

Integrative medicine is the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is evidence-based, and makes use of all appropriate therapeutic approaches, healthcare professionals, and disciplines to achieve optimal health and healing.

American Board of Integrative

Medicine

and

Consortium of Academic Health Centers for Integrative Medicine

#### INTEGRATIVE MEDICINE PRACTICE

- •Evaluating patient is a whole person, not sum of organs
- Patient is an active participant
- •Using least invasive treatments whenever possible
- Patient education as a cornerstone
- •Moving from disease management to health creation

# WHAT INTEGRATIVE MEDICINE IS NOT

voodoo

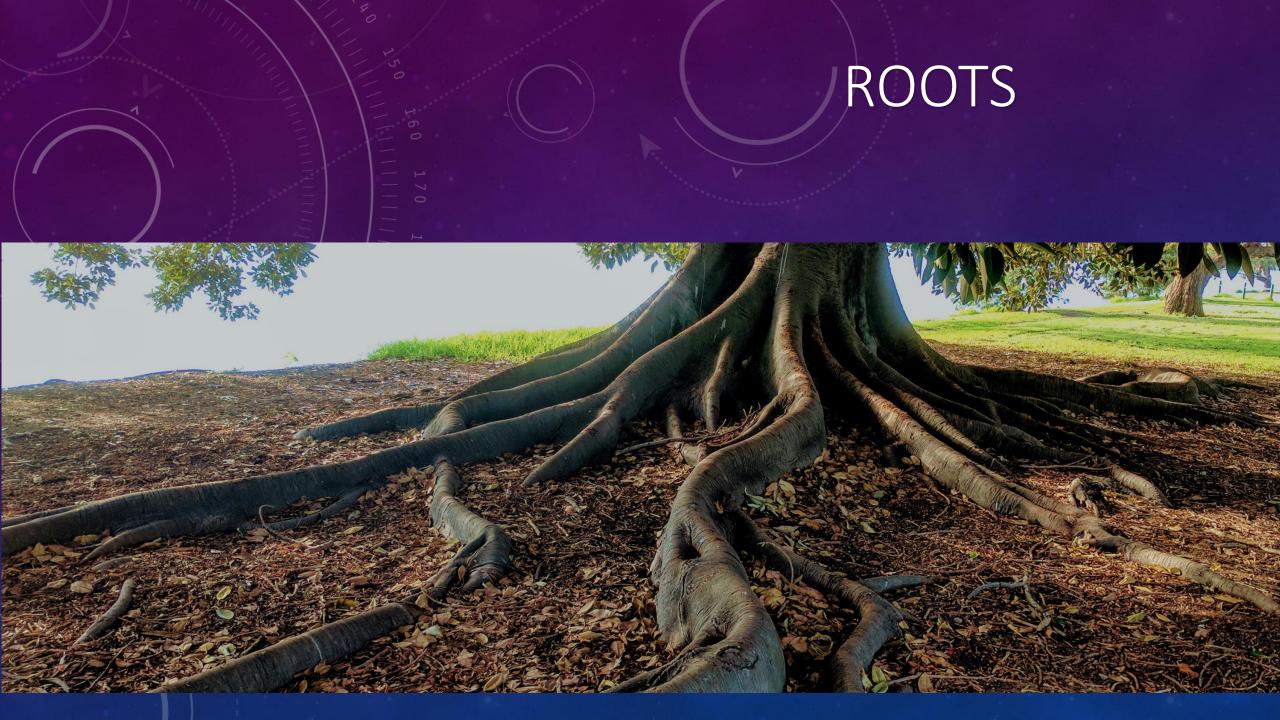


a religion practiced in parts of the Caribbean and the southern US, combining elements of Roman Catholic ritual with traditional African magical and religious rites, and characterized by sorcery and spirit possession.

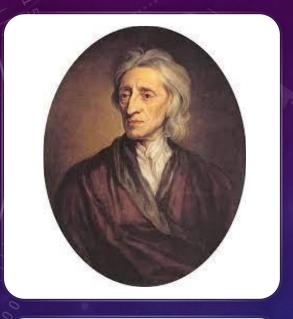
Magical cures

Anti-aging clinics

How I Cured My Fibromyalgia with One Simple Medicine <a href="https://www.pinterest.com">https://www.pinterest.com</a> pin The New Bible **Cure** for Chronic Fatigue and **Fibromyalgia** 











ARISTOTLE (384–322)

A PERSON IS A COMBINATION OF BOTH PHYSICAL AND SPIRITUAL PROPERTIES WITH NO SEPARATION BETWEEN MIND AND BODY.

RENE DESCARTES (1596-1650)

