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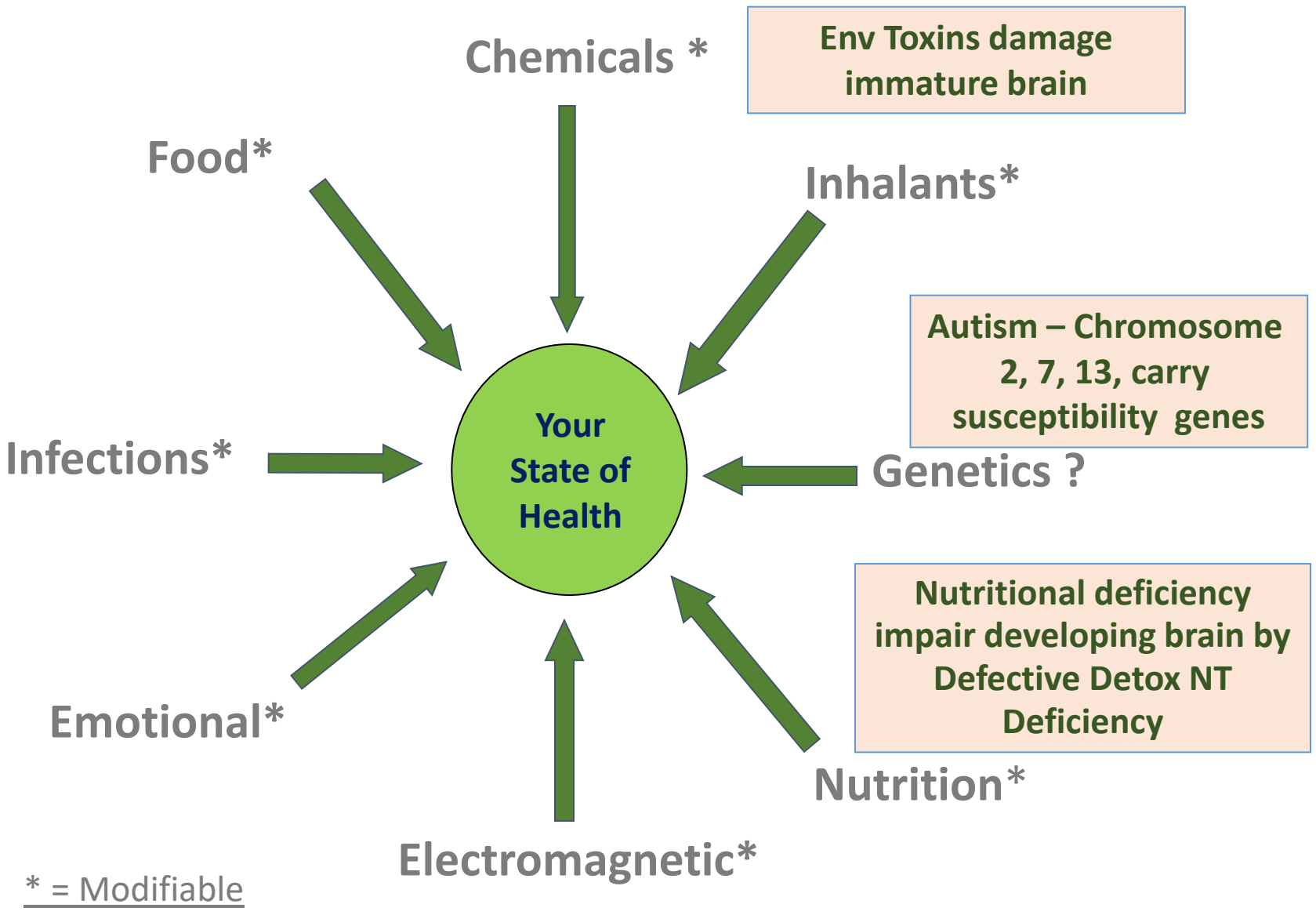
FOOD ADVERSE REACTION AND INTESTINAL MICROBIOTA

Webinar

September 11, 2024

Prof. Carmelo Rizzo, MD

The Total Load Effect:



* = Modifiable

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Nutrition, or we should say, the correct nutrition, is fundamental in the prevention of symptoms and must be the first therapeutic approach for any disease

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Many years of studies and researches enabled us to understand and explain many variables which link nutrition and the maintenance of the state of health in all individuals.

Knowledge of mechanisms of biochemical interactions opened new fields of studies and research in the science of nutrition.

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BASIC PRINCIPLES IN CLINICAL NUTRITION

- Some diseases can be caused and/or triggered by environmental factors
- Many diseases can be cured by the elimination of these factors
- Individual predisposition must be evaluated;
- In the diseases, environmental factors include foods, preservatives, chemicals present in the air and water, and the intestinal environment (gut flora).

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In any DISEASE we must always:

- Remove chemicals and/or toxics;
- Repair possible chronic damages in particularly sensitive organism which are exposed and/or inflamed.

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FATHER OF CLINICAL ECOLOGY

Theron Randolph, MD
1906 – 1995
Chicago, USA

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Shannon, W.R. “Neuropathic manifestations in infants and children as a result of anaphilactic reaction to foods contained in their dietary” *Am. Journal of Disease in Children , 1922*

Albert H. Rowe ““Elimination diet and the patient’s allergies” *H. Kimpton, London, 1944*

Rinkell H. J. “Rotation diet” *Annals of Allergy, 1944*

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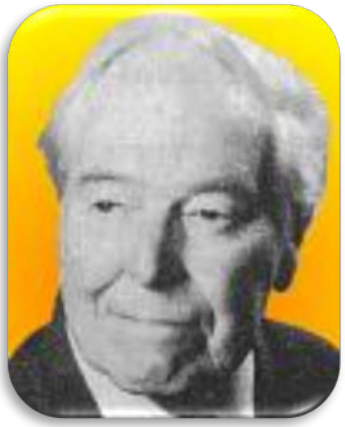
RICHARD MACKARNESS

(1916 – 1996)

Indian-English physician and writer who championed "Clinical Ecology" and established Britain's first obesity and food allergy clinic. Working outside of the academic mainstream, he revealed that various illnesses can be traced to food allergies, and could be cured by dietary restrictions.



"Clinical ecology [is] a new branch of medicine aimed at helping people made sick by a failure to adapt to facets of our modern, polluted environment."

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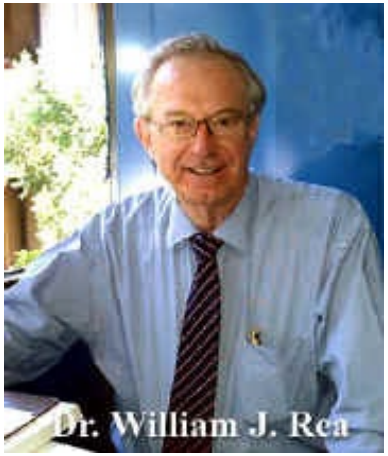
PIONIERS OF CLINICAL ECOLOGY

WILLIAM J. REA

Cardiovascular Surgery
Environmental Health Center (EHC-Dallas)



DORIS J. RAPP

Pediatric Allergy and Environmental Medicine
(Phoenix, Arizona)

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FOOD ADVERSE REACTIONS

FOOD ALLERGY (properly named) Immediate reaction.
IgE-mediated phenomena.

PSEUDOALLERGY Enzymatic Deficiency (lactose intolerance/malabsorption, favism, nickel intolerance , celiac disease)

HYPERSENSITIVITY Foods which release hystamine (chocolate, dried fruits, seasoned cheese etc.)

