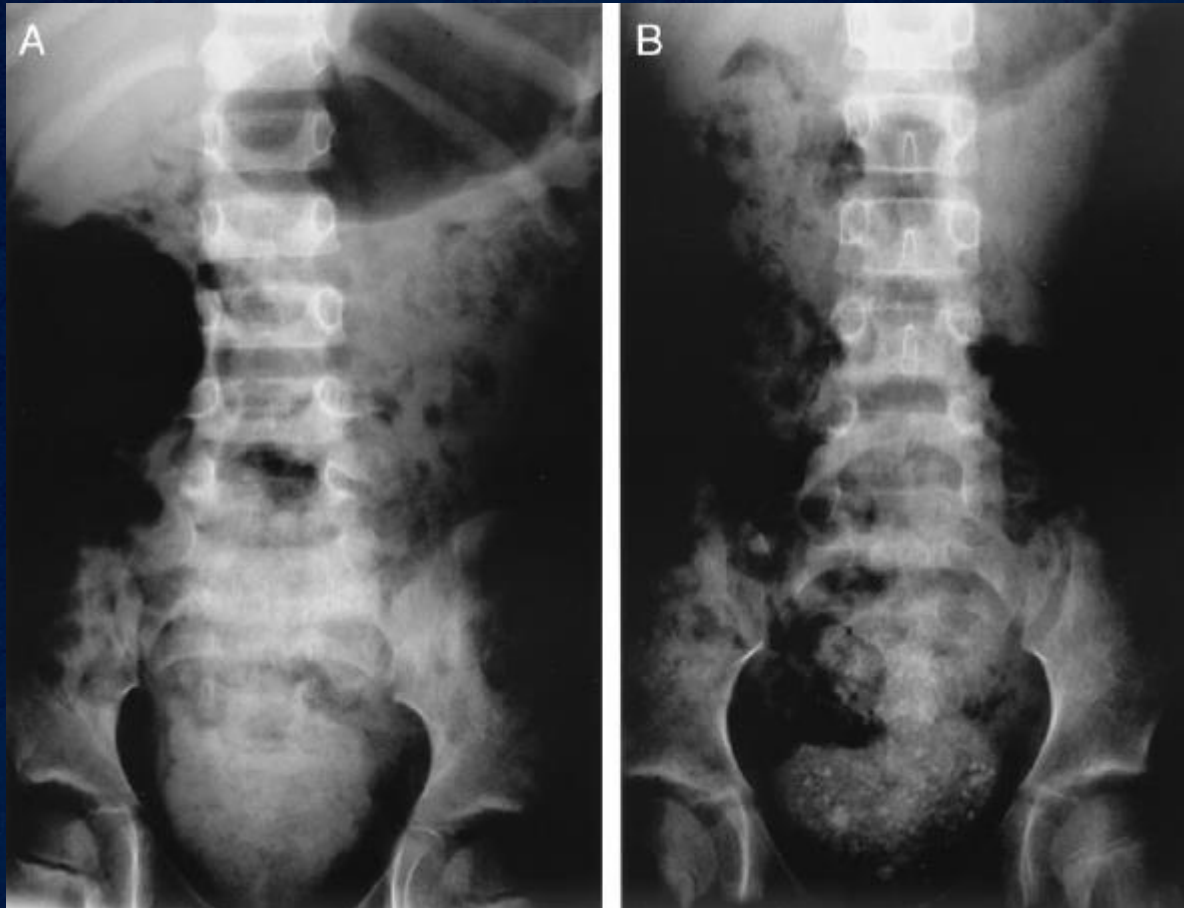




# Sforzo evacuativo/stipsi



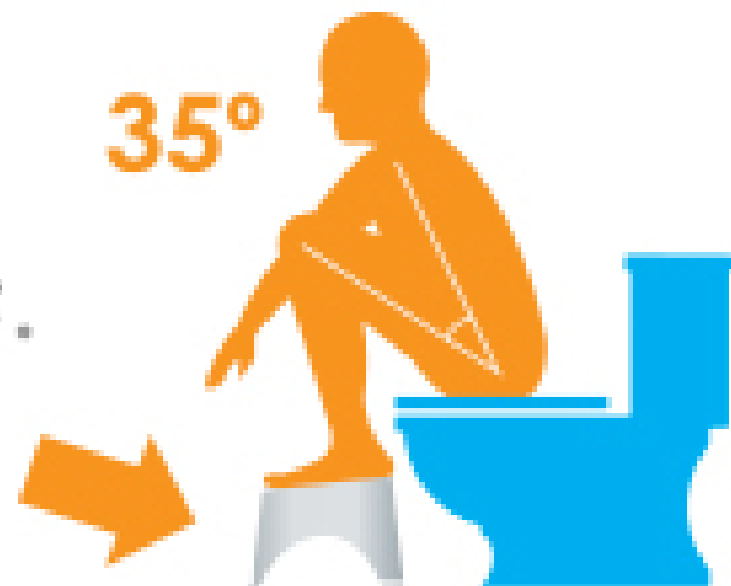
# Megarectto







*Vs.*



**UNHEALTHY**

**HEALTHY**

BATHROOM POSTURE

## Apparente autostimolazione





Reflusso







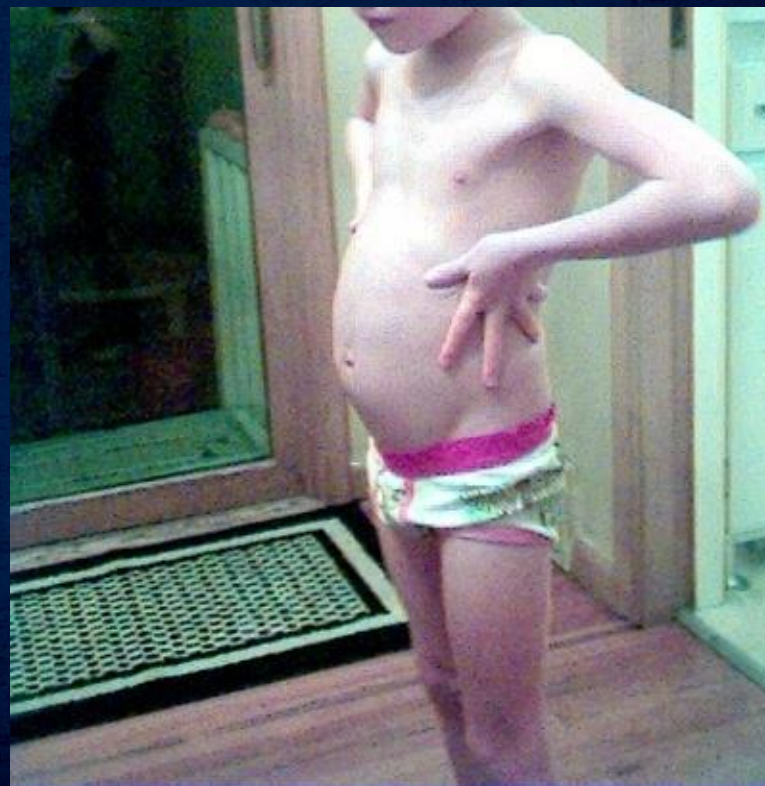








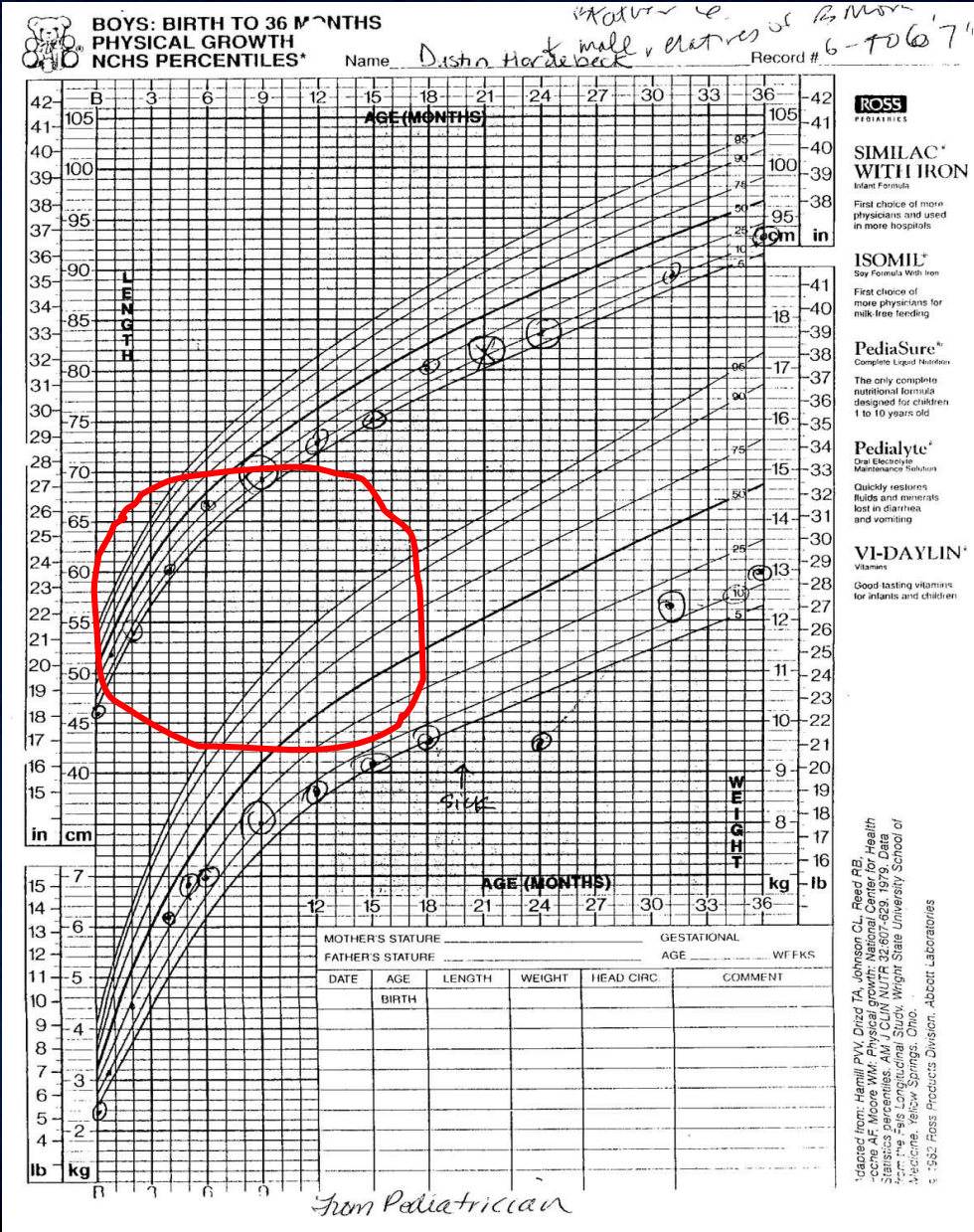
# Malassorbimento







# Ridotta crescita peso ed altezza



**ROSS PEDIATRICS**

**SIMILAC<sup>®</sup> WITH IRON**  
Infant Formula  
First choice of more physicians and used in more hospitals

**ISOMIL<sup>®</sup>**  
Soy Formula With Iron  
First choice of more physicians for milk free feeding

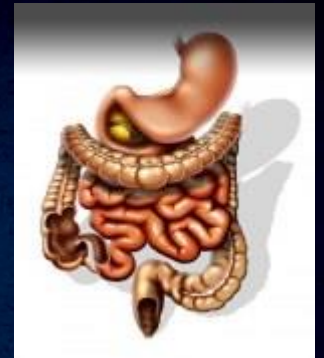
**PediaSure<sup>™</sup>**  
Complete Liquid Multivitamin  
The only complete nutritional formula designed for children 1 to 10 years old