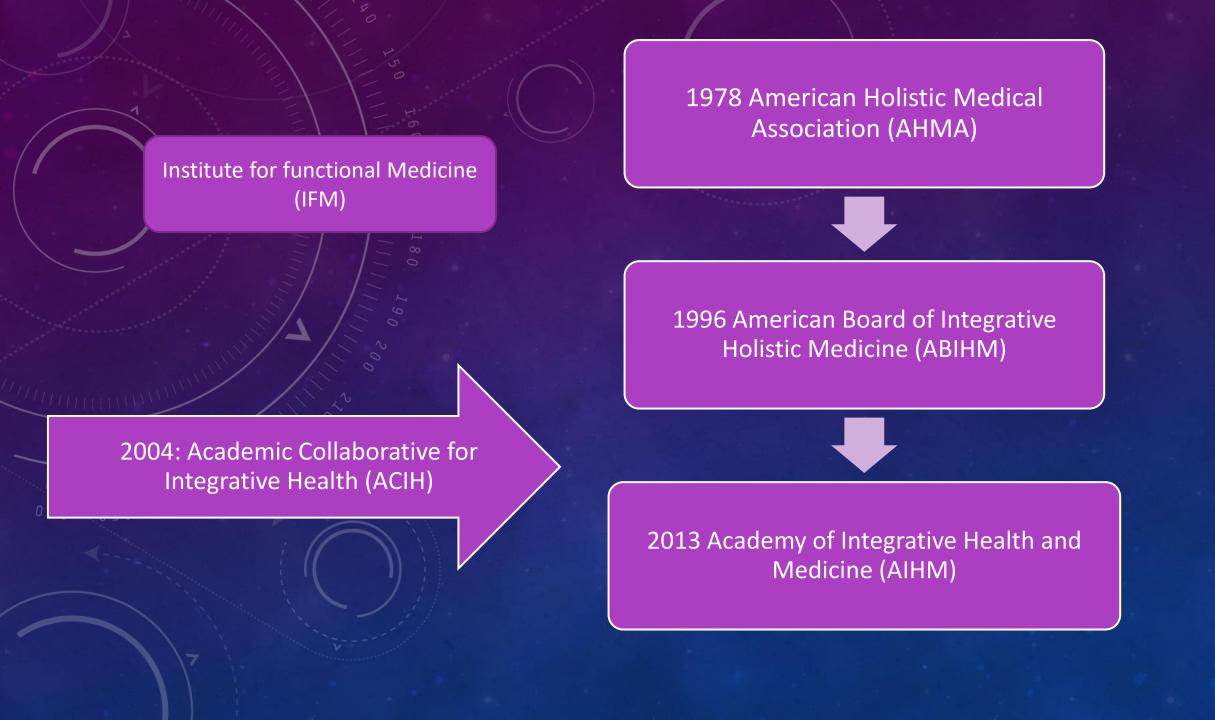
"CARTESIAN SPLIT"