TOXIC REACTIONS Mushrooms poisoning, botulism

FOOD INTOLERANCE Retarded reaction:
No IgE mediated

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INFLAMMATION / ALLERGY CONNECTION

Inflammation is a really matter of life or death:

It is an abnormal response of living tissues in relation to an insult or injury

It keeps us alive - protecting us by destroying bacteria, yeasts and viruses

It can kill us - destroying organs and tissues of our body

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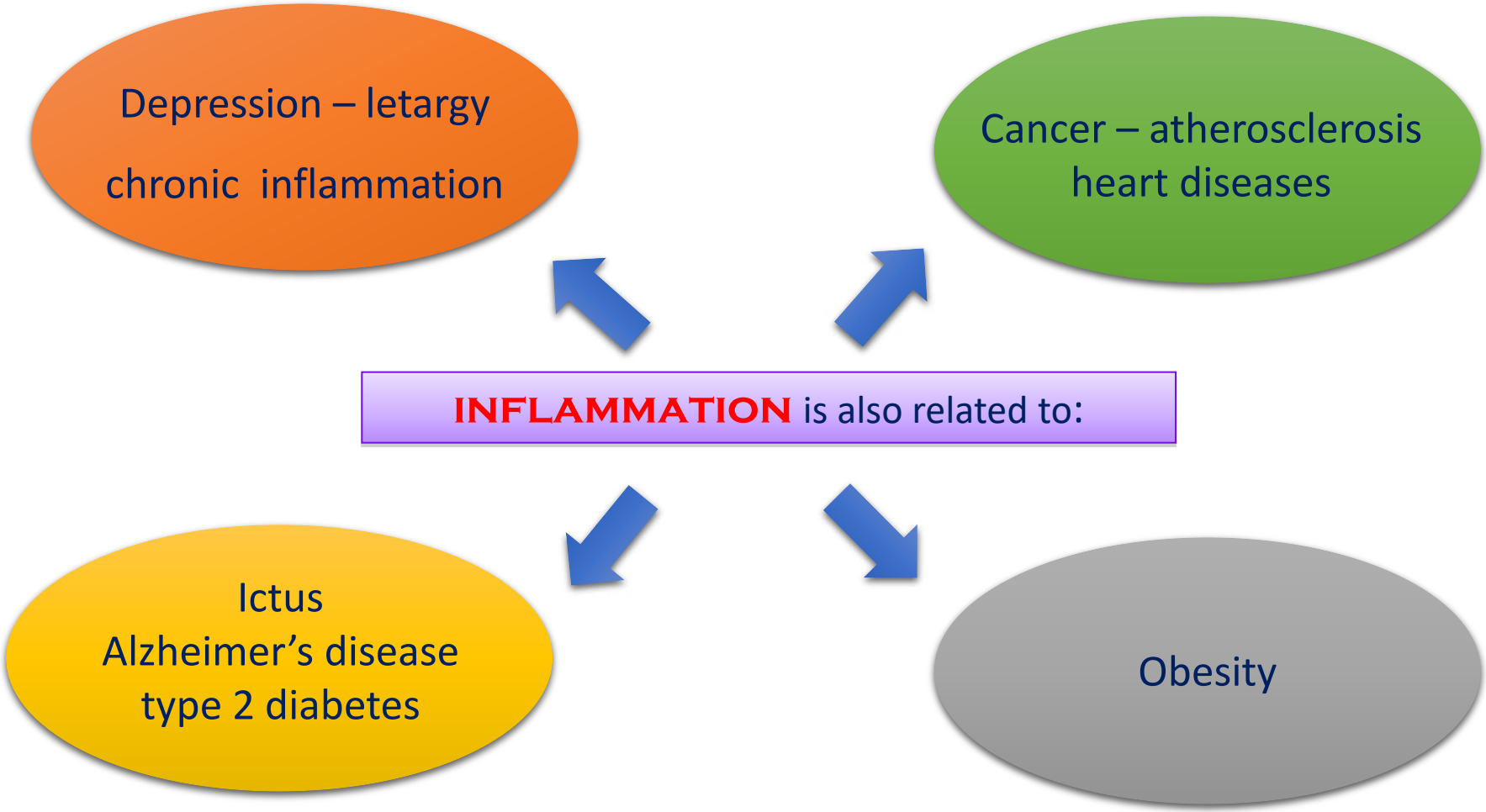
Inflammation may occur differently in different people with symptoms caused by external inflammatory reactions:

- ✧ Edema to the arts
- ✧ Osteoarthritis – rheumatoid arthritis
- ✧ Sore throat– gingivitis
- ✧ Gastric pyrosis – ulcer
- ✧ Skin pruritus– eczema
- ✧ Rhinitis – asthma – emphysema – allergy
- ✧ IBD – LES – multiple sclerosis
- ✧ Migraine – headache – type 1 diabetes mellitus


Depression – letargy
chronic inflammation
Cancer – atherosclerosis
heart diseases
INFLAMMATION is also related to:
Ictus
Alzheimer's disease
type 2 diabetes
Obesity

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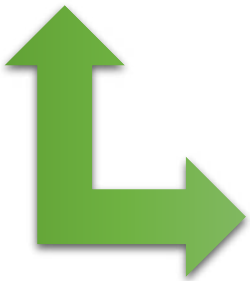
If we identify the causes that trigger inflammation, we can modify these factors and control inflammatory diseases by eliminating or reducing the individual risks for the development of an enormity of related symptoms.



INFLAMMATION involves hundreds of biological and chemical processes that have different effects on any organ.

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Many times our genes cause an over-reaction of our immune system by triggering autoimmune disorders in the family.

Often this chronicity persists for a short-circuit mechanism triggered by external environmental factors.

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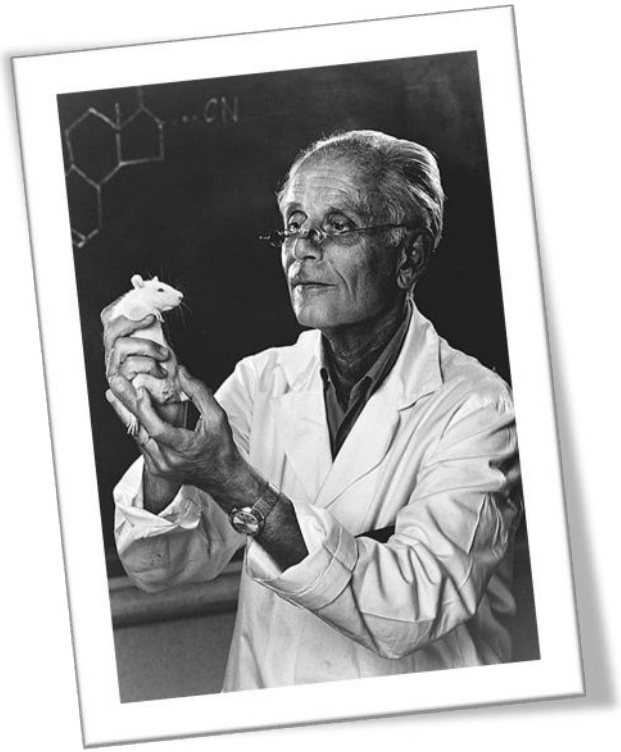
GENERAL ADAPTATION SYNDROME

Hans Selye (1907 - 1982)
Hungarian-Canadian Endocrinologist



Stress:

Non specific response of the body to a negative stimuli

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GENERAL ADAPTATION SYNDROME SELYE'S THEORY

Whatever is the stress agent (foods, chemicals, allergens, injuries, physical or psychological trauma), the body's response is divided into 3 phases:

1. **ALARM PHASE**
2. **ADAPTATION PHASE** in which the body maintains a certain balance with the stressful agent
3. **PHASE OF EXCURSION** resulting in the appearance of symptoms or illnesses

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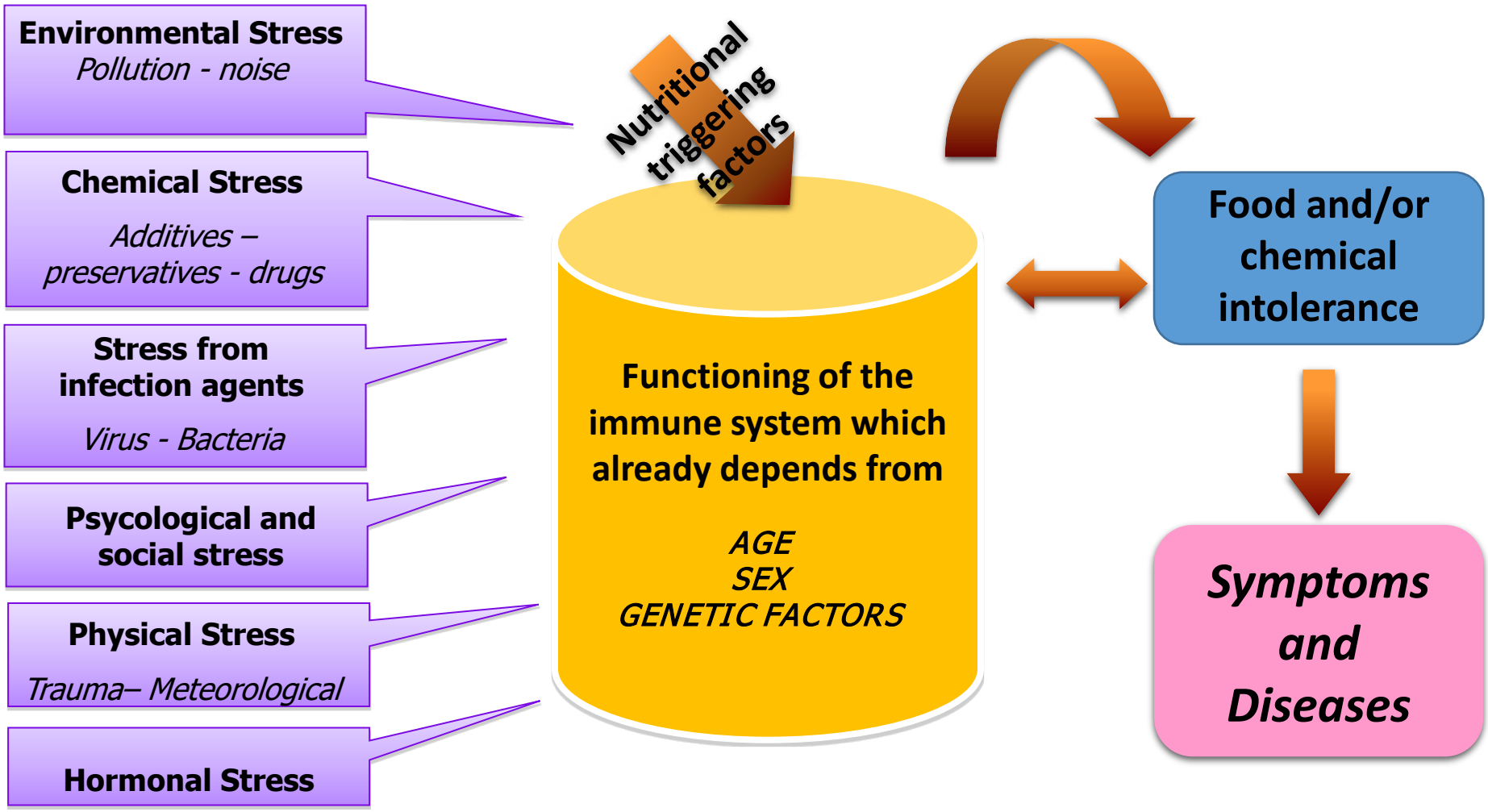
STRESS THEORY



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CONTROVERSIES

- **Traditional medicine**

If a person is sick he needs to introduce chemicals into the body

- **Clinical Ecology**

If a person is sick he needs to remove chemicals from the body

Complementary Medicine: If a person is ill, there are specific indications for taking chemical substances and specific indications to remove them from their body

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FOOD INTOLERANCE

Prof. C. Rizzo

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FOOD INTOLERANCE

DEFINITION

- Condition characterized by inability to absorbe or metabolize a nutrient
- Abnormal reaction of the body to a specific food

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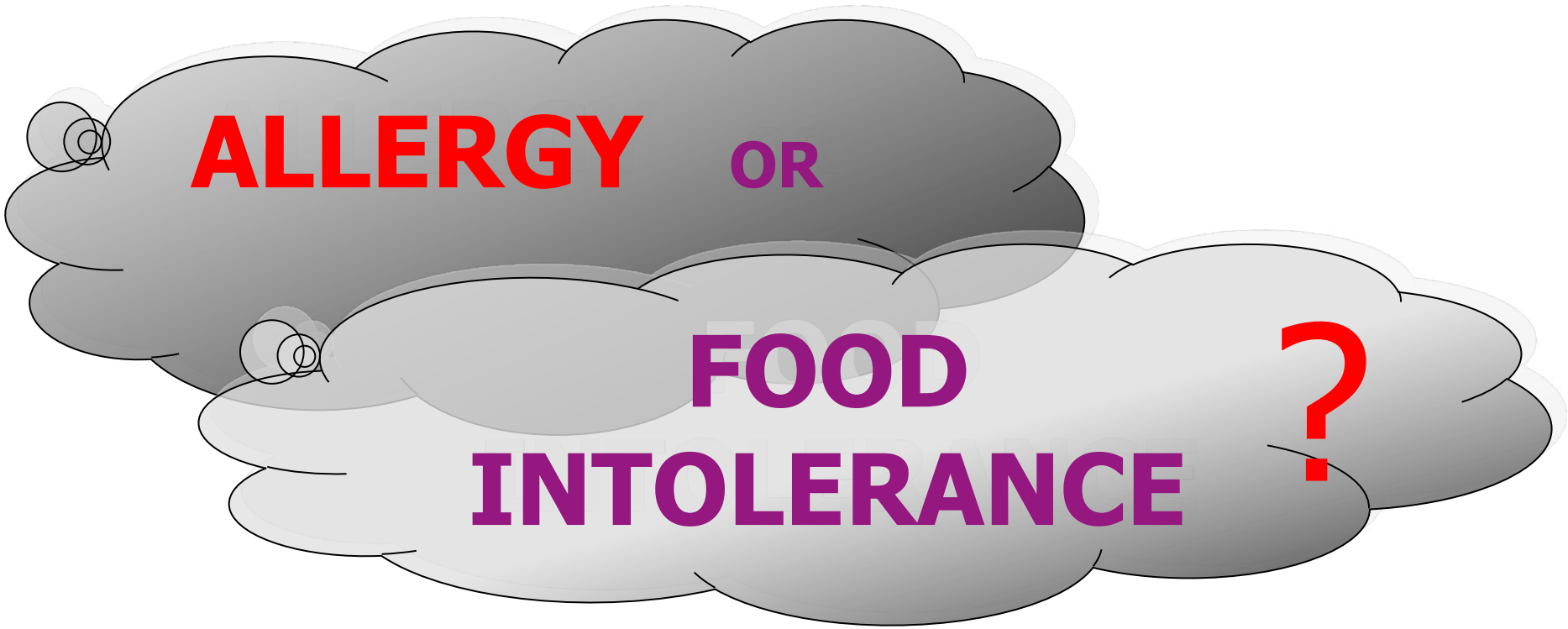
TERMINOLOGICAL CONFUSION