**PediaLyte<sup>®</sup>**  
Oral Electrolyte Maintenance Solution  
Quickly restores fluids and minerals lost in diarrhea and vomiting

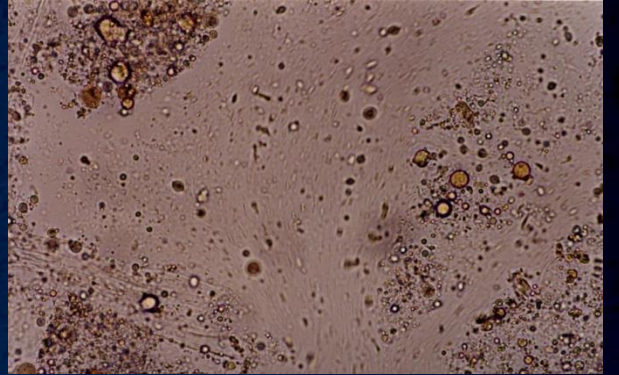
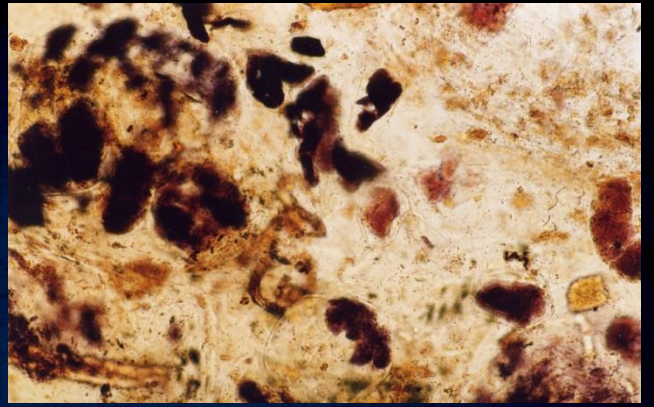
**VI-DAYLIN<sup>®</sup>**  
Vitamins  
Good-tasting vitamins for infants and children

Adapted from: Hamill PV, Dried TA, Johnson CL, Reed RB, Moore AF, Moore WK. Physical growth: National Center for Health Statistics percentiles. AM J CLIN NUTR 32:607-629, 1979. Data from the Fels Longitudinal Study, Wright State University School of Medicine, Yellow Springs, Ohio. © 1982 Ross Products Division, Abbott Laboratories





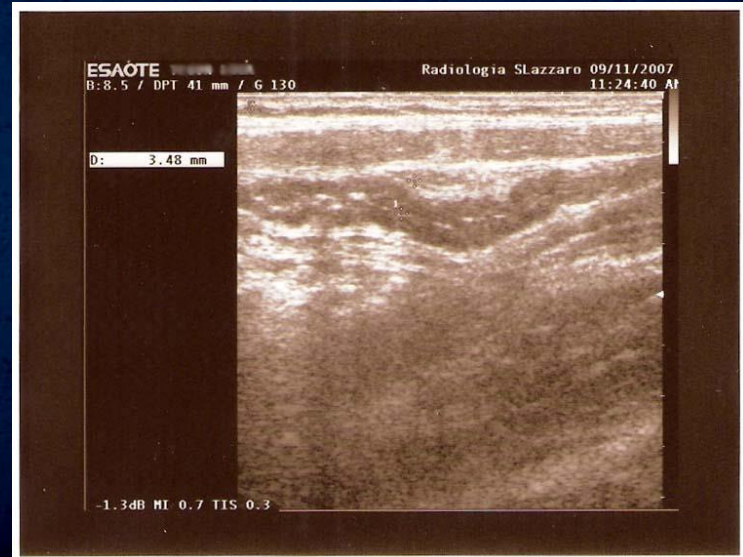








# Ecografia Intestinale





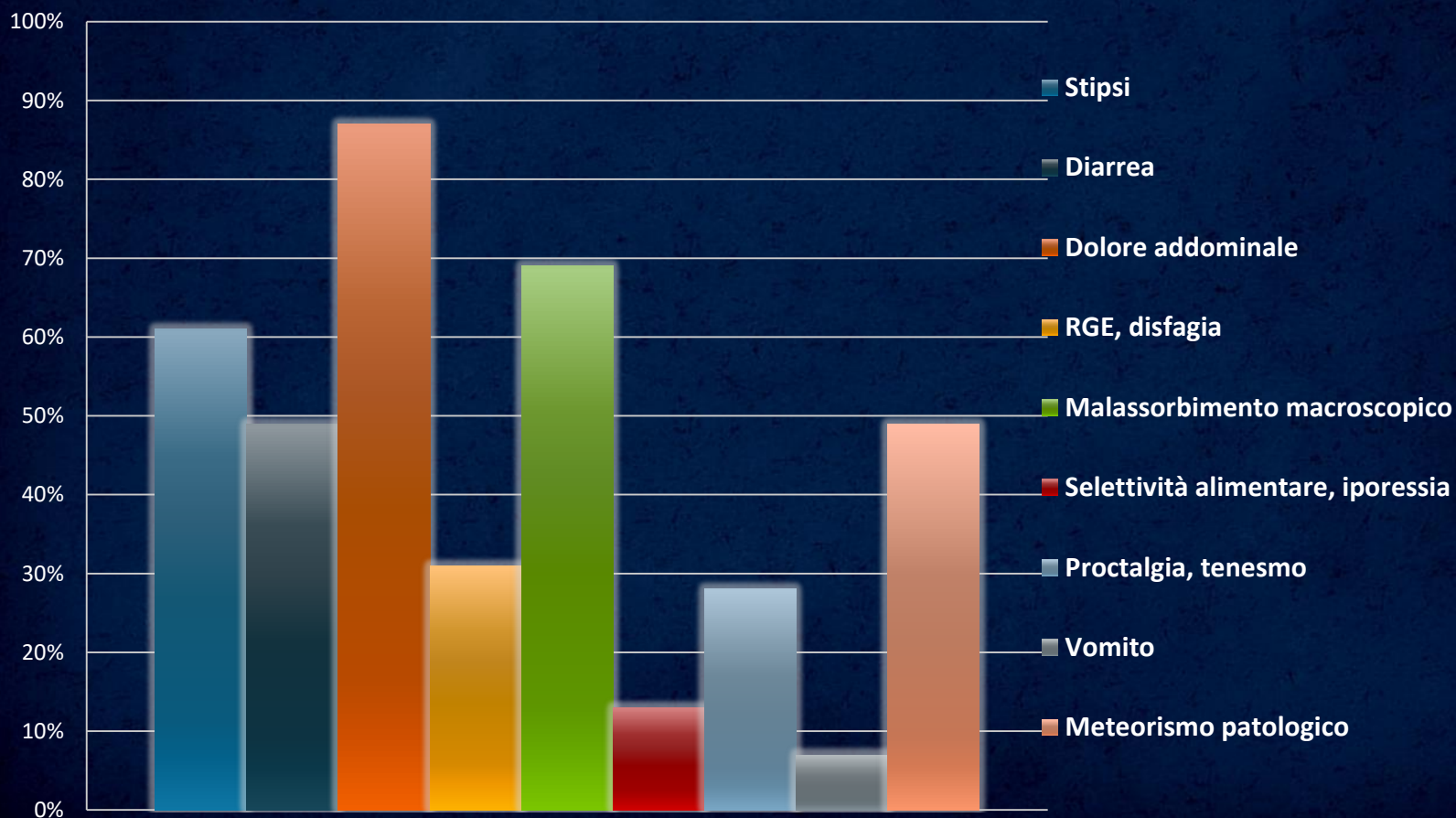
**1300 PAZIENTI:**



**450 PAZIENTI  
con esecuzione  
di EGDS e  
colonscopia.**

# Sintomi Gastrointestinali

## Prevalenza dei sintomi GEL



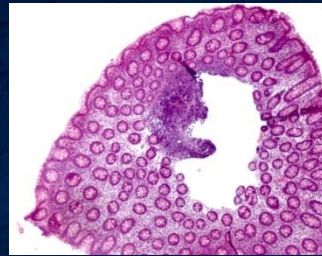
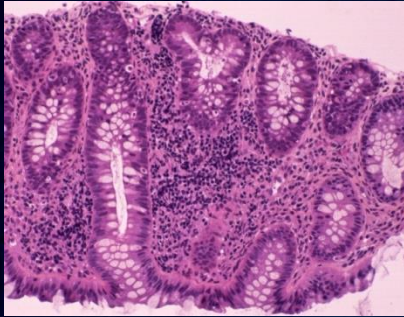