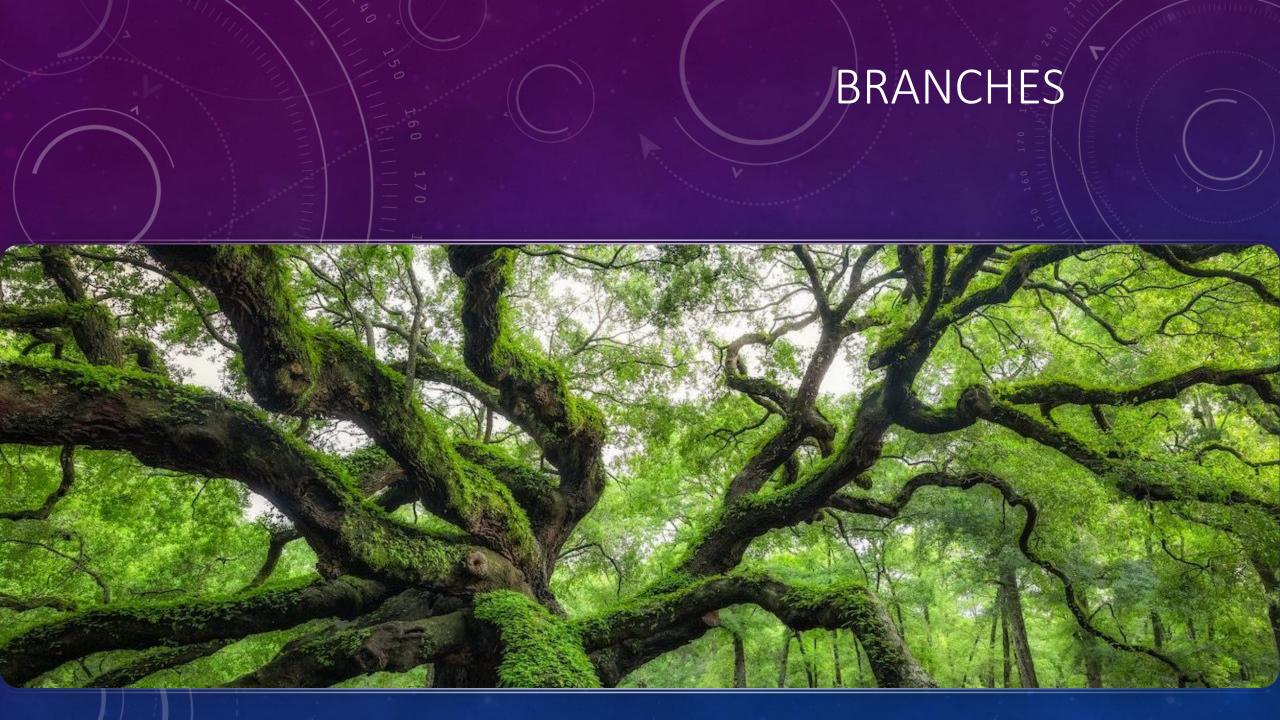
JOHN LOCKE (1632-1704) & DAVID HUME (1711-1776)
REDUCTIONISM

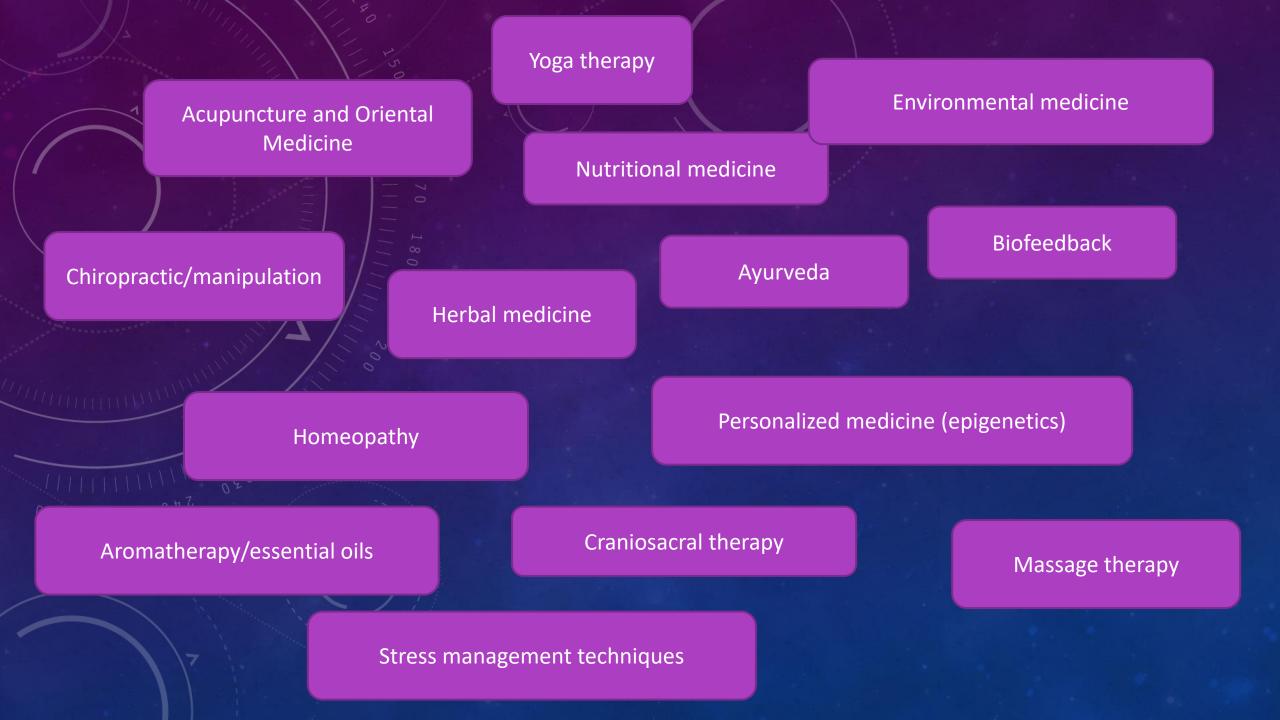
# INTEGRATIVE MEDICINE IN THE US

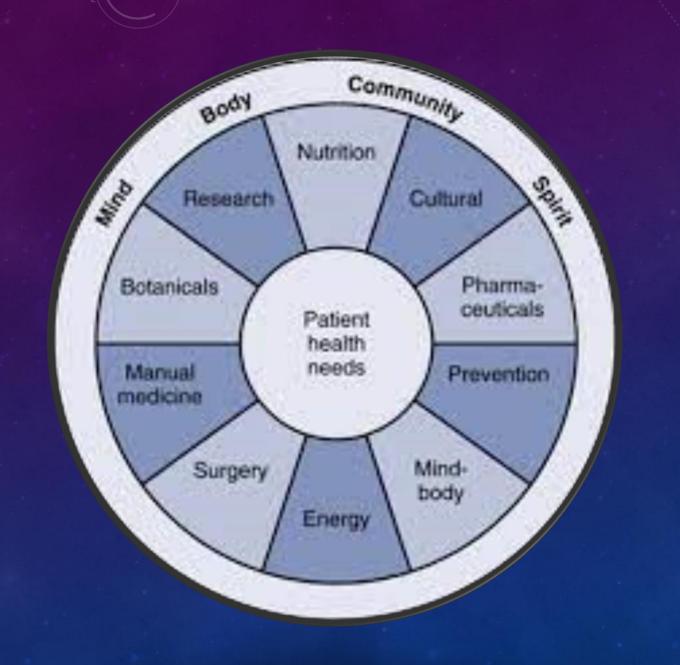
- •1910 Flexner report
- •1993 Office of Alternative Medicine within NIH
- •1997 fellowship program in integrative medicine at the University of Arizona
- 2006 ACP report (pending collapse of primary care)
- •2013 the American Board of integrative medicine formed (ABOIM)

