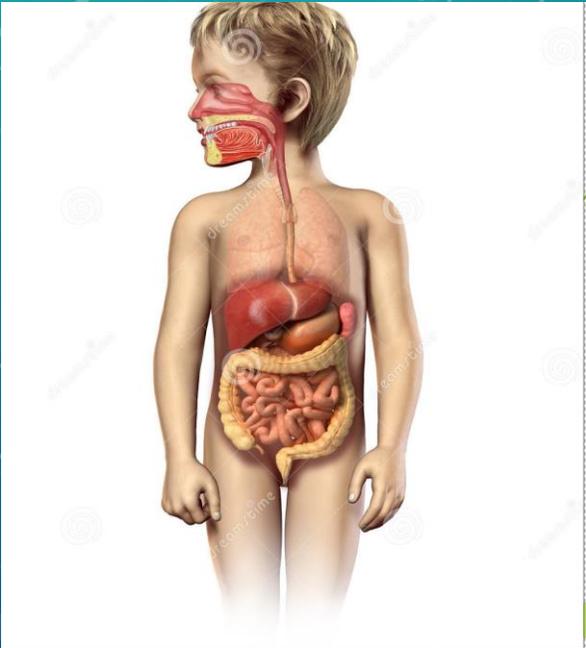


THE HUMAN MICROBIOME



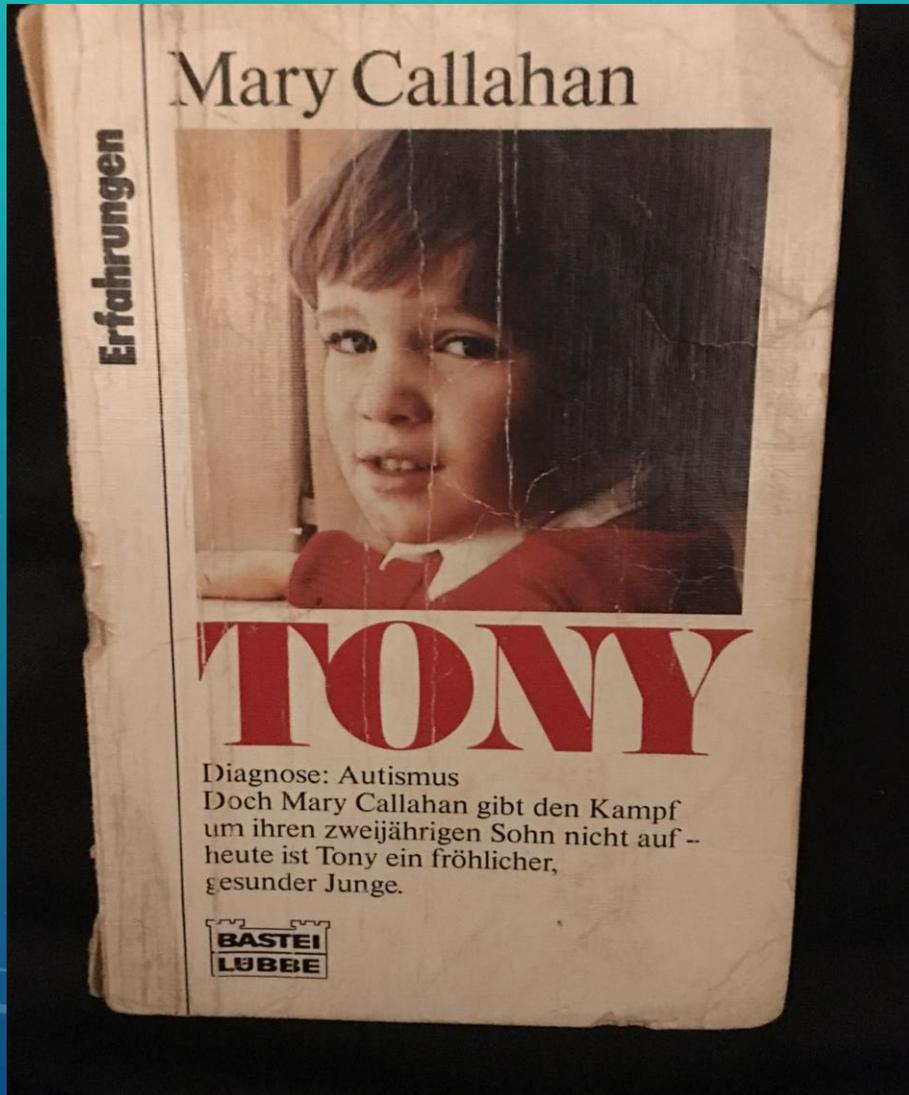
THE IMPORTANCE OF A WELL FUNCTIONING DIGESTIVE SYSTEM IN AUTISM

REBECCA SHERRY ESHRAGHI, PHD, DNM, BBA

DISCLAIMER

Information obtained in this presentation is for educational purposes only, it is not intended as diagnosis, prescription or treatment for any disease, mental or physical, and is not a substitute for regular medical care.

HOW IT ALL BEGAN:



- 1985 - read this book
- 2008 - daughter was diagnosed
- 2008 – Autism Awareness month April, First talks about autism recovery
- 2008 – present – started researching connection between autism and the digestive tract/ microbiome

Regression into Autism:



- Complete loss of eye contact
- Toe walking and hand flapping
- Irritability
- Extreme seeking for sensory input (obsession with water)
- Sleepless nights
- Completely unaware of surroundings
- Complete loss in interest for social interaction