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FOOD ADVERSE REACTIONS

IMMUNO MEDIATED → **FOOD ALLERGY**

NO IMMUNO MEDIATED → **FOOD INTOLERANCE**

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FOOD ADVERSE REACTIONS

The use of therms immuno-mediated to indicate allergies and no immuno-mediated to indicate intolerance is not really appropriate

FOOD INTOLERANCE is still an
IMMUNITY
HYPERSENSITIVITY REACTION.
It is just that DOES NOT DEPEND ONLY ON IgE

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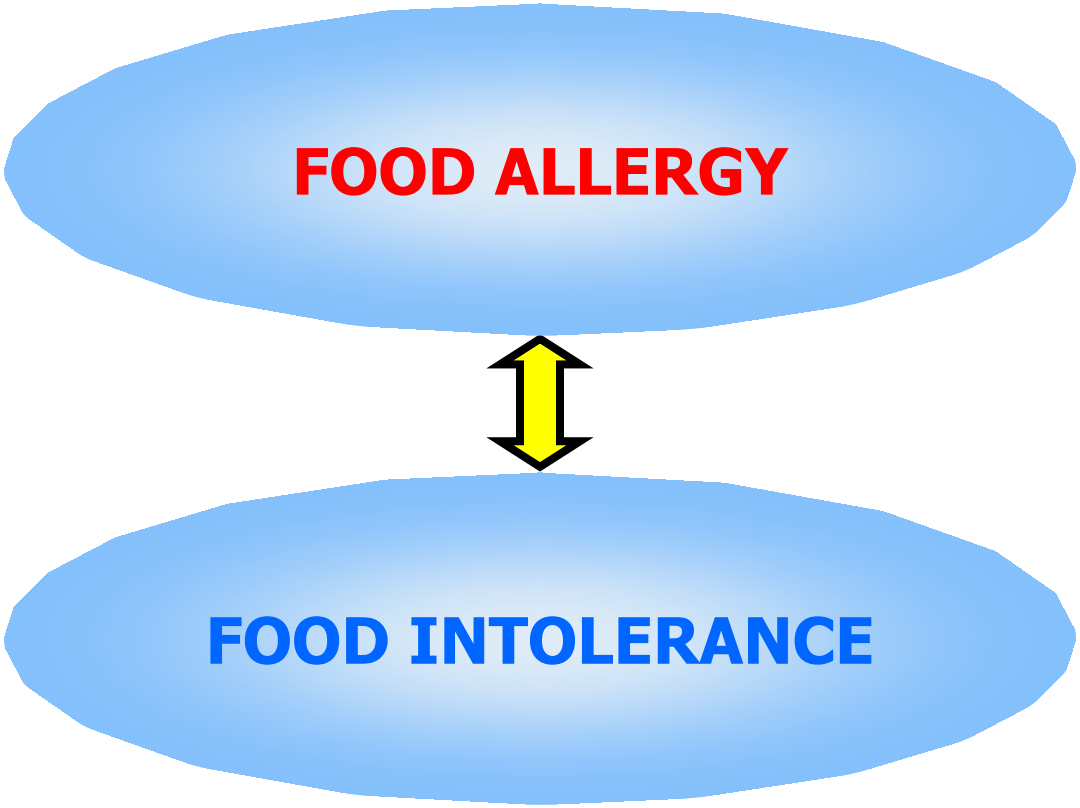

TWO PHENOMENOES THAT OFTEN ONE LEADS TO THE OTHER AS EXPRESSION OF AN IPER-REACTIVITY OF OUR IMMUNE SYSTEM

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FOOD ALLERGY

- Immediated reaction (strawberry hives, angioedema from shell fish, peanuts)
- Acute reaction
- Dose-dependent
- IgE - mediated
- No cross-reactivity
- Defined target organs

FOOD INTOLERANCE

- Retarded reaction (up to 72 h after)
- Cronic reaction
- No dose-dependent
- No IgE - mediated
- Cross-reactivity
- Any organs - apparatus

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MACROMOLECULE THEORY

JONATHAN BROSTOFF

Professor Emeritus of Allergy
and Environmental Health King's College
London UK

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THEORY OF THE ALTERED ABSORPTION OF MACROMOLECULES

- THE INTESTINAL BARRIER RULES A FUNDAMENTAL FUNCTION IN ABSORPTION OF FOODS AND STIMULATING IMMUNE SYSTEM
- 60% OF ALL IMMUNITY CELLS ARE CLOSE TO THE INTESTINAL WALLS
- ON THE INTESTINAL BARRIER THERE ARE NUMEROUS SAPROPHYTE CELLS (BACTERIAL FLORA)

AN ALTERATION OF BACTERIAL FLORA IS CALLED
INTESTINAL DISBIOSIS

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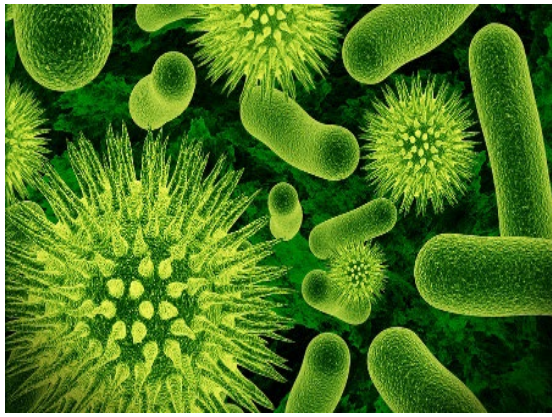
THEORY OF THE ALTERED ABSORPTION OF MACROMOLECULES

BACTERIA COLONIZING THE INTESTIN FROM BIRTH ARE ABOUT 1000 SPECIES (ACIDOPHILUS, BIFIDUS LACTOBACILLUS, ESCHERICHIA, ENTEROCOCCO ECC.)

- **SYNTHESIZE VITAMINS K-B1-B12- FOLIC ACID, PANTHOTENIC ACID**
- **METABOLIZE STEROID HORMONES**
- **REGULATE INTESTINAL GAS**
- **PRODUCE NATURAL ANTIBIOTICS**
- **PRODUCE ANTI BACTERIAL ACTION SUBSTANCES**



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INTESTINAL BARRIER

NON IMMUNOLOGIC

IMMUNOLOGIC

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NON IMMUNOLOGICAL INTESTINAL BARRIER

INTESTINAL EPITELIUM

- Pile of binded enterocites (apical tight junctions)
- Normally this barrier is little or totally unpenetrable to potential dangerous materials
- Any alteration or inflammation can alterate its permeability

IUXTAMUCOSAL ENVIRONMENT

- The mucus is a fundamental component of the barrier
- Traps microrganisms and other dangerous materials blocking its absorption
- Contains secretory IgA, enzymes for digestion of proteins, fats and anaerobic bacteria normally present on the mucosa

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IMMUNOLOGICAL INTESTINAL BARRIER

↓

MUCOSAL IMMUNE SYSTEM

↓

GUT ASSOCIATED ORGANIZED

LIMPHOID TISSUE

(GALT: Gut Associated Lymphoid Tissue)