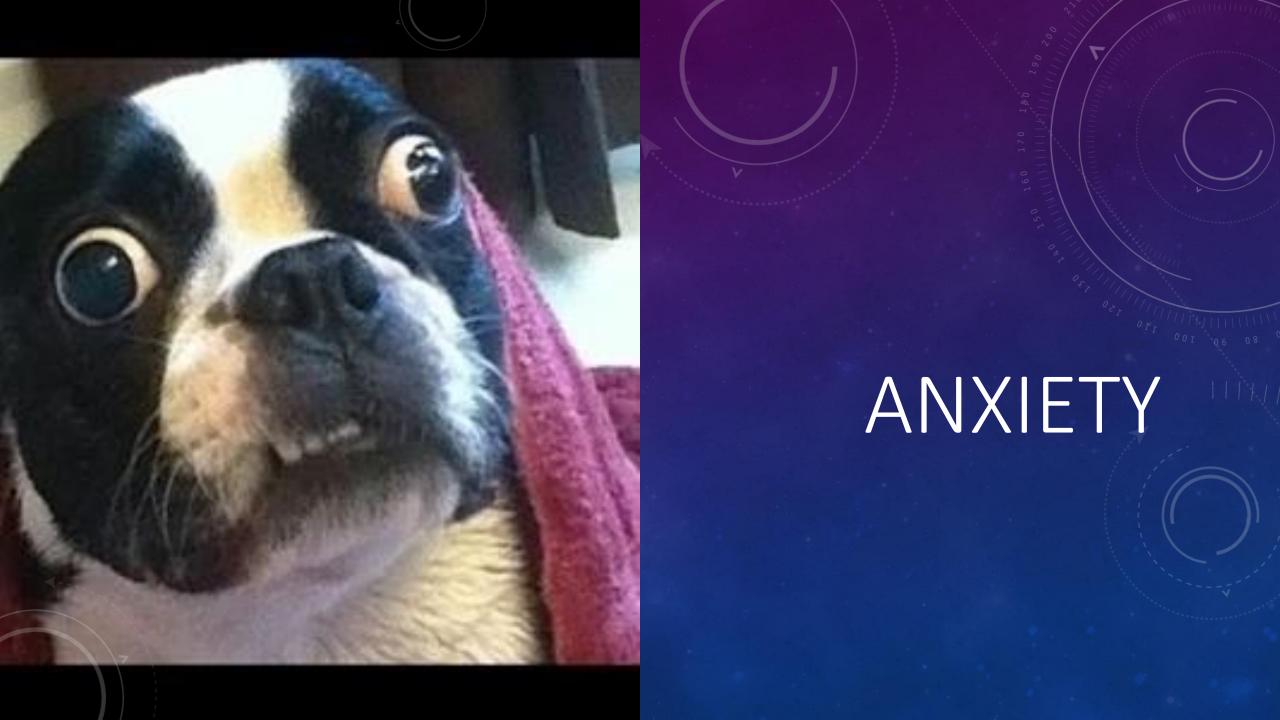












Longest differential diagnosis and all psychiatric disorders

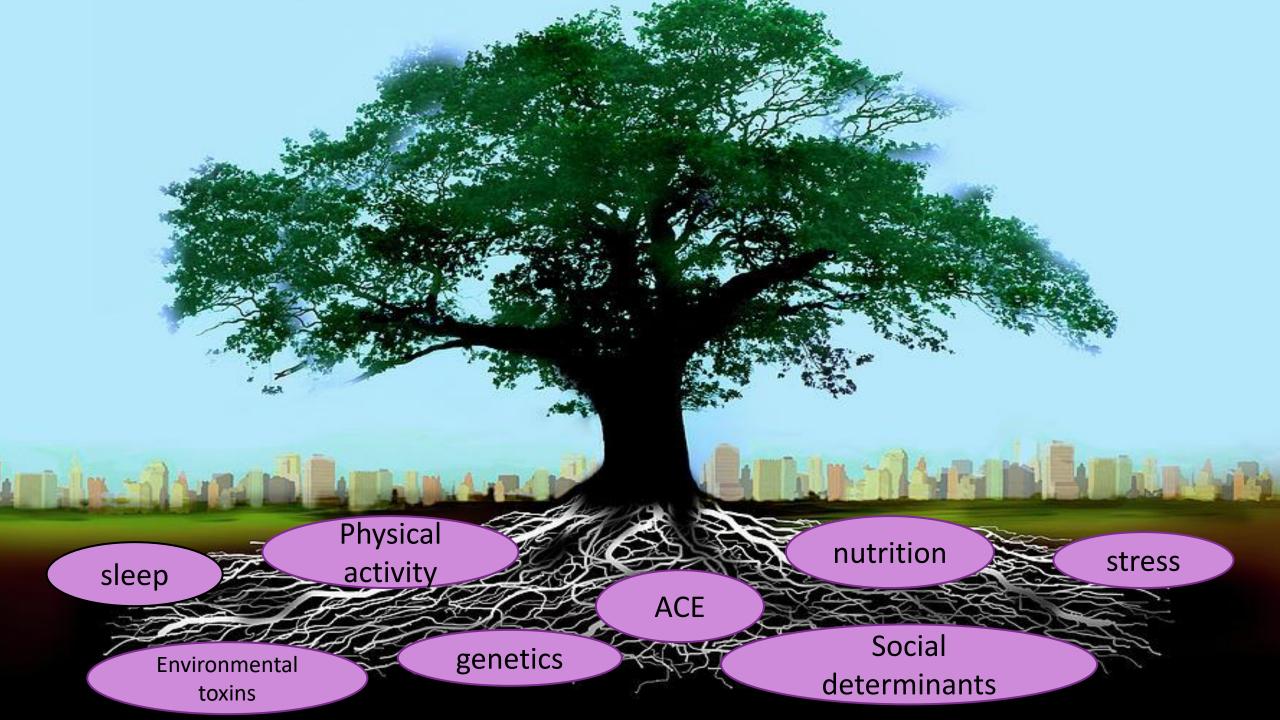
#### **Diagnostic criteria:**

- Worry more often than not (6 months)
- Worry is difficult to control
- At least 3 other somatic symptoms (Fatigue, restlessness, insomnia, myalgia, etc.)
- Difficult to carry out day-to-day functions
- Unrelated to other medical conditions/drugs/alcohol
- Not explained by another mental or medical disorder