# Endoscopy

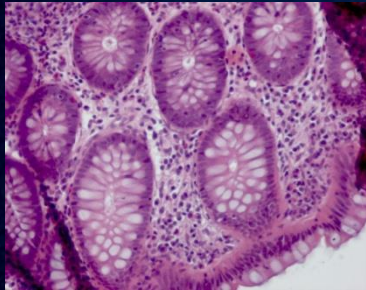




# Malattia infiammatoria cronica intestinale ad eccesso di eosinofili



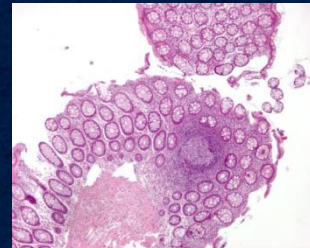
Colon dx



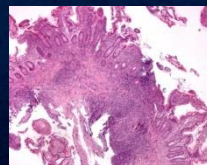
Colon sin



Colon Trasverso



Retto



Ileo Terminale



Serosa



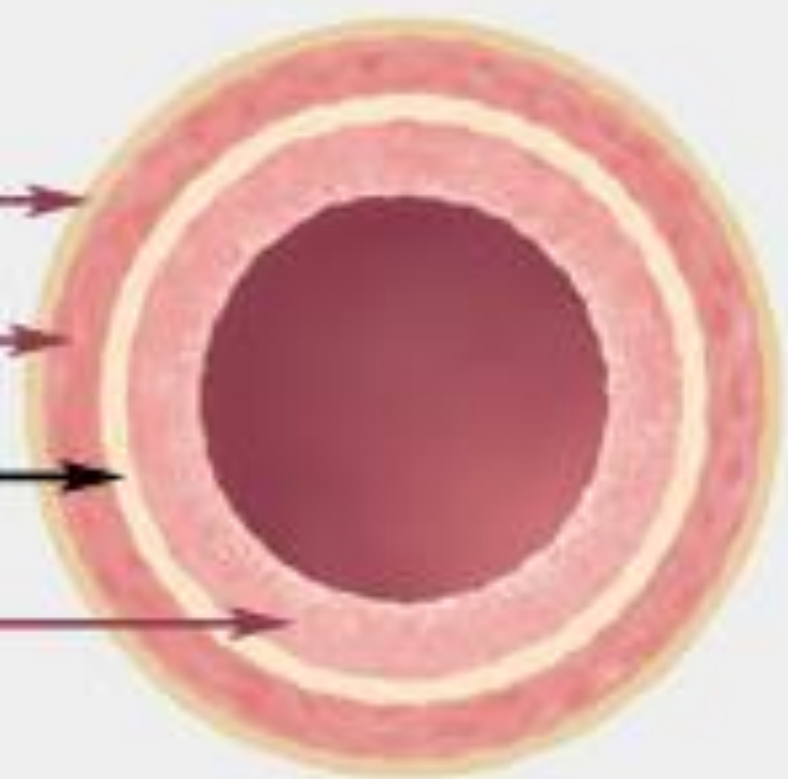
Muscle Layers



*Submucosa*



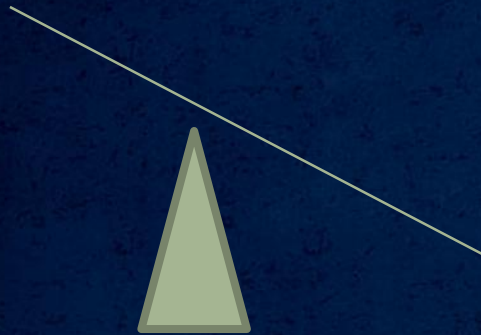
Mucosa



# Morbo di Crohn

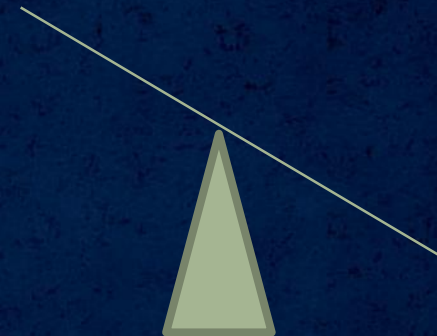
# Enteropatia eosinofila

Indici  
infiammatori



Dolore

Dolore



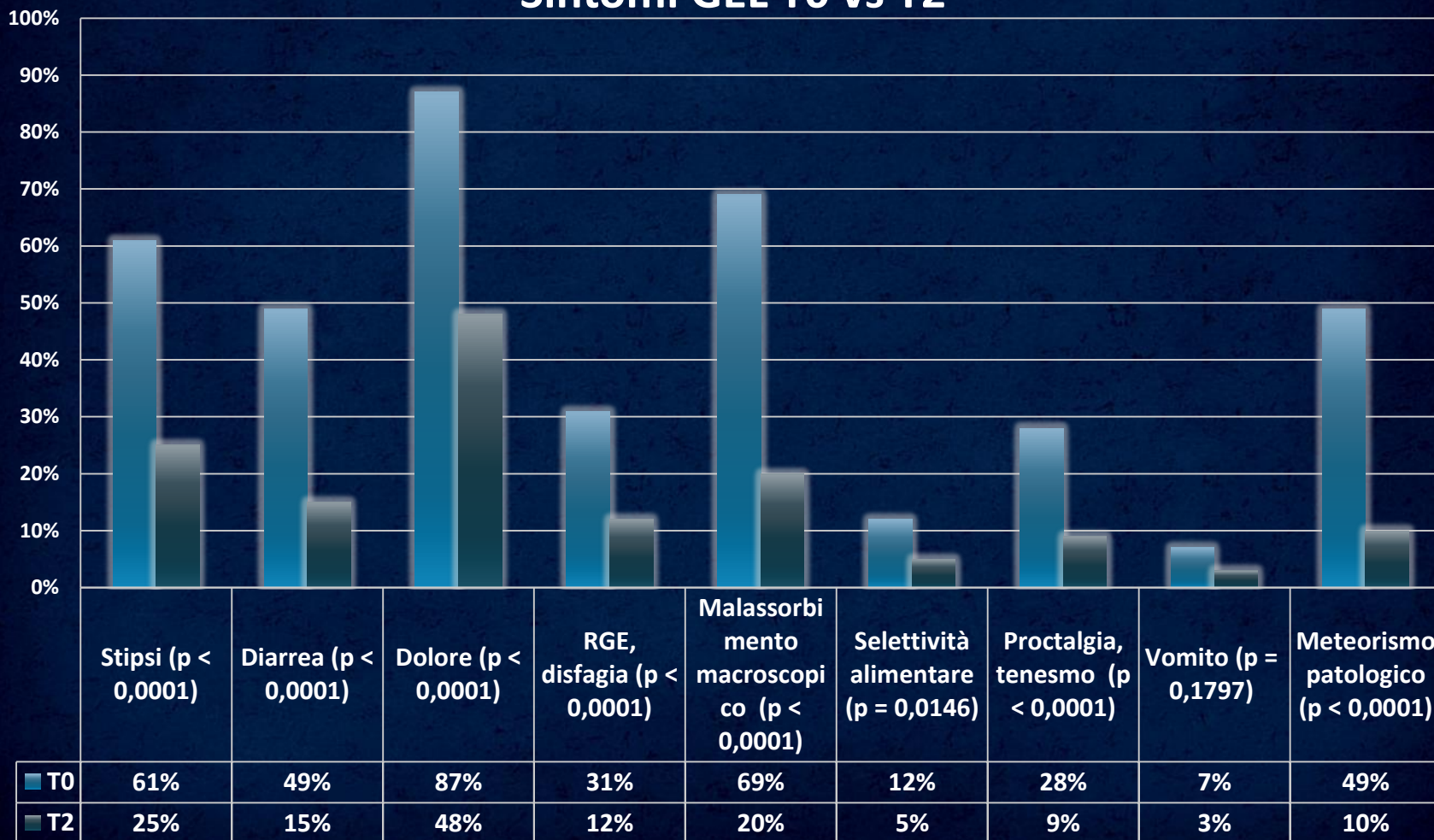
Indici  
infiammatori





# RISULTATI: FOLLOW-UP

## Sintomi GEL T0 vs T2





# Ileo dopo terapia

01:25:03

25 Feb 05



01:34:50

25 Feb 05



01:52:37

25 Feb 05



01:53:06

25 Feb 05



# Risultati

- **Miglioramento con utilizzo farmaci di anti-infiammatori e dieta di esclusione:**
  - Stipsi ( $p = 0,0071$ )
  - Intensità del dolore ( $p < 0,0001$ )
  - Proctalgia e tenesmo ( $p = 0,0127$ )
- **Miglioramento neuropsichiatrico globale ( $p = 0,0001$ ) ed in particolar modo nei campi relativi a:**
  - Agitazione ( $p = 0,004$ )
  - Motricità ( $p = 0,024$ )
  - Attenzione ( $p = 0,005$ )
  - Imitazione ( $p = 0,015$ )