400 mq

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ALTERATION OF INTESTINAL BARRIER

↓

INCREASES GUT PERMEABILITY

When the intestine looses its filter capacity, it can permit the transit of macromolecule that, being recognized as "non self", activate the body mechanisms of defence

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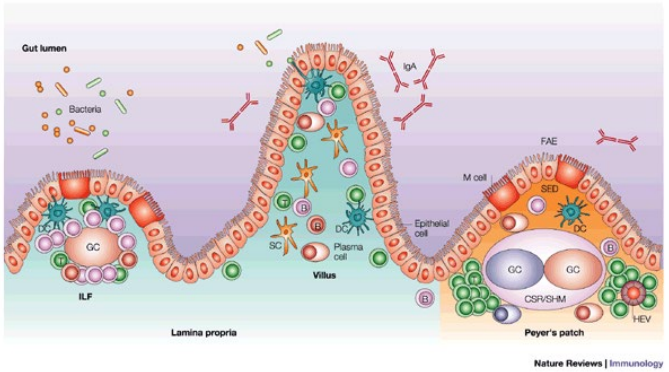
CAUSES FOR ALTERATION OF INTESTINAL BARRIER

- GENETIC CONDITIONS
- ENTERITIS, DIARRHEA,
- PROLONGED STEROID THERAPY
- PROLONGED ANTIBIOTICS THERAPY
- VIRAL INFECTIONS
- SURGERY
- EMOTIONAL STRESS



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FOOD INTOLERANCE

CONDITION IN WHICH

A FOOD IS AVOIDED

AND

SIMPTOMS DISAPPEAR

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FOOD INTOLERANCE

RECURRING CROSS – REACTIONS BETWEEN FOODS OF THE SAME BIOLOGICAL FAMILY OR GROUP

INGESTION OF COLLATERAL FOODS MEANS NOT TO DETOX THE BODY AND KEEP THE INTOLERANCE

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BIOLOGICAL FAMILIES

• WHEAT	OAT, CORN, BARLEY, RICE
• MILK	BEEF, LAMB
• EGGS	CHICKEN, COCKEREL, GUINEA-FOWL
• TOMATO	POTATOS, PEPPER, EGGPLANT
• COFFEE	TEA, COCOA, COLA, MATE', KARKADE'
• APPLE	ALMOND, PEACH, STRAWBERRY, CHERRY
• SUGAR	BEETROOT, SPINACH, SWISS CHARD
• SHRIMP	LOBSTER, CRUSTACEAN, CRAB
• TROUT	SALMON, HERRING

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BIOLOGICAL FAMILIES AND CROSS-REACTIONS

Gramineae	Rosaceae
Oat	Apricot
* Bamboo	Persimmon
* Kamut	Cherry
* Sugarcane	Quince
* Spelt	Strawberry
Bermuda grass	Raspberry
Wheat	Almond
Buckwheat	Apple
* Corn	Blackberry
Millet	Loquat
* Rice	** Pear
Rye	Plum

** Far from a biological point of view with grain*
*** Low allergenic power*

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BIOLOGICAL FAMILIES AND CROSS-REACTIONS

Solanaceae	**Rutaceae**
Cayenne pepper	Orange
Eggplant	Bergamot
Paprika	Citron
Potato	Chinotto
Chili pepper	Lime
Pepper	Lemon
Tomato	Mandarin
Tobaco	Grapefruit
Chenopodiace	**Cucurbitaceae**
Beet	Cucumber
Swiss chard	Watermelon
Spinach	Melon
	Pumpkin/ Zucchini

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BIOLOGICAL FAMILIES AND CROSS-REACTIONS

Cruciferae	Leguminosae
Broccoli	Peanut
Cabbage	Chickpeas
Brussells sprout	Carrob
Cauliflower	Beans
Kale	Fava beans
Water cress	Lentil
Mustard	Liquorice
Turnip	Lupin
Radish	Peas
Arugula	Soy – Soy Lecithin
	Tamarind
Umbelliferae	**Compositae**
Anis	Camomile
Carrot	Artichoke
Coriander	Chicory
Cumin	Sunflower
Fennel	Lettuce
Parsnip	Radicchio
	Parsley
	Celery

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BIOLOGICAL FAMILIES AND CROSS-REACTIONS

Labiate	**Vitaceae**
Basil	Black Currant
Marjoram	Red Currant
Oregano	Gooseberry
Rosemary	Grape
Thyme	
Liliaceae	**Lauraceae**
Garlic	Laurel
Asparagus	Avocado
Onion	Cinnamon
Leek	
Palmae (Arecaceae)	**Musaceae**
Coconut	Bananas
Date	
Sago	

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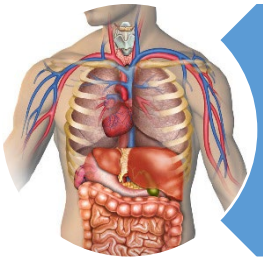
FOOD INTOLERANCE

DISTURBS ARE NOT ONLY IN RELATION TO DIRECT INGESTION, IT MAY LAST AT A DISTANCE OF 72 HOURS LATER.



IT CAN MANIFEST WITH SYMPTOMS AND DISEASES AT THE EXPENSE OF ANY ORGAN - APPARATUS - SYSTEM.

AFTER THE PERIOD OF RECOMMENDED AVOIDANCE, THE SUBSTANCE CAN BE REINTRODUCED IN THE DIET EVERY 3-4 DAYS

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SYMPTOMS RELATED TO THE PRESENCE OF FOOD INTOLERANCE

S.N.C.	HEADHACHE, LOW CONCENTRATION, DEPRESSION, IPERACTIVITY, VARIABLE MOOD, PERSISTENT ASTHENIA, MENTAL TORP
GENITO-URINARY	VAGINAL IRRITATION, CYCLIC CYSTITIS, ENURESIS
RESPIRATORY	NASAL CONGESTION, RHINITIS, SINUSITIS, RHEUM, ASTHMA, BRONCHITIS, OTITIS
SKELETAL MUSCLE	ARTICULAR DOLENCY, YOUNG ARTHRITIS, MUSCULAR CRAMPS
GASTROINTESTINAL	NAUSEA, AEROPHAGY, METEORISM, DIARRHEA, GASTRALGIA, IRRITABLE COLON SYNDROMES, CHRON DISEASE.
SKIN	ECZEMA, RASH, FACIAL PALENESS, PSORIASIS, ACNE

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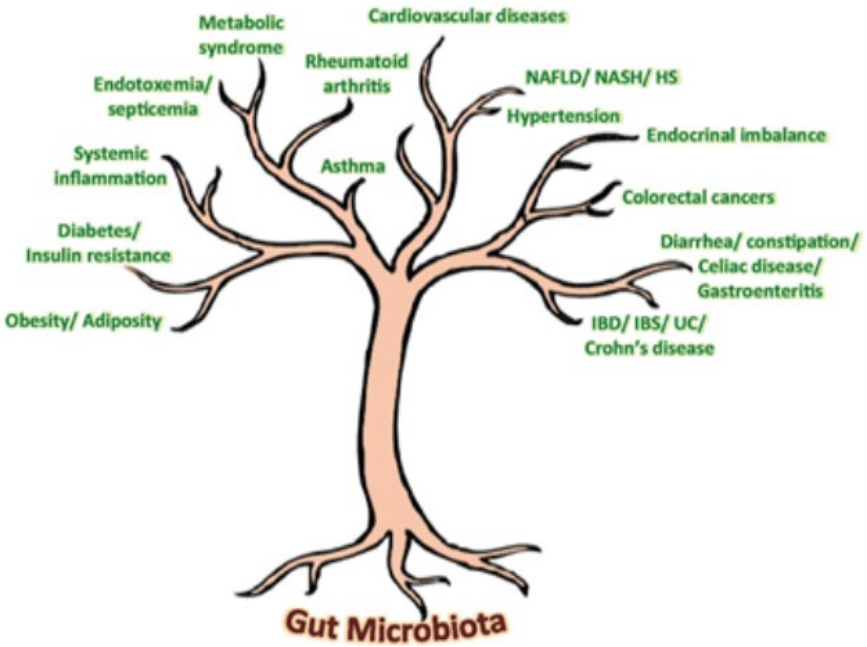
CHRONIC INFLAMMATION AND INTESTINAL MICROBIOTA