ANXIETY



**ONE CAUSE-MANY CONDITIONS** 







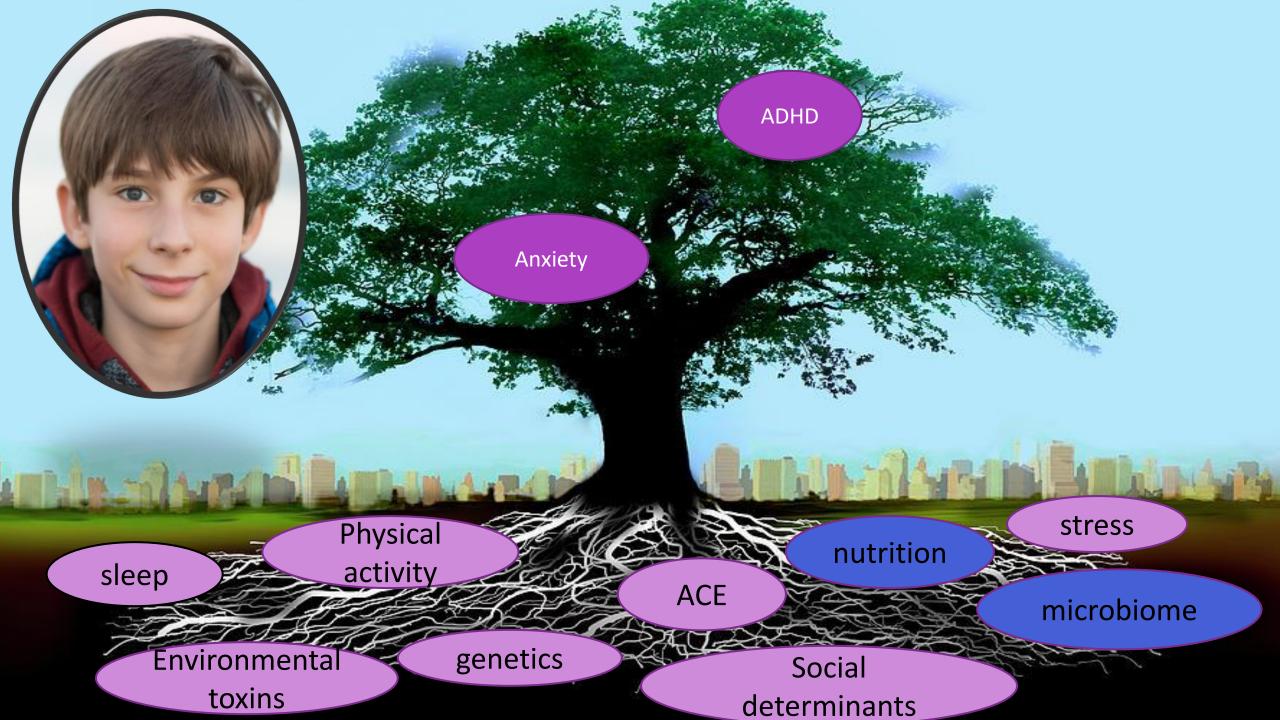
#### CODY

- 10-year-old white male
- Struggling with anxiety since first grade
- Extensive history of otitis media starting at age 2
- Intermittent abdominal pain and diarrhea
- Struggling at school
- Very good natured, but irritable when hungry
- Eats Standard American Diet (SAD)

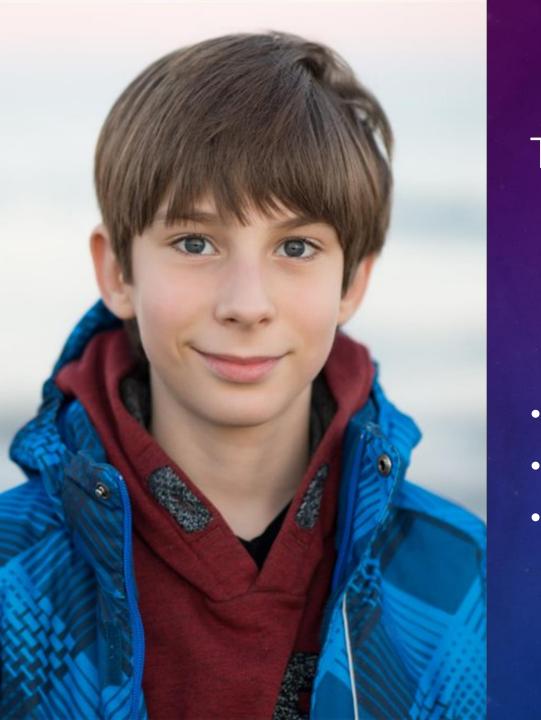


#### CODY

- Evaluated by his pediatrician and diagnosed with GAD
- Referred for counseling
- Zoloft 50 mg daily
- Diagnosed with ADHD, intolerant of stimulants







#### TESTING

- Testing for food intolerances (IgG4)
- Organic Acid Test (OAT)
- 3-hour glucose tolerance test



#### TREATMENT PLAN

- YEAST ERADICATION
- GUT REPAIR PROTOCOL
- NUTRITION
- PHYSICAL ACTIVITY
- Transcranial magnetic stimulation
- Headspace phone app
- SUPPLEMENTS: Magnesium Threonate, CBD, L-Theanine