# Cosa c'è sotto



Tornare alle origini



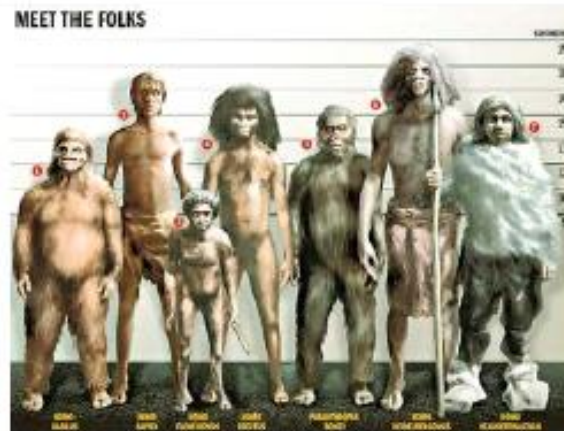


# Evoluzione alimenti e razza umana

Anni

2.5 M

La razza umana appare sulla faccia della terra



2018

10,000

Cambio da nomade, raccogliatore a stile di vita residenziale

Diet

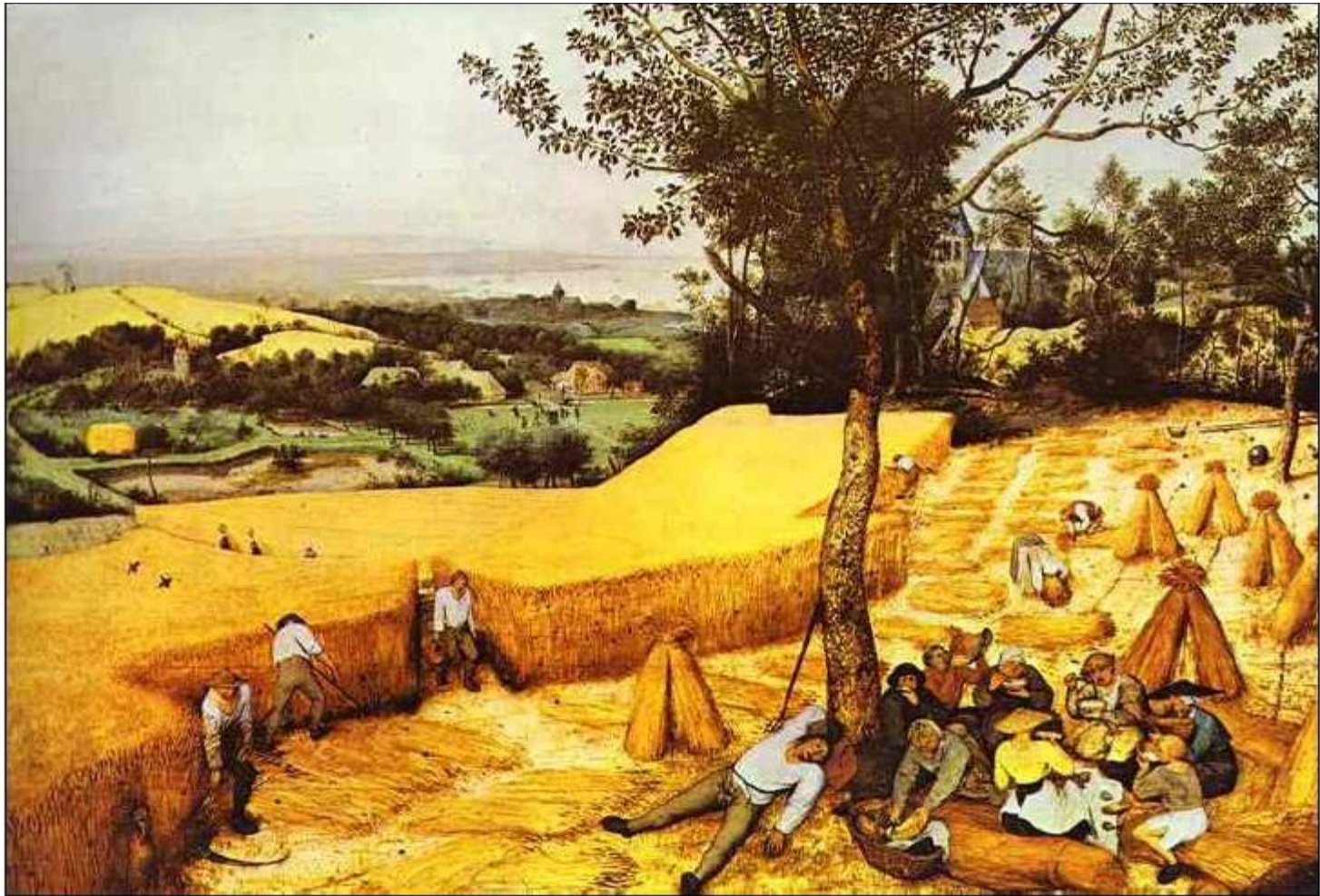
Frutta fresca, tuberi, frutta secca, digiuno, carne occasionalmente, conservazione non possibile



Domesticazione animali  
Avvento dell'agricoltura.  
Sviluppo alimenti contenenti **glutine** (graminacee: grano, segale, orzo) più adattabili rispetto riso, avena, miglio  
**Latte caprino**, **ovino** (latte vaccino solo dal '700 in avanti)

Fasano A. et al 2014

## Cambiamenti Ambientali/Nutrizionali



*Pieter Bruegel, 1565*





Esposizione ai batteri  
fin da molto piccolo

Scarsa esposizione alle infezioni  
e solo da più grande

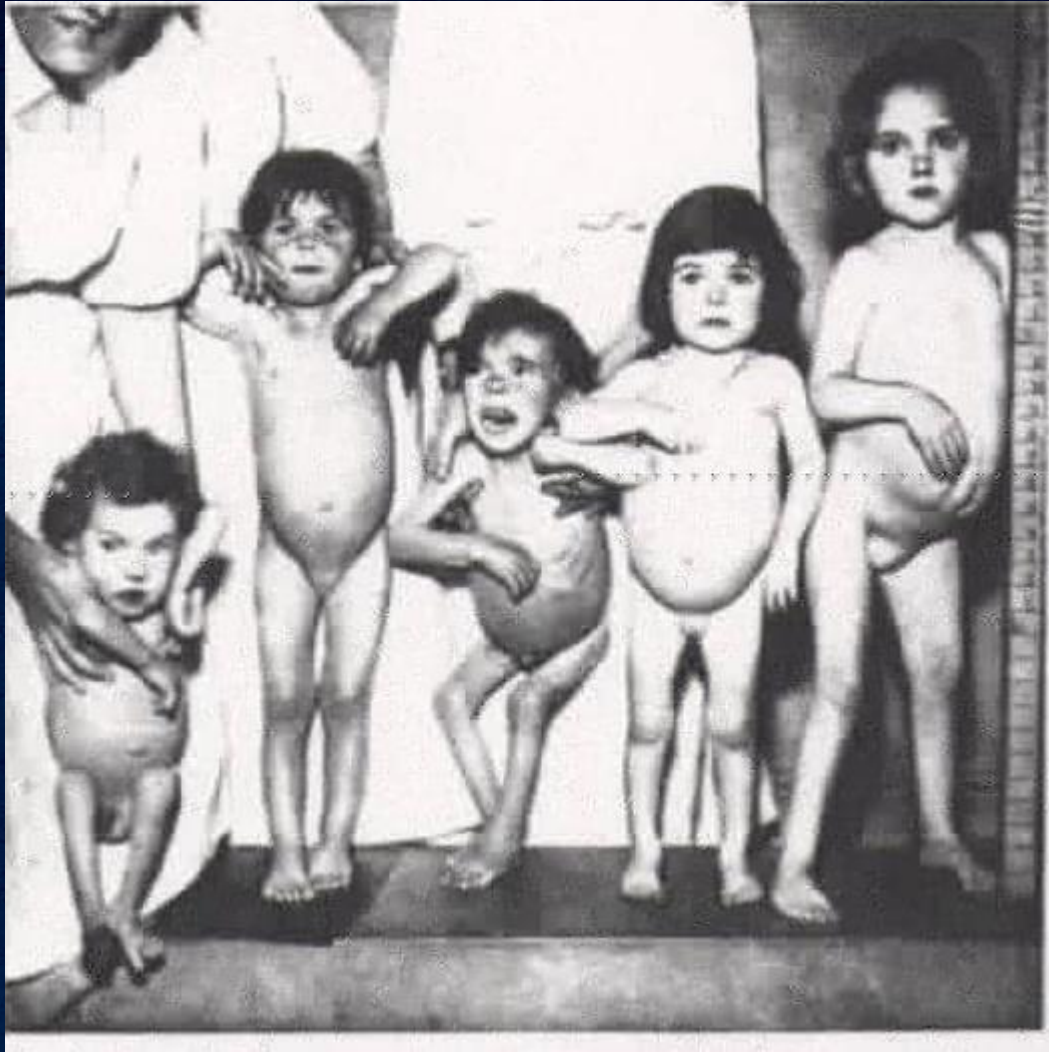
## Passato

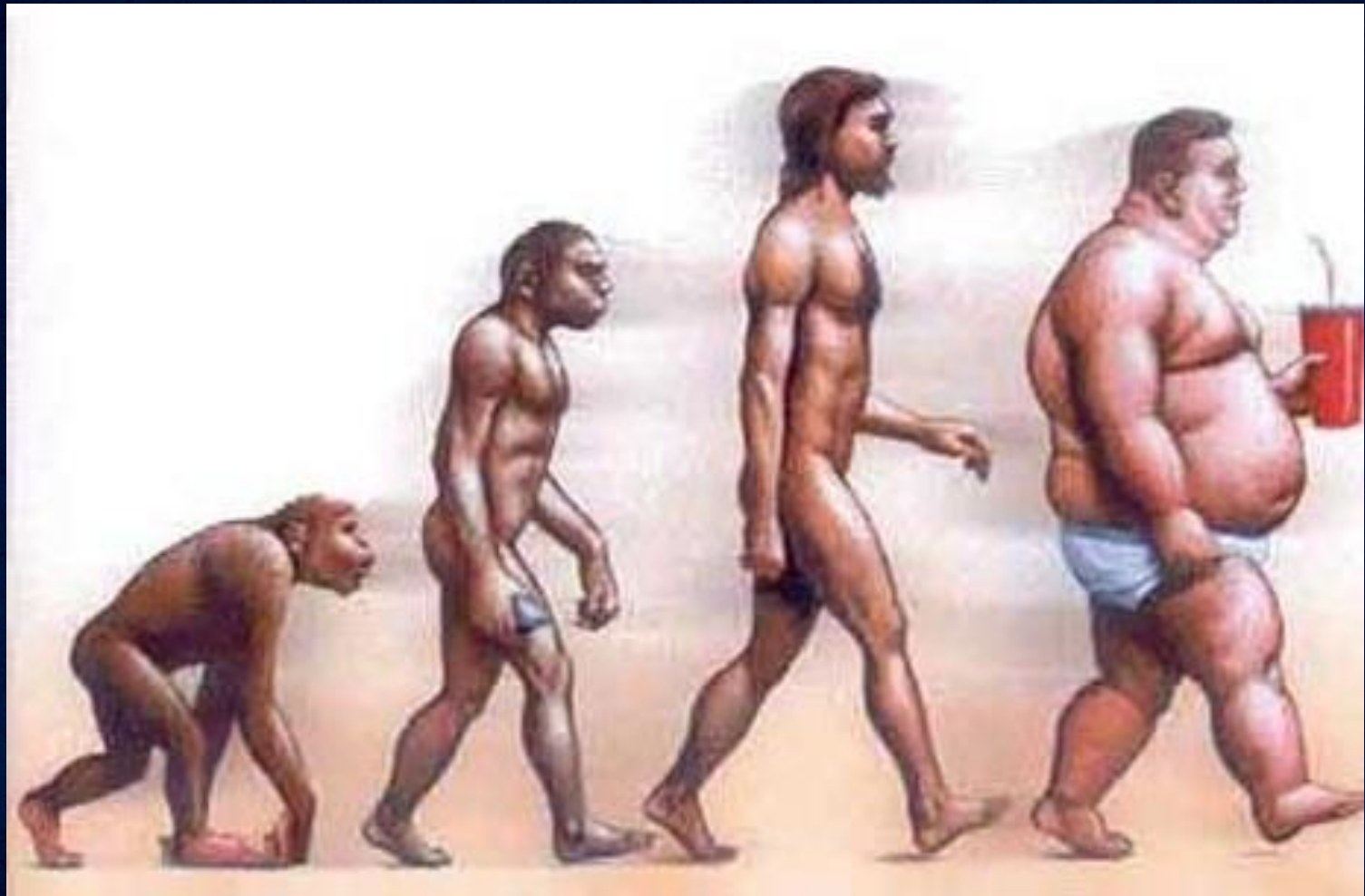
- Scarsa Igiene
- Molti batteri
- Meno cibo
- Vita più corta