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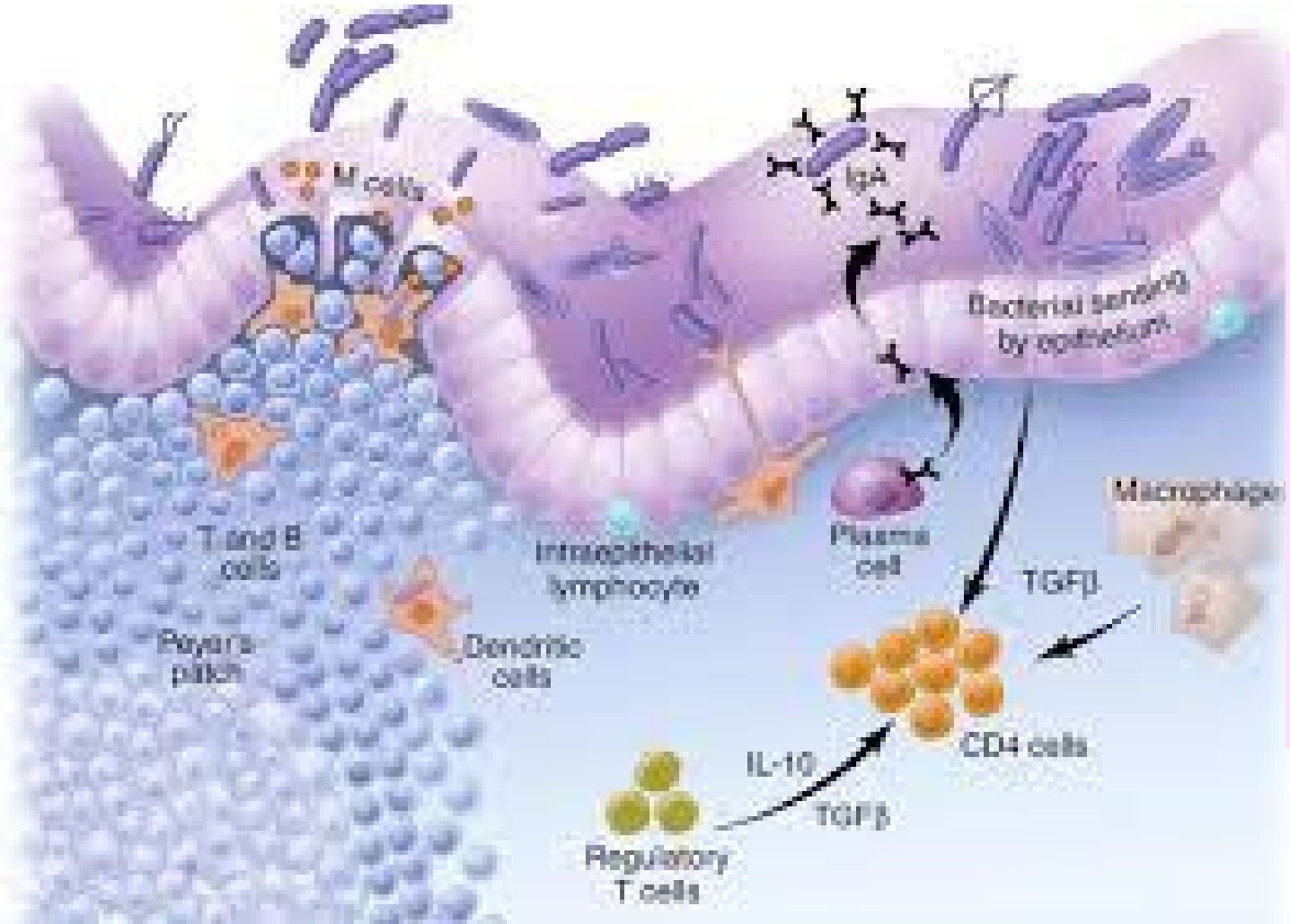
WHAT IS INTESTINAL MICROBIOTA



Billions of bacterial cells reside in our intestinal tract and are one of the richest and most complex ecosystems on the planet

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INTESTINAL MICROBIOTA

the largest and most complex bacterial ecosystem in the human body

75% - 80% not cultivable

Firmicutes (50-80%)

Bacteroidetes (40%)

Actinobacteria

Proteobacteria

Methanobrevibacter smithii

Candida

Penicillum

Aspergillus

Disordini metabolici:

Obesità, Diabete tipo I e

Malattie infiammatorie croniche intestinali (MICI)

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THE MICROBIOTA IN THE DIFFERENT LIFE STAGES

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INFANT

the intestinal microbiota is gradually assembled thanks to :

- Perinatal events
- feeding with breast milk
- contact with the bacteria present on the mother's body.

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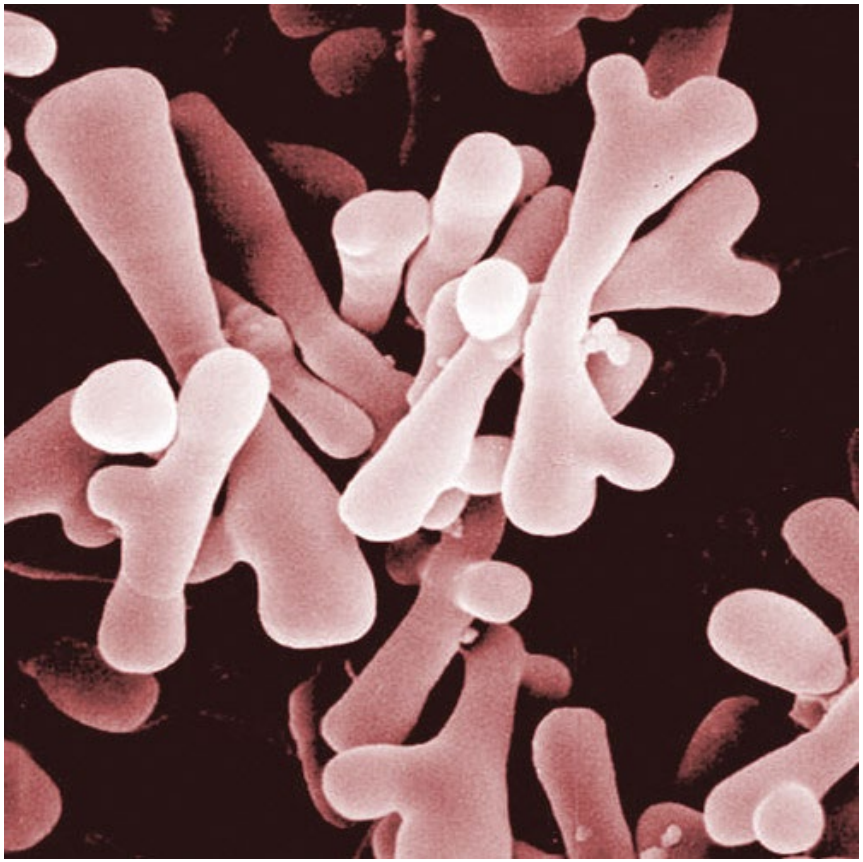
INFANT