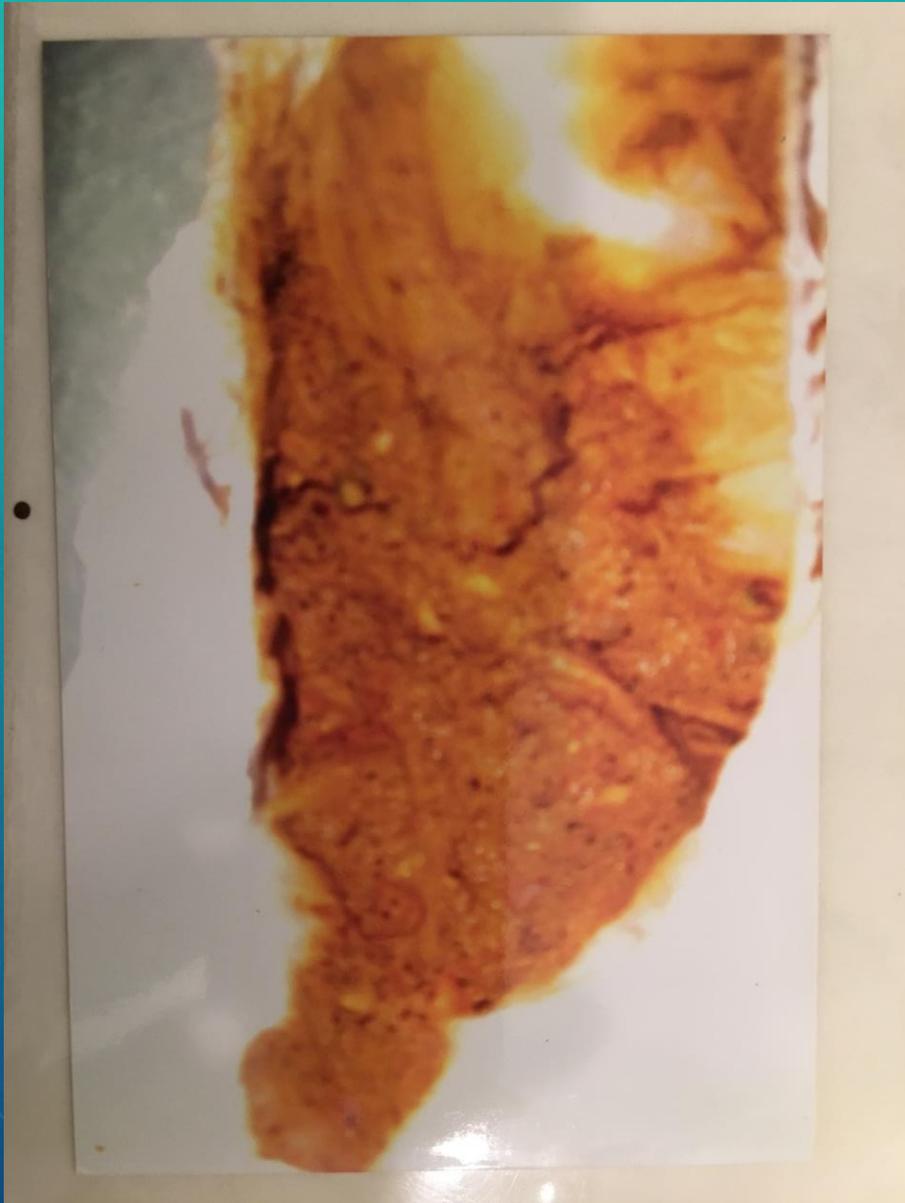
Additional Physical Symptoms:

- **Pale complexion**
- **Dark circles under her eyes**
- **Bloated belly**
- **Nails stopped growing**

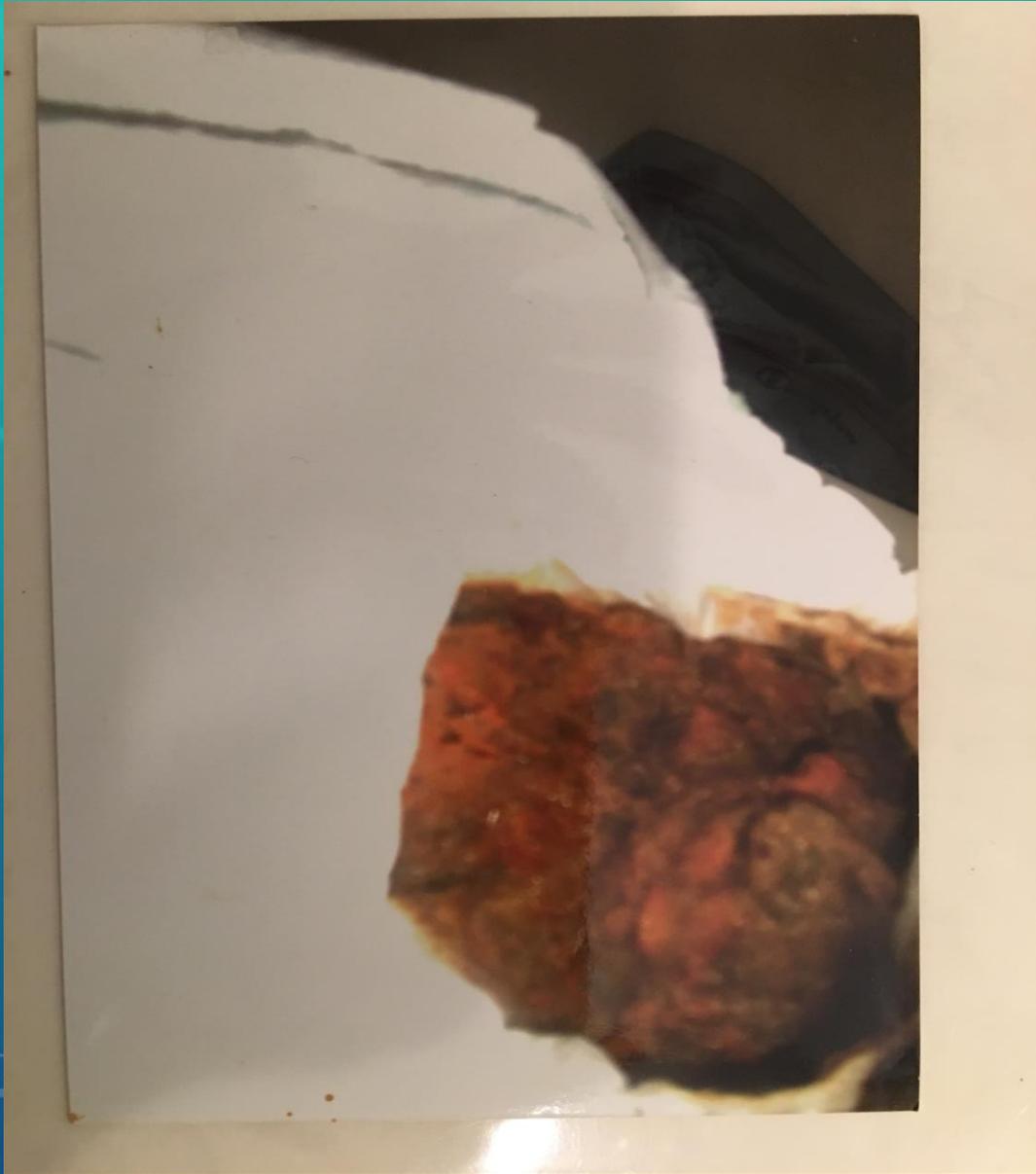
BREAKDOWN IN DIGESTIVE FUNCTIONING:

- **Liquid diarrhea with undigested food pieces**
- **Abdominal bloating**
- **Pain**
- **Up to 15 soiled diapers with diarrhea each day**

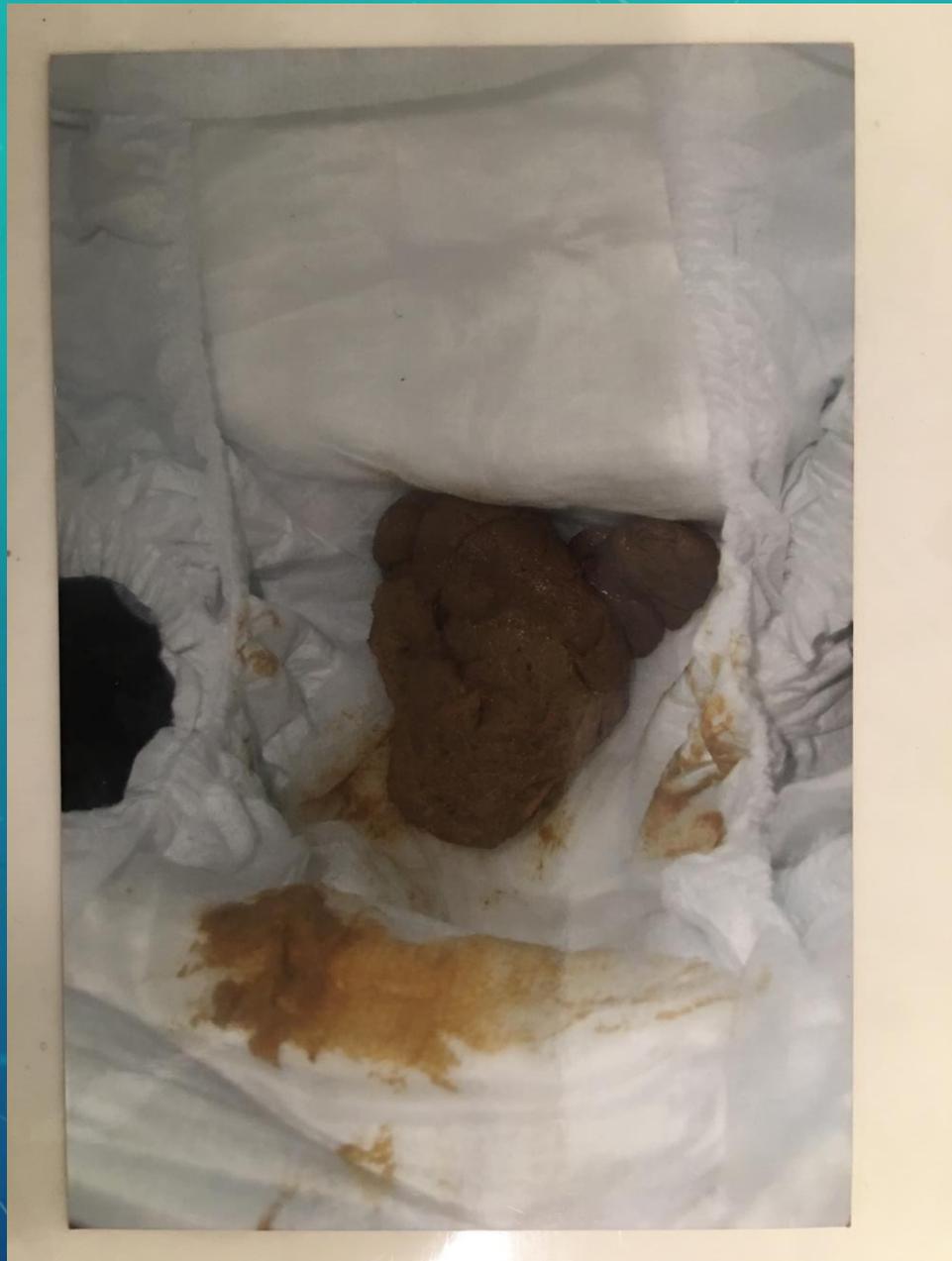




- **Grainy, orange, loose stools**



- **Colorful with undigested foods**



- **First formed, normal looking stool**

AUTISM PREVALENCE

AS REPORT BY CDC - ADDM REPORT: 2000 - 2014

Birth Year	Survey Year	Year Reported	Autism Rate
2006	2014	2018	1 in 59
2004	2012	2016	1 in 68
2002	2010	2014	1 in 68
2000	2008	2012	1 in 88
1998	2006	2009	1 in 110
1996	2004	2009	1 in 125
1994	2002	2007	1 in 150
1992	2000	2007	1 in 150

NOTES: ADDM = Autism and Developmental Disabilities Monitoring Network
Source: www.cdc.gov

- Currently 1 in 59 children are diagnosed with autism
- Better diagnosis?
- There is no genetic epidemic
- Genetics vs. Epigenetics

WHAT IS HAPPENING?