## Attualmente

- Maggior Igiene
- Meno batteri
- Più cibo
- Vita più lunga

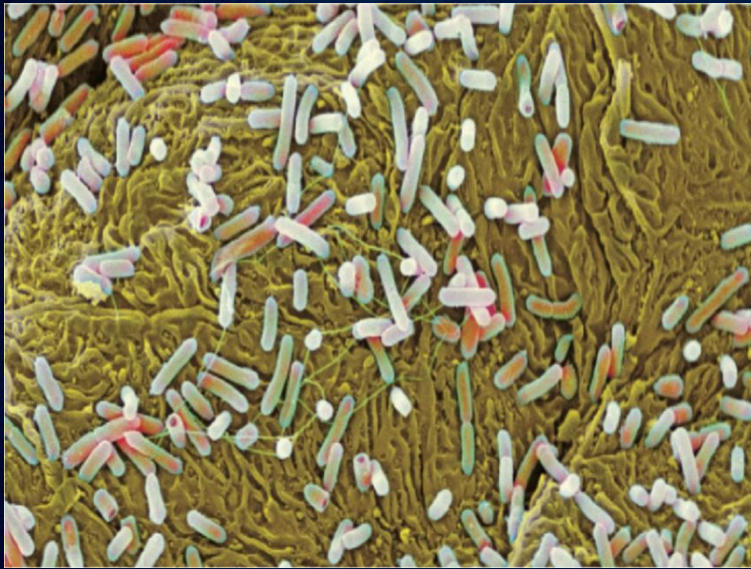




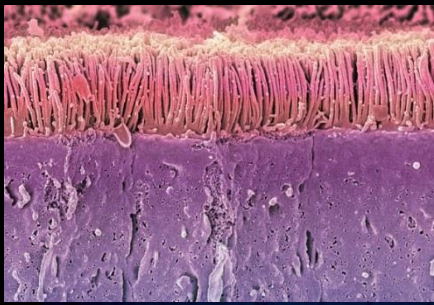




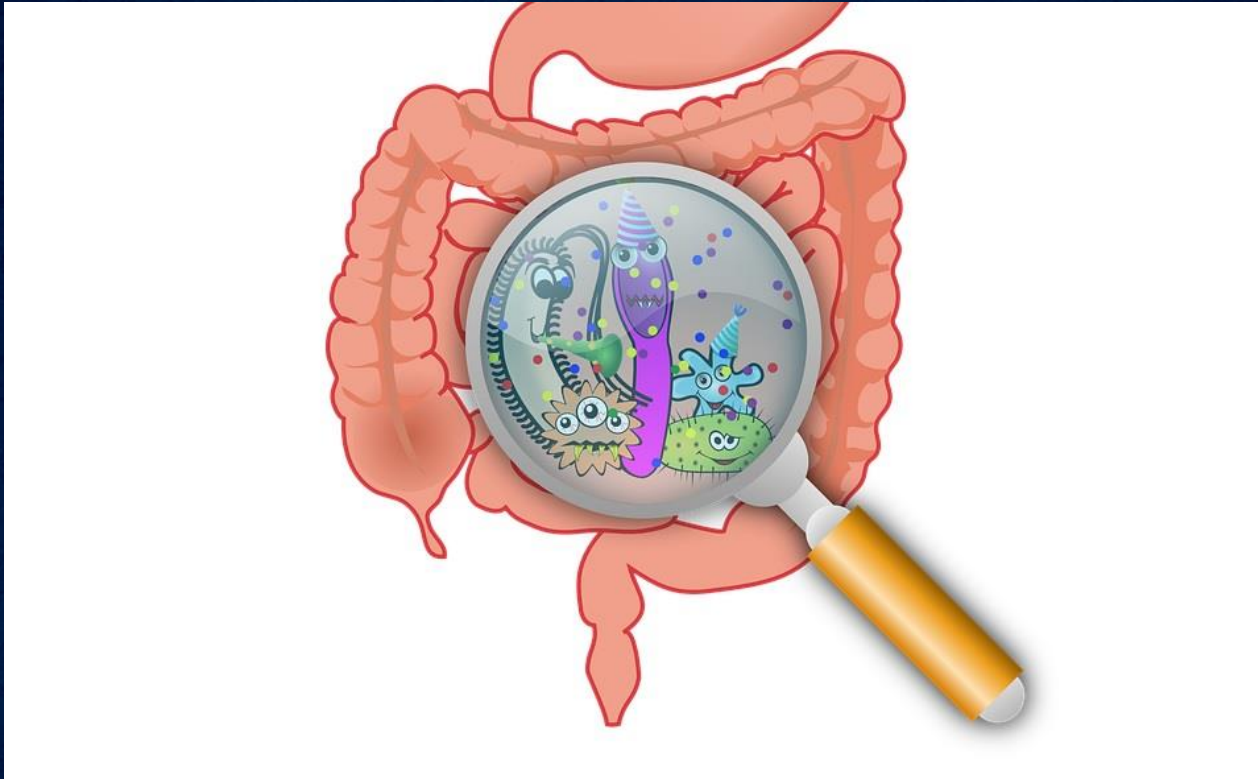
Batteri primi segni di vita sulla terra adattati anche alle  
condizioni più estreme e noi siamo in un certo senso  
il loro contenitore evoluto