A high abundance of bifidobacteria is crucial for:

- **Development** and education of the immune system
- **Protection** from infections by pathogenic microorganisms
- **Prevention** of onset of allergic diseases (asthma, eczema)

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CHILD

The microbiota slowly assumes the typical conformation of an healthy adult's microbiota

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CHILD

The balance of the intestinal microbiota helps to **prevent** the onset of diseases that may persist throughout life:

- Obesity
- Diabetes
- Metabolic disorders

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ADULT

An healthy intestinal microbiota permit to:

- **Preserve** the immune system balance
- **Preserve** the balance of the energy metabolism
- **Prevent** many local or systemic diseases
- **Preserve** the body's defenses even in stressful situations (travel, environmental changes or lifestyles)

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ELDERLY

A healthy microbiota helps to:

- **Maintain** proper nutritional status
- **Balance** the functioning of the immune system
- **Counteract** the effects of aging (immunosenescence, chronic and generalized inflammation)

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KNOW YOUR INTESTINAL MICROBIOTA FOR:

- **Prevent** many intestinal diseases (SCI, diverticulitis..) or systemic (obesity, diabetes, allergies..)
- **Design** personalized dietary approaches
- **Maintaining** the balance of the organism in every change of life: pregnancy, menopause, stressful situations….

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METABOLIC FUNCTIONS OF INTESTINAL MICROBIOTA

- Vitamin production
- Amino acid synthesis
- Biotransformation of bile acids
- Fermentation of non-digestible and muco-endogenous substrates

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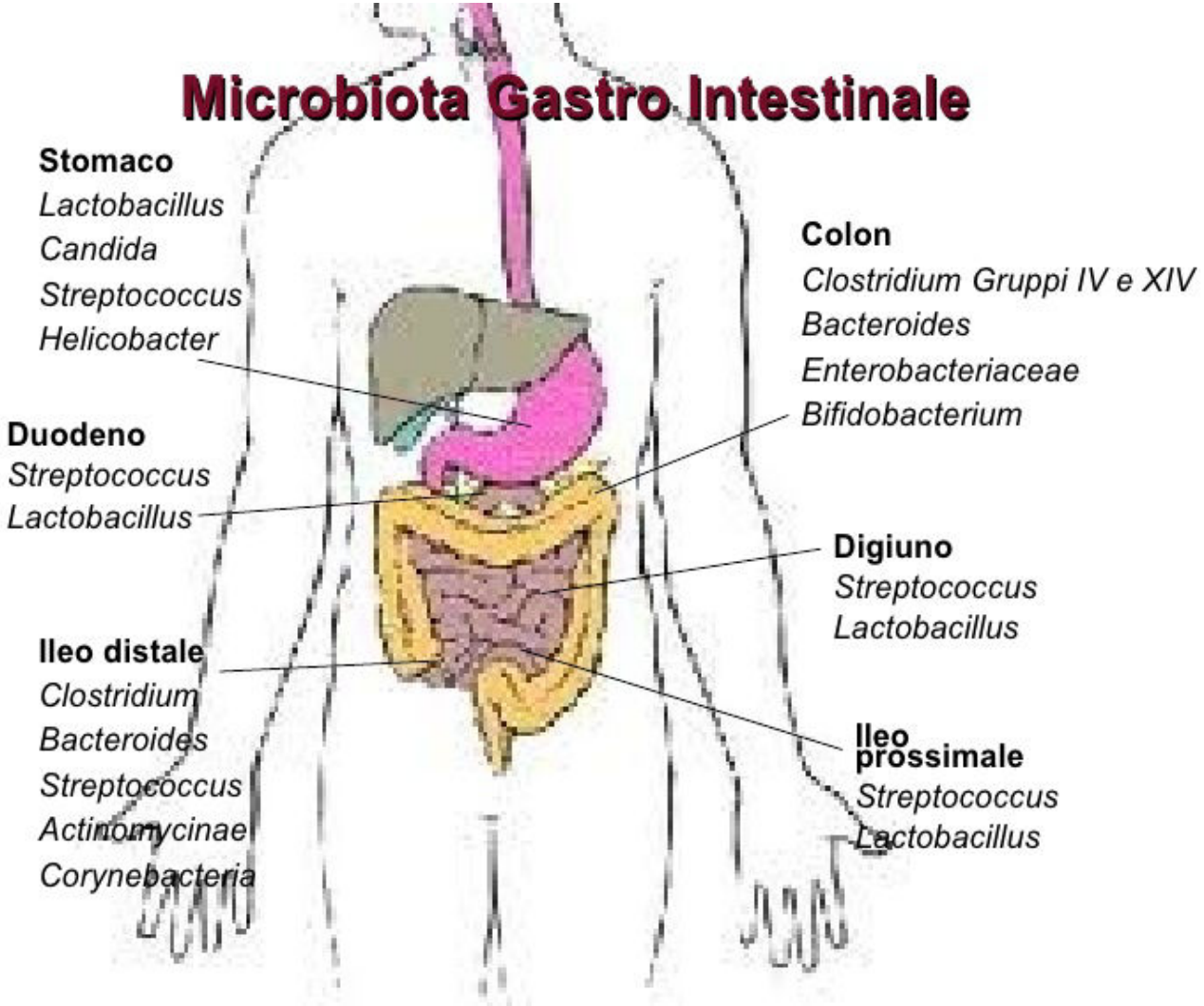
DISTRIBUTION OF THE MICROBIOTA



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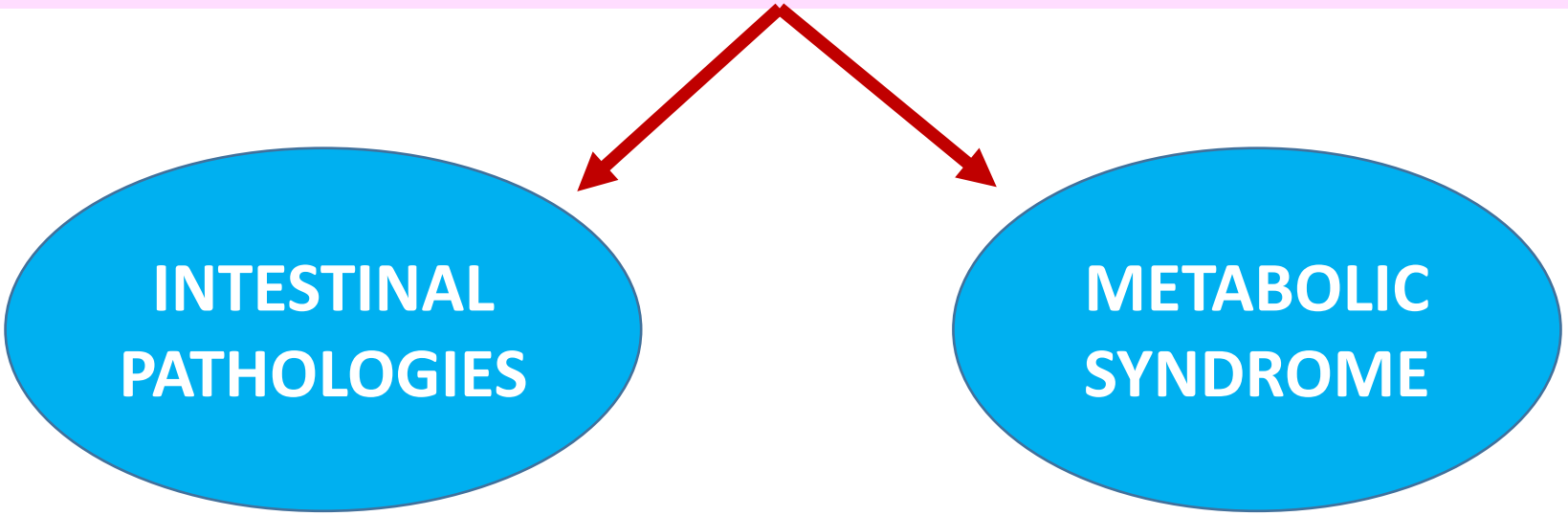
MICROBIOTA AND METABOLISM