THE MICROBIOME – OUR INNER ECOSYSTEM

- Human body contains 10 times more microbes such as bacteria and fungi, than actual human cells and bacteria are much smaller than human cells.
- The highest concentration of some 100 trillion microbes is found in the human gut.
- Our genes are outnumbered by a hundred to one by microbial genes (The Human Microbiome). The sum of all these microbes includes more than 60,000 genes, that's twice as many as the human genome. **(We are more bacteria than human cells)**
- Majority of our microbes are good and beneficial.
- Good bacteria and pathogenic bacteria both are present in the gut. **(the ecosystem is based on balance)**



ROLE AND IMPORTANCE OF THE GUT FLORA/ MICROBIOME:

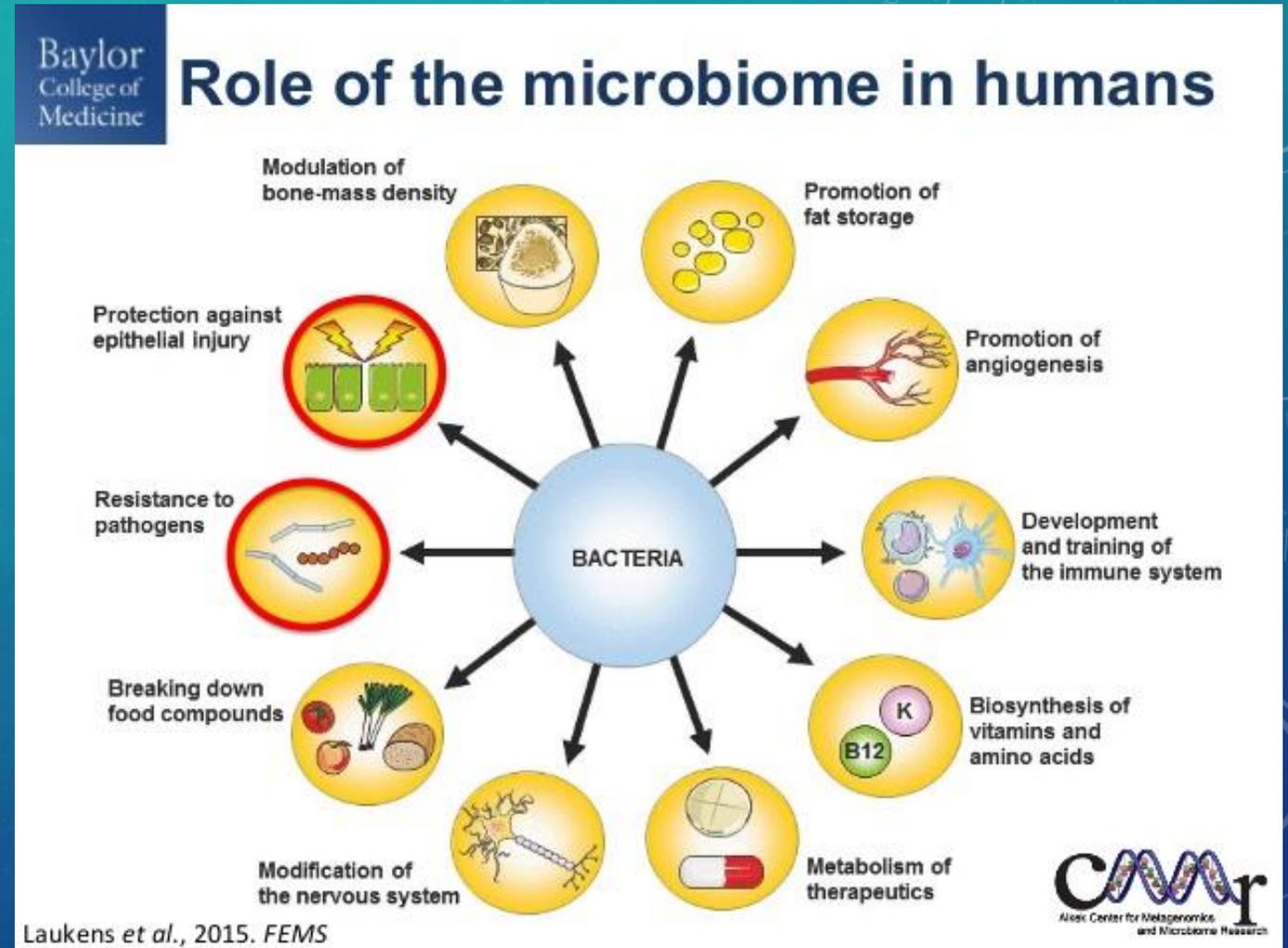
- **Regulates our immune system (80% of our immune system is regulated by our gut bacteria)**
- **Gut bacteria are responsible for producing hundreds of neuro-chemicals such as serotonin which influences mood and brain function, 90% of the serotonin which is a neurotransmitter resides in the gut.**
- **Gut bacteria determine how we metabolize food and helps us to extract energy from food.**
- **Helps with the production of some vitamins (B and K).**

DISEASES ASSOCIATED WITH THE MICROBIOME

- Autoimmune disease
- Allergies
- Autism
- Diabetes
- Multiple Sclerosis
- Asthma
- Eczema
- Colon cancer
- IBS
- Neurological Disorders
- CNS disorders
- Cardiovascular
- Inflammation
- Obesity

•

• ** These are common diseases in families with autism, especially autoimmune and GI



WHAT IS WRONG WITH THE GI TRACT IN AUTISM?