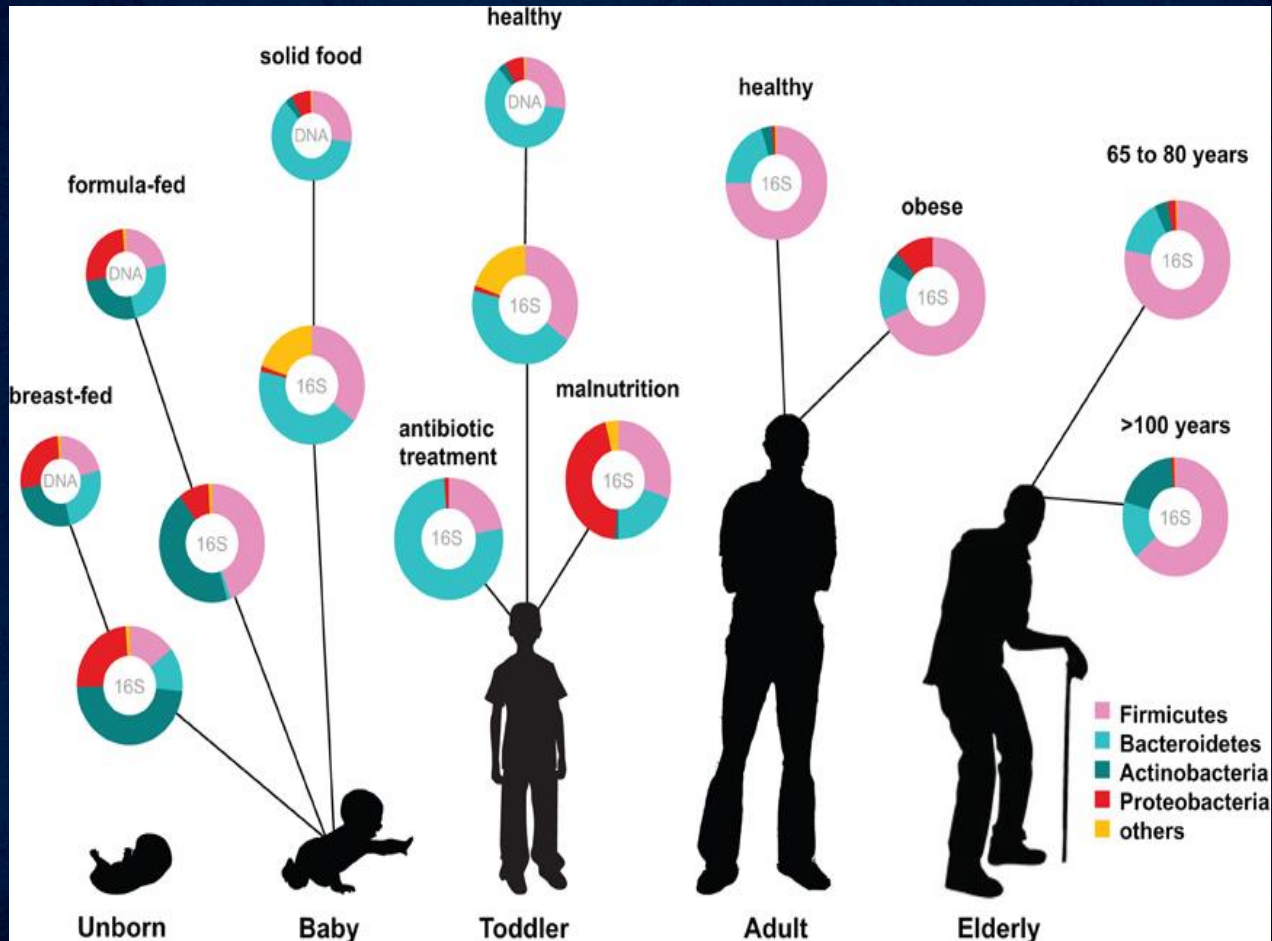


Microbioma Umano





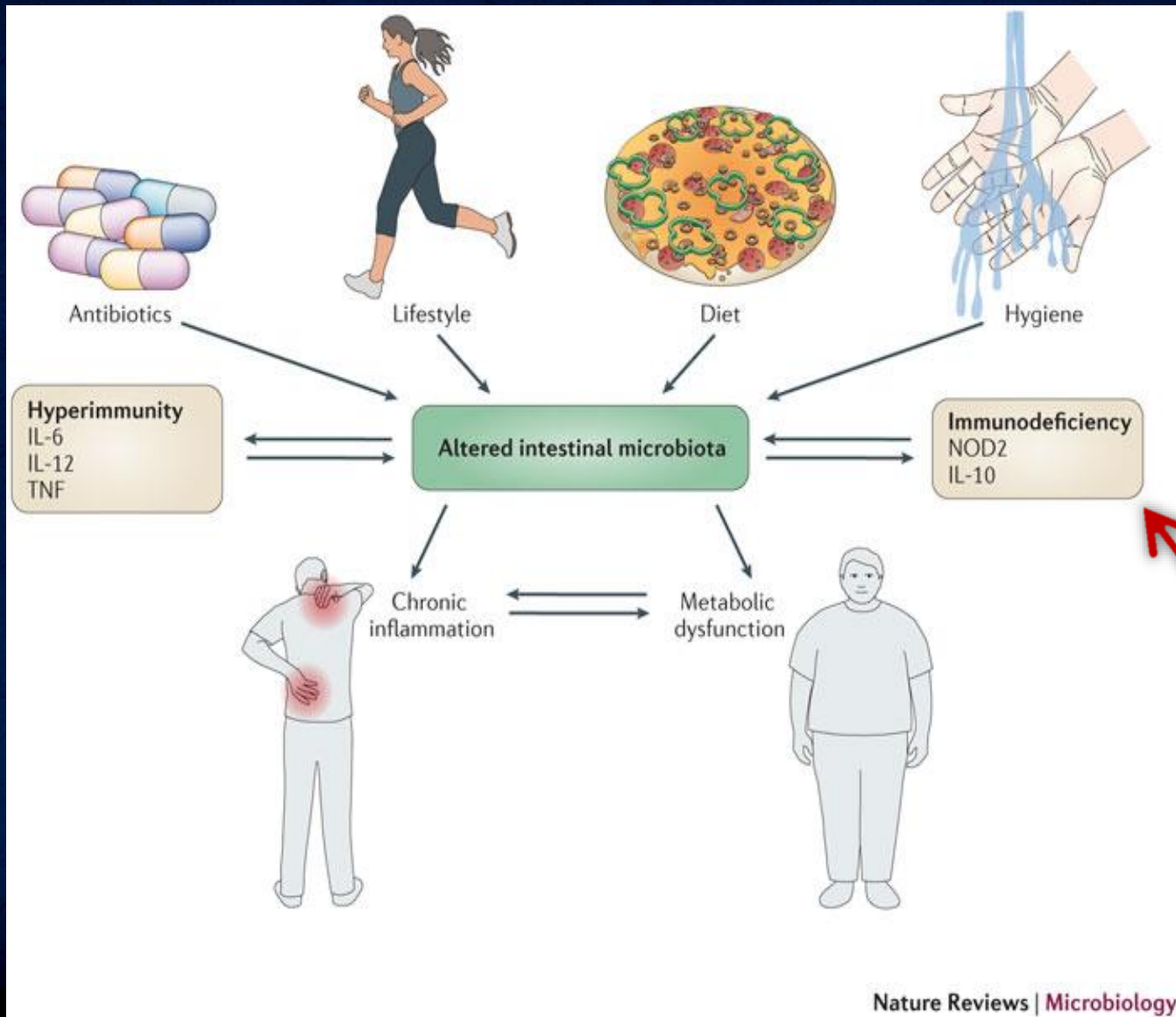
# Microbiota Intestinale: Alterazioni durante il ciclo di vita dell'uomo

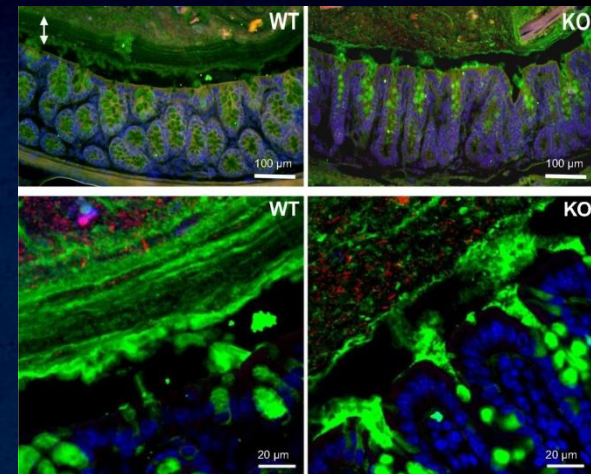
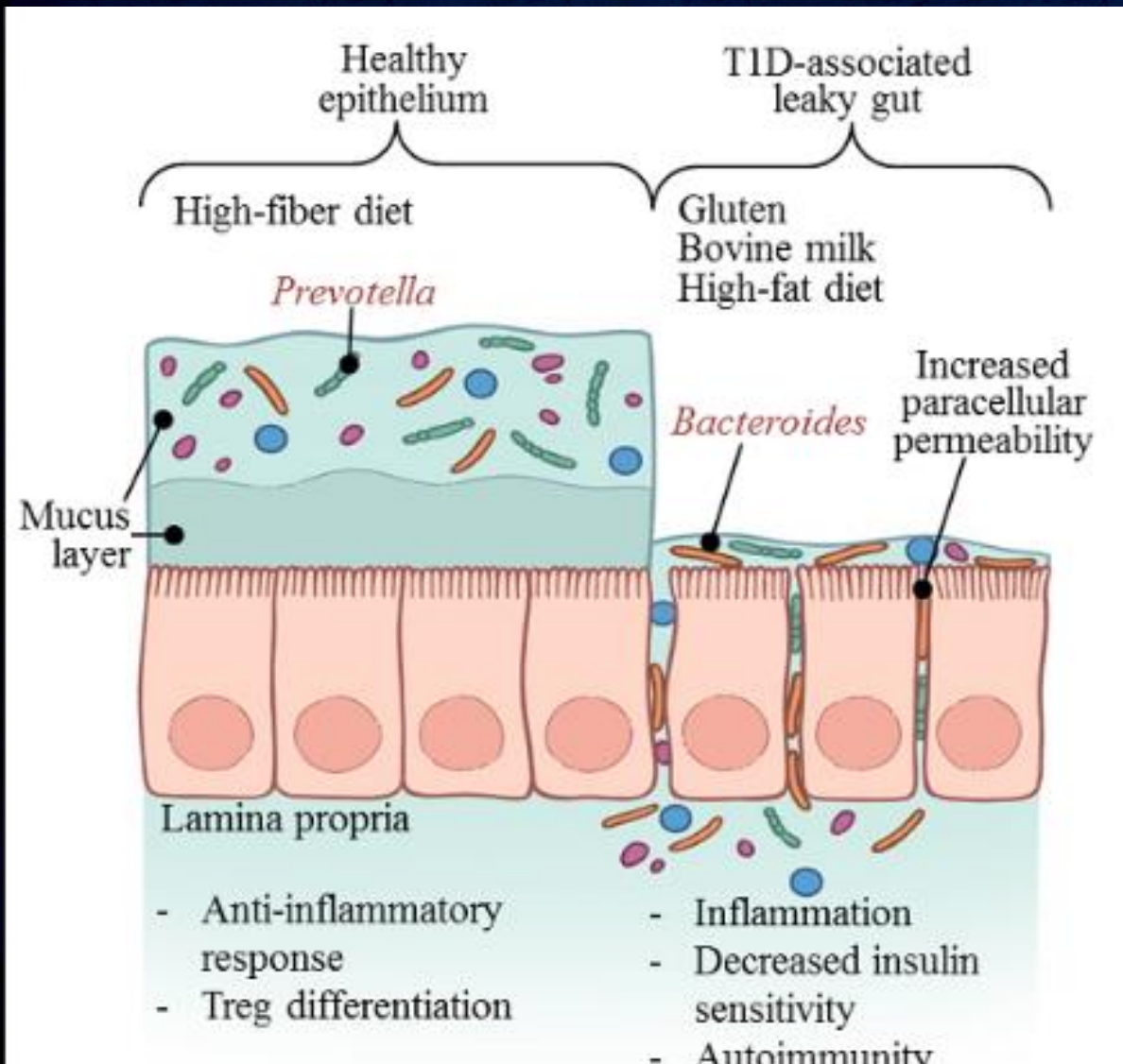