# NUTRITION





# PHYSICAL ACTIVITY



## STRESS MANAGEMENT



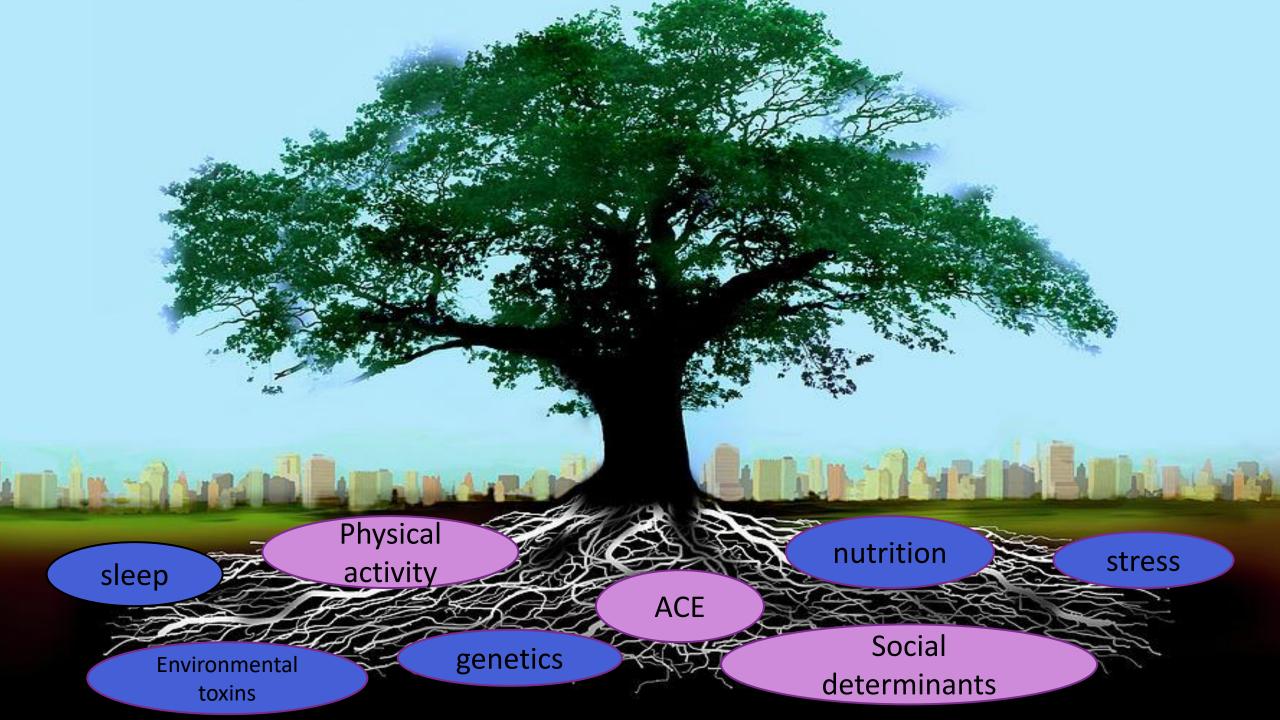
#### SHANTI

- 38-year-old female of Indian descent
- Cardiologist
- Always somewhat anxious, but progressively worsening over the past 5 years.
- Concerned about very slight cognitive issues (word finding)
- Anxiety worse after certain foods



#### SHANTI

- Eats healthy, well-balanced diet. Vegetarian.
- Has been practicing meditation for years.
- Has never smoked, glass of wine 3-4 x/week
- Expressed interest in genetic testing and personalized medicine.







#### PATIENT EDUCATION

- •Understanding pathophysiology of histamine intolerance
- •Understanding factors affecting integrity of GI mucosa
- Preventive measures
- •How to handle exacerbation



# NUTRITION





SLEEP

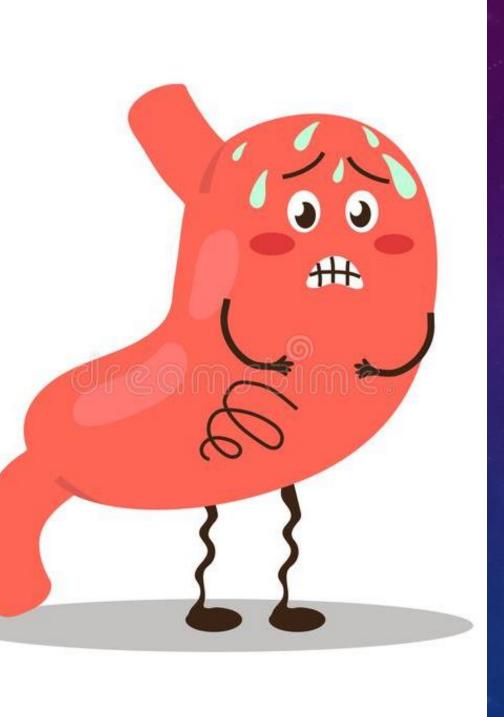




# PHYSICAL ACTIVITY



## STRESS MANAGEMENT



# ABDOMINAL PAIN AND DIARRHEA



#### TINA

- 56-year-old African-American female
- Executive of pharmaceutical company
- Stressful work environment
- Suffering from debilitating diarrhea: Up to 10 watery BM's /day, occasionally explosive. Associated tenesmus. Intermittent. Unable to identify precipitant. Abrupt onset after family picnic. Extensive prior diagnostic evaluation.
- Can eat the same meal at the same restaurant and be asymptomatic on one occasion and severely ill on another occasion



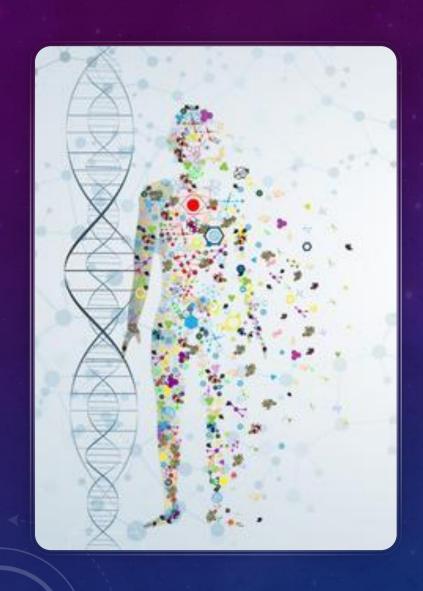
#### TINA

- Testing was negative for celiac disease, Crohn's disease or ulcerative colitis.
- Random gastric and colon biopsies showing nonspecific inflammation
- Diagnosed with IBD with diarrhea
- Lomotil, Bentyl and Cymbalta



### TINA

- Presented to integrative medicine clinic to explore possible further testing and treatment.
- Amongst other testing genetic evaluation completed.