The Prevalence of Gastrointestinal Problems in Children Across the United States With Autism Spectrum Disorders From Families With Multiple Affected Members

Wang, Lulu W. MD^{*†}; Tancredi, Daniel J. PhD[†]; Thomas, Dan W. MD[‡]

Journal of Developmental & Behavioral Pediatrics: June 2011 - Volume 32 - Issue 5 - p 351-360
doi: 10.1097/DBP.0b013e31821bd06a
Original Article

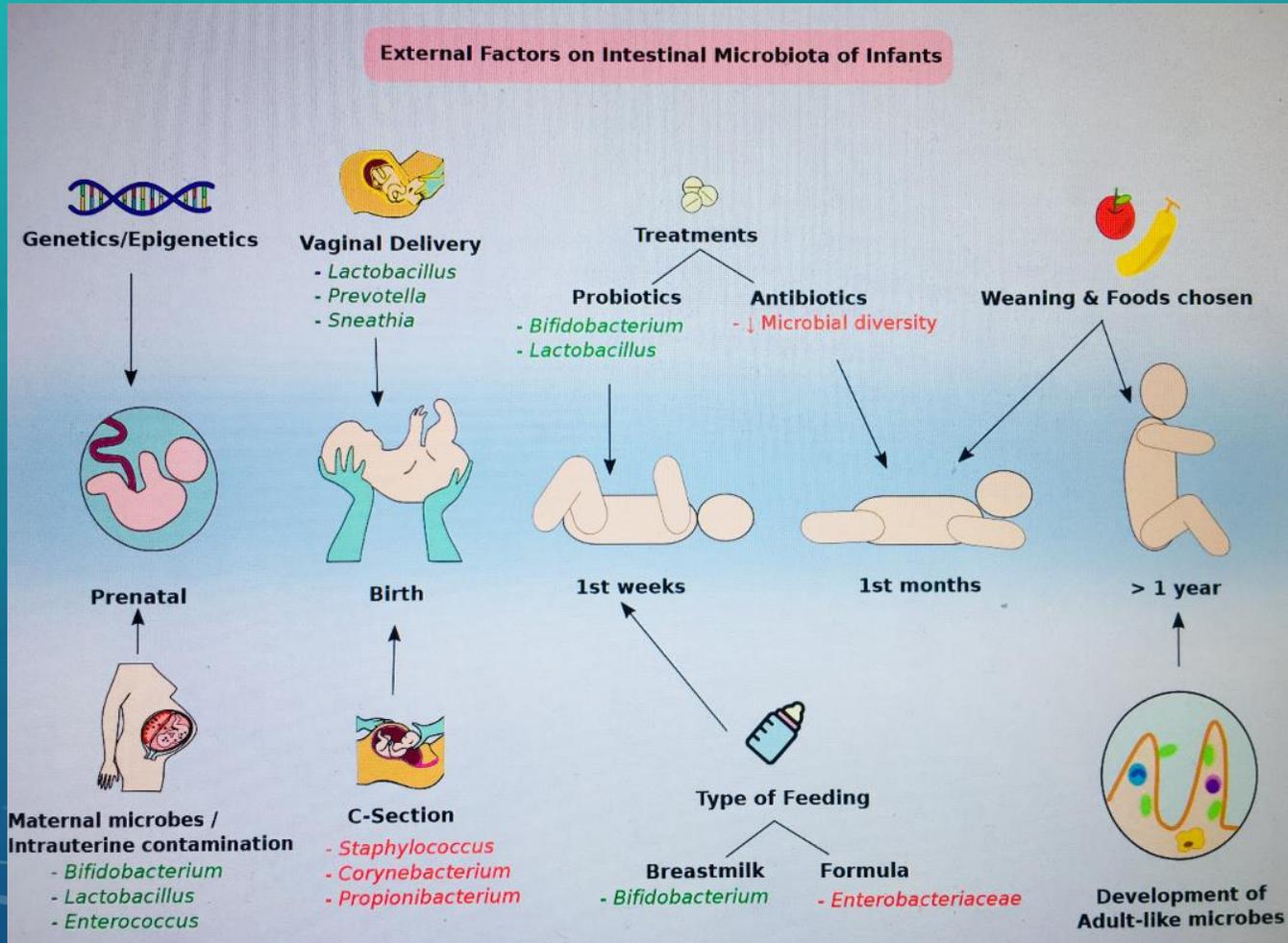
Autistic disorder and gastrointestinal disease

Horvath, Karoly MD, PhD^{*}; Perman, Jay A. MD[†]

Current Opinion in Pediatrics: October 2002 - Volume 14 - Issue 5 - p 583-587
Gastroenterology and nutrition

- **GI problems are the most common medical problems associated with Autism**
- **Symptoms: constipation, diarrhea, bloating, pain, indigestion, acid reflux, vomiting...**
- **Causes: Abnormal Intestinal Permeability (dysbiosis/ leaky gut), Inflammation, Gut Flora and microbial composition/ diversity**

What determines the development of the microbes?



- Microbial shifts during pregnancy
- Birth: Vaginal vs. C-section
- Breastmilk vs. Bottle feeding
- Environmental Exposures
- Food and Nutrition
- Drugs/ Antibiotics

=> The microbiome becomes more stable and individualized by the age of 3.

AUTISM RISK ALSO CONNECTED TO THE MOTHER'S MICROBIOME AND GUT HEALTH



UVAToday

HEALTH & MEDICINE

AUTISM RISK DETERMINED BY HEALTH OF MOM'S GUT, UVA RESEARCH REVEALS

The discovery raises the possibility that preventing forms of autism could be as simple as an expectant mother modifying her diet or taking custom probiotics.

- Pre-pregnancy (maternal inflammation)
- During pregnancy (maternal inflammation, trimester shifts in vaginal microbiome and risk of abortion and pre-term labor)
- During birthing process (C-section vs. Vaginal, vaginal flora, vaginal swapping)
- During lactation/ breastfeeding
- **Glyphosate?? Artificial sweeteners??**

WHAT CAN DISRUPT THE EARLY DEVELOPMENT OF THE MICROBIOME?

ANTIBIOTICS!!!!