# Microbiota intestinale: Influenze ambientali e risposta immune

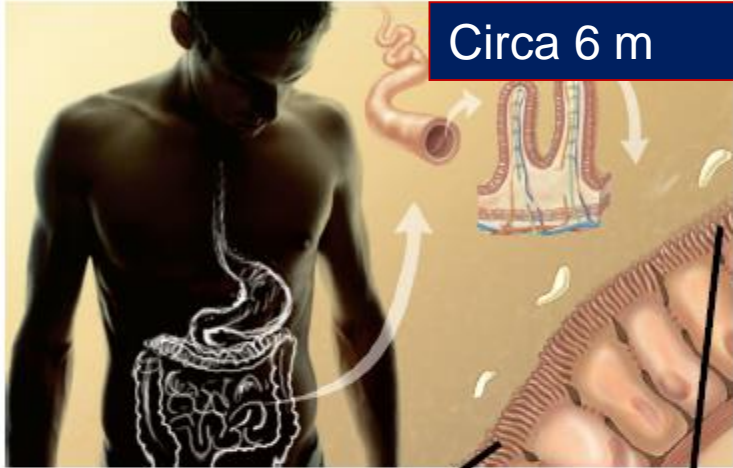






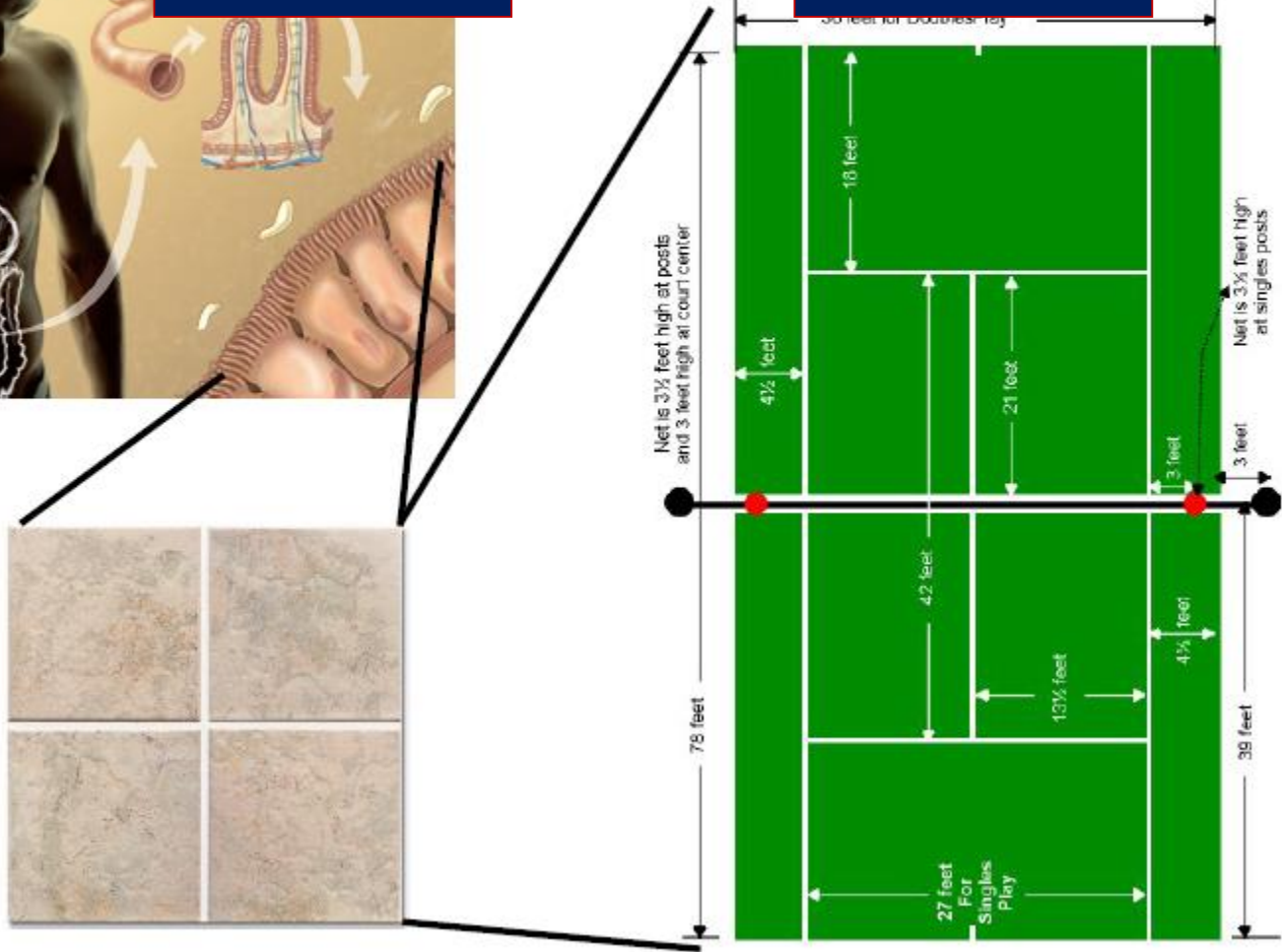


# Intestino ed Evoluzione



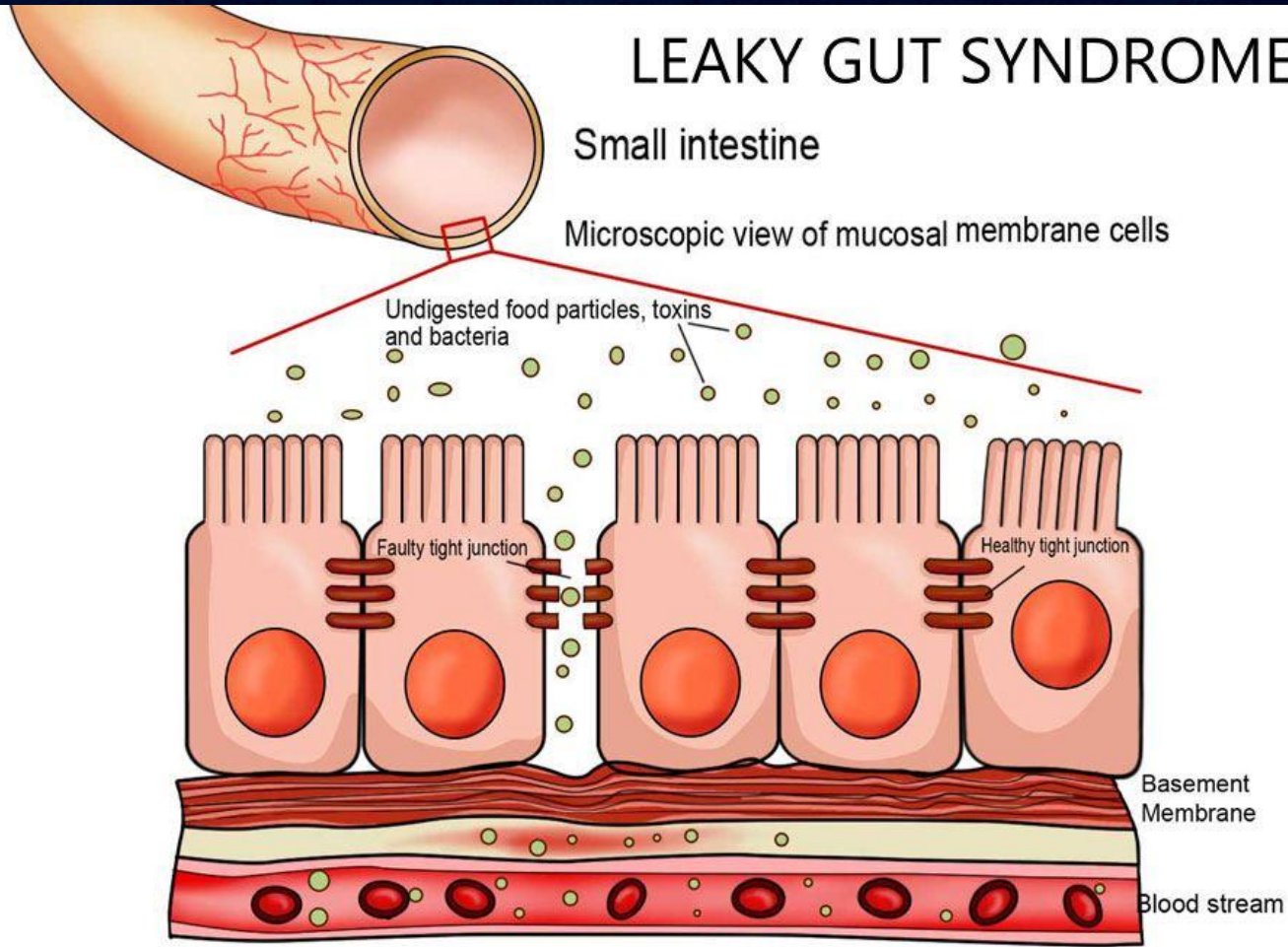
Circa 6 m

Circa 1000 m<sup>2</sup>





# LEAKY GUT SYNDROME



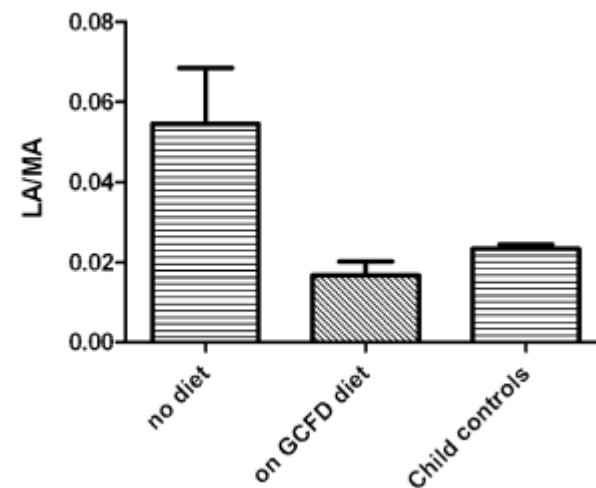
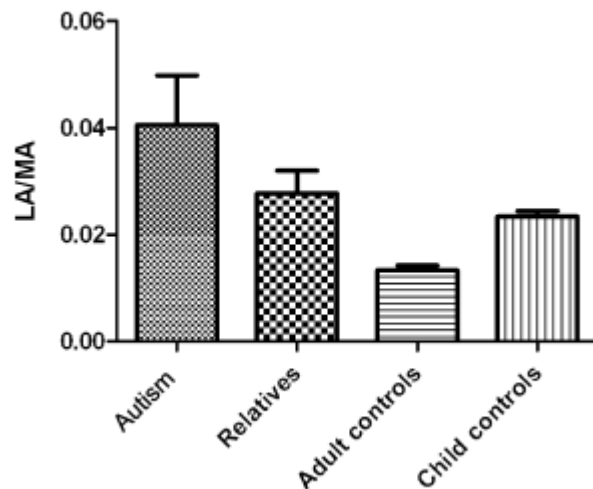
# Alterazione barriera GI

- Abnormal intestinal permeability in children with autism.
  - *D'Eufemia et al 1996*
- Alteration of intestinal barrier in patients with autism spectrum disorders and their first-degree relatives.
  - *De Magistris et al 2010*



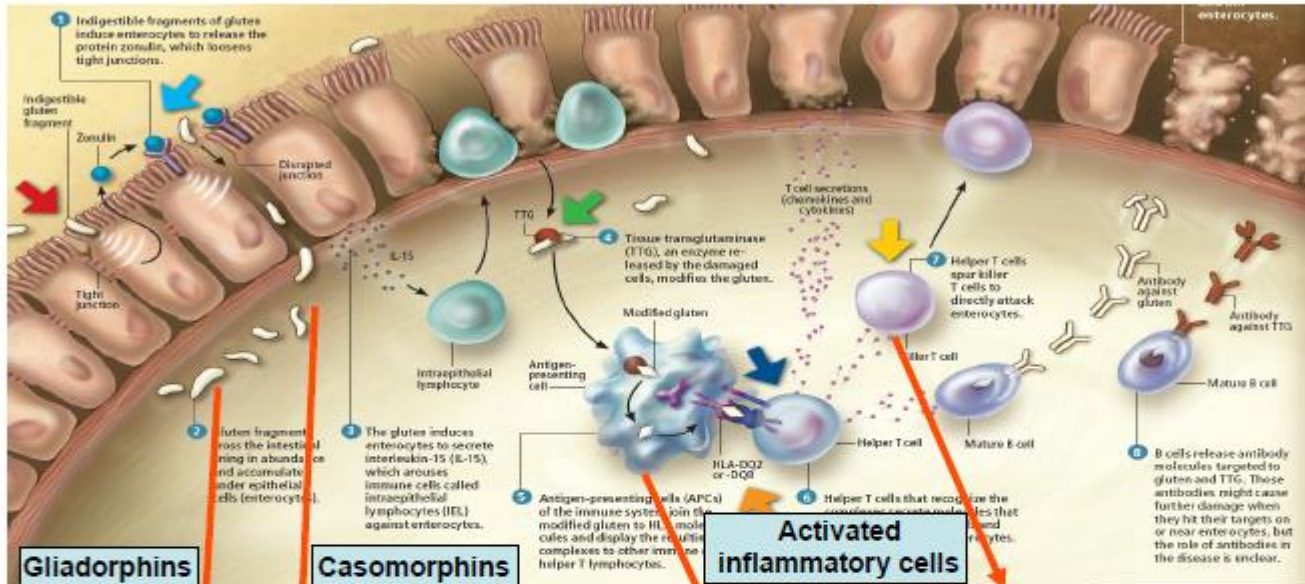
# Alterations of the Intestinal Barrier in Patients With Autism Spectrum Disorders and in Their First-degree Relatives

*\*Laura de Magistris, \*Valeria Familiari, <sup>†#</sup>Antonio Pascotto, \*Anna Sapone,  
<sup>†</sup>Alessandro Frolli, <sup>§</sup>Patrizia Iardino, <sup>‡</sup>Maria Carteni, <sup>‡</sup>Mario De Rosa,  
<sup>¶</sup>Ruggiero Francavilla, \*Gabriele Riegler, <sup>†</sup>Roberto Militerni, and <sup>||</sup>Carmela Bravaccio*