DYSBIOSIS → changes in the balance of the microbiota (GALT system)



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METABOLIC SYNDROME

The relationship between microbiota and metabolic syndrome involves the relative risk of developing

- type II diabetes
- cardiovascular diseases
- hyperglycemia
- hyperlipidemia
- insulin resistance
- fibrinolysis
- liver disease
- non-alcoholic fatty liver disease NAFLD

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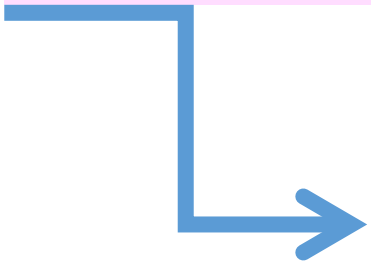
METABOLIC SYNDROME

In the obese, a high-fat diet causes:

- increase of *firmicutes*
- decrease of *bacteroidetes*
- increased glyco-hydroxylase and phosphotransferase enzymes



increase in fermentation products starting from polysaccharides (acetate, butyrate, propionate) which have a high energy value for enterocytes and increase caloric intake

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METABOLIC SYNDROME

The microbiota can act

- On intestinal enzymes involved in lipogenesis by increasing the deposition of fat in the liver (steatosis)
- On the composition of bile
- On choline levels
- On the permeability of the mucous membrane

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MICROBIOTA AND AUTISM

Individuals with autism have unique intestinal bacterial populations, responsible for the variety and severity of symptoms

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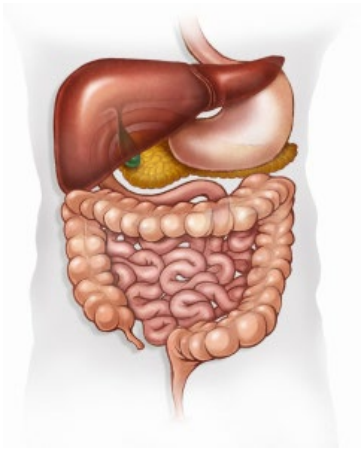
BOWEL AUTISM AND NUTRITION

Dott. Federico Balzola
U.O.A.D.U. Gastro-Epatologia
Città della Salute
Ospedale Molinette Torino



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BOWEL AUTISM AND NUTRITION

Since the beginning of the outpatient activity, in 2005, more than 900 patients have come to our observation who presented:

- Gastrointestinal symptoms (alvous disorders, abdominal pain, reflux, malabsorption, food selectivity)
- Autism spectrum neuropsychiatric pathology

All of them were prescribed first-level exams which included:

- Blood tests (IBD/malabsorption screening, HLA mutation for celiac disease)
- Feces (parasitological/fecal Hb/mycological/fecal calprotectin)
- Abdominal and intestinal ultrasound

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BOWEL AUTISM AND NUTRITION

Underwent endoscopy (EGDS/Colon with biopsies) + video capsule in selected cases

201 total patients with pervasive developmental disorder

169M, 32F
Average age 12 years (range 4-42)

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BOWEL AUTISM AND NUTRITION

The key symptoms were:

48% constipation,
28% diarrhea,
55% abdominal pain,
10% Gastroesophageal reflux

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BOWEL AUTISM AND NUTRITION

- ✓ Inflammatory index (alpha-2-globulins/platelets) 40%
- ✓ Celiac disease antibodies neg 90% AGA IgG 20%Malabsorption/malnutrition 88% (Hb faeces pos. 7%)
- ✓ Calprotectin 48%
- ✓ HLA DQ2-DQ8 + 55%
- ✓ Iron deficiency/anaemia 25% Microcythaemia 40%
- ✓ Low IgA 35% High IgE 40% (atopy 80% with specific IgE neg 90%)

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BOWEL AUTISM AND NUTRITION

Histological findings

- ✓ 62/190 (33%) esophagitis
- ✓ 68/190 (36%) chronic gastritis
- ✓ 4/190 (2%) eosinophilic gastritis
- ✓ 68/190 (36%) MARSH I°-II°
- ✓ 54/190 (81%) non-IBD chronic colitis
- ✓ 71/190 (37%) colitis with excess eosinophils
- ✓ Video capsule with signs of atypical IBD 19/25

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BOWEL AUTISM AND NUTRITION

Based on the histological data, was started a pharmacological therapy with mesalazine, budesonide, beclomethasone, immunosuppressants, anti-TNF:

- Gluten and casein free diet
- GEL drug therapy (different according to the patient)

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BOWEL AUTISM AND NUTRITION

At the 12-month follow-up of 150 patients

Gastrointestinal improvement:

- 65% pain
- 84% bowel complaints
- 41 % Reflux/dysphagia
- 40% Improved muscle mass/growth

Behavioral improvement (36 patients followed up for 12 months)

- 65% hyperactivity/aggression
- 34% attention
- 22.1% sleep-wake rhythm

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MICROBIOTA AND AUTISM

"In a sample of 2,973 children with ASD (ages 2-17 years, 81.6 % male), 24% experienced at least one type of chronic GI problem (constipation, abdominal pain, bloating, diarrhea, and/or nausea lasting three or more months). Children with each type of GI problem had significantly higher rates of both anxiety and sensory over-responsivity. Sensory over-responsivity and anxiety were highly associated, and each provided unique contributions to the prediction of chronic GI problems in logistic regression analyses. **The results indicate that anxiety, sensory over-responsivity and GI problems are possibly interrelated phenomenon for children with ASD, and may have common underlying mechanisms.**" *Mazurek MO, et Al., 2013*

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MICROBIOTA AND AUTISM

In a 2013 article, Macfabe D. of the Department of Psychology (Neuroscience) and Psychiatry, Division of Developmental Disabilities, Lawson Research Institute, University of Western in Ontario, Canada, examines the role of enteric fatty acids Short Chain Fatty Acids (SCFA), specifically propionic acid, which is produced by bacteria that have been associated with the autistic condition and which may play a role in the etiology of some forms of ASD (Macfabe , 2013).

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IMPLICATIONS FOR CLINICAL PRACTICE

- Being able to intervene effectively on the most important cardiovascular risk factors
- Prevent and control type II diabetes more effectively
- Treat and prevent obesity

intervening with lifestyle and nutraceutical diet

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CONCLUSIONS

The development of research and absolutely innovative knowledge in the field of the microbiota will involve in the future not only gastroenterologists but also internists, cardiologists, allergists, psychiatrists, veterinarians and other specialists who will find in this environment a strong and decisive ally for the prevention and the treatment of many pathological conditions.

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Thanks

for your attention

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