- With 1,365 courses per 1,000 babies, the highest percentage of antibiotics is prescribed for children below the age of two, meaning that the average child in America receives nearly 3 courses of antibiotics before the age of two.
- Pre-term babies routinely receive anti-biotics.
- According to a study children with autism had significantly more ear infections than the control group and because of this fact, they used antibiotics far more frequently. 34.5% of children with autism had used extensive and repeated broad-spectrum antibiotic treatments, a higher proportion of 54.5% of the children with autism had received more than six courses of antibiotics.
- 80% of total antibiotics is sold for live stock
- Martin Blaser: We are in the midst of extinguishing some of our irreplaceable microbes for good and causing major shift in our microbial composition. Even short term antibiotic treatment leaves antibiotic resistant genes for up to two years after treatment.

DISRUPTING THE DEVELOPING MICROBIOME IN EARLY STAGES

Early Disruption of the Microbiome Leading to Decreased Antioxidant Capacity and Epigenetic Changes: Implications for the Rise in Autism

 [Rebecca S. Eshraghi](#)^{1*},  [Richard C. Deth](#)²,  [Rahul Mittal](#)³,  [Mayank Aranke](#)³,
 [Sae-In S. Kay](#)⁴,  [Baharak Moshiree](#)¹ and
 [Adrien A. Eshraghi](#)³

¹Division of Gastroenterology, Department of Medicine, Miller School of Medicine, University of Miami, Miami, FL, United States

²Department of Pharmaceutical Sciences, College of Pharmacy, Nova Southeastern University, Fort Lauderdale, FL, United States

³Department of Otolaryngology, Miller School of

Effects of Antibiotics Overuse on the Microbiome

- Shifts the structure of the microbial community
- Changes the microbial and metabolic patterns of the gut => lower capacity to produce proteins, less ability to absorb iron, digest certain foods and produce essential molecules
- Causing imbalance between beneficial and pathogenic bacteria.
- Promotes growth of bacterial biofilms, which is a cause for reoccurring infections

Balance is Everything:

RESEARCH ARTICLE | MICROBIAL ECOLOGY

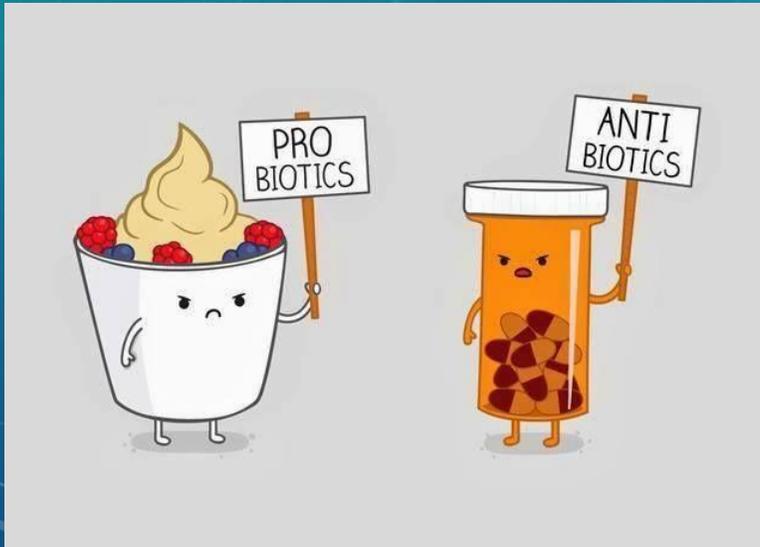
The microbiome of uncontacted Amerindians

Jose C. Clemente^{1,2,*}, Erica C. Pehrsson^{3,*}, Martin J. Blaser^{4,5}, Kuldi...

+ See all authors and affiliations

Science Advances 17 Apr 2015:
Vol. 1, no. 3, e1500183
DOI: 10.1126/sciadv.1500183

- Symbiotic relationship between our bacteria
- **Study:** Yanomami tribe have never been exposed to modern life, modern medicine and modern food, their microbiome had about 50 percent more ecological diversity than the average American.
- Microbes pass from parent to child just like our genes, hence with our lifestyles that are hostile towards our second genome, our microbes, we are fueling the transgenerational epidemic of missing but essential microbes.



Consequences of an imbalance of beneficial vs. pathogenic microbes in the gut:

LEAKY GUT/ GUT DYSBIOSIS AND INFLAMMATION!!!

- acute inflammation vs. chronic inflammation
- acute mucosal inflammation due to enteric bacterial pathogens will cause an inflammatory Response => activation of glial cells and microglia in the brain.
- Inflammation in the gut lining can cause gut permeability
 - ⇒ pathogenic bacteria can escape through the gut lining into the bloodstream
 - ⇒ => activates inflammatory cytokines that travel through the bloodstream causing oxidative stress and leading to a heightened immune response.

NEWS AND VIEWS • 16 MAY 2018

Brain inflammatory cascade controlled by gut-derived molecules

Metabolite molecules produced by the gut's microbes activate immune cells in the brain called microglia, which signal to astrocyte cells to mediate responses to inflammation in the central nervous system.

ScienceDirect

Outline



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Volume 23, Issue 5, 9 May 2018, Pages 653-660.e5

Brief Report

Early-Life Antibiotic-Driven Dysbiosis Leads to Dysregulated Vaccine Immune Responses in Mice

Miriam Anne Lynn^{1, 7} ... David John Lynn^{1, 3, 8}  

 Show more

<https://doi.org/10.1016/j.chom.2018.04.009>

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Inflammation and the Blood-Brain-Barrier connection

Science News

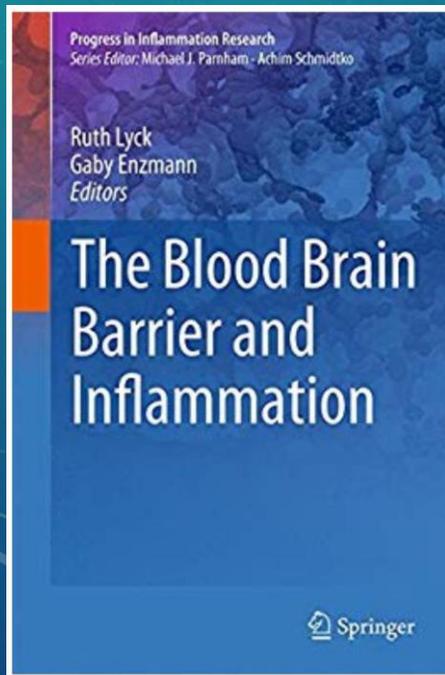
from research organizations

Changes in blood-brain barrier, intestinal permeability found in individuals with autism