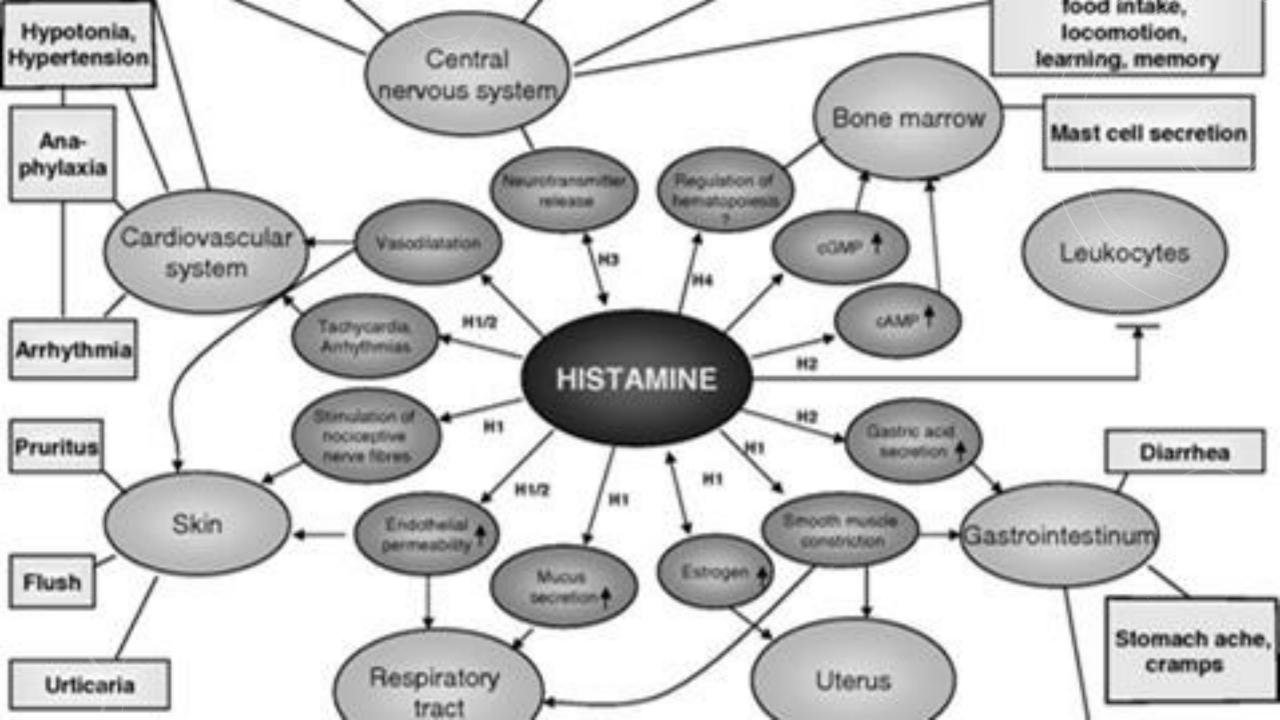
### GENOMIC EVALUATION

- •You can't change your DNA, but you can change DNA expression.
- Lifestyle, nutrition, habits, supplements and medications are potential interventions that can reduce risk and promote healthy gene expression.
- Your family history doesn't have to be your destiny

L-mistidine decarboxylase (mbc) NH<sub>2</sub> histamine (HA) histamine N-methyltransferase diamine oxidase (DAO) (HNMT)  $NH_2$ N<sub>t</sub>-methylimidazole-4histamine acetyldehyde Xanthine oxidase DAO OH imidazole-4-1-methylimidazoleacetic acid 4-acetyldehyde Xanthine oxidase Ribosyl transferase OH HO 1-ribosylimidazole-1-methylimidazole-4-acetic acid 4-acetic acid OH

## HISTAMINE INTOLERANCE

- •Histamine Intolerance: The Current State of the Art
- •Oriol Comas-Basté, Sònia Sánchez-<u>Pérez, Maria Teresa Veciana-</u> <u>Nogués, Mariluz Latorre-</u> <u>Moratalla, and María del Carmen</u> <u>Vidal-Carou. Biomolecules.</u> 2020 Aug; 10(8): 1181





## TINA'S TREATMENT PLAN

- Patient education
- Nutritional plan
- Supplements



## PATIENT EDUCATION

- •Understanding pathophysiology of histamine intolerance
- •Understanding factors affecting integrity of GI mucosa
- Preventive measures
- •How to handle exacerbation



## NUTRITION



## AVOID FOODS HIGH IN HISTAMINE

- Aged fish: mackerel or tuna has 600-1460 mg/kg (flash frozen has 1-20 mg/kg)
- Canned sardines/tuna: 3-2000 mg/kg
- Fermented alcoholic beverages:

champagne is 670 mg/L red wine is 0-30 mg/L, white wine 0-10 mg/L, beer is 0-17 mg/L

- Sauerkraut: 229 mg/kg
- Fermented milk/milks: ripened cheeses: 2.2-2500 mg/kg
- Fermented soy products: miso, soy sauce
- Dry aged sausages: up to 357 mg/kg