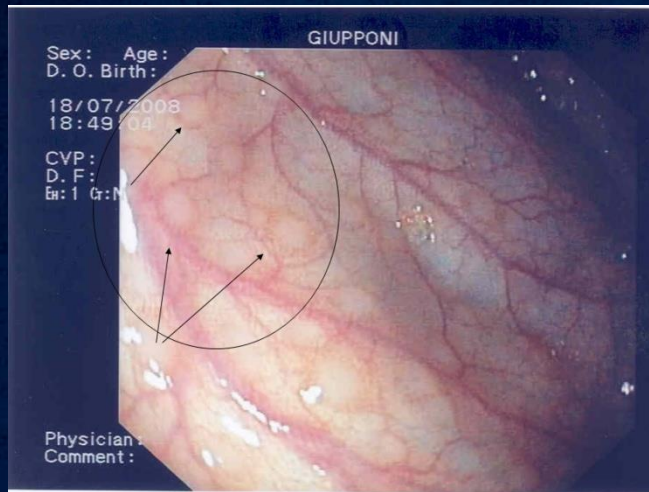
**Gladorphins**

**Casomorphins**

**Activated inflammatory cells**



# Cute Intestino Coinvolti





# Effect of gluten free diet on gastrointestinal and behavioral indices for children with autism spectrum disorders: a randomized clinical trial

Faezeh Ghalichi, Jamal Ghaemmaghami, Ayyoub Malek, Alireza Ostadrahimi

Tabriz, Iran

**Background:** Genetic and environmental factors are both responsible for the etiology of autism spectrum disorders (ASD). Although epidemiological studies have been conducted to clarify the association between restriction diets and ASD, the conclusion remains unclear. This study was undertaken to investigate the effect of gluten free diet (GFD) on gastrointestinal symptoms and behavioral indices in children with ASD.

**Methods:** In this randomized clinical trial, 80 children diagnosed with ASD by the Autism Diagnostic Interview-Revised (ADI-R) were assigned into GFD ( $n=40$ ) and regular diet (RD) ( $n=40$ ) groups for 6 weeks. At the beginning and end of the intervention, the ROME III questionnaire for evaluating gastrointestinal symptoms and Gilliam Autism Rating Scale 2 questionnaire (GARS-2) for assessing psychometric properties were completed.

**Results:** Of the 80 children, 53.9% had gastrointestinal abnormalities. In the GFD group, the prevalence of gastrointestinal symptoms decreased significantly ( $P<0.05$ ) after intake of GFD (40.57% vs. 17.10%) but increased insignificantly in the RD group (42.45% vs. 44.05%). GFD intervention resulted in a significant decrease in behavioral disorders (80.03=14.07 vs. 75.82=15.37,  $P<0.05$ ) but an insignificant increase in the RD group (79.92=15.49 vs. 80.92=16.24).

**Conclusion:** This study suggested that GFD may be

effective in controlling gastrointestinal symptoms and ASD behaviors.

*World J Pediatr June 2016; Online First*

**Key words:** autism;  
behavior disorders/problems;  
gastrointestinal system;  
gluten free diet

## Introduction

Autistic spectrum disorders (ASD) (autistic disorder; pervasive developmental disorder, not otherwise specified; and asperger syndrome) are severe neurodevelopmental disorders with diagnostic features including qualitative impairment in social interactions (e.g., lack of social reciprocity, marked impairment in eye-to eye gaze, lack of joint attention), qualitative impairments in communication (e.g., lack of language development, echolalia, stereotyped, and repetitive use of language), and restricted repetitive and stereotyped patterns of behaviors, interests, and activities.<sup>[1]</sup>

According to the Autism and Developmental Disabilities Monitoring Network of Centers for Disease Control and Prevention, the incidence of ASD has increased from about 1/88 children in 2012 up to 1/68 children in 2014. This means that the estimated incidence of ASD increased by 30% during the period of 2012-2014. According to the the Centers for Disease Control, boys with ASD were identified five times as many as girls (1/54 vs. 1/252).<sup>[2]</sup> Iran is one of the countries with a low incidence of ASD and an incidence of 6.26/10000 in children of 5 years old.<sup>[3]</sup>

At present, the etiology of ASD is unknown; however, genetic and environment factors are implied.<sup>[4]</sup> ASD is a complex and clinically heterogeneous disorder with a spectrum of symptoms.<sup>[5]</sup> In the past, ASD was thought to be merely a psychological or neurological disorder. But at present, there is increasing evidence that it affects multiple systems of the body, for example the metabolic, gastrointestinal, immunological, mitochondrial, and

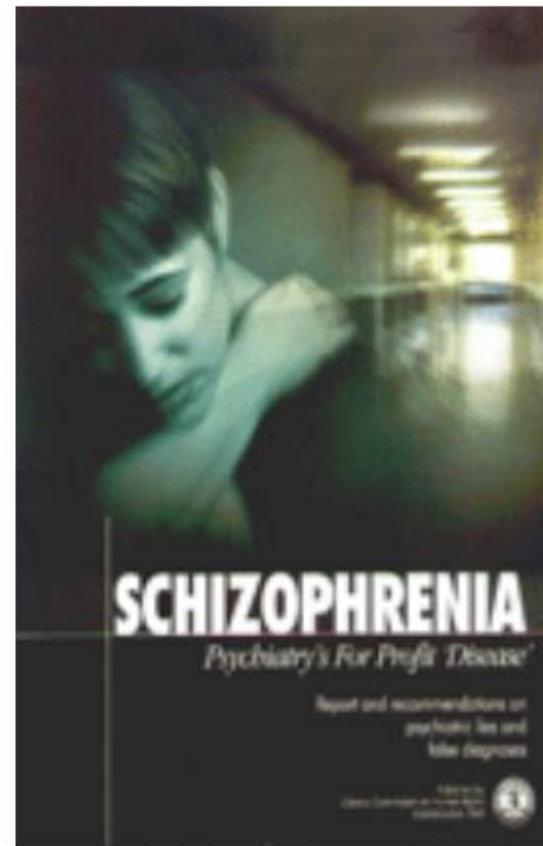
**Author Affiliations:** Nutrition Research Center, Faculty of Nutrition and Food Sciences, Biochemistry and Diet Therapy, Tabriz University of Medical Sciences, Tabriz, Iran (Ghalichi F); Faculty of Nutrition and Food Sciences, Biochemistry and Diet Therapy, Tabriz University of Medical Sciences, Tabriz, Iran (Ghaemmaghami J); Clinical Psychiatry Research Center, Department of Psychiatry, Tabriz University of Medical Sciences, Tabriz, Iran (Malek A); Department of Biochemistry and Diet Therapy, Tabriz University of Medical Sciences, Tabriz, Iran (Ostadrahimi A)

**Corresponding Author:** Alireza Ostadrahimi, PhD, MD, Department of Biochemistry and Diet Therapy, Tabriz University of Medical Sciences, Tabriz, Iran (Tel: +98 41 33357580; Email: Ostadrahimi@tbzmed.ac.ir)

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# Autismo & Schizofrenia





# Conclusioni



- Sintomi gastrointestinali sono presenti in una percentuale molto elevata dei pazienti
- E' presente un quadro infiammatorio intestinale specifico
- E' una malattia INTESTINALE curabile che migliora direttamente ed indirettamente il comportamento





*d'après Sir Luke Fildes, R. A. - Joseph Tomasek*

*Wyeth, Philadelphia*

*THE DOCTOR*



# Conclusioni



- Considerare il paziente con disturbo comportamentale come tutti gli altri pazienti
- Considerare la malattia NP come malattia multiorgano
- Considerare il coinvolgimento cerebrale come possibile complicanza extra-intestinale

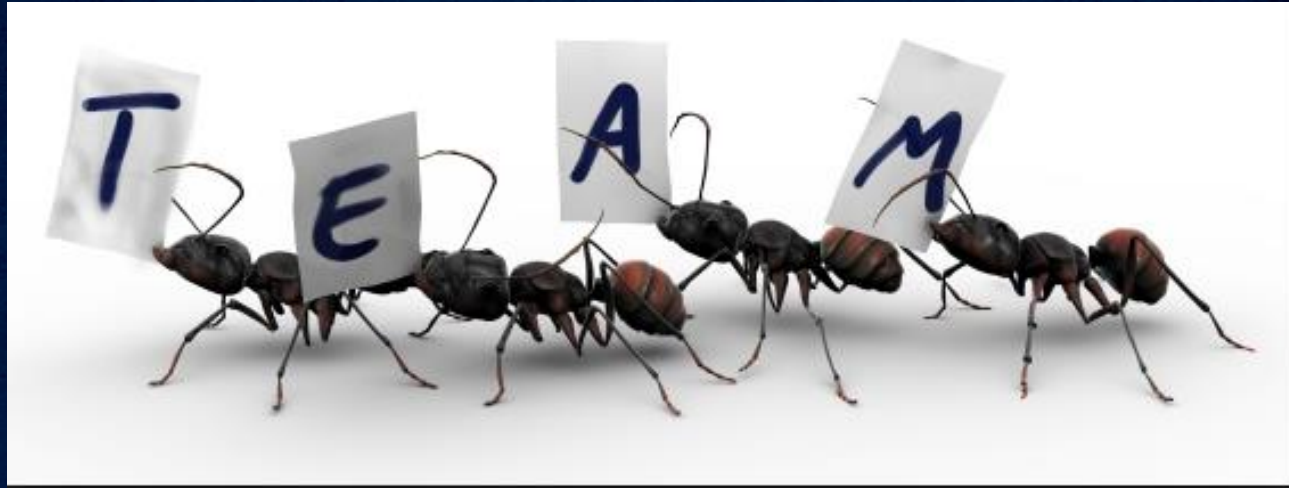
# Conclusioni



- Considerare bene l'espressività dei sintomi gastrointestinali nei pazienti con soglia del dolore più elevata, con insorgenza da sempre e con espressività non verbale
- Considerare l'opinione dei genitori, non banalizzare i loro sforzi come giustificazione per accettare una malattia di cui non si danno pace









*Tutte le verità passano attraverso  
tre stadi.*

*Primo: vengono ridicolizzate*

*Secondo: vengono violentemente  
contestate*

*Terzo: vengono accettate dandole come  
evidenti e proprie*

*A. Schopenhauer 1840*

"LA SPERANZA HA  
DUE BELLISSIMI FIGLI,  
LO SDEGNO E IL CORAGGIO.  
SDEGNO PER LE COSE COME SONO  
E CORAGGIO PER CAMBIARLE"  
ARISTOTELE







Dott. Federico Balzola  
Dott. Carlo Alessandria

Ambulatorio Intestino Autismo

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Prenotazione: C.U.P.A. 011/633.3710 e 011/633.3615  
dal lunedì al giovedì 14.00-15.30, il venerdì 14.00-  
15.00.