Date: January 18, 2017

Source: Massachusetts General Hospital

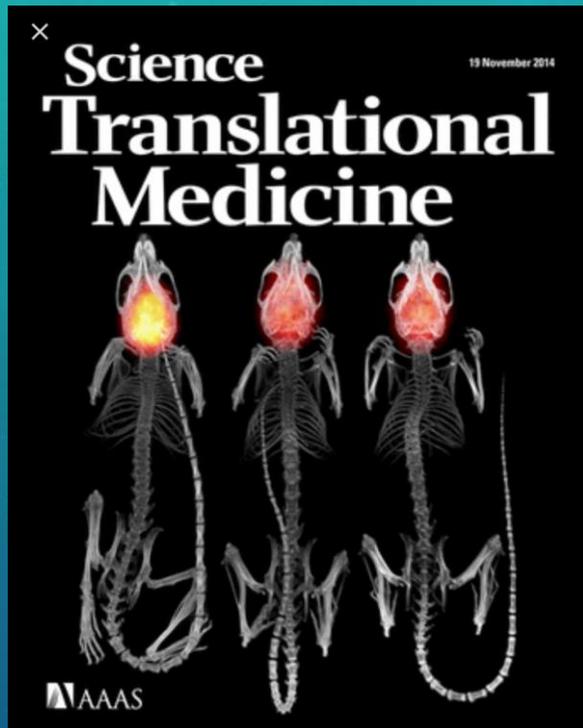
Summary: A new study finds reduced expression of genes involved in integrity of the blood-brain barrier, intestinal barrier in those with autism spectrum disorder.



- **BBB:** “A layer of tightly packed cells that make up the walls of brain capillaries and prevent substances in the blood from diffusing freely into the brain: passage across the cell membranes is determined by solubility in the lipid bilayer or recognition by a transport molecule”.
- **An inflammatory insult during brain development can change blood-brain barrier permeability and behavior in later life.**
- **Study:** germ-free adult mice underwent fecal transplantation from animals with normal microbiomes the junction proteins tightened resulting into less BBB permeability (“Blood-brain barrier dysfunction in disorders of the developing brain”, Moretti et al., *Frontiers in Neuroscience* 2015)

Blood-Brain-Barrier and Inflammation connection

“A new study in mice, conducted by researchers at Sweden's Karolinska Institutet together with colleagues in Singapore and the United States, shows that our natural gut-residing microbes can influence the integrity of the blood-brain barrier, which protects the brain from harmful substances in the blood. According to the authors, the findings provide experimental evidence that our indigenous microbes contribute to the mechanism that closes the blood-brain barrier before birth. The results also support previous observations that gut microbiota can impact brain development and function.”



“The gut microbiota influences blood-brain barrier permeability in mice”, *Science Translational Medicine* 19 Nov 2014:Vol. 6, Issue 263, pp. 263ra158
DOI: 10.1126/scitranslmed.3009759

THE LYMPHATIC SYSTEM AND BRAIN CONNECTION

IMPORTANT RECENT DISCOVERY:

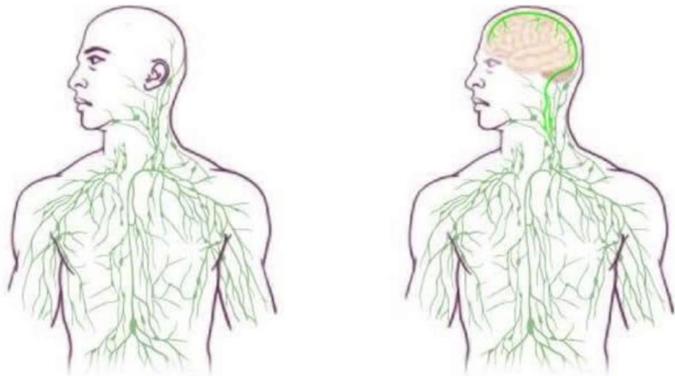
Neuroscience News



Researchers Find Missing Link Between the Brain and Immune System

Neuroscience News

3 years ago



Maps of the lymphatic system: old (left) and updated to reflect UVA's discovery. Image credit: University of Virginia Health System.

- The lymphatic system is a network of tissues and organs that help rid the body of toxins, waste and other unwanted materials. The primary function of the lymphatic system is to transport lymph, a fluid containing infection-fighting white blood cells, throughout the body.
- The brain is directly connected to the immune system by vessels previously thought not to exist.

=> overturns decades of textbook teaching

Glutathione Depletion/ Impaired Detoxification Capacity

- Glutathione is the most potent antioxidant and detoxifying agent in the body
- Children with autism have limited capacity in producing glutathione
- The production of glutathione is in part dependent on the GI tracts ability to absorb methionine, which is a precursor for making glutathione
- Other factors depleting glutathione: acetaminophen, heavy metals, pesticides, chemicals ...