## LIMIT INTAKE OF HISTAMINE-RELEASING FOODS

- Chocolate/cocoa powder
- •Most acidic fruits (kiwi, lemon, lime, pineapple, plums).
- •Cow's milk
- Nuts
- Papaya
- Shellfish
- Beans and pulses
- Tomatoes
- Wheat germ
- Many artificial preservatives and dyes (benzoate, sulphites, nitrites, glutamate)
- •Egg white only in raw form

Kohn JB. Is There a Diet for Histamine Intolerance? Journal of the Academy of Nutrition and Dietetics. 2014;114(11):1860. doi:10.1016/j.jand.2014.09.009

# INCREASE INTAKE OF FOODS THAT DEGRADE HISTAMINE

- •Foods high in luteolin, quercetin and rutin.
- Watercress
- Pea sprouts
- Onions, leafy green vegetables and apples

## PROBIOTIS

Lactobacillus rhamnosus

Thomas CM, Hong T, Pijkeren JP van, et al. Histamine Derived from Probiotic Lactobacillus reuteri Suppresses TNF via Modulation of PKA and ERK Signaling. PLOS ONE. 2012;7(2):e31951. doi:10.1371/journal.pone.003195

- Lactobacillus casei
- Lactobacillus bulgaricus
- Lactobacillus brevis
- Lactobacillus buchneri
- Lactobacillus fermentum
- Lactobacillus sp.

### DIAMINE OXIDASE REPLACEMENT

Manzotti G, Breda D, Gioacchino MD, Burastero SE. Serum diamine oxidase activity in patients with histamine intolerance. Int J Immunopathol Pharmacol. 2016;29(1):105-111. doi:10.1177/0394632015617170

Schnedl WJ, Schenk M, Lackner S, Enko D, Mangge H, Forster F. Diamine oxidase supplementation improves symptoms in patients with histamine intolerance. *Food Sci Biotechnol*. 2019;28(6):1779-1784. Published 2019 May 24. doi:10.1007/s10068-019-00627-3

# SUPPLEMENTS/MEDICATIONS THAT DECREASE HISTAMINE RELEASE

• Quercetin: Directly inhibits histamine release. <u>Usual dose: 250-1000 mg per day</u> (in divided doses before or between meals). *Mild CYP3A4 inhibitor and mild platelet/fibrin inhibitor*.

**Bromelain:** <u>Usual dose: 200 - 600 mg per day</u> in divided doses before or between meals. *Mild platelet/fibrin inhibitor*.

**Vitamin C:** <u>Usual dose: 500-2000 mg per day</u>. Shown to increase DAO levels compared to controls.

- Pycnogenol and Luteolin: Inhibits the release of histamine from mast cell.
- Cromolyn also works on this mast cell activation pathway. Mild platelet/fibrin inhibitor. Typical dose 50 mg twice a day.
- H2 blockers: The H2 receptor antagonists cimetidine and ranitidine block the histamine receptors in the gut.

#### REFERRENCES

Mlcek J, Jurikova T, Skrovankova S, Sochor J. Quercetin and Its Anti-Allergic Immune Response. Molecules. 2016;21(5):623. doi:10.3390/molecules21050623

Elbarbry F, Ung A, Abdelkawy K. Studying the Inhibitory Effect of Quercetin and Thymoquinone on Human Cytochrome P450 Enzyme Activities. Pharmacogn Mag. 2017;13(Suppl 4):S895-S899. doi:10.4103/0973-1296.224342

Horwitz RJ. Chapter 30 - The Allergic Patient. In: Rakel D, ed. Integrative Medicine (Fourth Edition). Elsevier; 2018:300-309.e2. doi:10.1016/B978-0-323-35868-2.00030-X

Gläser D, Hilberg T. The influence of bromelain on platelet count and platelet activity in vitro. Platelets. 2006;17(1):37-41. doi:10.1080/09537100500197489

Atlee JL. Complications in Anesthesia. Elsevier Health Sciences; 2007.

## CAUTION WITH SUPPLEMENTS/MEDICATIONS THAT CAN INCREASE HISTAMINE RELEASE:

- Supplements: Acetylcysteine (NAC).
- Immune Modulators: Humira, Envrel.
- Antidepressants: Doxepin, amitryptiline, mirtazapine (does not increase histamine release but blocks the reuptake of histamine leading to greater histamine levels).
- Antibiotics: Cefuroxime and Clavulanic Acid.
- BP Medications: Verapamil and Amilioride.
- NSAIDS: Ibuprofen, Aspirin and Aleve.

Barrett KE, Minor JR, Metcalfe DD. Histamine secretion induced by N-acetyl cysteine. Agents Actions. 1985;16(3-4):144-146. doi:10.1007/bf01983123
Paltiel M, Gober LM, Deng A, et al. Immediate Type I Hypersensitivity Response Implicated in Worsening Injection Site Reactions to Adalimumab. Arch Dermatol. 2008;144(9):1190-1194. doi:10.1001/archderm.144.9.1190

Pham DL, Kim J-H, Trinh THK, Park H-S. What we know about nonsteroidal anti-inflammatory drug hypersensitivity. Korean J Intern Med. 2016;31(3):417-432. doi:10.3904/kjim.2016.085



#### MIGUEL

- 32-year-old Hispanic male
- Small business owner
- Progressively worsening anxiety over the past 2 years
- Currently significantly affecting his ability to function
- Affecting his marriage
- Admits to occasional loose stools
- Describes himself as "laidback" prior to onset
- Does not smoke or drink alcohol



### MIGUEL

- Initially evaluated by his PCP and referred to psychiatrist
- Diagnosed with General Anxiety Disorder
- Started on Cymbalta
- Mindfulness Based Stress Reduction (MBSR)
- 60% improvement in his symptoms.