Glutathione-Related Factors and Oxidative Stress in Autism, A Review

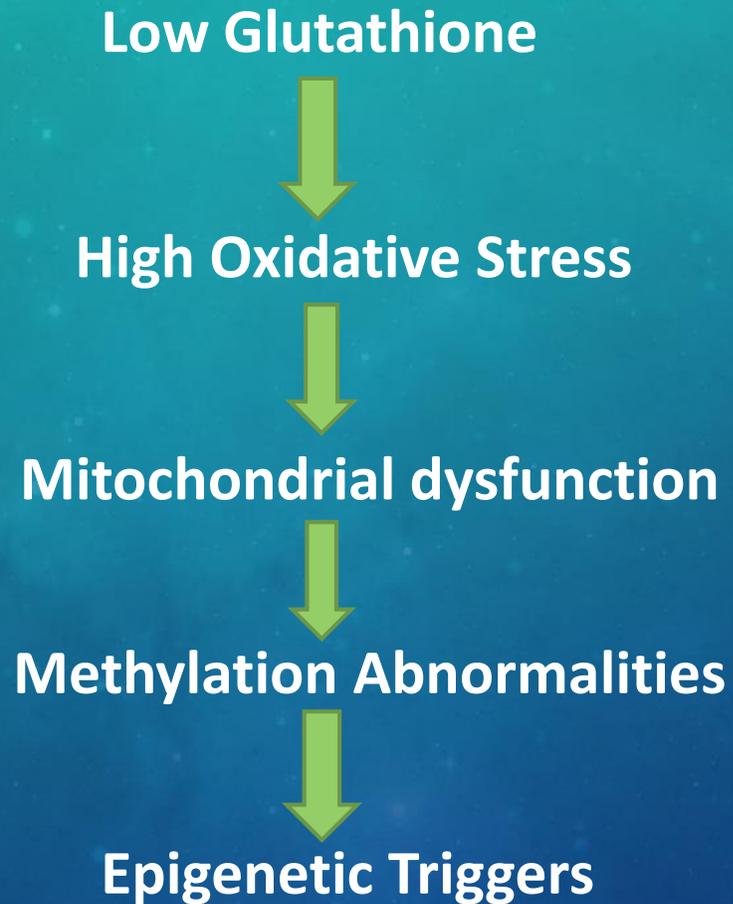
Author(s): A. Ghanizadeh, Research Center for Psychiatry and Behavioral Sciences, Department of Psychiatry, Hafez Hospital, Shiraz, Iran. S. Akhondzadeh, M. Hormozi, A. Makarem, M. Abotorabi-Zarchi, A. Firoozabadi.

Affiliation: Journal Name: Current Medicinal Chemistry

Volume 19 , Issue 23 , 2012

DOI : [10.2174/092986712802002572](https://doi.org/10.2174/092986712802002572)

Cascade of Interconnected Events:



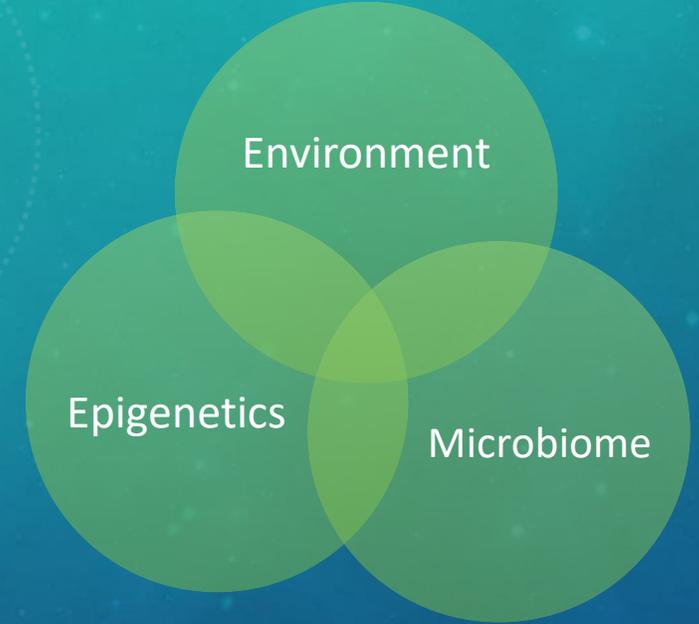
Mitochondrial dysfunction in the gastrointestinal mucosa of children with autism: A blinded case-control study

What is Epigenetics

“The study of biological mechanisms that will switch genes on and off. Epigenetics is in control of the genes.”

Only a very small part of our microbiome is heritable, the rest is shaped by our environment!

This means our microbiome that is connected to so many diseases, can be responsible for triggering genes on and off.



SD Menu ☰

Science News *from research organizations*

How good bacteria control your genes
Chemical signals from gut bacteria influence gene regulation in the gut lining

Date: January 9, 2018

Source: Babraham Institute

Summary: Scientists have discovered a way that bacteria in the gut can control genes in our cells. Their work shows that chemical messages from bacteria can alter chemical markers throughout the human genome. The signal chemicals are made when bacteria digest fruits and vegetables. By communicating in this way, the bacteria may help to fight infections and to prevent cancer.

Imbalanced/ insufficient Microbes

+ Added antibiotics

Inflammation in the gut lining

**Leaky gut, compromised blood-brain-barrier, formation of biofilms,
growth of pathogenic bacteria, impaired methylation**

Pathogens leaking into the bloodstream, glutathione depletion, oxidative stress

+ environmental toxins, chemicals and heavy metals

Epigenetic changes

+ infection, multiple vaccines, immune system activation

Brain inflammation = Encephalitis = Autism

What can we do to improve our child's digestive health?

- **Specific Diets:**
 - Ketogenic
 - GAPS
 - Anti-inflammatory
 - Elimination
 - Body-Ecology
 - Gluten-, Dairy-, Soy- Free Diet
- Add missing micronutrients, vitamins and mineral as supplements
- Gut healing supplements such as fiber, probiotic, prebiotics, digestive enzymes, curcumin...

Changing the gut flora has shown to reduce autism symptoms, such as change in diet, probiotics, prebiotics and fecal transplants.



SUMMARY

“The microbiome is responsible for many functions that are impaired in autism such as metabolizing food, regulating the immune system, eliminating toxins and waste, absorbing nutrients, producing neurotransmitters, preventing the colonization of the gut by pathogenic bacteria, and maintaining the tight junctions of intestinal epithelial cells. Microbial constitution and development in early childhood has been shown to affect the blood-brain barrier permeability.”

THANK YOU!

Rebecca Sherry Eshraghi, Ph.D., DNM

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